INTRODUCTION

• CDS1, a gap in B-cell marker, is a promising target for the treatment of B-cell malignancies because of its expression on most B-cell lymphomas and leukemias.

• Duvortuxizumab, also known as JNH-64052781 and MGDO11, is a Fc-bearing bispecific C19 x C03 DART® protein which contains binding domains for CD19 and CD3 antigens.

• Duvortuxizumab was designed to target CD19+ cells for recognition and elimination by CD3-expressing T-lymphocytes.

• A first-in-human (FIH), phase 1 dose-escalation trial of duvortuxizumab in patients with relapsed or refractory B-cell malignancies is ongoing (ClinicalTrials.gov NCT02454270).

• Here we report the results from a translational pharmacokinetic (PK) model that utilized duvortuxizumab PK data from cynomolgus monkeys to predict duvortuxizumab PK in humans.

METHODS

PK Studies in Cynomolgus Monkeys

Study 1

• Two groups of cynomolgus monkeys (n=5/group) were administered 4 intravenous (2-hr IV) doses of duvortuxizumab at 0.005 µg/kg, 0.05 µg/kg, or 0.5 µg/kg once weekly for 4 weeks.

• Serum concentrations above the lower limit of quantification were obtained at dose levels >0.5 µg/kg.

Study 2

• Groups of cynomolgus monkeys (n=5/group) were administered 2-hr IV infusions of duvortuxizumab at 0.2, 2.5, or 10 µg/kg once weekly for 4 weeks.

RESULTS

PK in Cynomolgus Monkeys

• Duvortuxizumab was reasonably characterized using a 2-compartment model with linear CL from the central compartment.

• PK parameters from the pooled studies are presented in Table 1.

Predicted Human PK

• Estimated human PK parameters were used to simulate serum concentration-time profiles for human doses ranging from 0.01 to 10 ng/kg (Figure 1).

CONCLUSIONS

• PK of duvortuxizumab in cynomolgus monkeys was reasonably characterized using a 2-compartment model with linear CL from the central compartment.

• The translational PK model has been used to aid dose escalation of duvortuxizumab in the ongoing FIH, phase 1 trial.

• This work showcases the potential of translational PK modeling in supporting the selection of a FIH dose escalation strategy utilizing preclinical PK information.

REFERENCES


ACKNOWLEDGMENTS

This study was funded by Janssen Research & Development, LLC. Writing assistance was provided by Tracy T. Cao, PhD (PRA Health Sciences), and editorial support was provided by Namit Ghildyal, PhD (Janssen Research & Development).