NCA Example Report

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Report (Final, V1.0)

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Statistic	DoseCohort	SubjectPart	Cmax (ng/mL)	Cmin (ng/mL)	tmax (h)	AUC 0-t (ng*h/mL)	AUC 0-24 (ng*h/mL)
n	40 mg QD	A1	6	6	6	6	6
Geomean	40 mg QD	A1	43.21	13.83	18	2333	776.9
Geo%CV	40 mg QD	A1	132.5	60.61	-	77.48	131
Minimum	40 mg QD	A1	8.79	6.72	6	998	145
Maximum	40 mg QD	A1	139	28.9	24	6150	2250
n	80 mg QD	A1	6	6	6	6	6
Geomean	80 mg QD	A1	114.4	11.12	10	7404	2245
Geo%CV	80 mg QD	A1	84.98	134	-	53.82	85.02
Minimum	80 mg QD	A1	65	1.85	6	4580	1150
Maximum	80 mg QD	A1	370	38.5	24	15300	6920
n	160 mg QD	A1	6	6	6	6	6
Geomean	160 mg QD	A1	138.4	15.53	24	9698	2202
Geo%CV	160 mg QD	A1	134.7	2613	-	150	194.2
Minimum	160 mg QD	A1	18.7	0.13	6	2310	186
Maximum	160 mg QD	A1	304	162	120	24900	5230

**Geomean value for tmax is the median not the geomean

Table 2.1.2 Summary Plasma AZD9291 Pharmacokinetic Parameters - - Cycle 1 (multiple dose)

Statistic	DoseCohort	SubjectPart	Cmax (ng/mL)	Cmin (ng/mL)	tmax (h)	AUC 0-t (ng*h/mL)	AUC 0-24 (ng*h/mL)
n	40 mg QD	A1	5	0	5	0	0
Geomean	40 mg QD	A1	159.5	-	8	-	-
Geo%CV	40 mg QD	A1	52.49	-	-	-	-
Minimum	40 mg QD	A1	97.6	-	4	-	-
Maximum	40 mg QD	A1	346	-	8	-	-
n	80 mg QD	A1	5	0	5	0	0
Geomean	80 mg QD	A1	432	-	8	-	-
Geo%CV	80 mg QD	A1	52.23	-	-	-	-
Minimum	80 mg QD	A1	269	-	4	-	-
Maximum	80 mg QD	A1	841	-	8	-	-
n	160 mg QD	A1	5	0	5	0	0
Geomean	160 mg QD	A1	635.7	-	8	-	-
Geo%CV	160 mg QD	A1	161.1	-	-	-	-
Minimum	160 mg QD	A1	164	-	4	-	-
Maximum	160 mg QD	A1	2320	-	8	-	-

**Geomean value for tmax is the median not the geomean

Table 2.1.3 Summary Plasma AZD9291 Pharmacokinetic Parameters - - Cycle 2 (multiple dose)

Statistic	DoseCohort	SubjectPart	Cmax (ng/mL)	Cmin (ng/mL)	tmax (h)	AUC 0-t (ng*h/mL)	AUC 0-24 (ng*h/mL)
n	40 mg QD	A1	5	4	5	5	5
Geomean	40 mg QD	A1	159.8	96.65	6	3202	3202
Geo%CV	40 mg QD	A1	30.63	31.17	-	20.55	20.55
Minimum	40 mg QD	A1	111	63.3	6	2480	2480
Maximum	40 mg QD	A1	237	121	24	4200	4200
n	80 mg QD	A1	4	4	4	4	4
Geomean	80 mg QD	A1	370.1	284.7	8	7989	7989
Geo%CV	80 mg QD	A1	39.16	23.47	-	33.03	33.03
Minimum	80 mg QD	A1	267	215	8	5830	5830
Maximum	80 mg QD	A1	635	370	10	12500	12500
n	160 mg QD	A1	5	5	5	5	5
Geomean	160 mg QD	A1	584.2	402.3	8	12320	12320
Geo%CV	160 mg QD	A1	116.4	232.5	-	140.5	140.5
Minimum	160 mg QD	A1	167	46.3	2	2690	2690
Maximum	160 mg QD	A1	1870	1740	12	42800	42800

**Geomean value for tmax is the median not the geomean

2.2 AZ5104 tables

Table 2.2.1 Summary Plasma AZD5104 Pharmacokinetic Parameters - - Cycle 0 (single dose)

Statistic	DoseCohort	SubjectPart	Cmax (ng/mL)	Cmin (ng/mL)	tmax (h)	AUC 0-t (ng*h/mL)	AUC 0-24 (ng*h/mL)
n	40 mg QD	A1	6	6	6	6	6
Geomean	40 mg QD	A1	3.752	1.548	24	213.1	52.66
Geo%CV	40 mg QD	A1	112.6	68.78	-	78.72	134.8
Minimum	40 mg QD	A1	0.89	0.69	12	86.3	10.4
Maximum	40 mg QD	A1	10.5	3.28	72	574	178
n	80 mg QD	A1	6	6	6	6	6
Geomean	80 mg QD	A1	8.623	1.372	24	684.2	122.4
Geo%CV	80 mg QD	A1	70.72	146.3	-	50.71	80.28
Minimum	80 mg QD	A1	5.23	0.25	12	421	70.7
Maximum	80 mg QD	A1	27.9	6.74	72	1240	502
n	160 mg QD	A1	6	6	6	6	6
Geomean	160 mg QD	A1	12.79	2.857	48	901.8	116.4
Geo%CV	160 mg QD	A1	123.9	309.2	-	156.8	242.9
Minimum	160 mg QD	A1	1.95	0.26	8	210	7.91
Maximum	160 mg QD	A1	30	17.6	120	2290	395

**Geomean value for tmax is the median not the geomean

Table 2.2.2 Summary Plasma AZD5104 Pharmacokinetic Parameters - - Cycle 1 (multiple dose)

Statistic	DoseCohort	SubjectPart	Cmax (ng/mL)	Cmin (ng/mL)	tmax (h)	AUC 0-t (ng*h/mL)	AUC 0-24 (ng*h/mL)
n	40 mg QD	A1	5	0	5	0	0
Geomean	40 mg QD	A1	15.15	-	8	-	-
Geo%CV	40 mg QD	A1	55.11	-	-	-	-
Minimum	40 mg QD	A1	9.58	-	0	-	-
Maximum	40 mg QD	A1	34.6	-	8	-	-
n	80 mg QD	A1	5	0	5	0	0
Geomean	80 mg QD	A1	39.4	-	8	-	-
Geo%CV	80 mg QD	A1	55.8	-	-	-	-
Minimum	80 mg QD	A1	23	-	8	-	-
Maximum	80 mg QD	A1	79.4	-	8	-	-
n	160 mg QD	A1	5	0	5	0	0
Geomean	160 mg QD	A1	60.35	-	8	-	-
Geo%CV	160 mg QD	A1	176.5	-	-	-	-
Minimum	160 mg QD	A1	14.5	-	4	-	-
Maximum	160 mg QD	A1	240	-	8	-	-

**Geomean value for tmax is the median not the geomean

Table 2.2.3 Summary Plasma AZD5104 Pharmacokinetic Parameters - - Cycle 2 (multiple dose)

Statistic	DoseCohort	SubjectPart	Cmax (ng/mL)	Cmin (ng/mL)	tmax (h)	AUC 0-t (ng*h/mL)	AUC 0-24 (ng*h/mL)
n	40 mg QD	A1	5	5	5	5	5
Geomean	40 mg QD	A1	14.02	11.12	10	300.2	300.2
Geo%CV	40 mg QD	A1	18.36	24.09	-	17.07	17.07
Minimum	40 mg QD	A1	10.8	8	8	239	239
Maximum	40 mg QD	A1	16.9	14	10	357	357
n	80 mg QD	A1	4	4	4	4	4
Geomean	80 mg QD	A1	35.04	31.15	10	784.7	784.7
Geo%CV	80 mg QD	A1	41.44	31.59	-	36.57	36.57
Minimum	80 mg QD	A1	24.7	22.3	6	551	551
Maximum	80 mg QD	A1	61.9	46.4	12	1280	1280
n	160 mg QD	A1	5	4	5	5	5
Geomean	160 mg QD	A1	55.97	43.99	8	1205	1205
Geo%CV	160 mg QD	A1	126.1	377.5	-	155.8	155.8
Minimum	160 mg QD	A1	15.1	4.26	6	237	237
Maximum	160 mg QD	A1	198	190	24	4570	4570

**Geomean value for tmax is the median not the geomean

3 Introduction

This training exercise uses trial data generated using the base Population PK model published in both https://bpspubs.onlinelibrary.wiley.com/doi/10.1111/bcp.13223 and the Clinical Pharmacology Review for Osimertinib published on the FDA website. The virtual trial data uses a clinical study design based on the clinical study protocol for Osimertinib.

4 Data summary

The list of numbers of patients in each dosing cohort and part is given in Table 4.0.1.

Table 4.0.1 List of numbers in each dosing cohort, part and cycle.

Dose cohort	Subject part	Cycle 0	Cycle 1	Cycle 2
40 mg QD	A1	6	6	6
80 mg QD	A1	6	6	6
160 mg QD	A1	6	6	6

Different API properties are given in Table 4.0.2.

Table 4.0.2 Selected API Properties.

Parameter	Compound	Species	Value	Unit	Source
MW	AZD9291	-	499.60	g/mol	WO_NCA_Training_Osimertinib
MW	AZ5104	-	485.58	g/mol	https://www.medchemexpress.com/AZ-5104.html

5 Methods

All of the work in this report was performed in accordance with Seda's best practice guide for NCA [1]. Explanations particular to this project are provided in Section B.

5.1 Plasma

5.1.1 Data cleaning, data visualisation and data manipulation

Data cleaning methods

Table 5.1.1 List of manual records manually excluded from NCA summaries

Subject	Dose cohort	Cycle	Day	Reason for exclusion
VST-003	40 mg QD	1	15	Missed Doses on C1D15
VST-005	40 mg QD	2	1	Missed Doses after C1D18 until to the last sample
VST-007	80 mg QD	1	15	Dose Reduction from 80mg to 40mg after C1D14
VST-007	80 mg QD	2	1	Dose Reduction from 80mg to 40mg after C1D14
VST-010	80 mg QD	2	1	Missed Doses on C1D20 and C1D21
VST-013	160 mg QD	1	15	Dose Reduction from 160mg to 80mg on C1D13 C1D14 and C1D15
VST-015	160 mg QD	2	1	Wasnt dosed in cycle 2

**Geomean value for tmax is the median not the geomean

Table 5.1.2 Details of manual modifications performed on individual data points (C1D15).

Subject	Dose cohort	Analyte	Nominal time post dose (h)	Measured Conc (ng/mL)	Conc (NCA analysis) (ng/mL)	Details of Modification
VST-002	40 mg QD	AZ5104	0	-	9.46	Copied concentration from C2 D1 H24.
VST-002	40 mg QD	AZD9291	0	-	94.81	Copied concentration from C2 D1 H24.
VST-009	80 mg QD	AZ5104	24	-	28.89	Copied concentration from C2 D1 H0.
VST-009	80 mg QD	AZD9291	24	-	265.77	Copied concentration from C2 D1 H0.
VST-011	80 mg QD	AZ5104	0	-	32.66	Copied concentration from C2 D1 H24.
VST-011	80 mg QD	AZD9291	0	-	310.87	Copied concentration from C2 D1 H24.

5.2 Data presentation

Note all non-calculable and non-quantifiable values are shown with a '-' in final presentation tables for ease of viewing.

6 Bibliography

[1] Jake Dickinson, Parmesh Gajjar, and Paul Dickinson. Best Practice Guide: Non-Compartmental Analysis of Clinical Pharmacokinetic Data. Technical Report V2.0, Seda Pharmaceutical Development Services, Unit D, Oakfield Road, Cheadle Royal Business Park, Stockport, SK8 3GX, 2023.

[2] Federico M. Giorgi, Carmine Ceraolo, and Daniele Mercatelli. The R Language: An Engine for Bioinformatics and Data Science. *Life*, 12 (5):648, apr 2022. ISSN 2075-1729. doi: 10.3390/life12050648.

[3] R: Regulatory Compliance and Validation Issues. A Guidance Document for the Use of R in Regulated Clinical Trial Environments. Technical report, Institute for Statistics and Mathematics, Wirtschaftsuniversitat Wien, Welthandelsplatz 1, 1020 Vienna, Austria, 2018. URL https://www.r-project.org/doc/R-FDA.pdf.

[4] William S. Denney, Sridhar Duvvuri, and Clare Buckeridge. Simple, Automatic Noncompartmental Analysis: The PKNCA R Package. In *Abstracts Accepted for American Conference on Pharmacometrics 2015 (ACoP6)*, volume 42. Springer Science and Business Media LLC, sep 2015. doi: 10.1007/s10928-015-9432-2.

[5] Yingbo Ma, Beatriz Guglieri-Lopez, Joga Gobburu, William Denney, and Vijay Ivaturi. Comparison of non-compartmental analysis results between PKNCA, Pumas and Phoenix WinNonlin. Poster, 2019. URL http://www.humanpredictions.com/wp-content/uploads/2020/01/ACOP_2019_T102_NCA_performance_evaluation_Yingbo_revised.pdf. Poster T-102 presented at ACOP 2019.

7 Plasma PK Data visualisation

7.1 Comparative Graphs

Figure 7.1.1 Geomean (×/÷ GeoSD) PK time-concentration profiles for all cohorts on cycle 0 day -6

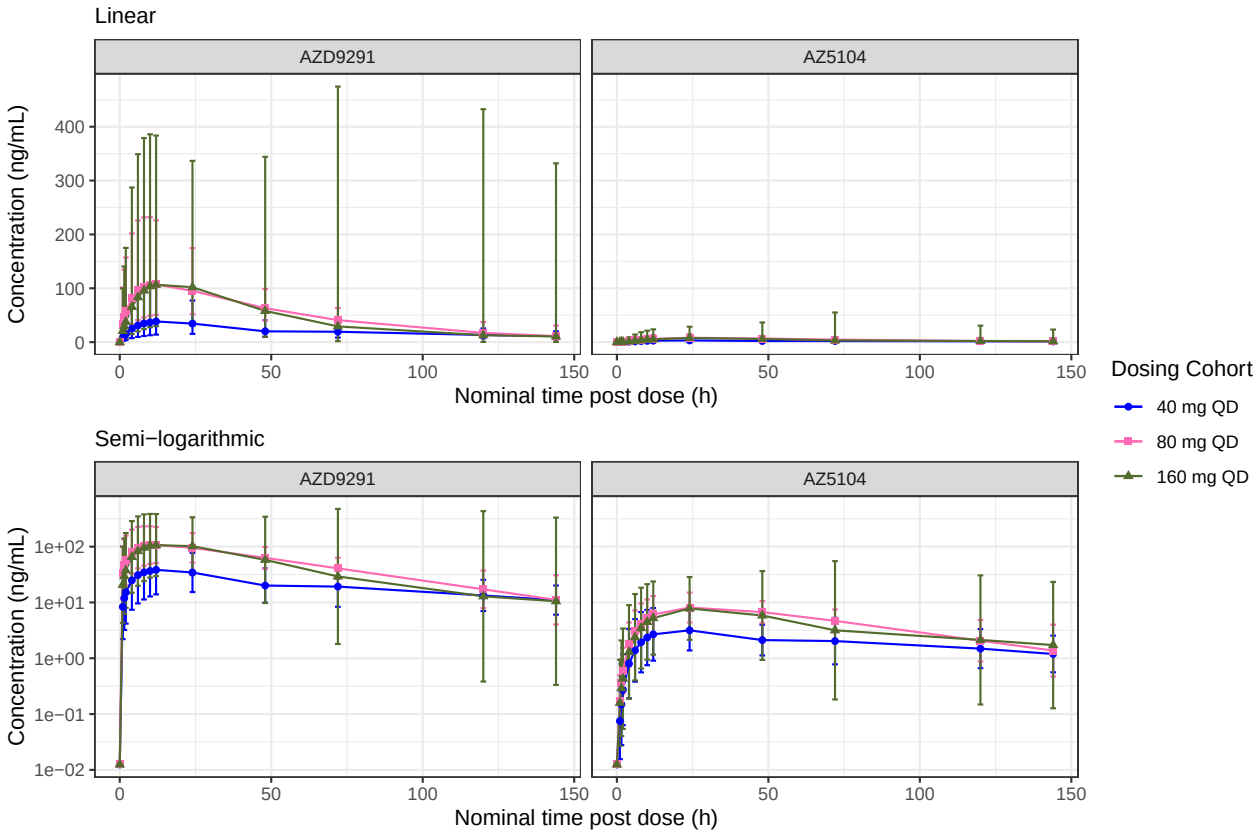
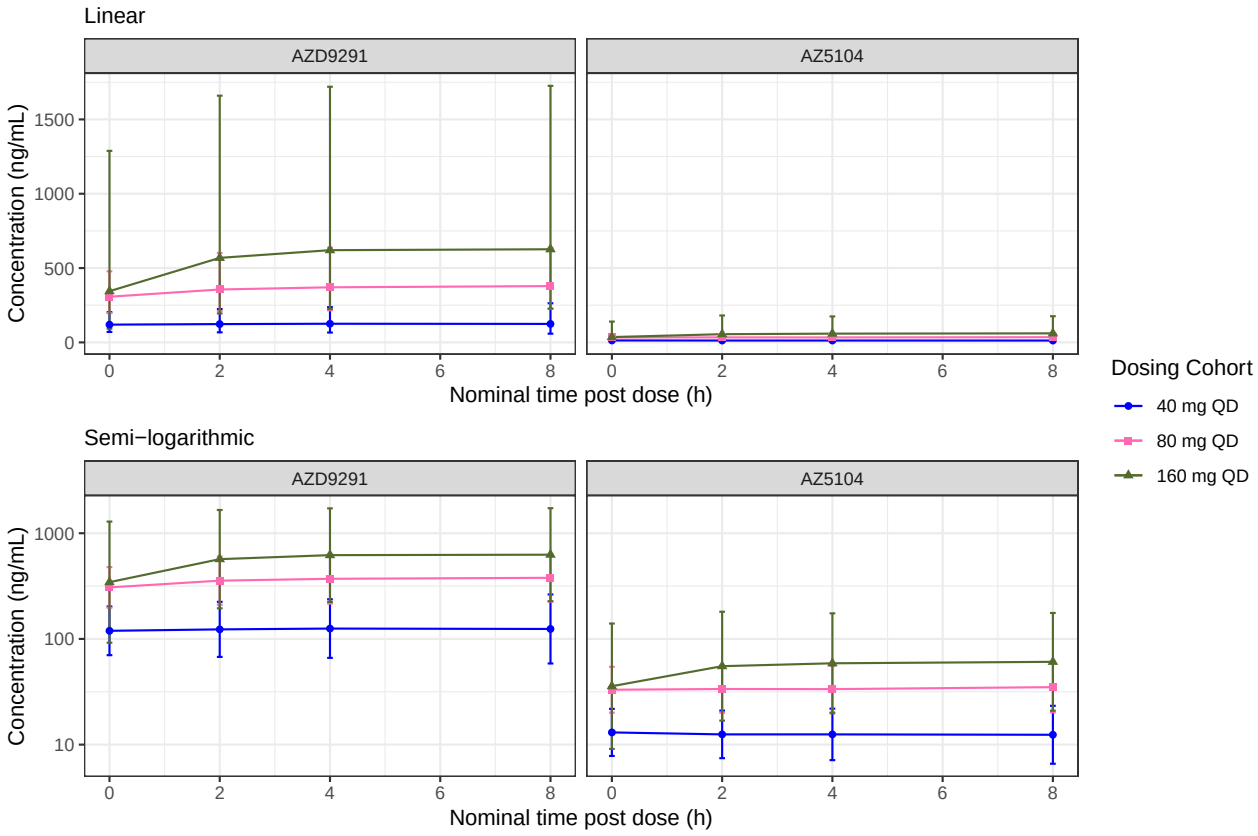


Figure 7.1.2 Geomean (×/÷ GeoSD) PK time-concentration profiles for all cohorts on cycle 1 day 15



7.2 40 mg QD

Figure 7.2.1 Geomean PK time-concentration profiles for 40 mg QD cohort

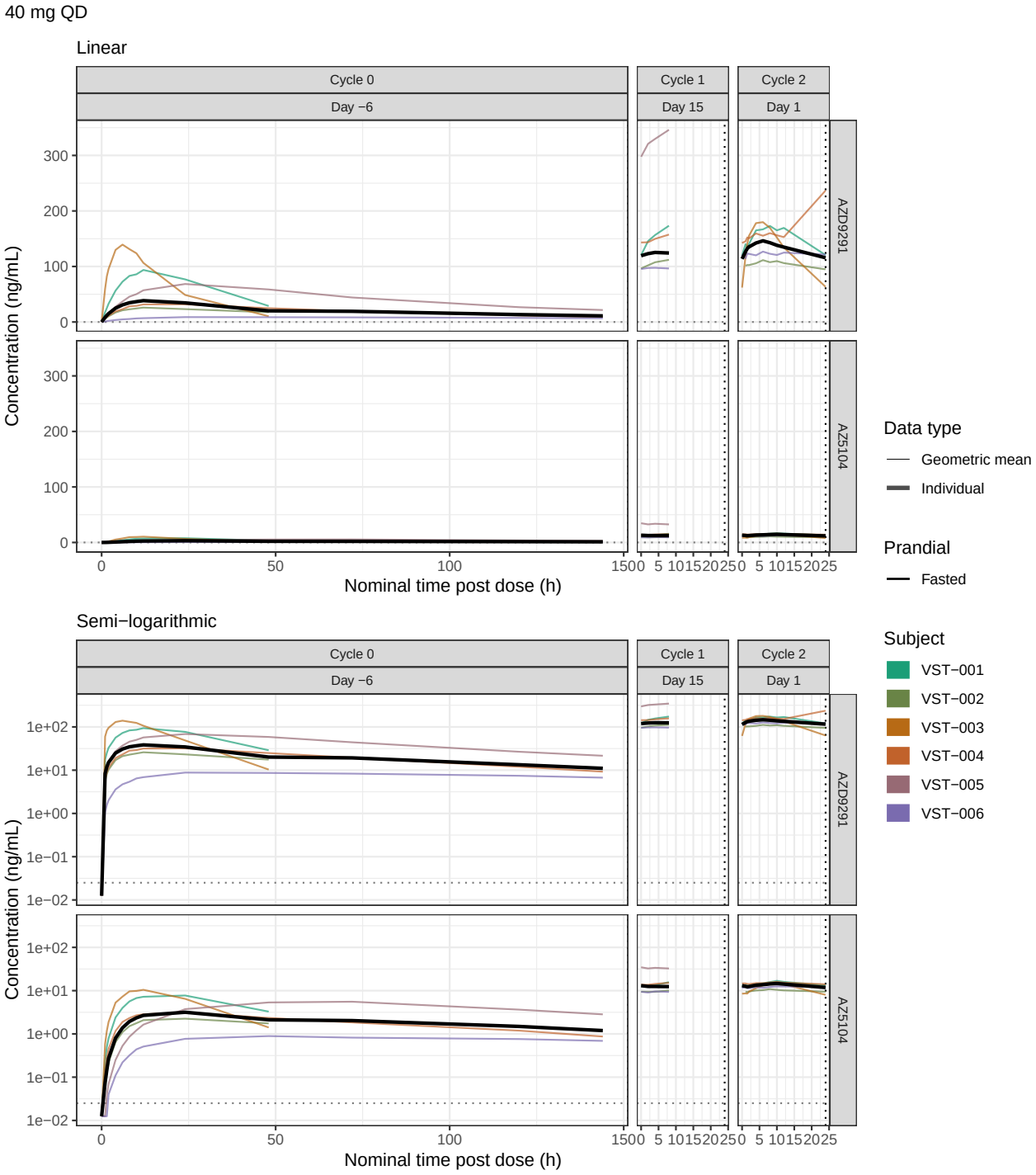


Figure 7.2.2 Plasma PK time-concentration profiles for subject VST-001

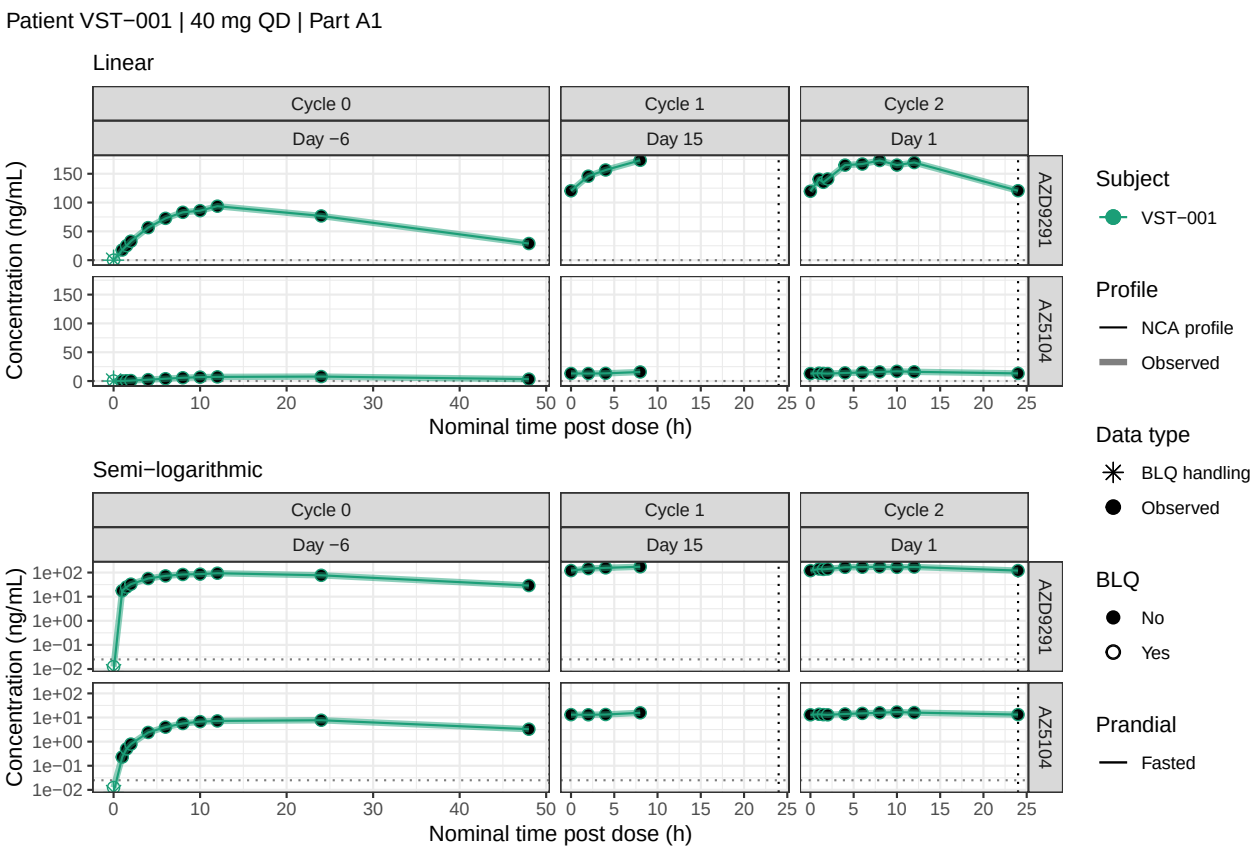


Figure 7.2.3 Plasma PK time-concentration profiles for subject VST-002

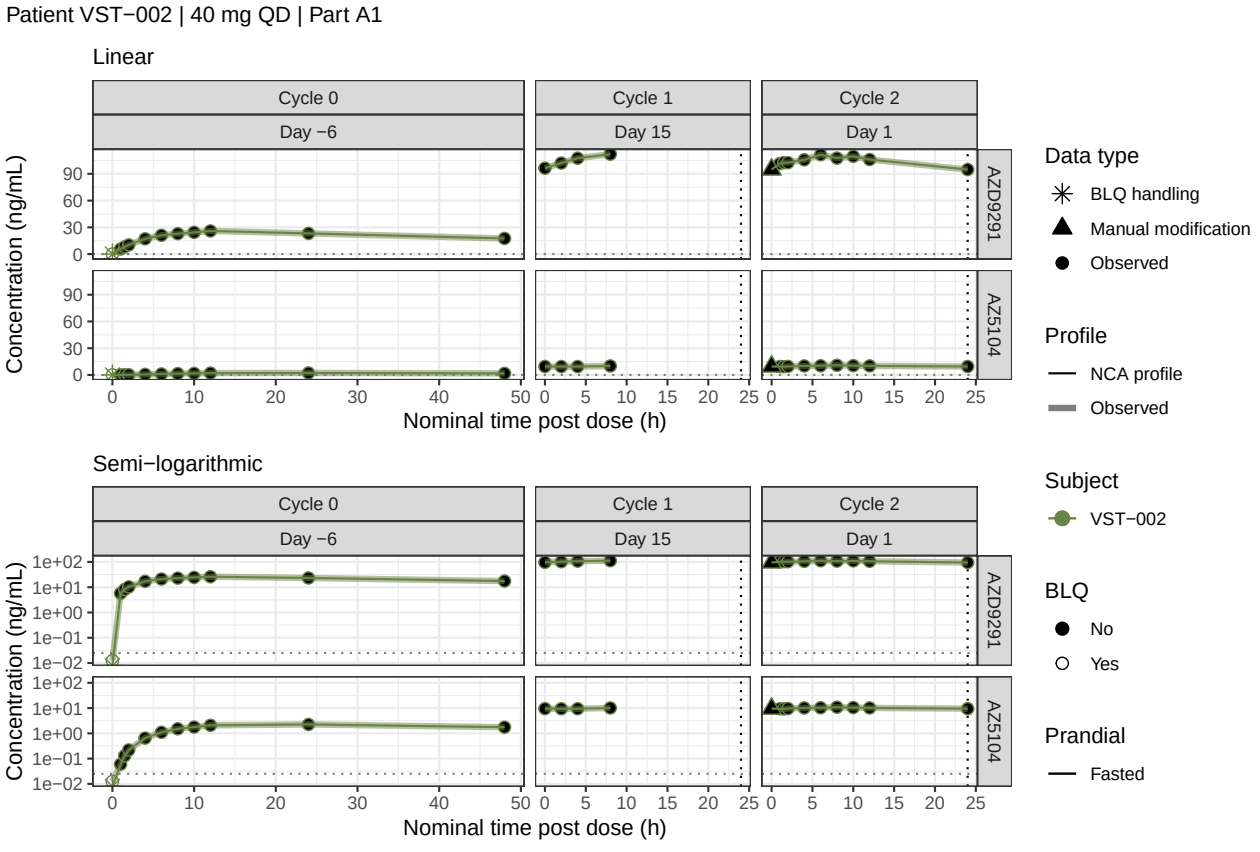


Figure 7.2.4 Plasma PK time-concentration profiles for subject VST-003

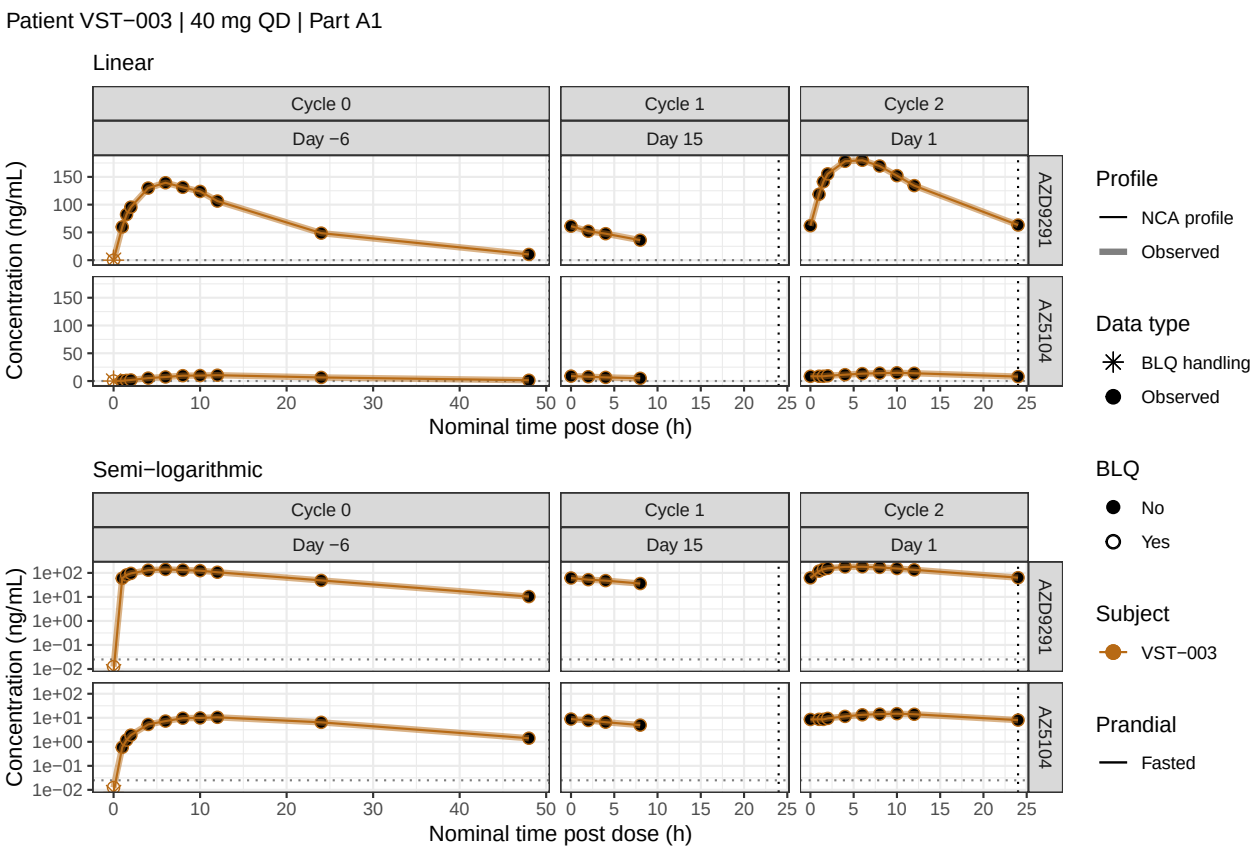


Figure 7.2.5 Plasma PK time-concentration profiles for subject VST-004

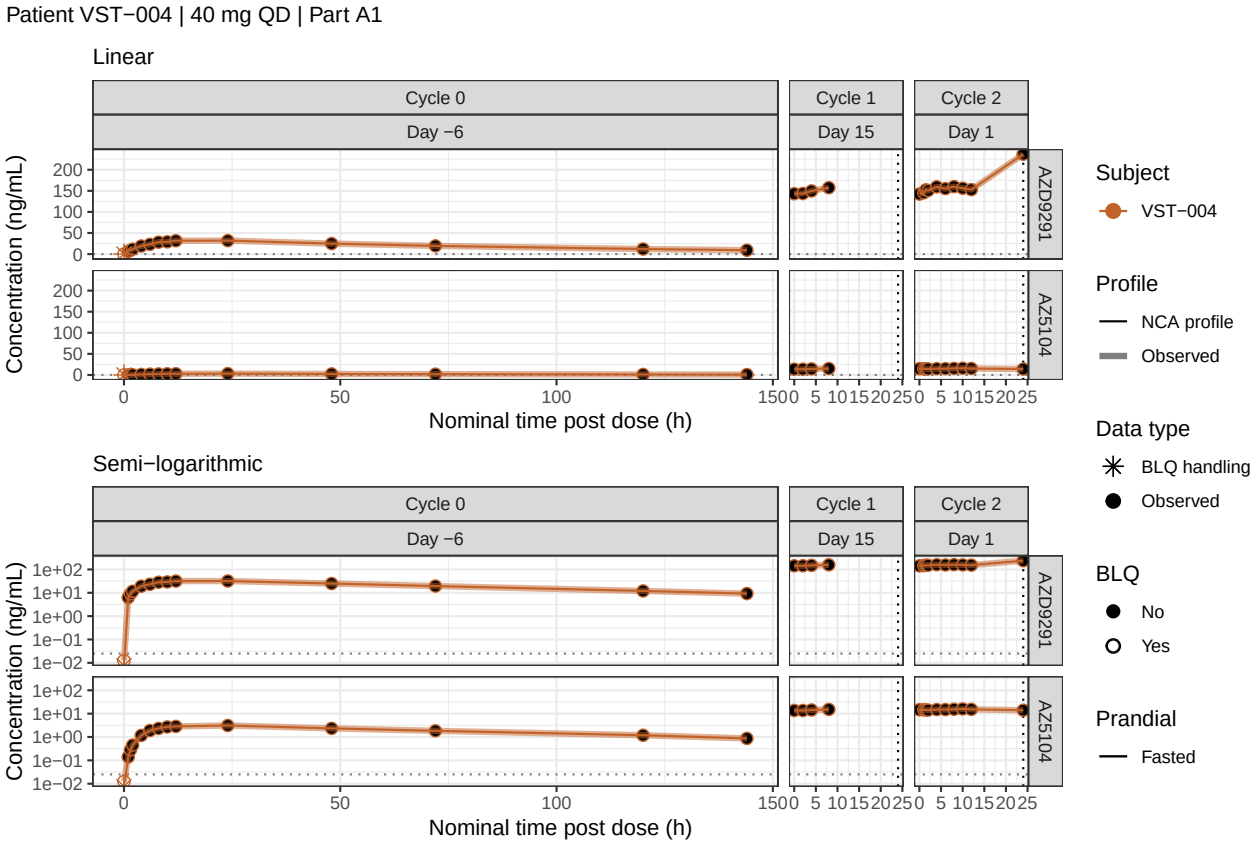


Figure 7.2.6 Plasma PK time-concentration profiles for subject VST-005

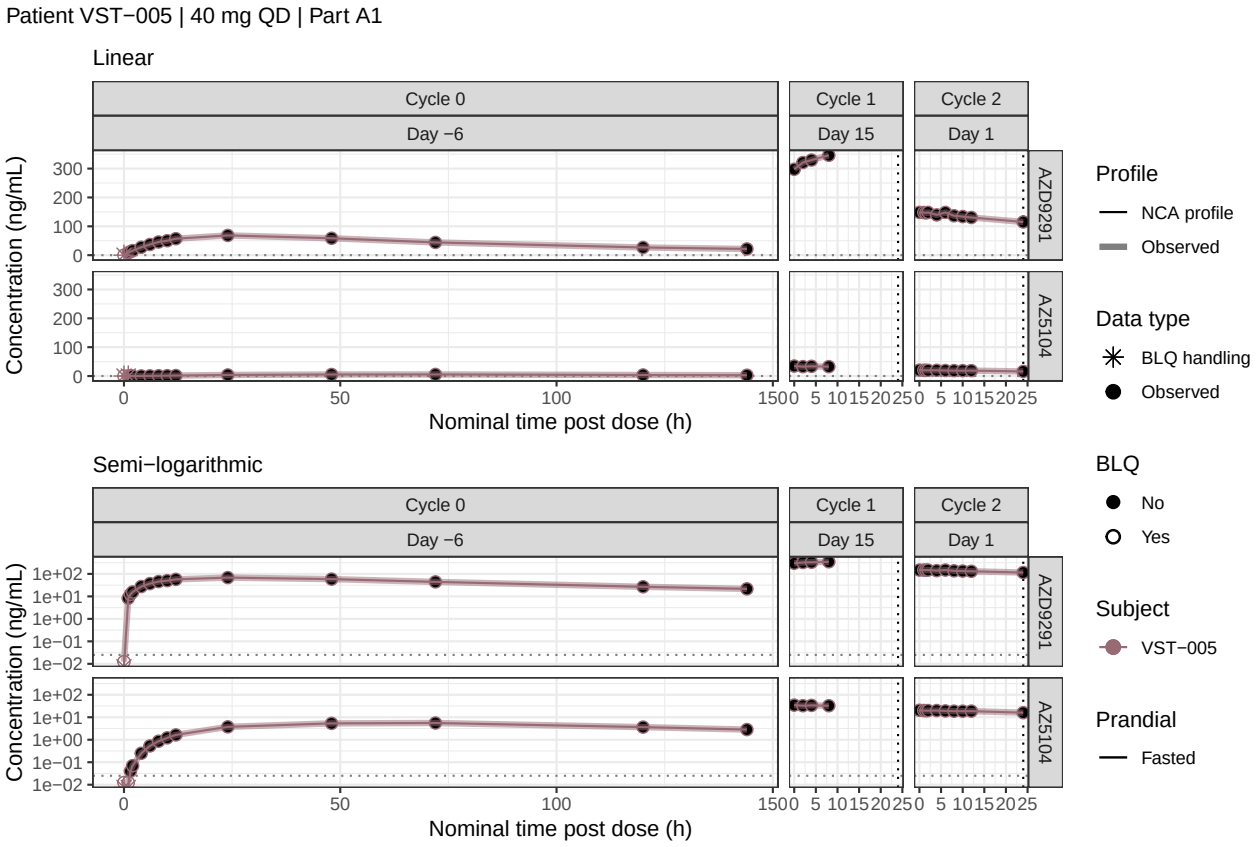
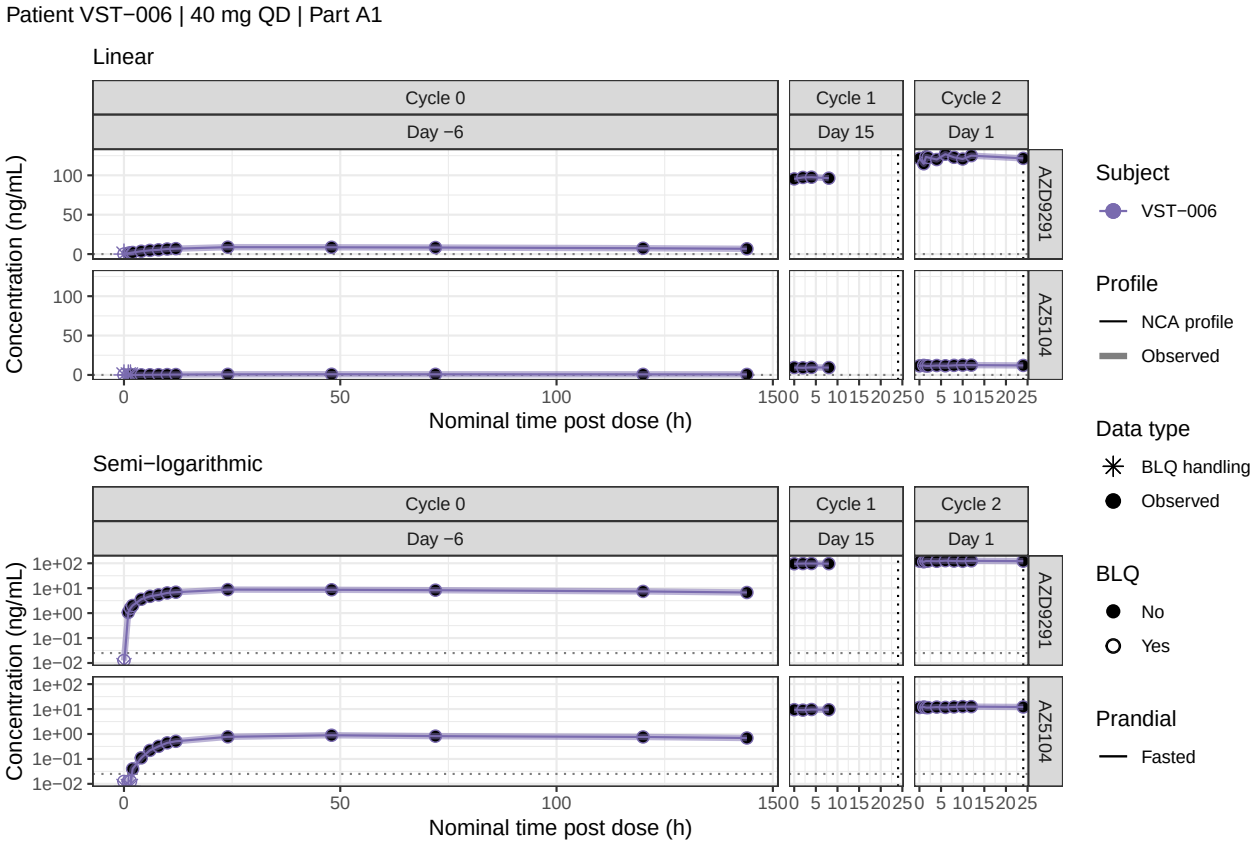


Figure 7.2.7 Plasma PK time-concentration profiles for subject VST-006



7.3 80 mg QD

Figure 7.3.1 Geomean PK time-concentration profiles for 80 mg QD cohort

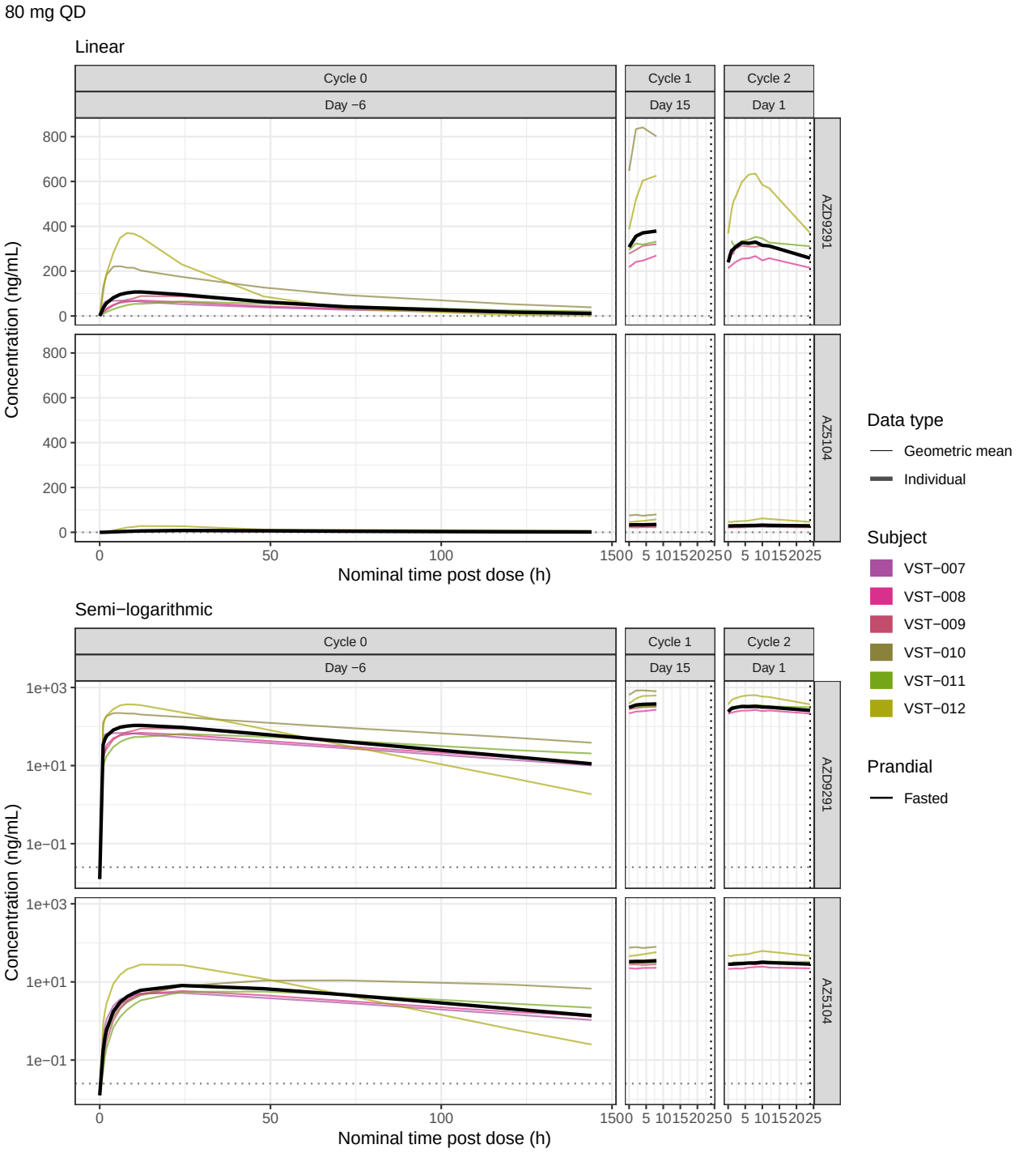


Figure 7.3.2 Plasma PK time-concentration profiles for subject VST-007

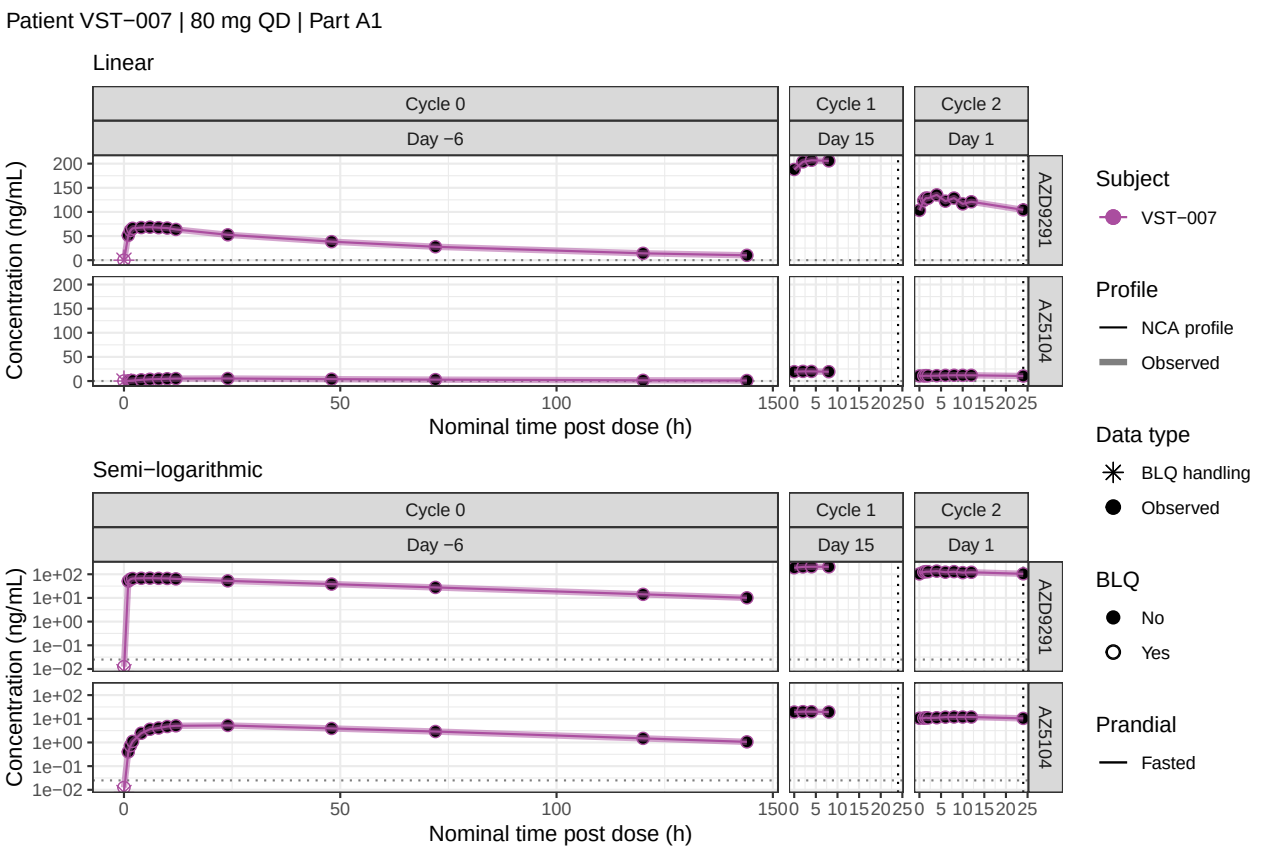


Figure 7.3.3 Plasma PK time-concentration profiles for subject VST-008

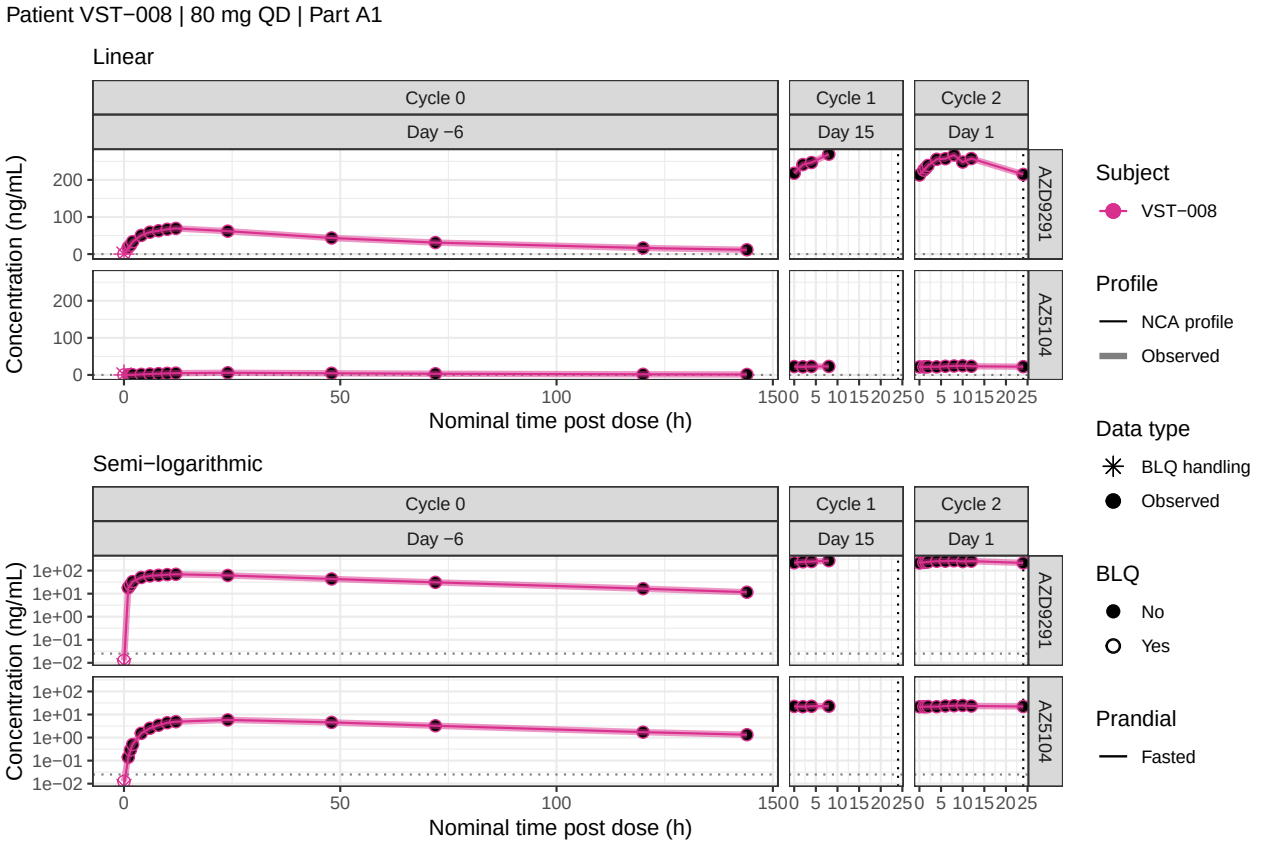


Figure 7.3.4 Plasma PK time-concentration profiles for subject VST-009

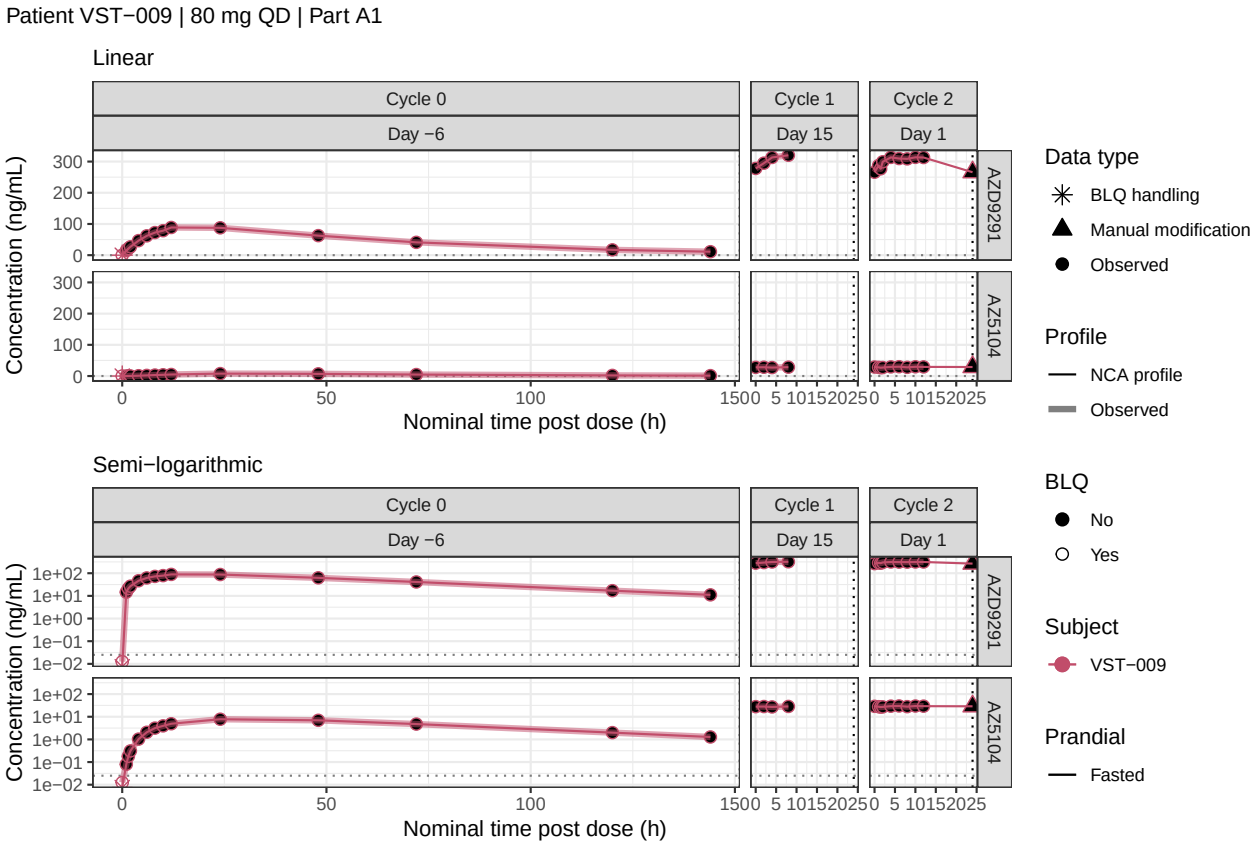


Figure 7.3.5 Plasma PK time-concentration profiles for subject VST-010

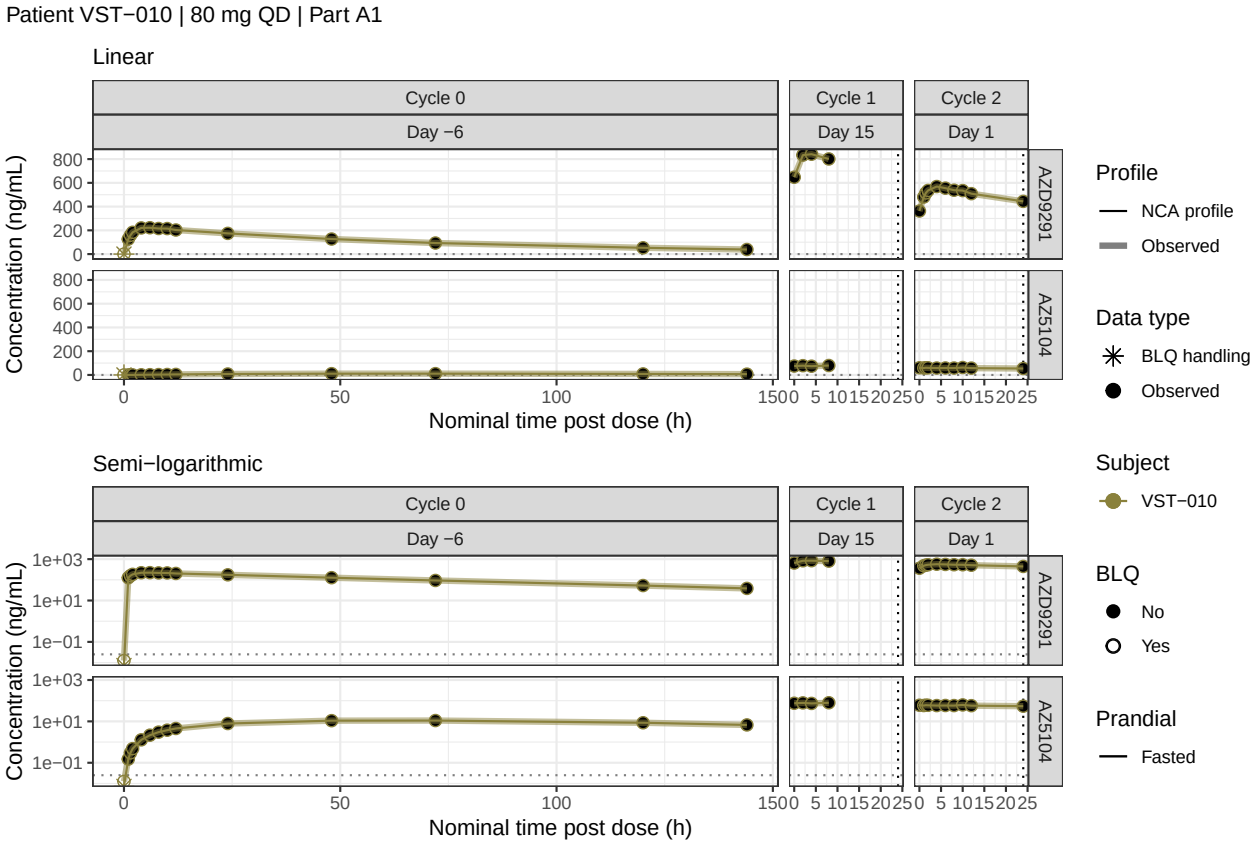


Figure 7.3.6 Plasma PK time-concentration profiles for subject VST-011

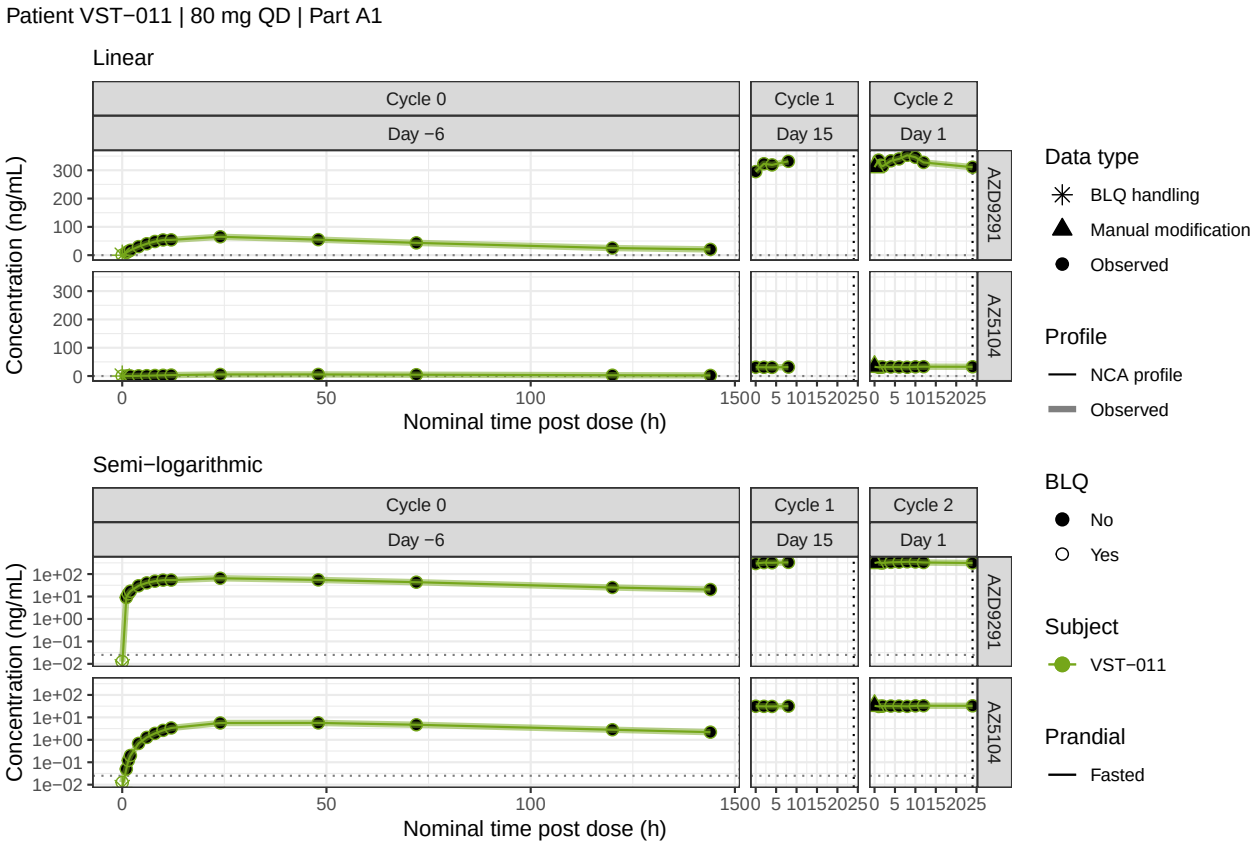
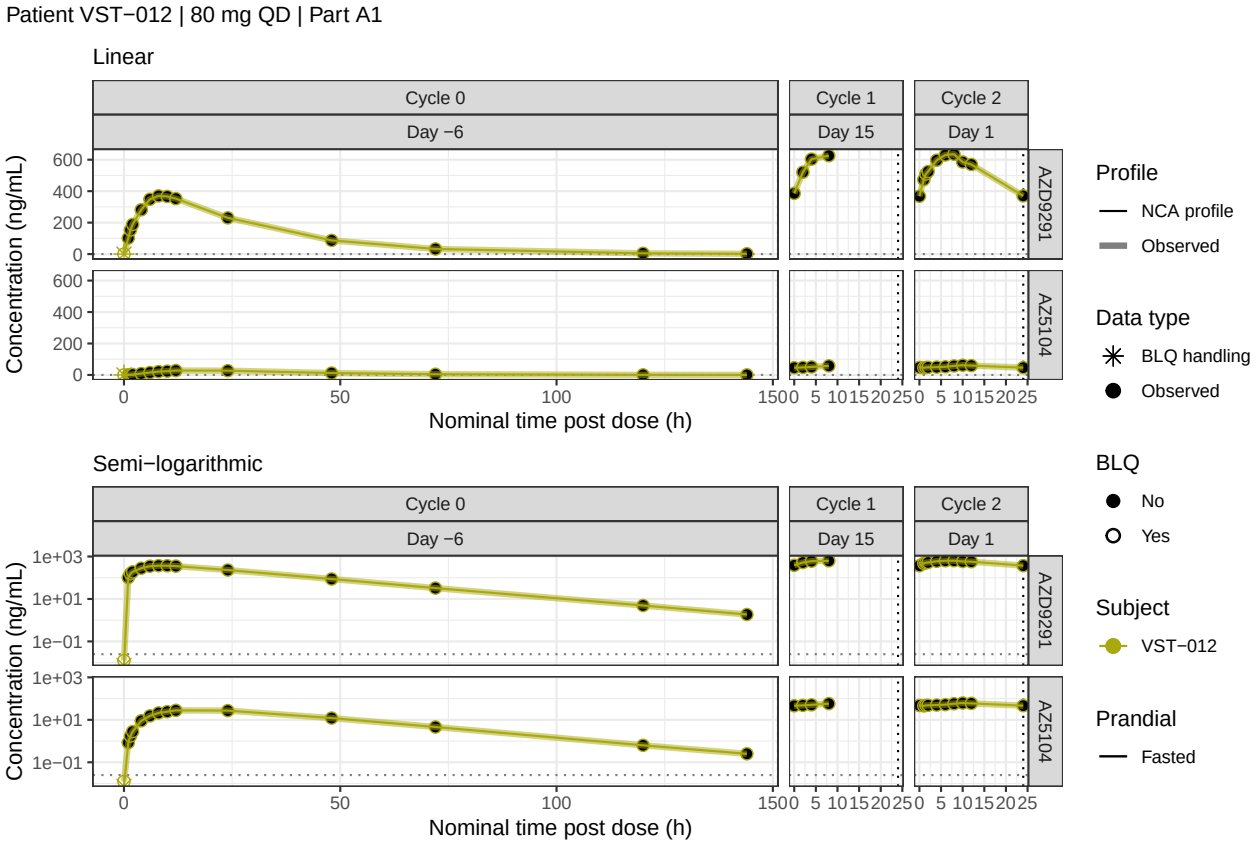


Figure 7.3.7 Plasma PK time-concentration profiles for subject VST-012



7.4 160 mg QD

Figure 7.4.1 Geomean PK time-concentration profiles for 160 mg QD cohort

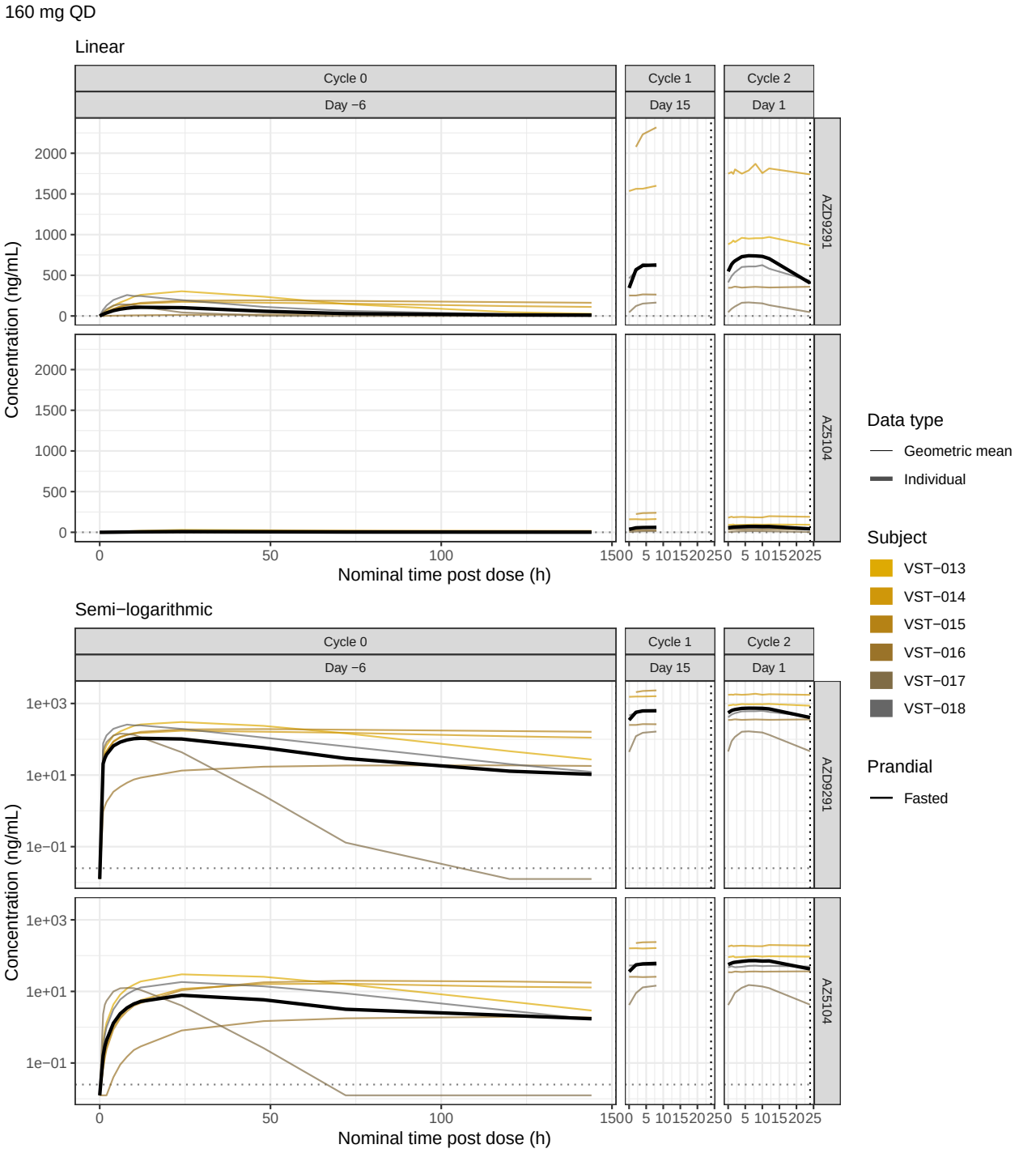


Figure 7.4.2 Plasma PK time-concentration profiles for subject VST-013

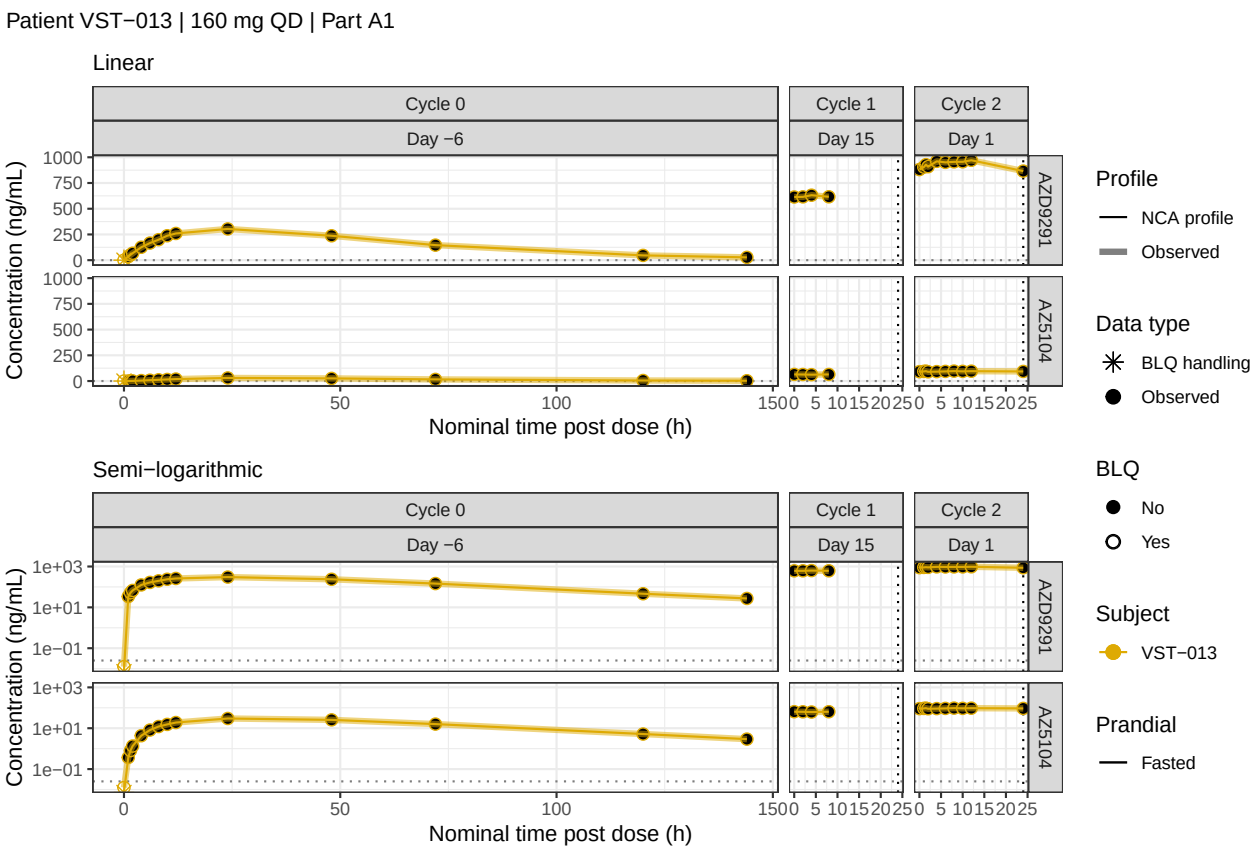


Figure 7.4.3 Plasma PK time-concentration profiles for subject VST-014

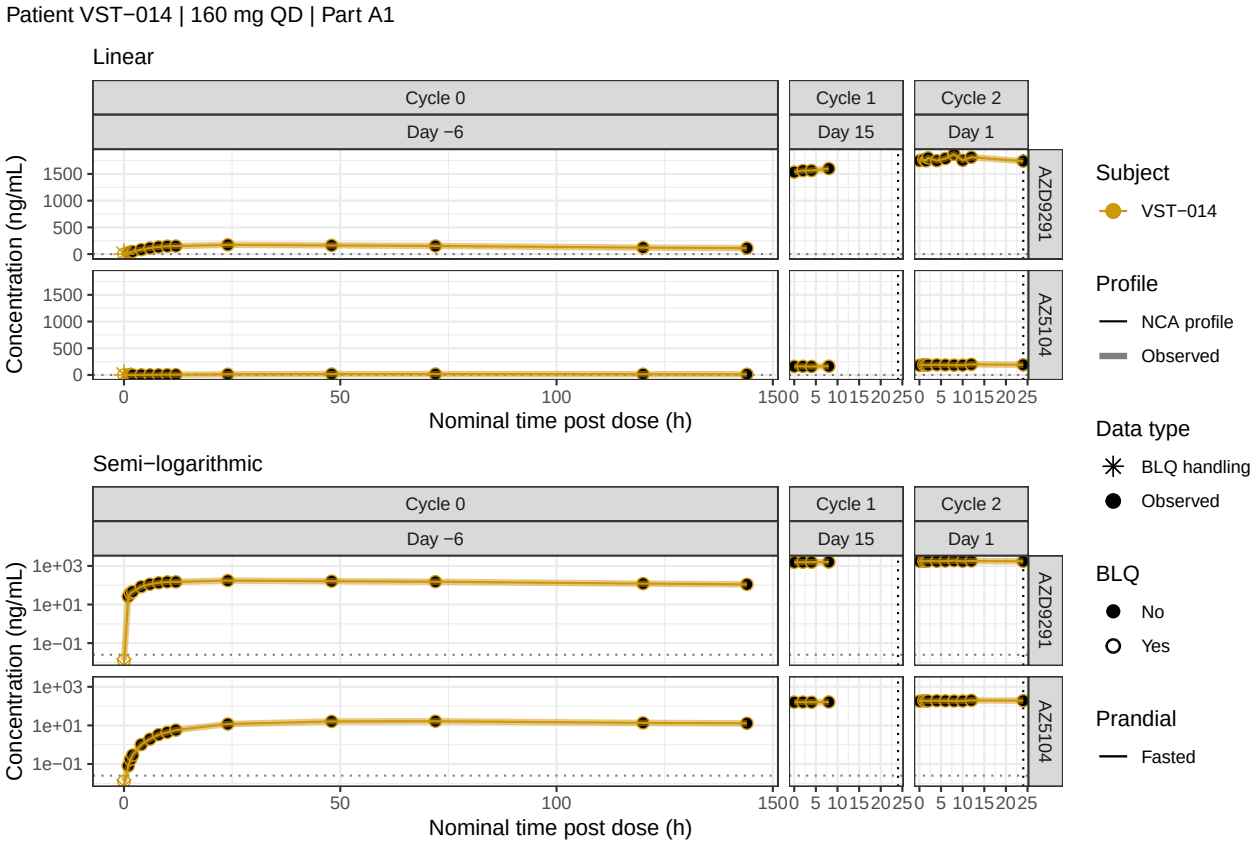


Figure 7.4.4 Plasma PK time-concentration profiles for subject VST-015

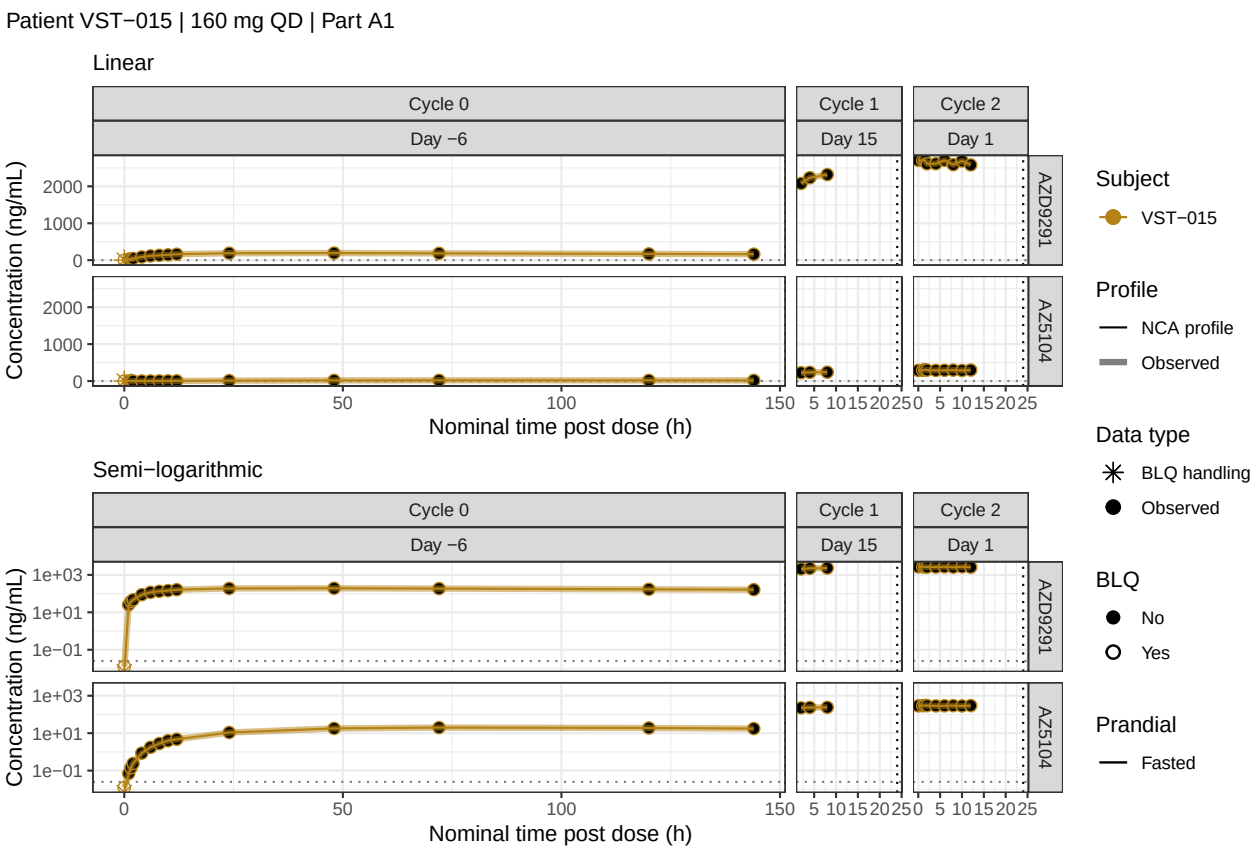


Figure 7.4.5 Plasma PK time-concentration profiles for subject VST-016

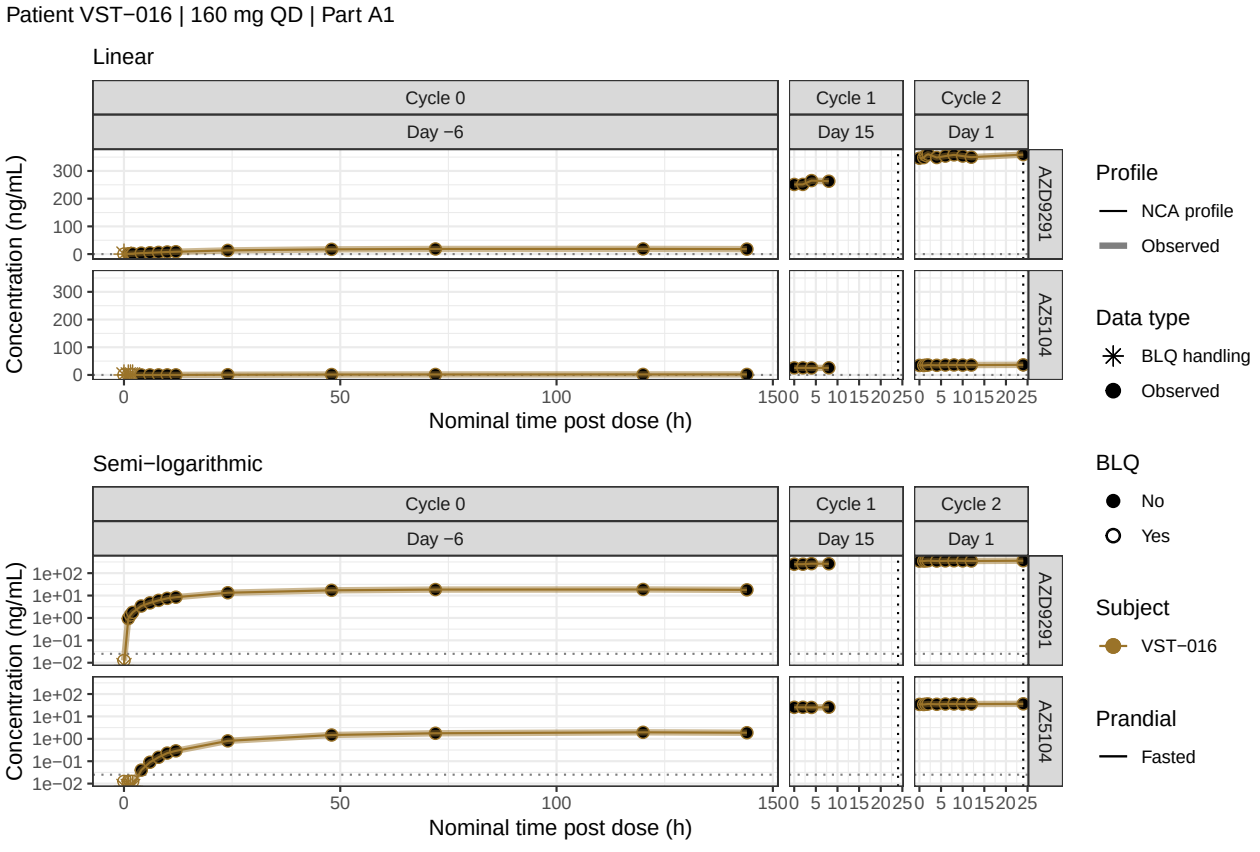


Figure 7.4.6 Plasma PK time-concentration profiles for subject VST-017

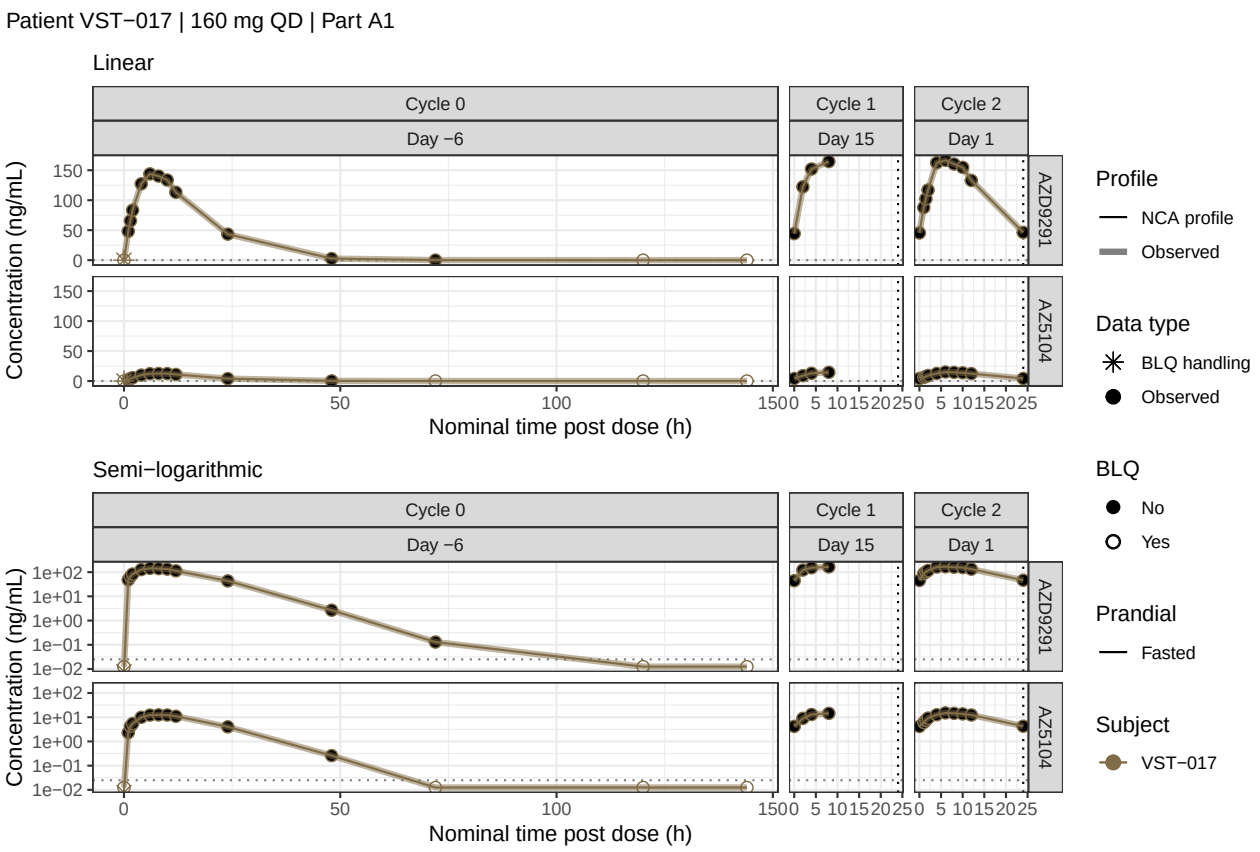
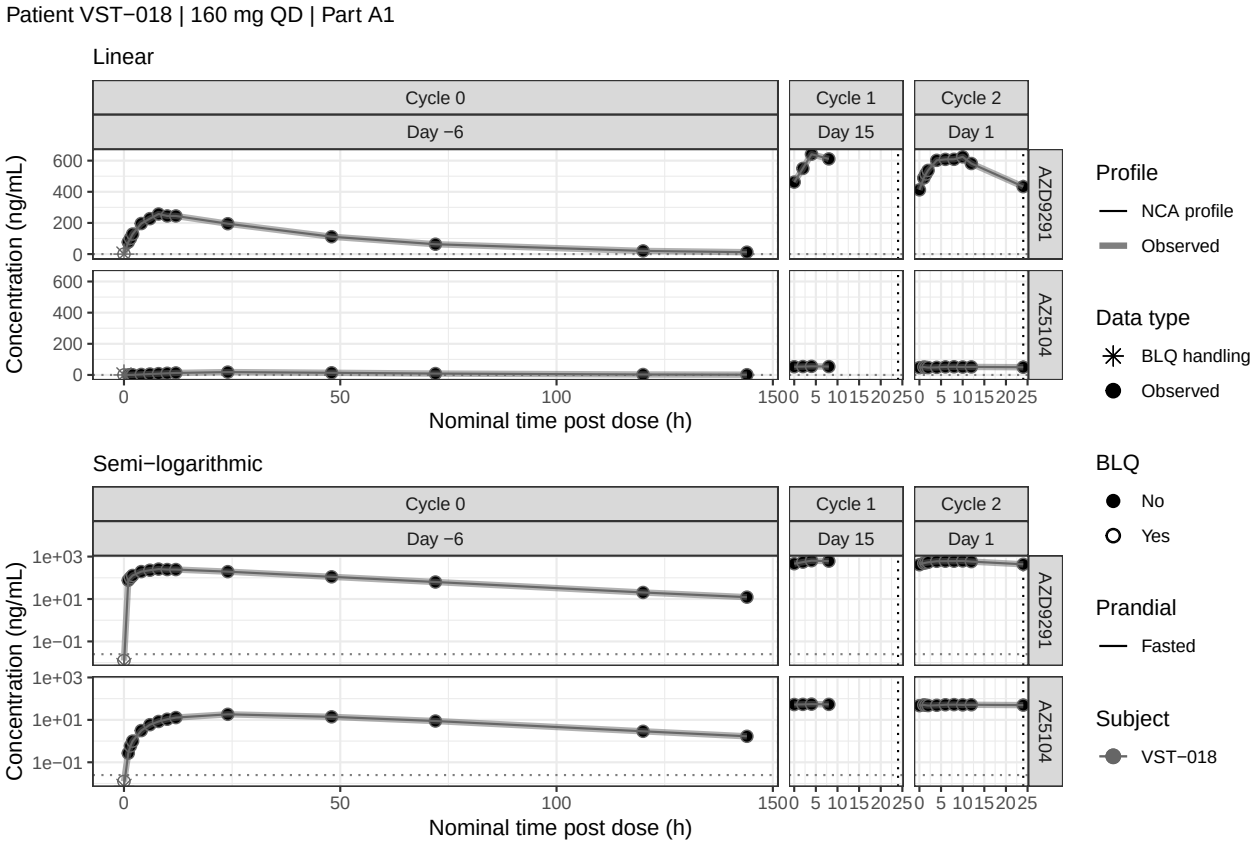


Figure 7.4.7 Plasma PK time-concentration profiles for subject VST-018



8 Selected plasma summary tables and graphs

8.1 Single dose tables

Table 8.1.1 Summary Plasma AZD9291 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCo-hort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h	48 h	72 h	120 h	144 h
n	40 mg QD	ng/mL	6	6	6	6	6	6	6	6	6	6	6	3	3	3
Geomean	40 mg QD	ng/mL	0.0125	8.349	11.97	15.11	24.87	30.84	34.68	36.69	38.43	34.43	20.09	19.25	13.34	11.02
GeoQ95	40 mg QD	ng/mL	0.0125	44.07	61.17	73.18	105.5	118.4	117	113	103.1	74.61	49.11	40.64	24.62	19.82
GeoQ05	40 mg QD	ng/mL	0.0125	1.628	2.37	3.034	5.313	6.862	7.747	8.993	9.597	11.2	9.027	9.056	7.794	6.937
GeoCV	40 mg QD	ng/mL	0	221.5	214.6	205.7	183.2	170	158.5	142.5	133.9	95.92	80.51	100.3	71.92	66.19
GeoSD	40 mg QD	ng/mL	1	3.791	3.717	3.62	3.364	3.208	3.068	2.866	2.755	2.243	2.028	2.303	1.907	1.827
Min	40 mg QD	ng/mL	0.0125	1.07	1.57	2.02	3.6	4.72	5.4	6.45	6.89	8.79	8.63	8.32	7.43	6.72
Max	40 mg QD	ng/mL	0.0125	59.8	82.3	95.5	130	139	131	124	106	76.8	58.6	44.1	26.7	21.6
Med	40 mg QD	ng/mL	0.0125	7.31	10.67	13.66	23.28	30.04	36.99	39.62	44.38	40.31	21.2	19.42	11.99	9.24
Mean	40 mg QD	ng/mL	0.0125	16.48	23.08	28.01	42.26	49.65	52.75	53.29	53.62	42.97	24.81	23.95	15.36	12.51

**Geomean value for tmax is the median not the geomean

Table 8.1.2 Summary Plasma AZ5104 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCo-hort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h	48 h	72 h	120 h	144 h
n	40 mg QD	ng/mL	6	6	6	6	6	6	6	6	6	6	6	3	3	3
Geomean	40 mg QD	ng/mL	0.0125	0.07501	0.1485	0.273	0.8015	1.384	1.936	2.35	2.683	3.165	2.117	2.031	1.488	1.193
GeoQ95	40 mg QD	ng/mL	0.0125	0.4662	0.952	1.52	4.335	6.264	8.428	8.959	9.534	7.384	4.727	4.97	3.255	2.515
GeoQ05	40 mg QD	ng/mL	0.0125	0.0125	0.01672	0.04601	0.1351	0.2741	0.4097	0.5666	0.6829	1.007	0.9985	0.889	0.7949	0.7062
GeoCV	40 mg QD	ng/mL	0	329.7	394.5	274.2	260	207.2	191.8	163.6	150.1	99.62	70.34	123	95.76	87.94
GeoSD	40 mg QD	ng/mL	1	4.821	5.341	4.321	4.185	3.636	3.463	3.13	2.963	2.294	1.885	2.612	2.241	2.132
Min	40 mg QD	ng/mL	0.0125	0.0125	0.0125	0.04	0.11	0.22	0.32	0.44	0.51	0.77	0.89	0.82	0.76	0.69
Max	40 mg QD	ng/mL	0.0125	0.59	1.18	1.89	5.28	7.28	9.63	9.85	10.5	7.72	5.34	5.55	3.64	2.83
Med	40 mg QD	ng/mL	0.0125	0.1	0.205	0.335	0.91	1.495	1.92	2.23	2.46	3.425	2.045	1.84	1.19	0.87
Mean	40 mg QD	ng/mL	0.0125	0.1742	0.3571	0.5767	1.643	2.502	3.383	3.783	4.125	4.008	2.502	2.737	1.863	1.463

**Geomean value for tmax is the median not the geomean

Table 8.1.3 Summary Plasma AZD9291 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCo-hort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h	48 h	72 h	120 h	144 h
n	80 mg QD	ng/mL	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Geomean	80 mg QD	ng/mL	0.0125	34.13	46.61	57.26	81.64	95.97	102.8	106.7	107.1	95.17	63.11	40.84	17.2	11.12
GeoQ95	80 mg QD	ng/mL	0.0125	119.4	157.3	187.1	264.8	311.5	323.2	320.7	307.1	214.9	115.5	76.98	43.93	32.87
GeoQ05	80 mg QD	ng/mL	0.0125	10.21	14.91	19.3	33.6	44.38	51.57	56.7	56.25	54.71	39.57	28.54	6.412	2.829
GeoCV	80 mg QD	ng/mL	0	151	144.3	133.1	112.6	103.9	96.75	91.06	86.52	66.7	47.04	46.06	90.92	134
GeoSD	80 mg QD	ng/mL	1	2.974	2.889	2.745	2.472	2.353	2.254	2.175	2.112	1.834	1.564	1.551	2.173	2.756
Min	80 mg QD	ng/mL	0.0125	9.06	13.3	17.3	30.1	40.3	48.3	53.8	54	52.5	38.4	27.8	4.92	1.85
Max	80 mg QD	ng/mL	0.0125	126	158	188	282	349	370	366	353	230	127	93.2	52.9	38.5
Med	80 mg QD	ng/mL	0.0125	34.76	43.02	49.68	58.96	65.16	69.87	72.63	78.97	76.33	58.72	36.79	16.7	11.34
Mean	80 mg QD	ng/mL	0.0125	53.46	72.1	85.89	116.1	133.4	139.4	141.1	138.5	112	68.87	44.81	21.76	15.6

**Geomean value for tmax is the median not the geomean

Table 8.1.4 Summary Plasma AZ5104 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCo-hort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h	48 h	72 h	120 h	144 h
n	80 mg QD	ng/mL	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Geomean	80 mg QD	ng/mL	0.0125	0.1745	0.3645	0.5984	1.771	3.045	4.19	5.192	6.105	8.108	6.717	4.684	2.065	1.372
GeoQ95	80 mg QD	ng/mL	0.0125	0.6978	1.382	2.21	6.508	10.68	14	16.05	18.22	19.91	11.77	8.893	6.491	5.089
GeoQ05	80 mg QD	ng/mL	0.0125	0.056230	.1328	0.2232	0.7627	1.442	2.159	2.876	3.631	5.323	4.061	2.984	0.7813	0.3587
GeoCV	80 mg QD	ng/mL	0	139.4	124.8	119.9	111.9	104.7	99.64	91.45	88.35	67.95	48.33	49.27	104.2	146.3
GeoSD	80 mg QD	ng/mL	1	2.827	2.635	2.57	2.462	2.364	2.294	2.181	2.137	1.852	1.581	1.594	2.357	2.915
Min	80 mg QD	ng/mL	0.0125	0.05	0.12	0.2	0.69	1.28	1.93	2.63	3.37	5.23	3.91	2.9	0.63	0.25
Max	80 mg QD	ng/mL	0.0125	0.84	1.71	2.78	9	15.3	21.1	24.1	27.9	27.1	12.1	11	8.58	6.74
Med	80 mg QD	ng/mL	0.0125	0.145	0.295	0.49	1.405	2.345	3.285	4.175	4.895	6.805	6.31	4.64	1.855	1.305
Mean	80 mg QD	ng/mL	0.0125	0.2767	0.555	0.8967	2.665	4.497	6.12	7.267	8.447	9.908	7.335	5.19	2.87	2.142

**Geomean value for tmax is the median not the geomean

Table 8.1.5 Summary Plasma AZD9291 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCo-hort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h	48 h	72 h	120 h	144 h
n	160 mg QD	ng/mL	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Geomean	160 mg QD	ng/mL	0.0125	20.74	29.63	37.47	65.41	83.36	95.83	103.8	106.6	101.9	57.99	29.23	12.86	10.51
GeoQ95	160 mg QD	ng/mL	0.0125	68.41	90.69	115.4	176	210.3	241.3	243.1	255.8	271.8	225.1	176	156	147.4
GeoQ05	160 mg QD	ng/mL	0.0125	2.144	3.098	4.019	7.6	10.41	13.17	15.42	16.17	17.93	4.262	0.4489	0.07773	0.06992
GeoCV	160 mg QD	ng/mL	0	328.7	320.7	312.4	281.5	260.3	237.2	214.7	203.8	177.9	477.7	4861	48260	38800
GeoSD	160 mg QD	ng/mL	1	4.812	4.744	4.671	4.391	4.187	3.956	3.718	3.599	3.302	5.933	16.23	33.63	31.59
Min	160 mg QD	ng/mL	0.0125	0.94	1.35	1.78	3.41	4.7	6.1	7.51	8.45	13.4	2.68	0.13	0.0125	0.0125
Max	160 mg QD	ng/mL	0.0125	76.9	101	129	196	227	257	245	260	304	237	185	170	162
Med	160 mg QD	ng/mL	0.0125	30.2	45.4	56.98	106.3	130	136.9	146.5	155.5	181	137	104.7	33.38	22.63
Mean	160 mg QD	ng/mL	0.0125	35.3	49.37	62.32	103.9	128.6	144.8	152.8	156.2	152.9	120.6	94.12	62.7	55.09

**Geomean value for tmax is the median not the geomean

Table 8.1.6 Summary Plasma AZ5104 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCo-hort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h	48 h	72 h	120 h	144 h
n	160 mg QD	ng/mL	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Geomean	160 mg QD	ng/mL	0.0125	0.1591	0.2902	0.4304	1.294	2.382	3.473	4.48	5.25	7.815	5.838	3.172	2.131	1.723
GeoQ95	160 mg QD	ng/mL	0.0125	1.466	2.799	3.838	8.066	11.05	12.38	14.57	17.21	26.51	23.45	18.98	17.4	16.3
GeoQ05	160 mg QD	ng/mL	0.0125	0.019230	.022870	.026170	.086130	.1893	0.3115	0.4688	0.5831	1.208	0.4016	0.043120	.044180	.04256
GeoCV	160 mg QD	ng/mL	0	474.6	691.7	849.8	640.8	479.3	388.6	321.5	296.1	208.7	526.9	5871	3474	2998
GeoSD	160 mg QD	ng/mL	1	5.913	7.185	7.941	6.915	5.944	5.297	4.75	4.526	3.653	6.251	17.36	14.35	13.57
Min	160 mg QD	ng/mL	0.0125	0.0125	0.0125	0.0125	0.04	0.09	0.15	0.23	0.29	0.81	0.26	0.0125	0.0125	0.0125
Max	160 mg QD	ng/mL	0.0125	2.32	4.25	5.45	9.94	12.2	12.5	15.4	19	30	25.6	19.9	18.9	17.6
Med	160 mg QD	ng/mL	0.0125	0.175	0.38	0.645	2.075	3.94	5.85	7.53	8.33	11.32	14.98	12.38	4.045	2.4
Mean	160 mg QD	ng/mL	0.0125	0.5204	0.9938	1.389	3.217	5.018	6.537	7.832	8.918	12.62	12.55	10.48	7.082	6.167

**Geomean value for tmax is the median not the geomean

8.2 Multiple dose tables

Table 8.2.1 Summary Plasma AZD9291 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	2 h	4 h	8 h
n	40 mg QD	ng/mL	6	6	6	6
Geomean	40 mg QD	ng/mL	119.4	123.1	125.3	124.2
GeoQ95	40 mg QD	ng/mL	247.9	263.5	273.7	291.2
GeoQ05	40 mg QD	ng/mL	68.42	60.97	57.04	46.07
GeoCV	40 mg QD	ng/mL	57.06	65.79	70.9	87.15
GeoSD	40 mg QD	ng/mL	1.7	1.822	1.893	2.121
Min	40 mg QD	ng/mL	61.2	52.2	47.7	36
Max	40 mg QD	ng/mL	298	321	330	346
Med	40 mg QD	ng/mL	108.4	122.9	128.6	134.7
Mean	40 mg QD	ng/mL	135.7	143.7	148.1	153.6

**Geomean value for tmax is the median not the geomean

Table 8.2.2 Summary Plasma AZ5104 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	2 h	4 h	8 h
n	40 mg QD	ng/mL	6	6	6	6
Geomean	40 mg QD	ng/mL	13.05	12.5	12.49	12.39
GeoQ95	40 mg QD	ng/mL	27.48	26.22	27.21	27.12
GeoQ05	40 mg QD	ng/mL	8.987	8.056	7.179	5.805
GeoCV	40 mg QD	ng/mL	54.87	55.46	60.81	69.96
GeoSD	40 mg QD	ng/mL	1.67	1.678	1.752	1.88
Min	40 mg QD	ng/mL	8.85	7.75	6.56	4.95
Max	40 mg QD	ng/mL	34.6	32.6	33.7	32.5
Med	40 mg QD	ng/mL	11.32	11.2	11.46	12.64
Mean	40 mg QD	ng/mL	14.87	14.24	14.48	14.64

**Geomean value for tmax is the median not the geomean

Table 8.2.3 Summary Plasma AZD9291 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	2 h	4 h	8 h
n	80 mg QD	ng/mL	6	6	6	6
Geomean	80 mg QD	ng/mL	307.1	355.9	370.6	378.6
GeoQ95	80 mg QD	ng/mL	568.9	741	774.3	753.1
GeoQ05	80 mg QD	ng/mL	195	212.6	216.3	220.1
GeoCV	80 mg QD	ng/mL	46.51	56.28	58.37	55.62
GeoSD	80 mg QD	ng/mL	1.557	1.69	1.719	1.681
Min	80 mg QD	ng/mL	188	204	207	206
Max	80 mg QD	ng/mL	647	834	841	801
Med	80 mg QD	ng/mL	286.5	308.9	316	325.8
Mean	80 mg QD	ng/mL	335.4	402.9	421.8	425.6

**Geomean value for tmax is the median not the geomean

Table 8.2.4 Summary Plasma AZ5104 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	2 h	4 h	8 h
n	80 mg QD	ng/mL	6	6	6	6
Geomean	80 mg QD	ng/mL	33.05	33.58	33.5	34.98
GeoQ95	80 mg QD	ng/mL	66.32	69.22	67.22	73.38
GeoQ05	80 mg QD	ng/mL	20.06	20.45	20.61	20.15
GeoCV	80 mg QD	ng/mL	53.21	55.29	53.73	59.35
GeoSD	80 mg QD	ng/mL	1.648	1.676	1.655	1.732
Min	80 mg QD	ng/mL	19.3	20	19.9	19.3
Max	80 mg QD	ng/mL	75.1	78.2	73.8	79.4
Med	80 mg QD	ng/mL	29.61	29.6	28.86	30.06
Mean	80 mg QD	ng/mL	36.97	37.87	37.51	39.94

**Geomean value for tmax is the median not the geomean

Table 8.2.5 Summary Plasma AZD9291 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	2 h	4 h	8 h
n	160 mg QD	ng/mL	5	6	6	6
Geomean	160 mg QD	ng/mL	344.4	568.5	620.4	626.4
GeoQ95	160 mg QD	ng/mL	1278	1935	2042	2113
GeoQ05	160 mg QD	ng/mL	62.64	146.4	174.7	184.9
GeoCV	160 mg QD	ng/mL	216.8	146.6	135.2	133.9
GeoSD	160 mg QD	ng/mL	3.741	2.919	2.772	2.755
Min	160 mg QD	ng/mL	44.3	122	152	164
Max	160 mg QD	ng/mL	1540	2080	2230	2320
Med	160 mg QD	ng/mL	462.1	582.6	636.5	613.6
Mean	160 mg QD	ng/mL	581.3	863.2	914.4	928.8

**Geomean value for tmax is the median not the geomean

Table 8.2.6 Summary Plasma AZ5104 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	2 h	4 h	8 h
n	160 mg QD	ng/mL	5	6	6	6
Geomean	160 mg QD	ng/mL	35.7	55.21	58.82	60.72
GeoQ95	160 mg QD	ng/mL	133.3	206.7	213.2	217.5
GeoQ05	160 mg QD	ng/mL	6.003	11.64	15.29	16.72
GeoCV	160 mg QD	ng/mL	233.6	175.6	150.6	145.2
GeoSD	160 mg QD	ng/mL	3.918	3.275	2.969	2.9
Min	160 mg QD	ng/mL	4.18	8.96	13	14.5
Max	160 mg QD	ng/mL	160	225	236	240
Med	160 mg QD	ng/mL	52.8	58.69	58.58	58.98
Mean	160 mg QD	ng/mL	61.34	89.59	91.46	93.43

**Geomean value for tmax is the median not the geomean

Table 8.2.7 Summary Plasma AZD9291 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h
n	40 mg QD	ng/mL	5	6	6	6	6	6	6	6	6	6
Geomean	40 mg QD	ng/mL	113.7	126.8	132.4	135.4	142.3	146.2	142.8	138.1	134.9	115.7
GeoQ95	40 mg QD	ng/mL	147.1	147.2	150.8	154.2	174.7	176.5	172.1	162.8	165.2	200.5
GeoQ05	40 mg QD	ng/mL	70.73	104.6	107.4	107.2	109.1	115.1	111.3	112.3	110.5	69.99
GeoCV	40 mg QD	ng/mL	36.31	15.36	14.53	16.05	20.34	17.93	19.33	16.14	16.39	44.99
GeoSD	40 mg QD	ng/mL	1.422	1.165	1.156	1.173	1.223	1.195	1.211	1.174	1.177	1.536
Min	40 mg QD	ng/mL	62	102	103	103	106	111	108	110	106	63.3
Max	40 mg QD	ng/mL	148	148	152	155	178	180	173	165	169	237
Med	40 mg QD	ng/mL	121.5	129.4	138.2	144.6	149.5	151.7	148.3	143	132.4	117.8
Mean	40 mg QD	ng/mL	118.8	128	133.5	136.8	144.6	148.1	144.9	139.6	136.4	125.4

**Geomean value for tmax is the median not the geomean

Table 8.2.8 Summary Plasma AZ5104 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h
n	40 mg QD	ng/mL	5	6	6	6	6	6	6	6	6	6
Geomean	40 mg QD	ng/mL	13.08	12.55	12.23	12.47	13.38	13.74	14.29	14.6	14.18	11.8
GeoQ95	40 mg QD	ng/mL	19.14	18.47	18.1	18.23	18.46	17.94	17.88	18.15	18.01	15.43
GeoQ05	40 mg QD	ng/mL	9.046	8.811	8.725	9.482	10.41	10.59	11.16	10.93	10.69	8.342
GeoCV	40 mg QD	ng/mL	33	31.44	31.05	28.35	24.24	21.9	19.61	21.39	21.5	26.26
GeoSD	40 mg QD	ng/mL	1.379	1.359	1.354	1.321	1.27	1.242	1.214	1.236	1.237	1.295
Min	40 mg QD	ng/mL	8.51	8.62	8.55	9.45	10.1	10.3	10.8	10.4	10.2	8
Max	40 mg QD	ng/mL	20.4	20	19.6	19.8	19.8	19.1	18.6	18.6	18.7	15.9
Med	40 mg QD	ng/mL	12.96	12.86	12.3	12.16	13.01	14.08	14.83	15.39	14.66	12.66
Mean	40 mg QD	ng/mL	13.64	13.06	12.72	12.9	13.72	14.01	14.51	14.87	14.45	12.12

**Geomean value for tmax is the median not the geomean

Table 8.2.9 Summary Plasma AZD9291 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h
n	80 mg QD	ng/mL	5	6	6	6	6	6	6	6	6	5
Geomean	80 mg QD	ng/mL	239	291.6	297.2	305.4	327.2	324.1	329.5	315.3	312.3	258
GeoQ95	80 mg QD	ng/mL	366.9	478.7	513.7	533.2	589.9	610.7	609.3	572.3	554	428.1
GeoQ05	80 mg QD	ng/mL	119.3	144	149.2	150	158.6	147.2	154.5	140.8	146.2	120.4
GeoCV	80 mg QD	ng/mL	55.96	54.52	55.99	57.35	59.39	64.54	61.58	64.03	60.01	62.4
GeoSD	80 mg QD	ng/mL	1.685	1.666	1.686	1.704	1.733	1.804	1.763	1.797	1.741	1.774
Min	80 mg QD	ng/mL	103	124	129	128	135	122	129	117	121	104
Max	80 mg QD	ng/mL	368	481	515	536	597	630	635	585	570	444
Med	80 mg QD	ng/mL	265.8	311.6	297.3	306.7	323.4	324.9	330.8	329.7	320.3	310.9
Mean	80 mg QD	ng/mL	262.5	321.2	330	340.3	367.3	369.1	371.7	357.4	349.7	288.8

**Geomean value for tmax is the median not the geomean

Table 8.2.10 Summary Plasma AZ5104 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h
n	80 mg QD	ng/mL	5	6	6	6	6	6	6	6	6	5
Geomean	80 mg QD	ng/mL	28.55	28.37	28.97	29.05	29.47	30.43	30.65	32.09	31.18	28.58
GeoQ95	80 mg QD	ng/mL	57.47	54.83	57.15	56.77	55.93	56.83	57.86	62.25	59.03	52.59
GeoQ05	80 mg QD	ng/mL	12.21	12.71	13.16	12.95	13.13	13.96	14.25	14.26	14.07	12.11
GeoCV	80 mg QD	ng/mL	77.47	65.47	66.03	66.79	65.62	63.43	64.8	68.79	66.14	74.01
GeoSD	80 mg QD	ng/mL	1.985	1.817	1.825	1.836	1.819	1.789	1.808	1.863	1.826	1.937
Min	80 mg QD	ng/mL	10.6	10.6	11.1	10.8	11.1	11.8	12	11.9	11.9	10.4
Max	80 mg QD	ng/mL	60.2	58.4	60.6	59.9	58.1	58.6	58	62.4	59.6	54.3
Med	80 mg QD	ng/mL	28.89	29.22	29.08	29.5	30.62	30.84	29.44	31.1	31.16	32.66
Mean	80 mg QD	ng/mL	33.79	32.43	33.26	33.37	33.68	34.55	35.06	37.17	35.77	33.2

**Geomean value for tmax is the median not the geomean

Table 8.2.11 Summary Plasma AZD9291 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h
n	160 mg QD	ng/mL	6	6	6	6	6	6	6	6	6	5
Geomean	160 mg QD	ng/mL	547.7	633.5	659.4	677.7	728.5	740.4	737.9	732.2	705	404.7
GeoQ95	160 mg QD	ng/mL	2426	2431	2423	2380	2363	2440	2385	2416	2363	1513
GeoQ05	160 mg QD	ng/mL	75.44	123.9	139.8	155	196.5	201.1	196	190.2	169.3	69.79
GeoCV	160 mg QD	ng/mL	271.2	189.5	174	161.1	137.5	138	139.3	141.5	152.1	232.2
GeoSD	160 mg QD	ng/mL	4.294	3.436	3.256	3.1	2.802	2.808	2.826	2.854	2.988	3.904
Min	160 mg QD	ng/mL	45.4	87.8	102	117	162	167	160	155	133	46.3
Max	160 mg QD	ng/mL	2710	2700	2700	2610	2610	2710	2590	2690	2580	1740
Med	160 mg QD	ng/mL	646.6	696.4	721.4	723	781.4	779.3	782.1	790.2	776.1	432.9
Mean	160 mg QD	ng/mL	1023	1050	1058	1056	1072	1095	1090	1089	1071	688.8

**Geomean value for tmax is the median not the geomean

Table 8.2.12 Summary Plasma AZ5104 Pharmacokinetic Parameters - single dose administration

Statistic	DoseCohort	Conc Unit	0 h	1 h	1.5 h	2 h	4 h	6 h	8 h	10 h	12 h	24 h
n	160 mg QD	ng/mL	6	6	6	6	6	6	6	6	6	5
Geomean	160 mg QD	ng/mL	56.26	61.63	64.09	65.31	68.86	72.15	72.32	70.44	71.06	42.37
GeoQ95	160 mg QD	ng/mL	256.2	262.7	268.9	264.5	258.9	260.4	262.6	255.9	269.1	165
GeoQ05	160 mg QD	ng/mL	7.072	9.313	11.04	12.92	16.27	18.7	18.18	17.41	16.11	6.545
GeoCV	160 mg QD	ng/mL	292.6	243	217.9	193.9	165.8	151.7	154.8	156.9	170.9	260.2
GeoSD	160 mg QD	ng/mL	4.493	4.015	3.753	3.487	3.156	2.982	3.022	3.048	3.218	4.187
Min	160 mg QD	ng/mL	4.17	6.04	7.52	9.19	12.6	15.1	14.5	13.7	12.4	4.26
Max	160 mg QD	ng/mL	289	292	305	298	287	291	296	286	298	190
Med	160 mg QD	ng/mL	68.92	72.08	72.49	68.56	70.07	72.55	74.44	72.42	73.69	49.57
Mean	160 mg QD	ng/mL	107.4	111.3	112.8	110.9	110.7	112.2	113.1	110.6	115.3	74.76

**Geomean value for tmax is the median not the geomean

9 Selected plasma NCA summary graphs

9.1 Summary graphs

Figure 9.1.1 Summary of NCA selected Cmax and AUC parameters.

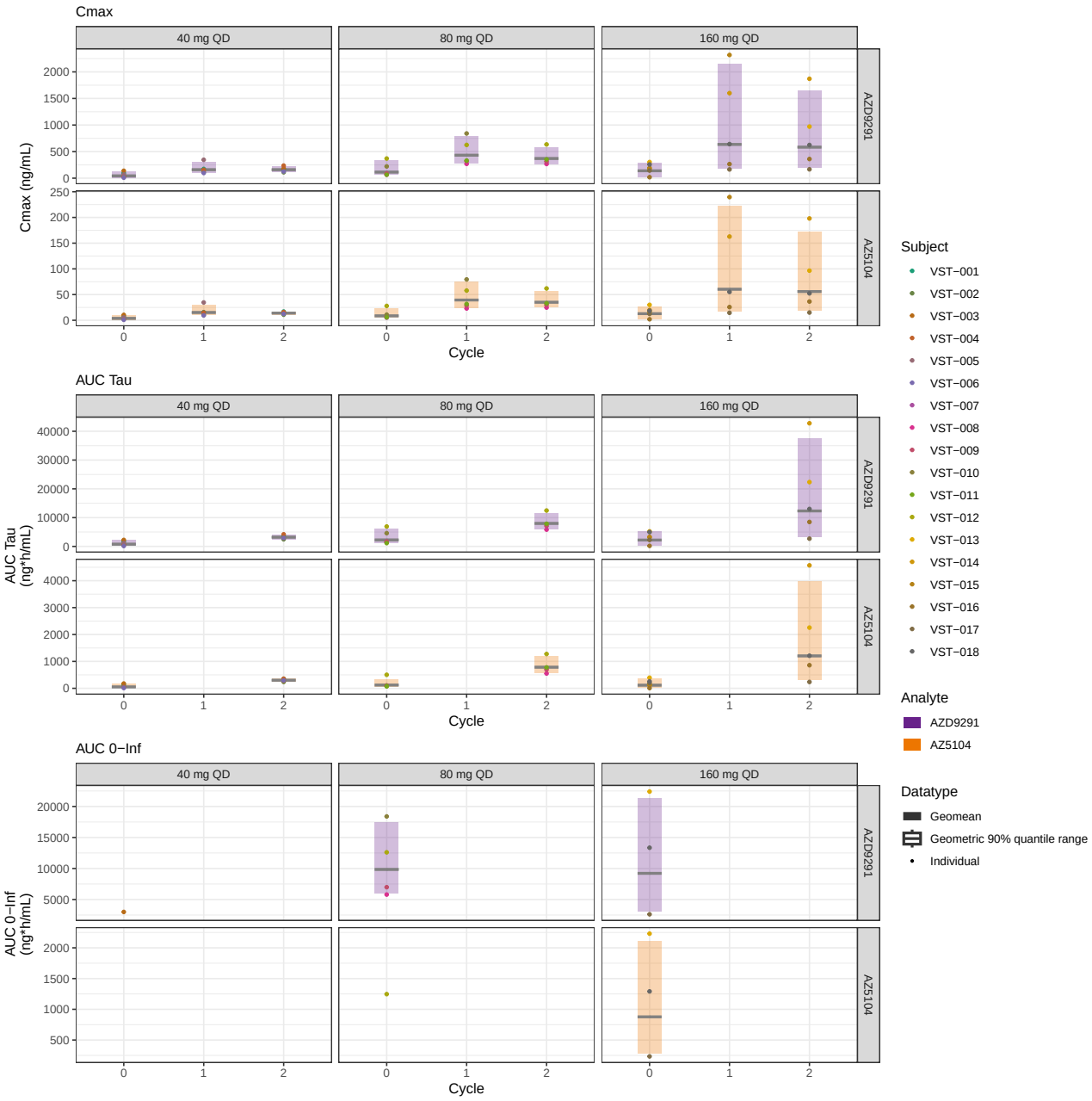


Figure 9.1.2 Summary of NCA calculated Half-lives.

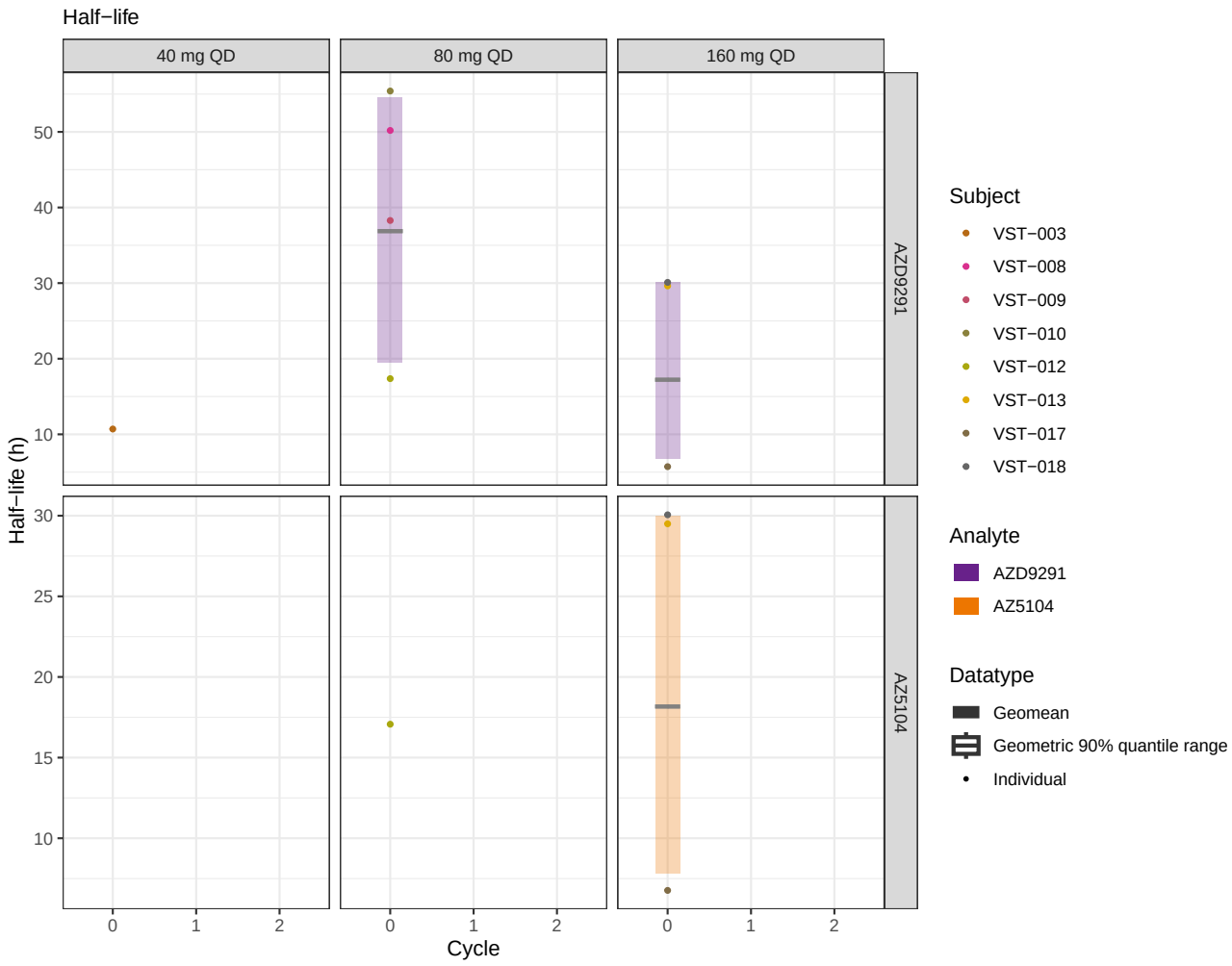
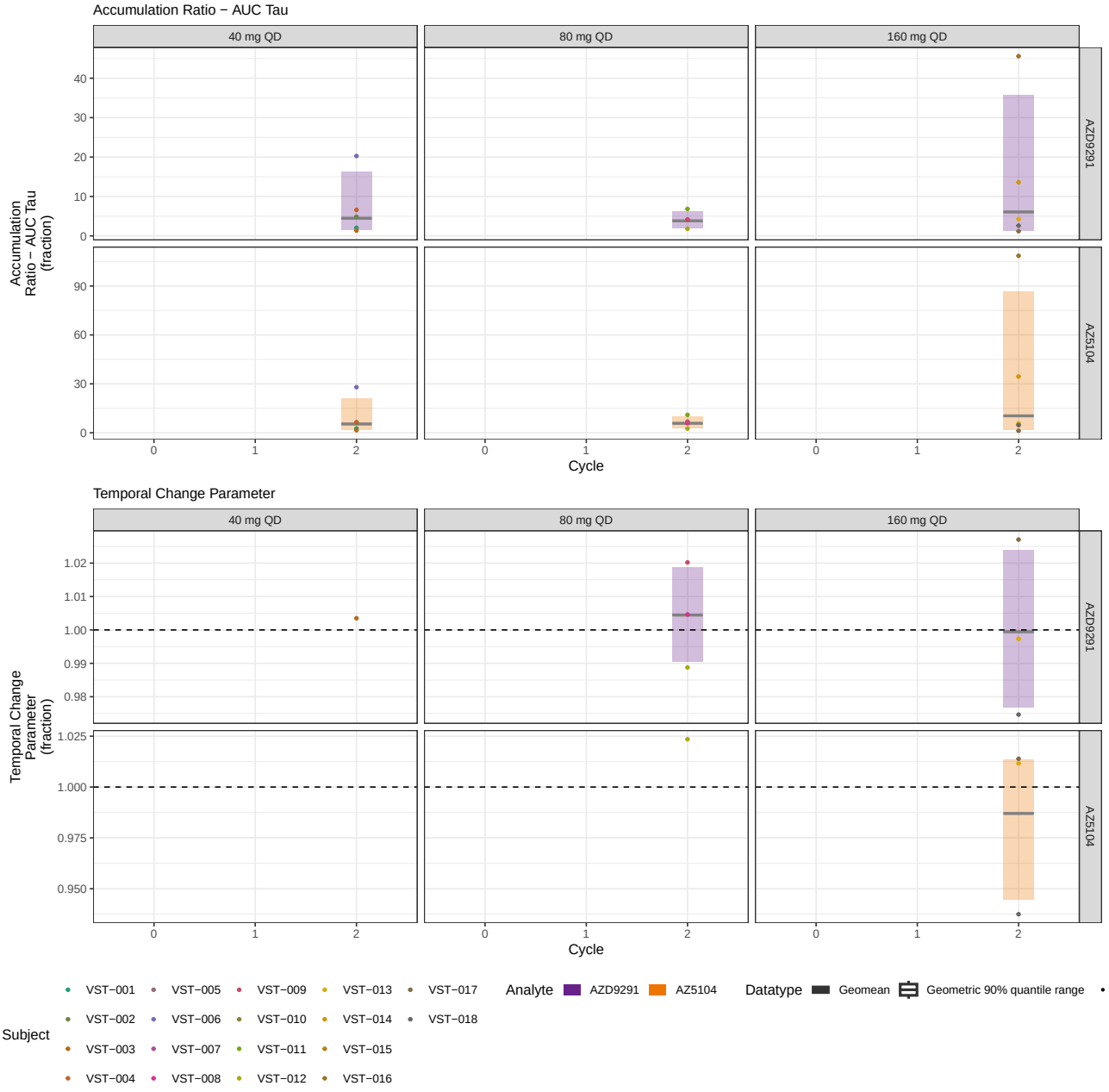


Figure 9.1.3 Summary of selected NCA ratios.



10 Plasma PK NCA results and tables listings by cohort

10.1 Part A1 40 mg QD

10.1.1 Cycle 0 Day -6 Fasted

Table 10.1.1 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-001	24	Inf	11	11	1	11	0	11	0	1
VST-002	24	Inf	11	11	1	11	0	11	0	1
VST-003	24	Inf	11	11	1	11	0	11	0	0
VST-004	24	Inf	14	14	1	14	0	14	0	1
VST-005	24	Inf	14	14	1	14	0	14	0	1
VST-006	24	Inf	14	14	1	14	0	14	0	1
n	-	-	-	6	6	6	6	6	-	-
Minimum	-	-	-	11	1	11	0	11	-	-
Maximum	-	-	-	14	1	14	0	14	-	-
Median	-	-	-	12	1	12	0	12	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.1.2 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-001	0	1	93.71	12	48	28.87
VST-002	0	1	25.94	12	48	17.54
VST-003	0	1	139.4	6	48	10.33
VST-004	0	1	31.92	24	140	9.24
VST-005	0	1	68.44	24	140	21.57
VST-006	0	1	8.79	24	140	6.72
n	-	6	6	6	6	6
Minimum	-	1	8.79	6	48	6.72
Maximum	-	1	139	24	140	28.9
Median	-	1	50.18	18	96	13.94
Arithmean	-	-	61.36	-	-	15.71
Arith%CV	-	-	80.07	-	-	54.19
ArithSD	-	-	49.13	-	-	8.515
Geomean	-	-	43.21	-	-	13.83
Geo%CV	-	-	132.5	-	-	60.61
GeoSD	-	-	2.737	-	-	1.75
GeoQ05	-	-	11.52	-	-	7.277
GeoQ95	-	-	126.2	-	-	26.84

Table 10.1.3 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-001	-	-	-	-	-	1	0	0	0	0	1
VST-002	-	-	-	-	-	1	0	0	0	0	1
VST-003	10.7	0.064757	3	1	3.36	0	0	0	0	0	0
VST-004	67.58	0.010257	4	1	1.42	0	0	0	1	0	1
VST-005	66.46	0.010429	4	0.997	1.44	0	0	0	1	0	1
VST-006	271.2	0.002556	4	0.958	0.354	0	0	0	1	0	1
n	1	1	1	1	1	-	-	-	-	-	-
Minimum	10.7	0.0648	3	1	3.36	-	-	-	-	-	-
Maximum	10.7	0.0648	3	1	3.36	-	-	-	-	-	-
Median	-	-	-	-	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.1.4 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC 0-Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-001	0	2952	756.7	1776	1776	-	-
VST-002	0	997.9	218	512.4	512.4	-	-
VST-003	0	2839	1360	2246	2246	2999	5.319
VST-004	0	2836	254.8	636.2	636.2	3737	24.11
VST-005	0	6150	409.5	1163	1163	8218	25.17
VST-006	0	1105	51.34	145.4	145.4	3734	70.41
n	-	6	6	6	6	1	4
Minimum	-	998	51.3	145	145	3000	5.32
Maximum	-	6150	1360	2250	2250	3000	70.4
Median	-	2838	332.1	899.5	899.5	-	24.64
Arithmean	-	2813	508.3	1080	1080	-	31.25
Arith%CV	-	66.24	94.49	74.58	74.58	-	88.48
ArithSD	-	1864	480.3	805.3	805.3	-	27.65
Geomean	-	2333	326.1	776.9	776.9	-	21.83
Geo%CV	-	77.48	162	131	131	-	144.9
GeoSD	-	1.985	3.111	2.717	2.717	-	2.897
GeoQ05	-	1024	73.7	199.2	199.2	-	6.672
GeoQ95	-	5119	1174	2118	2118	-	60.34

Table 10.1.5 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Half-life dependent parameters

Subject / Statistic	Manual exclusion flag	Half-life exclusion flag	AUMC 0-Inf (ng*h^2/mL)	MRT (h)	Cl/F (L/h)	Clss/F (L/h)	Vz/F (L)
VST-001	0	1	-	-	-	-	-
VST-002	0	1	-	-	-	-	-
VST-003	0	0	53910	17.98	13.34	-	206
VST-004	0	1	384700	103	10.71	-	1044
VST-005	0	1	872600	106.2	4.867	-	466.7
VST-006	0	1	1487000	398.3	10.71	-	4191
n	-	-	1	1	1	0	1
Minimum	-	-	53900	18	13.3	-	206
Maximum	-	-	53900	18	13.3	-	206
Median	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-

Table 10.1.6 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC 0-Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-001	0	2.343	44.41	-
VST-002	0	0.6485	12.81	-
VST-003	0	3.485	56.14	74.97
VST-004	0	0.798	15.91	93.41
VST-005	0	1.711	29.07	205.5
VST-006	0	0.2197	3.636	93.35
n	-	6	6	4
Minimum	-	0.22	3.64	75
Maximum	-	3.48	56.1	205
Median	-	1.255	22.49	93.38
Arithmean	-	1.534	27	116.8
Arith%CV	-	80.07	74.58	51.14
ArithSD	-	1.228	20.13	59.74
Geomean	-	1.08	19.42	107.7
Geo%CV	-	132.5	131	46.58
GeoSD	-	2.737	2.717	1.558
GeoQ05	-	0.288	4.981	77.48
GeoQ95	-	3.155	52.94	182.5

Table 10.1.7 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-001	24	Inf	11	11	1	11	0	11	0	1
VST-002	24	Inf	11	11	1	11	0	11	0	1
VST-003	24	Inf	11	11	1	11	0	11	0	1
VST-004	24	Inf	14	14	1	14	0	14	0	1
VST-005	24	Inf	14	14	2	14	0	14	0	1
VST-006	24	Inf	14	14	3	14	0	14	0	1
n	-	-	-	6	6	6	6	6	-	-
Minimum	-	-	-	11	1	11	0	11	-	-
Maximum	-	-	-	14	3	14	0	14	-	-
Median	-	-	-	12	1	12	0	12	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.1.8 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-001	0	1	7.72	24	48	3.28
VST-002	0	1	2.25	24	48	1.75
VST-003	0	1	10.46	12	48	1.41
VST-004	0	1	3.11	24	140	0.87
VST-005	0	1.5	5.55	72	140	2.83
VST-006	0	2	0.89	48	140	0.69
n	-	6	6	6	6	6
Minimum	-	1	0.89	12	48	0.69
Maximum	-	2	10.5	72	140	3.28
Median	-	1	4.33	24	96	1.58
Arithmean	-	-	4.997	-	-	1.805
Arith%CV	-	-	72.46	-	-	58.12
ArithSD	-	-	3.62	-	-	1.049
Geomean	-	-	3.752	-	-	1.548
Geo%CV	-	-	112.6	-	-	68.78
GeoSD	-	-	2.471	-	-	1.863
GeoQ05	-	-	1.122	-	-	0.7312
GeoQ95	-	-	9.695	-	-	3.161

Table 10.1.9 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-001	-	-	-	-	-	1	0	0	0	0	1
VST-002	-	-	-	-	-	1	0	0	0	0	1
VST-003	-	-	-	-	-	1	0	0	0	0	1
VST-004	68.89	0.010061	4	0.993	1.39	0	0	0	1	0	1
VST-005	-	-	-	-	-	1	0	0	0	0	1
VST-006	303.9	0.0022811	3	0.869	0.237	0	0	0	1	0	1
n	0	0	0	0	0	-	-	-	-	-	-
Minimum	-	-	-	-	-	-	-	-	-	-	-
Maximum	-	-	-	-	-	-	-	-	-	-	-
Median	-	-	-	-	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.1.10 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC 0-Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-001	0	260.3	46.19	135.8	135.8	-	-
VST-002	0	86.25	12.52	38.51	38.51	-	-
VST-003	0	257.2	77.94	177.5	177.5	-	-
VST-004	0	266.5	19.81	55.51	55.51	353	24.5
VST-005	0	573.9	7.448	39.73	39.73	-	-
VST-006	0	106.1	2.74	10.42	10.42	408.6	74.03
n	-	6	6	6	6	0	2
Minimum	-	86.3	2.74	10.4	10.4	-	24.5
Maximum	-	574	77.9	178	178	-	74
Median	-	258.7	16.17	47.62	47.62	-	-
Arithmean	-	258.4	27.77	76.25	76.25	-	-
Arith%CV	-	67.58	104.2	85.66	85.66	-	-
ArithSD	-	174.6	28.95	65.32	65.32	-	-
Geomean	-	213.1	16.22	52.66	52.66	-	-
Geo%CV	-	78.72	185	134.8	134.8	-	-
GeoSD	-	2.003	3.385	2.767	2.767	-	-
GeoQ05	-	90.84	3.518	14.45	14.45	-	-
GeoQ95	-	473.8	68.38	166	166	-	-

Table 10.1.11 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Half-life dependent parameters

Subject / Statistic	Manual exclusion flag	Half-life exclusion flag	AUMC 0-Inf (ng*h^2/mL)	MRT (h)	Cl/F (L/h)	Clss/F (L/h)	Vz/F (L)
VST-001	0	1	-	-	-	-	-
VST-002	0	1	-	-	-	-	-
VST-003	0	1	-	-	-	-	-
VST-004	0	1	37100	105.1	-	-	-
VST-005	0	1	-	-	-	-	-
VST-006	0	1	184200	450.8	-	-	-
n	-	-	0	0	0	0	0
Minimum	-	-	-	-	-	-	-
Maximum	-	-	-	-	-	-	-
Median	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-

Table 10.1.12 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC 0-Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-001	0	0.193	3.396	-
VST-002	0	0.05625	0.9626	-
VST-003	0	0.2615	4.438	-
VST-004	0	0.07775	1.388	8.824
VST-005	0	0.1387	0.9932	-
VST-006	0	0.02225	0.2605	10.22
n	-	6	6	2
Minimum	-	0.0222	0.26	8.82
Maximum	-	0.262	4.44	10.2
Median	-	0.1082	1.19	-
Arithmean	-	0.1249	1.906	-
Arith%CV	-	72.46	85.66	-
ArithSD	-	0.09051	1.633	-
Geomean	-	0.09381	1.317	-
Geo%CV	-	112.6	134.8	-
GeoSD	-	2.471	2.767	-
GeoQ05	-	0.02806	0.3612	-
GeoQ95	-	0.2424	4.151	-

Table 10.1.13 40 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Ratios

Subject / Statistic	Manual exclusion flag	Accumulation Ratio - Cmax (fraction)	Accumulation Ratio - AUC 0-Tau (fraction)	Temporal Change Parameter (fraction)	Metabolite to Parent Ratio - Cmax (fraction)	Metabolite to Parent Ratio - AUC 0-Tau (fraction)	Metabolite to Parent Ratio - AUC Inf (fraction)
VST-001	0	-	-	-	0.082	0.076	-
VST-002	0	-	-	-	0.087	0.075	-
VST-003	0	-	-	-	0.075	0.079	-
VST-004	0	-	-	-	0.097	0.087	0.094
VST-005	0	-	-	-	0.081	0.034	-
VST-006	0	-	-	-	0.101	0.072	0.109
n	-	0	0	0	6	6	2
Minimum	-	-	-	-	0.075	0.034	0.094
Maximum	-	-	-	-	0.101	0.087	0.109
Median	-	-	-	-	0.085	0.076	-
Arithmean	-	-	-	-	0.087	0.071	-
Arith%CV	-	-	-	-	11.572	26.355	-
ArithSD	-	-	-	-	0.01	0.019	-
Geomean	-	-	-	-	0.087	0.068	-
Geo%CV	-	-	-	-	11.493	35.228	-
GeoSD	-	-	-	-	1.121	1.408	-
GeoQ05	-	-	-	-	0.077	0.041	-
GeoQ95	-	-	-	-	0.1	0.085	-

10.1.2 Cycle 1 Day 15 Fasted

Table 10.1.14 40 mg QD Part A1 Cycle 1 Day 15 Fasted: AZD9291 (Parent) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-001	-	-	4	4	0	4	0	4	0	1
VST-002	-	-	4	4	0	4	0	4	0	1
VST-003	-	-	4	4	0	4	0	4	1	1
VST-004	-	-	4	4	0	4	0	4	0	1
VST-005	-	-	4	4	0	4	0	4	0	1
VST-006	-	-	4	4	0	4	0	4	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	4	0	4	0	4	-	-
Maximum	-	-	-	4	0	4	0	4	-	-
Median	-	-	-	4	0	4	0	4	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.1.15 40 mg QD Part A1 Cycle 1 Day 15 Fasted: AZD9291 (Parent) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-001	0	-	173.4	8	-	-
VST-002	0	-	112	8	-	-
VST-003	1	-	61.23	0	-	-
VST-004	0	-	157.5	8	-	-
VST-005	0	-	346.2	8	-	-
VST-006	0	-	97.6	4	-	-
n	-	0	5	5	0	0
Minimum	-	-	97.6	4	-	-
Maximum	-	-	346	8	-	-
Median	-	-	157.5	8	-	-
Arithmean	-	-	177.3	-	-	-
Arith%CV	-	-	56.06	-	-	-
ArithSD	-	-	99.41	-	-	-
Geomean	-	-	159.5	-	-	-
Geo%CV	-	-	52.49	-	-	-
GeoSD	-	-	1.638	-	-	-
GeoQ05	-	-	100.3	-	-	-
GeoQ95	-	-	301.4	-	-	-

Table 10.1.16 40 mg QD Part A1 Cycle 1 Day 15 Fasted: AZ5104 (Metabolite) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-001	-	-	4	4	0	4	0	4	0	1
VST-002	-	-	4	4	0	4	0	4	0	1
VST-003	-	-	4	4	0	4	0	4	1	1
VST-004	-	-	4	4	0	4	0	4	0	1
VST-005	-	-	4	4	0	4	0	4	0	1
VST-006	-	-	4	4	0	4	0	4	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	4	0	4	0	4	-	-
Maximum	-	-	-	4	0	4	0	4	-	-
Median	-	-	-	4	0	4	0	4	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.1.17 40 mg QD Part A1 Cycle 1 Day 15 Fasted: AZ5104 (Metabolite) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-001	0	-	15.69	8	-	-
VST-002	0	-	10.09	8	-	-
VST-003	1	-	8.85	0	-	-
VST-004	0	-	15.18	8	-	-
VST-005	0	-	34.65	0	-	-
VST-006	0	-	9.58	4	-	-
n	-	0	5	5	0	0
Minimum	-	-	9.58	0	-	-
Maximum	-	-	34.6	8	-	-
Median	-	-	15.18	8	-	-
Arithmean	-	-	17.04	-	-	-
Arith%CV	-	-	60.1	-	-	-
ArithSD	-	-	10.24	-	-	-
Geomean	-	-	15.15	-	-	-
Geo%CV	-	-	55.11	-	-	-
GeoSD	-	-	1.674	-	-	-
GeoQ05	-	-	9.68	-	-	-
GeoQ95	-	-	29.57	-	-	-

10.1.3 Cycle 2 Day 1 Fasted

Table 10.1.18 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-001	24	24	10	10	0	10	0	10	0	1
VST-002	24	24	10	9	0	10	0	10	0	1
VST-003	24	24	10	10	0	10	0	10	0	1
VST-004	24	24	10	10	0	10	0	10	0	1
VST-005	24	24	10	10	0	10	0	10	1	1
VST-006	24	24	10	10	0	10	0	10	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	9	0	10	0	10	-	-
Maximum	-	-	-	10	0	10	0	10	-	-
Median	-	-	-	10	0	10	0	10	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.1.19 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-001	0	0	173	8	24	120.6
VST-002	0	0	111.4	6	24	94.81
VST-003	0	0	179.9	6	24	63.26
VST-004	0	0	236.9	24	24	-
VST-005	1	0	148.3	0	24	115
VST-006	0	0	126.8	6	24	120.7
n	-	5	5	5	5	4
Minimum	-	0	111	6	24	63.3
Maximum	-	0	237	24	24	121
Median	-	0	173	6	24	107.7
Arithmean	-	-	165.6	-	-	99.83
Arith%CV	-	-	29.86	-	-	27.29
ArithSD	-	-	49.45	-	-	27.25
Geomean	-	-	159.8	-	-	96.65
Geo%CV	-	-	30.63	-	-	31.17
GeoSD	-	-	1.349	-	-	1.356
GeoQ05	-	-	114.3	-	-	67.22
GeoQ95	-	-	224.2	-	-	120.7

Table 10.1.20 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-001	28.3	0.024494	3	0.919	0.495	0	0	0	1	0	1
VST-002	69.06	0.010037	3	0.984	0.203	0	0	0	1	0	1
VST-003	11.06	0.062692	3	1	1.27	0	0	0	1	0	1
VST-004	-	-	-	-	-	1	0	0	0	0	1
VST-005	64.68	0.010717	4	1	0.247	0	0	0	1	1	1
VST-006	1370	0.00050595	4	-0.416	0.0117	0	0	1	1	0	1
n	0	0	0	0	0	-	-	-	-	-	-
Minimum	-	-	-	-	-	-	-	-	-	-	-
Maximum	-	-	-	-	-	-	-	-	-	-	-
Median	-	-	-	-	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.1.21 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-001	0	3642	1918	3642	3642	-	-
VST-002	0	2482	1278	2482	2482	-	-
VST-003	0	3009	1877	3009	3009	-	-
VST-004	0	4198	1859	4198	4198	-	-
VST-005	1	3161	1690	3161	3161	-	-
VST-006	0	2947	1468	2947	2947	-	-
n	-	5	5	5	5	0	0
Minimum	-	2480	1280	2480	2480	-	-
Maximum	-	4200	1920	4200	4200	-	-
Median	-	3009	1859	3009	3009	-	-
Arithmean	-	3255	1680	3255	3255	-	-
Arith%CV	-	20.56	17.21	20.56	20.56	-	-
ArithSD	-	669.2	289.2	669.2	669.2	-	-
Geomean	-	3202	1659	3202	3202	-	-
Geo%CV	-	20.55	18.35	20.55	20.55	-	-
GeoSD	-	1.226	1.2	1.226	1.226	-	-
GeoQ05	-	2569	1314	2569	2569	-	-
GeoQ95	-	4080	1910	4080	4080	-	-

Table 10.1.22 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Half-life dependent parameters

Subject / Statistic	Manual exclusion flag	Half-life exclusion flag	AUMC 0-Inf (ng*h^2/mL)	MRT (h)	Cl/F (L/h)	Clss/F (L/h)	Vz/F (L)
VST-001	0	1	-	-	-	10.98	-
VST-002	0	1	-	-	-	16.12	-
VST-003	0	1	-	-	-	13.29	-
VST-004	0	1	-	-	-	9.529	-
VST-005	1	1	-	-	-	12.65	-
VST-006	0	1	-	-	-	13.57	-
n	-	-	0	0	0	5	0
Minimum	-	-	-	-	-	9.53	-
Maximum	-	-	-	-	-	16.1	-
Median	-	-	-	-	-	13.29	-
Arithmean	-	-	-	-	-	12.7	-
Arith%CV	-	-	-	-	-	19.99	-
ArithSD	-	-	-	-	-	2.539	-
Geomean	-	-	-	-	-	12.49	-
Geo%CV	-	-	-	-	-	20.55	-
GeoSD	-	-	-	-	-	1.226	-
GeoQ05	-	-	-	-	-	9.804	-
GeoQ95	-	-	-	-	-	15.57	-

Table 10.1.23 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-001	0	4.325	91.04	-
VST-002	0	2.786	62.05	-
VST-003	0	4.496	75.24	-
VST-004	0	5.922	104.9	-
VST-005	1	3.707	79.04	-
VST-006	0	3.17	73.67	-
n	-	5	5	0
Minimum	-	2.79	62	-
Maximum	-	5.92	105	-
Median	-	4.325	75.24	-
Arithmean	-	4.14	81.39	-
Arith%CV	-	29.86	20.56	-
ArithSD	-	1.236	16.73	-
Geomean	-	3.995	80.04	-
Geo%CV	-	30.63	20.55	-
GeoSD	-	1.349	1.226	-
GeoQ05	-	2.859	64.21	-
GeoQ95	-	5.605	102	-

Table 10.1.24 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Ratios

Subject / Statistic	Manual exclusion flag	Accumulation Ratio - Cmax (fraction)	Accumulation Ratio - AUC Tau (fraction)	Temporal Change Parameter (fraction)	Metabolite to Parent Ratio - Cmax (fraction)	Metabolite to Parent Ratio - AUC Tau (fraction)	Metabolite to Parent Ratio - AUC Inf (fraction)
VST-001	0	1.846	2.05	-	-	-	-
VST-002	0	4.295	4.844	-	-	-	-
VST-003	0	1.29	1.34	1.003	-	-	-
VST-004	0	7.421	6.598	-	-	-	-
VST-005	1	2.166	2.719	-	-	-	-
VST-006	0	14.428	20.263	-	-	-	-
n	-	5	5	1	0	0	0
Minimum	-	1.29	1.34	1.003	-	-	-
Maximum	-	14.428	20.263	1.003	-	-	-
Median	-	4.295	4.844	-	-	-	-
Arithmean	-	5.856	7.019	-	-	-	-
Arith%CV	-	91.673	109.727	-	-	-	-
ArithSD	-	5.369	7.702	-	-	-	-
Geomean	-	4.054	4.467	-	-	-	-
Geo%CV	-	128.751	144.261	-	-	-	-
GeoSD	-	2.688	2.889	-	-	-	-
GeoQ05	-	1.386	1.459	-	-	-	-
GeoQ95	-	12.632	16.19	-	-	-	-

Table 10.1.25 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-001	24	24	10	10	0	10	0	10	0	1
VST-002	24	24	10	9	0	10	0	10	0	1
VST-003	24	24	10	10	0	10	0	10	0	1
VST-004	24	24	10	10	0	10	0	10	0	1
VST-005	24	24	10	10	0	10	0	10	1	1
VST-006	24	24	10	10	0	10	0	10	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	9	0	10	0	10	-	-
Maximum	-	-	-	10	0	10	0	10	-	-
Median	-	-	-	10	0	10	0	10	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.1.26 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-001	0	0	16.87	10	24	13.24
VST-002	0	0	10.85	8	24	9.46
VST-003	0	0	14.82	10	24	8
VST-004	0	0	15.96	10	24	14.02
VST-005	1	0	20.44	0	24	15.93
VST-006	0	0	12.52	10	24	12.09
n	-	5	5	5	5	5
Minimum	-	0	10.8	8	24	8
Maximum	-	0	16.9	10	24	14
Median	-	0	14.82	10	24	12.09
Arithmean	-	-	14.2	-	-	11.36
Arith%CV	-	-	17.48	-	-	22.46
ArithSD	-	-	2.483	-	-	2.552
Geomean	-	-	14.02	-	-	11.12
Geo%CV	-	-	18.36	-	-	24.09
GeoSD	-	-	1.2	-	-	1.268
GeoQ05	-	-	11.17	-	-	8.273
GeoQ95	-	-	16.68	-	-	13.86

Table 10.1.27 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-001	-	-	-	-	-	1	0	0	0	0	1
VST-002	104.5	0.0066313	3	0.956	0.134	0	0	0	1	0	1
VST-003	-	-	-	-	-	1	0	0	0	0	1
VST-004	-	-	-	-	-	1	0	0	0	0	1
VST-005	70.03	0.009898	7	0.94	0.314	0	0	0	1	1	1
VST-006	-	-	-	-	-	1	0	0	0	0	1
n	0	0	0	0	0	-	-	-	-	-	-
Minimum	-	-	-	-	-	-	-	-	-	-	-
Maximum	-	-	-	-	-	-	-	-	-	-	-
Median	-	-	-	-	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.1.28 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-001	0	353.2	178.4	353.2	353.2	-	-
VST-002	0	239.5	121.8	239.5	239.5	-	-
VST-003	0	277.1	148.3	277.1	277.1	-	-
VST-004	0	356.9	181.1	356.9	356.9	-	-
VST-005	1	438.4	230.8	438.4	438.4	-	-
VST-006	0	291.4	143.9	291.4	291.4	-	-
n	-	5	5	5	5	0	0
Minimum	-	239	122	239	239	-	-
Maximum	-	357	181	357	357	-	-
Median	-	291.4	148.3	291.4	291.4	-	-
Arithmean	-	303.6	154.7	303.6	303.6	-	-
Arith%CV	-	16.69	16.13	16.69	16.69	-	-
ArithSD	-	50.68	24.96	50.68	50.68	-	-
Geomean	-	300.2	153.1	300.2	300.2	-	-
Geo%CV	-	17.07	16.58	17.07	17.07	-	-
GeoSD	-	1.185	1.179	1.185	1.185	-	-
GeoQ05	-	246.5	126	246.5	246.5	-	-
GeoQ95	-	356.2	180.5	356.2	356.2	-	-

Table 10.1.29 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-001	0	0.4218	8.83	-
VST-002	0	0.2712	5.986	-
VST-003	0	0.3705	6.926	-
VST-004	0	0.399	8.923	-
VST-005	1	0.511	10.96	-
VST-006	0	0.313	7.285	-
n	-	5	5	0
Minimum	-	0.271	5.99	-
Maximum	-	0.422	8.92	-
Median	-	0.3705	7.285	-
Arithmean	-	0.3551	7.59	-
Arith%CV	-	17.48	16.69	-
ArithSD	-	0.06207	1.267	-
Geomean	-	0.3505	7.504	-
Geo%CV	-	18.36	17.07	-
GeoSD	-	1.2	1.185	-
GeoQ05	-	0.2791	6.164	-
GeoQ95	-	0.4171	8.905	-

Table 10.1.30 40 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Ratios

Subject / Statistic	Manual exclusion flag	Accumulation Ratio - Cmax (fraction)	Accumulation Ratio - AUC Tau (fraction)	Temporal Change Parameter (fraction)	Metabolite to Parent Ratio - Cmax (fraction)	Metabolite to Parent Ratio - AUC Tau (fraction)	Metabolite to Parent Ratio - AUC Inf (fraction)
VST-001	0	2.185	2.6	-	0.098	0.097	-
VST-002	0	4.822	6.219	-	0.097	0.096	-
VST-003	0	1.417	1.561	-	0.082	0.092	-
VST-004	0	5.132	6.43	-	0.067	0.085	-
VST-005	1	3.683	11.034	-	0.138	0.139	-
VST-006	0	14.067	27.966	-	0.099	0.099	-
n	-	5	5	0	5	5	0
Minimum	-	1.417	1.561	-	0.067	0.085	-
Maximum	-	14.067	27.966	-	0.099	0.099	-
Median	-	4.822	6.219	-	0.097	0.096	-
Arithmean	-	5.525	8.955	-	0.089	0.094	-
Arith%CV	-	91.247	121.087	-	15.42	5.91	-
ArithSD	-	5.041	10.843	-	0.014	0.006	-
Geomean	-	4.041	5.387	-	0.088	0.094	-
Geo%CV	-	108.712	153.137	-	16.669	6.066	-
GeoSD	-	2.419	3.001	-	1.18	1.062	-
GeoQ05	-	1.545	1.728	-	0.07	0.086	-
GeoQ95	-	11.498	20.842	-	0.098	0.099	-

10.2 Part A1 80 mg QD

10.2.1 Cycle 0 Day -6 Fasted

Table 10.2.1 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-007	24	Inf	14	14	1	14	0	14	0	1
VST-008	24	Inf	14	14	1	14	0	14	0	0
VST-009	24	Inf	14	14	1	14	0	14	0	0
VST-010	24	Inf	14	14	1	14	0	14	0	0
VST-011	24	Inf	14	14	1	14	0	14	0	1
VST-012	24	Inf	14	14	1	14	0	14	0	0
n	-	-	-	6	6	6	6	6	-	-
Minimum	-	-	-	14	1	14	0	14	-	-
Maximum	-	-	-	14	1	14	0	14	-	-
Median	-	-	-	14	1	14	0	14	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.2.2 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-007	0	1	68.37	6	140	10.11
VST-008	0	1	69.22	12	140	11.57
VST-009	0	1	88.72	12	140	11.1
VST-010	0	1	221.9	6	140	38.51
VST-011	0	1	65.02	24	140	20.43
VST-012	0	1	370	8	140	1.85
n	-	6	6	6	6	6
Minimum	-	1	65	6	140	1.85
Maximum	-	1	370	24	140	38.5
Median	-	1	78.97	10	140	11.34
Arithmean	-	-	147.2	-	-	15.6
Arith%CV	-	-	84.67	-	-	81.31
ArithSD	-	-	124.6	-	-	12.68
Geomean	-	-	114.4	-	-	11.12
Geo%CV	-	-	84.98	-	-	134
GeoSD	-	-	2.09	-	-	2.756
GeoQ05	-	-	65.84	-	-	2.829
GeoQ95	-	-	325.6	-	-	32.87

Table 10.2.3 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-007	49.81	0.013916	4	1	1.93	0	0	0	1	0	1
VST-008	50.19	0.01381	5	0.999	2.39	0	0	0	2	0	0
VST-009	38.28	0.018106	4	1	2.51	0	0	0	2	0	0
VST-010	55.41	0.012511	6	1	2.38	0	0	0	2	0	0
VST-011	66.04	0.010497	4	0.997	1.45	0	0	0	1	0	1
VST-012	17.37	0.039915	6	1	7.6	0	0	0	0	0	0
n	4	4	4	4	4	-	-	-	-	-	-
Minimum	17.4	0.0125	4	0.999	2.38	-	-	-	-	-	-
Maximum	55.4	0.0399	6	1	7.6	-	-	-	-	-	-
Median	44.24	0.015958	5	1	2.45	-	-	-	-	-	-
Arithmean	40.31	0.021085	5	1	3.72	-	-	-	-	-	-
Arith%CV	41.9	60.604	18	0.0219	69.6	-	-	-	-	-	-
ArithSD	16.89	0.012779	0	0.000219	2.59	-	-	-	-	-	-
Geomean	36.87	0.018798	5	1	3.23	-	-	-	-	-	-
Geo%CV	56.43	56.428	19	0.0219	62.1	-	-	-	-	-	-
GeoSD	1.692	1.6918	1	1	1.77	-	-	-	-	-	-
GeoQ05	19.55	0.012697	4	0.999	2.38	-	-	-	-	-	-
GeoQ95	54.59	0.035452	6	1	6.44	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.2.4 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC 0-Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-007	0	4579	755.2	1450	1450	5306	13.69
VST-008	0	4965	614.6	1400	1400	5802	14.44
VST-009	0	6375	662.5	1721	1721	6988	8.774
VST-010	0	15320	2350	4609	4609	18390	16.74
VST-011	0	5909	434.1	1148	1148	7856	24.78
VST-012	0	12560	3475	6921	6921	12610	0.3676
n	-	6	6	6	6	4	6
Minimum	-	4580	434	1150	1150	5800	0.368
Maximum	-	15300	3470	6920	6920	18400	24.8
Median	-	6142	708.8	1585	1585	9798	14.07
Arithmean	-	8284	1382	2875	2875	10950	13.13
Arith%CV	-	54.46	89.89	82.17	82.17	52.83	62.11
ArithSD	-	4512	1242	2362	2362	5784	8.155
Geomean	-	7404	1015	2245	2245	9847	8.011
Geo%CV	-	53.82	99.93	85.02	85.02	57.19	315.1
GeoSD	-	1.656	2.298	2.091	2.091	1.702	4.694
GeoQ05	-	4673	473.6	1206	1206	5966	0.8125
GeoQ95	-	14580	3151	6252	6252	17380	22.46

Table 10.2.5 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Half-life dependent parameters

Subject / Statistic	Manual exclusion flag	Half-life exclusion flag	AUMC 0-Inf (ng*h^2/mL)	MRT (h)	Cl/F (L/h)	Clss/F (L/h)	Vz/F (L)
VST-007	0	1	387500	73.04	15.08	-	1083
VST-008	0	0	442800	76.31	13.79	-	998.4
VST-009	0	0	446500	63.89	11.45	-	632.3
VST-010	0	0	1490000	81.01	4.349	-	347.7
VST-011	0	1	825900	105.1	10.18	-	970.2
VST-012	0	0	362800	28.77	6.345	-	159
n	-	-	4	4	4	0	4
Minimum	-	-	363000	28.8	4.35	-	159
Maximum	-	-	1490000	81	13.8	-	998
Median	-	-	444600	70.1	8.897	-	490
Arithmean	-	-	685500	62.5	8.982	-	534.3
Arith%CV	-	-	78.45	37.79	48.78	-	68.4
ArithSD	-	-	537800	23.62	4.382	-	365.5
Geomean	-	-	571800	58.06	8.124	-	432.2
Geo%CV	-	-	71.93	50.76	57.19	-	93.8
GeoSD	-	-	1.907	1.614	1.702	-	2.213
GeoQ05	-	-	373800	32.43	4.603	-	178.8
GeoQ95	-	-	1244000	80.29	13.41	-	932.3

Table 10.2.6 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC 0-Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-007	0	0.8546	18.13	66.32
VST-008	0	0.8652	17.5	72.53
VST-009	0	1.109	21.51	87.35
VST-010	0	2.774	57.62	229.9
VST-011	0	0.8128	14.35	98.2
VST-012	0	4.624	86.52	157.6
n	-	6	6	6
Minimum	-	0.813	14.4	66.3
Maximum	-	4.62	86.5	230
Median	-	0.9871	19.82	92.77
Arithmean	-	1.84	35.94	118.7
Arith%CV	-	84.67	82.17	53.52
ArithSD	-	1.558	29.53	63.5
Geomean	-	1.43	28.06	106.9
Geo%CV	-	84.98	85.02	51.19
GeoSD	-	2.09	2.091	1.62
GeoQ05	-	0.823	15.08	67.82
GeoQ95	-	4.07	78.16	209.2

Table 10.2.7 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-007	24	Inf	14	14	1	14	0	14	0	1
VST-008	24	Inf	14	14	1	14	0	14	0	1
VST-009	24	Inf	14	14	1	14	0	14	0	1
VST-010	24	Inf	14	14	1	14	0	14	0	1
VST-011	24	Inf	14	14	1	14	0	14	0	1
VST-012	24	Inf	14	14	1	14	0	14	0	0
n	-	-	-	6	6	6	6	6	-	-
Minimum	-	-	-	14	1	14	0	14	-	-
Maximum	-	-	-	14	1	14	0	14	-	-
Median	-	-	-	14	1	14	0	14	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.2.8 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-007	0	1	5.23	24	140	1.06
VST-008	0	1	5.84	24	140	1.33
VST-009	0	1	7.77	24	140	1.28
VST-010	0	1	10.96	72	140	6.74
VST-011	0	1	5.66	48	140	2.19
VST-012	0	1	27.92	12	140	0.25
n	-	6	6	6	6	6
Minimum	-	1	5.23	12	140	0.25
Maximum	-	1	27.9	72	140	6.74
Median	-	1	6.805	24	140	1.305
Arithmean	-	-	10.56	-	-	2.142
Arith%CV	-	-	82.96	-	-	109.1
ArithSD	-	-	8.764	-	-	2.337
Geomean	-	-	8.623	-	-	1.372
Geo%CV	-	-	70.72	-	-	146.3
GeoSD	-	-	1.891	-	-	2.915
GeoQ05	-	-	5.334	-	-	0.3587
GeoQ95	-	-	22.1	-	-	5.089

Table 10.2.9 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-007	49.64	0.013963	3	1	1.45	0	0	0	1	0	1
VST-008	53.73	0.012901	4	0.997	1.79	0	0	0	1	0	1
VST-009	38.09	0.0182	3	1	1.89	0	0	0	1	0	1
VST-010	-	-	-	-	-	1	0	0	0	0	1
VST-011	65.45	0.01059	3	1	1.1	0	0	0	1	0	1
VST-012	17.07	0.040604	4	1	5.62	0	0	0	0	0	0
n	1	1	1	1	1	-	-	-	-	-	-
Minimum	17.1	0.0406	4	1	5.62	-	-	-	-	-	-
Maximum	17.1	0.0406	4	1	5.62	-	-	-	-	-	-
Median	-	-	-	-	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.2.10 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC 0-Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-007	0	420.6	36.85	98.59	98.59	496.5	15.29
VST-008	0	462.4	29.52	93.84	93.84	565.5	18.23
VST-009	0	608.2	25.85	101.9	101.9	678.6	10.36
VST-010	0	1236	25.82	100.2	100.2	-	-
VST-011	0	565.6	16.78	70.66	70.66	772.4	26.77
VST-012	0	1241	172.1	502.4	502.4	1247	0.4938
n	-	6	6	6	6	1	5
Minimum	-	421	16.8	70.7	70.7	1250	0.494
Maximum	-	1240	172	502	502	1250	26.8
Median	-	586.9	27.68	99.41	99.41	-	15.29
Arithmean	-	755.5	51.15	161.3	161.3	-	14.23
Arith%CV	-	50.29	116.5	103.9	103.9	-	68.32
ArithSD	-	379.9	59.6	167.5	167.5	-	9.722
Geomean	-	684.2	35.77	122.4	122.4	-	8.249
Geo%CV	-	50.71	96.49	80.28	80.28	-	351.9
GeoSD	-	1.613	2.251	2.024	2.024	-	5.006
GeoQ05	-	430.7	18.69	75.85	75.85	-	0.9077
GeoQ95	-	1239	117.1	337.2	337.2	-	24.79

Table 10.2.11 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Half-life dependent parameters

Subject / Statistic	Manual exclusion flag	Half-life exclusion flag	AUMC 0-Inf (ng*h^2/mL)	MRT (h)	Cl/F (L/h)	Clss/F (L/h)	Vz/F (L)
VST-007	0	1	39920	80.4	-	-	-
VST-008	0	1	49750	87.98	-	-	-
VST-009	0	1	49390	72.78	-	-	-
VST-010	0	1	-	-	-	-	-
VST-011	0	1	87160	112.8	-	-	-
VST-012	0	0	44330	35.55	-	-	-
n	-	-	1	1	0	0	0
Minimum	-	-	44300	35.5	-	-	-
Maximum	-	-	44300	35.5	-	-	-
Median	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-

Table 10.2.12 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC 0-Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-007	0	0.06538	1.232	6.206
VST-008	0	0.073	1.173	7.069
VST-009	0	0.09712	1.274	8.482
VST-010	0	0.137	1.253	-
VST-011	0	0.07075	0.8832	9.655
VST-012	0	0.349	6.28	15.59
n	-	6	6	5
Minimum	-	0.0654	0.883	6.21
Maximum	-	0.349	6.28	15.6
Median	-	0.08506	1.243	8.482
Arithmean	-	0.132	2.016	9.4
Arith%CV	-	82.96	103.9	39.38
ArithSD	-	0.1095	2.094	3.702
Geomean	-	0.1078	1.529	8.905
Geo%CV	-	70.72	80.28	36.72
GeoSD	-	1.891	2.024	1.427
GeoQ05	-	0.06668	0.9481	6.37
GeoQ95	-	0.2762	4.215	14.16

Table 10.2.13 80 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Ratios

Subject / Statistic	Manual exclusion flag	Accumulation Ratio - Cmax (fraction)	Accumulation Ratio - AUC 0-Tau (fraction)	Temporal Change Parameter (fraction)	Metabolite to Parent Ratio - Cmax (fraction)	Metabolite to Parent Ratio - AUC 0-Tau (fraction)	Metabolite to Parent Ratio - AUC Inf (fraction)
VST-007	0	-	-	-	0.076	0.068	0.094
VST-008	0	-	-	-	0.084	0.067	0.097
VST-009	0	-	-	-	0.088	0.059	0.097
VST-010	0	-	-	-	0.049	0.022	-
VST-011	0	-	-	-	0.087	0.062	0.098
VST-012	0	-	-	-	0.075	0.073	0.099
n	-	0	0	0	6	6	5
Minimum	-	-	-	-	0.049	0.022	0.094
Maximum	-	-	-	-	0.088	0.073	0.099
Median	-	-	-	-	0.08	0.064	0.097
Arithmean	-	-	-	-	0.077	0.058	0.097
Arith%CV	-	-	-	-	18.723	31.803	2.141
ArithSD	-	-	-	-	0.014	0.019	0.002
Geomean	-	-	-	-	0.075	0.055	0.097
Geo%CV	-	-	-	-	21.933	48.084	2.164
GeoSD	-	-	-	-	1.242	1.578	1.022
GeoQ05	-	-	-	-	0.055	0.028	0.094
GeoQ95	-	-	-	-	0.087	0.071	0.099

10.2.2 Cycle 1 Day 15 Fasted

Table 10.2.14 80 mg QD Part A1 Cycle 1 Day 15 Fasted: AZD9291 (Parent) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-007	-	-	4	4	0	4	0	4	1	1
VST-008	-	-	4	4	0	4	0	4	0	1
VST-009	-	-	4	4	0	4	0	4	0	1
VST-010	-	-	4	4	0	4	0	4	0	1
VST-011	-	-	4	4	0	4	0	4	0	1
VST-012	-	-	4	4	0	4	0	4	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	4	0	4	0	4	-	-
Maximum	-	-	-	4	0	4	0	4	-	-
Median	-	-	-	4	0	4	0	4	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.2.15 80 mg QD Part A1 Cycle 1 Day 15 Fasted: AZD9291 (Parent) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-007	1	-	207	4	-	-
VST-008	0	-	269.2	8	-	-
VST-009	0	-	320.1	8	-	-
VST-010	0	-	841.2	4	-	-
VST-011	0	-	331.6	8	-	-
VST-012	0	-	625.6	8	-	-
n	-	0	5	5	0	0
Minimum	-	-	269	4	-	-
Maximum	-	-	841	8	-	-
Median	-	-	331.6	8	-	-
Arithmean	-	-	477.5	-	-	-
Arith%CV	-	-	51.69	-	-	-
ArithSD	-	-	246.8	-	-	-
Geomean	-	-	432	-	-	-
Geo%CV	-	-	52.23	-	-	-
GeoSD	-	-	1.634	-	-	-
GeoQ05	-	-	278.7	-	-	-
GeoQ95	-	-	792.9	-	-	-

Table 10.2.16 80 mg QD Part A1 Cycle 1 Day 15 Fasted: AZ5104 (Metabolite) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-007	-	-	4	4	0	4	0	4	1	1
VST-008	-	-	4	4	0	4	0	4	0	1
VST-009	-	-	4	4	0	4	0	4	0	1
VST-010	-	-	4	4	0	4	0	4	0	1
VST-011	-	-	4	4	0	4	0	4	0	1
VST-012	-	-	4	4	0	4	0	4	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	4	0	4	0	4	-	-
Maximum	-	-	-	4	0	4	0	4	-	-
Median	-	-	-	4	0	4	0	4	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.2.17 80 mg QD Part A1 Cycle 1 Day 15 Fasted: AZ5104 (Metabolite) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-007	1	-	20.01	2	-	-
VST-008	0	-	22.95	8	-	-
VST-009	0	-	28.47	8	-	-
VST-010	0	-	79.45	8	-	-
VST-011	0	-	31.65	8	-	-
VST-012	0	-	57.8	8	-	-
n	-	0	5	5	0	0
Minimum	-	-	23	8	-	-
Maximum	-	-	79.4	8	-	-
Median	-	-	31.65	8	-	-
Arithmean	-	-	44.06	-	-	-
Arith%CV	-	-	54.23	-	-	-
ArithSD	-	-	23.9	-	-	-
Geomean	-	-	39.4	-	-	-
Geo%CV	-	-	55.8	-	-	-
GeoSD	-	-	1.683	-	-	-
GeoQ05	-	-	23.96	-	-	-
GeoQ95	-	-	74.55	-	-	-

10.2.3 Cycle 2 Day 1 Fasted

Table 10.2.18 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-007	24	24	10	10	0	10	0	10	1	1
VST-008	24	24	10	10	0	10	0	10	0	1
VST-009	24	24	10	9	0	10	0	10	0	1
VST-010	24	24	10	10	0	10	0	10	1	1
VST-011	24	24	10	9	0	10	0	10	0	1
VST-012	24	24	10	10	0	10	0	10	0	1
n	-	-	-	4	4	4	4	4	-	-
Minimum	-	-	-	9	0	10	0	10	-	-
Maximum	-	-	-	10	0	10	0	10	-	-
Median	-	-	-	9	0	10	0	10	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.2.19 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-007	1	0	135.3	4	24	104.2
VST-008	0	0	267	8	24	214.7
VST-009	0	0	313.5	10	24	265.8
VST-010	1	0	568.9	4	24	443.9
VST-011	0	0	352.9	8	24	310.9
VST-012	0	0	635.1	8	24	370.1
n	-	4	4	4	4	4
Minimum	-	0	267	8	24	215
Maximum	-	0	635	10	24	370
Median	-	0	333.2	8	24	288.3
Arithmean	-	-	392.1	-	-	290.4
Arith%CV	-	-	42.27	-	-	22.76
ArithSD	-	-	165.7	-	-	66.09
Geomean	-	-	370.1	-	-	284.7
Geo%CV	-	-	39.16	-	-	23.47
GeoSD	-	-	1.459	-	-	1.261
GeoQ05	-	-	273.5	-	-	221.7
GeoQ95	-	-	581.5	-	-	360.5

Table 10.2.20 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-007	60.28	0.011499	4	0.796	0.265	0	0	1	1	1	1
VST-008	57.88	0.011975	3	0.789	0.242	0	0	1	1	0	1
VST-009	-	-	-	-	-	1	0	0	0	0	1
VST-010	55.79	0.012423	5	0.985	0.323	0	0	0	1	1	1
VST-011	106.8	0.0064883	3	0.695	0.131	0	0	1	1	0	1
VST-012	20.47	0.033866	3	0.987	0.684	0	0	0	1	0	1
n	0	0	0	0	0	-	-	-	-	-	-
Minimum	-	-	-	-	-	-	-	-	-	-	-
Maximum	-	-	-	-	-	-	-	-	-	-	-
Median	-	-	-	-	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.2.21 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-007	1	2845	1496	2845	2845	-	-
VST-008	0	5829	3003	5829	5829	-	-
VST-009	0	7129	3664	7129	7129	-	-
VST-010	1	12080	6372	12080	12080	-	-
VST-011	0	7861	4031	7861	7861	-	-
VST-012	0	12470	6914	12470	12470	-	-
n	-	4	4	4	4	0	0
Minimum	-	5830	3000	5830	5830	-	-
Maximum	-	12500	6910	12500	12500	-	-
Median	-	7495	3847	7495	7495	-	-
Arithmean	-	8322	4403	8322	8322	-	-
Arith%CV	-	34.72	39.22	34.72	34.72	-	-
ArithSD	-	2889	1727	2889	2889	-	-
Geomean	-	7989	4185	7989	7989	-	-
Geo%CV	-	33.03	36.81	33.03	33.03	-	-
GeoSD	-	1.38	1.428	1.38	1.38	-	-
GeoQ05	-	6008	3094	6008	6008	-	-
GeoQ95	-	11630	6376	11630	11630	-	-

Table 10.2.22 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Half-life dependent parameters

Subject / Statistic	Manual exclusion flag	Half-life exclusion flag	AUMC 0-Inf (ng*h^2/mL)	MRT (h)	Cl/F (L/h)	Clss/F (L/h)	Vz/F (L)
VST-007	1	1	-	-	-	28.12	-
VST-008	0	1	-	-	-	13.72	-
VST-009	0	1	-	-	-	11.22	-
VST-010	1	1	-	-	-	6.622	-
VST-011	0	1	-	-	-	10.18	-
VST-012	0	1	-	-	-	6.417	-
n	-	-	0	0	0	4	0
Minimum	-	-	-	-	-	6.42	-
Maximum	-	-	-	-	-	13.7	-
Median	-	-	-	-	-	10.7	-
Arithmean	-	-	-	-	-	10.38	-
Arith%CV	-	-	-	-	-	29.23	-
ArithSD	-	-	-	-	-	3.035	-
Geomean	-	-	-	-	-	10.01	-
Geo%CV	-	-	-	-	-	33.03	-
GeoSD	-	-	-	-	-	1.38	-
GeoQ05	-	-	-	-	-	6.876	-
GeoQ95	-	-	-	-	-	13.32	-

Table 10.2.23 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-007	1	1.692	35.56	-
VST-008	0	3.337	72.87	-
VST-009	0	3.919	89.11	-
VST-010	1	7.111	151	-
VST-011	0	4.411	98.26	-
VST-012	0	7.938	155.8	-
n	-	4	4	0
Minimum	-	3.34	72.9	-
Maximum	-	7.94	156	-
Median	-	4.165	93.69	-
Arithmean	-	4.901	104	-
Arith%CV	-	42.27	34.72	-
ArithSD	-	2.072	36.11	-
Geomean	-	4.626	99.86	-
Geo%CV	-	39.16	33.03	-
GeoSD	-	1.459	1.38	-
GeoQ05	-	3.418	75.1	-
GeoQ95	-	7.269	145.4	-

Table 10.2.24 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Ratios

Subject / Statistic	Manual exclusion flag	Accumulation Ratio - Cmax (fraction)	Accumulation Ratio - AUC Tau (fraction)	Temporal Change Parameter (fraction)	Metabolite to Parent Ratio - Cmax (fraction)	Metabolite to Parent Ratio - AUC Tau (fraction)	Metabolite to Parent Ratio - AUC Inf (fraction)
VST-007	1	1.98	1.962	-	-	-	-
VST-008	0	3.857	4.165	1.005	-	-	-
VST-009	0	3.534	4.143	1.02	-	-	-
VST-010	1	2.563	2.621	0.657	-	-	-
VST-011	0	5.427	6.847	-	-	-	-
VST-012	0	1.717	1.801	0.989	-	-	-
n	-	4	4	3	0	0	0
Minimum	-	1.717	1.801	0.989	-	-	-
Maximum	-	5.427	6.847	1.02	-	-	-
Median	-	3.695	4.154	1.005	-	-	-
Arithmean	-	3.634	4.239	1.005	-	-	-
Arith%CV	-	41.894	48.646	1.565	-	-	-
ArithSD	-	1.522	2.062	0.016	-	-	-
Geomean	-	3.357	3.819	1.004	-	-	-
Geo%CV	-	51.366	59.892	1.566	-	-	-
GeoSD	-	1.622	1.74	1.016	-	-	-
GeoQ05	-	1.913	2.041	0.99	-	-	-
GeoQ95	-	5.156	6.355	1.019	-	-	-

Table 10.2.25 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-007	24	24	10	10	0	10	0	10	1	1
VST-008	24	24	10	10	0	10	0	10	0	1
VST-009	24	24	10	9	0	10	0	10	0	1
VST-010	24	24	10	10	0	10	0	10	1	1
VST-011	24	24	10	9	0	10	0	10	0	1
VST-012	24	24	10	10	0	10	0	10	0	1
n	-	-	-	4	4	4	4	4	-	-
Minimum	-	-	-	9	0	10	0	10	-	-
Maximum	-	-	-	10	0	10	0	10	-	-
Median	-	-	-	9	0	10	0	10	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.2.26 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-007	1	0	11.96	8	24	10.4
VST-008	0	0	24.69	10	24	22.29
VST-009	0	0	29.89	6	24	27.88
VST-010	1	0	62.36	10	24	54.26
VST-011	0	0	33	12	24	32.66
VST-012	0	0	61.91	10	24	46.4
n	-	4	4	4	4	4
Minimum	-	0	24.7	6	24	22.3
Maximum	-	0	61.9	12	24	46.4
Median	-	0	31.44	10	24	30.27
Arithmean	-	-	37.37	-	-	32.31
Arith%CV	-	-	44.72	-	-	31.9
ArithSD	-	-	16.71	-	-	10.31
Geomean	-	-	35.04	-	-	31.15
Geo%CV	-	-	41.44	-	-	31.59
GeoSD	-	-	1.489	-	-	1.361
GeoQ05	-	-	25.41	-	-	23.05
GeoQ95	-	-	56.33	-	-	44.02

Table 10.2.27 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-007	69.2	0.010017	3	0.962	0.202	0	0	0	1	1	1
VST-008	-	-	-	-	-	1	0	0	0	0	1
VST-009	400.4	0.0017313	3	0.753	0.035	0	0	1	1	0	1
VST-010	-	-	-	-	-	1	0	0	0	1	1
VST-011	-	-	-	-	-	1	0	0	0	0	1
VST-012	-	-	-	-	-	1	0	0	0	0	1
n	0	0	0	0	0	-	-	-	-	-	-
Minimum	-	-	-	-	-	-	-	-	-	-	-
Maximum	-	-	-	-	-	-	-	-	-	-	-
Median	-	-	-	-	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.2.28 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-007	1	271	137.6	271	271	-	-
VST-008	0	550.9	277	550.9	550.9	-	-
VST-009	0	694.8	345.5	694.8	694.8	-	-
VST-010	1	1381	710.7	1381	1381	-	-
VST-011	0	776.2	382.2	776.2	776.2	-	-
VST-012	0	1276	643.8	1276	1276	-	-
n	-	4	4	4	4	0	0
Minimum	-	551	277	551	551	-	-
Maximum	-	1280	644	1280	1280	-	-
Median	-	735.5	363.8	735.5	735.5	-	-
Arithmean	-	824.5	412.1	824.5	824.5	-	-
Arith%CV	-	38.23	38.94	38.23	38.23	-	-
ArithSD	-	315.2	160.5	315.2	315.2	-	-
Geomean	-	784.7	391.7	784.7	784.7	-	-
Geo%CV	-	36.57	36.91	36.57	36.57	-	-
GeoSD	-	1.425	1.43	1.425	1.425	-	-
GeoQ05	-	570.4	286.4	570.4	570.4	-	-
GeoQ95	-	1185	595.3	1185	1185	-	-

Table 10.2.29 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-007	1	0.1495	3.388	-
VST-008	0	0.3086	6.887	-
VST-009	0	0.3736	8.684	-
VST-010	1	0.7795	17.26	-
VST-011	0	0.4125	9.702	-
VST-012	0	0.7739	15.95	-
n	-	4	4	0
Minimum	-	0.309	6.89	-
Maximum	-	0.774	16	-
Median	-	0.3931	9.193	-
Arithmean	-	0.4672	10.31	-
Arith%CV	-	44.72	38.23	-
ArithSD	-	0.2089	3.94	-
Geomean	-	0.438	9.809	-
Geo%CV	-	41.44	36.57	-
GeoSD	-	1.489	1.425	-
GeoQ05	-	0.3176	7.131	-
GeoQ95	-	0.7042	14.81	-

Table 10.2.30 80 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Ratios

Subject / Statistic	Manual exclusion flag	Accumulation Ratio - Cmax (fraction)	Accumulation Ratio - AUC Tau (fraction)	Temporal Change Parameter (fraction)	Metabolite to Parent Ratio - Cmax (fraction)	Metabolite to Parent Ratio - AUC Tau (fraction)	Metabolite to Parent Ratio - AUC Inf (fraction)
VST-007	1	2.287	2.749	-	0.088	0.095	-
VST-008	0	4.228	5.871	-	0.092	0.095	-
VST-009	0	3.847	6.816	-	0.095	0.097	-
VST-010	1	5.69	13.778	-	0.11	0.114	-
VST-011	0	5.83	10.985	-	0.094	0.099	-
VST-012	0	2.217	2.54	1.024	0.097	0.102	-
n	-	4	4	1	4	4	0
Minimum	-	2.217	2.54	1.024	0.092	0.095	-
Maximum	-	5.83	10.985	1.024	0.097	0.102	-
Median	-	4.037	6.344	-	0.094	0.098	-
Arithmean	-	4.031	6.553	-	0.095	0.098	-
Arith%CV	-	36.798	53.064	-	2.319	3.312	-
ArithSD	-	1.483	3.477	-	0.002	0.003	-
Geomean	-	3.808	5.781	-	0.095	0.098	-
Geo%CV	-	41.885	67.117	-	2.312	3.307	-
GeoSD	-	1.495	1.84	-	1.023	1.034	-
GeoQ05	-	2.408	2.88	-	0.093	0.095	-
GeoQ95	-	5.556	10.226	-	0.097	0.102	-

10.3 Part A1 160 mg QD

10.3.1 Cycle 0 Day -6 Fasted

Table 10.3.1 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-013	24	Inf	14	14	1	14	0	14	0	0
VST-014	24	Inf	14	14	1	14	0	14	0	1
VST-015	24	Inf	14	14	1	14	0	14	0	1
VST-016	24	Inf	14	14	1	14	0	14	0	1
VST-017	24	Inf	14	14	3	14	2	12	0	0
VST-018	24	Inf	14	14	1	14	0	14	0	0
n	-	-	-	6	6	6	6	6	-	-
Minimum	-	-	-	14	1	14	0	12	-	-
Maximum	-	-	-	14	3	14	2	14	-	-
Median	-	-	-	14	1	14	0	14	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.3.2 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-013	0	1	303.6	24	140	27.28
VST-014	0	1	173.6	24	140	111
VST-015	0	1	192.8	48	140	162
VST-016	0	1	18.69	120	140	17.98
VST-017	0	1	143.9	6	72	0.13
VST-018	0	1	257.4	8	140	12.24
n	-	6	6	6	6	6
Minimum	-	1	18.7	6	72	0.13
Maximum	-	1	304	120	140	162
Median	-	1	183.2	24	140	22.63
Arithmean	-	-	181.7	-	-	55.1
Arith%CV	-	-	54.38	-	-	119.2
ArithSD	-	-	98.78	-	-	65.67
Geomean	-	-	138.4	-	-	15.53
Geo%CV	-	-	134.7	-	-	2613
GeoSD	-	-	2.765	-	-	12.87
GeoQ05	-	-	31.13	-	-	0.405
GeoQ95	-	-	291.3	-	-	147.4

Table 10.3.3 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-013	29.63	0.023393	3	0.999	2.43	0	0	0	2	0	0
VST-014	158.1	0.0043852	3	0.993	0.456	0	0	0	1	0	1
VST-015	376.9	0.0018392	3	0.999	0.191	0	0	0	1	0	1
VST-016	-	-	-	-	-	1	0	0	0	0	1
VST-017	5.726	0.12106	3	0.999	8.38	0	0	0	0	0	0
VST-018	30.1	0.023029	6	1	4.39	0	0	0	0	0	0
n	3	3	3	3	3	-	-	-	-	-	-
Minimum	5.73	0.023	3	0.999	2.43	-	-	-	-	-	-
Maximum	30.1	0.121	6	1	8.38	-	-	-	-	-	-
Median	29.63	0.023393	3	0.999	4.39	-	-	-	-	-	-
Arithmean	21.82	0.055828	4	0.999	5.07	-	-	-	-	-	-
Arith%CV	63.88	101.19	43	0.0362	59.9	-	-	-	-	-	-
ArithSD	13.94	0.056494	1	0.000362	3.03	-	-	-	-	-	-
Geomean	17.22	0.040252	3	0.999	4.47	-	-	-	-	-	-
Geo%CV	121.8	121.77	41	0.0362	68.4	-	-	-	-	-	-
GeoSD	2.595	2.5951	1	1	1.86	-	-	-	-	-	-
GeoQ05	6.749	0.023065	3	0.999	2.58	-	-	-	-	-	-
GeoQ95	30.05	0.10271	5	1	7.86	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.3.4 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC 0-Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-013	0	21240	1851	5230	5230	22400	5.205
VST-014	0	20240	1205	3144	3144	45550	55.56
VST-015	0	24910	1218	3317	3317	113000	77.95
VST-016	0	2312	55.5	186.3	186.3	-	-
VST-017	0	2621	1376	2249	2249	2622	0.04096
VST-018	0	12820	2366	4993	4993	13350	3.981
n	-	6	6	6	6	3	5
Minimum	-	2310	55.5	186	186	2620	0.041
Maximum	-	24900	2370	5230	5230	22400	78
Median	-	16530	1297	3230	3230	13350	5.205
Arithmean	-	14020	1345	3187	3187	12790	28.55
Arith%CV	-	69.72	57.56	58.44	58.44	77.41	125.5
ArithSD	-	9777	774.3	1862	1862	9902	35.82
Geomean	-	9698	888.1	2202	2202	9221	5.165
Geo%CV	-	150	240.5	194.2	194.2	158.2	9552
GeoSD	-	2.961	3.989	3.491	3.491	3.063	20.49
GeoQ05	-	2386	119.8	347.3	347.3	3085	0.1023
GeoQ95	-	23940	2225	5170	5170	21270	72.85

Table 10.3.5 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Half-life dependent parameters

Subject / Statistic	Manual exclusion flag	Half-life exclusion flag	AUMC 0-Inf (ng*h^2/mL)	MRT (h)	Cl/F (L/h)	Clss/F (L/h)	Vz/F (L)
VST-013	0	0	1285000	57.37	7.142	-	305.3
VST-014	0	1	10820000	237.5	3.512	-	801
VST-015	0	1	62400000	552.2	1.416	-	769.8
VST-016	0	1	-	-	-	-	-
VST-017	0	0	36320	13.85	61.03	-	504.1
VST-018	0	0	624600	46.79	11.99	-	520.4
n	-	-	3	3	3	0	3
Minimum	-	-	36300	13.9	7.14	-	305
Maximum	-	-	1290000	57.4	61	-	520
Median	-	-	624600	46.79	11.99	-	504.1
Arithmean	-	-	648700	39.34	26.72	-	443.3
Arith%CV	-	-	96.31	57.7	111.6	-	27.02
ArithSD	-	-	624800	22.7	29.81	-	119.8
Geomean	-	-	307800	33.38	17.35	-	431.1
Geo%CV	-	-	583.2	89.71	158.2	-	30.6
GeoSD	-	-	6.591	2.156	3.063	-	1.349
GeoQ05	-	-	48270	15.65	7.522	-	321
GeoQ95	-	-	1196000	56.21	51.86	-	518.8

Table 10.3.6 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZD9291 (Parent) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC 0-Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-013	0	1.898	32.69	140
VST-014	0	1.085	19.65	284.7
VST-015	0	1.205	20.73	706.3
VST-016	0	0.1168	1.164	-
VST-017	0	0.8991	14.06	16.38
VST-018	0	1.608	31.21	83.44
n	-	6	6	5
Minimum	-	0.117	1.16	16.4
Maximum	-	1.9	32.7	706
Median	-	1.145	20.19	140
Arithmean	-	1.135	19.92	246.2
Arith%CV	-	54.38	58.44	111.9
ArithSD	-	0.6174	11.64	275.6
Geomean	-	0.8651	13.76	130.9
Geo%CV	-	134.7	194.2	251.7
GeoSD	-	2.765	3.491	4.103
GeoQ05	-	0.1946	2.17	22.69
GeoQ95	-	1.821	32.31	588.9

Table 10.3.7 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-013	24	Inf	14	14	1	14	0	14	0	0
VST-014	24	Inf	14	14	1	14	0	14	0	1
VST-015	24	Inf	14	14	1	14	0	14	0	1
VST-016	24	Inf	14	14	4	14	0	14	0	1
VST-017	24	Inf	14	14	4	14	3	11	0	0
VST-018	24	Inf	14	14	1	14	0	14	0	0
n	-	-	-	6	6	6	6	6	-	-
Minimum	-	-	-	14	1	14	0	11	-	-
Maximum	-	-	-	14	4	14	3	14	-	-
Median	-	-	-	14	1	14	0	14	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.3.8 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-013	0	1	29.99	24	140	2.93
VST-014	0	1	16.45	72	140	12.87
VST-015	0	1	19.91	72	140	17.64
VST-016	0	4	1.95	120	140	1.87
VST-017	0	1	12.48	8	48	0.26
VST-018	0	1	18.3	24	140	1.68
n	-	6	6	6	6	6
Minimum	-	1	1.95	8	48	0.26
Maximum	-	4	30	120	140	17.6
Median	-	1	17.38	48	140	2.4
Arithmean	-	-	16.51	-	-	6.208
Arith%CV	-	-	55.81	-	-	116.3
ArithSD	-	-	9.216	-	-	7.218
Geomean	-	-	12.79	-	-	2.857
Geo%CV	-	-	123.9	-	-	309.2
GeoSD	-	-	2.624	-	-	4.643
GeoQ05	-	-	3.102	-	-	0.4145
GeoQ95	-	-	27.07	-	-	16.3

Table 10.3.9 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-013	29.5	0.023498	3	1	2.44	0	0	0	2	0	0
VST-014	-	-	-	-	-	1	0	0	0	0	1
VST-015	-	-	-	-	-	1	0	0	0	0	1
VST-016	-	-	-	-	-	1	0	0	0	0	1
VST-017	6.765	0.10245	4	0.991	5.62	0	0	0	0	0	0
VST-018	30.06	0.023062	3	1	2.4	0	0	0	2	0	0
n	3	3	3	3	3	-	-	-	-	-	-
Minimum	6.77	0.0231	3	0.991	2.4	-	-	-	-	-	-
Maximum	30.1	0.102	4	1	5.62	-	-	-	-	-	-
Median	29.5	0.023498	3	1	2.44	-	-	-	-	-	-
Arithmean	22.11	0.049671	3	0.997	3.48	-	-	-	-	-	-
Arith%CV	60.11	92.028	17	0.524	53	-	-	-	-	-	-
ArithSD	13.29	0.045711	0	0.00523	1.85	-	-	-	-	-	-
Geomean	18.17	0.038149	3	0.997	3.2	-	-	-	-	-	-
Geo%CV	103.9	103.89	16	0.525	51.7	-	-	-	-	-	-
GeoSD	2.353	2.3528	1	1.01	1.63	-	-	-	-	-	-
GeoQ05	7.839	0.023105	3	0.992	2.4	-	-	-	-	-	-
GeoQ95	30	0.088425	3	1	5.17	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.3.10 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC 0-Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-013	0	2106	101.3	395.1	395.1	2231	5.59
VST-014	0	1890	27.5	132.6	132.6	-	-
VST-015	0	2288	23.92	117.3	117.3	-	-
VST-016	0	209.5	1.31	7.91	7.91	-	-
VST-017	0	231.4	115.6	198.5	198.5	233.9	1.085
VST-018	0	1218	70.89	257.7	257.7	1291	5.642
n	-	6	6	6	6	3	3
Minimum	-	210	1.31	7.91	7.91	234	1.08
Maximum	-	2290	116	395	395	2230	5.64
Median	-	1554	49.19	165.5	165.5	1291	5.59
Arithmean	-	1324	56.74	184.8	184.8	1252	4.105
Arith%CV	-	70.12	81.33	71.89	71.89	79.79	63.72
ArithSD	-	928.4	46.14	132.9	132.9	999	2.616
Geomean	-	901.8	29.9	116.4	116.4	876.6	3.246
Geo%CV	-	156.8	388.9	242.9	242.9	172.9	120.9
GeoSD	-	3.047	5.298	4.014	4.014	3.243	2.584
GeoQ05	-	214.8	2.708	15.52	15.52	277.5	1.278
GeoQ95	-	2241	111.8	355.1	355.1	2112	5.637

Table 10.3.11 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Half-life dependent parameters

Subject / Statistic	Manual exclusion flag	Half-life exclusion flag	AUMC 0-Inf (ng*h^2/mL)	MRT (h)	Cl/F (L/h)	Clss/F (L/h)	Vz/F (L)
VST-013	0	0	137100	61.45	-	-	-
VST-014	0	1	-	-	-	-	-
VST-015	0	1	-	-	-	-	-
VST-016	0	1	-	-	-	-	-
VST-017	0	0	3404	14.55	-	-	-
VST-018	0	0	77650	60.13	-	-	-
n	-	-	3	3	0	0	0
Minimum	-	-	3400	14.6	-	-	-
Maximum	-	-	137000	61.5	-	-	-
Median	-	-	77650	60.13	-	-	-
Arithmean	-	-	72710	45.38	-	-	-
Arith%CV	-	-	92.11	58.85	-	-	-
ArithSD	-	-	66980	26.71	-	-	-
Geomean	-	-	33090	37.74	-	-	-
Geo%CV	-	-	717.5	98.84	-	-	-
GeoSD	-	-	7.316	2.283	-	-	-
GeoQ05	-	-	4653	16.77	-	-	-
GeoQ95	-	-	129500	61.32	-	-	-

Table 10.3.12 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC 0-Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-013	0	0.1874	2.469	13.94
VST-014	0	0.1028	0.8285	-
VST-015	0	0.1244	0.7334	-
VST-016	0	0.01219	0.04944	-
VST-017	0	0.078	1.24	1.462
VST-018	0	0.1144	1.611	8.07
n	-	6	6	3
Minimum	-	0.0122	0.0494	1.46
Maximum	-	0.187	2.47	13.9
Median	-	0.1086	1.034	8.07
Arithmean	-	0.1032	1.155	7.825
Arith%CV	-	55.81	71.89	79.79
ArithSD	-	0.0576	0.8305	6.244
Geomean	-	0.07993	0.7275	5.479
Geo%CV	-	123.9	242.9	172.9
GeoSD	-	2.624	4.014	3.243
GeoQ05	-	0.01938	0.09702	1.734
GeoQ95	-	0.1692	2.219	13.2

Table 10.3.13 160 mg QD Part A1 Cycle 0 Day -6 Fasted: AZ5104 (Metabolite) Ratios

Subject / Statistic	Manual exclusion flag	Accumulation Ratio - Cmax (fraction)	Accumulation Ratio - AUC 0-Tau (fraction)	Temporal Change Parameter (fraction)	Metabolite to Parent Ratio - Cmax (fraction)	Metabolite to Parent Ratio - AUC 0-Tau (fraction)	Metabolite to Parent Ratio - AUC Inf (fraction)
VST-013	0	-	-	-	0.099	0.076	0.1
VST-014	0	-	-	-	0.095	0.042	-
VST-015	0	-	-	-	0.103	0.035	-
VST-016	0	-	-	-	0.104	0.042	-
VST-017	0	-	-	-	0.087	0.088	0.089
VST-018	0	-	-	-	0.071	0.052	0.097
n	-	0	0	0	6	6	3
Minimum	-	-	-	-	0.071	0.035	0.089
Maximum	-	-	-	-	0.104	0.088	0.1
Median	-	-	-	-	0.097	0.047	0.097
Arithmean	-	-	-	-	0.093	0.056	0.095
Arith%CV	-	-	-	-	13.475	37.866	5.62
ArithSD	-	-	-	-	0.013	0.021	0.005
Geomean	-	-	-	-	0.092	0.053	0.095
Geo%CV	-	-	-	-	14.55	37.288	5.694
GeoSD	-	-	-	-	1.156	1.434	1.059
GeoQ05	-	-	-	-	0.075	0.037	0.09
GeoQ95	-	-	-	-	0.104	0.085	0.099

10.3.2 Cycle 1 Day 15 Fasted

Table 10.3.14 160 mg QD Part A1 Cycle 1 Day 15 Fasted: AZD9291 (Parent) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-013	-	-	4	4	0	4	0	4	1	1
VST-014	-	-	4	4	0	4	0	4	0	1
VST-015	-	-	4	3	0	3	0	3	0	1
VST-016	-	-	4	4	0	4	0	4	0	1
VST-017	-	-	4	4	0	4	0	4	0	1
VST-018	-	-	4	4	0	4	0	4	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	3	0	3	0	3	-	-
Maximum	-	-	-	4	0	4	0	4	-	-
Median	-	-	-	4	0	4	0	4	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.3.15 160 mg QD Part A1 Cycle 1 Day 15 Fasted: AZD9291 (Parent) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-013	1	-	631.6	4	-	-
VST-014	0	-	1600	8	-	-
VST-015	0	-	2318	8	-	-
VST-016	0	-	265.2	4	-	-
VST-017	0	-	164.4	8	-	-
VST-018	0	-	641.3	4	-	-
n	-	0	5	5	0	0
Minimum	-	-	164	4	-	-
Maximum	-	-	2320	8	-	-
Median	-	-	641.3	8	-	-
Arithmean	-	-	997.9	-	-	-
Arith%CV	-	-	93.26	-	-	-
ArithSD	-	-	930.7	-	-	-
Geomean	-	-	635.7	-	-	-
Geo%CV	-	-	161.1	-	-	-
GeoSD	-	-	3.099	-	-	-
GeoQ05	-	-	180.9	-	-	-
GeoQ95	-	-	2153	-	-	-

Table 10.3.16 160 mg QD Part A1 Cycle 1 Day 15 Fasted: AZ5104 (Metabolite) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-013	-	-	4	4	0	4	0	4	1	1
VST-014	-	-	4	4	0	4	0	4	0	1
VST-015	-	-	4	3	0	3	0	3	0	1
VST-016	-	-	4	4	0	4	0	4	0	1
VST-017	-	-	4	4	0	4	0	4	0	1
VST-018	-	-	4	4	0	4	0	4	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	3	0	3	0	3	-	-
Maximum	-	-	-	4	0	4	0	4	-	-
Median	-	-	-	4	0	4	0	4	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.3.17 160 mg QD Part A1 Cycle 1 Day 15 Fasted: AZ5104 (Metabolite) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-013	1	-	64.36	0	-	-
VST-014	0	-	162.8	8	-	-
VST-015	0	-	239.6	8	-	-
VST-016	0	-	25.68	8	-	-
VST-017	0	-	14.49	8	-	-
VST-018	0	-	55.14	4	-	-
n	-	0	5	5	0	0
Minimum	-	-	14.5	4	-	-
Maximum	-	-	240	8	-	-
Median	-	-	55.14	8	-	-
Arithmean	-	-	99.55	-	-	-
Arith%CV	-	-	98.28	-	-	-
ArithSD	-	-	97.83	-	-	-
Geomean	-	-	60.35	-	-	-
Geo%CV	-	-	176.5	-	-	-
GeoSD	-	-	3.286	-	-	-
GeoQ05	-	-	16.25	-	-	-
GeoQ95	-	-	221.8	-	-	-

10.3.3 Cycle 2 Day 1 Fasted

Table 10.3.18 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-013	24	24	10	10	0	10	0	10	0	1
VST-014	24	24	10	10	0	10	0	10	0	1
VST-015	24	24	10	9	0	9	0	9	1	1
VST-016	24	24	10	10	0	10	0	10	0	1
VST-017	24	24	10	10	0	10	0	10	0	1
VST-018	24	24	10	10	0	10	0	10	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	10	0	10	0	10	-	-
Maximum	-	-	-	10	0	10	0	10	-	-
Median	-	-	-	10	0	10	0	10	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.3.19 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-013	0	0	970.8	12	24	865.9
VST-014	0	0	1870	8	24	1740
VST-015	1	0	2706	6	12	2580
VST-016	0	0	360.5	2	24	348.5
VST-017	0	0	166.5	6	24	46.34
VST-018	0	0	624.4	10	24	432.9
n	-	5	5	5	5	5
Minimum	-	0	167	2	24	46.3
Maximum	-	0	1870	12	24	1740
Median	-	0	624.4	8	24	432.9
Arithmean	-	-	798.5	-	-	686.7
Arith%CV	-	-	84	-	-	95.77
ArithSD	-	-	670.7	-	-	657.7
Geomean	-	-	584.2	-	-	402.3
Geo%CV	-	-	116.4	-	-	232.5
GeoSD	-	-	2.522	-	-	3.907
GeoQ05	-	-	194.4	-	-	69.38
GeoQ95	-	-	1640	-	-	1513

Table 10.3.20 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-013	-	-	-	-	-	1	0	0	0	0	1
VST-014	429.7	0.0016132	3	-0.367	0.0326	0	0	1	1	0	1
VST-015	1257	0.00055164	3	-0.995	0.00318	0	0	1	1	1	1
VST-016	-	-	-	-	-	1	0	0	0	0	1
VST-017	7.993	0.086714	3	0.999	1.75	0	0	0	1	0	1
VST-018	-	-	-	-	-	1	0	0	0	0	1
n	0	0	0	0	0	-	-	-	-	-	-
Minimum	-	-	-	-	-	-	-	-	-	-	-
Maximum	-	-	-	-	-	-	-	-	-	-	-
Median	-	-	-	-	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.3.21 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-013	0	22340	11330	22340	22340	-	-
VST-014	0	42780	21460	42780	42780	-	-
VST-015	1	31760	31760	62620	62620	-	-
VST-016	0	8493	4241	8493	8493	-	-
VST-017	0	2692	1706	2692	2692	-	-
VST-018	0	13010	6969	13010	13010	-	-
n	-	5	5	5	5	0	0
Minimum	-	2690	1710	2690	2690	-	-
Maximum	-	42800	21500	42800	42800	-	-
Median	-	13010	6969	13010	13010	-	-
Arithmean	-	17860	9143	17860	17860	-	-
Arith%CV	-	87.73	84.84	87.73	87.73	-	-
ArithSD	-	15670	7757	15670	15670	-	-
Geomean	-	12320	6573	12320	12320	-	-
Geo%CV	-	140.5	123.7	140.5	140.5	-	-
GeoSD	-	2.84	2.62	2.84	2.84	-	-
GeoQ05	-	3388	2047	3388	3388	-	-
GeoQ95	-	37570	18890	37570	37570	-	-

Table 10.3.22 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Half-life dependent parameters

Subject / Statistic	Manual exclusion flag	Half-life exclusion flag	AUMC 0-Inf (ng*h^2/mL)	MRT (h)	Cl/F (L/h)	Clss/F (L/h)	Vz/F (L)
VST-013	0	1	-	-	-	7.161	-
VST-014	0	1	-	-	-	3.74	-
VST-015	1	1	-	-	-	2.555	-
VST-016	0	1	-	-	-	18.84	-
VST-017	0	1	-	-	-	59.42	-
VST-018	0	1	-	-	-	12.3	-
n	-	-	0	0	0	5	0
Minimum	-	-	-	-	-	3.74	-
Maximum	-	-	-	-	-	59.4	-
Median	-	-	-	-	-	12.3	-
Arithmean	-	-	-	-	-	20.29	-
Arith%CV	-	-	-	-	-	111.4	-
ArithSD	-	-	-	-	-	22.6	-
Geomean	-	-	-	-	-	12.98	-
Geo%CV	-	-	-	-	-	140.5	-
GeoSD	-	-	-	-	-	2.84	-
GeoQ05	-	-	-	-	-	4.259	-
GeoQ95	-	-	-	-	-	47.23	-

Table 10.3.23 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-013	0	6.067	139.6	-
VST-014	0	11.69	267.4	-
VST-015	1	16.91	391.4	-
VST-016	0	2.253	53.08	-
VST-017	0	1.041	16.83	-
VST-018	0	3.903	81.32	-
n	-	5	5	0
Minimum	-	1.04	16.8	-
Maximum	-	11.7	267	-
Median	-	3.903	81.32	-
Arithmean	-	4.99	111.6	-
Arith%CV	-	84	87.73	-
ArithSD	-	4.192	97.94	-
Geomean	-	3.651	77.03	-
Geo%CV	-	116.4	140.5	-
GeoSD	-	2.522	2.84	-
GeoQ05	-	1.215	21.17	-
GeoQ95	-	10.25	234.8	-

Table 10.3.24 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZD9291 (Parent) Ratios

Subject / Statistic	Manual exclusion flag	Accumulation Ratio - Cmax (fraction)	Accumulation Ratio - AUC Tau (fraction)	Temporal Change Parameter (fraction)	Metabolite to Parent Ratio - Cmax (fraction)	Metabolite to Parent Ratio - AUC Tau (fraction)	Metabolite to Parent Ratio - AUC Inf (fraction)
VST-013	0	3.197	4.272	0.997	-	-	-
VST-014	0	10.775	13.608	-	-	-	-
VST-015	1	14.03	18.877	-	-	-	-
VST-016	0	19.289	45.59	-	-	-	-
VST-017	0	1.158	1.197	1.027	-	-	-
VST-018	0	2.426	2.606	0.975	-	-	-
n	-	5	5	3	0	0	0
Minimum	-	1.158	1.197	0.975	-	-	-
Maximum	-	19.289	45.59	1.027	-	-	-
Median	-	3.197	4.272	0.997	-	-	-
Arithmean	-	7.369	13.455	1	-	-	-
Arith%CV	-	103.816	138.3	2.628	-	-	-
ArithSD	-	7.65	18.608	0.026	-	-	-
Geomean	-	4.51	6.074	0.999	-	-	-
Geo%CV	-	164.004	259.839	2.625	-	-	-
GeoSD	-	3.135	4.183	1.027	-	-	-
GeoQ05	-	1.342	1.399	0.977	-	-	-
GeoQ95	-	17.169	35.798	1.024	-	-	-

Table 10.3.25 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Sample counts*

Subject / Statistic	Tau (h)	Maximum time for NCA purposes (h)	No. expected datapoints	No. observed datapoints	No. observed datapoints - BLQ	No. timepoints in NCA profile	No. timepoints that are non-quantifiable	No.timepoints available for NCA	Manual exclusion flag	Half-life exclusion flag
VST-013	24	24	10	10	0	10	0	10	0	1
VST-014	24	24	10	10	0	10	0	10	0	1
VST-015	24	24	10	9	0	9	0	9	1	1
VST-016	24	24	10	10	0	10	0	10	0	1
VST-017	24	24	10	10	0	10	0	10	0	1
VST-018	24	24	10	10	0	10	0	10	0	1
n	-	-	-	5	5	5	5	5	-	-
Minimum	-	-	-	10	0	10	0	10	-	-
Maximum	-	-	-	10	0	10	0	10	-	-
Median	-	-	-	10	0	10	0	10	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-

*Flag and exclude columns have a value 1 to mark an exclusion.

Table 10.3.26 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Minimum & maximum concentration and timepoint summary

Subject / Statistic	Manual exclusion flag	tfirst (h)	Cmax (ng/mL)	tmax (h)	tlast (h)	Cmin (ng/mL)
VST-013	0	0	96.51	8	24	93.22
VST-014	0	0	198	12	24	190.3
VST-015	1	0	305.1	1.5	12	286.1
VST-016	0	0	36.46	24	24	-
VST-017	0	0	15.06	6	24	4.26
VST-018	0	0	52.36	8	24	49.57
n	-	5	5	5	5	4
Minimum	-	0	15.1	6	24	4.26
Maximum	-	0	198	24	24	190
Median	-	0	52.36	8	24	71.4
Arithmean	-	-	79.68	-	-	84.34
Arith%CV	-	-	91.1	-	-	94.19
ArithSD	-	-	72.59	-	-	79.44
Geomean	-	-	55.97	-	-	43.99
Geo%CV	-	-	126.1	-	-	377.5
GeoSD	-	-	2.652	-	-	5.211
GeoQ05	-	-	17.97	-	-	6.156
GeoQ95	-	-	171.5	-	-	171

Table 10.3.27 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Half-life parameters**

Subject / Statistic	Half-life (h)	Lambda z (1/h)	No. points in half-life fit	Adj R-squared	Span Ratio (fraction)	Flag on half-life calculation	Flag on half-life value	Flag on adj R2	Flag on span ratio	Manual exclusion flag	Half-life exclusion flag
VST-013	576.6	0.0012021	3	-0.163	0.0243	0	0	1	1	0	1
VST-014	-	-	-	-	-	1	0	0	0	0	1
VST-015	-	-	-	-	-	1	0	0	0	1	1
VST-016	-	-	-	-	-	1	0	0	0	0	1
VST-017	8.122	0.085341	3	0.995	1.72	0	0	0	1	0	1
VST-018	300.3	0.0023082	3	0.528	0.0466	0	0	1	1	0	1
n	0	0	0	0	0	-	-	-	-	-	-
Minimum	-	-	-	-	-	-	-	-	-	-	-
Maximum	-	-	-	-	-	-	-	-	-	-	-
Median	-	-	-	-	-	-	-	-	-	-	-
Arithmean	-	-	-	-	-	-	-	-	-	-	-
Arith%CV	-	-	-	-	-	-	-	-	-	-	-
ArithSD	-	-	-	-	-	-	-	-	-	-	-
Geomean	-	-	-	-	-	-	-	-	-	-	-
Geo%CV	-	-	-	-	-	-	-	-	-	-	-
GeoSD	-	-	-	-	-	-	-	-	-	-	-
GeoQ05	-	-	-	-	-	-	-	-	-	-	-
GeoQ95	-	-	-	-	-	-	-	-	-	-	-

**Flag and exclude columns have a value 1 for an error (i.e. exclusion from summary statistics) and a value 2 for a warning (i.e. treat with caution but included in summary statistics).

Table 10.3.28 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Calculated AUC

Subject / Statistic	Manual exclusion flag	AUC 0-t (ng*h/mL)	AUC 0-12 (ng*h/mL)	AUC 0-24 (ng*h/mL)	AUC Tau (ng*h/mL)	AUC 0-Inf (ng*h/mL)	AUC 0-Inf extrapolated Pc (%)
VST-013	0	2257	1122	2257	2257	-	-
VST-014	0	4570	2241	4570	4570	-	-
VST-015	1	3506	3506	-	-	-	-
VST-016	0	858.7	425.4	858.7	858.7	-	-
VST-017	0	237.1	145.9	237.1	237.1	-	-
VST-018	0	1211	603.7	1211	1211	-	-
n	-	5	5	5	5	0	0
Minimum	-	237	146	237	237	-	-
Maximum	-	4570	2240	4570	4570	-	-
Median	-	1211	603.7	1211	1211	-	-
Arithmean	-	1827	907.7	1827	1827	-	-
Arith%CV	-	93.05	90.99	93.05	93.05	-	-
ArithSD	-	1700	825.9	1700	1700	-	-
Geomean	-	1205	623.6	1205	1205	-	-
Geo%CV	-	155.8	137.3	155.8	155.8	-	-
GeoSD	-	3.034	2.799	3.034	3.034	-	-
GeoQ05	-	306.7	180.8	306.7	306.7	-	-
GeoQ95	-	3969	1951	3969	3969	-	-

Table 10.3.29 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Dose normalised parameters

Subject / Statistic	Manual exclusion flag	Dose normalised Cmax (ng/mL/mg)	Dose normalised AUC Tau (ng*h/mL/mg)	Dose normalised AUC 0-Inf (ng*h/mL/mg)
VST-013	0	0.6032	14.1	-
VST-014	0	1.238	28.57	-
VST-015	1	1.907	-	-
VST-016	0	0.2279	5.367	-
VST-017	0	0.09412	1.482	-
VST-018	0	0.3272	7.566	-
n	-	5	5	0
Minimum	-	0.0941	1.48	-
Maximum	-	1.24	28.6	-
Median	-	0.3272	7.566	-
Arithmean	-	0.498	11.42	-
Arith%CV	-	91.1	93.05	-
ArithSD	-	0.4537	10.62	-
Geomean	-	0.3498	7.532	-
Geo%CV	-	126.1	155.8	-
GeoSD	-	2.652	3.034	-
GeoQ05	-	0.1123	1.917	-
GeoQ95	-	1.072	24.81	-

Table 10.3.30 160 mg QD Part A1 Cycle 2 Day 1 Fasted: AZ5104 (Metabolite) Ratios

Subject / Statistic	Manual exclusion flag	Accumulation Ratio - Cmax (fraction)	Accumulation Ratio - AUC Tau (fraction)	Temporal Change Parameter (fraction)	Metabolite to Parent Ratio - Cmax (fraction)	Metabolite to Parent Ratio - AUC Tau (fraction)	Metabolite to Parent Ratio - AUC Inf (fraction)
VST-013	0	3.218	5.712	1.012	0.099	0.101	-
VST-014	0	12.038	34.479	-	0.106	0.107	-
VST-015	1	15.326	-	-	0.113	-	-
VST-016	0	18.697	108.564	-	0.101	0.101	-
VST-017	0	1.207	1.195	1.014	0.09	0.088	-
VST-018	0	2.861	4.697	0.937	0.084	0.093	-
n	-	5	5	3	5	5	0
Minimum	-	1.207	1.195	0.937	0.084	0.088	-
Maximum	-	18.697	108.564	1.014	0.106	0.107	-
Median	-	3.218	5.712	1.012	0.099	0.101	-
Arithmean	-	7.604	30.929	0.988	0.096	0.098	-
Arith%CV	-	98.712	146.816	4.402	9.221	7.566	-
ArithSD	-	7.506	45.409	0.043	0.009	0.007	-
Geomean	-	4.782	10.371	0.987	0.096	0.098	-
Geo%CV	-	158.587	473.275	4.463	9.43	7.663	-
GeoSD	-	3.068	5.904	1.046	1.099	1.08	-
GeoQ05	-	1.434	1.571	0.945	0.085	0.089	-
GeoQ95	-	17.121	86.31	1.014	0.105	0.106	-

11 Plasma PK NCA Terminal Half-life fits

11.1 40 mg QD Part A1

Figure 11.1.1 Terminal half-life fit for subject VST-001

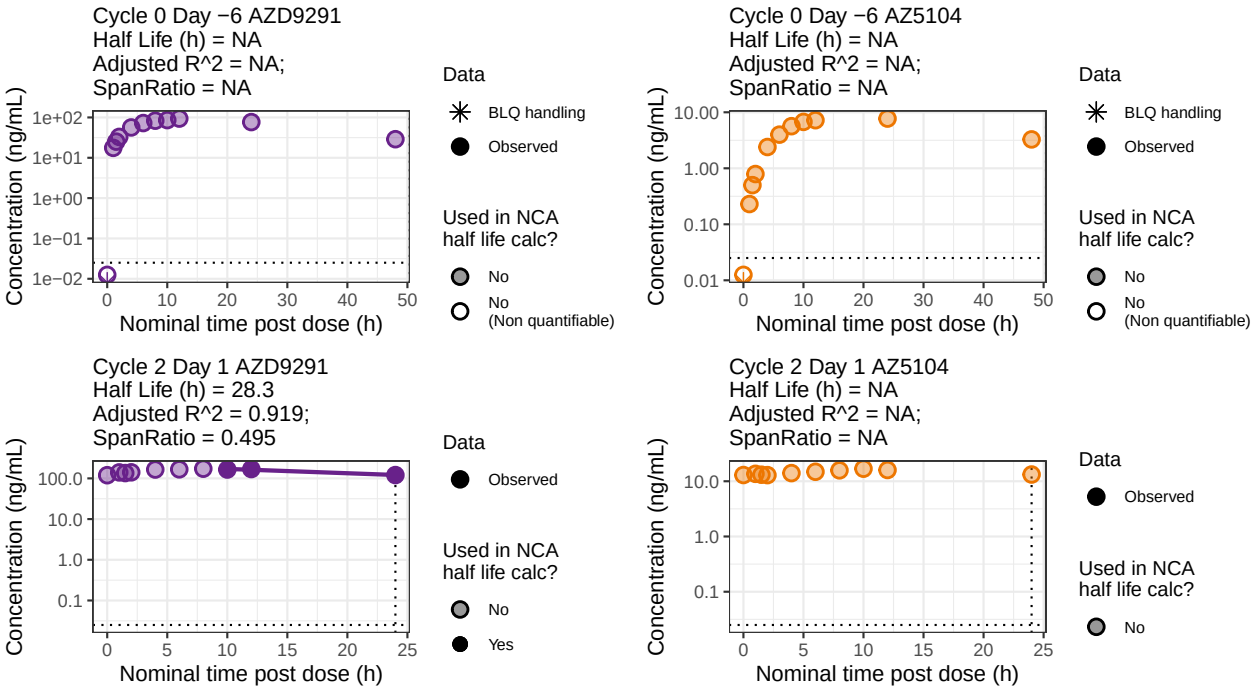


Figure 11.1.2 Terminal half-life fit for subject VST-002

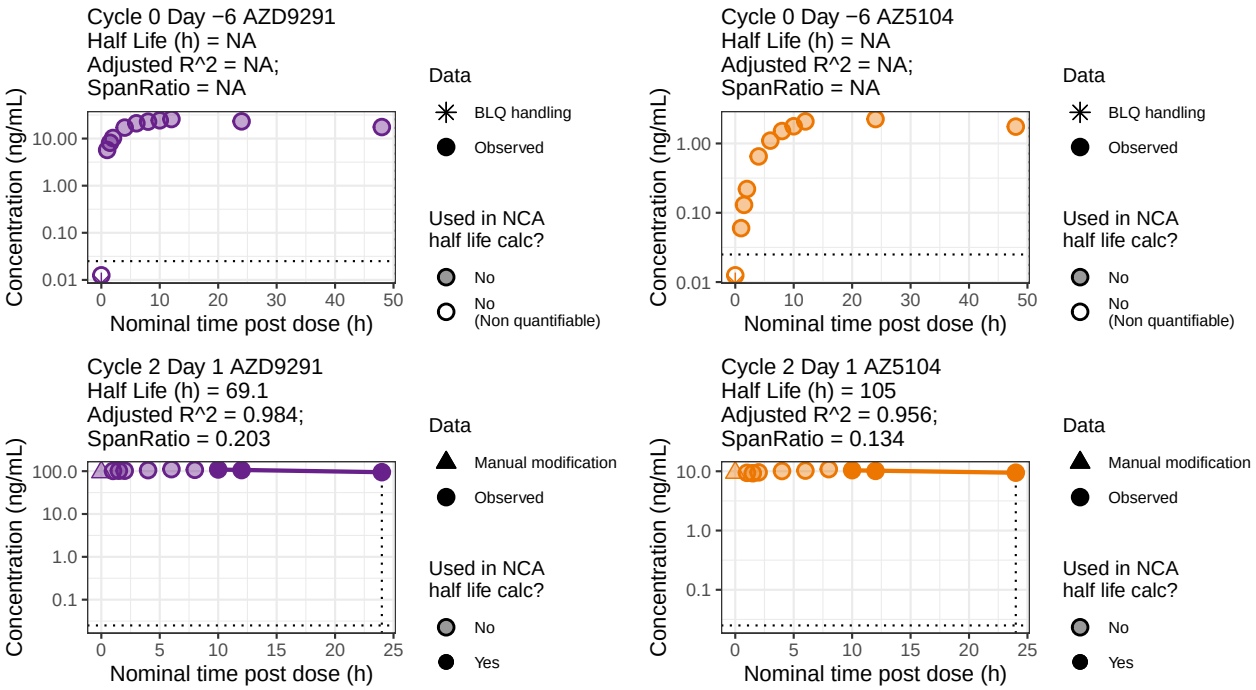


Figure 11.1.3 Terminal half-life fit for subject VST-003

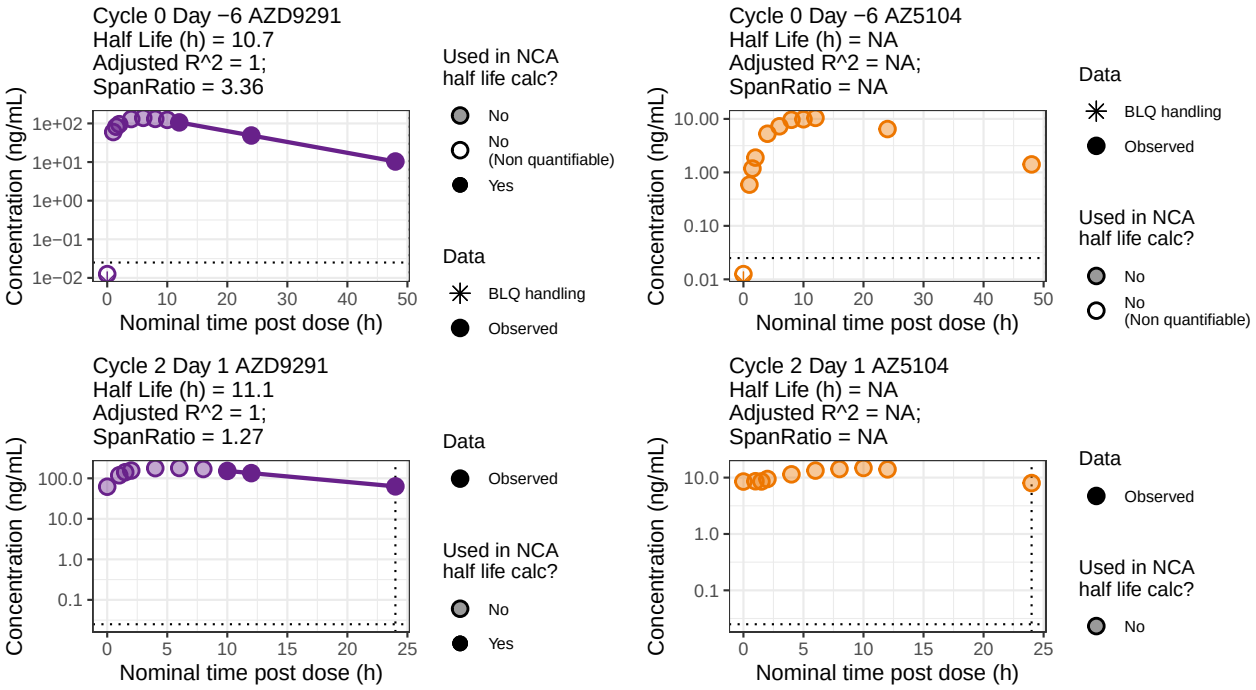


Figure 11.1.4 Terminal half-life fit for subject VST-004

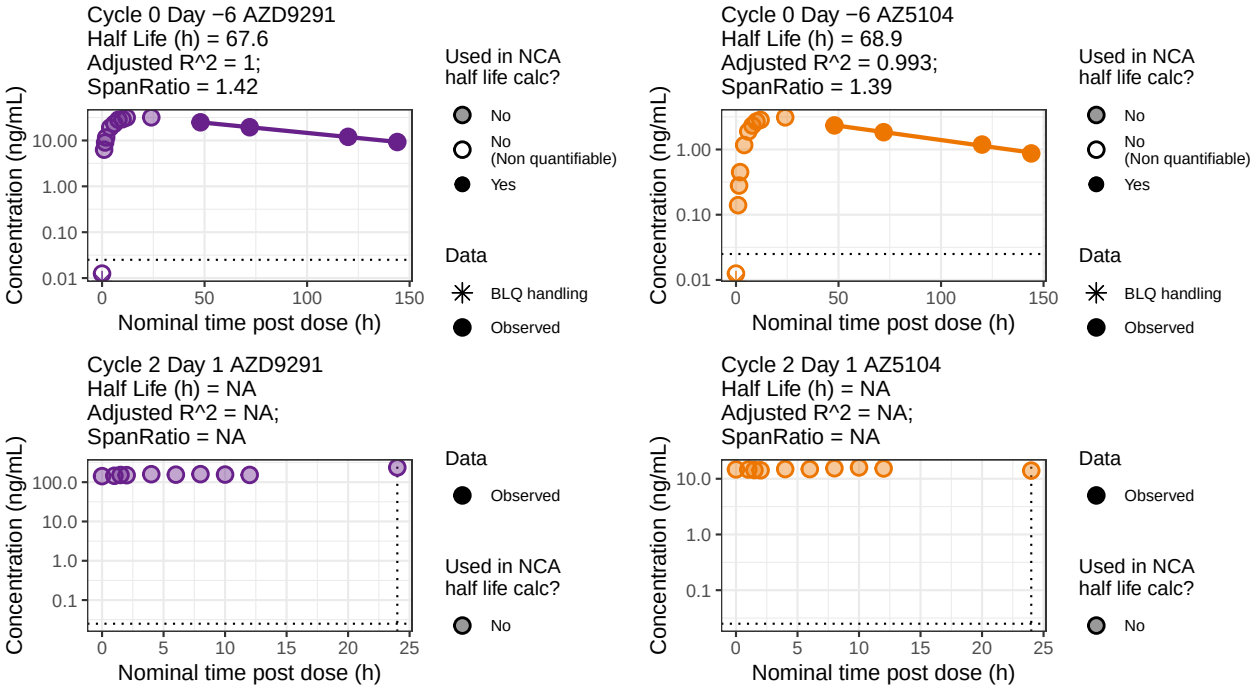


Figure 11.1.5 Terminal half-life fit for subject VST-005

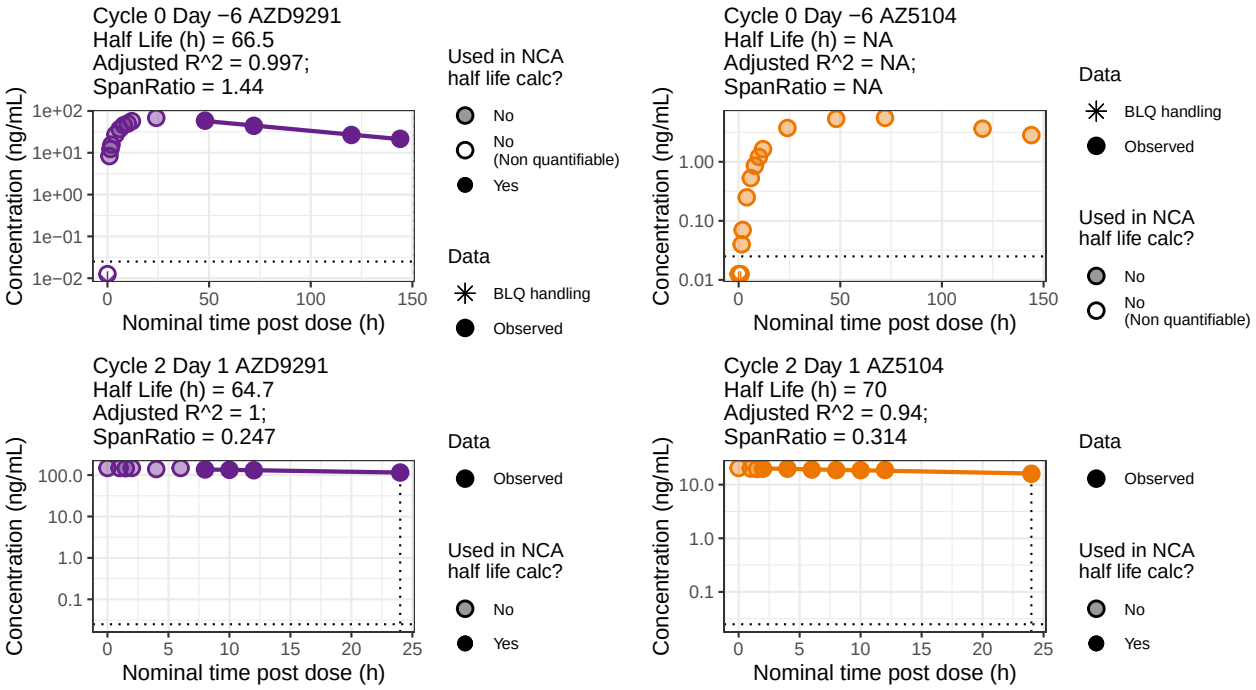
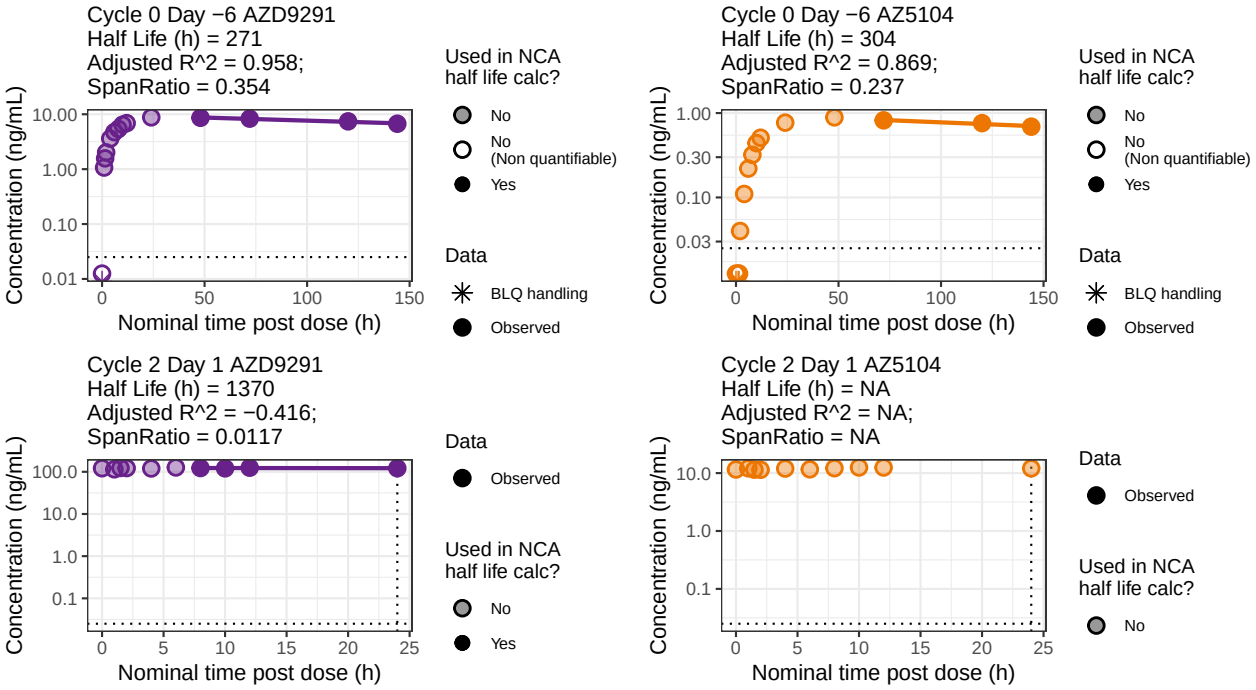


Figure 11.1.6 Terminal half-life fit for subject VST-006



11.2 80 mg QD Part A1

Figure 11.2.1 Terminal half-life fit for subject VST-007

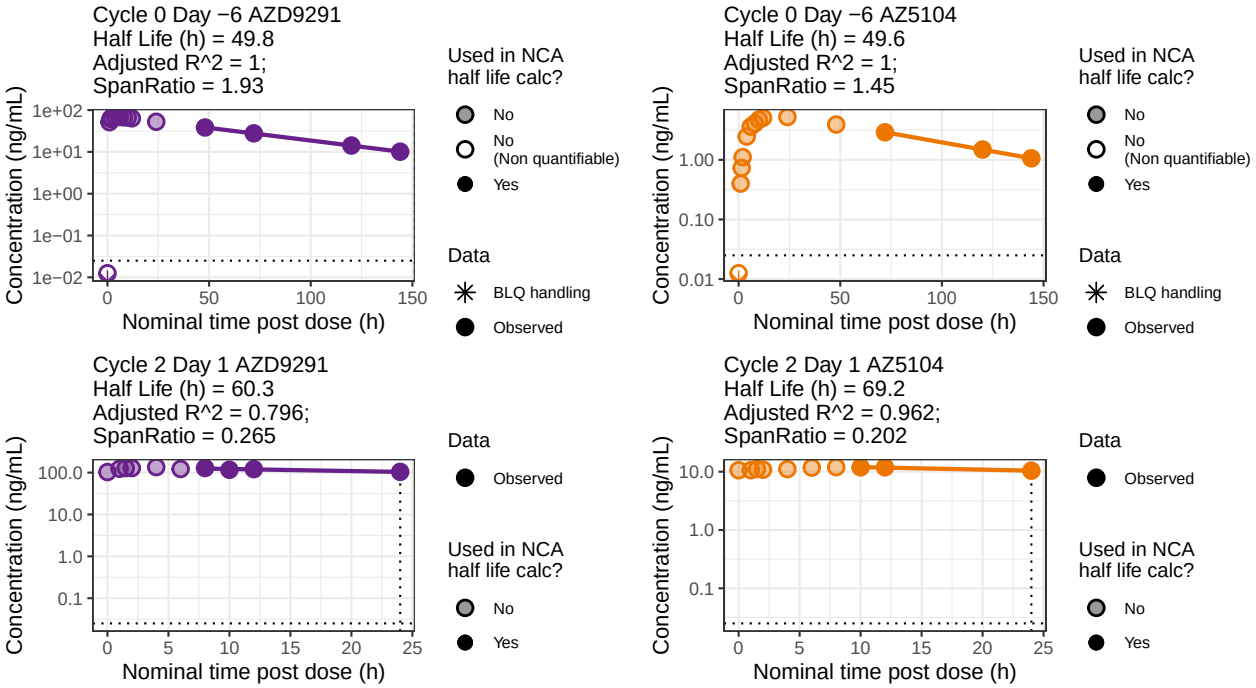


Figure 11.2.2 Terminal half-life fit for subject VST-008

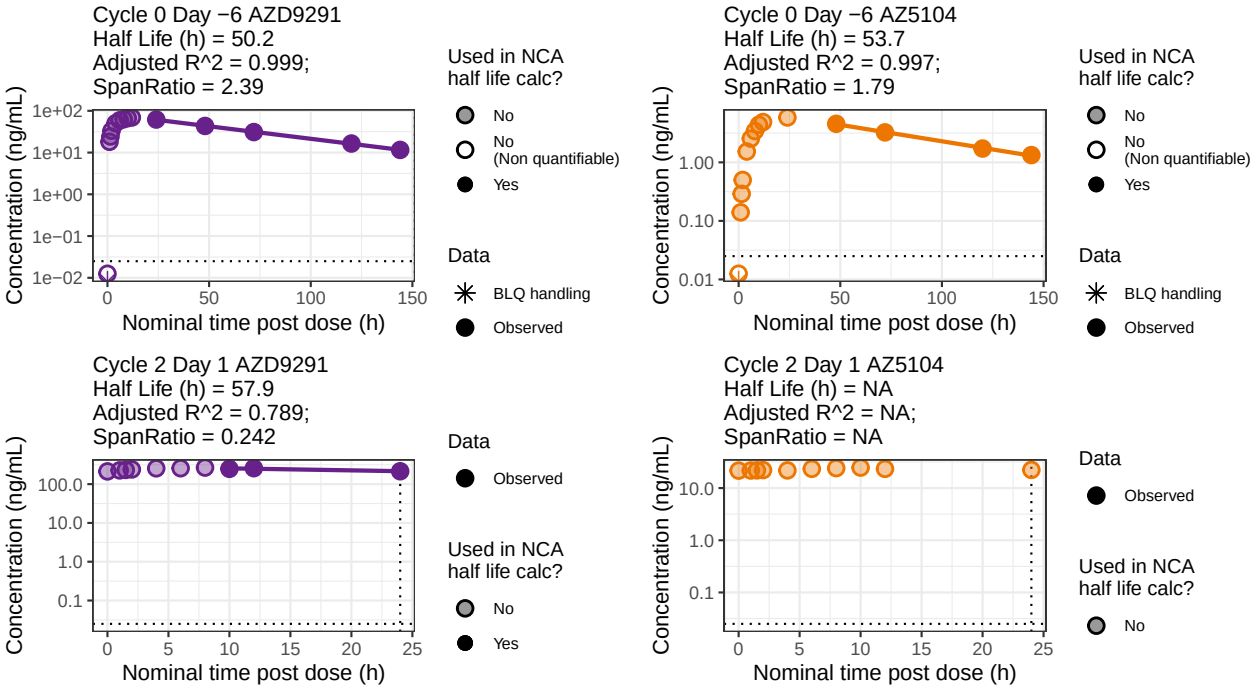


Figure 11.2.3 Terminal half-life fit for subject VST-009

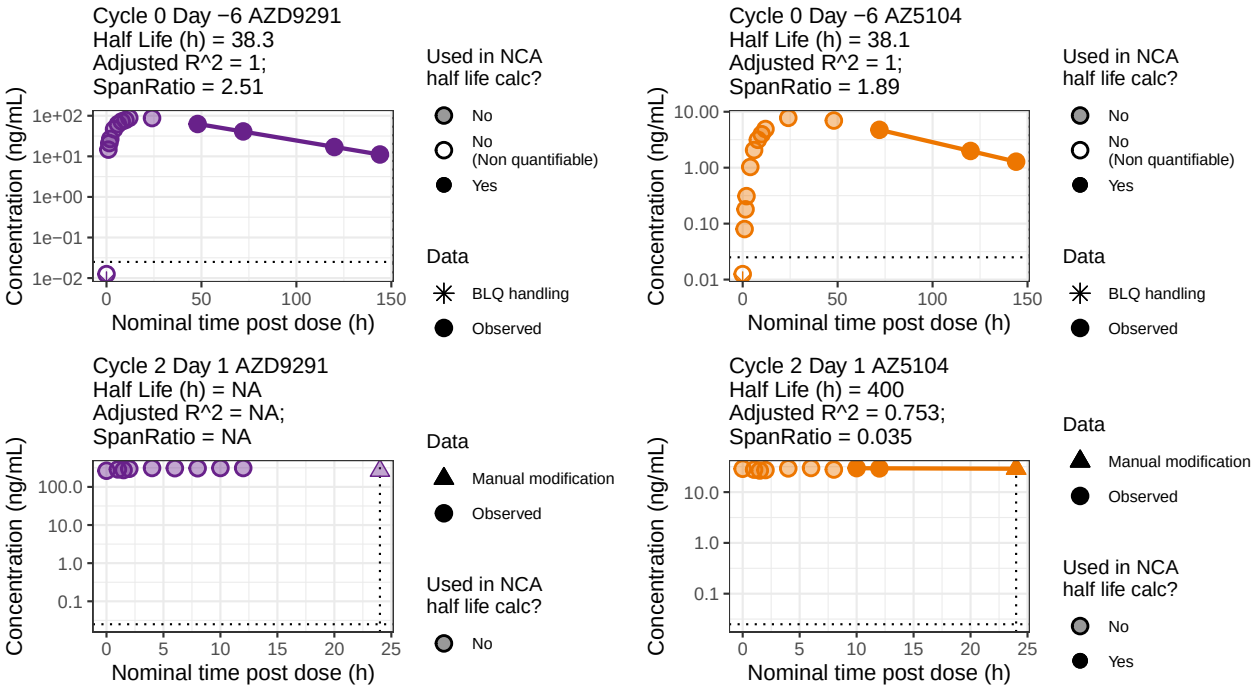


Figure 11.2.4 Terminal half-life fit for subject VST-010

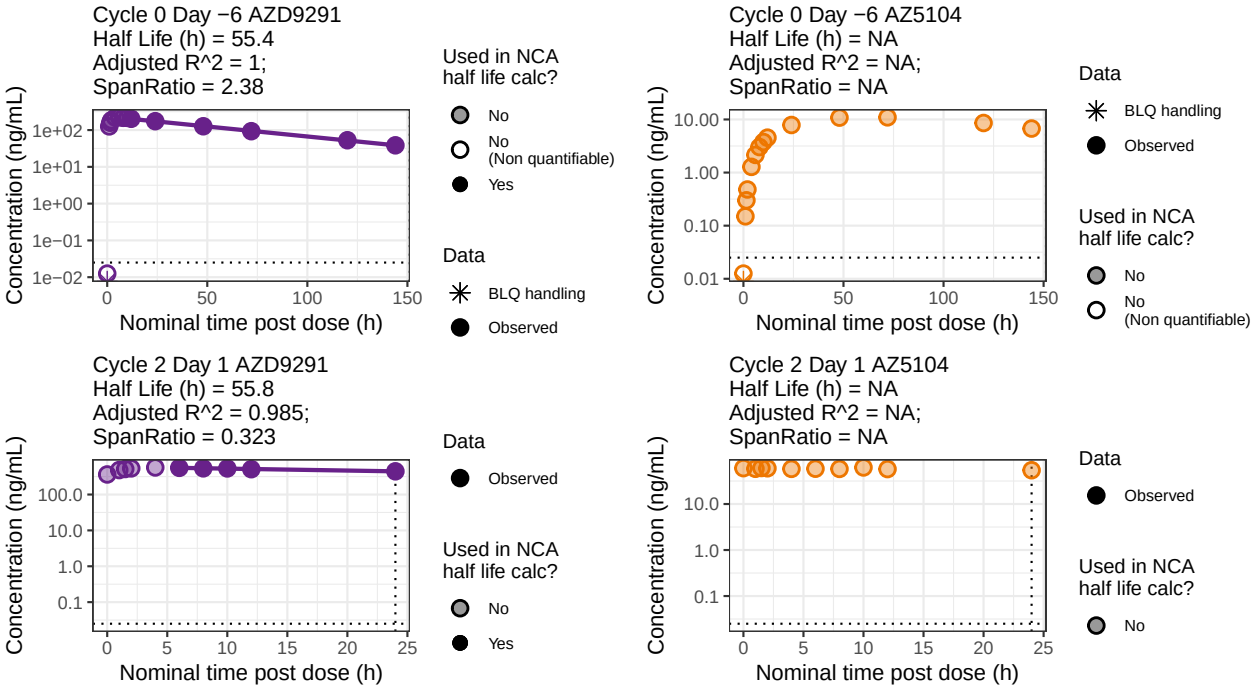


Figure 11.2.5 Terminal half-life fit for subject VST-011

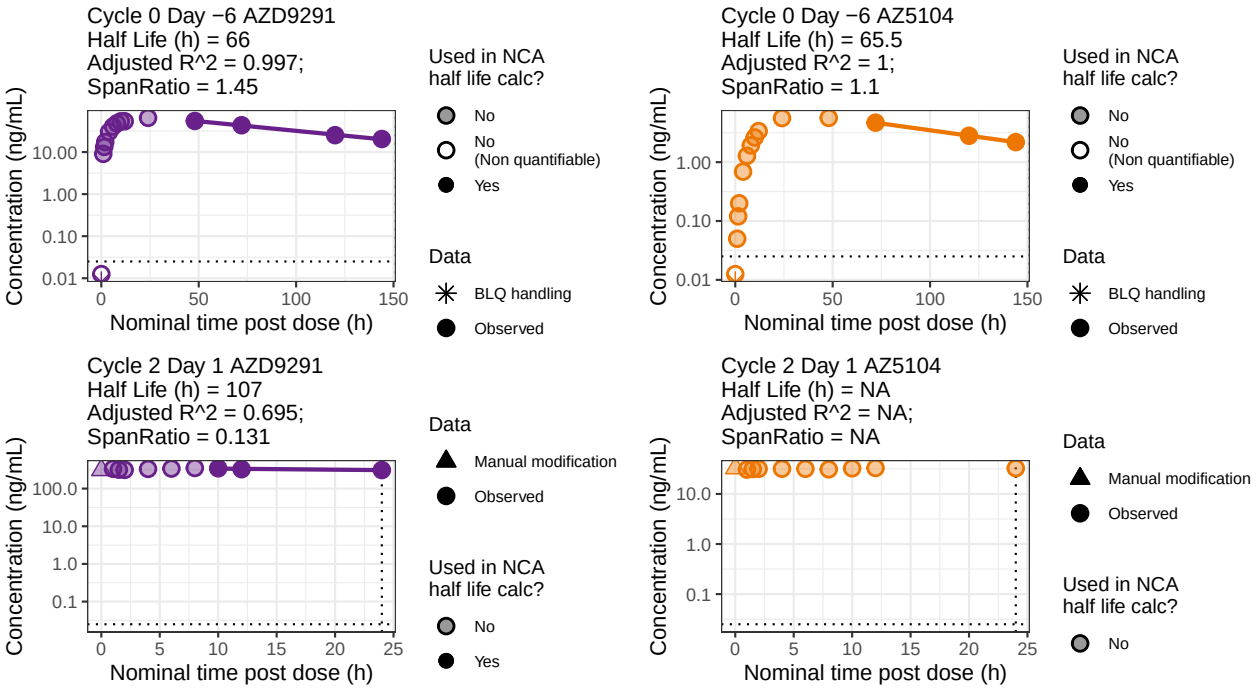
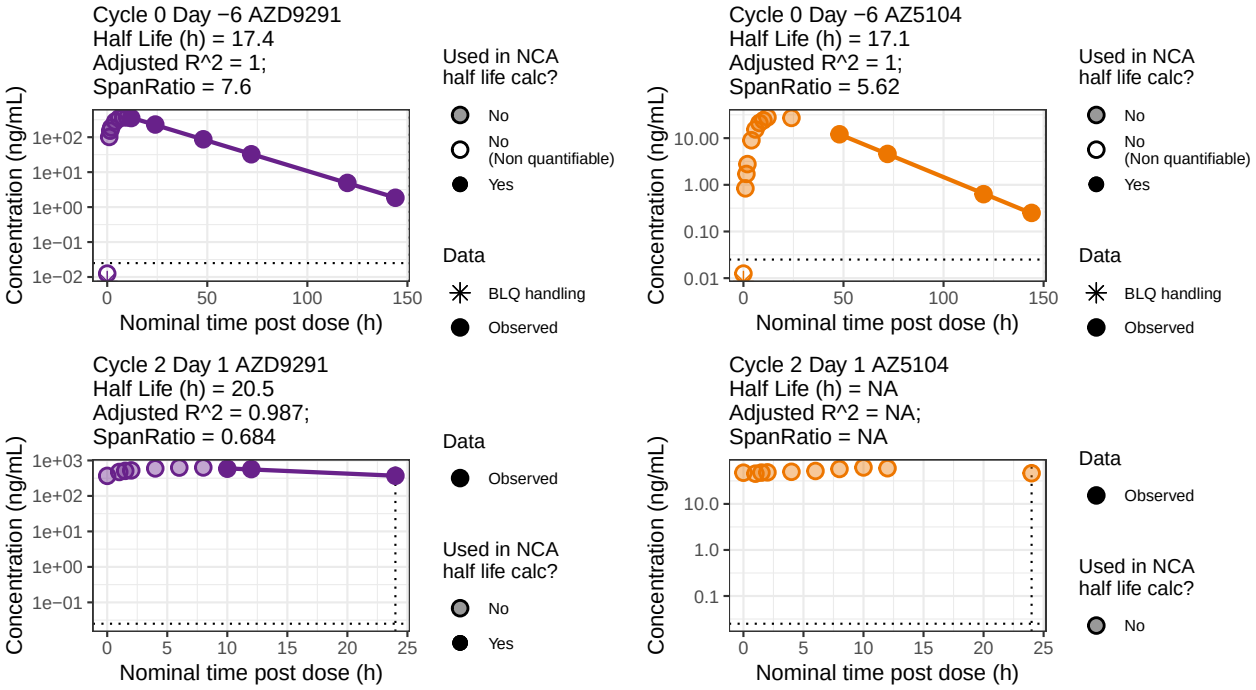


Figure 11.2.6 Terminal half-life fit for subject VST-012



11.3 160 mg QD Part A1

Figure 11.3.1 Terminal half-life fit for subject VST-013

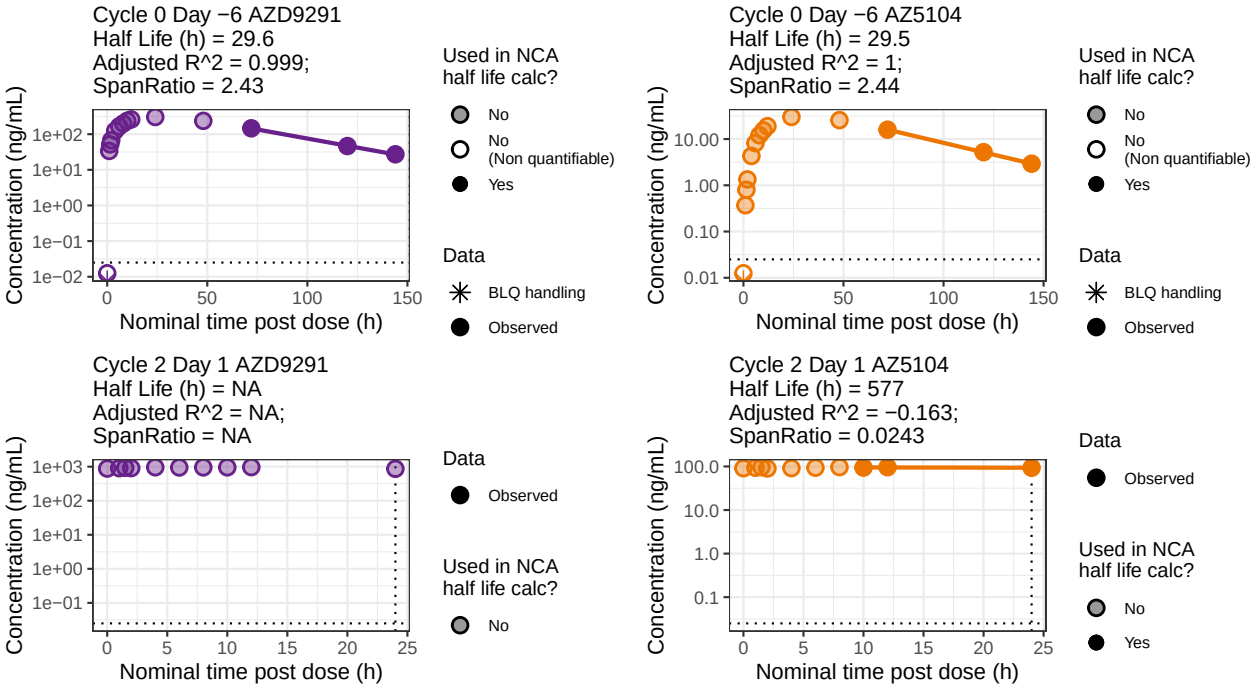


Figure 11.3.2 Terminal half-life fit for subject VST-014

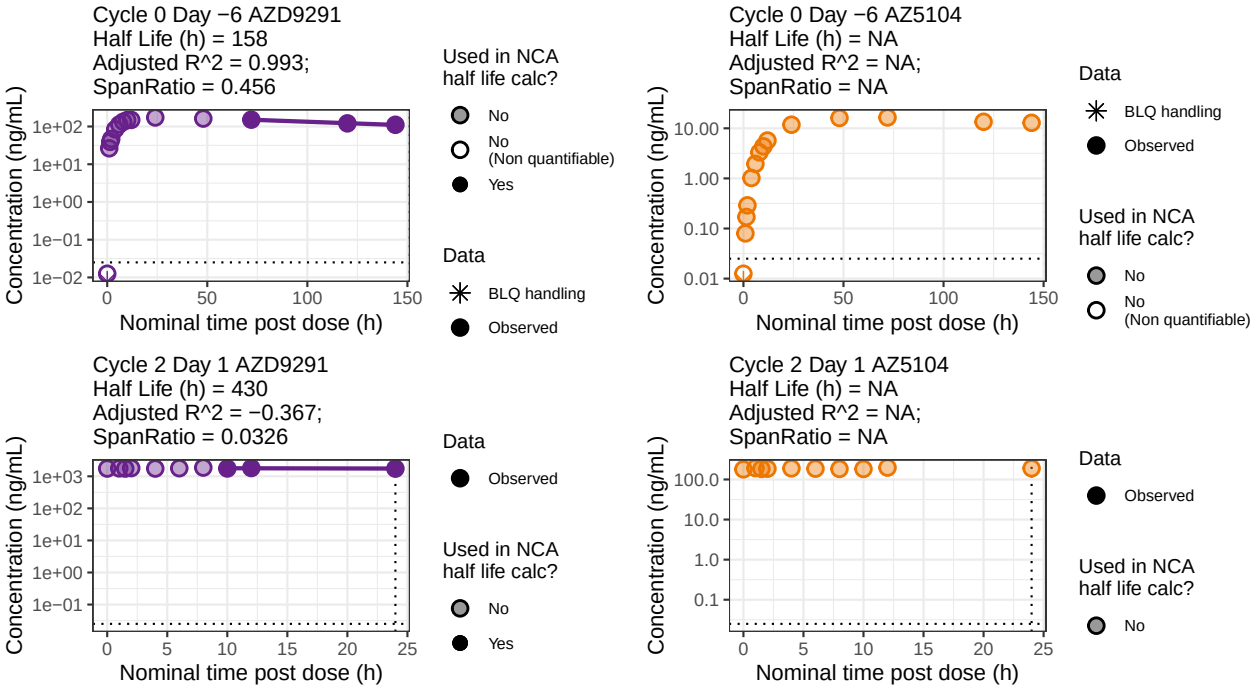


Figure 11.3.3 Terminal half-life fit for subject VST-015

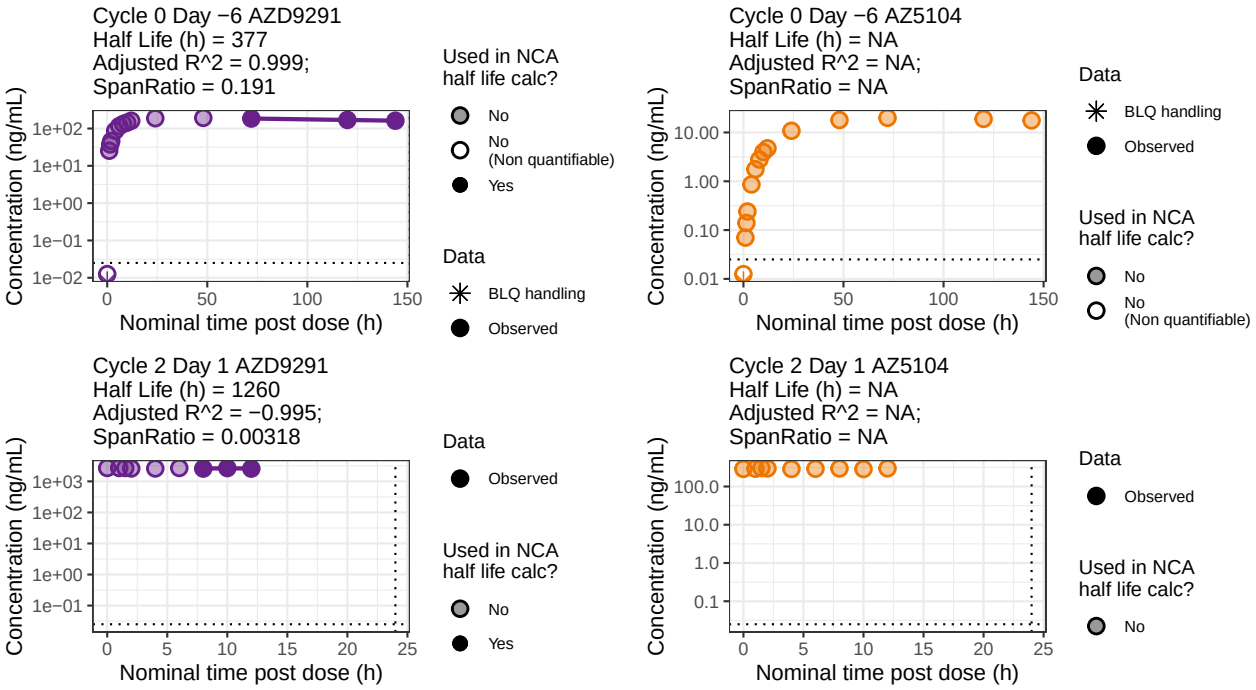


Figure 11.3.4 Terminal half-life fit for subject VST-016

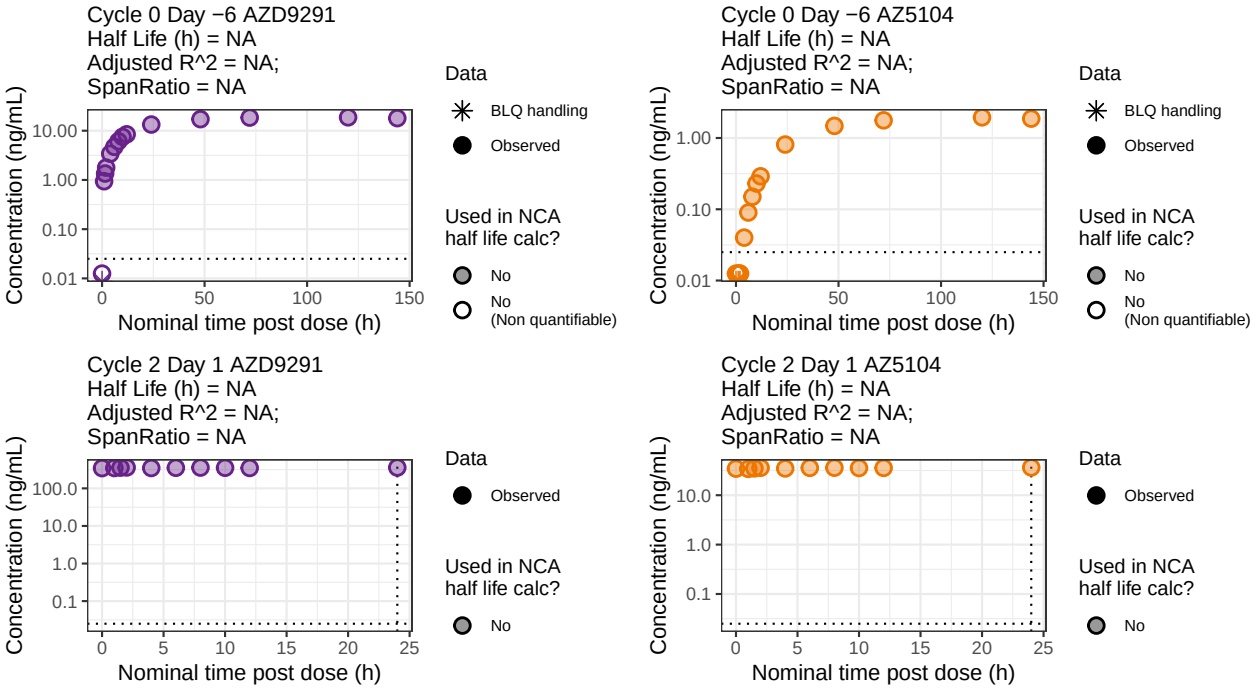


Figure 11.3.5 Terminal half-life fit for subject VST-017

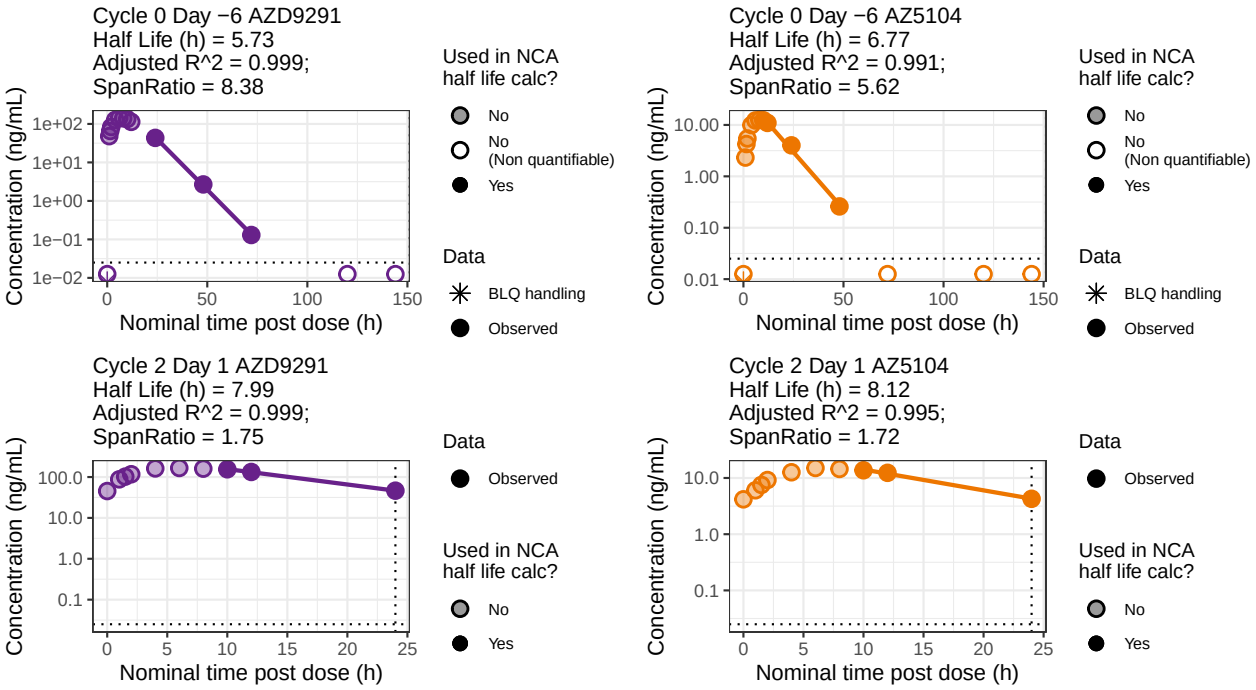
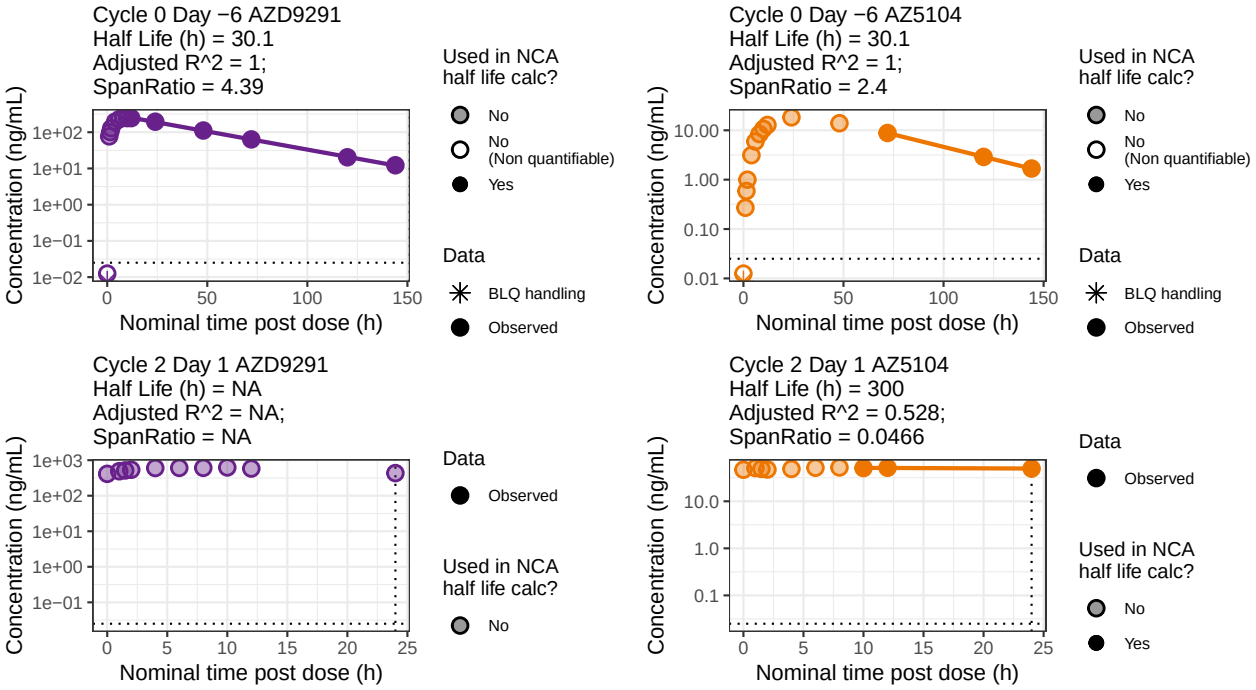


Figure 11.3.6 Terminal half-life fit for subject VST-018



A Email records

A.1 API properties

The following pages give email trails of API properties

A.2 Electronic files, software and other documentation

All data manipulation, visualisation and NCA was performed in the opensource datascience and statistics language R [2, 3], version 4.2.2 run within the RStudio IDE on Windows 10. A list of packages and their version numbers can be found in Table A.2.1. In particular, NCA calculations were performed using the R package PKNCA [4]. This has been shown to be consistent with NCA performed using other (commercial) software such as Phoenix WinNonlin [5].

Table A.2.1 Details of R packages used.

Package	Version
here	1.0.1
knitr	1.49
tidyverse	2.0.0
kableExtra	1.4.0
testthat	3.2.1.1
rlang	1.1.4
PKNCA	0.11.0
ggh4x	0.2.8
patchwork	1.3.0
RColorBrewer	1.1.3
dplyr	1.1.4
units	0.8.5
ggpackets	0.2.1
ggplot2	3.5.1
stats	4.4.1
pdftools	3.4.1
readr	2.1.5
renv	1.0.11
rmarkdown	2.28
xfun	0.48
readxl	1.4.3

Code was stored and managed using Seda's private GitLab account for source control management. Details of the repository can be found in Table A.2.2. Details of the scripts, and verification history can be found in Table A.2.3.

Table A.2.2 Code repository details

Parameter	Value
Repository name	https://gitlab.com/sedapds/sedainternal/nca/nca_training/osimertinib_genericscipts_v2
Project ID	58584663
Subfolder	PKUK
Last commit code	
Tag	
Authors	Emily Fell
Verifiers	Harri Dickinson
Signed Code PDF	NCA Example Report

Table A.2.3 Details of script verification.

Folder	Script	Commit Code	Author	Checked by	Check date	LastModifySHA	Verification up to date?
Clinical/NCA/Generic-Scripts/Utilities	CleanProject.R	08ec14c8	PG/EF	JD	04/01/2024	08ec14c8	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Validation_PKNCA_package.R	353463b0	PG/EF	JD	04/01/2024	353463b0	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Validation_PKNCA_Calculation-Theoph_Seda_function.R	c7e530d3	PG/EF	JD	04/01/2024	c7e530d3	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	PKNCA_package_Validation.R	08ec14c8	PG/EF	JD	04/01/2024	08ec14c8	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Utilities_Data.R	5f7a17a4	PG/EF	JD	17/01/2024	5f7a17a4	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Utilities_Tables.R	08ec14c8	PG/EF	JD	04/01/2024	08ec14c8	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Utilities_NCA_Manipulation.R	3d2cf030	PG/EF	JD	12/01/2023	3d2cf030	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	Data_Summarise_PK.R	ea1ed1c1	PG/EF	JD	04/01/2024	ea1ed1c1	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Utilities_generateLaTeXCode.R	ffd22fe1	PG/EF	JD	04/01/2024	ffd22fe1	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	Data_generateLaTeX.R	ea1ed1c1	PG/EF	JD	04/01/2024	ea1ed1c1	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Utilities_DataVisualisation.R	40288b0f	PG/EF	JD	04/01/2024	40288b0f	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	DataVisualisation_Individuals.R	9f52d360	PG/EF	JD	16/01/2024	9f52d360	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	DataVisualisation_Summarised.R	d1717a1b	PG/EF	JD	16/01/2024	d1717a1b	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	DataVisualisation_generateLaTeX.R	d1717a1b	PG/EF	JD	17/01/2023	d1717a1b	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Utilities_NCA_Calculate.R	d1717a1b	PG/EF	JD	04/01/2024	d1717a1b	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_Calculate.R	b40edb05	PG/EF	JD	04/01/2024	b40edb05	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Utilities_NCA_HalfLifePlot.R	ea1ed1c1	PG/EF	JD	04/01/2024	ea1ed1c1	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_PlotHalfLifeFit.R	9f52d360	PG/EF	JD	16/01/2024	9f52d360	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_HalfLifePlots_generateLaTeX.R	08ec14c8	PG/EF	JD	04/01/2024	08ec14c8	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_PostProcess.R	f5d9dfb6	PG/EF	JD	04/01/2024	f5d9dfb6	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_CohortListing.R	4b7ac16e	PG/EF	JD	29/01/2024	4b7ac16e	TRUE
Clinical/NCA/Generic-Scripts/Utilities	Utilities_NCA_Summarise.R	08ec14c8	PG/EF	JD	04/01/2024	08ec14c8	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_Summarise.R	08ec14c8	PG/EF	JD	04/01/2024	08ec14c8	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_CohortListingTables.R	5f7a17a4	PG/EF	JD	04/01/2024	5f7a17a4	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_CohortListingTables_generateLaTeX.R	5f7a17a4	PG/EF	JD	04/01/2024	5f7a17a4	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	SummaryTables.R	40288b0f	EF	JD	04/01/2024	40288b0f	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_SummaryTables.R	5f7a17a4	PG/EF	JD	04/01/2024	5f7a17a4	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	NCA_SummaryGraphs.R	c7e530d3	PG/EF	JD	16/01/2024	c7e530d3	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	runNCAPipeline.R	2a37ec30	PG/EF	JD	04/01/2024	2a37ec30	TRUE
Clinical/NCA/Generic-Scripts/AnalysisPipeline-Scripts	RenderRscripts.R	08ec14c8	PG/EF	JD	04/01/2024	08ec14c8	TRUE
Clinical/NCA/Generic-Scripts/Lists	NCA_formatSpec.csv	4b7ac16e	PG/EF	JD	04/01/2024	4b7ac16e	TRUE

Table A.2.3 Details of script verification. *(continued)*

Folder	Script	Commit Code	Author	Checked by	Check date	LastModifySHA	Verification up to date?
Clinical/NCA/Generic-Scripts/Lists	NCAunits.csv	c7e530d3	PG/EF	JD	04/01/2024	c7e530d3	TRUE
Clinical/NCA/Generic-Scripts/Lists	PKData_ColumnList.csv	cd9d15b1	PG/EF	JD	04/01/2024	cd9d15b1	TRUE
Clinical/NCA/Generic-Scripts/Lists	SampleExpectedNumbers.csv	ea1ed1c1	PG/EF	JD	04/01/2024	ea1ed1c1	TRUE
Clinical/NCA/Generic-Scripts/Utilities	BuildProject.R	08ec14c8	PG/EF	JD	04/01/2024	08ec14c8	TRUE
DataClean/	PKUK.DataClean_PK.R	10ddc1aa	EF	HD	12/11/2024	10ddc1aa	TRUE
DataClean/	PKUK.DataManipulation_PK.R	10ddc1aa	EF	HD	12/11/2024	10ddc1aa	TRUE
NCA/	PKUK.NCA_SummaryTablesGraphs_generate-LaTeX.R	10ddc1aa	EF	HD	12/11/2024	10ddc1aa	TRUE
NA	PKUK.runAnalysis.R	41d7bf87	EF	HD	12/11/2024	41d7bf87	TRUE

B NCA Methods

B.1 Data visualisation

Individual time-plasma concentration profiles were plotted for each individual and inspected for any non-plausible profiles. BLQ concentration values (as received and unprocessed) were plotted as LLQ/2, with the LLQ value shown with a horizontal dotted line.

Where data has been truncated for NCA (e.g. only a 12 hr profile for BID dosing), this has been marked with a vertical dotted line.

Additionally, the processed data (manual modifications if applicable and BLQ handling) used for NCA is shown alongside the as received data for comparison.

Plasma geometric mean profiles and geometric 90% quantile ranges were calculated using the post-exclusion data for each dosing cohort. Note these statistics were only calculated if more than 50% of the data points at that nominal time point are quantifiable. The geometric means and geometric quantile ranges were visualised for each cohort. All data visualisation (individual and mean) is provided in Section 7.

B.2 NCA calculations

NCA was performed for each individual profile using nominal times. For the purposes of NCA, multiple dose profiles were restricted to 24 hours for QD dosing and 12 hours for BID dosing. BLQ values were treated as per Seda's NCA best practice guide [1]. In particular, any BLQ values before the first measurable concentration are set to be 0 ng/ml for single dose (and treated as quantifiable) or treated as missing otherwise. If two BLQ values occur in succession then the profile is deemed to have ended at the last concentration above the LLQ. Full details are given in [1]. Where a measured PK profile followed a dosing holiday (e.g for on-off dosing regimes), BLQ values before the first measurable concentration were treated as a single dose. In other cases, by discretion, a BLQ value before the first measurable concentration may be set as the LLQ value for NCA purposes.

For each individual (where data is available), the following ratios were calculated for multiple dose profile:

1. Accumulation ratio on C_{max}, which is the ratio of C_{max} compared to C_{max} in Cycle 0.
2. Accumulation ratio on AUC_{Tau}, which is the ratio of AUC_{Tau} compared to $AUC_{0\text{-}Tau}$ in Cycle 0.
3. Temporal change parameter, which is the ratio of AUC_{Tau} $AUC_{0\text{-}inf}$ in Cycle 0.

Average concentration Cav is calculated as $AUC_{0\text{-}24}$/24 for Cycle 0 and AUC_{Tau}/Tau for Cycles 1 and 2. Free average concentration 'Free Cav' is calculated by converting Cav to molar concentrations using the analyte molecular weights and fractions unbound provided in Table 4.0.2.

Summarised statistics were produced in accordance with Seda's NCA best practice guide [1], on those PK results not subject to the exclusions detailed in Section B.3. Individual and summarised listings are provided in Section 10. Half-life fitting plots for each individual are provided in Section 11. Summary graphs are provided in Section 8.

The parameter 'AUC 0-Tau' in Cycle 0 refers to AUC from 0 to the dosing interval for that cohort, i.e. 24 hours for QD dosing and 12 hours for BID dosing.

B.3 Warnings and exclusions

Flags for automatically calculated errors and warnings are recorded in the following columns: 'Flag on half-life calculation', 'Flag on half-life value', 'Flag on adj R2' and 'Flag on span ratio'. An automatically generated error flag is marked by a 1, whilst a warning flag was marked with a 2. Exclusions from summary statistics are marked by a 1 in the column 'Exclude on half-life' for an exclusion on parameters linked to half-life and the column 'Exclude manual' for manual exclusions on all parameters. Any such manual exclusions are detailed in Section 5.1.

The following warnings flags are automatically generated during the analysis:

- 'Flag on span ratio': Span ratio is less than or equal to 3

The following error flags are automatically generated during the analysis, and lead to an exclusion on parameters linked to half-life in the summary statistics:

- 'Flag on half-life calculation': When PKNCA is unable to calculate a half-life

- ‘Flag on adj R2’: When the adjusted R squared value is less than 0.8
- ‘Flag on span ratio’: When the span-ratio is less than or equal to 2

C PK Data

C.1 Final PK Data for NCA analysis

Table C.1.1 Final PK data.

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-001	40 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	1.0	h	17.62	ng/mL	No	17.6200	17.62	17.6200	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	1.5	h	25.11	ng/mL	No	25.1100	25.11	25.1100	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	2.0	h	32.93	ng/mL	No	32.9300	32.93	32.9300	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	4.0	h	56.48	ng/mL	No	56.4800	56.48	56.4800	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	6.0	h	72.6	ng/mL	No	72.6000	72.60	72.6000	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	8.0	h	83.07	ng/mL	No	83.0700	83.07	83.0700	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	10.0	h	85.9	ng/mL	No	85.9000	85.90	85.9000	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	12.0	h	93.71	ng/mL	No	93.7100	93.71	93.7100	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	24.0	h	76.79	ng/mL	No	76.7900	76.79	76.7900	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	0	-6	48.0	h	28.87	ng/mL	No	28.8700	28.87	28.8700	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	1.0	h	0.23	ng/mL	No	0.2300	0.23	0.2300	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	1.5	h	0.5	ng/mL	No	0.5000	0.50	0.5000	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	2.0	h	0.79	ng/mL	No	0.7900	0.79	0.7900	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	4.0	h	2.4	ng/mL	No	2.4000	2.40	2.4000	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	6.0	h	3.99	ng/mL	No	3.9900	3.99	3.9900	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	8.0	h	5.65	ng/mL	No	5.6500	5.65	5.6500	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	10.0	h	6.74	ng/mL	No	6.7400	6.74	6.7400	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	12.0	h	7.22	ng/mL	No	7.2200	7.22	7.2200	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	24.0	h	7.72	ng/mL	No	7.7200	7.72	7.7200	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	0	-6	48.0	h	3.28	ng/mL	No	3.2800	3.28	3.2800	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	1	15	0.0	h	120.42	ng/mL	No	120.4200	120.42	120.4200	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	1	15	2.0	h	145.76	ng/mL	No	145.7600	145.76	145.7600	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	1	15	4.0	h	156.54	ng/mL	No	156.5400	156.54	156.5400	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	1	15	8.0	h	173.38	ng/mL	No	173.3800	173.38	173.3800	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	1	15	0.0	h	13.15	ng/mL	No	13.1500	13.15	13.1500	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	1	15	2.0	h	12.98	ng/mL	No	12.9800	12.98	12.9800	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	1	15	4.0	h	13.33	ng/mL	No	13.3300	13.33	13.3300	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	1	15	8.0	h	15.69	ng/mL	No	15.6900	15.69	15.6900	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	0.0	h	119.61	ng/mL	No	119.6100	119.61	119.6100	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	1.0	h	140.26	ng/mL	No	140.2600	140.26	140.2600	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	1.5	h	135.16	ng/mL	No	135.1600	135.16	135.1600	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	2.0	h	140.92	ng/mL	No	140.9200	140.92	140.9200	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	4.0	h	165	ng/mL	No	165.0000	165.00	165.0000	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	6.0	h	166.85	ng/mL	No	166.8500	166.85	166.8500	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	8.0	h	173.01	ng/mL	No	173.0100	173.01	173.0100	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	10.0	h	165.02	ng/mL	No	165.0200	165.02	165.0200	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	12.0	h	169.47	ng/mL	No	169.4700	169.47	169.4700	No	-	No	-
VST-001	40 mg QD	A1	AZD9291	2	1	24.0	h	120.57	ng/mL	No	120.5700	120.57	120.5700	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-001	40 mg QD	A1	AZ5104	2	1	0.0	h	12.96	ng/mL	No	12.9600	12.96	12.9600	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	2	1	1.0	h	13.62	ng/mL	No	13.6200	13.62	13.6200	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	2	1	1.5	h	13.13	ng/mL	No	13.1300	13.13	13.1300	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	2	1	2.0	h	12.91	ng/mL	No	12.9100	12.91	12.9100	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	2	1	4.0	h	14.04	ng/mL	No	14.0400	14.04	14.0400	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	2	1	6.0	h	14.84	ng/mL	No	14.8400	14.84	14.8400	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	2	1	8.0	h	15.76	ng/mL	No	15.7600	15.76	15.7600	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	2	1	10.0	h	16.87	ng/mL	No	16.8700	16.87	16.8700	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	2	1	12.0	h	15.98	ng/mL	No	15.9800	15.98	15.9800	No	-	No	-
VST-001	40 mg QD	A1	AZ5104	2	1	24.0	h	13.24	ng/mL	No	13.2400	13.24	13.2400	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	1.0	h	5.73	ng/mL	No	5.7300	5.73	5.7300	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	1.5	h	8.15	ng/mL	No	8.1500	8.15	8.1500	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	2.0	h	10.28	ng/mL	No	10.2800	10.28	10.2800	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	4.0	h	17.08	ng/mL	No	17.0800	17.08	17.0800	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	6.0	h	21.09	ng/mL	No	21.0900	21.09	21.0900	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	8.0	h	22.87	ng/mL	No	22.8700	22.87	22.8700	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	10.0	h	24.38	ng/mL	No	24.3800	24.38	24.3800	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	12.0	h	25.94	ng/mL	No	25.9400	25.94	25.9400	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	24.0	h	23.18	ng/mL	No	23.1800	23.18	23.1800	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	0	-6	48.0	h	17.54	ng/mL	No	17.5400	17.54	17.5400	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	1.0	h	0.06	ng/mL	No	0.0600	0.06	0.0600	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	1.5	h	0.13	ng/mL	No	0.1300	0.13	0.1300	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	2.0	h	0.22	ng/mL	No	0.2200	0.22	0.2200	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	4.0	h	0.65	ng/mL	No	0.6500	0.65	0.6500	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	6.0	h	1.1	ng/mL	No	1.1000	1.10	1.1000	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	8.0	h	1.51	ng/mL	No	1.5100	1.51	1.5100	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	10.0	h	1.77	ng/mL	No	1.7700	1.77	1.7700	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	12.0	h	2.08	ng/mL	No	2.0800	2.08	2.0800	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	24.0	h	2.25	ng/mL	No	2.2500	2.25	2.2500	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	0	-6	48.0	h	1.75	ng/mL	No	1.7500	1.75	1.7500	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	1	15	0.0	h	96.37	ng/mL	No	96.3700	96.37	96.3700	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	1	15	2.0	h	102.08	ng/mL	No	102.0800	102.08	102.0800	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	1	15	4.0	h	107.55	ng/mL	No	107.5500	107.55	107.5500	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	1	15	8.0	h	112.03	ng/mL	No	112.0300	112.03	112.0300	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	1	15	0.0	h	9.48	ng/mL	No	9.4800	9.48	9.4800	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	1	15	2.0	h	9.41	ng/mL	No	9.4100	9.41	9.4100	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	1	15	4.0	h	9.41	ng/mL	No	9.4100	9.41	9.4100	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	1	15	8.0	h	10.09	ng/mL	No	10.0900	10.09	10.0900	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	2	1	0.0	h	-	ng/mL	No	-	94.81	94.8100	No	-	Yes	Copied concentration from C2 D1 H24.
VST-002	40 mg QD	A1	AZD9291	2	1	1.0	h	101.5	ng/mL	No	101.5000	101.50	101.5000	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	2	1	1.5	h	102.58	ng/mL	No	102.5800	102.58	102.5800	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-002	40 mg QD	A1	AZD9291	2	1	2.0	h	102.53	ng/mL	No	102.5300	102.53	102.5300	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	2	1	4.0	h	105.72	ng/mL	No	105.7200	105.72	105.7200	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	2	1	6.0	h	111.42	ng/mL	No	111.4200	111.42	111.4200	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	2	1	8.0	h	107.66	ng/mL	No	107.6600	107.66	107.6600	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	2	1	10.0	h	109.69	ng/mL	No	109.6900	109.69	109.6900	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	2	1	12.0	h	106.05	ng/mL	No	106.0500	106.05	106.0500	No	-	No	-
VST-002	40 mg QD	A1	AZD9291	2	1	24.0	h	94.81	ng/mL	No	94.8100	94.81	94.8100	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	2	1	0.0	h	-	ng/mL	No	-	9.46	9.4600	No	-	Yes	Copied concentration from C2 D1 H24.
VST-002	40 mg QD	A1	AZ5104	2	1	1.0	h	9.41	ng/mL	No	9.4100	9.41	9.4100	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	2	1	1.5	h	9.27	ng/mL	No	9.2700	9.27	9.2700	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	2	1	2.0	h	9.58	ng/mL	No	9.5800	9.58	9.5800	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	2	1	4.0	h	10.09	ng/mL	No	10.0900	10.09	10.0900	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	2	1	6.0	h	10.27	ng/mL	No	10.2700	10.27	10.2700	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	2	1	8.0	h	10.85	ng/mL	No	10.8500	10.85	10.8500	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	2	1	10.0	h	10.44	ng/mL	No	10.4400	10.44	10.4400	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	2	1	12.0	h	10.15	ng/mL	No	10.1500	10.15	10.1500	No	-	No	-
VST-002	40 mg QD	A1	AZ5104	2	1	24.0	h	9.46	ng/mL	No	9.4600	9.46	9.4600	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	1.0	h	59.83	ng/mL	No	59.8300	59.83	59.8300	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	1.5	h	82.3	ng/mL	No	82.3000	82.30	82.3000	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	2.0	h	95.5	ng/mL	No	95.5000	95.50	95.5000	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	4.0	h	129.85	ng/mL	No	129.8500	129.85	129.8500	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	6.0	h	139.39	ng/mL	No	139.3900	139.39	139.3900	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	8.0	h	131.2	ng/mL	No	131.2000	131.20	131.2000	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	10.0	h	123.78	ng/mL	No	123.7800	123.78	123.7800	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	12.0	h	106.4	ng/mL	No	106.4000	106.40	106.4000	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	24.0	h	48.7	ng/mL	No	48.7000	48.70	48.7000	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	0	-6	48.0	h	10.33	ng/mL	No	10.3300	10.33	10.3300	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	1.0	h	0.59	ng/mL	No	0.5900	0.59	0.5900	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	1.5	h	1.18	ng/mL	No	1.1800	1.18	1.1800	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	2.0	h	1.89	ng/mL	No	1.8900	1.89	1.8900	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	4.0	h	5.28	ng/mL	No	5.2800	5.28	5.2800	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	6.0	h	7.28	ng/mL	No	7.2800	7.28	7.2800	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	8.0	h	9.63	ng/mL	No	9.6300	9.63	9.6300	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	10.0	h	9.85	ng/mL	No	9.8500	9.85	9.8500	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	12.0	h	10.46	ng/mL	No	10.4600	10.46	10.4600	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	24.0	h	6.46	ng/mL	No	6.4600	6.46	6.4600	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	0	-6	48.0	h	1.41	ng/mL	No	1.4100	1.41	1.4100	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	1	15	0.0	h	61.23	ng/mL	No	61.2300	61.23	61.2300	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	1	15	2.0	h	52.17	ng/mL	No	52.1700	52.17	52.1700	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	1	15	4.0	h	47.69	ng/mL	No	47.6900	47.69	47.6900	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	1	15	8.0	h	36.02	ng/mL	No	36.0200	36.02	36.0200	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-003	40 mg QD	A1	AZ5104	1	15	0.0	h	8.85	ng/mL	No	8.8500	8.85	8.8500	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	1	15	2.0	h	7.75	ng/mL	No	7.7500	7.75	7.7500	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	1	15	4.0	h	6.56	ng/mL	No	6.5600	6.56	6.5600	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	1	15	8.0	h	4.95	ng/mL	No	4.9500	4.95	4.9500	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	0.0	h	62.02	ng/mL	No	62.0200	62.02	62.0200	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	1.0	h	118.6	ng/mL	No	118.6000	118.60	118.6000	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	1.5	h	141.29	ng/mL	No	141.2900	141.29	141.2900	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	2.0	h	155.4	ng/mL	No	155.4000	155.40	155.4000	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	4.0	h	178.07	ng/mL	No	178.0700	178.07	178.0700	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	6.0	h	179.85	ng/mL	No	179.8500	179.85	179.8500	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	8.0	h	169.49	ng/mL	No	169.4900	169.49	169.4900	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	10.0	h	152.16	ng/mL	No	152.1600	152.16	152.1600	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	12.0	h	134.23	ng/mL	No	134.2300	134.23	134.2300	No	-	No	-
VST-003	40 mg QD	A1	AZD9291	2	1	24.0	h	63.26	ng/mL	No	63.2600	63.26	63.2600	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	0.0	h	8.51	ng/mL	No	8.5100	8.51	8.5100	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	1.0	h	8.62	ng/mL	No	8.6200	8.62	8.6200	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	1.5	h	8.55	ng/mL	No	8.5500	8.55	8.5500	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	2.0	h	9.45	ng/mL	No	9.4500	9.45	9.4500	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	4.0	h	11.43	ng/mL	No	11.4300	11.43	11.4300	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	6.0	h	13.32	ng/mL	No	13.3200	13.32	13.3200	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	8.0	h	14.2	ng/mL	No	14.2000	14.20	14.2000	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	10.0	h	14.82	ng/mL	No	14.8200	14.82	14.8200	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	12.0	h	14.01	ng/mL	No	14.0100	14.01	14.0100	No	-	No	-
VST-003	40 mg QD	A1	AZ5104	2	1	24.0	h	8	ng/mL	No	8.0000	8.00	8.0000	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	1.0	h	6.29	ng/mL	No	6.2900	6.29	6.2900	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	1.5	h	9.03	ng/mL	No	9.0300	9.03	9.0300	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	2.0	h	11.63	ng/mL	No	11.6300	11.63	11.6300	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	4.0	h	19.13	ng/mL	No	19.1300	19.13	19.1300	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	6.0	h	23.12	ng/mL	No	23.1200	23.12	23.1200	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	8.0	h	28.32	ng/mL	No	28.3200	28.32	28.3200	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	10.0	h	29.1	ng/mL	No	29.1000	29.10	29.1000	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	12.0	h	31.66	ng/mL	No	31.6600	31.66	31.6600	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	24.0	h	31.92	ng/mL	No	31.9200	31.92	31.9200	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	48.0	h	24.86	ng/mL	No	24.8600	24.86	24.8600	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	72.0	h	19.42	ng/mL	No	19.4200	19.42	19.4200	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	120.0	h	11.99	ng/mL	No	11.9900	11.99	11.9900	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	0	-6	144.0	h	9.24	ng/mL	No	9.2400	9.24	9.2400	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	1.0	h	0.14	ng/mL	No	0.1400	0.14	0.1400	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	1.5	h	0.28	ng/mL	No	0.2800	0.28	0.2800	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	2.0	h	0.45	ng/mL	No	0.4500	0.45	0.4500	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	4.0	h	1.17	ng/mL	No	1.1700	1.17	1.1700	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	6.0	h	1.89	ng/mL	No	1.8900	1.89	1.8900	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	8.0	h	2.33	ng/mL	No	2.3300	2.33	2.3300	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-004	40 mg QD	A1	AZ5104	0	-6	10.0	h	2.69	ng/mL	No	2.6900	2.69	2.6900	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	12.0	h	2.84	ng/mL	No	2.8400	2.84	2.8400	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	24.0	h	3.11	ng/mL	No	3.1100	3.11	3.1100	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	48.0	h	2.34	ng/mL	No	2.3400	2.34	2.3400	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	72.0	h	1.84	ng/mL	No	1.8400	1.84	1.8400	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	120.0	h	1.19	ng/mL	No	1.1900	1.19	1.1900	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	0	-6	144.0	h	0.87	ng/mL	No	0.8700	0.87	0.8700	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	1	15	0.0	h	143.21	ng/mL	No	143.2100	143.21	143.2100	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	1	15	2.0	h	143.65	ng/mL	No	143.6500	143.65	143.6500	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	1	15	4.0	h	149.71	ng/mL	No	149.7100	149.71	149.7100	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	1	15	8.0	h	157.45	ng/mL	No	157.4500	157.45	157.4500	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	1	15	0.0	h	13.7	ng/mL	No	13.7000	13.70	13.7000	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	1	15	2.0	h	13.65	ng/mL	No	13.6500	13.65	13.6500	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	1	15	4.0	h	14.32	ng/mL	No	14.3200	14.32	14.3200	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	1	15	8.0	h	15.18	ng/mL	No	15.1800	15.18	15.1800	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	0.0	h	142.35	ng/mL	No	142.3500	142.35	142.3500	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	1.0	h	145.31	ng/mL	No	145.3100	145.31	145.3100	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	1.5	h	152.34	ng/mL	No	152.3400	152.34	152.3400	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	2.0	h	150.68	ng/mL	No	150.6800	150.68	150.6800	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	4.0	h	159.41	ng/mL	No	159.4100	159.41	159.4100	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	6.0	h	155.31	ng/mL	No	155.3100	155.31	155.3100	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	8.0	h	160.01	ng/mL	No	160.0100	160.01	160.0100	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	10.0	h	156.2	ng/mL	No	156.2000	156.20	156.2000	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	12.0	h	152.85	ng/mL	No	152.8500	152.85	152.8500	No	-	No	-
VST-004	40 mg QD	A1	AZD9291	2	1	24.0	h	236.89	ng/mL	No	236.8900	236.89	236.8900	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	0.0	h	14.72	ng/mL	No	14.7200	14.72	14.7200	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	1.0	h	14.65	ng/mL	No	14.6500	14.65	14.6500	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	1.5	h	14.33	ng/mL	No	14.3300	14.33	14.3300	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	2.0	h	14.2	ng/mL	No	14.2000	14.20	14.2000	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	4.0	h	14.93	ng/mL	No	14.9300	14.93	14.9300	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	6.0	h	14.9	ng/mL	No	14.9000	14.90	14.9000	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	8.0	h	15.46	ng/mL	No	15.4600	15.46	15.4600	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	10.0	h	15.96	ng/mL	No	15.9600	15.96	15.9600	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	12.0	h	15.31	ng/mL	No	15.3100	15.31	15.3100	No	-	No	-
VST-004	40 mg QD	A1	AZ5104	2	1	24.0	h	14.02	ng/mL	No	14.0200	14.02	14.0200	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	1.0	h	8.33	ng/mL	No	8.3300	8.33	8.3300	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	1.5	h	12.31	ng/mL	No	12.3100	12.31	12.3100	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	2.0	h	15.68	ng/mL	No	15.6800	15.68	15.6800	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	4.0	h	27.43	ng/mL	No	27.4300	27.43	27.4300	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	6.0	h	36.97	ng/mL	No	36.9700	36.97	36.9700	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	8.0	h	45.66	ng/mL	No	45.6600	45.66	45.6600	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	10.0	h	50.15	ng/mL	No	50.1500	50.15	50.1500	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	12.0	h	57.1	ng/mL	No	57.1000	57.10	57.1000	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	24.0	h	68.44	ng/mL	No	68.4400	68.44	68.4400	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	48.0	h	58.62	ng/mL	No	58.6200	58.62	58.6200	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	72.0	h	44.12	ng/mL	No	44.1200	44.12	44.1200	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-005	40 mg QD	A1	AZD9291	0	-6	120.0	h	26.67	ng/mL	No	26.6700	26.67	26.6700	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	0	-6	144.0	h	21.57	ng/mL	No	21.5700	21.57	21.5700	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	1.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	1.5	h	0.04	ng/mL	No	0.0400	0.04	0.0400	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	2.0	h	0.07	ng/mL	No	0.0700	0.07	0.0700	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	4.0	h	0.25	ng/mL	No	0.2500	0.25	0.2500	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	6.0	h	0.53	ng/mL	No	0.5300	0.53	0.5300	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	8.0	h	0.86	ng/mL	No	0.8600	0.86	0.8600	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	10.0	h	1.21	ng/mL	No	1.2100	1.21	1.2100	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	12.0	h	1.64	ng/mL	No	1.6400	1.64	1.6400	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	24.0	h	3.74	ng/mL	No	3.7400	3.74	3.7400	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	48.0	h	5.34	ng/mL	No	5.3400	5.34	5.3400	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	72.0	h	5.55	ng/mL	No	5.5500	5.55	5.5500	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	120.0	h	3.64	ng/mL	No	3.6400	3.64	3.6400	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	0	-6	144.0	h	2.83	ng/mL	No	2.8300	2.83	2.8300	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	1	15	0.0	h	297.6	ng/mL	No	297.6000	297.60	297.6000	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	1	15	2.0	h	320.99	ng/mL	No	320.9900	320.99	320.9900	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	1	15	4.0	h	329.7	ng/mL	No	329.7000	329.70	329.7000	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	1	15	8.0	h	346.15	ng/mL	No	346.1500	346.15	346.1500	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	1	15	0.0	h	34.65	ng/mL	No	34.6500	34.65	34.6500	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	1	15	2.0	h	32.59	ng/mL	No	32.5900	32.59	32.5900	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	1	15	4.0	h	33.7	ng/mL	No	33.7000	33.70	33.7000	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	1	15	8.0	h	32.54	ng/mL	No	32.5400	32.54	32.5400	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	0.0	h	148.27	ng/mL	No	148.2700	148.27	148.2700	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	1.0	h	147.88	ng/mL	No	147.8800	147.88	147.8800	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	1.5	h	146.42	ng/mL	No	146.4200	146.42	146.4200	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	2.0	h	148.26	ng/mL	No	148.2600	148.26	148.2600	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	4.0	h	139.58	ng/mL	No	139.5800	139.58	139.5800	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	6.0	h	148.12	ng/mL	No	148.1200	148.12	148.1200	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	8.0	h	136.59	ng/mL	No	136.5900	136.59	136.5900	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	10.0	h	133.74	ng/mL	No	133.7400	133.74	133.7400	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	12.0	h	130.54	ng/mL	No	130.5400	130.54	130.5400	No	-	No	-
VST-005	40 mg QD	A1	AZD9291	2	1	24.0	h	115.04	ng/mL	No	115.0400	115.04	115.0400	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	0.0	h	20.44	ng/mL	No	20.4400	20.44	20.4400	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	1.0	h	19.96	ng/mL	No	19.9600	19.96	19.9600	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	1.5	h	19.57	ng/mL	No	19.5700	19.57	19.5700	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	2.0	h	19.81	ng/mL	No	19.8100	19.81	19.8100	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	4.0	h	19.82	ng/mL	No	19.8200	19.82	19.8200	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	6.0	h	19.09	ng/mL	No	19.0900	19.09	19.0900	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	8.0	h	18.65	ng/mL	No	18.6500	18.65	18.6500	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	10.0	h	18.6	ng/mL	No	18.6000	18.60	18.6000	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	12.0	h	18.74	ng/mL	No	18.7400	18.74	18.7400	No	-	No	-
VST-005	40 mg QD	A1	AZ5104	2	1	24.0	h	15.93	ng/mL	No	15.9300	15.93	15.9300	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-006	40 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	1.0	h	1.07	ng/mL	No	1.0700	1.07	1.0700	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	1.5	h	1.57	ng/mL	No	1.5700	1.57	1.5700	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	2.0	h	2.02	ng/mL	No	2.0200	2.02	2.0200	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	4.0	h	3.6	ng/mL	No	3.6000	3.60	3.6000	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	6.0	h	4.72	ng/mL	No	4.7200	4.72	4.7200	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	8.0	h	5.4	ng/mL	No	5.4000	5.40	5.4000	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	10.0	h	6.45	ng/mL	No	6.4500	6.45	6.4500	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	12.0	h	6.89	ng/mL	No	6.8900	6.89	6.8900	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	24.0	h	8.79	ng/mL	No	8.7900	8.79	8.7900	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	48.0	h	8.63	ng/mL	No	8.6300	8.63	8.6300	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	72.0	h	8.32	ng/mL	No	8.3200	8.32	8.3200	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	120.0	h	7.43	ng/mL	No	7.4300	7.43	7.4300	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	0	-6	144.0	h	6.72	ng/mL	No	6.7200	6.72	6.7200	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	1.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	1.5	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	2.0	h	0.04	ng/mL	No	0.0400	0.04	0.0400	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	4.0	h	0.11	ng/mL	No	0.1100	0.11	0.1100	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	6.0	h	0.22	ng/mL	No	0.2200	0.22	0.2200	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	8.0	h	0.32	ng/mL	No	0.3200	0.32	0.3200	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	10.0	h	0.44	ng/mL	No	0.4400	0.44	0.4400	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	12.0	h	0.51	ng/mL	No	0.5100	0.51	0.5100	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	24.0	h	0.77	ng/mL	No	0.7700	0.77	0.7700	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	48.0	h	0.89	ng/mL	No	0.8900	0.89	0.8900	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	72.0	h	0.82	ng/mL	No	0.8200	0.82	0.8200	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	120.0	h	0.76	ng/mL	No	0.7600	0.76	0.7600	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	0	-6	144.0	h	0.69	ng/mL	No	0.6900	0.69	0.6900	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	1	15	0.0	h	95.46	ng/mL	No	95.4600	95.46	95.4600	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	1	15	2.0	h	97.3	ng/mL	No	97.3000	97.30	97.3000	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	1	15	4.0	h	97.6	ng/mL	No	97.6000	97.60	97.6000	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	1	15	8.0	h	96.39	ng/mL	No	96.3900	96.39	96.3900	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	1	15	0.0	h	9.41	ng/mL	No	9.4100	9.41	9.4100	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	1	15	2.0	h	9.05	ng/mL	No	9.0500	9.05	9.0500	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	1	15	4.0	h	9.58	ng/mL	No	9.5800	9.58	9.5800	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	1	15	8.0	h	9.36	ng/mL	No	9.3600	9.36	9.3600	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	2	1	0.0	h	121.54	ng/mL	No	121.5400	121.54	121.5400	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	2	1	1.0	h	114.66	ng/mL	No	114.6600	114.66	114.6600	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	2	1	1.5	h	123.43	ng/mL	No	123.4300	123.43	123.4300	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	2	1	2.0	h	122.72	ng/mL	No	122.7200	122.72	122.7200	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	2	1	4.0	h	120.04	ng/mL	No	120.0400	120.04	120.0400	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	2	1	6.0	h	126.82	ng/mL	No	126.8200	126.82	126.8200	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-006	40 mg QD	A1	AZD9291	2	1	8.0	h	122.88	ng/mL	No	122.8800	122.88	122.8800	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	2	1	10.0	h	120.68	ng/mL	No	120.6800	120.68	120.6800	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	2	1	12.0	h	125	ng/mL	No	125.0000	125.00	125.0000	No	-	No	-
VST-006	40 mg QD	A1	AZD9291	2	1	24.0	h	121.53	ng/mL	No	121.5300	121.53	121.5300	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	0.0	h	11.55	ng/mL	No	11.5500	11.55	11.5500	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	1.0	h	12.11	ng/mL	No	12.1100	12.11	12.1100	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	1.5	h	11.47	ng/mL	No	11.4700	11.47	11.4700	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	2.0	h	11.42	ng/mL	No	11.4200	11.42	11.4200	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	4.0	h	11.98	ng/mL	No	11.9800	11.98	11.9800	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	6.0	h	11.63	ng/mL	No	11.6300	11.63	11.6300	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	8.0	h	12.16	ng/mL	No	12.1600	12.16	12.1600	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	10.0	h	12.52	ng/mL	No	12.5200	12.52	12.5200	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	12.0	h	12.49	ng/mL	No	12.4900	12.49	12.4900	No	-	No	-
VST-006	40 mg QD	A1	AZ5104	2	1	24.0	h	12.09	ng/mL	No	12.0900	12.09	12.0900	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	1.0	h	51.43	ng/mL	No	51.4300	51.43	51.4300	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	1.5	h	61.77	ng/mL	No	61.7700	61.77	61.7700	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	2.0	h	66.04	ng/mL	No	66.0400	66.04	66.0400	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	4.0	h	67.57	ng/mL	No	67.5700	67.57	67.5700	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	6.0	h	68.37	ng/mL	No	68.3700	68.37	68.3700	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	8.0	h	67.33	ng/mL	No	67.3300	67.33	67.3300	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	10.0	h	66.5	ng/mL	No	66.5000	66.50	66.5000	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	12.0	h	63.66	ng/mL	No	63.6600	63.66	63.6600	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	24.0	h	52.54	ng/mL	No	52.5400	52.54	52.5400	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	48.0	h	38.38	ng/mL	No	38.3800	38.38	38.3800	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	72.0	h	27.78	ng/mL	No	27.7800	27.78	27.7800	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	120.0	h	14.19	ng/mL	No	14.1900	14.19	14.1900	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	0	-6	144.0	h	10.11	ng/mL	No	10.1100	10.11	10.1100	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	1.0	h	0.4	ng/mL	No	0.4000	0.40	0.4000	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	1.5	h	0.73	ng/mL	No	0.7300	0.73	0.7300	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	2.0	h	1.11	ng/mL	No	1.1100	1.11	1.1100	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	4.0	h	2.46	ng/mL	No	2.4600	2.46	2.4600	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	6.0	h	3.61	ng/mL	No	3.6100	3.61	3.6100	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	8.0	h	4.08	ng/mL	No	4.0800	4.08	4.0800	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	10.0	h	4.72	ng/mL	No	4.7200	4.72	4.7200	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	12.0	h	5.06	ng/mL	No	5.0600	5.06	5.0600	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	24.0	h	5.23	ng/mL	No	5.2300	5.23	5.2300	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	48.0	h	3.91	ng/mL	No	3.9100	3.91	3.9100	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	72.0	h	2.9	ng/mL	No	2.9000	2.90	2.9000	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	120.0	h	1.49	ng/mL	No	1.4900	1.49	1.4900	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	0	-6	144.0	h	1.06	ng/mL	No	1.0600	1.06	1.0600	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	1	15	0.0	h	187.92	ng/mL	No	187.9200	187.92	187.9200	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	1	15	2.0	h	203.81	ng/mL	No	203.8100	203.81	203.8100	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	1	15	4.0	h	206.99	ng/mL	No	206.9900	206.99	206.9900	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-007	80 mg QD	A1	AZD9291	1	15	8.0	h	205.75	ng/mL	No	205.7500	205.75	205.7500	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	1	15	0.0	h	19.3	ng/mL	No	19.3000	19.30	19.3000	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	1	15	2.0	h	20.01	ng/mL	No	20.0100	20.01	20.0100	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	1	15	4.0	h	19.94	ng/mL	No	19.9400	19.94	19.9400	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	1	15	8.0	h	19.3	ng/mL	No	19.3000	19.30	19.3000	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	0.0	h	103.22	ng/mL	No	103.2200	103.22	103.2200	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	1.0	h	123.84	ng/mL	No	123.8400	123.84	123.8400	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	1.5	h	128.7	ng/mL	No	128.7000	128.70	128.7000	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	2.0	h	128.4	ng/mL	No	128.4000	128.40	128.4000	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	4.0	h	135.34	ng/mL	No	135.3400	135.34	135.3400	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	6.0	h	122.26	ng/mL	No	122.2600	122.26	122.2600	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	8.0	h	128.73	ng/mL	No	128.7300	128.73	128.7300	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	10.0	h	116.61	ng/mL	No	116.6100	116.61	116.6100	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	12.0	h	121.05	ng/mL	No	121.0500	121.05	121.0500	No	-	No	-
VST-007	80 mg QD	A1	AZD9291	2	1	24.0	h	104.19	ng/mL	No	104.1900	104.19	104.1900	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	0.0	h	10.59	ng/mL	No	10.5900	10.59	10.5900	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	1.0	h	10.63	ng/mL	No	10.6300	10.63	10.6300	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	1.5	h	11.11	ng/mL	No	11.1100	11.11	11.1100	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	2.0	h	10.83	ng/mL	No	10.8300	10.83	10.8300	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	4.0	h	11.08	ng/mL	No	11.0800	11.08	11.0800	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	6.0	h	11.75	ng/mL	No	11.7500	11.75	11.7500	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	8.0	h	11.96	ng/mL	No	11.9600	11.96	11.9600	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	10.0	h	11.87	ng/mL	No	11.8700	11.87	11.8700	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	12.0	h	11.88	ng/mL	No	11.8800	11.88	11.8800	No	-	No	-
VST-007	80 mg QD	A1	AZ5104	2	1	24.0	h	10.4	ng/mL	No	10.4000	10.40	10.4000	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	1.0	h	18.1	ng/mL	No	18.1000	18.10	18.1000	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	1.5	h	24.27	ng/mL	No	24.2700	24.27	24.2700	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	2.0	h	33.32	ng/mL	No	33.3200	33.32	33.3200	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	4.0	h	50.34	ng/mL	No	50.3400	50.34	50.3400	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	6.0	h	59.07	ng/mL	No	59.0700	59.07	59.0700	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	8.0	h	62.78	ng/mL	No	62.7800	62.78	62.7800	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	10.0	h	66.84	ng/mL	No	66.8400	66.84	66.8400	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	12.0	h	69.22	ng/mL	No	69.2200	69.22	69.2200	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	24.0	h	61.76	ng/mL	No	61.7600	61.76	61.7600	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	48.0	h	43.37	ng/mL	No	43.3700	43.37	43.3700	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	72.0	h	30.93	ng/mL	No	30.9300	30.93	30.9300	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	120.0	h	16.44	ng/mL	No	16.4400	16.44	16.4400	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	0	-6	144.0	h	11.57	ng/mL	No	11.5700	11.57	11.5700	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	1.0	h	0.14	ng/mL	No	0.1400	0.14	0.1400	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	1.5	h	0.29	ng/mL	No	0.2900	0.29	0.2900	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	2.0	h	0.5	ng/mL	No	0.5000	0.50	0.5000	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	4.0	h	1.53	ng/mL	No	1.5300	1.53	1.5300	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	6.0	h	2.54	ng/mL	No	2.5400	2.54	2.5400	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-008	80 mg QD	A1	AZ5104	0	-6	8.0	h	3.42	ng/mL	No	3.4200	3.42	3.4200	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	10.0	h	4.39	ng/mL	No	4.3900	4.39	4.3900	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	12.0	h	4.88	ng/mL	No	4.8800	4.88	4.8800	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	24.0	h	5.84	ng/mL	No	5.8400	5.84	5.8400	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	48.0	h	4.55	ng/mL	No	4.5500	4.55	4.5500	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	72.0	h	3.25	ng/mL	No	3.2500	3.25	3.2500	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	120.0	h	1.72	ng/mL	No	1.7200	1.72	1.7200	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	0	-6	144.0	h	1.33	ng/mL	No	1.3300	1.33	1.3300	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	1	15	0.0	h	217.87	ng/mL	No	217.8700	217.87	217.8700	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	1	15	2.0	h	241.25	ng/mL	No	241.2500	241.25	241.2500	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	1	15	4.0	h	246.73	ng/mL	No	246.7300	246.73	246.7300	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	1	15	8.0	h	269.22	ng/mL	No	269.2200	269.22	269.2200	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	1	15	0.0	h	22.53	ng/mL	No	22.5300	22.53	22.5300	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	1	15	2.0	h	21.81	ng/mL	No	21.8100	21.81	21.8100	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	1	15	4.0	h	22.78	ng/mL	No	22.7800	22.78	22.7800	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	1	15	8.0	h	22.95	ng/mL	No	22.9500	22.95	22.9500	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	0.0	h	213.05	ng/mL	No	213.0500	213.05	213.0500	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	1.0	h	226.41	ng/mL	No	226.4100	226.41	226.4100	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	1.5	h	232.21	ng/mL	No	232.2100	232.21	232.2100	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	2.0	h	238.97	ng/mL	No	238.9700	238.97	238.9700	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	4.0	h	255.53	ng/mL	No	255.5300	255.53	255.5300	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	6.0	h	257.06	ng/mL	No	257.0600	257.06	257.0600	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	8.0	h	266.96	ng/mL	No	266.9600	266.96	266.9600	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	10.0	h	247.98	ng/mL	No	247.9800	247.98	247.9800	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	12.0	h	257.52	ng/mL	No	257.5200	257.52	257.5200	No	-	No	-
VST-008	80 mg QD	A1	AZD9291	2	1	24.0	h	214.74	ng/mL	No	214.7400	214.74	214.7400	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	0.0	h	21.61	ng/mL	No	21.6100	21.61	21.6100	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	1.0	h	21.71	ng/mL	No	21.7100	21.71	21.7100	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	1.5	h	21.85	ng/mL	No	21.8500	21.85	21.8500	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	2.0	h	22.11	ng/mL	No	22.1100	22.11	22.1100	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	4.0	h	21.82	ng/mL	No	21.8200	21.82	21.8200	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	6.0	h	23.4	ng/mL	No	23.4000	23.40	23.4000	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	8.0	h	24.1	ng/mL	No	24.1000	24.10	24.1000	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	10.0	h	24.69	ng/mL	No	24.6900	24.69	24.6900	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	12.0	h	23.37	ng/mL	No	23.3700	23.37	23.3700	No	-	No	-
VST-008	80 mg QD	A1	AZ5104	2	1	24.0	h	22.29	ng/mL	No	22.2900	22.29	22.2900	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	1.0	h	14.64	ng/mL	No	14.6400	14.64	14.6400	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	1.5	h	21.19	ng/mL	No	21.1900	21.19	21.1900	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	2.0	h	26.79	ng/mL	No	26.7900	26.79	26.7900	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	4.0	h	46.59	ng/mL	No	46.5900	46.59	46.5900	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	6.0	h	61.94	ng/mL	No	61.9400	61.94	61.9400	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	8.0	h	72.41	ng/mL	No	72.4100	72.41	72.4100	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	10.0	h	78.42	ng/mL	No	78.4200	78.42	78.4200	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	12.0	h	88.72	ng/mL	No	88.7200	88.72	88.7200	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	24.0	h	87.65	ng/mL	No	87.6500	87.65	87.6500	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-009	80 mg QD	A1	AZD9291	0	-6	48.0	h	62.62	ng/mL	No	62.6200	62.62	62.6200	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	72.0	h	41.1	ng/mL	No	41.1000	41.10	41.1000	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	120.0	h	16.96	ng/mL	No	16.9600	16.96	16.9600	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	0	-6	144.0	h	11.1	ng/mL	No	11.1000	11.10	11.1000	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	1.0	h	0.08	ng/mL	No	0.0800	0.08	0.0800	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	1.5	h	0.18	ng/mL	No	0.1800	0.18	0.1800	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	2.0	h	0.31	ng/mL	No	0.3100	0.31	0.3100	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	4.0	h	1.03	ng/mL	No	1.0300	1.03	1.0300	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	6.0	h	2.06	ng/mL	No	2.0600	2.06	2.0600	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	8.0	h	3.15	ng/mL	No	3.1500	3.15	3.1500	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	10.0	h	3.96	ng/mL	No	3.9600	3.96	3.9600	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	12.0	h	4.91	ng/mL	No	4.9100	4.91	4.9100	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	24.0	h	7.77	ng/mL	No	7.7700	7.77	7.7700	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	48.0	h	6.96	ng/mL	No	6.9600	6.96	6.9600	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	72.0	h	4.75	ng/mL	No	4.7500	4.75	4.7500	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	120.0	h	1.99	ng/mL	No	1.9900	1.99	1.9900	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	0	-6	144.0	h	1.28	ng/mL	No	1.2800	1.28	1.2800	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	1	15	0.0	h	278.01	ng/mL	No	278.0100	278.01	278.0100	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	1	15	2.0	h	294.85	ng/mL	No	294.8500	294.85	294.8500	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	1	15	4.0	h	313.15	ng/mL	No	313.1500	313.15	313.1500	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	1	15	8.0	h	320.08	ng/mL	No	320.0800	320.08	320.0800	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	1	15	0.0	h	27.87	ng/mL	No	27.8700	27.87	27.8700	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	1	15	2.0	h	28.2	ng/mL	No	28.2000	28.20	28.2000	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	1	15	4.0	h	27.09	ng/mL	No	27.0900	27.09	27.0900	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	1	15	8.0	h	28.47	ng/mL	No	28.4700	28.47	28.4700	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	0.0	h	265.77	ng/mL	No	265.7700	265.77	265.7700	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	1.0	h	287.37	ng/mL	No	287.3700	287.37	287.3700	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	1.5	h	276.75	ng/mL	No	276.7500	276.75	276.7500	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	2.0	h	299.28	ng/mL	No	299.2800	299.28	299.2800	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	4.0	h	313.37	ng/mL	No	313.3700	313.37	313.3700	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	6.0	h	309.69	ng/mL	No	309.6900	309.69	309.6900	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	8.0	h	308.62	ng/mL	No	308.6200	308.62	308.6200	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	10.0	h	313.51	ng/mL	No	313.5100	313.51	313.5100	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	12.0	h	312.96	ng/mL	No	312.9600	312.96	312.9600	No	-	No	-
VST-009	80 mg QD	A1	AZD9291	2	1	24.0	h	-	ng/mL	No	-	265.77	265.7700	No	-	Yes	Copied concentration from C2 D1 H0.
VST-009	80 mg QD	A1	AZ5104	2	1	0.0	h	28.89	ng/mL	No	28.8900	28.89	28.8900	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	2	1	1.0	h	27.75	ng/mL	No	27.7500	27.75	27.7500	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	2	1	1.5	h	26.66	ng/mL	No	26.6600	26.66	26.6600	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	2	1	2.0	h	27.22	ng/mL	No	27.2200	27.22	27.2200	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	2	1	4.0	h	29.32	ng/mL	No	29.3200	29.32	29.3200	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	2	1	6.0	h	29.89	ng/mL	No	29.8900	29.89	29.8900	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	2	1	8.0	h	27.88	ng/mL	No	27.8800	27.88	27.8800	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	2	1	10.0	h	29.71	ng/mL	No	29.7100	29.71	29.7100	No	-	No	-
VST-009	80 mg QD	A1	AZ5104	2	1	12.0	h	29.32	ng/mL	No	29.3200	29.32	29.3200	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-009	80 mg QD	A1	AZ5104	2	1	24.0	h	-	ng/mL	No	-	28.89	28.8900	No	-	Yes	Copied concentration from C2 D1 H0.
VST-010	80 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	1.0	h	126	ng/mL	No	126.0000	126.00	126.0000	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	1.5	h	158.5	ng/mL	No	158.5000	158.50	158.5000	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	2.0	h	183.5	ng/mL	No	183.5000	183.50	183.5000	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	4.0	h	220.14	ng/mL	No	220.1400	220.14	220.1400	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	6.0	h	221.92	ng/mL	No	221.9200	221.92	221.9200	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	8.0	h	215.45	ng/mL	No	215.4500	215.45	215.4500	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	10.0	h	214.86	ng/mL	No	214.8600	214.86	214.8600	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	12.0	h	202.76	ng/mL	No	202.7600	202.76	202.7600	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	24.0	h	174.43	ng/mL	No	174.4300	174.43	174.4300	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	48.0	h	126.86	ng/mL	No	126.8600	126.86	126.8600	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	72.0	h	93.16	ng/mL	No	93.1600	93.16	93.1600	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	120.0	h	52.87	ng/mL	No	52.8700	52.87	52.8700	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	0	-6	144.0	h	38.51	ng/mL	No	38.5100	38.51	38.5100	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	1.0	h	0.15	ng/mL	No	0.1500	0.15	0.1500	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	1.5	h	0.3	ng/mL	No	0.3000	0.30	0.3000	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	2.0	h	0.48	ng/mL	No	0.4800	0.48	0.4800	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	4.0	h	1.28	ng/mL	No	1.2800	1.28	1.2800	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	6.0	h	2.15	ng/mL	No	2.1500	2.15	2.1500	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	8.0	h	3.02	ng/mL	No	3.0200	3.02	3.0200	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	10.0	h	3.76	ng/mL	No	3.7600	3.76	3.7600	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	12.0	h	4.54	ng/mL	No	4.5400	4.54	4.5400	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	24.0	h	7.86	ng/mL	No	7.8600	7.86	7.8600	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	48.0	h	10.83	ng/mL	No	10.8300	10.83	10.8300	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	72.0	h	10.96	ng/mL	No	10.9600	10.96	10.9600	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	120.0	h	8.58	ng/mL	No	8.5800	8.58	8.5800	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	0	-6	144.0	h	6.74	ng/mL	No	6.7400	6.74	6.7400	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	1	15	0.0	h	647.35	ng/mL	No	647.3500	647.35	647.3500	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	1	15	2.0	h	833.55	ng/mL	No	833.5500	833.55	833.5500	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	1	15	4.0	h	841.24	ng/mL	No	841.2400	841.24	841.2400	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	1	15	8.0	h	801.11	ng/mL	No	801.1100	801.11	801.1100	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	1	15	0.0	h	75.08	ng/mL	No	75.0800	75.08	75.0800	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	1	15	2.0	h	78.17	ng/mL	No	78.1700	78.17	78.1700	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	1	15	4.0	h	73.8	ng/mL	No	73.8000	73.80	73.8000	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	1	15	8.0	h	79.45	ng/mL	No	79.4500	79.45	79.4500	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	2	1	0.0	h	362.78	ng/mL	No	362.7800	362.78	362.7800	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	2	1	1.0	h	480.57	ng/mL	No	480.5700	480.57	480.5700	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	2	1	1.5	h	515.27	ng/mL	No	515.2700	515.27	515.2700	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	2	1	2.0	h	536.02	ng/mL	No	536.0200	536.02	536.0200	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	2	1	4.0	h	568.87	ng/mL	No	568.8700	568.87	568.8700	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	2	1	6.0	h	555.3	ng/mL	No	555.3000	555.30	555.3000	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-010	80 mg QD	A1	AZD9291	2	1	8.0	h	537.95	ng/mL	No	537.9500	537.95	537.9500	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	2	1	10.0	h	534.93	ng/mL	No	534.9300	534.93	534.9300	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	2	1	12.0	h	508.93	ng/mL	No	508.9300	508.93	508.9300	No	-	No	-
VST-010	80 mg QD	A1	AZD9291	2	1	24.0	h	443.92	ng/mL	No	443.9200	443.92	443.9200	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	0.0	h	60.23	ng/mL	No	60.2300	60.23	60.2300	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	1.0	h	58.4	ng/mL	No	58.4000	58.40	58.4000	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	1.5	h	60.64	ng/mL	No	60.6400	60.64	60.6400	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	2.0	h	59.86	ng/mL	No	59.8600	59.86	59.8600	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	4.0	h	58.14	ng/mL	No	58.1400	58.14	58.1400	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	6.0	h	58.57	ng/mL	No	58.5700	58.57	58.5700	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	8.0	h	58.03	ng/mL	No	58.0300	58.03	58.0300	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	10.0	h	62.36	ng/mL	No	62.3600	62.36	62.3600	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	12.0	h	57.48	ng/mL	No	57.4800	57.48	57.4800	No	-	No	-
VST-010	80 mg QD	A1	AZ5104	2	1	24.0	h	54.26	ng/mL	No	54.2600	54.26	54.2600	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	1.0	h	9.06	ng/mL	No	9.0600	9.06	9.0600	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	1.5	h	13.26	ng/mL	No	13.2600	13.26	13.2600	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	2.0	h	17.3	ng/mL	No	17.3000	17.30	17.3000	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	4.0	h	30.13	ng/mL	No	30.1300	30.13	30.1300	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	6.0	h	40.35	ng/mL	No	40.3500	40.35	40.3500	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	8.0	h	48.3	ng/mL	No	48.3000	48.30	48.3000	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	10.0	h	53.77	ng/mL	No	53.7700	53.77	53.7700	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	12.0	h	53.98	ng/mL	No	53.9800	53.98	53.9800	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	24.0	h	65.02	ng/mL	No	65.0200	65.02	65.0200	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	48.0	h	54.83	ng/mL	No	54.8300	54.83	54.8300	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	72.0	h	43.43	ng/mL	No	43.4300	43.43	43.4300	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	120.0	h	25.19	ng/mL	No	25.1900	25.19	25.1900	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	0	-6	144.0	h	20.43	ng/mL	No	20.4300	20.43	20.4300	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	1.0	h	0.05	ng/mL	No	0.0500	0.05	0.0500	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	1.5	h	0.12	ng/mL	No	0.1200	0.12	0.1200	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	2.0	h	0.2	ng/mL	No	0.2000	0.20	0.2000	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	4.0	h	0.69	ng/mL	No	0.6900	0.69	0.6900	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	6.0	h	1.28	ng/mL	No	1.2800	1.28	1.2800	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	8.0	h	1.93	ng/mL	No	1.9300	1.93	1.9300	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	10.0	h	2.63	ng/mL	No	2.6300	2.63	2.6300	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	12.0	h	3.37	ng/mL	No	3.3700	3.37	3.3700	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	24.0	h	5.61	ng/mL	No	5.6100	5.61	5.6100	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	48.0	h	5.66	ng/mL	No	5.6600	5.66	5.6600	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	72.0	h	4.69	ng/mL	No	4.6900	4.69	4.6900	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	120.0	h	2.81	ng/mL	No	2.8100	2.81	2.8100	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	0	-6	144.0	h	2.19	ng/mL	No	2.1900	2.19	2.1900	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	1	15	0.0	h	295.06	ng/mL	No	295.0600	295.06	295.0600	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	1	15	2.0	h	323.04	ng/mL	No	323.0400	323.04	323.0400	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	1	15	4.0	h	318.91	ng/mL	No	318.9100	318.91	318.9100	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-011	80 mg QD	A1	AZD9291	1	15	8.0	h	331.6	ng/mL	No	331.6000	331.60	331.6000	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	1	15	0.0	h	31.35	ng/mL	No	31.3500	31.35	31.3500	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	1	15	2.0	h	30.99	ng/mL	No	30.9900	30.99	30.9900	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	1	15	4.0	h	30.64	ng/mL	No	30.6400	30.64	30.6400	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	1	15	8.0	h	31.65	ng/mL	No	31.6500	31.65	31.6500	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	2	1	0.0	h	-	ng/mL	No	-	310.87	310.8700	No	-	Yes	Copied concentration from C2 D1 H24.
VST-011	80 mg QD	A1	AZD9291	2	1	1.0	h	335.9	ng/mL	No	335.9000	335.90	335.9000	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	2	1	1.5	h	317.86	ng/mL	No	317.8600	317.86	317.8600	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	2	1	2.0	h	314.11	ng/mL	No	314.1100	314.11	314.1100	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	2	1	4.0	h	333.36	ng/mL	No	333.3600	333.36	333.3600	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	2	1	6.0	h	340.12	ng/mL	No	340.1200	340.12	340.1200	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	2	1	8.0	h	352.88	ng/mL	No	352.8800	352.88	352.8800	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	2	1	10.0	h	345.88	ng/mL	No	345.8800	345.88	345.8800	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	2	1	12.0	h	327.61	ng/mL	No	327.6100	327.61	327.6100	No	-	No	-
VST-011	80 mg QD	A1	AZD9291	2	1	24.0	h	310.87	ng/mL	No	310.8700	310.87	310.8700	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	2	1	0.0	h	-	ng/mL	No	-	32.66	32.6600	No	-	Yes	Copied concentration from C2 D1 H24.
VST-011	80 mg QD	A1	AZ5104	2	1	1.0	h	30.69	ng/mL	No	30.6900	30.69	30.6900	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	2	1	1.5	h	31.49	ng/mL	No	31.4900	31.49	31.4900	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	2	1	2.0	h	31.79	ng/mL	No	31.7900	31.79	31.7900	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	2	1	4.0	h	31.91	ng/mL	No	31.9100	31.91	31.9100	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	2	1	6.0	h	31.79	ng/mL	No	31.7900	31.79	31.7900	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	2	1	8.0	h	31	ng/mL	No	31.0000	31.00	31.0000	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	2	1	10.0	h	32.49	ng/mL	No	32.4900	32.49	32.4900	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	2	1	12.0	h	33	ng/mL	No	33.0000	33.00	33.0000	No	-	No	-
VST-011	80 mg QD	A1	AZ5104	2	1	24.0	h	32.66	ng/mL	No	32.6600	32.66	32.6600	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	1.0	h	101.53	ng/mL	No	101.5300	101.53	101.5300	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	1.5	h	153.64	ng/mL	No	153.6400	153.64	153.6400	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	2.0	h	188.37	ng/mL	No	188.3700	188.37	188.3700	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	4.0	h	281.67	ng/mL	No	281.6700	281.67	281.6700	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	6.0	h	348.82	ng/mL	No	348.8200	348.82	348.8200	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	8.0	h	369.95	ng/mL	No	369.9500	369.95	369.9500	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	10.0	h	366.48	ng/mL	No	366.4800	366.48	366.4800	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	12.0	h	352.71	ng/mL	No	352.7100	352.71	352.7100	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	24.0	h	230.36	ng/mL	No	230.3600	230.36	230.3600	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	48.0	h	87.15	ng/mL	No	87.1500	87.15	87.1500	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	72.0	h	32.48	ng/mL	No	32.4800	32.48	32.4800	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	120.0	h	4.92	ng/mL	No	4.9200	4.92	4.9200	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	0	-6	144.0	h	1.85	ng/mL	No	1.8500	1.85	1.8500	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	1.0	h	0.84	ng/mL	No	0.8400	0.84	0.8400	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	1.5	h	1.71	ng/mL	No	1.7100	1.71	1.7100	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-012	80 mg QD	A1	AZ5104	0	-6	2.0	h	2.78	ng/mL	No	2.7800	2.78	2.7800	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	4.0	h	9	ng/mL	No	9.0000	9.00	9.0000	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	6.0	h	15.34	ng/mL	No	15.3400	15.34	15.3400	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	8.0	h	21.12	ng/mL	No	21.1200	21.12	21.1200	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	10.0	h	24.14	ng/mL	No	24.1400	24.14	24.1400	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	12.0	h	27.92	ng/mL	No	27.9200	27.92	27.9200	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	24.0	h	27.14	ng/mL	No	27.1400	27.14	27.1400	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	48.0	h	12.1	ng/mL	No	12.1000	12.10	12.1000	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	72.0	h	4.59	ng/mL	No	4.5900	4.59	4.5900	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	120.0	h	0.63	ng/mL	No	0.6300	0.63	0.6300	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	0	-6	144.0	h	0.25	ng/mL	No	0.2500	0.25	0.2500	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	1	15	0.0	h	386.16	ng/mL	No	386.1600	386.16	386.1600	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	1	15	2.0	h	520.61	ng/mL	No	520.6100	520.61	520.6100	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	1	15	4.0	h	603.8	ng/mL	No	603.8000	603.80	603.8000	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	1	15	8.0	h	625.59	ng/mL	No	625.5900	625.59	625.5900	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	1	15	0.0	h	45.71	ng/mL	No	45.7100	45.71	45.7100	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	1	15	2.0	h	48.05	ng/mL	No	48.0500	48.05	48.0500	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	1	15	4.0	h	50.81	ng/mL	No	50.8100	50.81	50.8100	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	1	15	8.0	h	57.8	ng/mL	No	57.8000	57.80	57.8000	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	0.0	h	367.92	ng/mL	No	367.9200	367.92	367.9200	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	1.0	h	473.04	ng/mL	No	473.0400	473.04	473.0400	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	1.5	h	509.12	ng/mL	No	509.1200	509.12	509.1200	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	2.0	h	524.79	ng/mL	No	524.7900	524.79	524.7900	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	4.0	h	597.11	ng/mL	No	597.1100	597.11	597.1100	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	6.0	h	630.31	ng/mL	No	630.3100	630.31	630.3100	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	8.0	h	635.07	ng/mL	No	635.0700	635.07	635.0700	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	10.0	h	585.32	ng/mL	No	585.3200	585.32	585.3200	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	12.0	h	569.84	ng/mL	No	569.8400	569.84	569.8400	No	-	No	-
VST-012	80 mg QD	A1	AZD9291	2	1	24.0	h	370.1	ng/mL	No	370.1000	370.10	370.1000	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	0.0	h	47.62	ng/mL	No	47.6200	47.62	47.6200	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	1.0	h	45.38	ng/mL	No	45.3800	45.38	45.3800	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	1.5	h	47.84	ng/mL	No	47.8400	47.84	47.8400	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	2.0	h	48.43	ng/mL	No	48.4300	48.43	48.4300	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	4.0	h	49.79	ng/mL	No	49.7900	49.79	49.7900	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	6.0	h	51.91	ng/mL	No	51.9100	51.91	51.9100	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	8.0	h	57.36	ng/mL	No	57.3600	57.36	57.3600	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	10.0	h	61.91	ng/mL	No	61.9100	61.91	61.9100	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	12.0	h	59.56	ng/mL	No	59.5600	59.56	59.5600	No	-	No	-
VST-012	80 mg QD	A1	AZ5104	2	1	24.0	h	46.4	ng/mL	No	46.4000	46.40	46.4000	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	1.0	h	33.93	ng/mL	No	33.9300	33.93	33.9300	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	1.5	h	51.68	ng/mL	No	51.6800	51.68	51.6800	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	2.0	h	67.39	ng/mL	No	67.3900	67.39	67.3900	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	4.0	h	125.46	ng/mL	No	125.4600	125.46	125.4600	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	6.0	h	166.23	ng/mL	No	166.2300	166.23	166.2300	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	8.0	h	198.93	ng/mL	No	198.9300	198.93	198.9300	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-013	160 mg QD	A1	AZD9291	0	-6	10.0	h	237.47	ng/mL	No	237.4700	237.47	237.4700	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	12.0	h	259.54	ng/mL	No	259.5400	259.54	259.5400	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	24.0	h	303.62	ng/mL	No	303.6200	303.62	303.6200	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	48.0	h	237.07	ng/mL	No	237.0700	237.07	237.0700	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	72.0	h	146.15	ng/mL	No	146.1500	146.15	146.1500	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	120.0	h	46.45	ng/mL	No	46.4500	46.45	46.4500	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	0	-6	144.0	h	27.28	ng/mL	No	27.2800	27.28	27.2800	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	1.0	h	0.37	ng/mL	No	0.3700	0.37	0.3700	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	1.5	h	0.8	ng/mL	No	0.8000	0.80	0.8000	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	2.0	h	1.34	ng/mL	No	1.3400	1.34	1.3400	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	4.0	h	4.31	ng/mL	No	4.3100	4.31	4.3100	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	6.0	h	8.15	ng/mL	No	8.1500	8.15	8.1500	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	8.0	h	12.1	ng/mL	No	12.1000	12.10	12.1000	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	10.0	h	15.4	ng/mL	No	15.4000	15.40	15.4000	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	12.0	h	18.98	ng/mL	No	18.9800	18.98	18.9800	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	24.0	h	29.99	ng/mL	No	29.9900	29.99	29.9900	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	48.0	h	25.63	ng/mL	No	25.6300	25.63	25.6300	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	72.0	h	15.94	ng/mL	No	15.9400	15.94	15.9400	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	120.0	h	5.2	ng/mL	No	5.2000	5.20	5.2000	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	0	-6	144.0	h	2.93	ng/mL	No	2.9300	2.93	2.9300	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	1	15	0.0	h	613.88	ng/mL	No	613.8800	613.88	613.8800	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	1	15	2.0	h	615.15	ng/mL	No	615.1500	615.15	615.1500	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	1	15	4.0	h	631.56	ng/mL	No	631.5600	631.56	631.5600	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	1	15	8.0	h	616.04	ng/mL	No	616.0400	616.04	616.0400	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	1	15	0.0	h	64.36	ng/mL	No	64.3600	64.36	64.3600	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	1	15	2.0	h	63.62	ng/mL	No	63.6200	63.62	63.6200	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	1	15	4.0	h	62.01	ng/mL	No	62.0100	62.01	62.0100	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	1	15	8.0	h	64.17	ng/mL	No	64.1700	64.17	64.1700	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	0.0	h	880.61	ng/mL	No	880.6100	880.61	880.6100	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	1.0	h	904.4	ng/mL	No	904.4000	904.40	904.4000	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	1.5	h	928.21	ng/mL	No	928.2100	928.21	928.2100	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	2.0	h	908.7	ng/mL	No	908.7000	908.70	908.7000	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	4.0	h	960.68	ng/mL	No	960.6800	960.68	960.6800	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	6.0	h	950.48	ng/mL	No	950.4800	950.48	950.4800	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	8.0	h	955.62	ng/mL	No	955.6200	955.62	955.6200	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	10.0	h	955.98	ng/mL	No	955.9800	955.98	955.9800	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	12.0	h	970.75	ng/mL	No	970.7500	970.75	970.7500	No	-	No	-
VST-013	160 mg QD	A1	AZD9291	2	1	24.0	h	865.86	ng/mL	No	865.8600	865.86	865.8600	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	2	1	0.0	h	90.96	ng/mL	No	90.9600	90.96	90.9600	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	2	1	1.0	h	93.35	ng/mL	No	93.3500	93.35	93.3500	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	2	1	1.5	h	96.19	ng/mL	No	96.1900	96.19	96.1900	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	2	1	2.0	h	89.74	ng/mL	No	89.7400	89.74	89.7400	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	2	1	4.0	h	91.41	ng/mL	No	91.4100	91.41	91.4100	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	2	1	6.0	h	93.5	ng/mL	No	93.5000	93.50	93.5000	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	2	1	8.0	h	96.51	ng/mL	No	96.5100	96.51	96.5100	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	2	1	10.0	h	94.03	ng/mL	No	94.0300	94.03	94.0300	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-013	160 mg QD	A1	AZ5104	2	1	12.0	h	95.82	ng/mL	No	95.8200	95.82	95.8200	No	-	No	-
VST-013	160 mg QD	A1	AZ5104	2	1	24.0	h	93.22	ng/mL	No	93.2200	93.22	93.2200	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	1.0	h	26.47	ng/mL	No	26.4700	26.47	26.4700	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	1.5	h	39.12	ng/mL	No	39.1200	39.12	39.1200	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	2.0	h	46.56	ng/mL	No	46.5600	46.56	46.5600	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	4.0	h	84.12	ng/mL	No	84.1200	84.12	84.1200	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	6.0	h	112.98	ng/mL	No	112.9800	112.98	112.9800	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	8.0	h	133.52	ng/mL	No	133.5200	133.52	133.5200	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	10.0	h	148.21	ng/mL	No	148.2100	148.21	148.2100	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	12.0	h	149.57	ng/mL	No	149.5700	149.57	149.5700	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	24.0	h	173.56	ng/mL	No	173.5600	173.56	173.5600	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	48.0	h	162.48	ng/mL	No	162.4800	162.48	162.4800	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	72.0	h	151.64	ng/mL	No	151.6400	151.64	151.6400	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	120.0	h	121.07	ng/mL	No	121.0700	121.07	121.0700	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	0	-6	144.0	h	110.99	ng/mL	No	110.9900	110.99	110.9900	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	1.0	h	0.08	ng/mL	No	0.0800	0.08	0.0800	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	1.5	h	0.17	ng/mL	No	0.1700	0.17	0.1700	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	2.0	h	0.29	ng/mL	No	0.2900	0.29	0.2900	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	4.0	h	1.02	ng/mL	No	1.0200	1.02	1.0200	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	6.0	h	1.95	ng/mL	No	1.9500	1.95	1.9500	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	8.0	h	3.31	ng/mL	No	3.3100	3.31	3.3100	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	10.0	h	4.36	ng/mL	No	4.3600	4.36	4.3600	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	12.0	h	5.71	ng/mL	No	5.7100	5.71	5.7100	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	24.0	h	11.8	ng/mL	No	11.8000	11.80	11.8000	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	48.0	h	16.07	ng/mL	No	16.0700	16.07	16.0700	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	72.0	h	16.45	ng/mL	No	16.4500	16.45	16.4500	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	120.0	h	13.5	ng/mL	No	13.5000	13.50	13.5000	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	0	-6	144.0	h	12.87	ng/mL	No	12.8700	12.87	12.8700	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	1	15	0.0	h	1535.2	ng/mL	No	1535.2000	1535.20	1535.2000	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	1	15	2.0	h	1562.74	ng/mL	No	1562.7400	1562.74	1562.7400	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	1	15	4.0	h	1564.13	ng/mL	No	1564.1300	1564.13	1564.1300	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	1	15	8.0	h	1600.35	ng/mL	No	1600.3500	1600.35	1600.3500	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	1	15	0.0	h	159.84	ng/mL	No	159.8400	159.84	159.8400	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	1	15	2.0	h	161.08	ng/mL	No	161.0800	161.08	161.0800	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	1	15	4.0	h	157.85	ng/mL	No	157.8500	157.85	157.8500	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	1	15	8.0	h	162.82	ng/mL	No	162.8200	162.82	162.8200	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	2	1	0.0	h	1748.62	ng/mL	No	1748.6200	1748.62	1748.6200	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	2	1	1.0	h	1769.89	ng/mL	No	1769.8900	1769.89	1769.8900	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	2	1	1.5	h	1745.86	ng/mL	No	1745.8600	1745.86	1745.8600	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	2	1	2.0	h	1801.69	ng/mL	No	1801.6900	1801.69	1801.6900	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	2	1	4.0	h	1748.73	ng/mL	No	1748.7300	1748.73	1748.7300	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	2	1	6.0	h	1788.2	ng/mL	No	1788.2000	1788.20	1788.2000	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	2	1	8.0	h	1870.08	ng/mL	No	1870.0800	1870.08	1870.0800	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-014	160 mg QD	A1	AZD9291	2	1	10.0	h	1755.43	ng/mL	No	1755.4300	1755.43	1755.4300	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	2	1	12.0	h	1813.19	ng/mL	No	1813.1900	1813.19	1813.1900	No	-	No	-
VST-014	160 mg QD	A1	AZD9291	2	1	24.0	h	1739.89	ng/mL	No	1739.8900	1739.89	1739.8900	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	0.0	h	179.17	ng/mL	No	179.1700	179.17	179.1700	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	1.0	h	192.04	ng/mL	No	192.0400	192.04	192.0400	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	1.5	h	184	ng/mL	No	184.0000	184.00	184.0000	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	2.0	h	185.89	ng/mL	No	185.8900	185.89	185.8900	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	4.0	h	189.5	ng/mL	No	189.5000	189.50	189.5000	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	6.0	h	186.21	ng/mL	No	186.2100	186.21	186.2100	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	8.0	h	183.56	ng/mL	No	183.5600	183.56	183.5600	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	10.0	h	183.14	ng/mL	No	183.1400	183.14	183.1400	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	12.0	h	198.02	ng/mL	No	198.0200	198.02	198.0200	No	-	No	-
VST-014	160 mg QD	A1	AZ5104	2	1	24.0	h	190.31	ng/mL	No	190.3100	190.31	190.3100	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	1.0	h	25.43	ng/mL	No	25.4300	25.43	25.4300	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	1.5	h	37.42	ng/mL	No	37.4200	37.42	37.4200	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	2.0	h	46.24	ng/mL	No	46.2400	46.24	46.2400	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	4.0	h	87.19	ng/mL	No	87.1900	87.19	87.1900	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	6.0	h	116.16	ng/mL	No	116.1600	116.16	116.1600	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	8.0	h	132.45	ng/mL	No	132.4500	132.45	132.4500	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	10.0	h	144.76	ng/mL	No	144.7600	144.76	144.7600	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	12.0	h	161.38	ng/mL	No	161.3800	161.38	161.3800	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	24.0	h	188.48	ng/mL	No	188.4800	188.48	188.4800	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	48.0	h	192.85	ng/mL	No	192.8500	192.85	192.8500	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	72.0	h	185.03	ng/mL	No	185.0300	185.03	185.0300	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	120.0	h	169.69	ng/mL	No	169.6900	169.69	169.6900	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	0	-6	144.0	h	162.01	ng/mL	No	162.0100	162.01	162.0100	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	1.0	h	0.07	ng/mL	No	0.0700	0.07	0.0700	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	1.5	h	0.14	ng/mL	No	0.1400	0.14	0.1400	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	2.0	h	0.24	ng/mL	No	0.2400	0.24	0.2400	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	4.0	h	0.86	ng/mL	No	0.8600	0.86	0.8600	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	6.0	h	1.76	ng/mL	No	1.7600	1.76	1.7600	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	8.0	h	2.79	ng/mL	No	2.7900	2.79	2.7900	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	10.0	h	3.97	ng/mL	No	3.9700	3.97	3.9700	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	12.0	h	4.74	ng/mL	No	4.7400	4.74	4.7400	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	24.0	h	10.83	ng/mL	No	10.8300	10.83	10.8300	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	48.0	h	17.97	ng/mL	No	17.9700	17.97	17.9700	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	72.0	h	19.91	ng/mL	No	19.9100	19.91	19.9100	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	120.0	h	18.94	ng/mL	No	18.9400	18.94	18.9400	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	0	-6	144.0	h	17.64	ng/mL	No	17.6400	17.64	17.6400	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	1	15	2.0	h	2077.92	ng/mL	No	2077.9200	2077.92	2077.9200	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	1	15	4.0	h	2232.17	ng/mL	No	2232.1700	2232.17	2232.1700	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	1	15	8.0	h	2318.15	ng/mL	No	2318.1500	2318.15	2318.1500	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	1	15	2.0	h	224.56	ng/mL	No	224.5600	224.56	224.5600	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-015	160 mg QD	A1	AZ5104	1	15	4.0	h	235.67	ng/mL	No	235.6700	235.67	235.6700	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	1	15	8.0	h	239.61	ng/mL	No	239.6100	239.61	239.6100	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	2	1	0.0	h	2705.29	ng/mL	No	2705.2900	2705.29	2705.2900	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	2	1	1.0	h	2702.98	ng/mL	No	2702.9800	2702.98	2702.9800	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	2	1	1.5	h	2703.43	ng/mL	No	2703.4300	2703.43	2703.4300	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	2	1	2.0	h	2610.7	ng/mL	No	2610.7000	2610.70	2610.7000	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	2	1	4.0	h	2611.7	ng/mL	No	2611.7000	2611.70	2611.7000	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	2	1	6.0	h	2705.66	ng/mL	No	2705.6600	2705.66	2705.6600	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	2	1	8.0	h	2586.08	ng/mL	No	2586.0800	2586.08	2586.0800	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	2	1	10.0	h	2687.59	ng/mL	No	2687.5900	2687.59	2687.5900	No	-	No	-
VST-015	160 mg QD	A1	AZD9291	2	1	12.0	h	2580.38	ng/mL	No	2580.3800	2580.38	2580.3800	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	2	1	0.0	h	288.57	ng/mL	No	288.5700	288.57	288.5700	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	2	1	1.0	h	291.56	ng/mL	No	291.5600	291.56	291.5600	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	2	1	1.5	h	305.14	ng/mL	No	305.1400	305.14	305.1400	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	2	1	2.0	h	297.52	ng/mL	No	297.5200	297.52	297.5200	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	2	1	4.0	h	287.21	ng/mL	No	287.2100	287.21	287.2100	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	2	1	6.0	h	291.2	ng/mL	No	291.2000	291.20	291.2000	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	2	1	8.0	h	295.82	ng/mL	No	295.8200	295.82	295.8200	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	2	1	10.0	h	286.06	ng/mL	No	286.0600	286.06	286.0600	No	-	No	-
VST-015	160 mg QD	A1	AZ5104	2	1	12.0	h	298.03	ng/mL	No	298.0300	298.03	298.0300	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	1.0	h	0.94	ng/mL	No	0.9400	0.94	0.9400	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	1.5	h	1.35	ng/mL	No	1.3500	1.35	1.3500	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	2.0	h	1.78	ng/mL	No	1.7800	1.78	1.7800	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	4.0	h	3.41	ng/mL	No	3.4100	3.41	3.4100	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	6.0	h	4.7	ng/mL	No	4.7000	4.70	4.7000	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	8.0	h	6.1	ng/mL	No	6.1000	6.10	6.1000	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	10.0	h	7.51	ng/mL	No	7.5100	7.51	7.5100	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	12.0	h	8.45	ng/mL	No	8.4500	8.45	8.4500	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	24.0	h	13.35	ng/mL	No	13.3500	13.35	13.3500	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	48.0	h	17.14	ng/mL	No	17.1400	17.14	17.1400	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	72.0	h	18.49	ng/mL	No	18.4900	18.49	18.4900	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	120.0	h	18.69	ng/mL	No	18.6900	18.69	18.6900	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	0	-6	144.0	h	17.98	ng/mL	No	17.9800	17.98	17.9800	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	1.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	1.5	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	2.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	4.0	h	0.04	ng/mL	No	0.0400	0.04	0.0400	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	6.0	h	0.09	ng/mL	No	0.0900	0.09	0.0900	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-016	160 mg QD	A1	AZ5104	0	-6	8.0	h	0.15	ng/mL	No	0.1500	0.15	0.1500	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	10.0	h	0.23	ng/mL	No	0.2300	0.23	0.2300	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	12.0	h	0.29	ng/mL	No	0.2900	0.29	0.2900	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	24.0	h	0.81	ng/mL	No	0.8100	0.81	0.8100	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	48.0	h	1.48	ng/mL	No	1.4800	1.48	1.4800	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	72.0	h	1.77	ng/mL	No	1.7700	1.77	1.7700	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	120.0	h	1.95	ng/mL	No	1.9500	1.95	1.9500	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	0	-6	144.0	h	1.87	ng/mL	No	1.8700	1.87	1.8700	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	1	15	0.0	h	251.26	ng/mL	No	251.2600	251.26	251.2600	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	1	15	2.0	h	251.47	ng/mL	No	251.4700	251.47	251.4700	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	1	15	4.0	h	265.25	ng/mL	No	265.2500	265.25	265.2500	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	1	15	8.0	h	262.92	ng/mL	No	262.9200	262.92	262.9200	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	1	15	0.0	h	25.53	ng/mL	No	25.5300	25.53	25.5300	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	1	15	2.0	h	25.56	ng/mL	No	25.5600	25.56	25.5600	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	1	15	4.0	h	25.11	ng/mL	No	25.1100	25.11	25.1100	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	1	15	8.0	h	25.68	ng/mL	No	25.6800	25.68	25.6800	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	0.0	h	345.96	ng/mL	No	345.9600	345.96	345.9600	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	1.0	h	348.23	ng/mL	No	348.2300	348.23	348.2300	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	1.5	h	356.25	ng/mL	No	356.2500	356.25	356.2500	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	2.0	h	360.52	ng/mL	No	360.5200	360.52	360.5200	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	4.0	h	348.5	ng/mL	No	348.5000	348.50	348.5000	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	6.0	h	353.73	ng/mL	No	353.7300	353.73	353.7300	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	8.0	h	358.12	ng/mL	No	358.1200	358.12	358.1200	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	10.0	h	353.81	ng/mL	No	353.8100	353.81	353.8100	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	12.0	h	349.71	ng/mL	No	349.7100	349.71	349.7100	No	-	No	-
VST-016	160 mg QD	A1	AZD9291	2	1	24.0	h	359.01	ng/mL	No	359.0100	359.01	359.0100	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	0.0	h	34.49	ng/mL	No	34.4900	34.49	34.4900	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	1.0	h	34.14	ng/mL	No	34.1400	34.14	34.1400	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	1.5	h	34.96	ng/mL	No	34.9600	34.96	34.9600	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	2.0	h	35.92	ng/mL	No	35.9200	35.92	35.9200	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	4.0	h	34.82	ng/mL	No	34.8200	34.82	34.8200	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	6.0	h	35.81	ng/mL	No	35.8100	35.81	35.8100	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	8.0	h	36.04	ng/mL	No	36.0400	36.04	36.0400	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	10.0	h	35.55	ng/mL	No	35.5500	35.55	35.5500	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	12.0	h	35.76	ng/mL	No	35.7600	35.76	35.7600	No	-	No	-
VST-016	160 mg QD	A1	AZ5104	2	1	24.0	h	36.46	ng/mL	No	36.4600	36.46	36.4600	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	1.0	h	48.17	ng/mL	No	48.1700	48.17	48.1700	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	1.5	h	65.66	ng/mL	No	65.6600	65.66	65.6600	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	2.0	h	83.36	ng/mL	No	83.3600	83.36	83.3600	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	4.0	h	127.26	ng/mL	No	127.2600	127.26	127.2600	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	6.0	h	143.85	ng/mL	No	143.8500	143.85	143.8500	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	8.0	h	140.19	ng/mL	No	140.1900	140.19	140.1900	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	10.0	h	133.62	ng/mL	No	133.6200	133.62	133.6200	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	12.0	h	113.19	ng/mL	No	113.1900	113.19	113.1900	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	24.0	h	43.41	ng/mL	No	43.4100	43.41	43.4100	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	48.0	h	2.68	ng/mL	No	2.6800	2.68	2.6800	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-017	160 mg QD	A1	AZD9291	0	-6	72.0	h	0.13	ng/mL	No	0.1300	0.13	0.1300	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	120.0	h	BLQ	ng/mL	Yes	0.0125	-	0.0125	No	Treat as missing	No	-
VST-017	160 mg QD	A1	AZD9291	0	-6	144.0	h	BLQ	ng/mL	Yes	0.0125	-	0.0125	No	Treat as missing	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	1.0	h	2.32	ng/mL	No	2.3200	2.32	2.3200	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	1.5	h	4.25	ng/mL	No	4.2500	4.25	4.2500	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	2.0	h	5.45	ng/mL	No	5.4500	5.45	5.4500	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	4.0	h	9.94	ng/mL	No	9.9400	9.94	9.9400	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	6.0	h	12.23	ng/mL	No	12.2300	12.23	12.2300	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	8.0	h	12.48	ng/mL	No	12.4800	12.48	12.4800	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	10.0	h	12.33	ng/mL	No	12.3300	12.33	12.3300	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	12.0	h	10.95	ng/mL	No	10.9500	10.95	10.9500	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	24.0	h	4.01	ng/mL	No	4.0100	4.01	4.0100	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	48.0	h	0.26	ng/mL	No	0.2600	0.26	0.2600	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	72.0	h	BLQ	ng/mL	Yes	0.0125	-	0.0125	No	Treat as missing	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	120.0	h	BLQ	ng/mL	Yes	0.0125	-	0.0125	No	Treat as missing	No	-
VST-017	160 mg QD	A1	AZ5104	0	-6	144.0	h	BLQ	ng/mL	Yes	0.0125	-	0.0125	No	Treat as missing	No	-
VST-017	160 mg QD	A1	AZD9291	1	15	0.0	h	44.26	ng/mL	No	44.2600	44.26	44.2600	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	1	15	2.0	h	122.25	ng/mL	No	122.2500	122.25	122.2500	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	1	15	4.0	h	152.01	ng/mL	No	152.0100	152.01	152.0100	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	1	15	8.0	h	164.44	ng/mL	No	164.4400	164.44	164.4400	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	1	15	0.0	h	4.18	ng/mL	No	4.1800	4.18	4.1800	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	1	15	2.0	h	8.96	ng/mL	No	8.9600	8.96	8.9600	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	1	15	4.0	h	12.96	ng/mL	No	12.9600	12.96	12.9600	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	1	15	8.0	h	14.49	ng/mL	No	14.4900	14.49	14.4900	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	0.0	h	45.41	ng/mL	No	45.4100	45.41	45.4100	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	1.0	h	87.78	ng/mL	No	87.7800	87.78	87.7800	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	1.5	h	102.33	ng/mL	No	102.3300	102.33	102.3300	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	2.0	h	117	ng/mL	No	117.0000	117.00	117.0000	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	4.0	h	162.39	ng/mL	No	162.3900	162.39	162.3900	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	6.0	h	166.54	ng/mL	No	166.5400	166.54	166.5400	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	8.0	h	160.34	ng/mL	No	160.3400	160.34	160.3400	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	10.0	h	154.7	ng/mL	No	154.7000	154.70	154.7000	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	12.0	h	132.98	ng/mL	No	132.9800	132.98	132.9800	No	-	No	-
VST-017	160 mg QD	A1	AZD9291	2	1	24.0	h	46.34	ng/mL	No	46.3400	46.34	46.3400	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	0.0	h	4.17	ng/mL	No	4.1700	4.17	4.1700	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	1.0	h	6.04	ng/mL	No	6.0400	6.04	6.0400	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	1.5	h	7.52	ng/mL	No	7.5200	7.52	7.5200	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	2.0	h	9.19	ng/mL	No	9.1900	9.19	9.1900	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	4.0	h	12.63	ng/mL	No	12.6300	12.63	12.6300	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	6.0	h	15.06	ng/mL	No	15.0600	15.06	15.0600	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	8.0	h	14.47	ng/mL	No	14.4700	14.47	14.4700	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	10.0	h	13.72	ng/mL	No	13.7200	13.72	13.7200	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	12.0	h	12.35	ng/mL	No	12.3500	12.35	12.3500	No	-	No	-
VST-017	160 mg QD	A1	AZ5104	2	1	24.0	h	4.26	ng/mL	No	4.2600	4.26	4.2600	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-018	160 mg QD	A1	AZD9291	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	1.0	h	76.89	ng/mL	No	76.8900	76.89	76.8900	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	1.5	h	101	ng/mL	No	101.0000	101.00	101.0000	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	2.0	h	128.59	ng/mL	No	128.5900	128.59	128.5900	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	4.0	h	196.15	ng/mL	No	196.1500	196.15	196.1500	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	6.0	h	227.49	ng/mL	No	227.4900	227.49	227.4900	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	8.0	h	257.36	ng/mL	No	257.3600	257.36	257.3600	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	10.0	h	244.97	ng/mL	No	244.9700	244.97	244.9700	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	12.0	h	244.81	ng/mL	No	244.8100	244.81	244.8100	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	24.0	h	195.04	ng/mL	No	195.0400	195.04	195.0400	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	48.0	h	111.44	ng/mL	No	111.4400	111.44	111.4400	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	72.0	h	63.31	ng/mL	No	63.3100	63.31	63.3100	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	120.0	h	20.3	ng/mL	No	20.3000	20.30	20.3000	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	0	-6	144.0	h	12.24	ng/mL	No	12.2400	12.24	12.2400	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	0.0	h	BLQ	ng/mL	Yes	0.0125	0.00	0.0000	Yes	Single dose before measureable concentration	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	1.0	h	0.27	ng/mL	No	0.2700	0.27	0.2700	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	1.5	h	0.59	ng/mL	No	0.5900	0.59	0.5900	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	2.0	h	1	ng/mL	No	1.0000	1.00	1.0000	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	4.0	h	3.13	ng/mL	No	3.1300	3.13	3.1300	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	6.0	h	5.93	ng/mL	No	5.9300	5.93	5.9300	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	8.0	h	8.39	ng/mL	No	8.3900	8.39	8.3900	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	10.0	h	10.7	ng/mL	No	10.7000	10.70	10.7000	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	12.0	h	12.84	ng/mL	No	12.8400	12.84	12.8400	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	24.0	h	18.3	ng/mL	No	18.3000	18.30	18.3000	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	48.0	h	13.9	ng/mL	No	13.9000	13.90	13.9000	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	72.0	h	8.82	ng/mL	No	8.8200	8.82	8.8200	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	120.0	h	2.89	ng/mL	No	2.8900	2.89	2.8900	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	0	-6	144.0	h	1.68	ng/mL	No	1.6800	1.68	1.6800	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	1	15	0.0	h	462.14	ng/mL	No	462.1400	462.14	462.1400	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	1	15	2.0	h	549.95	ng/mL	No	549.9500	549.95	549.9500	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	1	15	4.0	h	641.35	ng/mL	No	641.3500	641.35	641.3500	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	1	15	8.0	h	611.11	ng/mL	No	611.1100	611.11	611.1100	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	1	15	0.0	h	52.8	ng/mL	No	52.8000	52.80	52.8000	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	1	15	2.0	h	53.76	ng/mL	No	53.7600	53.76	53.7600	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	1	15	4.0	h	55.14	ng/mL	No	55.1400	55.14	55.1400	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	1	15	8.0	h	53.8	ng/mL	No	53.8000	53.80	53.8000	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	2	1	0.0	h	412.51	ng/mL	No	412.5100	412.51	412.5100	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	2	1	1.0	h	488.5	ng/mL	No	488.5000	488.50	488.5000	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	2	1	1.5	h	514.63	ng/mL	No	514.6300	514.63	514.6300	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	2	1	2.0	h	537.27	ng/mL	No	537.2700	537.27	537.2700	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	2	1	4.0	h	602.04	ng/mL	No	602.0400	602.04	602.0400	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	2	1	6.0	h	608.11	ng/mL	No	608.1100	608.11	608.1100	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	2	1	8.0	h	608.56	ng/mL	No	608.5600	608.56	608.5600	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	2	1	10.0	h	624.45	ng/mL	No	624.4500	624.45	624.4500	No	-	No	-
VST-018	160 mg QD	A1	AZD9291	2	1	12.0	h	581.48	ng/mL	No	581.4800	581.48	581.4800	No	-	No	-

Table C.1.1 Final PK data. *(continued)*

Subject	Dose cohort	Sub-ject part	Analyte	Cycle	Day	Nominal time post dose	Time unit	Measured Conc	Conc Unit	BLQ	Conc (visualisation)	Conc (NCA analysis)	Conc (NCA visualisation)	BLQ handling?	Details of BLQ handling	Conc manually modified?	Details of Modification
VST-018	160 mg QD	A1	AZD9291	2	1	24.0	h	432.92	ng/mL	No	432.9200	432.92	432.9200	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	0.0	h	46.88	ng/mL	No	46.8800	46.88	46.8800	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	1.0	h	50.82	ng/mL	No	50.8200	50.82	50.8200	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	1.5	h	48.79	ng/mL	No	48.7900	48.79	48.7900	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	2.0	h	47.37	ng/mL	No	47.3700	47.37	47.3700	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	4.0	h	48.73	ng/mL	No	48.7300	48.73	48.7300	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	6.0	h	51.6	ng/mL	No	51.6000	51.60	51.6000	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	8.0	h	52.36	ng/mL	No	52.3600	52.36	52.3600	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	10.0	h	50.82	ng/mL	No	50.8200	50.82	50.8200	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	12.0	h	51.57	ng/mL	No	51.5700	51.57	51.5700	No	-	No	-
VST-018	160 mg QD	A1	AZ5104	2	1	24.0	h	49.57	ng/mL	No	49.5700	49.57	49.5700	No	-	No	-

D Validation

Validation tests were performed on 2024-11-13 15:51:39.824173 on PKNCA version 0.11.0. Session infomation and R version information are given below.

D.1 Validation session infomation

- R version 4.4.1 (2024-06-14 ucrt), `x86_64-w64-mingw32`
- Locale: `LC_COLLATE=English_United Kingdom.utf8`, `LC_CTYPE=English_United Kingdom.utf8`, `LC_MONETARY=English_United Kingdom.utf8`, `LC_NUMERIC=C`, `LC_TIME=English_United Kingdom.utf8`
- Time zone: `Europe/London`
- TZcode source: `internal`
- Running under: `Windows 10 x64 (build 19045)`
- Matrix products: default
- Base packages: base, datasets, graphics, grDevices, methods, stats, utils
- Other packages: dplyr 1.1.4, forcats 1.0.0, ggplot2 3.5.1, here 1.0.1, kableExtra 1.4.0, lubridate 1.9.3, PKNCA 0.11.0, purrr 1.0.2, readr 2.1.5, rlang 1.1.4, stringr 1.5.1, testthat 3.2.1.1, tibble 3.2.1, tidyr 1.3.1, tidyverse 2.0.0
- Loaded via a namespace (and not attached): backports 1.5.0, brio 1.1.5, checkmate 2.3.2, cli 3.6.3, colorspace 2.1-1, compiler 4.4.1, desc 1.4.3, digest 0.6.37, evaluate 1.0.1, fansi 1.0.6, fastmap 1.2.0, generics 0.1.3, glue 1.8.0, grid 4.4.1, gtable 0.3.6, hms 1.1.3, htmltools 0.5.8.1, knitr 1.49, lattice 0.22-6, lifecycle 1.0.4, magrittr 2.0.3, munsell 0.5.1, nlme 3.1-166, parallel 4.4.1, pillar 1.9.0, pkgconfig 2.0.3, R6 2.5.1, Rcpp 1.0.13, rmarkdown 2.28, rprojroot 2.0.4, rstudioapi 0.17.1, scales 1.3.0, stringi 1.8.4, svglite 2.1.3, systemfonts 1.1.0, tidyselect 1.2.1, timechange 0.3.0, tools 4.4.1, tzdb 0.4.0, units 0.8-5, utf8 1.2.4, vctrs 0.6.5, viridisLite 0.4.2, waldo 0.6.1, withr 3.0.2, xfun 0.48, xml2 1.3.6

D.2 R version infomation

Table D.2.1 Details of R version utilised.

Description	Value
platform	x86_64-w64-mingw32
arch	x86_64
os	mingw32
crt	ucrt
system	x86_64, mingw32
status	
major	4
minor	4.1
year	2024
month	06
day	14
svn rev	86737
language	R
version.string	R version 4.4.1 (2024-06-14 ucrt)
nickname	Race for Your Life

D.3 PKNCA Package Validation

Installation of the PKNCA package was performed using the “testthat” package in R. A summary of PKNCA package test results are provided in Table D.3.1. All tests passed successfully.

Table D.3.1 Summary of PKNCA package tests.

Failed	Warning	Skipped	Passed
0	0	0	1639

D.4 PKNCA Calculation Validation

Internal tests were performed to validate PKNCA calculations using first principle methods on a theophylline dataset. Results of the tests are provided in Table D.4.1.

Table D.4.1 Details of PKNCA calculation tests.

Parameter	Expected Value	Calculated Value	Outcome
Half Life (hr)	7.99	7.99	Pass
AUClast (hr.mg/L)	98.7	98.7	Pass
AUC0-24 (hr.mg/L)	98.3	98.3	Pass
AUC0-Inf (hr.mg/L)	115	115	Pass
Cl (L/hr.kg)	0.0398	0.0398	Pass
V (L/kg)	0.458	0.458	Pass