Abstract 11568, POSTER 502: INTRATUMORAL INT230-6 (CISPLATIN, VINBLASTINE, SHAO) ALONE OR WITH IPILIMUMAB PROLONGED SURVIVAL WITH FAVORABLE SAFETY IN ADULTS WITH REFRACTORY SARCOMAS (NCT 03058289)

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BACKGROUND AND METHODS

- Metastatic **soft tissue sarcomas are a deadly and diverse group of solid tumors** derived from mesenchymal cells; highly toxic chemotherapy provides only limited benefit and **immunotherapy to date has shown to be mostly ineffective as treatment.**
- **A new localized method of cancer killing has been created** using a novel formulation (INT230-6) consisting of cisplatin (CIS),vinblastine (VIN) and a diffusion enhancer molecule (SHAO) specifically designed to **enable drug dispersion throughout a tumor and cancer cell penetration** via a passive process following intratumoral (IT) injection.
- The **drug causes apoptosis and necrosis** resulting in dendritic & T-cells flux to the tumor.
- IT-01 is an open-label phase 1/2 study in adults with locally advanced, unresectable or metastatic solid tumors, including sarcoma. INT230-6 dose was set by tumor diameter or volume and was given IT Q2W for up to 5 doses alone or with IPI IV at 3mg/kg Q3 weeks for 4 doses. Maintenance dosing of INT230-6 was Q9W.
- **Previously reported results showed INT230-6 alone induced tumor regression in uninjected lesions[1]** (an abscopal effect) in multiple cancer types both immunogenic (hot) and non-immunogenic (cold) with T-cell infiltrates identified within the tumor.

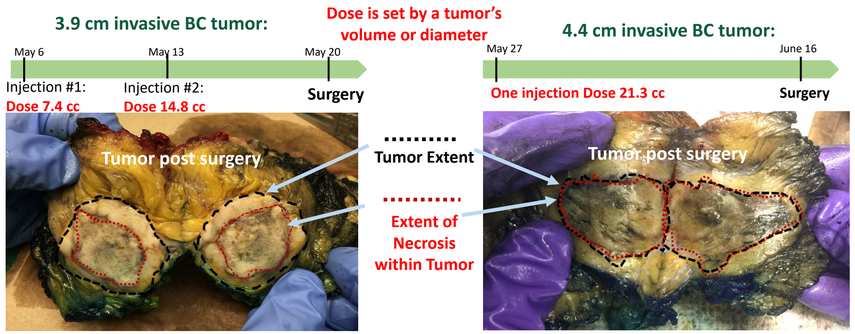
Primary Outcome Measures for Phase 1/2 study: Assess the preliminary efficacy of INT230-6 alone or in combination with immunotherapy as measured by overall survival and disease control rate in specific cancer types.

Additional Outcome Measures for Phase 1/2:
Characterize the overall safety of INT230-6 alone or in combination with immunotherapy by the rate of grade 3 or higher adverse events (AEs) attributed to the study treatments.

Characterize the pharmacokinetic (PK) profile of multiple doses of the three INT230-6 components (CIS, VBL, and SHAO) after single and then multiple IT tumor site injections.

INTRATUMORAL INJECTION OF INT230-6 LEADS TO DRUG DISPERSION THROUGHOUT THE LESION AND HIGH PERCENTAGES OF NECROSIS IN LARGE HUMAN TUMORS

Tumor death is dependent on total dose given per treatment (images below are from a neoadjuvant study in breast cancer)



Final Pathology (significant necrosis ~85%)

Final Pathology (significant necrosis >95%)
Residual cancer is mostly ghost cells

1. Thomas, J. S, et. al. SITC 2021 Abstract Number: 501

INT230-6, a locally delivered cytotoxic treatment leading to a systemic immune response in hot or cold tumors, **is a new way to treat cancer**

Compared to synthetic controls[2] INT230-6 alone **extended survival in refractory soft tissue sarcoma subjects by nearly 450 days** with favorable safety; OS may be improved with IPI

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SCAN ME

SARCOMA SUBJECTS DEMOGRAPHICS

Demographics (Datalock)	INT230-6 (n=15)	INT230-6 + IPI (n=14)
Age (median, range)	64 (41.9-76.1)	63.2 (33-82.1)
Gender	73.3% male	50% male
ECOG	0 (13.3%), 1 (80%) 2 (6.7%)	0 (42.9%) 1 (57.1%)
Median # of prior therapies, (range)	3 (0-8)	5 (0-9)
# of tumors injected (% deep)	120 (47.5)	127 (69.4%)

SAFETY

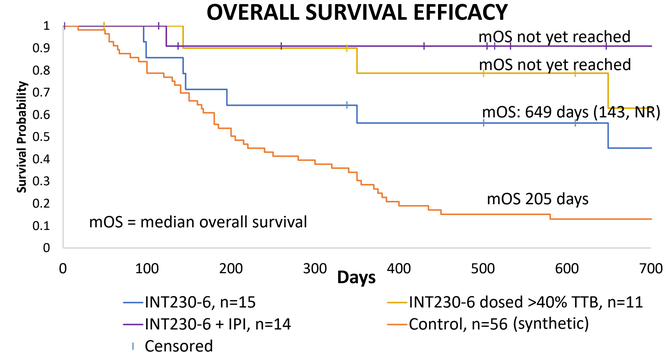
The vast majority of TEAEs related to the drug regimen were grade 1 or 2; two monotherapy and one combination subject had a grade 3 AE. There were no related grade 4 or grade 5 drug regimen AEs in either arm

Treatment-Emergent Adverse Events (TEAEs), n (%), Considered Related To Drug Regimen by MedDRA Coded SOC/PT – All Sarcoma Treated Population 3 or more events for category.

Data as of February 22, 2023	Monotherapy Sarcoma (N=15)	INT230-6 + IPI Sarcoma (N=14)
Total # of TEAEs Related to Study Drug	107	76
Subjects With at Least One TEAEs Related to Study Drug	14 (93.3%)	12 (85.7%)
Localized tumor-related pain	12 (80.0%)	6 (42.9%)
Fatigue	6 (40.0%)	5 (35.7%)
Nausea	7 (46.7%)	4 (28.6%)
Vomiting	5 (33.3%)	3 (21.4%)
Decreased appetite	5 (33.3%)	2 (14.3%)
Pruritus	0	3 (21.4%)
Rash maculo-papular	0	3 (21.4%)
Anaemia	3 (20.0%)	2 (14.3%)

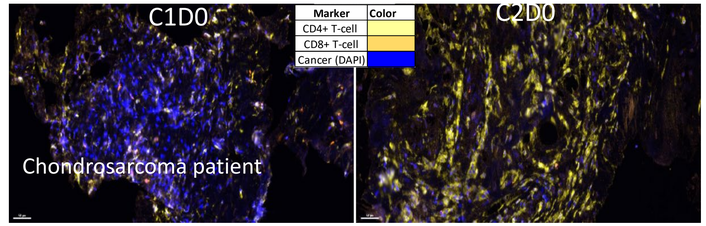
2. Synthetic control: Using survival results based on Royal Marsden Hospital scoring (RMHS) reported in Subbiah V, et al. Sci Rep. 2016;6:35448, we created a synthetic control (n=56) using our study's sarcoma subject's RMHS parameters

OVERALL SURVIVAL EFFICACY



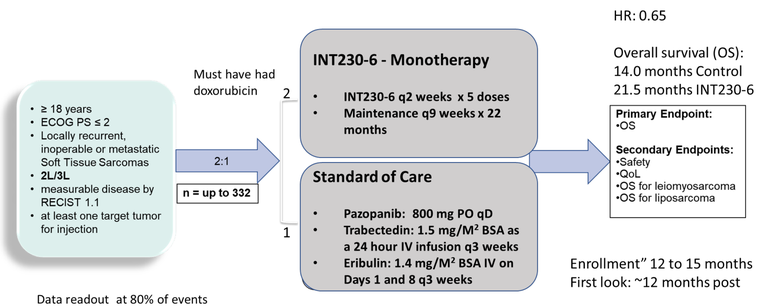
Dosing relative to presenting total tumor burden (TTB) show increased survival with higher drug volume loaded for sarcoma subjects administered INT230-6 with or without ipilimumab compared to a synthetic control[2]. Abscopal responses for INT230-6 alone (previously reported) were primarily in subjects dosed ≥ 40% of TTB. The disease control rate (DCR; Stable disease + partial response + complete response divided by number of subjects) for the all-treated population (those who received at least one dose of INT230-6) was 93% for monotherapy and 86% for the ipi combo. For combo, one subject had yet to reach first timepoint for SD.

INCREASE IN IMMUNE BIOMARKERS IN SARCOMA



Biopsies taken pretreatment cycle 1 day 0 (C1D0) and Day 28 (C2D0) for immunohistochemistry analysis. There was a notable reduction in cancer cells (blue) post 2 doses of INT230-6 at day 28 and an increase CD4+ (yellow) CD8+ T-cells.

FUTURE DIRECTIONS: PHASE 3 STUDY DESIGN



Two interim looks at 50% and 75% of events: test for futility and efficacy