INT230-6, a novel intratumoral (IT) formulation demonstrated a favorable safety profile during injections into a variety of refractory and superficial tumors with evidence of tumor regression and immune activation.

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Unintended Therapeutics and the National Cancer Institute’s Vaccine Branch have collaborated to evaluate the safety of intratumoral (IT) injections of a novel formulation of cisplatin (CIS), vinblastine (VIN) and an adjuvant (SHAO) that improves intratumal and tissue diffusion by passive diffusion.

INT230-6 has demonstrated the ability to induce an adaptive immune response in animal models and to component in initiating an anti-tumor immune response is priming the immune system with a low burden of antigens. Cisplatin, a component in INT230-6, has properties that can induce immunotoxicity can potentially target in the tumor to recruit immune cells and stimulate a systemic immune response. Given the increased diffusion into cancer cells of the cytotoxic agents using the specific technical data package for INT230-6, this antigen presentation increases influx of antigen priming cells (APCs) to the tumor microenvironment and improves APCs ability to recognize antigens potentially more effectively then local destructive modalities such as radiation.

The role of cytotoxic agents in augmenting the response of checkpoint inhibitors, was explored based on the Merck Keynote 189 trial in NSCLC. It is our aim to determine the role of INT230-6 and antigenspecific cytotoxic agents in the clinic.

INT230-6 is now in a Phase 1/2 clinical trial in the US and Canada at 5 major academic centers. Here we report preliminary safety and response data from 34 subjects having different tumor types.

ENDPOINTS

Primary Outcome Measures for Phase 1:

• The primary objective was to assess the safety and tolerability of multiple intratumoral doses of INT230-6 in heavily advanced or recurrent malignancies. This was assessed by the rate of 2 grade 3 adverse events attributed to INT230-6 and the underlying disease

Additional Outcome Measures for Phase 1:

• Characterized the pharmacokinetic profile of multiple doses of the three INT230-6 components (CIS, VIN, and SHAO) after single and then multiple IT tumor site injections.
• Assessed the preliminary efficacy of INT230-6 by measuring the injected tumor response using RECIST 1.1 response thresholds.
• Monitored tumor response in non-small cell lung cancer (NSCLC) patients.
• Evaluated various tumor- and anti-tumor immune response biomarkers that may correlate with tumor response.

SAFETY

There were no DLTs and one drug related SAE (grade 3 abdominal pain) 20 unrelated SAEs were reported in 10 subjects, all related to underlying disease.

Related AE by max severity in more than 1 patient

• Most adverse events were mild grade and transient.
• Syncope side effects do not appear dose-related to severe or with repeat dosing.

BIOMARKERS

Blood samples at 2 weeks show increases in CD8+ and CD4+ T-cells compared to baseline (n=25 evaluable).

Example of a breast cancer subject with a pre- and one month post first dose biopsy. There was a 75% reduction in IV 67Ga (magnetic) and 75% reduction in F18Fa (fluorine) intensity increase in CD8 and CD4 T-cells (using whole section image analysis)

RESULTS AND CONCLUSIONS

• INT230-6 was well tolerated at doses up to 120 mL in multiple deep and superficial tumor injections.
• Some patients received IT twice the approved IV dose for VIN without substantial cytotoxic side effects
• PK suggests that the majority of the drug remains in the tumor (based on AUC comparison to historical IV data)
• The study drug and dosing procedure were well tolerated.
• Multiple different types of injected tumors demonstrated visible necrosis, decreased contrast uptake and size reduction.
• Some patients reported decreases in cancer related symptoms.
• Eight patients had a decrease in size of un-injected lesions
• Increases in tumor and circulating CD8 and CD4 T-cells and absopocal responses in non-injected tumors support preclinical findings of immune cell engagement following INT230-6 treatment.

Enrollment of various tumor types is ongoing to better characterize the safety and efficacy at higher doses. Future cohorts to include INT230-6 plus anti-PD-1 and anti-CTLA-4 drugs. Tumor specific phase 2 expansion cohorts will be determined by the steing steering committee.