INTRATUMORAL INT230-6 SHOWS A FAVORABLE SAFETY PROFILE AND EARLY SIGNS OF EFFICACY IN ADVANCED SOFT TISSUE SARCOMA WITH MONOTHERAPY AND IN COMBINATION WITH IPILUMUMAB [INTENSITY IT-01; BMS#CA184–592]

1Matthew Ingham*, 2James Hu, 3Giles Whalen, 4Jacob Thomas, 5Anthony El-Khoueiry, 6Diana Hanna, 7Anthony El-Khoueiry, 8Christian Meyer, 9Nilofer Azad, 10Syed Mahmood, 11Lewis Bender, 12Ian Walters, 13Alibruni Razak, 14New York Presbyterian Hospital/Columbia, New York, NY, USA; 15Keek School of Medicine of USC, Los Angeles, CA, USA; 16UMass Memorial Medical Center, Worcester, MA, USA; 17Fox Chase Cancer Center, Philadelphia, PA, USA; 18 Johns Hopkins, Baltimore, MD, USA; 19Intensity Therapeutics, Inc., Westport, CT, USA; 20Princess Margaret Cancer Centre, Toronto, Canada

Background Study IT-01 evaluates INT230-6, a novel formulation of cisplatin (CIS) and vinblastine (VIN) with an amphiphilic cell penetration enhancer designed for intratumoral (IT) administration, as monotherapy or in combination with ipilimumab (IPI). In preclinical studies, INT230-6 increases drug dispersion throughout the tumor, allows drug diffusion into cancer cells and recruits dendritic, CD4 and CD8 T-cells. Further, the addition of IPI has shown to improve INT230-6 responses in preclinical models. 1

Methods IT-01 is an open-label phase 1/2 study, currently enrolling adult subjects with locally advanced, unresectable or metastatic solid tumors, including soft tissue sarcoma (STS). The study assesses the safety and efficacy of INT230-6 administered IT Q2W up to 5 treatment sessions as monotherapy or with IPI 3mg/kg IV Q3W for 4 doses. Biopsies from injected tumor are taken pretreatment and Day 28 for immunohistochemistry (IHC) analysis.

Results 22 subjects with STS (14 INT230-6 monotherapy, 8 IPI combination) have been enrolled with a median age was 65, having a median of 4 (2,10) prior therapies. INT230-6 doses of up to 175 mL (87.5 mg of CIS, 17.5 mg VIN) were injected in one or more tumors at a single dosing session, which contains doses exceeding the typical IV doses of the cytotoxic drugs. 2 PK analysis estimates that 95% of INT230-6 active agents remain in the tumor. The most common (>25%) related adverse events (AEs) in evaluable monotherapy subjects (n=13) were localized pain (77%), fatigue (39%), decreased appetite (31%), and nausea (31%). The most common (>25%) related AEs in evaluable IPI subjects (n=4) were anemia (50%), fatigue (50%), pruritus (50%), and rash maculo-papular (50%). There were no related grade 4 or 5 AEs in either cohort. The median overall survival (OS) estimate for the monotherapy population (n=14) has not been reached with a median follow-up of 425 days, which compares favorably to results seen in basket studies of patients with similar prognostic factors (ECOG, LDH, # of metastatic sites). 3 4 IHC results indicate influx of CD4 and CD8 T-cells without meaningful changes in circulating inflammatory cytokines. Abscopal effects in the monotherapy arm were observed in multiple lesions in 4 subjects. OS data for the 8 IPI combination subjects is immature.

Conclusions IT INT230-6 is well tolerated when administered as monotherapy and combined with IPI in STS subjects. INT230-6 monotherapy survival compares favorably to published basket studies in STS with similar prognostic factors. IHC and abscopal effects indicate dosing may activate a T-cell mediated immune response.

Trial Registration NCT # 03058289

REFERENCES

Ethics Approval The protocol was approved by an institutional review board, independent ethics committee, or research ethics board at each institution. All subjects or their legally acceptable representative provided written informed consent before screening. The study was designed, undertaken, and reported in accordance with the Declaration of Helsinki, and is registered with clinicaltrial.gov with registration no NCT03058289.

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