Rationale for CD137 agonists in cancer

CD137 (TNFRSF9, 4-1BB) is a member of the tumor necrosis factor receptor superfamily that functions as a potent co-stimulator of adaptive and innate immune cells1 (Figure 1). The antitumor activity from targeting the CD137 pathway in preclinical models2 has provided rationale for pharmacologic modulation of the CD137 axis in cancer patients. Antibody-mediated stimulation of CD137 is anticipated to augment T cell co-stimulation, enhance NK cell cytotoxicity, promote maturation of antigen presenting cells (APCs), and suppress T regulatory cells (Tregs).1 Despite signs of clinical activity, the development of first-generation anti-CD137 antibodies has been hampered by on-target, dose-limiting hepatotoxicity3,4. Emerging data also suggest that pharmacologic optimization of epitope and Fc interactions is critical for realizing maximal efficacy for this class of molecule6.

Translating CD137 co-stimulation to the clinic

To overcome clinical limitations, Agens has developed AGEN2373, a novel anti-CD137 antibody designed to stimulate CD137 signaling only in the context of ongoing immune cell activation.

Conclusion

The pharmacologic and non-clinical safety profile of AGEN2373, a novel anti-CD137 antibody designed to provide potent yet restricted CD137 pathway co-stimulation, supports the potential for a therapeutic window in patients as a monotherapy or in combination with other therapeutic modalities.