Clinical Activity and Safety of SYNC-T Therapy SV-102 in Patients with Metastatic Prostate Cancer

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BACKGROUND

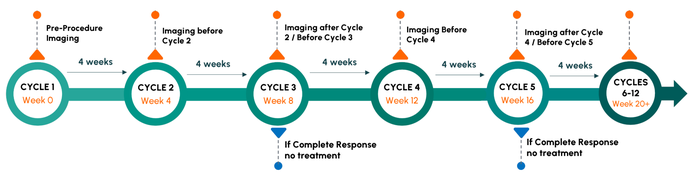
- Conventional systemically administered immunotherapies for metastatic prostate cancer have limited efficacy and significant rates of severe immune-related adverse events, especially when two or more drugs are combined.
- SYNC-T is a novel *in situ* therapy that synchronizes the location of tumor antigens, the SV-102 immunotherapy drug, and immune cells in the tumor microenvironment and locoregional lymph nodes.
- SYNC-T Therapy is initiated with partial oncolysis of a target tumor to release patient-specific tumor antigens, followed immediately by intratumoral infusion of SV-102, leading to immune system education, T cell activation and a systemic anti-tumor immune response.
- SV-102 is designed to target multiple mechanisms of cancer, comprised of 4 active immunotherapies: a PD-1 inhibitor (abazistobart), CTLA-4 inhibitor (futermestotug), CD40 agonist (ciltistotug), and TLR9 agonist (sitmutolimod).
- Herein we report on the first 15 subjects treated with SYNC-T Therapy SV-102.

METHODS

STUDY DESIGN & KEY ELIGIBILITY CRITERIA

- 15 patients with metastatic prostate cancer (10 had failed hormone therapy and 5 had refused hormone therapy) were recruited into a single-arm Phase 1 study (NCT05544227)
- Primary objectives included safety and toxicity, with secondary objectives to assess efficacy and pharmacokinetics
- All were treated and evaluable and received the same dose of SV-102 q4 weeks for up to 12 cycles (median = 6).
- For each cycle a single tumor site was treated, and the primary prostate tumor was targeted in all subjects
- Combination therapy utilizes partial oncolysis of a target tumor with the infusion of SV-102 fixed dose of 15 mL
- Baseline imaging of bone scan and/or PET/CT, and MRI of prostate
- Response assessment every 8 weeks
- Durability of response measured every 12 weeks after completion of therapy
- **Key Inclusion Criteria**: Histologically confirmed metastatic prostate cancer, failure of previous treatment with one or more approved second-generation androgen-receptor-pathway inhibitors with or without prior chemotherapy or refused hormone therapy, and measurable disease by RECIST 1.1 criteria, soft-tissue disease that can be targeted by SYNC-T Therapy
- **Key Exclusion Criteria:** Known other primary malignancy other than prostate cancer that is progressing or has required active treatment in previous 3 years, obstructed urinary system before or after stenting, or undergone major surgery or local prostate intervention within 28 days prior to first SYNC-T cycle

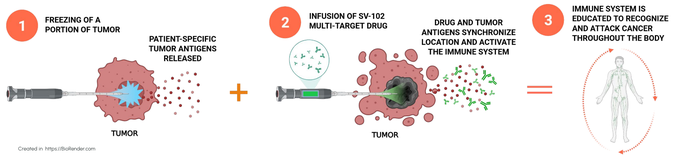
Figure 1. Phase 1 Study Design



SYNC-T THERAPY SV-102 PROCEDURE OVERVIEW

- Utilizing a proprietary needle-like immunotherapy delivery device, partial oncolysis is performed via a proprietary freeze-thaw method that disrupts tumor cell membranes, resulting in immunogenic cell death and the release of damage-associated molecular patterns (DAMPs) and patient-specific tumor antigens.
- Next, the combination immunotherapeutic SV-102, which is designed to target multiple cancer mechanisms, is infused through the same needle delivery device directly into the tumor in the zone of oncolysis.
- The infusion functions to synchronize the location of the SV-102 immunotherapeutic with patient-specific tumor antigens and immune cells in the locoregional tumor microenvironment (TME) and draining lymph nodes.

Figure 2. SYNC-T Therapy SV-102 Procedure Steps



RESULTS

RESPONSE SUMMARY

- Eight patients (53%, the two-sided 95% confidence interval (CI), 29 to 79) demonstrated a complete response (CR)
- Five patients had a partial response (PR) with an overall response rate (ORR) of 87%
- Among 15 patients, 3 have died resulting in 80% survival with 17 months median follow-up
- At baseline, 13/15 patients (87%) had skeletal metastases (range 1-54); 5/13 (38%) had >20 bone metastases. After therapy, all bone metastases resolved in 7/13 (54%) patients when visualized by bone scan and/or PSMA PET scan.

Table 1. Subject Characteristics

Baseline Characteristics		(n = 15)
Demographics	White	9 (60%)
	Hispanic	5 (33%)
	Black	1 (7%)
Age		Median: 61 (Range: 49-74)
ECOG	PS-0	7 (47%)
	PS-1	7 (47%)
	PS-2	1 (6%)
Bone Mets		13 (87%)

Table 2. Overview of Prior Therapy

Prior Therapy	(n = 15)
ADT and/or 2nd generation anti-androgen or subject refused	15 (100%)
Chemotherapy	3 (20%)
Radiation Therapy	5 (33%)
Immunotherapy	2 (13%)

Figure 3. RECIST 1.1 Assessment

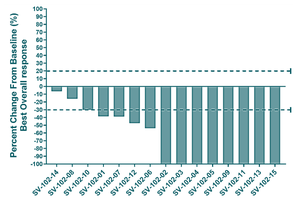


Table 3. Summary of Best Response

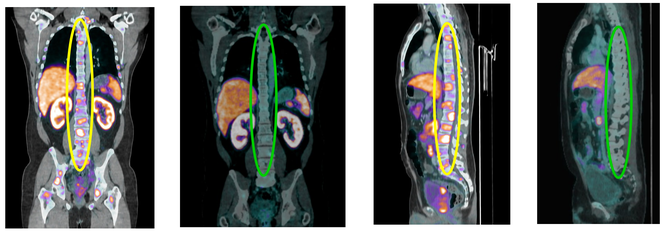
Best Response in Evaluable Subjects (n=15)*	
Disease Control Rate	15 (100%)
Complete Response	8 (53%)
Partial Response	5 (33%)
Stable Disease	2 (13%)
Progressive Disease	0 (0%)
Overall Response Rate	13 (87%)

*Independent radiological review completed on 5/24/2025 reported ORR of 87%, CR of 40% and PR of 47%

Table 4. Summary of Key Results

Summary of Key Results in Months (n=15)	
Median Time to Response (range)	2.9 (1.8–4.8)
Median Duration of Response (range)	12.1 (1.1–22.4)
Median rPFS (range)	14.2 (4.8–24.1)
Median OS (range)	Not Reached (6.1–24.6)

Figure 4. Subject SV-102-09: Complete Response and Complete Resolution of > 50 Bone Metastases



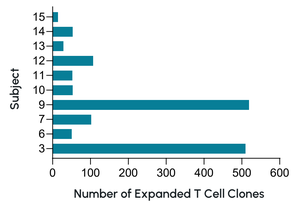
PRE-THERAPY. May 2023 coronal PSMA PET/CT shows extensive bone metastases (greater than 50)

POST-THERAPY. December 2023 coronal PSMA PET/CT shows complete resolution of all bone metastases

PRE-THERAPY. May 2023 sagittal PSMA PET/CT shows extensive bone metastases

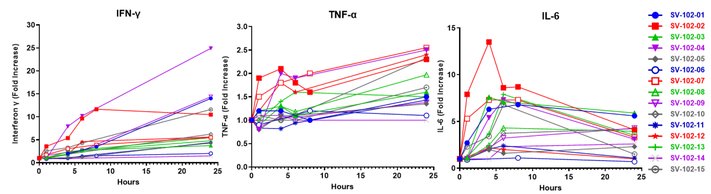
POST-THERAPY. December 2023 sagittal PSMA PET/CT shows complete resolution of all bone metastases

Figure 5. Increase in Frequency of New T Cell Clones



- SYNC-T therapy induced a robust peripheral polyclonal T cell expansion, which increases after additional treatment cycles
- Data shows expanded TCRß clones associated with known MHC-restricted tumor antigens
- SYNC-T therapy may drive a positive selection of polyclonal responses against some tumor antigens

Figure 6. Anti-Tumor Cytokines are Rapidly Induced by SYNC-T Therapy



- Pro-inflammatory cytokines increase during the first 24 hours after SYNC-T Therapy
- IFNγ, TNFα and IL-6 all show significant increases from pre-treatment

KEY TAKEAWAYS

- SYNC-T SV-102 first in human study achieved proof of concept, demonstrating that combining partial oncolysis with a multi-target immunotherapy can effectively generate a systemic anti-tumor immune response in metastatic prostate cancer
- Robust clinical activity: 87% overall response rate (ORR) with 53% complete responses (CR), including complete resolution of widespread bone metastases in 54% of patients
- Favorable safety profile: Predominantly Grade 1 or 2 adverse events (95%) due to low dose and minimal systemic drug exposure, despite infusion of 4 potent immunotherapies
- Innovative therapeutic approach: Synchronizes the location of patient-specific tumor antigens, immune effectors, and SV-102 immunotherapy at the tumor site and in lymphatics
- Next steps: Multi-center LEGION-100 Phase 2 trial (NCT06533644) is enrolling in the U.S.

SAFETY & TOLERABILITY

- SYNC-T demonstrated the ability to target multiple cancer mechanisms while avoiding systemic autoimmune side effects
- The therapy was well-tolerated with adverse events (AE) in 13 patients
- The majority (95%) of AEs were Grade 1 or 2 , most commonly fever and hematuria
- There were two Grade 2 immune-related AEs of hepatitis and hypothyroidism and two Grade 3 AEs of urinary retention and spinal cord compression
- No Grade 4 or 5 TEAEs

Table 5. Overview of Treatment Emergent Adverse Events

Treatment Emergent Adverse Events (TEAEs)	All TEAEs N (%) Events	Grade 1+2 TEAEs	Grade 3 TEAEs	Grade 4/5 TEAEs
Anemia	1 (6.7) 1	1 (6.7) 1	0	0
Chest Pain	1 (6.7) 1	1 (6.7) 1	0	0
Vertigo	1 (6.7) 1	1 (6.7) 1	0	0
Hypothyroidism	1 (6.7) 1	1 (6.7) 1	0	0
Polydipsia	1 (6.7) 1	1 (6.7) 1	0	0
Diarrhea	2 (13.3) 2	2 (13.3) 2	0	0
Rectal Discomfort	1 (6.7) 1	1 (6.7) 1	0	0
Vomiting	2 (13.3) 2	2 (13.3) 2	0	0
Fever	3 (20.0) 4	3 (20.0) 4	0	0
Fatigue	1 (6.7) 2	1 (6.7) 2	0	0
COVID-19	1 (6.7) 1	1 (6.7) 1	0	0
Right Shoulder Fracture	1 (6.7) 1	1 (6.7) 1	0	0
Hepatic Enzymes Increased	1 (6.7) 1	1 (6.7) 1	0	0
Low back pain	1 (6.7) 1	1 (6.7) 1	0	0
Myalgias	1 (6.7) 2	1 (6.7) 2	0	0
Skin Squamous Cell Carcinoma	1 (6.7) 1	1 (6.7) 1	0	0
Spinal Cord Compression	1 (6.7) 1	0	1 (6.7) 1	0
Hematuria	4 (26.7) 4	4 (26.7) 4	0	0
Urethral Discomfort	1 (6.7) 1	1 (6.7) 1	0	0
Urinary Hesitancy	1 (6.7) 1	1 (6.7) 1	0	0
Urinary Retention	2 (13.3) 4	1 (6.7) 3	1 (6.7) 1	0
Urinary Tract Infection	2 (13.3) 2	2 (13.3) 2	0	0
Diaphoresis / hyperhidrosis	2 (13.3) 2	2 (13.3) 2	0	0
Rash	2 (13.3) 2	2 (13.3) 2	0	0
Perineal Hematoma	1 (6.7) 1	1 (6.7) 1	0	0

CONCLUSIONS AND ADDITIONAL INFORMATION

CONCLUSIONS

- These data demonstrate an initial proof of concept that SV-102 can be safely administered, and metastatic prostate cancer can be effectively treated by via a combination of partial oncolysis and intratumoral infusion
- SYNC-T Therapy SV-102 has an acceptable safety profile
- LEGION-100, a multi-center Phase 2 trial is currently enrolling in the US (NCT06533644).

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