Pharmaceutical Development

Claire Patterson
Senior Principal Scientist, Seda Pharmaceutical Development Services
Biopharmaceutics in Complex Parenteral Formulation Design

November 2020
Patient Centric Formulation Design

Traditional PK

Optimise PK and Biodistribution to Maximise Therapeutic Index

Biopharmaceutics in Complex Parenteral Formulation Design
Complex Medicines in Oncology

'Small' molecules

Biologics

Complex Medicines

Complex APIs

Complex Formulation

Complex RoD

mAbs, recombinant proteins, vaccines etc.

RoD = route of delivery
ASOs = Antisense oligonucleotides
siRNA = small interfering RNA
ADCs = antibody-drug conjugates

'Naked' siRNA
ASOs
Synthetic proteins/ peptides
Complex Medicines in Oncology

Complex Medicines

- 'Small' molecules
- Biologics

- Complex API (conjugated to targeting moeity)
  - Dendrimers, glatiramoids, polymeric conjugates, ADCs, oligo conjugates, GalNAc-siRNA conjugates

- Complex Formulation
  - Nanomeds e.g. liposomes, polymeric/solid-lipid/inorganic NPs, polymersomes, micelles, nanocrystals, colloids, microbubbles, other carriers (e.g. chitosan-based), albumin-bound agents, extracellular vesicles (exosomes, microvesicles)

- Complex RoD
  - Non-systemic site of action including intratumoural injection, targeted therapies

'Naked' siRNA
ASOs
Synthetic proteins/peptides

mAbs, recombinant proteins, vaccines etc.

RoD = route of delivery
ASOs = Antisense oligonucleotides
siRNA = small interfering RNA
ADCs = antibody-drug conjugates
Nanomedicines

Drug chemically linked to a carrier

Drug encapsulated in a carrier

Drug-Polymer Conjugates

Dendrimers

Antibody Drug Conjugates

Micelles

Liposomes

Polymeric nanoparticles

Inorganic nanoparticles

Lipid nanoparticles

Polymersomes
Nanoparticles for Biophysical Targeting: Critical Quality Attributes

- Size
- Opsonisation potential
- API Release rate

Liver
RES
Tumor
Kidney
<=10 um
Patients Prefer Subcutaneous Trastuzumab Administration in HER2-Positive Metastatic Breast Cancer

European Journal of Cancer

TAKE-HOME MESSAGE

- This randomized study was designed to evaluate patients’ preference of subcutaneous or intravenous trastuzumab for the management of metastatic, HER2-positive breast cancer. The subcutaneous formulation was preferred by 85.9% of patients vs. 14.1% who preferred the intravenous formulation (P < 0.001). Toxicity was consistent with the known safety profile.

- The definitive preference for subcutaneous trastuzumab is consistent with what has been previously reported in patients with early-stage breast cancer.

— Neil Majithia, MD

<table>
<thead>
<tr>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient convenience – less chair time</td>
<td>Bleeding risk in patients with low platelet counts</td>
</tr>
<tr>
<td>Less time and manipulation from Pharmacy</td>
<td>Sites of admin need to be rotated</td>
</tr>
<tr>
<td>Less nurse administration time – i.e., more patients treated</td>
<td>Max injection volume is limited to ~2ml, multiple injections per dose may be required</td>
</tr>
<tr>
<td>Potential for home administration</td>
<td>Injection site reactions/allergic reaction</td>
</tr>
<tr>
<td>Potential for improved safety profile</td>
<td></td>
</tr>
</tbody>
</table>

Biopharmaceutics in Complex Parenteral Formulation Design
Biopharmaceutics Challenges

- Biopharm tools for SC formulations are in their infancy compared with oral delivery
- Preclinical to clinical and cross species translation of SC bioavailability/absorption rate is poor
- In vitro release models are often non compendial, lack guidance, poorly predictive
- In vitro in vivo correlation is challenging

Active research efforts ongoing to develop novel biorelevant in vitro methods and mechanistic in silico models to improve IVIVR and enable smarter formulation and in-vivo study design

Seda Pharmaceutical Development Services® is the business name and registered trademark of SEDA Pharma Development Services Ltd, a company incorporated in England and Wales with registered number: 9442533 and registered office: 3 Castlebrook Close, Unsworth, Bury, Lancashire, UK, BL9 8JE. © Copyright 2015-2017