AB598, a Therapeutic Anti-Human CD39 Antibody, Binds and Inhibits CD39 Enzymatic Activity In Vivo to Promote Anti-Tumor Immunity

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INTRODUCTION

CD39, which poorly binds and inhibits CD39 enzymatic activity, is being developed as a cancer immunotherapy. CD39 catalyzes the conversion of extracellular adenosine monophosphate (AMP) into adenosine diphosphate (ADP), resulting in decreased amounts of immunosuppressive ATP and increased levels of immunostimulatory adenosine in the tumor microenvironment (TME). By blocking CD39 in the TME, levels of ATP increase, leading to myeloid cell activation and improved tumor control.

AB598 is a highly potent and specific, binding and inhibiting human CD39 with sub-micromolar potency, AB598 does not bind or inhibit murine CD39, preventing a challenge for studying CD39 inhibition in an immunosuppressive syngeneic tumor model. Surface CD39 knockout (KO) mice were engineered with a tumor-specific promoter to drive expression of human CD39, allowing for a more physiological assessment of CD39 inhibition in solid tumors compared to the alternative use of human cells growing in immunodeficient mice.

RESULTS

AB598 Bolsters Extracellular ATP In Combination With Oxisplatin

Oxisplatin Induces the Hallmarks of CD3

Human CD39 Knock-In Mice are an Immunocompetent Model Amenable to CD39 Inhibition

AB598.mlg2a + OXA Combination Shows Efficacy Compared to Single Agents in a C57BL/6 hCD39KI MC38 Model

Peripheral Blood from hCD39KI Mice Treated with AB598.mlg2a Shows Full Receptor Occupancy

Peripheral Blood from hCD39KI Mice Treated with AB598.mlg2a Shows a Decrease in Cell Surface CD39

Surface Expression of CD39 Decreases with AB598.mlg2a Treatment in Tumor Draining Lymph Nodes

Peripheral Pathology of hCD39KI Mice Treated with AB598.mlg2a in a C57BL/6 hCD39KI MC38 Tumor Model

CONCLUSION

Our results indicate the superb ability of AB598.mlg2a to inhibit intratumoral CD39 enzymatic activity, resulting in tumor growth inhibition. The findings presented here provide a rationale for the combination of CD39 inhibition with ICD-inducing chemotherapy in the clinic.

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Figure 3: Human CD39 Knock-In Mice are an Immunocompetent Model Amenable to CD39 Inhibition

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