Phase 1 Trial Safety and Efficacy of Ragistomig, a Bispecific Antibody Targeting PD-L1 and 4-1BB in Advanced Solid Tumors

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Introduction

ABL503 and Mechanism of Action

- Ragistomig (ABL503/TJ-L-14B) is a full-length anti-PD-L1 mAb (R-) linked human immunoglobin G1 fused with single chain variable fragment of anti-4-1BB engaging mAb **Figure 1**
  - PD-1 (PD-L1) blockade enhances the amplitude of tumor immunity by reprogramming suppressive and stimulatory signals that yielded more powerful cancer control
  - 4-1BB is a co-stimulatory receptor of the tumor necrosis factor receptor family, which is expressed on a wide variety of cell types. Anti-4-1BB antibodies have shown to possess strong antitumor properties due to CD8+ T-cell activation, production of interferon-γ, and induction of cytolytic marker[1]
- Activation of T-cells in the tumor microenvironment by 4-1BB agonist antibodies is a promising approach to augment PD-(L)1 inhibitor efficacy. Ragistomig is a bispecific antibody combining PD-L1 antagonist with 4-1BB agonistic activity, designed to induce 4-1BB signaling only when bound to the PD-L1 tumor antigen on cancer cells, which may overcome resistance to PD-(L)1 inhibition and avoid hepatotoxicity seen with previously developed 4-1BB mAbs[2] **Figure 1**

Figure 1
Ragistomig (ABL503/TJ-L-14B) and mechanism of action.

Major Preclinical Observation

- ABL503-induced anti-tumor response was protective against tumor re-challenge in efficacy model (hPD-L1+MC38) due to increase of immunological memory function[1] **Figure 2**
- ABL503 induces cell killing in PD-L1 blockade-resistant lung cancer organoids **Figure 3**

Figure 2 Immunological memory function (in vivo)

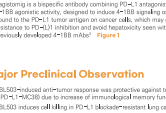
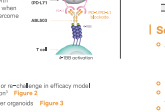


Figure 3 Tumor killing activity in anti-PD-L1 non-responder (in vitro)


% of killing
IgG1
Anti-PD-L1
ABL503
Donor(M)
Donor(F)
Donor(M)
Donor(F)
Donor(M)
Donor(F)