PK/PD MODELLING AND SIMULATION OF STAVUDINE NANOPARTICLES IN HIV PATIENTS

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Objective

To develop a PK/PD model to simulate, using Monte Carlo simulation, the antiviral intra and extracellular activity of stavudine, by administering the drug by oral or nanoparticles system.

Methods

* Dosage schedules

Conventional tablets (Oral) (40 mg / 12 h)
Nanoparticles system (NP) (1 mg / 12 h by i.v.)
Combined treatment (Oral + NP) (40 mg oral + 1 mg NP i.v / 12 h)

* PK/PD Model

Pharmacokinetic model (PK): one-compartment model

\[
\frac{dC(t)}{dt} = \frac{K_A}{V} \cdot A - \frac{C}{V} \cdot k
\]

Inhibition model: INH = \( (I_{\text{max}} \cdot C_Y) / (I_{C_{50}} + C_Y) \)

Pharmacodynamic model (PD):

- T cells: \( \frac{dT(t)}{dt} = \lambda_T - d_T \cdot T - k_T \cdot T \cdot V \cdot (1 - \text{INH}) \)
- Macrophage cells: \( \frac{dM(t)}{dt} = \lambda_M - d_M \cdot M - k_M \cdot M \cdot V \cdot (1 - \text{INH}) \)
- Viral Load: \( \frac{dV(t)}{dt} = \pi_T \cdot (k_T \cdot T + V \cdot (1 - \text{INH}) - \delta_T \cdot T) + \pi_M \cdot (k_M \cdot M + V \cdot (1 - \text{INH}) - \delta_M \cdot M) - c \cdot V \)

Fig. 1. Stavudine nanoparticles PK/PD model

Results

Fig. 1. Evolution of Viral Load in different cells throughout the treatment, using Monte Carlo Simulation.

Fig. 2. Evolution of T cells and macrophages with Oral+NP treatment, using Monte Carlo Simulation.

Fig. 3. Probability of exceeding HIV virions/µL and T cells/µL target values at the end of the treatment.

Conclusions

- The PK/PD model developed may simulate antiviral activity of stavudine using oral and/or nanoparticles administration.
- NP treatment may decrease the viral load inside macrophages better than standard oral treatments.
- Oral+NP treatment controls the levels of immunologic cells (T cells and Macrophages).
- The Oral+NP treatment increase the probability to achieve suitable virions/µL and T cells/µL target values in comparison with standard oral treatments.

References