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CASE REPORT

Dramatic Clinical Response to a Novel Form of Cell Therapy SL-28 in a Patient with Prostate Cancer and Bone Metastasis: A Case Report

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Purpose: Prostate cancer is the most common malignancy among older man and often a challenge owing to its rapid spread and age-related comorbidities. SL-28 (Leukocyte-Tells) is a novel cell therapy that uses allogeneic leukocytes whose anticancer activity is altered ex vivo using the recently discovered Universal Receptive System.

Patients and Methods: A 79-year-old man with T2cNOMx1, Gleason 7 (3+4) adenocarcinoma of the prostate, with a total PSA level of 10.6 ng/mL and free PSA:total PSA ratio of 11.4% received hormone therapy. Due to an insufficient clinical response and poor tolerance to the therapy, the patient underwent novel allogeneic SL-28 cell therapy.

Results: SL-28 therapy was well-tolerated, with no serious adverse effects. The levels of laboratory markers of prostate cancer, such as prostate-specific antigen, gradually improved from the second week of SL-28 therapy. Complete responses, including the resolution of bone metastasis within 4 months of therapy, were confirmed by computed tomography and histology.

Conclusion: SL-28 was efficient and safe approach in a patient with stage IV prostate cancer, supporting its potential in an allogeneic cell therapy for advanced malignancies.

Keywords: prostate cancer, oncology, cell therapy, leucocyte-tells, SL-28, teazeled receptors, TezR, Universal receptive system

Introduction

Prostate cancer is the most common malignancy among older males, particularly those over 65 years of age.[1] While some tumors progress slowly, others grow rapidly and metastasize early, particularly to the bones and lymph nodes.[2] Managing prostate cancer in older adults poses significant challenges due to the presence of age-related comorbidities such as cardiovascular disease, diabetes, and reduced renal function, which can limit treatment options.[3]

Complete responses to cell therapies remain rare and challenging to achieve in patients with advanced solid tumors. The only exception is the use of tumor-infiltrating lymphocyte (TIL) therapy for melanoma, which has a reported complete response rate of 4%.[4] Achieving a complete response for other types of solid tumors, using either TILs or chimeric antigen receptor (CAR) T cells, remains challenging and is rarely reported.[5]

Recently, we discovered a novel Universal Receptive System present across the whole tree of life.[6–10] This system orchestrates cellular responses to different environmental stimuli and regulates cell memory and forgetting.[7]

We developed a method using the TezR receptors of the Universal Receptive System, without direct genetic modification, to orchestrate leukocyte activity (ie, lymphocytes and granulocytes, no dendritic cells) and generate so called "Leukocyte-Tells", as previously described.[10,11] Compared to CAR-T (exerting modified anticancer activity

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through the gene editing allowing for the elimination of target cells that express the corresponding antigen) or TILs (involving a T-cell subpopulation of the patient expanded outside the body and reinfused to eliminate a specific tumor type in the same patient), Leukocyte-Tells are not genetically modified and are not trained against any specific tumor.[12] Their enhanced antitumor activity is generated through novel regulatory pathways triggered upon TezRs receptor destruction.[10,11] Leukocyte-Tells exhibit unusually high activity against various microorganisms, including antibiotic-resistant strains and cancer cells. RNA-Seq data and differential expression analyses for the transcriptional profiles identified approximately 1,300 upregulated differentially expressed genes in Leukocyte-Tells compared with that to Leukocyte-Controls. The functional pathway analysis revealed that these genes were enriched in four broad functional categories: immune cell signaling, immune cell migration, membrane uptake, and enhanced energy metabolism.[11] SL-28 is an allogeneic, non-HLA-matched, cell-based therapy composed of Leukocyte-Tells obtained from the blood of healthy donors, with increased activity through the Universal Receptive System.[10,11] Access to and use of investigational cell therapies for patients with advanced solid tumors varies across countries, with the allowance to use them based on local IRB approvals in the Eurasian Union, including Kazakhstan. For this study, the compassionate use (expanded access) pathway was employed under NCT06872489.

Here, we report a complete response in a patient with stage IV prostate cancer following the therapy with SL-28.

Case Presentation

A 79-year- old man is presented in January 2024 with a chief complaint of increased urgency, frequent urination, and pelvic pain. The first complaint of dysuria with episodes of incontinence dates back to November 2022, when benign prostatic hyperplasia was diagnosed.

Based on the results of clinical examinations and laboratory analyses, the patient was clinically suspected of having prostatic cancer. The serum prostate-specific antigen (PSA) (normal range, <4.50 ng/mL) and free PSA levels were >10.4 ng/mL and 1.21 ng/mL respectively, resulting in a low free PSA to total PSA percentage ratio of 11.4% (free PSA above 25% is considered normal)[13] (Figure 1).

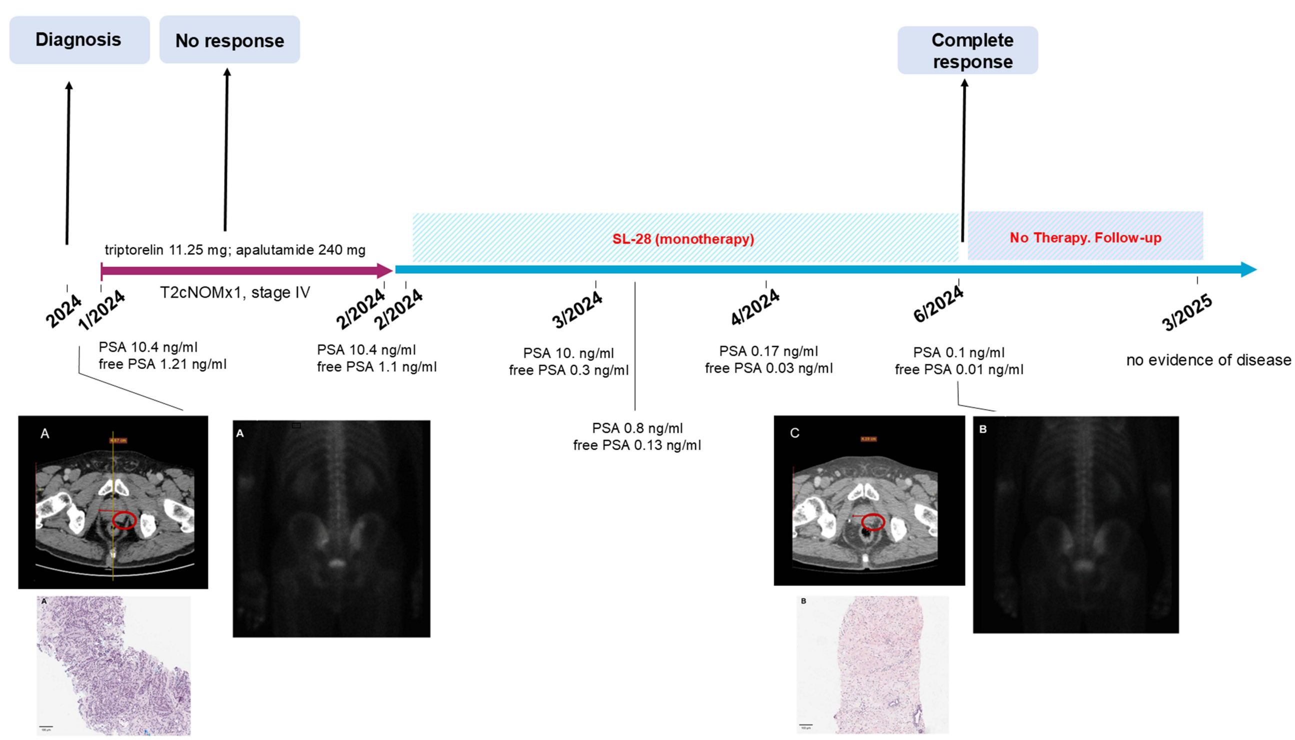

Figure 1 Timeline of events.

Computed tomography (CT) (Figure 2A and B) revealed a prostatic neoplasm 32×21 mm. Bone scintigraphy confirmed the presence of a metastatic lesion, measuring 26×15 mm in the right side of the pelvic bone (Figure 3A). Transrectal ultrasound-guided needle biopsy was performed, and the specimens were subjected to histopathological evaluation. Microscopic examination confirmed acinar adenocarcinoma of the prostate with a Gleason score of 4 + 3 = 7 (Figure 4A). Imaging and biopsy findings revealed a tumor classified as T2cNOMx1, stage IV. The patient was treated with a single daily dose of triptorelin 11.25 mg and apalutamide 240 mg. After 4 weeks, there were no positive dynamics, with the levels of total PSA at 10.4 ng/mL and free PSA at 1.1 ng/mL (10.6% free PSA) (Figure 1). The patient's course was complicated by multiple episodes of high blood pressure with severe headaches and vision changes, most likely attributed to androgen ablation therapy.

Considering these concerns and the nature of prostate tumors with bone metastasis, experimental SL-28 therapy was recommended. After obtaining written informed consent from the patient, the SL-28 administration was approved by the Institutional Review Board under NCT06872489, and the study was conducted in accordance with the approved protocol. The institutional approval from the local ethical committee of (approval number 298–55-4) was granted to publish the case details. No commercial sponsors were involved in this study.

SL-28 therapy began in February 2024. SL-28 was administered at a dose from 1 × 10^7 to 1 × 10^8 cells per injection once or twice daily, five times a week. SL-28 was administered as a slow (3 min) 5-mL I.V. cell suspension injection without any premedication. Initial doses were administered in the inpatient settings, followed by subsequent doses being administered at the patient's home by trained nurses. The infusions, cryopreserved prior to administration, were delivered over the course of 2 weeks.

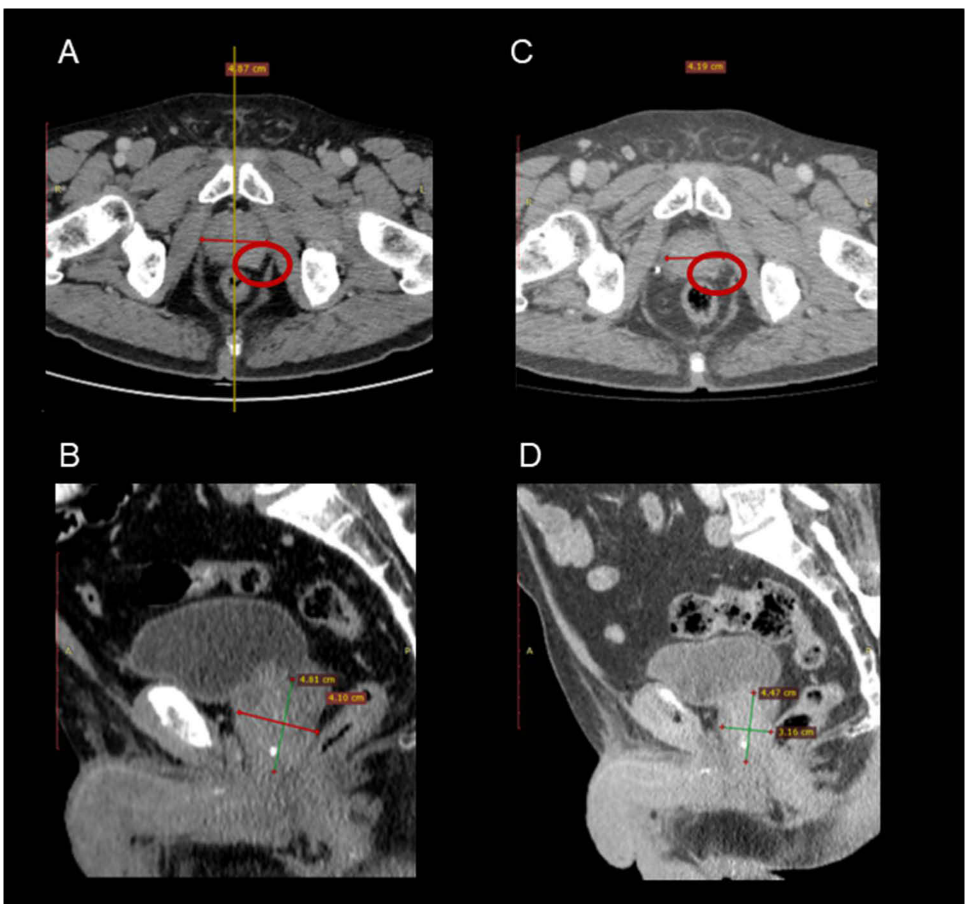

Figure 2 Comparison of pre- and post-therapy CT scans of the pelvis. (**A** and **B**) CT scans of the pelvis before SL-28 therapy showing the presence of clinically evident extraprostatic extension in the left lobe of the prostate. (**C** and **D**) CT scans of the pelvis after four months of SL-28 therapy showing a reduction in prostate volume, with a reduced degree of extraprostatic extension (red circle).

Abbreviation: CT, computed tomography.

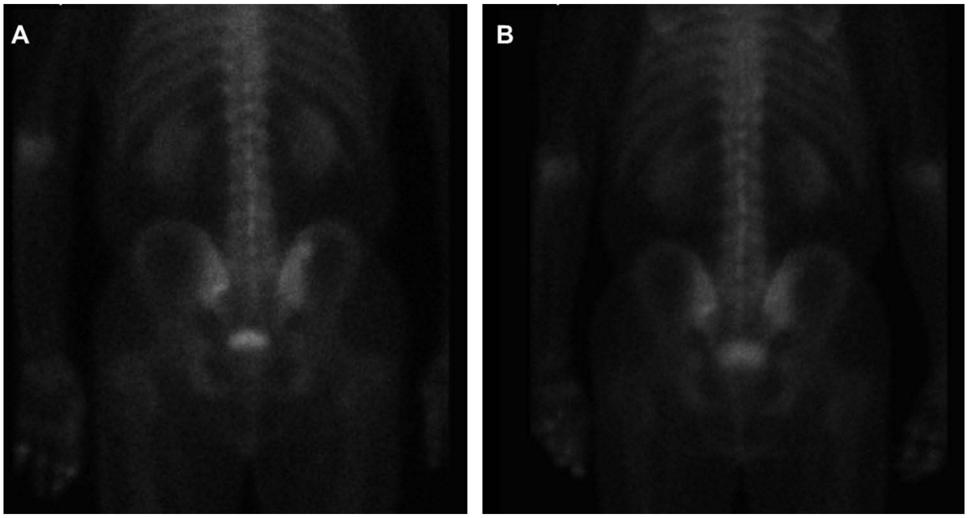

Figure 3 Bone scintigraphy (**A**) Baseline bone scans showing osteoblastic lesions at the pelvis. (**B**) Bone scans performed 3 months after SL-28 therapy showing no metabolic activity in the pelvis compared with the baseline bone scan (**A**).

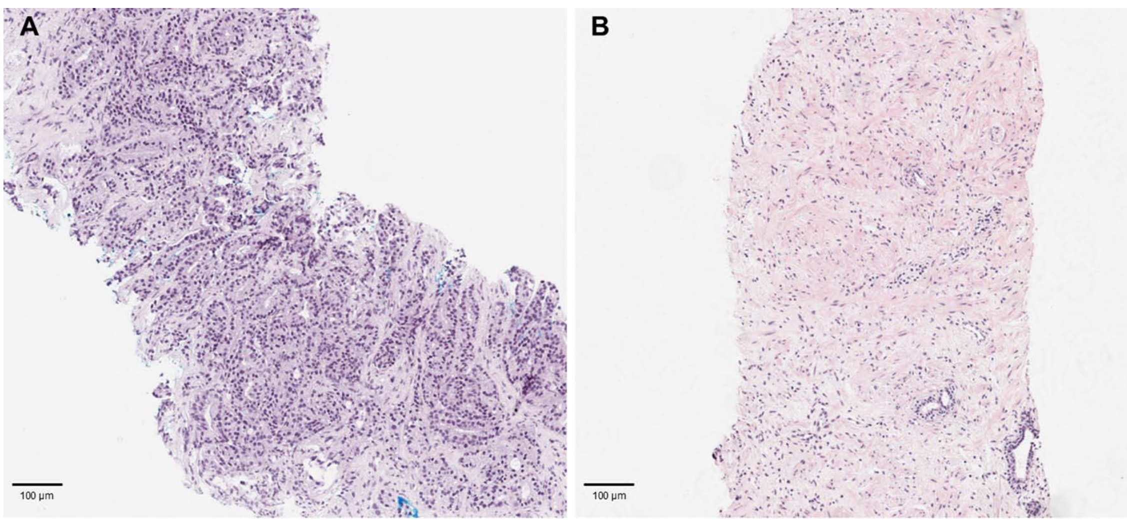

Figure 4 Hematoxylin and eosin-stained section of needle biopsy of prostate. (**A**) Baseline showing acinar adenocarcinoma of the prostate with enlarged, pleomorphic cells infiltrating as solid nests and cords with poorly differentiated glands (Gleason score 4+3 = 7); x10 magnification. (**B**) Post-therapy section showing variable fibrosis; x10 magnification.

Outcome and Follow-Up

SL-28 therapy was well tolerated, with no significant adverse effects such as graft-versus-host disease (GvHD), cytokine release syndrome (CRS), or immune effector cell-associated neurotoxicity syndrome (ICANS). A mild fever (peaking at a temperature of 38.0 °C) occasionally occurred within 2–3 hours post-infusion, lasted 3–4 hours, and was either self-limiting or was effectively managed with symptomatic treatment. Within the first month, the patient experienced a reduction in urination frequency and urgency. Pain in the pelvic area and during urination notably reduced. PSA levels exhibited minimal change, with the levels of total and free PSA at 10.0 and 0.3 ng/mL, respectively.

Ten days later, PSA levels dropped significantly with the total PSA levels at 0.8 ng/mL and free PSA level at 0.13 ng/mL. By the end of the second month, total and free PSA levels dropped to 0.17 ng/mL and 0.03 ng/mL, respectively. Clinical improvements continued, with nocturia reduced from 4–5 times per night to 1–2 episodes per night. The patient also noticed improved urine flow and no longer experienced difficulty urinating.

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The same trend continued, and by the end of the fourth month of therapy, total and free PSA levels were 0.1 and 0.01 ng/mL, respectively. Repeated CT revealed the disappearance of contrast enhancement in the lesion located in the left peripheral lobe (Figure 2C and D). Repeated bone scintigraphy revealed reduced pathological accumulation (Figure 3B). Histopathological examination (Figure 4B) revealed widespread glandular atrophy with focal basal cell hyperplasia but no adenocarcinoma structures. Therefore, SL-28 treatment was discontinued.

Eight months after the completion of SL-28 therapy, the patient showed no evidence of the disease, interpreted as complete response according to the RECIST 1.1 criteria. Currently, the patient's PSA levels are monitored every three months without any supporting therapy.

Discussion

Prostate cancer in older adults is known for its rapid progression, metastasis, and poor prognosis.[14] Age-associated comorbidities narrow down therapeutic choices owing to underlying toxicity and adverse cardiac effects. Moreover, prostate cancer that has spread to the bones responds poorly to available therapies.[15]

SL-28 therapy is a novel type of cell therapy with intravenous injections of Leukocyte-Tells, which are donor-derived leukocytes and platelets whose activity is increased through the Universal Receptive System. SL-28 has shown high efficacy against different types of cancer in previous laboratory studies.[10,11] Specifically, Leukocyte-Tells exhibited multiple antitumor mechanisms that were upregulated compared with the naïve white blood cells. First, Leukocyte-Tells, displayed enhanced production of anticancer and antimicrobial bioactive compounds (AABCs) with identified over 700 unique or differentially produced peptide and nonpeptide metabolites showing > 100,000 times higher activity than control leukocyte-derived AABCs.[10] Second, the antimicrobial and anticancer activities of Leukocyte-Tells exceeded those of control leukocytes and exhibited up to 1,000,000 times higher activities against various microorganisms and cancer cell lines, likely due to increased phagocytic activity, granule enzyme production, and enhanced cytokine production. Finally, Leukocyte-Tell gene-expression analysis revealed the enrichment of genes associated with numerous functional pathways including cell membrane uptake, immune cell signaling, and, interestingly, immune cell migration with upregulation of ESAM, JAM3, RAP1GDS1, and RAPGEF, suggesting that Leukocyte-Tells may have high capacity to migrate toward the tumors.[16–19] Together these findings suggest that SL-28 may provide a superior antitumor effect in patients.

In the present study, because of low therapeutic response and poor tolerance to androgen ablation therapy with severe side effects, the patient underwent investigational SL-28 therapy. Here, we report the case of a 79-year-old man with a T2cNOMx1 prostate cancer who achieved a complete response (per RECIST 1.1) within 4 months of SL-28 therapy. The patient in this study received intravenous injections of SL-28 at a dose up 1×10^8 cells per injection QD, 5 days a week for 4 months as monotherapy. Although a month before the initiation of SL-28 therapy, the patient received a single injection of triptorelin 11.25 mg, which had a sustained effect over 3 months, it is highly unlikely that the observed complete response was due to the therapeutic effect of triptorelin.[20] First, after triptorelin injection, PSA level was stable for the first 4 weeks, after which SL-28 therapy was initiated. Second, triptorelin has never been reported to induce a complete response, including the disappearance of bone metastases. Finally, triptorelin requires one to three months of therapeutic injections to maintain the level of PSA, whereas the patient in this study received only a single triptorelin injection more than 12 months ago. At the same time, due to the limitations of the single case study, additional clinical research is required to fully elucidate the effect of Sl-28 in the patients with prostate cancer.

During the study, the patient tolerated the SL-28 therapy well, with no severe adverse effects, and cell blood tests and biochemical analyses did not identify any major changes. Despite numerous injections throughout the therapeutic course, SL-28 cells exhibited a lack of engraftment or proliferation with no signs of GvHD, CRS, or ICANS, which is typical for other allogeneic cell therapies.

A pronounced effect was observed starting from the second week of SL-28 therapy, with an improvement in urinary function, followed by the normalization of PSA level in the second month of therapy, along with continuous improvement in urinary function and disappearance of the complaints. The observed initial stability during the first 4 weeks, followed by a rapid reduction in serum PSA levels, highlights the possibility that SL-28 is sensitive to the tumor microenvironment and requires time to overcome it, showing a pattern similar to that reported for TIL cell therapy.[21]

A complete response was confirmed by computed tomography and histological examinations after 4th month of therapy. One limitation of this case report is the absence of a control or comparison group, highlighting the need for a larger controlled study. Our preliminary findings underscore the potential of SL-28 therapy and support further investigations related to SL-28 in patients with different tumor types; however, full-scale multicenter clinical trials are needed to confirm efficacy. Specifically, future clinical research should particularly focus on the pharmacokinetic profile of SL-28 to optimize dosage. Moreover, along with the standard RECIST criteria used to assess cell therapeutic activity, additional biomarkers (eg, immune profiling, cytokine levels, and potential tumor microenvironment analysis) should be applied to support the mechanism of action of SL-28.

Conclusion

This study evaluated the efficacy and safety of SL-28, a novel adoptive cell therapy, in a patient with stage IV prostate cancer. This case supports the hypothesis that SL-28 might offer clinical benefit in advanced prostate cancer and warrants further clinical evaluation in controlled studies.

Ethics and Consent Declaration

Written informed consent was obtained from the patient to have the case details and any accompanying image published. The study was conducted in accordance with the Declaration of Helsinki. This is a care report. The study was conducted in accordance with the local legislation and institutional requirements. The institutional approval to publish the case details was granted by the Ethics Committee of a State Medical Institute and Private Hospital International Almaty (approval number 298-55-4).

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Disclosure

VT and GT are stockholders and either current or previous employees at Second Life Therapeutics, Inc. and may be listed as co-inventors on various pending patent applications related to the cell-based therapy presented in this study. The authors report no other conflicts of interest in this work.

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