

PHARMACOKINETICS OF A NOVEL VISCOELASTIC SUSPENSION OF TRASTUZUMAB BIOSIMILAR FOR HIGH-CONCENTRATION, LOW-VOLUME SUBCUTANEOUS INJECTION

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Abstract LB024

Background:

- The proprietary XeriJect™ technology (Xeris Pharmaceuticals, Inc., Chicago, IL, USA) uses a novel viscoelastic suspension for delivery of high-concentration, low-volume subcutaneous (SC) injections of therapeutic antibodies
- Trastuzumab (TmAb) is a monoclonal antibody that selectively binds and inhibits human epidermal growth factor receptor 2 protein (HER2). It is:
 - Widely used to treat certain types of breast, stomach, and esophageal cancer
 - Commercially available for both intravenous (IV) infusion (Herceptin®, Genentech Inc., South San Francisco, CA, USA) [Herceptin IV] and SC injection (Herceptin Hylecta®, Genentech Inc., South San Francisco, CA, USA) [Hylecta SC]
- XeriJect TmAb (XJ TmAb) is a stable formulation of a trastuzumab biosimilar at a higher concentration (432 mg/mL) than Hylecta (120 mg/mL) for SC administration, thus enabling lower injection volumes.

Goal:

This study evaluated the pharmacokinetic profiles of XJ TmAb SC compared with Herceptin IV and Hylecta SC in a preclinical pharmacokinetic model.

Methods:

- 12 female minipigs were administered (n=4 each treatment):

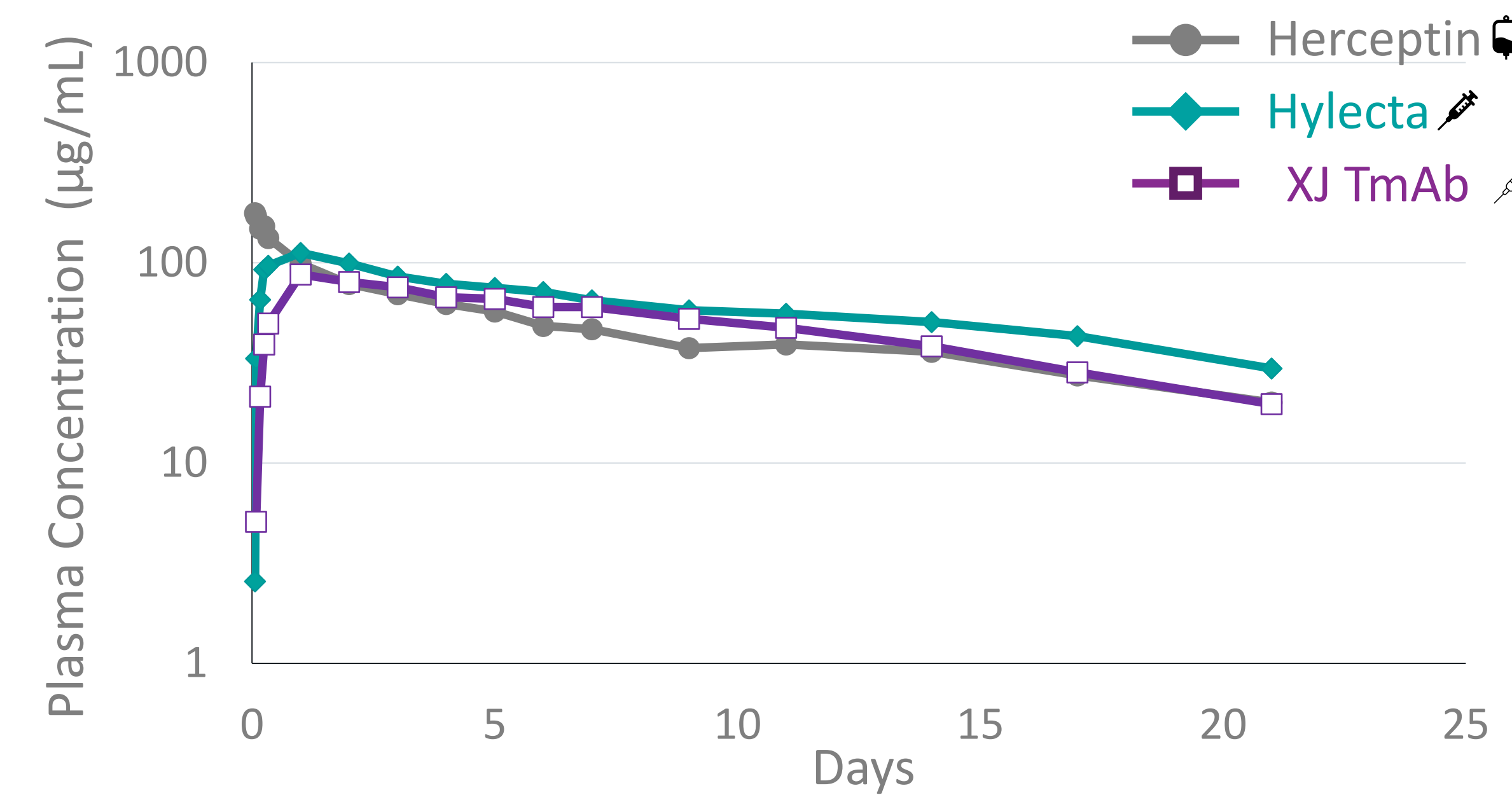
Treatment	Herceptin IV	Hylecta SC	XJ TmAb SC
Route	IV*	SC	SC
Dose conc. (mg/mL)	21	120	431.8
Dose volume	0.48 mg/kg	1 mL	0.28 mL
Dose level	10 mg/kg	120 mg/animal	120 mg/animal

*Administered over 90 minutes

- Plasma collected over 21 days
- Non-compartmental analysis conducted on plasma trastuzumab concentration-time levels using Phoenix software version 8.2.0.4383 (Certara, USA)

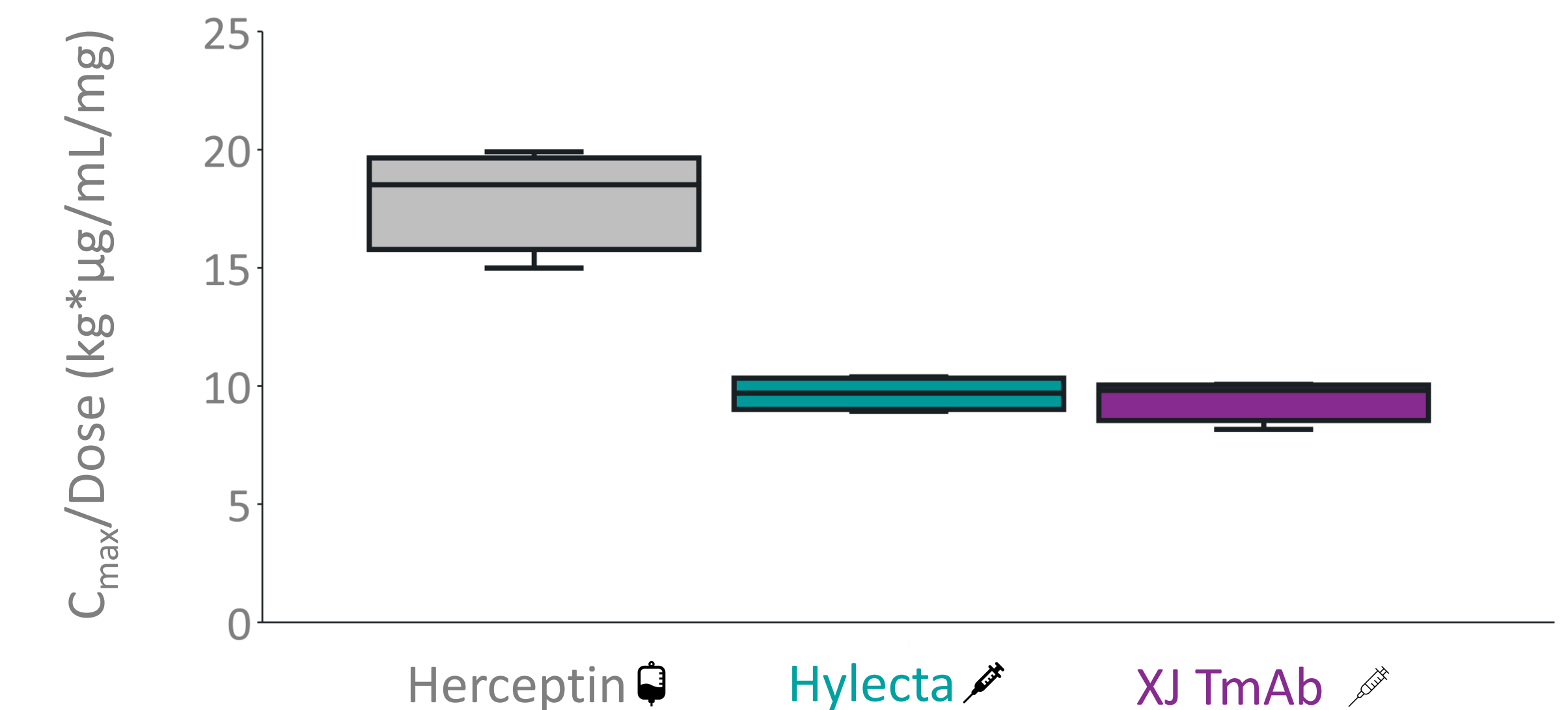
RESULTS

Plasma Trastuzumab Concentration Time-Curve



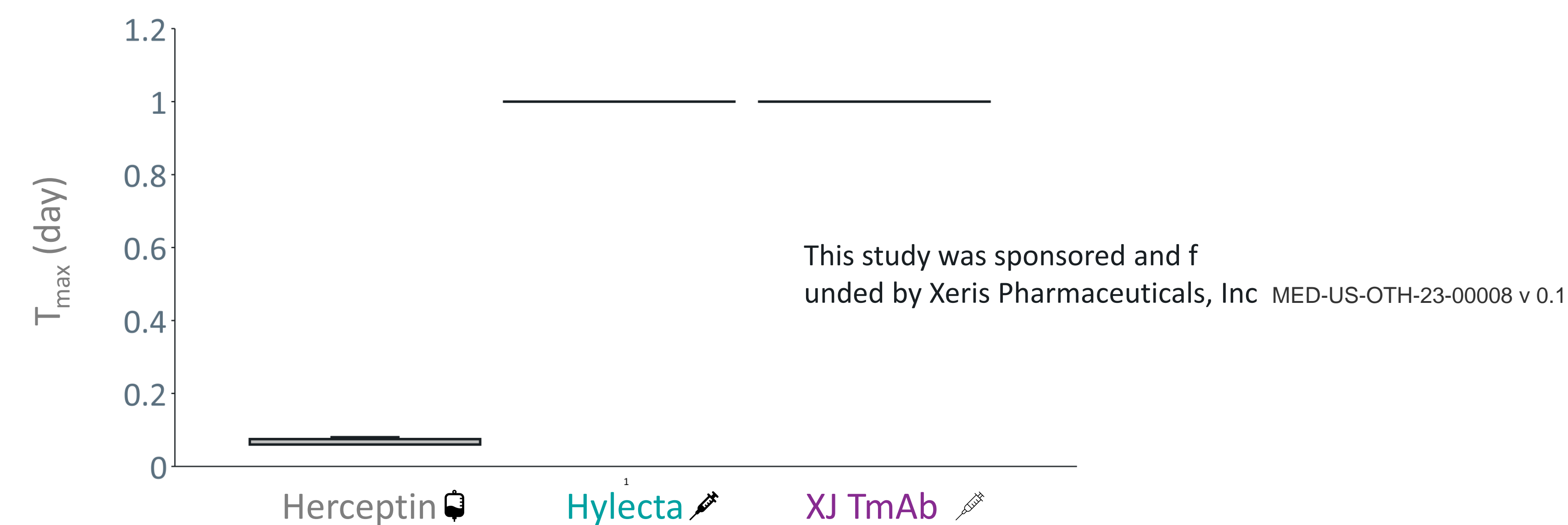
Semi-log scale of mean trastuzumab plasma concentration over time

Maximum Plasma Concentration Relative to Dose Similar Between XJ TmAb and Hylecta Administered SC



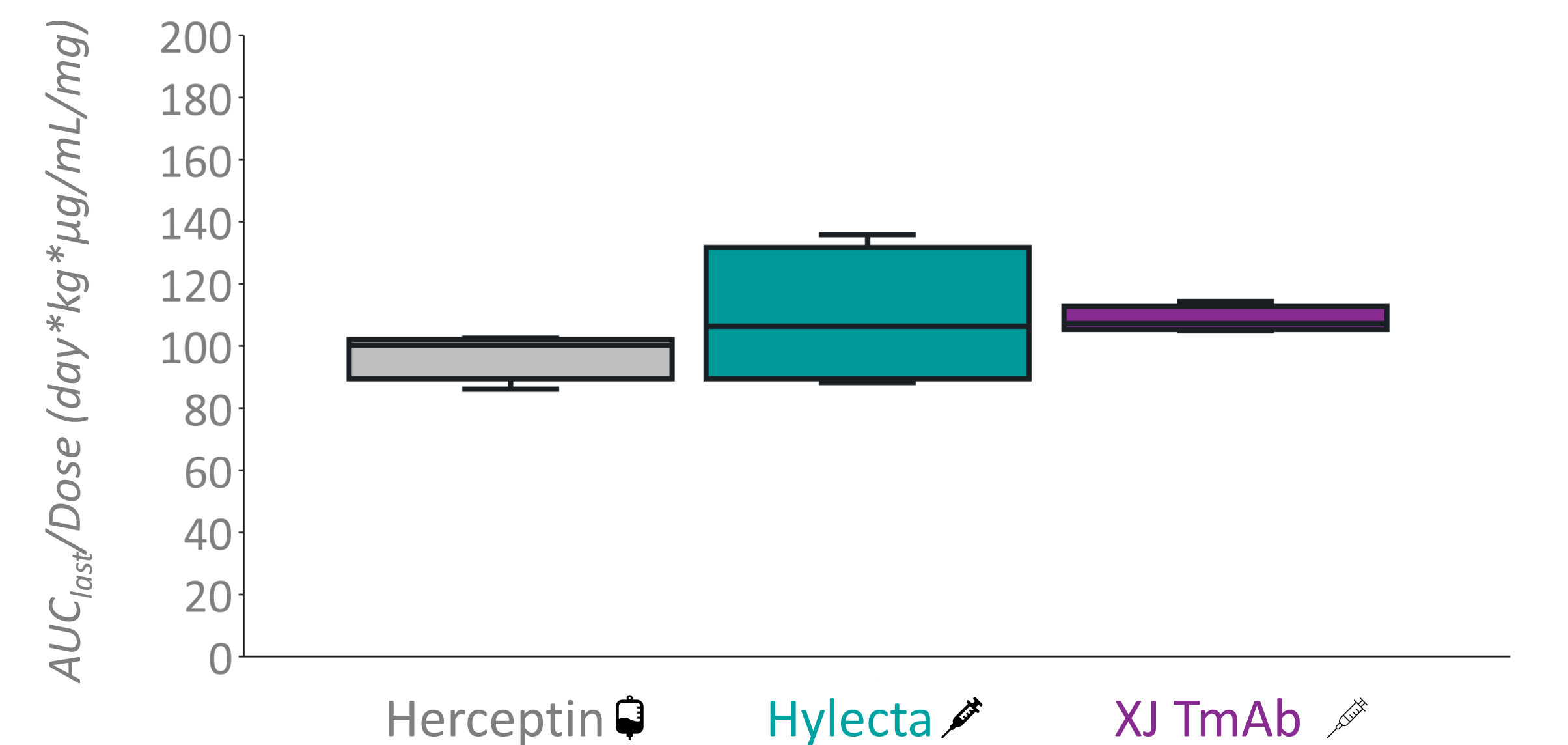
Box values are 25th to 75th percentiles; solid line is the mean; whiskers are values within the 1.5 interquartile range

Time to Peak Drug Concentration Similar Between XJ TmAb and Hylecta SC



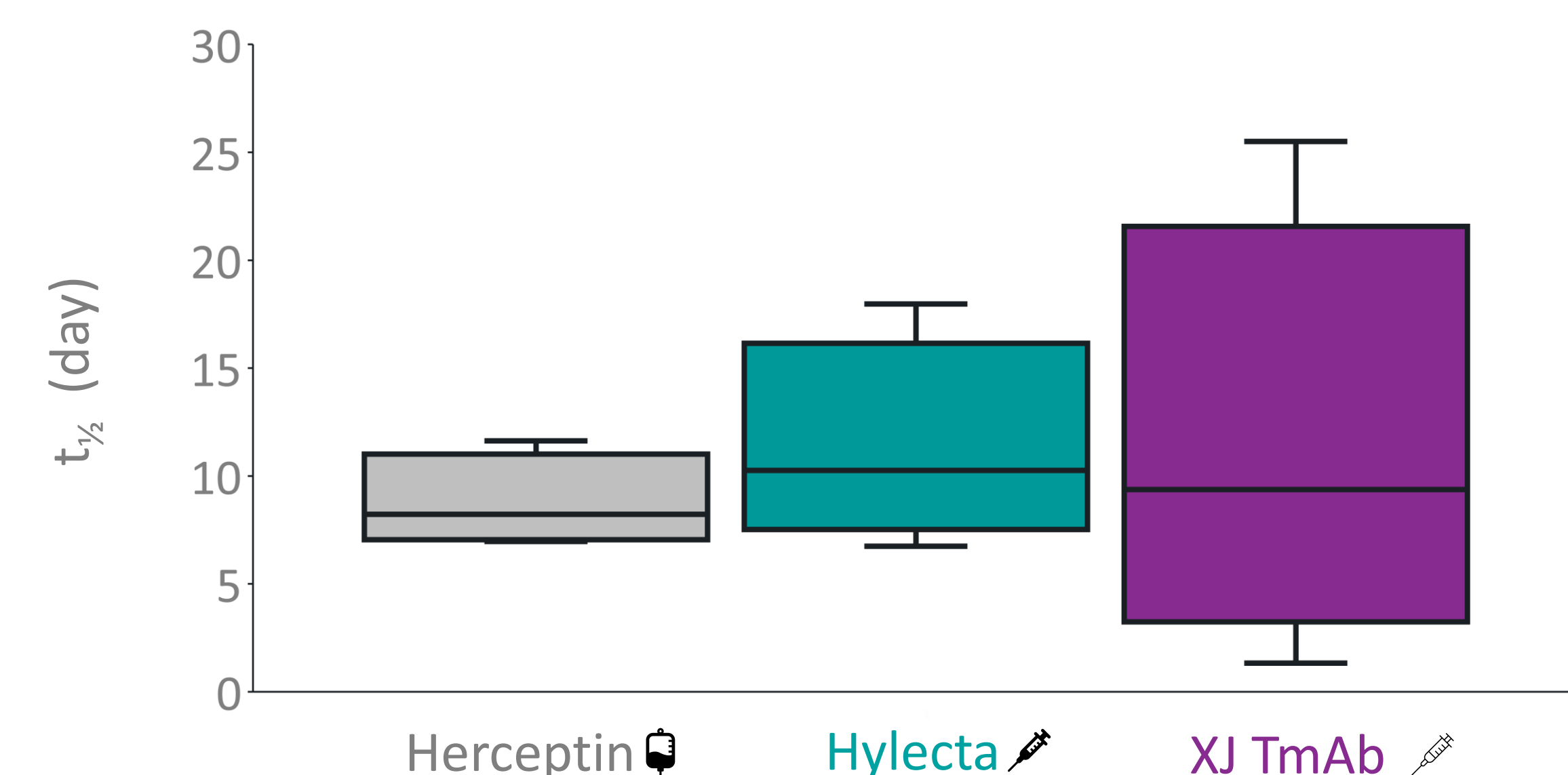
Box values are 25th to 75th percentiles; solid line is the mean; whiskers are values within the 1.5 interquartile range

Exposure Relative to Dose Similar Across All Formulations



Box values are 25th to 75th percentiles; solid line is the mean; whiskers are values within the 1.5 interquartile range

Elimination Half-Life Similar Across All Formulations



Box values are 25th to 75th percentiles; solid line is the mean; whiskers are values within the 1.5 interquartile range

CONCLUSIONS:

We have demonstrated for the first time that administration of XeriJect TmAb, a stable high-concentration formulation of trastuzumab administered SC, produced rapid absorption and similar pharmacokinetics to commercially available Herceptin IV and Hylecta SC in a preclinical pharmacokinetic model.