A human challenge model for respiratory syncytial virus kinetics, the pharmacological effect of a novel fusion inhibitor, and the modeling of symptoms scores

Julia Korell, Bruce Green, John DeVincenzo, Dymphy Huntjens

PII: S0928-0987(17)30342-1
DOI: doi:10.1016/j.ejps.2017.05.070
Reference: PHASCI 4092

To appear in:

Received date: 25 May 2017
Accepted date: 30 May 2017

Please cite this article as: Korell, Julia, Green, Bruce, DeVincenzo, John, Huntjens, Dymphy, A human challenge model for respiratory syncytial virus kinetics, the pharmacological effect of a novel fusion inhibitor, and the modeling of symptoms scores, (2017), doi:10.1016/j.ejps.2017.05.070

A human challenge model for respiratory syncytial virus kinetics, the pharmacological effect of a novel fusion inhibitor, and the modeling of symptoms scores

Julia Korell[a], Bruce Green[a*], John DeVincenzo[b], Dymphy Huntjens[c**]

[a]*Model Answers Pty Ltd, Brisbane, Australia*
[b]*Department of Pediatrics and Microbiology, Immunology and Biochemistry, University of Tennessee Center for Health Sciences, Children's Foundation Research Institute at LeBonheur Children's Hospital, Memphis, TN, USA.*
[c]*Janssen R&D, a division of Janssen Pharmaceutica NV, Beerse, Belgium*

Abstract

Respiratory syncytial virus (RSV) causes acute lower respiratory tract infections, and is a major cause of hospital admissions and death in young children. Limited treatments currently exist that can prevent or minimise exacerbation of the disease. The aims of this work were: 1) to develop a population pharmacodynamic model to describe RSV kinetics (RSVK) in nasal lavage, 2) evaluate the impact of an investigational fusion inhibitor, JNJ-53718678, on RSVK, and 3) determine the relationship between RSVK and symptoms scores.

The best model to fit the RSVK data was a target-cell limited viral kinetics model previously developed for influenza A infections (Baccam P, Beauchemin C, Macken, CA, Hayden FG, Perelson AS, 2006), which included a series of compartments for infected, non-producing and infected, and producing cell populations. The model was adapted to account for longer incubation times seen in RSV, by including 4 additional transit compartments, with the virus elimination rate constant and initial number of target cells fixed to literature values to ensure model parameter identifiability. Between-subject

*Primary author for correspondence
**Additional author for correspondence
Email addresses: bruce@model-a.com.au (Bruce Green[a]), DHUNTJES@its.jnj.com (Dymphy Huntjens[c])