Mechanism of action of a novel agonist TNFR2-antibody that induces co-stimulation of T cells and promotes robust anti-tumor immunity


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Abstract: A PASSION FOR OUTTUMCANCER

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Co-stimulatory activity increases proliferation and functionality of murine T cells in vitro

Anti-TNF2 antibody activity requires Fcg receptor binding

Anti-TNF2 co-stimulation enhances the magnitude and effector function of CD8 T-cells

Mechanisms of action summary

- Co-stimulatory activity on T cells
- Increases magnitude and effector function of tumor infiltrating CD8 T-cells
- TNFR2 receptor downregulation
- Dependence on immuno-stimulating and activating Fcg receptors
- Comparative activity of mAbs, agonists and patients with advanced disease binding to activating Fcg receptors
- TNF2 binding induces tumor infiltrating CD8 T-cells
- No consistent reduction in the frequency of T cells subsets in the tumor and periphery

Conclusions and Clinical Relevance

Anti-TNF2 and TNF2/2 antibodies may both be able to deliver robust immunostimulation and an advantageous toxicity profile compared to anti-CTLA4 in a long-term efficacy study in mice (see Richards et al at Almirall, A). A human anti TNFR2 antibody (M168) with similar efficacy and lower toxicity, is the same analog for the murine anti T cell co-stimulating rig, then is being developed for use as a potential new treatment option in cancer patients. See inspection of data in table for characterization of M168.

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