Results from phase I dose escalation of IMC-F106C, the first PRAME × CD3 ImmTAC bispecific protein in solid tumors


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Background

IMC-F106C is the first TCR bispecific protein targeting CD3 and PRAME, the most broadly expressed cancer testis antigen, which is homogenously expressed in multiple tumors (eg, lung, ovarian, endometrial, melanoma, breast). ImmTAC bispecifics redirect polyclonal T cells to target intra/extracellular cancer proteins, as validated by tebentafusp (tebe; gp100×CD3 ImmTAC) with an overall survival benefit in metastatic uveal melanoma (mUM).

Methods

HLA-A*02:01+ patients (pts) with selected advanced tumors are eligible. Prospective PRAME testing required in low PRAME prevalence tumors. Primary objectives: safety and recommended dose. Secondary/exploratory objectives: efficacy, biomarkers and ctDNA response. IMC-F106C is dosed weekly with extended monitoring for intra-patient dose escalation during first 3 wks until target dose (TD).

Results

As of April 2022, 42 heavily pre-treated pts, across tumor types, were treated in 9 cohorts (TD 0.3-160 mcg) during dose escalation. 86% of tumors were confirmed PRAME+, median H score = 203. Most common (>30%) related AEs were consistent with the mechanism of action: pyrexia 64%; cytokine release syndrome (CRS) 45%; hypotension, fatigue 38% each; chills 36%; and nausea 33%. These were mostly Grade (G) 1/2, occurred in first 3 wks and rapidly resolved. 31% pts had related G3/4 AEs, most commonly lymphopenia 14% and AST increase 7%. There were no G3/4 CRS, treatment related discontinuations or deaths. Confirmed PRs were seen at TD of ≥ 20 mcg, a threshold dose for consistent and robust T cell activation. 18 pts at ≥ 20mcg were confirmed PRAME+, including 5 mUM pts who progressed on prior tebe. In 13 tebe-naive pts, 69% (9/13) had tumor shrinkage and 38% (5/13) had a partial response (PR) including 2 of 3 cutaneous melanoma (all failed prior anti-PD1 & CTLA4), 1 of 2 ovarian, 2 of 5 mUM. All PRs are confirmed, 4 PRs ongoing. ctDNA response was observed across multiple tumor types and included some pts with complete clearance.

Conclusions

IMC-F106C, the first PRAME×CD3 ImmTAC, is well tolerated and demonstrated durable RECIST partial responses and ctDNA response in PRAME+ pts across multiple tumor types. Dose escalation and multiple expansions are ongoing.

Clinical trial identification

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Legal entity responsible for the study

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Disclosure