**INTRODUCTION**

- Bintrafusp alfa is a first-in-class bifunctional fusion protein composed of the extracellular domain of the TGF-βRII receptor, to function as a TGF-β "trap," fused to a human IgG1 antibody blocking PD-L1 (Figure 1).

**RESULTS**

- **Figure 2. Change in target lesions assessed by investigator**
  - NK
  - Tumor cells are also a major source of TGF-
  - PD-1

- **Figure 3. Best change in target lesions from baseline assessed by investigator**
  - Patients with a BOR of NE (n=5) are not included in this figure. Five additional patients were not included in this figure because it closely mimics human stage IV

- **Figure 4. HMGA2 expression by investigator-assessed BOR**
  - HMGA2 expression was 32-fold higher in patients who experienced disease control with bintrafusp alfa compared with those who had PDI (Figure 4).

- **Figure 5. Association between HMGA2 and TGF-β signaling, and bintrafusp alfa pharmacodynamic effects in a TNBC model**
  - Bintrafusp alfa or Trap control (TGF-β trap linked to an inactive anti-PD-L1) reduced expression of these HMGA2-correlated TGF-β signaling-related genes relative to anti-PD-L1 or isotype control treatment (Figure 6), suggesting that HMGA2 is correlated with TGF-β-induced signaling more strongly in the presence of TGF-β sequestration.

- **Figure 6. Effects of bintrafusp alfa on HMGA2 expression and TGF-β signaling activity**
  - Gene expression

- **Figure 7. Correlation between HMGA2 and TGF-β genes Core genes**
  - HMGA2 expression significantly correlated with the expression of TGF-β receptors, ligands, collagen, and EMT-related genes in bintrafusp alfa-treated mice (Figure 7).

**CONCLUSIONS**

- **Patients with TNBC who experienced disease control with bintrafusp alfa had high expression of HMGA2**

- **In a murine model, the correlation of HMGA2 and TGF-β signaling was stronger in bintrafusp alfa-treated tumors compared with isotype control-treated tumors**

- **These data demonstrate a link between HMGA2 expression and TGF-β; bintrafusp alfa and Trap control reduced expression of HMGA2 and individual TGF-β signaling-related genes relative to anti-PD-L1**

- **Collectively, these observations warrant further analysis of the potential link between bintrafusp alfa antitumor activity and HMGA2**

- **Based on phase 1 trial results and biomarker analysis, a phase 2 study is planned to evaluate the clinical activity of bintrafusp alfa in patients with HMGA2-high TNBC**

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**REFERENCES**


**Table No. 1573**

- **Figure 8. Correlation between HMGA2 and TGF-β genes Core genes**

- **Table 1. **

**Poster No. 1573**

**Association between TGF-β signaling and HMGA2, a potential biomarker for bintrafusp alfa in triple-negative breast cancer**


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