S+ SimulationsPlus

G+ GastroPlus®

BIOL

BIOLOGICS

The Biologics Module simulates the systemic absorption and pharmacokinetics of biologics – for both monoclonal antibodies (mAb) and antibody-drug conjugates. Both mAbs and ADCs administered as an intravenous bolus dose, intravenous infusion, subcutaneous, and intramuscular injections can be modeled.

What is the Biologics module?

As with other GastroPlus® modules, there is no equation or code writing required. All major organs are connected in an anatomical fashion with plasma flow represented by blue solid arrows and lymph flow by red dashed arrows.

The lymph node collects the lymphatic drainage from organs and lymph fluid is returned to the systemic circulation. Each organ in the PBPK models divided into three major compartments representing the vascular, endosomal, and interstitial spaces.

PBPK models for antibody-drug conjugates (ADCs) - processes considered:

- ✓ Distribution and elimination processes of multiple ADC species with different DAR (drug-to-antibody ratio)
- ✓ Clearance defined through nonspecific mechanisms
- ✓ Binding to target receptor, internalize, and be cleared in the cell lysosome
- ✓ Release and clearance of the toxin molecule

PBPK models for monoclonal antibodies (mAb) - processes considered:

- ✓ Convective transport and fluid phase endocytosis describing uptake of antibody into the tissue
- ✓ mAb-FcRn (neonatal FC receptor) binding & recycling – including pH-dependent binding kinetics
- ✓ Target mediated elimination in the interstitial space to include the influence of specific antigen-mAb interactions on mAb disposition
- ✓ Within the endosomal space, the competition for binding to FcRn between endogenous IgG and the therapeutic mAb
- ✓ mAb administration by either intravenous (IV), subcutaneous (SQ), or intramuscular injections

Payload
- Toxins can fall off antibody due to deconjugation
- Released toxins can be cleared through metabolism or renally

Two types of deconjugation models included
- Series of transit processes to describe deconjugation from high to low DARs
- Average DAR used to describe deconjugation step

Interested in collaborating?

Email us! info@simulations-plus.com

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