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TheraMAB starts oncology clinical program with its mAb targeting an immune checkpoint

Tumor cells use various strategies to avoid immune reactions. Most efforts by researchers to circumvent these tactics have focused on monoclonal antibodies (mAbs) that target inhibitory checkpoints to reactivate the immune response against tumor cells. The rapidly growing field of immuno-oncology has seen the approval of several promising drugs of this kind.

A potential drawback, however, of altering the body's natural suppressive mechanisms is an increased risk of immune-related adverse events. In addition, a combination of inhibitory drugs may be required to achieve higher success rates. For these reasons, molecules targeting direct activation of immune cells, including antibodies to receptors such as OX40, CD40 and others on immune cells with a stimulatory mechanism of action (stimulatory checkpoints), have also been developed. Preclinical and clinical investigations are showing promising results for these approaches.

TheraMAB believes that therapy with stimulatory drugs—as well as a currently untested combination of stimulatory and inhibitory approaches—may result in greater benefits for patients with cancer. The company is developing a drug, TAB08, that may have exclusive properties in this area.

TAB08 is a mAb that targets the key co-stimulatory receptor CD28 on T lymphocytes. Unlike with other drugs, binding of TAB08 to CD28 allows direct activation of T cells with only tonic T cell receptor signaling required.

In vitro studies using blood samples from patients with B cell chronic lymphocytic leukemia have revealed that TAB08 efficiently induces T cell expansion, corrects T cell dysfunction and induces immunogenicity of B cell chronic lymphocytic leukemia cells, leading to their elimination. Interestingly, TAB08 also stimulated the expression of other receptors related to immunological checkpoints, including OX40 and CD40.

Furthermore, slow recovery of the number and function of T cells after cytotoxic therapies contributes to the high incidence of life-threatening infections after treatment. In *in vivo* experiments repopulation from a small inoculum of mature T cells accelerates dramatically after administration of an ortholog of TAB08 in bone-marrow-reconstituted rats.

TAB08 administered in combination with new immunological checkpoints or current therapies could be beneficial for patients with cancer, with an expected synergistic effect. TAB08 could be administered intravenously, and potentially could also be efficacious when injected directly into solid tumors.

Good safety of TAB08 at low doses has already been demonstrated in a recent clinical trial in healthy volunteers and further confirmed in ongoing phase 2 clinical trials in patients with autoimmune diseases. The first phase 1 clinical trial of TAB08 in the oncology setting is currently under way in patients with solid tumors. TheraMAB is open to new opportunities as it develops its promising oncology program for TAB08.

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