

A Phase 1b/2 Open Label Study of Tivozanib in Combination with Durvalumab in Subjects with Advanced Hepatocellular Carcinoma: DEDUCTIVE

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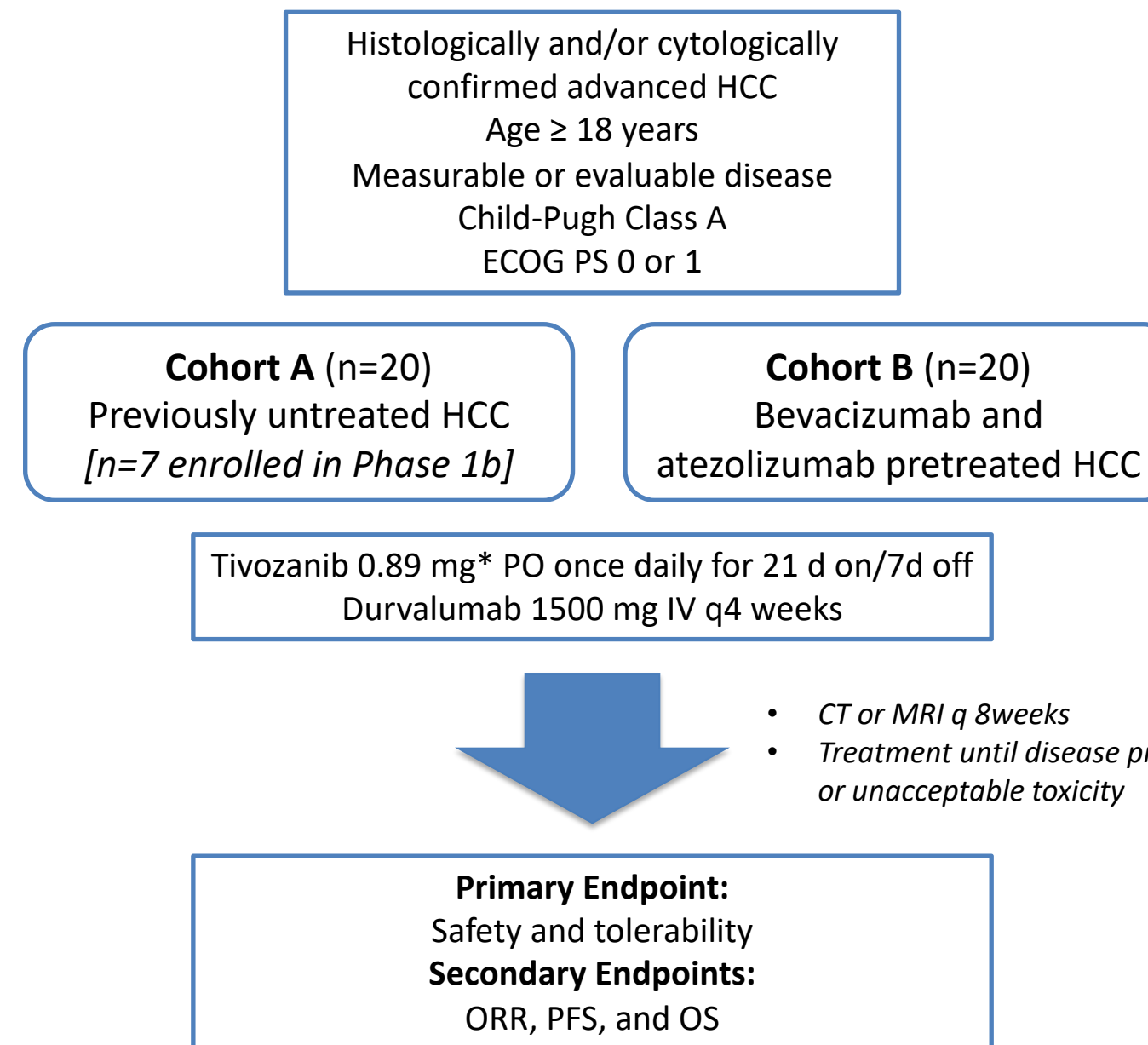
Background

- Tivozanib, a potent and selective VEGFR 1, 2 and 3 TKI, and durvalumab, an anti-PD-L1 antibody, have both demonstrated single agent activity in hepatocellular cancer (HCC).^{1,2}
- The combination of atezolizumab, a PD-L1 antibody, and bevacizumab, a VEGF-A monoclonal antibody, has improved the standard of care in untreated advanced HCC with a median PFS of 6.8 months and a 1-year overall survival of 67.2%. Serious toxic effects were noted in 38% of patients who received the combination.³
- The currently approved agents used in the 2nd line setting have all been evaluated in patients with HCC only after exposure to 1st line sorafenib, which may no longer be the standard of care.
- Evidence-based treatment options for HCC patients that progress on atezolizumab and bevacizumab are therefore limited; and opportunities to improve the toxicity profile of effective combination therapy in untreated HCC are needed.

Rationale for Tivozanib plus Durvalumab

- Tivozanib has been shown to reduce production of regulatory T cells (**Figure 1**),⁴ thus potentially facilitating immune-mediated responses.
- Durvalumab blocks the interaction of programmed death ligand 1 with the immune checkpoint receptor PD-1, thus facilitating cytotoxic T cell proliferation.²
- The selectivity and favorable tolerability of the VEGFR TKI tivozanib¹ may allow it to be used more readily as a combination therapy with an immune checkpoint inhibitor, potentially leading to improved safety and efficacy in previously treated and untreated HCC.
- These mechanisms may act additively or synergistically to remove inhibition of the immune response that mediates antitumor activity.⁴
- DEDUCTIVE is a Phase 1b/2, multicenter, open-label study to assess the safety and efficacy of tivozanib with durvalumab in patients with advanced HCC previously untreated (cohort A) or bevacizumab- and atezolizumab-pretreated HCC (cohort B).

Study Design and Methods:



*equivalent to 1 mg tivozanib hydrochloride salt

Cohort A has completed enrollment and Cohort B is currently enrolling.

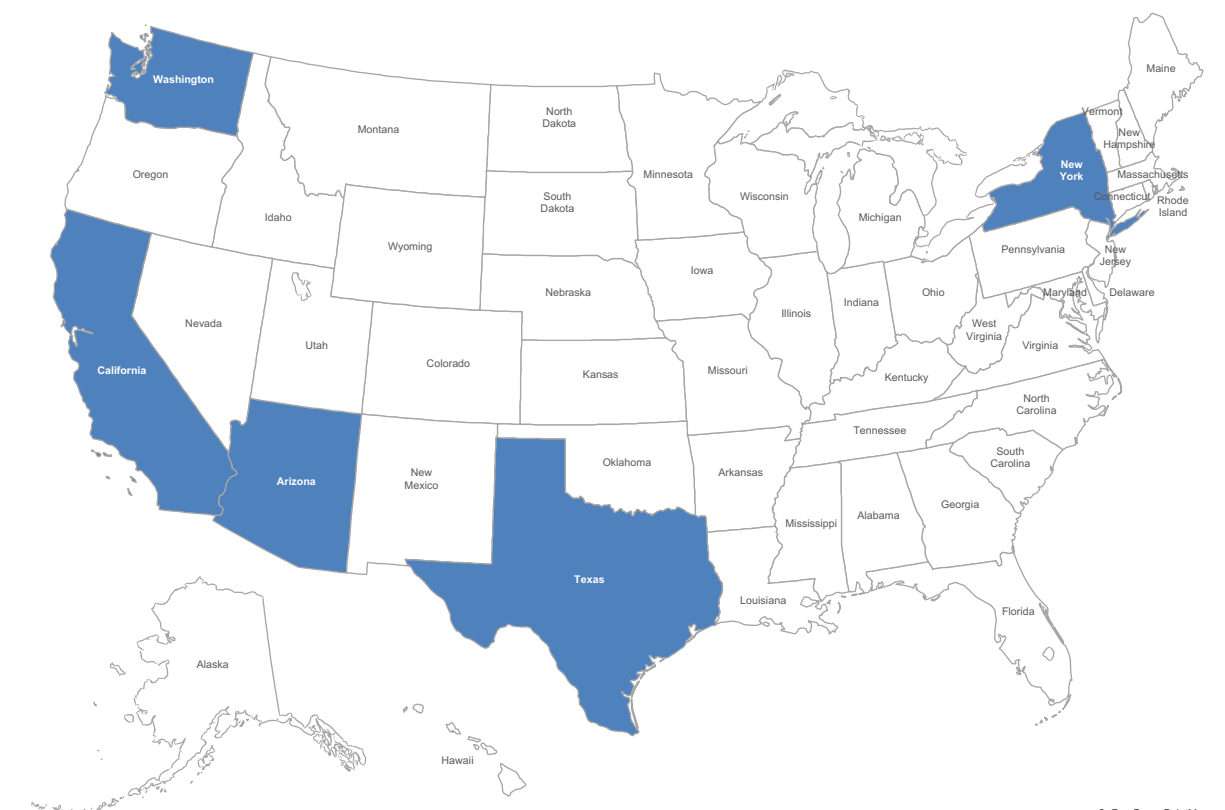
DEDUCTIVE will evaluate the safety, tolerability, and efficacy of tivozanib in combination with durvalumab in advanced HCC previously untreated (cohort A) or bevacizumab- and atezolizumab-pretreated HCC (cohort B).

Previously Reported Phase 1b Results

- Phase 1b dose-escalation portion of DEDUCTIVE enrolled n=7 previously untreated subjects and was presented at ASCO-GI 2021 (Abstract 294).
- The recommended phase 2 dose (RP2D) of tivozanib was 0.89 mg (equivalent to 1 mg commercially available tivozanib hydrochloride) PO once daily for 21 d on/7 d off combined with durvalumab 1500 mg IV q4 weeks.
- Safety:
 - There were no ≥ grade 3 AEs in Cycle 1
 - 6 of 7 subjects experienced an adverse drug reaction
 - The most common AEs (each seen in 2/7 patients) were: cough; diarrhea; fatigue; hypertension; and PPE
 - 1 subject experienced a treatment-related SAE for grade 3 GI hemorrhage, which resolved
- Efficacy and safety results for Phase 2, Cohort A (previously untreated HCC) are presented in a separate poster (ASCO GI 2022, Abstract 462)**

DEDUCTIVE Study Sites

- DEDUCTIVE is currently enrolling at 12 sites in the United States.



References and Acknowledgements

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Figure 1. Reduction in regulatory T cells with Tivozanib⁴

