Abstract #9534: Phase 1b trial of IFx-Hu2.0, a novel personalized cancer vaccine, in checkpoint inhibitor resistant Merkel cell carcinoma and cutaneous squamous cell carcinoma

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Background: Merkel cell carcinoma (MCC) and cutaneous squamous cell carcinoma (cSCC) exhibit high response rate to immune checkpoint inhibitor (ICI). However, patients with advanced disease who fail initial ICI therapy have limited treatment options. IFx-Hu2.0 (IFx) is a plasmid DNA encoding for an immunogenic bacterial protein, Emm55m, formulated with a transfection agent for direct intratumoral injection. In a phase 1 study in advanced melanoma, biomarker analyses demonstrated robust immune priming effects of IFx administration. As part of an ongoing Phase 1b study, we evaluated the safety and immunologic response of different schedules of IFx intratumoral administration in patients with advanced MCC or cSCC. We report the initial results of the first stage of this study. ClinicalTrials.gov Identifier NCT01460065.

Methods: Methods: In the first trial stage (n=11), IFx was administered intratumorally in up to 3 lesions on 3 schedules; weekly x 1, 2, or 3. We report safety and efficacy data for these patients as well as preliminary correlative studies. Given the proposed potential for immune priming effects of IFx, we performed an unplanned exploratory analysis of post-protocol treatment efficacy to evaluate for response to ICI rechallenge if given. Data cutoff for clinical outcomes was February 2023.

Trial Design: This study follows a two-stage design with primary goal to assess the safety and tolerability of repeated dosing schemes of the study agent. In the first trial stage (exposure escalation), a 3+3 trial design was utilized to assess safety of repeated weekly intratumoral vaccinations using a fixed dose of IFx (Cohort 1 ± single dose, Cohort 2 ± 2 doses, 1 week apart, Cohort 3 ± 3 doses, weekly). If successful, the second trial stage (expansion) would be conducted to increase the total study sample size to 20.

Study Timeline:
- Week 1 (screening to treatment)
- 1-3 weeks (treatment cycles)
- 4 weeks (DLT window and time from last dose to final trial assessment)
- Total on-protocol time ± 6-8 weeks.

Efficacy: Best response to trial therapy was SD in 2 patients and PD in 7. One MCC patient experienced complete clinical response in 2 injected lesions, but had progression of disease overall with development of new disease areas. Both patients with SD (one MCC, one cSCC) had only the injected site as a known disease area and experienced a clinical response in injected site (not meeting RECIST criteria for PR).

Results: Patient Demographics

Five patients with advanced MCC and four with cSCC were enrolled. Prior to trial enrollment, all patients with MCC received ICI with pembrolizumab (4) oravelumab (1), all had progressive disease with median 3 months treatment (2.3-4.5mo). All 4 patients with cSCC previously received cemiplimab with median 6 months treatment (3.0-11.5mo).

Toxicity: IFx was well tolerated at all dose schedules evaluated with no treatment-related significant adverse events (SAEs) observed. As per protocol, 3 patients were enrolled in each predefined study cohort and cohort #3 (weekly dosing x 3) was selected for the second stage of the study (expansion).

Results: Post-protocol ICI Rechallenge

Following completion of protocol therapy, all 5 MCC patients and 2 of 4 cSCC patients were treated with anti-PD-1 therapy as the immediate post-protocol therapy: pembrolizumab (3) oravelumab (2) in MCC and cemiplimab (2) in cSCC. Four of 5 MCC patients and 1 of 2 cSCC patients, or 5 of 7 total (71%), experienced objective response to ICI rechallenge in this setting, with duration of response ongoing in 4 patients (7+8+9+20 months) and one response lasting 23 months. All 4 MCC patients with post-protocol response to anti-PD(L)1 therapy had previously experienced progression to this same drug class prior to treatment on protocol.

Conclusions:

I	IFx-Hu2.0 is safe and well tolerated at weekly dosing repeated up to 3 weeks. In an exploratory post-hoc analysis, five of seven patients (71%) treated with standard of care ICI agents immediately following protocol therapy experienced a durable objective response despite prior failure of the same drug class prior to protocol enrollment suggesting an "immune priming" effect of study therapy. An additional 11 patients are planned for enrollment in the expansion stage of the study using the weekly x 3 dosing schedule. Exploratory biomarker analyses are ongoing.

References