1129 A NOVEL CPG MOTIF INTRODUCED INTO A BISPECIFC AM003 COMPOUND FOR THE TREATMENT OF SOLID TUMORS

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Background Despite clinical activity of immunotherapy agents in a broad range of cancer indications, there is still a substantial percentage of patients who fail to respond to those therapies, and hence, an unmet need to address mechanisms of tumor immune resistance. One of the most promising approaches is to turn a "cold" tumor into "hot" tumor.

CpG motif is a DNA sequence rich in unmethylated Cytosine- phosphate Guanine (CpG) nucleotides, prevalent in bacterial DNA, eliciting host immune reaction.

AM003 is a Bispecific Personalized Aptamer comprised of a T cell engager arm and a tumor-targeting arm, which is the outcome of Aummune's innovative tailored therapeutic platform that identifies functional aptamers capable of killing tumor target cells. The two ssDNA aptameric arms of AM003, when hybridized, are designed to form a novel immunostimulant CpG motif

Methods In vitro evaluation of the AM003 CpG mode-of-action was performed using B cell and dendritic cells (DC) flow cytometry analyses, cytokines measurements and co-culture assays. Moreover, in vivo immunologic effects were investigated in syngeneic mice tumor models.

Results The AM003 CpG motif induced a potent stimulation of antigen presenting cells. Stimulated dendritic cells (DC) had an increased cell surface expression of different co-stimulatory receptors and elevated TNF-a secretion.

DC cultured with AM003 demonstrated enhanced CD4 T cells stimulation in a mixed lymphocyte reaction (MLR) model with higher levels of IFN-gamma detected. Furthermore, anti-PD1 led to a synergistic effect when combined with AM003 in the MLR assay, where IFN gamma levels were further elevated, compared with both single agents.

In line with the observed results of innate immune stimulation, in vivo, intratumoral injection of AM003 effectively transformed the immune landscape of the injected tumor, with increased infiltration of CD8+ CD4+ T cells and of B cells.

Conclusions Our findings suggest that AM003 addresses the challenges of immune resistance by activating the innate immune system, improving T cell infiltration and enabling a follow-on effective T cell activation by the compound's T cell engager arm.

These data provide a framework for the clinical development of this novel personally tailored immunotherapy. Aummune has initiated a first-in-human clinical study of AM003 in subjects with solid tumors.

Ethics Approval

TLV medical center ethics committee TLVMC – IL – 2205 – 113 – 5 (Animals study)

Helsinki approval number 0297-15-TLV (Buffy coat)

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