SAFETY AND SURVIVAL RESULTS FROM A PHASE 1/2 TRIAL OF INTRATUMORAL AGENT INT230-6 (CISPLATIN VINBLASTINE) INDUCES IMMUNOLOGICAL CANCER CELL DEATH ALONE OR WITH PEMBROLIZUMAB IN PATIENTS WITH FRAGILEXITY, METASTATIC CANCERS

Background Study IT-01, KN-A10: INT230-6 is a new product with a unique dual anti-cancer mechanism. The drug is comprised of cisplatin and vinblastine co-formulated into a molecule that enables drug dispersion throughout an injected tumor and diffusion into cancer cells. The drug directly kills cancer and activates an immune response. Results from a neo-adjuvant breast cancer study confirm that a single injection induces necrosis in up to 95% of a tumor and recruits TILs.

Methods INT230-6 intratumoral (IT) treatments are Q2W up to 5 followed by maintenance dosing Q9W. Dose is set by the tumor’s longest diameter or volume. Pembrolizumab is 200mg IV Q3W in the INT230-6 combination arm. Biopsies from the injected tumor at pretreatment and day 28 are sent for immunohistochemistry analysis. Endpoints are safety and exploratory efficacy by overall survival.

Results Sixty-four subjects received INT230-6 alone (median 4 prior treatments). Thirty received INT230-6 + pembrolizumab (median 3 prior). There were 652 image-guided INT230-6 IT injections (378 to visceral tumors eg lung, liver, pancreas) median 5 injections, range (1,50). Doses ranged from 0.14 up to 175mL (87.5 mg of cisplatin, 17.5mg vinblastine – much higher than typical IV doses). The INT230-6 arm enrolled 19 cancer types; the PEM combination recruited primarily colon, pancreatic, TNBC or bile duct cancers. IHC results show marked reduction in DAPI of proliferating cancer cells with influx of CD4 and CD8 T-cells. Non-injected visceral tumors shrank in several INT230-6 monotherapy subjects. Due to drug absorption or immune influx RECIST is not ideal for use with INT230-6 (ASCO2022). Overall survival is preferred. The estimated median OS (mOS) was 361 days for INT230-6; the mOS for the combination has not been reached (173 days of median follow-up). Pharmacokinetics shows >95% of the active agents remain in the injected tumor at 1 hour compared to IV. The most common (>20%) treatment-related adverse events (TRAEs) for INT230-6 alone/combination were localized pain (59%/50%), nausea (39%/13%), fatigue (28%/20%) and vomiting (23%/20%). The incidence of grade 3 TRAEs for the INT230-6 and combination arms were 10% and 20%. One combination patient had a grade 4 neutrophil decrease that quickly resolved. No patient discontinued therapy due to treatment toxicities.

Conclusions Intratumoral injections of large drug volumes into visceral tumors was feasible and well-tolerated. Biopsies confirmed immunological cell death. OS was compelling for this heavily pretreated population lacking standard therapeutic options. INT230-6 may offer a well-tolerated treatment for refractory patients and is entering randomized controlled trials.

Trial Registration [Intensity-IT-01, Merck-KN-A10] NCT03058289

REFERENCES