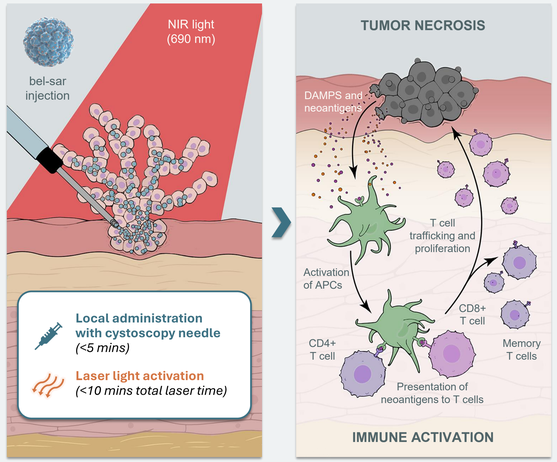
Immune response and preliminary efficacy of bel-sar (AU-011), a first-in-class virus-like drug conjugate (VDC), in NMIBC

Seth P. Lerner, MD[1], Piyush K. Agarwal, MD[2], Joseph McQuaid, MD[3], Xianne Penny, PhD[3], Jennifer Linehan, MD[4], Max Kates, MD[5], Joseph Jacob, MD MCR[6], Gary D. Steinberg, MD[7], Neal D. Shore, MD[8], and Sabine D. Brookman-May, MD[3,9]

[1]Baylor College of Medicine, Houston, TX; [2]University of Chicago, Chicago, IL; [3]Aura Biosciences, Boston, MA; [4]John Wayne Cancer Institute, Santa Monica, CA; [5]Johns Hopkins School of Medicine, Baltimore, MD; [6]SUNY Upstate Medical University, Syracuse, NY; [7]Rush University, Chicago, IL; [8]Carolina Urologic Research Center and Genesis Care US, Myrtle Beach, SC; [9]Ludwig Maximilian University of Munich, Munich, Germany

INTRODUCTION

- Current standard-of-care with TURBT and adjuvant intravesical therapy for NMIBC leaves a **significant unmet need** due to high recurrence rates and the need for repeat surgeries and adjuvant treatment
- **Belzupacap sarotalocan (bel-sar; AU-011)** is a **focally administered virus-like drug conjugate (VDC),** coupling tumor-specific necrosis with robust immune activation
- Preclinical models and clinical ocular melanoma studies demonstrated **durable anti-tumor responses** with **minimal toxicity**



Bel-sar has a novel, dual mechanism of action:

1. **Robust targeted cytotoxicity** designed to rapidly destroy cancer cells
2. **Long-term anti-tumor immune memory** with the potential to provide immune surveillance, urothelial field effect, and prevent recurrence

METHODS

Bel-sar is currently under investigation in a phase 1b/2 clinical trial in participants with IR and HR NMIBC (NCT05483868)[a]

- 17 participants with NMIBC received a single low dose of intratumoral bel-sar with light activation (n=12) or without light activation (n=5), followed by SoC TURBT 7–12 (+7) days later
- Response was assessed histologically by a central pathologist
- Immune response was evaluated using multiplex immunofluorescence (24-marker panel) performed on pre- and post-treatment biopsies from 5 participants who had cCRs or visually smaller lesions after bel-sar treatment

[a] Bel-sar (AU-011) is an investigational product candidate. The effectiveness and safety of bel-sar have not been established, and bel-sar is not approved for use in any jurisdiction

PRELIMINARY EFFICACY

A single dose of bel-sar produced cCR in participants with IR and HR NMIBC

Intermediate risk (n=5)
- **4/5 treated tumors achieved cCR**, while the fifth showed visual tumor shrinkage
- **3/5** participants demonstrated **cCR** in at least 1 **untreated tumor**
- **Visual changes** on cystoscopy identified in **4/5** participants
- **100%** of treated and untreated tumors demonstrated **immune response**[a]

High risk (n=5)
- **3/5 treated tumors** demonstrated **visual tumor shrinkage**
- **1/5** participants achieved **cCR** in both the **treated tumor and an untreated tumor**
- **Visual changes** on cystoscopy identified in **4/5** participants
- **100%** of treated and untreated tumors demonstrated **immune response**[a]

Favorable safety profile (n=17)[b]
- <10% of participants experienced Grade 1 TEAEs related to study drug
- No Grade 2/3 TEAEs related to study drug
- No SAEs or DLTs

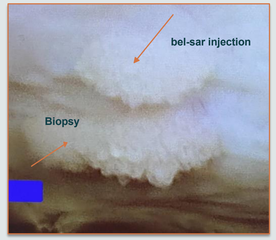
For purposes of this analysis, cCR is defined as absence of tumor cells on histopathologic evaluation. [a]Immune response defined by immunocyte infiltration on post-treatment histopathology. [b]Safety data includes all light-activated cohorts (A, B, and C), including two participants treated but not efficacy evaluable (n=12), plus the drug-only cohort that received no light activation (n=5). [c]Confirmed with histopathologic evaluation. Data cutoff March 3, 2025.

Case study: cCR confirmed in a patient with highly recurrent disease

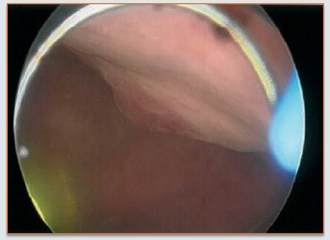
Cohort A:
72-year-old male
Single dose bel-sar + light activation

- Multiple Ta low-grade tumors, intermediate risk (no CIS)
- History of Ta high-grade (<3cm), intermediate risk
- Multiple prior TURBT surgery (x6)
- Prior BCG induction and maintenance

cCR visualized at time of TURBT[c]



Tumor pre-injection/pre-biopsy

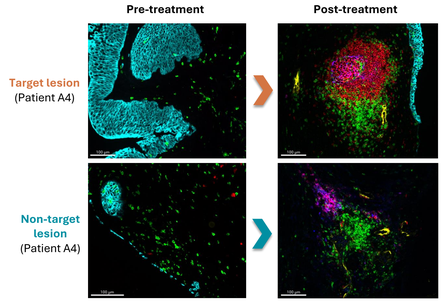


Post-injection edema and ecchymosis at injection site

IMMUNE RESPONSE

Objectives of multiplex immunofluorescence:
- Confirm and characterize bel-sar immune MoA in the clinic
- Identify cell populations associated with clinical response
- Determine whether bel-sar can induce immune memory
- Evaluate potential immune response in untreated tumors

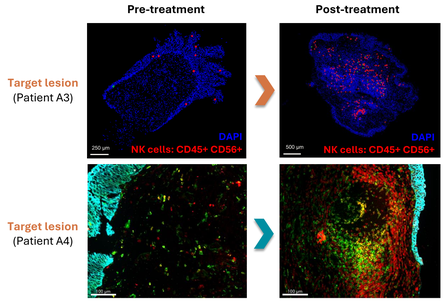
Bel-sar induced adaptive immune memory through generation of *de novo* mature tertiary lymphoid structures (TLS)



In **5/5** participants, **mature TLS** were present in **target lesions** (3 formed TLS *de novo*)

In **2/5** participants, mature TLS were also present in **non-target lesions**, supporting a **urothelial field effect**

Bel-sar generated innate and adaptive effectors regardless of immune environment



In treated lesions:
- **NK cell** density increased up to **40x**
- **CD4+ cytolytic T cell** density increased up to **7x**
- In **5/5** participants, **CD4+ and CD8+ memory T cells** were observed after bel-sar treatment

PHASE 1 CONCLUSIONS

In both IR and HR NMIBC patients, focal administration of a single, low-dose of bel-sar induced cCRs through rapid tumor necrosis, effector cell infiltration, localized immune memory, and a urothelial field effect.

- Grade 1 drug-related adverse events only
- Bel-sar induced adaptive immune memory through generation of *de novo* mature TLS
- Bel-sar generated innate and adaptive effectors regardless of immune environment, converted "cold" to "hot" tumors, and reversed dysfunction in exhausted tumors

These results support evaluation of additional bel-sar doses and cycles in participants with NMIBC.

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Study disclosures
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Abbreviations
APC, antigen-presenting cell; **bel-sar**, belzupacap sarotalocan; **BCG**, Bacillus Calmette-Guerin; **CIS**, carcinoma in situ; **cCR**, clinical complete response; **DAMP**, damage-associated molecular pattern; **DLT**, dose-limiting toxicity; **HR**, high risk; **IR**, intermediate risk; **MoA**, mechanism of action; **NIR**, near-infrared; **NK**, natural killer; **NMIBC**, non-muscle-invasive bladder cancer; **SAE**, serious adverse event; **SoC**, standard of care; **TEAE**, treatment-emergent adverse event; **TLS**, tertiary lymphoid structure; **TURBT**, transurethral resection of bladder tumor; **VDC**, virus-like drug conjugate.

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