Press Release

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Mendus Publishes Preclinical Data Demonstrating Significant Anti-Tumor Synergies of Intratumoral Immune Priming with CTLA-4 Inhibition

- Intratumoral injection of allogeneic pro-inflammatory dendritic cells ("ilixadencel") substantially and sustainably enhanced an otherwise ineffective systemic anti-CTLA-4 treatment in an established in vivo cancer model
- Effects were shown to be T-cell-dependent and included a profound remodeling of the tumor microenvironment (TME), the formation of immune memory cells, and delivered results indicating the spread of the therapeutic effects into the periphery via the bloodstream and lymphoid organs
- Cured mice in the combination arm (7 out of 10) stayed tumor-free and survived for at least 70 days and sustained a subsequent tumor re-challenge

Mendus AB ("Mendus" publ; IMMUST), a biopharmaceutical company focused on improving survival outcomes for cancer patients with tumor recurrence through cell-based immunotherapies, today announced the publication of in vivo data demonstrating significant anti-tumor synergies between the Company’s allogeneic dendritic cell-based immune primer program ilixadencel and immune checkpoint inhibition via CTLA-4 blockade in the peer-reviewed journal ONCOIMMUNOLOGY.

“These preclinical data underpin the rationale behind our immune primer in playing multiple roles in overcoming immunosuppression and rewiring the TME rather than just providing for a simple inflammatory signal,” commented Alex Karlsson-Parra, M.D., Ph.D., Chief Scientific Officer at Mendus. “Taken together, these early-stage findings warrant further clinical investigation with our current generation allogeneic immune primer and future generation immune primers in cancer patients receiving anti-CTLA-4 therapy and in indications where this immune checkpoint strategy has previously failed to make a substantial impact on patient outcomes.”

Cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) is an inhibitory checkpoint receptor and blocking has the potential to release the “brakes” on patients’ endogenous immune systems. The US Food and Drug Administration (FDA) approved the first anti-CTLA-4 antibody, ipilimumab (Yervoy®), for the treatment of late-stage melanoma in 2011 and several CTLA-4 targeting programs are in clinical development today. Despite achieving durable responses and improved overall survival using CTLA-4 blockade in many patients, it is estimated that up to 80% still do not respond possibly attributed to a lack of pre-existing immunity. Mendus’ current generation immune primer, ilixadencel, has been evaluated in a broad range of tumors and has demonstrated an excellent safety profile across all studies with encouraging signs of efficacy when combined with other treatment modalities including checkpoint inhibitor pembrolizumab and kinase inhibitors.

In the preclinical study published today, mice were transplanted subcutaneously with CT-26 colorectal cancer cells and were subsequently treated with an intratumoral injection of ilixadencel, an intravenously given antagonistic anti-CTLA-4 antibody, a combination of both or placebo. Neither ilixadencel, nor anti-CTLA-4 treatment alone affected tumor progression or prolonged survival significantly. However, combined treatment with ilixadencel and anti-CTLA-4 significantly delayed tumor progression and led to tumor remission with 7 out of 10 mice surviving longer than 70 days with no detectable tumor. All surviving mice were subsequently re-challenged with CT-26 cells and...
all mice rejected the newly inoculated tumors compared to the control mice, where none rejected the reintroduced CT-26 cells, indicating the establishment of an immunological memory response.

Several findings of the study demonstrated a profound remodeling of the initially immunosuppressive tumor microenvironment following the combined use of ilixadencel and the anti-CTLA-4 inhibitor. Changes to the TME were visible in gene set analyses of significant pathway signatures including upregulated pathways that affect the myeloid compartment, antigen presentation, the lymphoid compartment, and cytokines/chemokine regulation. On a cellular level, changes in the combination arm included intratumoral infiltration of immune cells with anti-cancer features, including host dendritic cells with high antigen-presenting capacity and activation phenotypes, macrophages with M1-like phenotype, activated neutrophils and inflammatory monocytes.

Combined, these changes led to a suitable TME for the expansion of CD8+ tissue-resident memory T cells which was positively correlated with elevated potential tumor-reactive CD8+ T cells in the tumor and “tumor-matching” CD8+ T cells in peripheral blood. Moreover, splenocytes from mice in the combination treatment group secreted significantly higher IFN-γ upon stimulation with a CT-26-derived model neoantigen, confirming the induction of a tumor-specific CD8+ T-cell response. Depletion of CD8+ T cells totally abolished the therapeutic benefit.

The publication titled: “Intratumoral administration of pro-inflammatory allogeneic dendritic cells improved the anti-tumor response of systemic anti-CTLA-4 treatment via unleashing a T cell-dependent response” is available via: https://doi.org/10.1080/2162402X.2022.2099642

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ABOUT MENDUS AB (PUBL)
Mendus is dedicated to changing the course of cancer treatment by addressing tumor recurrence and improving survival outcomes for cancer patients, while preserving quality of life. We are leveraging our unparalleled expertise in allogeneic dendritic cell biology to develop an advanced clinical pipeline of novel, off-the-shelf, cell-based immunotherapies which combine clinical efficacy with a benign safety profile. Based in Sweden and The Netherlands, Mendus is publicly traded on the Nasdaq Stockholm under the ticker IMMU.ST. http://www.mendus.com/