Desired time horizon for tumour elimination $t_p$ (1-3 months)

Rate constants of therapy compartments $\kappa_p$, $\kappa_M$, $\kappa_L$, $\kappa_I$ [eq.(40)]

Determine Bias level to shift baseline $T^*$ [formula of eq.(4)] (see fig. 2B)

Patient’s clinical parameters:
cell populations $T$, $N$, $L$, $C$ (Figure 3)

Normal tissue protection:
If leucocyte levels $N$, $C$ fall outside bounds:
increase time horizon gradually until levels within bounds

Start therapy simulation process:
find the drug dosages [eq.(37)-(39)]

Continue until tumour regression completes
(i.e. when its cell population $T = 0$)

Drug toxicity precaution:
Drug doses to be kept bounded (Table 2)
(also item B.4, Additional file 2)

Any drug stopped if computed dose is negative:
Continue other drugs & resume former drug
when its computed dose becomes positive

Biological parameters of tumour action:
cell-drug interaction rates $a$, $b$, $c$, $d$. (Table 1)

Therapy weights for minimizing drug-toxicity
adjust parameters $r_T$, $r_T$, $r_L$, $r_I$ (Addl. file 2)

Bounds of cell population & drug dosages:
limits of $N$, $L$, $C$ and $v_M$, $v_L$, $v_I$ (Table 2)

Colour codes:
Computational process to derive dose-time profile of drugs: **Black panels**
Preparation of the Bias shift for depressing tumour curve: **Green panels**
Precautions to prevent toxicity of therapy agents on patient: **Brown panels**
Final output of the therapeutic agents for administration: **Blue panels**

Calculated dosing of therapeutic agents to patient
Dose rate flow $v_{AP}$, $v_L$, $v_I$