Final Results of a Phase II Multicenter Trial of HF10, a Replication-competent HSV-1 Oncolytic Virus, and Ipilimumab Combination Treatment in Patients with Stage IIIB-IV Unresectable or Metastatic Melanoma

Abstract #166420

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Introduction

HF10 is a bioselected replication-competent oncolytic virus derived from HSV-1. In preclinical studies, combining ipilimumab (CTLA-4 antibody) with HF10 has shown a higher rate of complete tumor disappearance and significant improvement in the median overall survival compared with either HF10 or ipilimumab alone. The current Phase II trial of HF10 and ipilimumab combination treatment was designed to assess the efficacy and safety of patients with Stage IIIB, IIIC, or IV metastatic malignant melanoma.

Phase II Study Design

Study Objectives

Evaluate the efficacy, safety and tolerability of HF10 at 1x10^7 $TCID_{50}$/mL in combination with 3mg/kg ipilimumab (ipi) in patients with Stage IIIB, Stage IIIC, or Stage IV unresectable or metastatic malignant melanoma.

Endpoints

Primary:

- Best overall response rate (BORR) at Week 24

Secondary:

- Safety and tolerability
- Objective response rate (ORR) at Weeks 12, 18 ,24
- Progression-free survival (PFS)
- Durable response rate (DRR)
- 1-year survival rate
- Evaluation of correlative studies

Key Inclusion Criteria

- Stage IIIB, IIIC or IV unresectable/unresected or histologically confirmed diagnosis of metastatic malignant melanoma
- Measurable (mWHO & irRC) superficial tumor suitable for injection
- Ipilimumab-eligible patients including patients previously treated with antitumor agents other than i.v. Ipilimumab.
- Adequate hepatic, renal, bone marrow function
- ECOG 0, 1, 2
- Life expectancy ≥24 weeks
- No known bleeding diathesis or coagulopathy

Study Treatment

- Intratumoral injection of HF10 at 1x10^7 $TCID_{50}$ /mL in combination with intravenous infusions of 3mg/kg ipilimumab
- Up to 5.0mL of HF10, the injection volume to be adjusted based on the size of tumor mass

Phase II Overall Results

Table 1: Safety Summary

Treatment-Emergent Adverse Events (TEAEs)	Number of Patients (%)
Safety evaluable patients	46
With any TEAEs	46 (100%)
With any TEAEs related to HF10	42 (91%)
With severity ≥ Gr 3 for HF10 related TEAEs	3 (6.5%)
With any TEAEs related to Ipilimumab	43 (93%)
With severity ≥ Gr 3 for Ipilimumab related TEAEs	10 (22%)
With any serious, HF10 related TEAEs	2 (4%)
With any serious, Ipilimumab related TEAEs	10 (22%)
Who discontinued drug due to HF10 related TEAEs	0 (0%)

Table 2: Responses in the Efficacy Evaluable Population

Best Overall Response (N=44)	24 weeks (N%)	48 weeks (N%)
Overall Response (ircR + irPR)	18 (40.9%)	20 (45.5%)
Disease Stability rate (ircR +irPR+irSD)	30 (68.2%)	30 (68.2%)
Complete Response (ircR)	8 (18.2%)	8 (18.2%)
Partial Response (irPR)	10 (22.7%)	12 (27.3%)
Stable Disease (irSD)	12 (27.3%)	10 (22.7%)
Unconfirmed Progressive Disease (unconfirmed irPD)	11 (25.0%)	11 (25.0%)
Confirmed Progressive Disease (confirmed irPD)	3 (6.8%)	3 (6.8%)

Figure 1: Best Overall Response at 24 Weeks

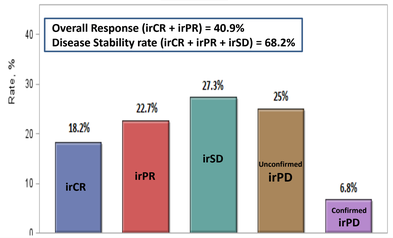


Figure 2: Response in Treatment Naïve vs ≥ 1 Prior Therapy

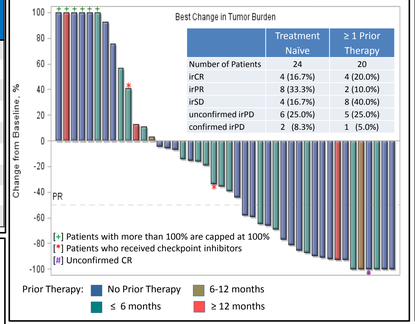


Figure 3: Kaplan-Meier Curve for Overall Survival in the Efficacy Evaluable Population

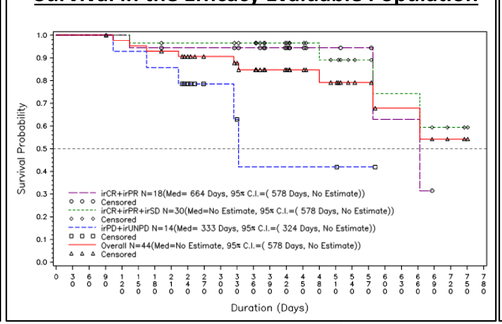


Figure 4: Cytokine Changes in Responders and Non-Responders

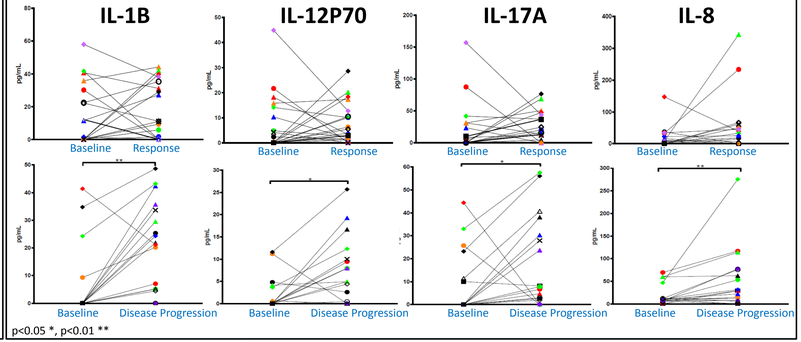


Figure 5: Responses in Injected and Never Injected Lesions

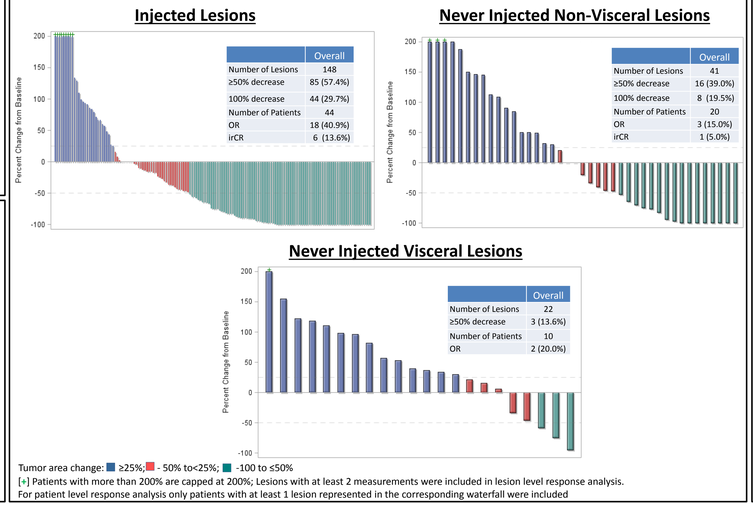
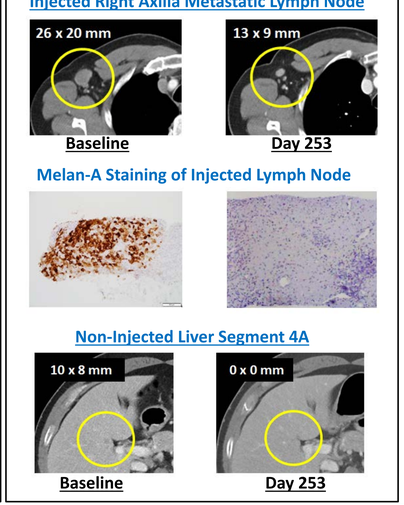


Figure 6: Response of Patient 001-040



Discussion/Conclusions

Treatment with HF10 plus ipilimumab was well-tolerated. Of 46 patients enrolled and treated: 59% men, median age 67 yrs (range 28 to 91); disease stage 20% IIIB, 43% IIIC and 37% IV. Most HF10-related AEs were ≤Grade 2, similar to HF10 monotherapy. No DLTs were reported. 37% had ≥Grade 3 AEs, the majority due to ipi. HF10-related ≥Grade 3 AEs (n=3) were embolism, lymphedema, diarrhea, hypoglycemia, and groin pain. Of the 44 efficacy evaluable pts per irRC, BORR at 24 weeks was 40.9% (18.2% ircR and 22.7% irPR); disease stability rate was 68.2% (27.3% irSD). HF10+ipi treatment resulted in a decrease in lesion size by ≥50% in 57.4% of injected lesions, 39% of never injected non-visceral lesions,and 13.6% of never injected visceral lesions. Complete resolution of lesions occurred in 29.7% of injected lesions and 19.5% of never injected non-visceral lesions. Of 44 efficacy evaluable pts, BORR at 24wks in treatment naïve pts was 50% (16.7% ircR, 33.3% irPR) and pts with ≥1 prior cancer therapies was 30% (20% ircR, 10% irPR). As of 19APR2017, median PFS was 19 months; 1-year overall survival rate was 85%. We are currently analyzing the cytokine profiles of responders versus non-responders.

Conclusions

The combination HF10 and ipilimumab treatment demonstrated a favorable benefit/risk profile and encouraging antitumor activity in pts with stage IIIB, IIIC, or IV unresectable or metastatic melanoma.

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