

administered A+T, and with HNSCC administered A+P are also reported as of 30 June 2020.

Results Fifty-five pts enrolled into this portion of the study. Twelve patients with ≥ 2 L GC received A+T+ram+pac and were evaluated for safety. No DLTs were reported, and the ALX148 maximum administered dose was 15 mg/kg QW. Out of the 9 pts who experienced any adverse event, 7 pts reported treatment-related adverse events (TRAE). The most common TRAEs were low grade diarrhea, fatigue, pruritus and rash (each n=2, 17%). Nine of the 12 patients were response-evaluable and reported a 66% ORR with 6PR and 3SD (including one ongoing near PR, 29.6%). Three patients with 1L HNSCC were administered A+P+5FU+platinum. No DLTs were reported and accrual to 15 mg/kg QW continues. Three pts experienced any AE, none were treatment-related. Of 3 evaluable patients with HNSCC, 2PR and 1SD were reported. Initial ALX148 combination PK and CD47 target occupancy are similar to that of single agent administration. Response duration and survival follow-up of 19 pts with HER2-positive GC administered A+T (2nd or later-line; 21% ORR) and of 10 pts with checkpoint inhibitor naïve HNSCC administered A+P (2nd or later-line; 40% ORR) will be reported. Results of all cohorts will be updated at time of presentation.

Conclusions Initial data suggests the myeloid checkpoint inhibitor, ALX148, is well tolerated in combination with the above anticancer antibodies, T-cell checkpoint inhibitor, and cytotoxic chemotherapy regimens with early anticancer signals in GC and HNSCC that compare favorably with historic controls. No MTD has been reached in any combination to date and accrual to chemotherapy combination regimens is ongoing.

Trial Registration ClinicalTrials.gov identifier NCT03013218

Ethics Approval The study was approved by all participating institutions' Ethics and/or Review Boards

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CDX1140-01, A PHASE 1 DOSE-ESCALATION/ EXPANSION STUDY OF CDX-1140 ALONE (PART 1) AND IN COMBINATION WITH CDX-301 (PART 2) OR PEMBROLIZUMAB (PART 3)

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Background CDX-1140 is an agonist anti-CD40 mAb selected to optimize systemic exposure and hence tumor microenvironment (TME) ingress. CDX-1140 activity may be enhanced by combining with CDX-301 (recombinant Flt3L), a dendritic cell growth factor, or with pembrolizumab, an anti-PD-1 mAb.

Methods Patients with advanced solid or hematologic (Part 1 only) tumors are enrolled. Part 1 dose-escalation results have been presented (SITC 2019). In Part 2, CDX-1140 dose-escalation (0.09–1.5 mg/kg q4w) is in combination with CDX-301 (75 mcg/kg sc QD x 5 for 2 cycles). In Part 3, CDX-1140 dose-escalation (0.72–1.5 mg/kg q3w) is in combination with pembrolizumab 200 mg q3w. Part 1 and 2 expansion cohorts are dosed at the CDX-1140 MTD, 1.5 mg/kg q4w. Part 3 expansion cohorts are planned. Peripheral blood and tumor biomarkers analysis are ongoing.

Results 92 patients have been treated (Part 1 n=57, Part 2 n=31, Part 3 n=4). Part 1 expansion cohorts in SCCHN (n=7) and RCC (n=5) are fully enrolled. Part 2 dose-escalation completed to the highest CDX-1140 dose and a SCCHN expansion cohort is ongoing. Part 3 dose-escalation recently initiated. Safety data is available for 23 and 10 patients at the MTD in Part 1 and 2, respectively. In general, the safety profiles were similar, with arthralgia (52% vs. 50%), pyrexia (44% vs 50%), fatigue (30% vs. 50%), chills (39% vs. 40%), vomiting (30% vs. 20%), nausea (26% vs 40%), myalgia (22% vs. 30%), increased ALT (22% vs. 20%), and increased AST (22% vs. 30%) being the most common drug related AEs at the MTD in Part 1 and 2, respectively. Most AEs were low grade. Across all cohorts, cytokine release syndrome (CRS) (G2 n=4, G3 n=2) occurred in 6 (Part 1 n=2; Part 2 n=4) and pneumonitis (G3) occurred in 5 (Part 1 n=4; Part 2 n=1) patients. Immune activation in the TME consistent with CD40 agonism and increases serum inflammatory cytokines were observed. Evidence of anti-tumor activity/clinical benefit include SD (n=13), tumor cavitation (n=2) and a uPR in solid tumors. A patient with follicular lymphoma has an ongoing durable complete metabolic response.

Conclusions The CDX-1140 MTD dose of 1.5 mg/kg, a dose level expected to provide good systemic exposure and TME penetration, is generally well tolerated alone and with CDX-301. Transaminitis and CRS have generally been low grade and infrequent. A cohort combining CDX-1140 with chemotherapy will be initiated in patients with previously untreated metastatic pancreatic adenocarcinoma.

Trial Registration NCT03329950

Ethics Approval The study was approved by the following: Providence St. Joseph Health IRB, approval number MOD2020001128; WIRB, approval number 1188814 (Hauke, Gabrail, Bordon & Gordon); University of Pennsylvania IRB, approval number UPCC 18917; Mount Sinai School of Medicine IRB, approval number 18-00202; Memorial Sloan Kettering Cancer Center IRB, approval number 18-225A; Houston Methodist IRB, approval number MOD00000836

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