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NOVEL, IMMUNE AGONISTIC CEACAM1/5 ANTIBODY (YB-200) DEMONSTRATES ANTI-TUMOR EFFICACY AND SIGNIFICANTLY INCREASES B-CELL RESPONSE IN SYNGENEIC LIVER HEPA1-6 TUMOR MICROENVIRONMENT

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Background Carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1) and 5 (CEACAM5, CEA) are members of the carcinoembryonic antigen (CEA) family. CEACAM1 is expressed on a variety of immune cells and acts as a cell–cell communication molecule. The signal transduction process is associated with immune cell activation, apoptosis, proliferation and differentiation. In the pathophysiological stage, CEACAM1 and 5 are dysregulated in various malignancies including, for instance, breast, lung, and gastrointestinal cancer. This seems associated with poor prognosis linked to a novel checkpoint blockade mechanism mediated by homophilic CEACAM1–1 and heterophilic CEACAM1–5 interaction between immune and tumor cells, respectively. YB-200 is a novel IgG1 antibody targeting CEACAM 1/5, which has shown to preserve the immune agonistic function of CEACAM1 on leukocytes in addition to potentially inhibiting both the homophilic and heterophilic checkpoint blockade of CEACAM1 and 5 on tumor cells. The present study was designed to test the *in vivo* anti-tumor activity of YB-200 and its effect on immune cells.

Methods Anti-tumor activity of YB-200 was assessed using the validated ReactionBiology's SubQperior[®] experimental syngeneic liver Hepa-1-6 tumor model. The tumor cells were injected into the mammary fat pad of C57BL/6 mice. On Day 5 after tumor cell injection, animals were randomized (median tumor size ~50 mm³) in two groups and treatment started. Mice were treated i.p. BIWx3 with either isotype control or YB-200 at 10 mg/kg/administration. Animals were euthanized on Day 20, and tumors harvested for flow cytometry analysis. Flow cytometry for immune-cell profiling was performed using the ReactionBiology All-in-one[®] staining panel.

Results Treatment with YB-200 induced statistically significant tumor growth inhibition by ~80% compared to isotype control, at well-tolerated dose. Flow cytometry analysis revealed that YB-200 led to a 10-fold increase in B-cells in the tumor micro-environment compared to the isotype control. In addition, a statistically significant increase in CD3+ and CD4+ T-cells was observed while granulocytes decreased.

Conclusions This study demonstrates that treatment with YB-200 induced statistically significant tumor growth inhibition compared to isotype control in a validated hepatocellular carcinoma model. Consistent with the role of CEACAM1 as cell–cell communication molecule the anti-tumor activity of YB-200 was correlated with a strong modulation of the immune cell compartment in the tumor micro environment.

Ethics Approval This animal study has been approved by the Ethics Committee for Animal Experimentation and is registered by the regional board Freiburg, Germany. Mice were handled according to the German animal welfare law and the GV-SOLAS guidelines.

<http://dx.doi.org/10.1136/jitc-2022-SITC2022.1384>