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

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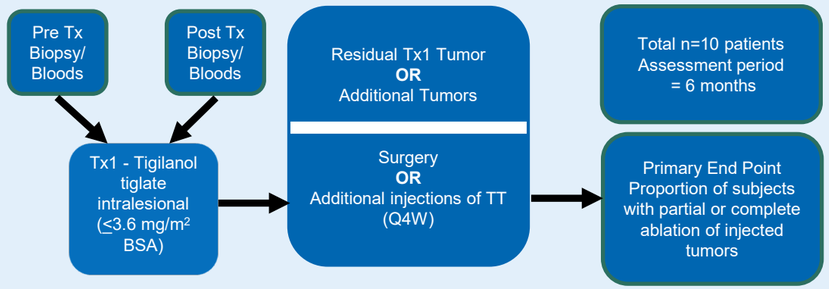
Background and Objectives

- Tigilanol tiglate (TT) is an epoxytigliane small molecule that directly induces tumor cell necrosis and tumor vascular disruption, with potential to induce systemic immunity via immunogenic cell death.
- In a Phase I, dose escalation study, TT was well-tolerated with clinical activity observed in 9 tumor types including an abscopal response.
- Based on these promising results, this current 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 tumor 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

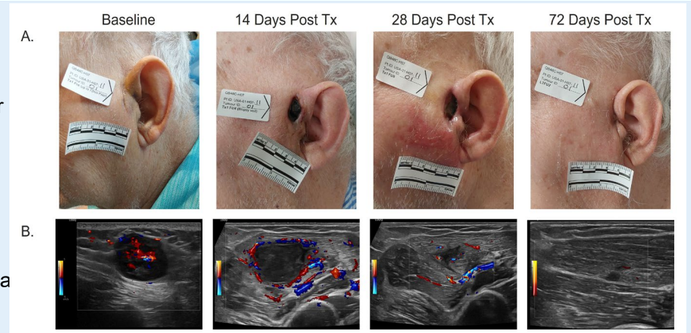


Figure 1. Example responses after first injection. A) Patient with cutaneous angiosarcoma. B) Patient with intramuscular leiomyosarcoma

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 2. Subsequent responses to systemic therapy. 3 patients with pre-existing metastatic sarcoma that was initially non-responsive to systemic therapy, proceeded from TT to subsequent systemic therapy. A) Patient with myxofibrosarcoma treated with gemcitabine/docetaxel/PD-1 inhibition as 4th line. B) Patient with myxofibrosarcoma treated with gemcitabine/docetaxel inhibition as 2nd line. C) Patient with leiomyosarcoma treated with temozolimide in 7th line.

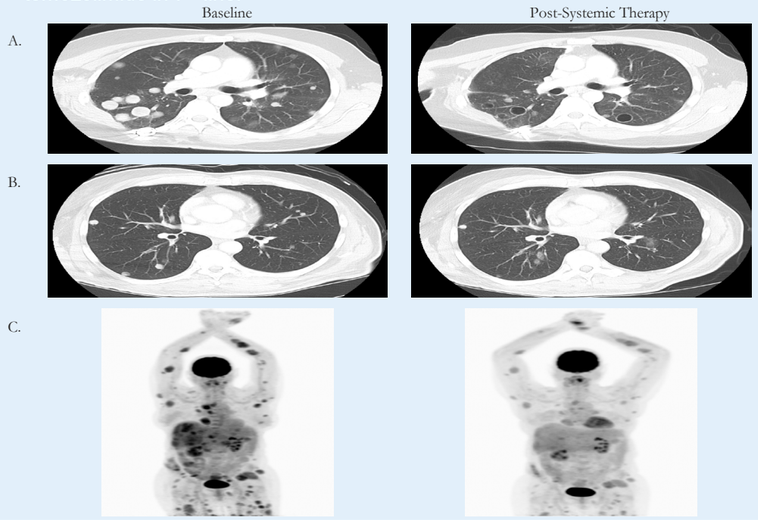


Figure 3. Response rate in injected lesion(s) per patient. 7 of 10 patients had response ≥30%

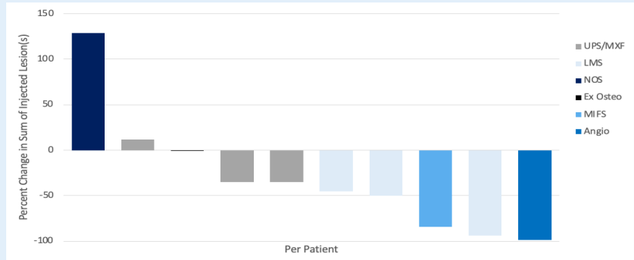


Figure 4. Response rate at 4 weeks in each injected lesion. 10 CR, 8 PR, 2 SD, 6 PD.

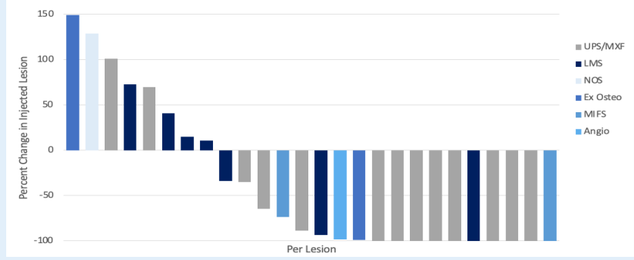


Table 2. Common adverse events.

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

- Intra-tumoral 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
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- A portion of this data was previously presented at ESMO conference, Barcelona, 2024

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