A patient-derived anti-CD9 antibody induces tumor rejection and synergistically enhances anti-PD1 activity

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Background
- AT1412 was isolated using AIMSelect from B cells of a patient who was cured of stage IV metastatic melanoma with brain metastasis following adoptive T-cell therapy.
- AT1412 is a fully human antibody specifically recognizing the tetraspanin CD9.
- AT1412 binds CD9 positive solid tumors (e.g. melanoma, gastric) and B-ALL (Abstract #1912 Poster #531).
- In sharp contrast to previously described CD9 antibodies, AT1412 does not induce aggregation of platelets.
- Here we explore the efficacy of human antibody AT1412 for potential treatment of solid tumors.

1. AT1412 recognizes a unique epitope on CD9

AT1412 is a CD9 antibody generated from the B cells of a cured melanoma patient. (A) AT1412 recognizes a novel epitope on CD9 as determined by crystallography. (B) Melanoma cells and primary melanocytes were incubated with AT1412. Binding was visualized using an anti IgG1 PE and flow cytometry. Median fluorescence intensities were corrected for isotype control antibody staining. Mel06.07 is the brain metastasis derived from the AT1412 donor patient.

2. AT1412 has single agent activity and synergizes with nivolumab (anti-PD1) to induce tumor rejection of melanoma tumors in a Human Immune System (HIS) mouse model

NSG mice carrying a human immune system subcutaneously transplanted with luciferase expressing melanoma tumors were treated twice per week with AT1412 in the presence or absence of Nivolumab (anti-PD1) (15 + 2.5 mg/kg). Tumor growth is followed during the experiment by whole body bioluminescence detection. Mice were transplanted with melanoma (A) A375 or (B) SK-MEL5 cell-lines.

Conclusion
AT1412
- Is a fully human monoclonal antibody derived from a cured melanoma patient.
- Targets a novel epitope on the tetraspanin CD9 and does not induce platelet aggregation.
- Has broad tumor reactivity to both solid cancers and B-ALL (Poster #531).
- Induced ADCC of tumor cells.
- Enhanced trans-endothelial migration and tumor immune cell infiltration of T cells and monocytes.
- Has single agent activity and can synergized with a PD1 antibody in inhibition of tumor growth.
- Induced transient thrombocytopenia in non-human primates without increased risk of bleeding and bruising.
- AT1412 is currently under preclinical development. First in Human is scheduled for Q1 2021.

Conflict of interest disclosure. IR, JV, MK, DQ, CF, GM, EV, MC, EF, SvdB, PVt, HvE are employees of AIMM Therapeutics. IR, JV, MK, DQ, CF, GM, EV, MC, EF, SvdB, PVt, HvE, HS have equity ownership in AIMM Therapeutics.

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