

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

$$\frac{dC(t)}{dt} = K_a * A - K_e * C$$

Inhibition model: $INH = (I_{max} * C^Y) / (IC_{50}^Y + C^Y)$

Pharmacodynamic model (PD):

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

* Monte Carlo Simulation

1000 HIV individual patients

4000 days of treatment

Software: GoldSim Pro, versión 10.1.

* Variables studied

Viral Load

Number of T cells and macrophages

Probability of exceeding { * Number of T cells
* Viral Load

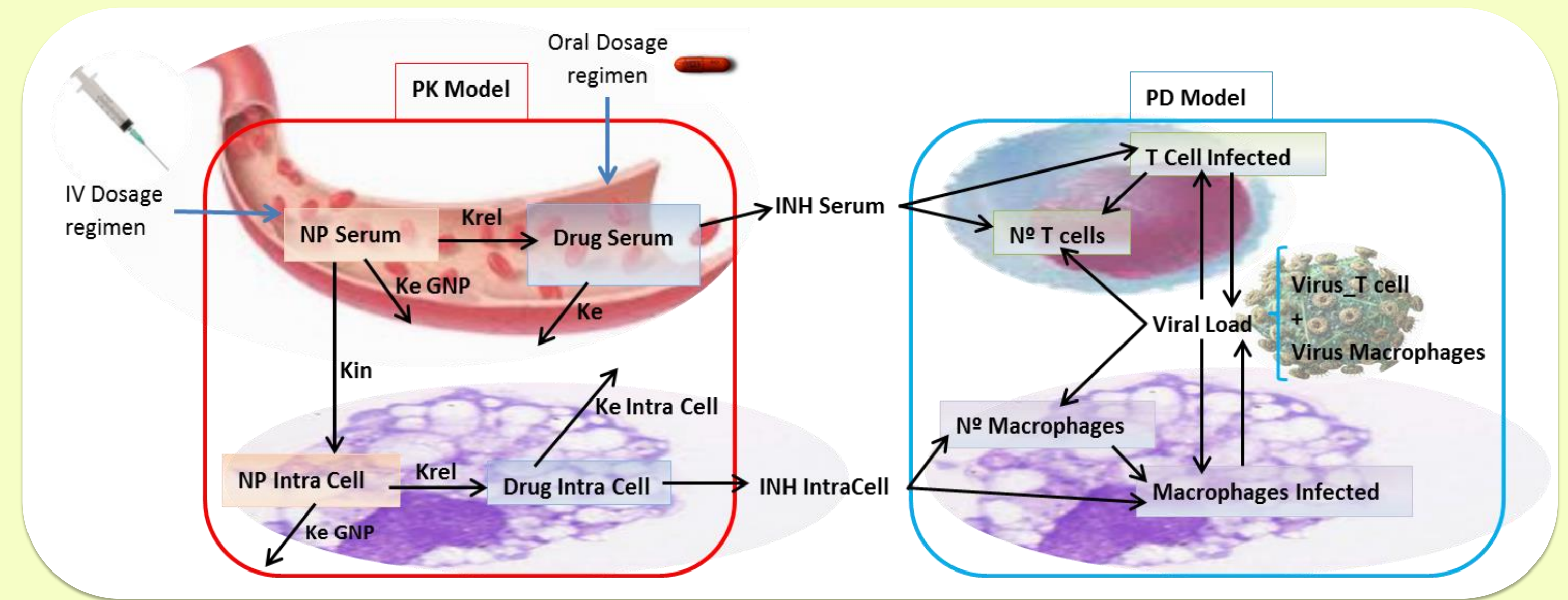


Fig. 1. Stavudine nanoparticles PK/PD model

RESULTS

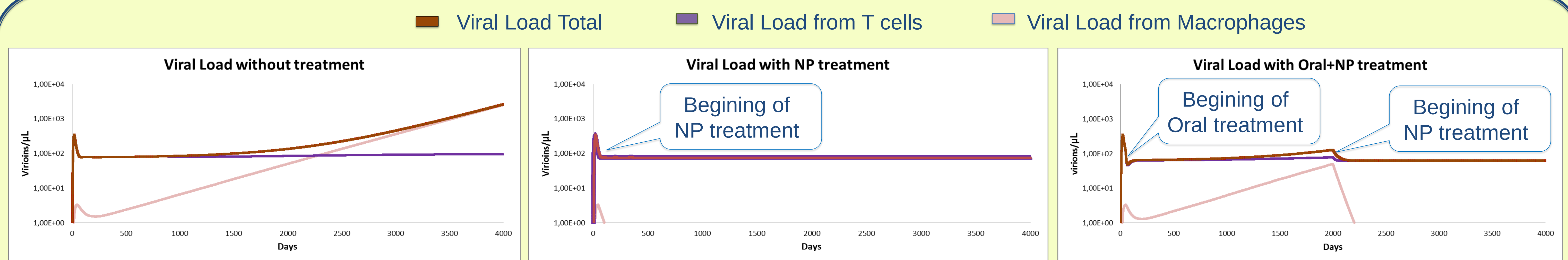


Fig. 1. Evolution of Viral Load in different cells throughout the treatment, using Monte Carlo Simulation.

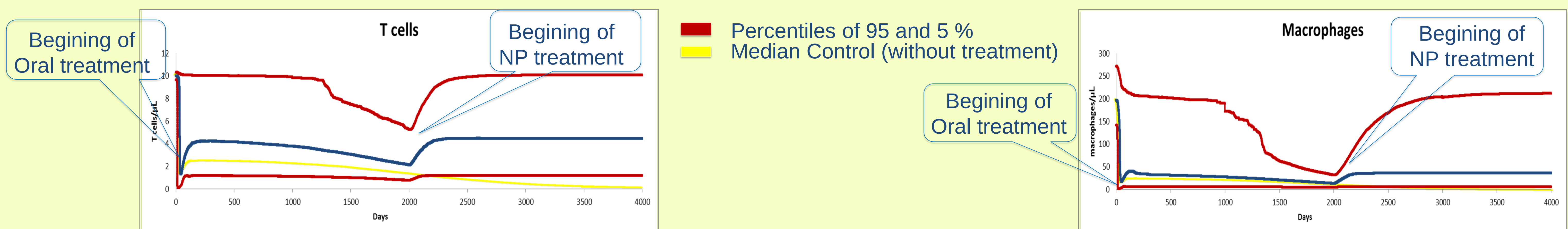


Fig. 2. Evolution of T cells and macrophages with Oral+NP treatment, using Monte Carlo Simulation.

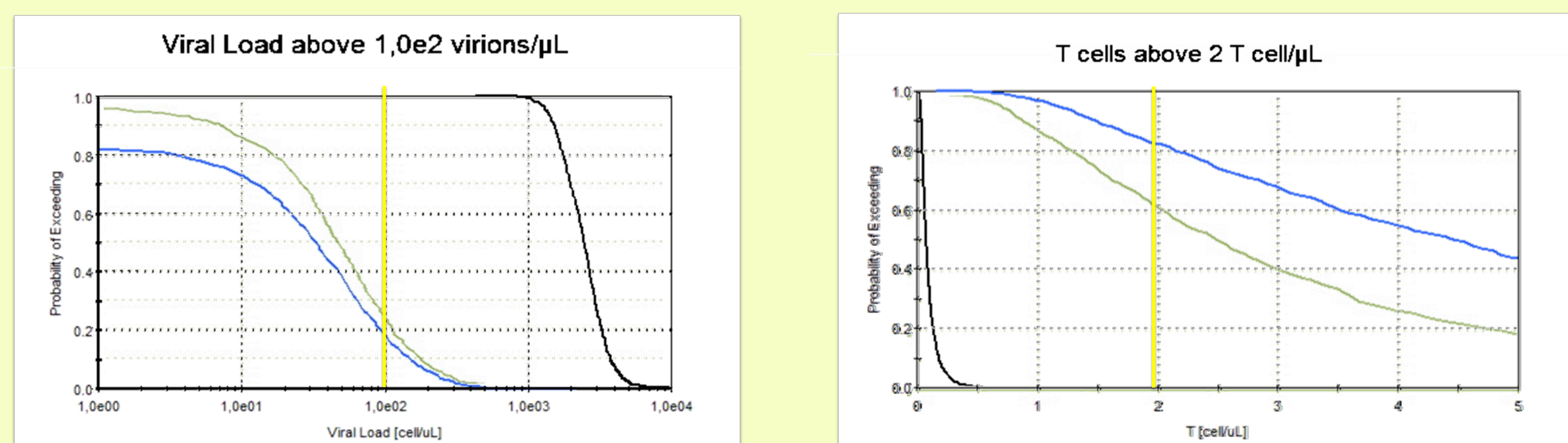


Fig. 3. Probability of exceeding HIV virions/μL and T cells/μL target values at the end of the treatment.

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

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