DEVELOPMENT SCIENCES: Innovation & Technology

TITLE

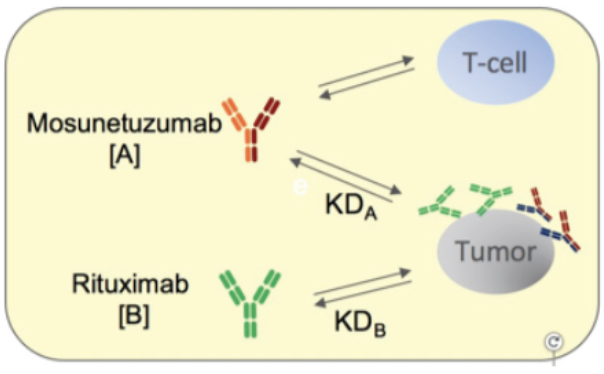
Quantitative Pharmacology to Broaden the Therapeutic Window of Mosunetuzumab to Enhance Benefit/Risk

SUMMARY

Quantitative pharmacology approaches informed the clinical dosing regimen which mitigates the mechanism-based toxicities, leading to a broad therapeutic window of mosunetuzumab (anti-CD20/CD3 bispecific antibody). Model-based understanding of target engagement kinetics elucidated clear relationship to clinical efficacy and informed the clinical dose selection with enhanced benefit/risk profiles in r/r NHL patients.

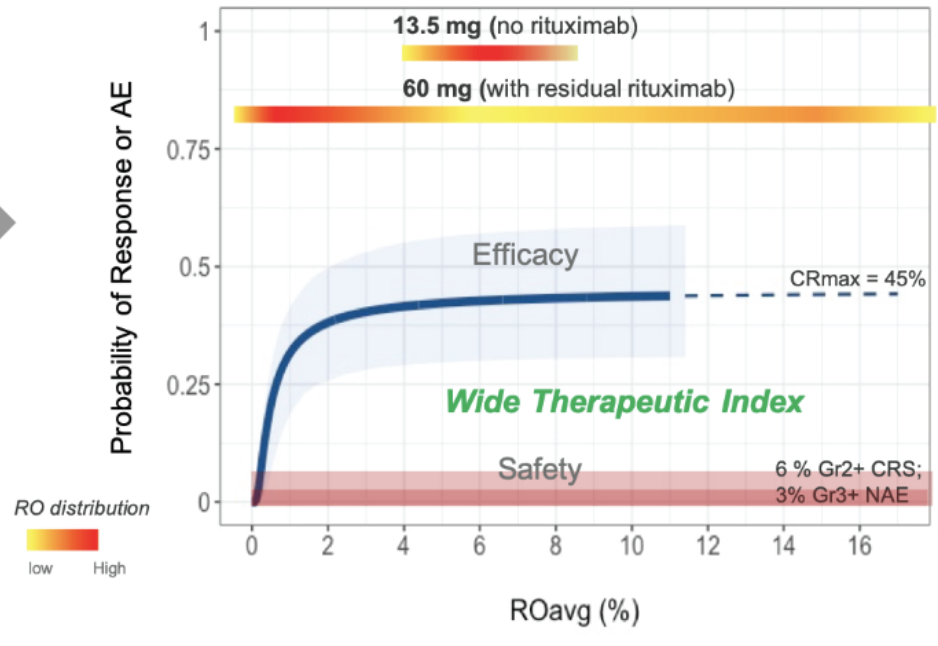
IMPACT

- Discovered a key predictor of clinical responses through model-based CD20 receptor occupancy (RO%)
- Informed clinical dose and regimen selection which effectively mitigated clinical cytokine release syndrome (CRS) and maximized benefit/risk



CD20 target engagement (% RO) of mosunetuzumab was modeled in the presence of residual levels of prior anti-CD20 therapies:

$$RO(A) = \frac{[A]}{KD_A + [A] + \frac{KD_A}{KD_B}[B]}$$



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