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Summary

FUNCTIONAL DIFFERENTIATION OF AFIMKIBART'S PREFERENCE FOR TRIMERIC TL1A IN BLOCKING ACTIVE TL1A SIGNALING

Domagoj Vucic

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Afimkibart, a fully human monoclonal antibody in Phase 3 studies for IBD, selectively neutralizes trimeric TL1A and potently inhibits NF-κB signaling and IFN-γ production, while monomeric TL1A shows minimal functional activity.

KEY POINTS

- Trimeric recombinant human TL1A robustly induced NF-κB activation in peripheral T lymphocytes and significantly enhanced IFN-γ production in human PBMCs with IL12 and IL18 co-stimulation, both potently inhibited by afimkibart.
- Monomeric recombinant human TL1A, even at concentrations exceeding 100 ng/mL, elicited only minimal NF-κB activation and marginal IFN-γ response.
- Afimkibart does not bind monomeric TL1A, selectively recognizing the active trimeric species, preventing sequestration by non-signaling monomers.
- In comparative cellular assays, afimkibart demonstrated greater NF-κB inhibition than PRA-023, an antibody binding both monomeric and trimeric TL1A, when blocking endogenous active TL1A.
- The selective binding of afimkibart to trimeric TL1A may represent a mechanistically distinct profile for optimal pharmacokinetic and pharmacodynamic properties, with clinical impact currently under investigation in IBD.
- Study funded by F. Hoffmann-La Roche, Ltd.

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