A Pilot Phase II Study to Evaluate the Small Molecule Tigilanol Tiglate in Patients with Advanced Soft Tissue Sarcoma (NCT05755113)

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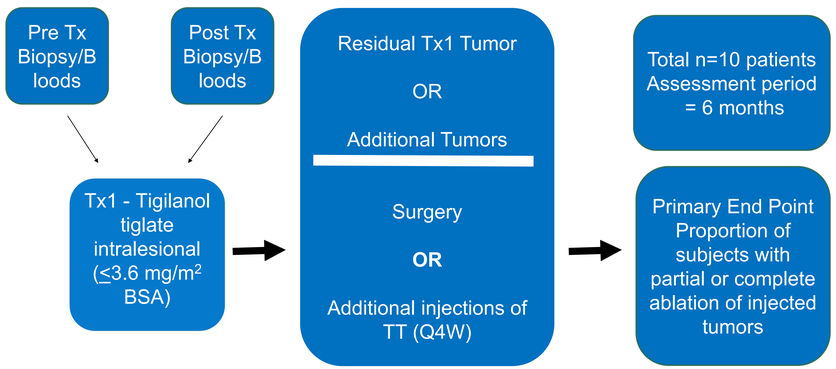
Background and Objectives

- Tigilanol tiglate (TT) is an epoxytigliane small molecule that induces tumor cell necrosis and tumor vascular disruption with potential to induce systemic immunity via immunogenic cell death when injected intratumorally
- In a Phase I, dose escalation study, TT was well-tolerated with clinical activity observed in 9 tumour types including an abscopal response
- One patient with angiosarcoma had a complete response from a single injection of TT 43 days post-injection. The patient was disease free at 25 months post-injection.
- Based on these promising results, this study was designed to investigate the preliminary efficacy of TT specifically in patients with advanced and/or metastatic soft tissue sarcomas (STS).

Methods

- Single center, single arm, open label, pilot Phase II study
- Adults with advanced and/or metastatic STS with tumours accessible for injection
- ECOG PS ≤ 2
- Lesion(s) volume measured by ultrasound (±CT or MRI)



- Observing response in ≥ 20% of patients was predefined as promising
- **Secondary endpoints**: Adverse events; pharmacokinetic assessments
- **Exploratory endpoints**: Tumor microenvironment change in blood and tumor samples

Results

Table 1. Baseline Demographics and Disease Characteristics. 11 patients were enrolled. One was lost to follow-up and was replaced.

Characteristic	Patients, No. N=11
Age, median (range)	
Sex	
Female	4
Male	7
ECOG Performance Status	
0	2
1	8
2	1
Sarcoma Histologic Type	
Leiomyosarcoma	4
Myxofibrosarcoma/UPS	3
Myxoinflammatory fibroblastic sarcoma	1
Extraskeletal Osteosarcoma	1
Angiosarcoma	1
Sarcoma NOS	1
Clinical disease status	
Recurrent/Locally Advanced	6
Distant Metastases	5
Prior Resections, median (range)	3 (0-9)
Prior Radiation	8
Prior Lines of Systemic Therapy, median (range)	3 (0-5)

Figure 1. Example responses after first injection. A) Patient with cutaneous angiosarcoma. B) Patient with intramuscular leiomyosarcoma

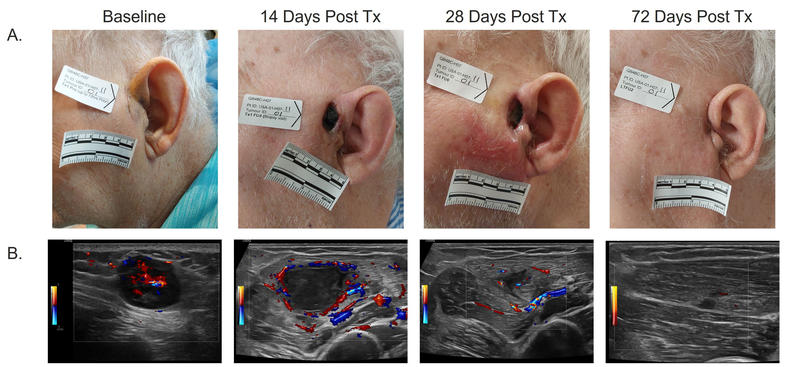


Figure 2. Response rate in injected lesion(s) per patient. 7 of 10 patients had response ≥30%

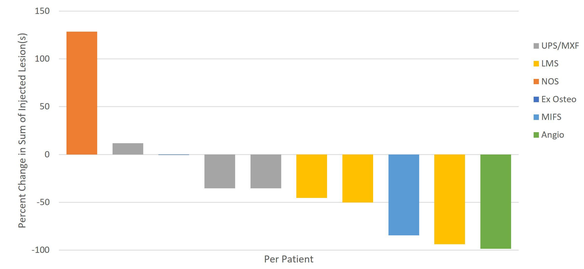


Figure 3. Response rate at 4 weeks in each injected lesion. 10 CR, 8 PR, 2 SD, 5 PD.

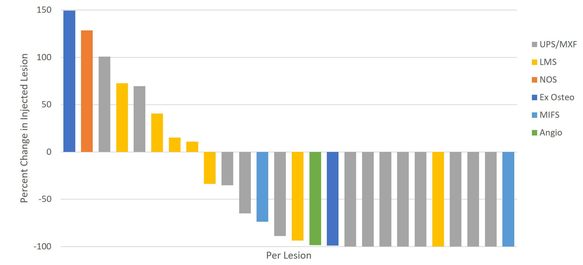


Table 2. Common adverse events.

Adverse Events	N=11	
Grade ≥3 AEs	1	
AEs leading to discontinuation	0	
AEs in ≥2 patients	Grade 1-2	Grade 3
Injection site wound	8	0
Pain at injection site	8	0
Injection site infection	3	1
Odor at injection site	4	0
Drainage at injection site	2	0
Flushing	4	0
Fever	3	0
Bleeding	2	0

Discussion

- Intratumoral TT appears safe for patients with STS.
- Efficacy was observed across numerous STS histologic types, exceeding the primary endpoint for a promising response.
- The tolerability and activity warrant further investigation of TT in patients with STS either alone or in combination with other agents.

References & Disclosures

- Boyle et al. 2014 PLoS One; Panizza et al. 2019 EBioMedicine; Cullen *et al.*2021 Scientific Reports; Cullen *et al.* 2024 Journal of Immunotherapy of Cancer
- Dr. Bartlett receives institutional research support from QBiotics Group and SkylineDx
- This study was sponsored by QBiotics Group

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