show that non-GCB subjects had a higher proportion of clinical response (4/8, 50%), compared to 3/10 (30%) in GCB subjects. DPX-Survivac-induced T cell responses were observed in 8/19 subjects (42.1%) including 6 subjects with clinical response (PR, CR), one SD and one PD. Multiplex-IHC analyses demonstrated baseline tumor PD-L1 expression in 6/7 subjects with a clinical response (85.7%, p<0.05). Similarly, subjects with higher baseline CD4+ and CD8+ T cell infiltration demonstrated a trend towards clinical response (table 1).

Conclusions DPX-Survivac, intermittent low-dose CPA and pembrolizumab is generally well tolerated and can induce clinical responses in subjects with r/r DLBCL (7/11, 63.6% of evaluable subjects), including subjects with both non-GCB and GCB subtypes. Pre-treatment biopsies of clinical responders were characterized by higher baseline tumor PD-L1 expression and CD4 and CD8 infiltration. Extending this exploratory data in a larger cohort may define a r/r DLBCL patient population with a higher likelihood to respond to this novel combination immunotherapy.

Trial Registration NCT03349450

Ethics Approval This study was approved by the Ontario Cancer Research Ethics Board, approval number 0981.

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Abstract 357 Figure 1 Proposed Mechanism of Action of TAK-573

doses ≥ 0.2 mg/kg. The duration of saturation was dose dependent with doses ≥ 0.75 mg/kg saturating CD38 RO through 24 hours. All dose levels tested resulted in increases in the type I IFN gene signature at 24 hours. Consistent with CD38 being an IFN stimulated gene, TAK-573 treatment resulted in CD38 RD increases most notably on NK cells, but also on other CD38+ cells including MM cells. Circulating levels of IFN-associated cytokines were also elevated, with maximal induction 4 hours after the EOI. CD8+ T-cells in BM showed increased CD69 expression in 7 of 9 patients analyzed, 3 of whom also showed increases in both IFNγ and granzyme B positivity suggesting TAK-573 treatment results in increased BM cytolytic CD8+ T-cells, in a subset of patients.

Conclusions These preliminary biomarker data indicate that TAK-573 is a pharmacologically active molecule that mediates its effect through IFNAR pathway modulation. Additional data are being collected to further refine the mechanism of action (Image 1), which will inform the recommended phase 2 dose and optimal schedule of administration for the development of TAK-573.

Trial Registration ClinicalTrials.gov: NCT03215030

Ethics Approval The TAK-573-1501 study is approved by WIRB-Copernicus Group, University of Nebraska Medical Center, Dana Farber Cancer Institute and Advarra IRBs.

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Abstract 358 TRIAL IN PROGRESS: A PILOT STUDY OF COMBINED IMMUNE CHECKPOINT INHIBITION IN COMBINATION WITH ABLATIVE THERAPIES IN SUBJECTS WITH HEPATOCELLULAR CARCINOMA (HCC)

Background Locoregional therapies for hepatocellular carcinoma, such as transcatheter arterial chemoembolization (TACE) or ablation, can induce a peripheral anti-tumor immune response. This may be amplified by immune checkpoint inhibitors (ICI). Early and higher anti-CTLA4 dosing could potentially lead to better priming and a stronger immune response. Recent data has suggested that early (Day 1 only), increased doses of anti-CTLA4 therapy, was associated with encouraging clinical activity and a tolerable safety profile. This study will evaluate dual immune checkpoint, CTLA4 (tremelimumab, day 1-only dosing) and PD-L1 (durvalumab) blockade in combination with TACE in patients with advanced