KEYNOTE-001

AUC 0-28

AUC 0-inf

Cmax

Tmax

Half-life

AUC 0-21

AUC21-42

Ctrough

Max change in Tumor size

# Basic Specs

N\_Tcell = 1200-3475 cells/microL blood (lymphocytes, healthy Cuban adults)

= 536-1787 cells/microL blood (T cells, healthy adult Switzerland)[[1]](#footnote-1)

= 1473 cells/microL blood (700-2508 ref values) (T cells, 253 healthy donors 19 to 67)[[2]](#footnote-2)

=1500 cells/microL blood (1000-3000 lymphocytes from tumor patient!)[[3]](#footnote-3)

V\_blood = 5L (assumption or 70mL/kg)[[4]](#footnote-4)

%\_PD1\_T = 0.3 (percent T cells expressing PD1)3

N\_PD1\_TC = 10000 PD1/T cell

AV = 6.0221415\*10^23 Avrogadro’s number

MW = 149000 g/mol

(PD-1 concentration in blood, nM) (magnitude is 10%~15% of the drug concentration (10mg/L) under very low dose so ignore the central volume effect. Assume to be constant)

(PD-1 concentration in tumor interstitial volume, nmol)

The ratio of PD1 in tumor vs blood. 1000 is the initial guess from the paper. The multiplier is used to align the Tmulti with the paper.

# Central compartment:

From Elassaiss[[5]](#footnote-5).

# Tumor compartment:

## Drug binding:

Assumption: k\_prod = k\_deg when no drug comes in, steady state of PD1. In amount form.

. From Shah et al.[[6]](#footnote-6)

/day Allometrically scaled from 20g mouse

In vitro value

In vitriol value

;

nM

## Tumor growth

(interstitial space volume)

Exponential growth

(1/day) has three values:

Fast growth: 0.0088

Medium growth: 0.0036

Slow growth: 0.0017

(error term: exp(), variance = 0.05 and mean = 0)

Drug effect

Receptor occupancy (gamma = 2.28)

is the slope (1/%day), there are two scalings:

(mouse is 20 g in the study)

(mouse is 0.113)

SLtg is converted into 1/day in equation by multiplying with 100. It is also corrected by multiplying another 100 to obtain reasonable tumor growth.

Note: BSLD effect is removed from CL since it is considered in the tumor compartment.

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2. Apoil PA, Puissant-Lubrano B, Congy-Jolivet N, Peres M, Tkaczuk J, Roubinet F, Blancher A. Reference values for T, B and NK human lymphocyte subpopulations in adults. Data Brief. 2017 Apr 21;12:400-404. doi: 10.1016/j.dib.2017.04.019. PMID: 28491945; PMCID: PMC5415546. [↑](#footnote-ref-2)
3. Hu X, Gu Y, Li D, Zhao S, Hua S, Jiang Y. Analyzing the percentage of different PD-1+ T cell subsets in peripheral blood and bronchoalveolar lavage fluid of small cell lung cancer patients: A prospective study. Clin Exp Pharmacol Physiol. 2019 Dec;46(12):1074-1083. doi: 10.1111/1440-1681.13153. Epub 2019 Aug 30. PMID: 31381177. [↑](#footnote-ref-3)
4. https://transfusion.com.au/disease\_therapeutics/haemorrhage [↑](#footnote-ref-4)
5. Elassaiss‐Schaap, J. Allometric scaling in oncology disease progression from xenograft tumor growth to human non‐small‐cell lung cancer. 19th Annual Meeting of the Population Approach Group in Europe June 8–11; Berlin, Germany; 2010. [↑](#footnote-ref-5)
6. Shah, D.K. & Betts, A.M. Towards a platform PBPK model to characterize the plasma

   and tissue disposition of monoclonal antibodies in preclinical species and human.

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