Title: Clinical development of BeiGene TIGIT and OX40 targeted therapies

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Over the last decade, development of targeted therapies for treatment of solid tumors has advanced considerably. At the forefront of this development were inhibitors targeting immune checkpoint proteins of the PD-1/L1 axis. However, clinical responses observed with these checkpoint inhibitors are often limited due to primary and secondary resistance. Given the high unmet medical need among patients with solid tumors, novel targets and new treatment combinations are needed.

Targeting additional immune proteins may help overcome tumor immune escape and enhance antitumor response in patients with advanced solid tumors who are sensitive or resistant to anti-PD-1/L1 treatments. T cell immunoreceptor with Ig and ITIM domains (TIGIT) and OX40 are immune checkpoint proteins expressed on several types of immune cells; both TIGIT and OX40 play important regulatory roles in innate cancer immunity. TIGIT is a co-inhibitory receptor that can suppress T cell activation, promote T cell exhaustion, and increase NK cell cytotoxicity. Co-stimulatory signals from OX40 during T cell activation mediates survival and expansion of both CD4+ and CD8+ T cells and are involved in controlling effector and memory T cell response. As inhibition of these checkpoint proteins has multiple immunological effects that may complement the activity of PD-1/L1 blockade, they have been identified as potential targets for anti-cancer drug development.

BeiGene, a global, science-driven, biopharmaceutical company, has successfully developed tislelizumab, a next-generation monoclonal antibody against PD-1. Tislelizumab was specifically engineered to minimize FcγR binding on macrophages to abrogate antibody-dependent phagocytosis—a potential mechanism of T-cell clearance and resistance to anti-PD-1 therapy. Currently, BeiGene is actively developing ociperlimab, an anti-TIGIT antibody, as well as BGB-A445, a non-ligand competing OX40 agonist antibody. Given the possible synergistic effects of the dual mechanisms of actions, combination of tislelizumab with either ociperlimab or BGB-A445 may enhance immune cell activation and improve antitumor activity in both PD-1 sensitive and resistant patients.

This presentation will discuss the scientific rationale for the development of ociperlimab and BGB-A445 as well as present available preclinical and clinical data.