NOVEL INTRATUMORAL AGENT, INT230–6 INDUCES CANCER CELL DEATH, INCREASES TUMOR INFILTRATES AND RESULTS IN DURABLE BENEFIT ALONE OR IN COMBINATION WITH PEMBROLIZUMAB IN REFRACTORY PATIENTS

1Anthony El-Khoueiry*, 1Jacob Thomas, 1Anthony Olszanski, 1Nilofar Azad, 1Lewis Bender, 1Ian Walters, 2Giles Whalen, 2Diana Hanna, 2Matthew Ingam, 2Ukran Su, 1University of Southern California, Los Angeles, CA, USA; 3Fox Chase Cancer Center, Philadelphia, PA, USA; 4Johns Hopkins, Chevy Chase, MD, USA; 5Intensity Therapeutics, Westport, CT, USA; 6University of Massachusetts, Worcester, MA, USA; 7Columbia University, New York, NY, USA; 8Princess Margaret Cancer Center, Toronto, ON, Canada

Background INT230-6 is a novel formulation of cisplatin and vinblinutane with an amphiphilic cell penetration enhancer that has been shown to enhance dispersion of the drug throughout tumors and allow diffusion into cells when given intratumorally. In preclinical models, INT230-6 has resulted in cell death, dendritic cell influx, antigen presentation and T-cell engagement with strong synergy when combined with checkpoint inhibitors

Methods This phase 1/2 study evaluated Q2week injections of INT230-6 x 5 dose by tumor volume alone or with 200 mg pembrolizumab IV Q3 weeks. Eligible patients had any advanced malignancy refractory to standard therapy with an injectable tumor.

Results Sixty subjects (median 3 prior therapies (range 0–10)) were enrolled (53 monotherapy, 7 combo). Median age was 60 (42–85). 19 different cancer types were accrued with breast cancer and sarcoma being the most frequent. Over 200 deep tumor injections were administered at doses of up to 172 ml of INT230-6 (86 mg of CIS, 17 mg of Vin). PK analysis revealed <5% of the drugs were measured in systemic circulation, indicative of minimal systemic exposure. There was no dose limiting toxicity. The most frequent monotherapy drug related AE’s reported were: injection-site pain 58%, nausea 37%, fatigue 33%, and vomiting 27% with only 18% of subjects experiencing a grade 3 AE (no grade 4 or 5). Rates were comparable for the single agent INT230-6 and the combination with pembrolizumab. In the overall monotherapy cohort, patients completing all 5 doses of INT230-6 over 56 days (n=16), the median overall survival has not yet been reached. After a median followup of 408 days. In the 5 evaluable patients who received the pembrolizumab combination, the median TTP has not been reached with a median follow up of 6 mo. Paired biopsies (pre, 1 month) were available in 10 monotherapy patients and revealed a median of 63% reduction in viable cancer cells on H&E (30% had no viable cancer) that was also associated with qualitative decreases in Ki67, increases of CD4 and CD8 T-cells and reduction in FoxP3 Tregs. Despite receiving only 2 month of monotherapy, short half lives of the active agents, and no subsequent therapies, 8 injected tumors continued to regress past 1 year.

Conclusions INT230-6 is well tolerated when administered intratumorally alone or in combination with pembrolizumab. Pharmacodynamic assessments provides proof of concept that this drug can reduce viable cancer cells and increases CD4/CD8 T-cell infiltrates leading to durable clinical benefit off treatment.

Trial Registration NCT 03058289

Ethics Approval The study was approved by USC, Princess Margaret Cancer Center, Fox Chase, UMass, Columbia, and Johns Hopkins Institution’s Ethics Board

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0411