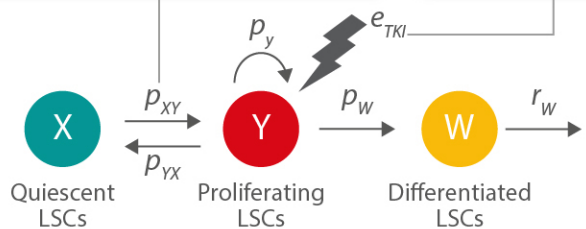
Development of a mathematical model to analyze and describe biphasic treatment responses from tyrosine kinase inhibitor (TKI) treated patients with chronic myeloid leukemia

The matematical model considers 3 leukemic cell types:

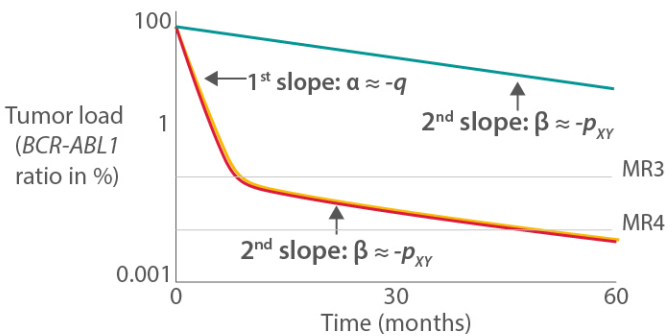
- Quiescent leukemic stem-cells (X)
- Proliferating leukemic stem-cells (Y)
- Differentiated leukemic cells (W)

1.Mechanism of activation/deactivation of quiescent/proliferating LSCs with rates p_{XY} and p_{YX}

2. Cytotoxic effect of TKI on proliferating LSCs with intensity e_{TKI}



p_{XY} activation rate of quiescient LSCs
p_{YX} activation rate of proliferating LSCs
p_Y proliferation rate of proliferating LSCs
p_W differentiation rate of proliferating LSCs
e_{TKI} citotoxicity rate
r_W mortality rate



The ratio α/β can be used to identify patients that are likely to benefit from dose reduction

α/β > 15	very likely retaining the original long-term treatment efficacy after a 50% dose reduction
α/β < 2	patients would benefit from dose escalation
α/β ≥ 2	patients benefit from dose escalation

Dose halving should be considered as a long-term treatment option for well-responding chronic myeloid leukemia patients under continuing maintenance therapy with tyrosine kinase inhibitor

Fassoni *et al.*, Haematologica, 2018