2132

A PHASE 1, OPEN-LABEL TRIAL TO DETERMINE FEASIBILITY AND SAFETY OF INTRAMURAL INJECTION OF BELZUPACAP SAROTALOCAN (AU-011) IN NON-MUSCLE INVASIVE BLADDER CANCER (NMIBC) - NCT05483868

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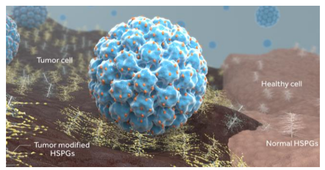
Background and Introduction

Bladder cancer is the ninth most common cancer globally and sixth most common in the US. [1,2] Approximately 70-80% of patients diagnosed with bladder cancer initially present with non-muscle invasive bladder cancer (NMIBC). [2,3,4] Standard treatment for NMIBC is transurethral resection of bladder tumor (TURBT) with or without intravesical therapy (i.e. Bacillus Calmette-Guerin [BCG] or chemotherapy). [3] Although BCG has been shown to reduce recurrence of NMIBC better than the intravesical chemotherapy, up to 20% of patients discontinue BCG therapy due to side effects and 50% fail BCG treatment completely. [3,5,6] These patients are treated with radical cystectomy and radiation, with a poor prognosis and a 5-year overall survival rate of ~50%.[3] Due to the limitations of current therapies and the BCG drug shortage, alternative therapies for the treatment of NMIBC are in development [5], such as the use of viruses as vehicles to target tumor cells. [7]

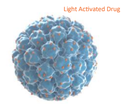
Belzupacap Sarotalocan - a Virus-Like Drug Conjugate (VDC)

Belzupacap sarotalocan (AU-011) is comprised of a virus-like particle (VLP) conjugated to a cytotoxic payload to form a VDC. A single VDC can deliver hundreds of cytotoxic molecules conjugated to its capsid proteins.

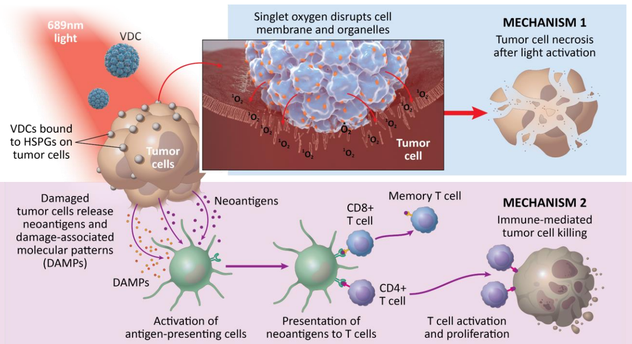


The VDC targets and binds to tumor-modified glycosaminoglycans (GAGs) without binding to normal cells, limiting off-target toxicity.

Belzupacap Sarotalocan - Dual Mechanism of Action

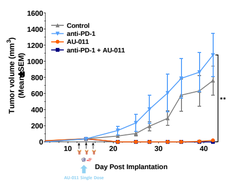


The dual mechanism of action consists of belzupacap sarotalocan selectively binding to malignant tumor cells, causing acute necrosis upon light activation and potential long term anti-tumor immunity as demonstrated in preclinical models.[3]

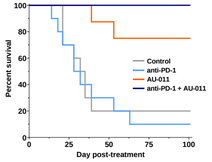


Preclinical Data Supports Initiation of Clinical Trials

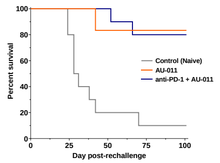
1. Tumor Growth



2. Survival



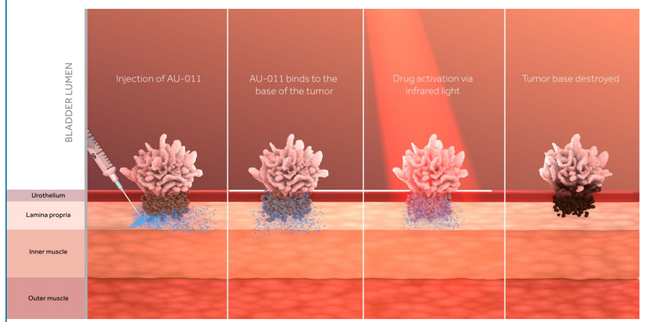
3. Survival After Rechallenge



1. Treatment of tumor caused complete responses in 80% of animals and addition of anti-PD-1 improved this to 100% complete responses.
2. Treatment leads to increased survival with belzupacap sarotalocan alone and in combination with the anti-PD-1.
3. In animals with complete responses, belzupacap sarotalocan alone or in combination with the anti-PD-1 prevented tumor growth after re-challenge 100 days later in approximately 80% of the animals demonstrating a long-term anti-tumor immunity. [7]

Syngeneic Mouse Tumor Bladder Model (MB49 Model in C57BL/6 Mice) (N=8 -10/group)

Intramural Administration



In contrast to many existing therapies delivered via intravesical administration, belzupacap sarotalocan (AU-011) will be administered in the lamina propria close to the base of the tumor.

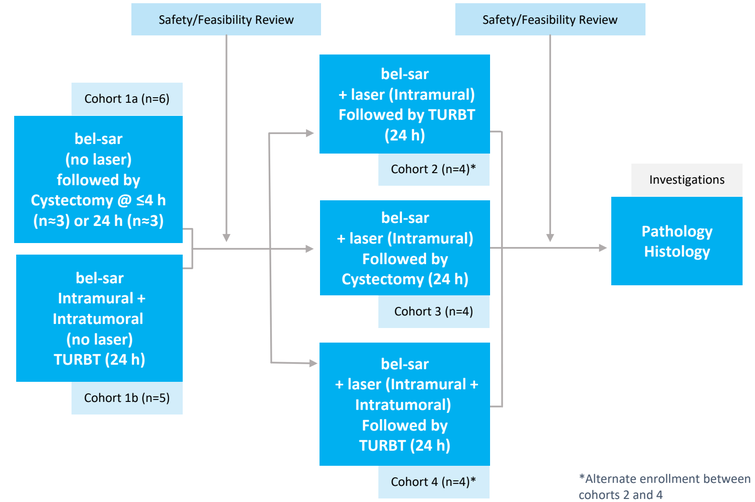
Window of Opportunity Trial in NMIBC

A window of opportunity trial allows for the early clinical assessment of belzupacap sarotalocan:

- Assess safety and tolerability of belzupacap sarotalocan alone and with laser activation.
- Evaluate belzupacap sarotalocan in patients with low, intermediate and high-risk NMIBC undergoing TURBT or cystectomy.
- Surgery samples allow the evaluation of intramural distribution in the bladder wall and other pathological assessments (see Trial Design).
- Evaluate the treatment of papillary and CIS disease both clinically and pathologically to help guide further development of belzupacap sarotalocan.

Trial Design

Trial design allows assessment of belzupacap sarotalocan (bel-sar) with and without laser in multiple NMIBC risk levels and with and without intratumoral administration.



*Alternate enrollment between cohorts 2 and 4

DEVELOPMENT OBJECTIVES: 1) Evaluate the feasibility of intramural +/- intratumoral administration of belzupacap sarotalocan in the treatment of NMIBC. 2) Evaluate degree of necrosis in the tumor after belzupacap sarotalocan therapy 3) Assess immune response at 1 week after treatment 4) Assess the safety and tolerability of belzupacap sarotalocan.

Trial Status

- One subject has been enrolled as of November 20, 2022, and enrollment is continuing in Cohorts 1a (cystectomy) and Cohort 1b (TURBT).
- The trial utilizes a novel approach to treating bladder cancer with intratumoral injection of belzupacap sarotalocan with the potential to kill the tumor from the basal side.
- The distribution of belzupacap sarotalocan alone will be assessed in Cohorts 1a and 1b.
- Upon confirmation of the safety of belzupacap sarotalocan alone, the trial will then progress to the second phase, with belzupacap sarotalocan plus light activation, where potential tumor necrosis and the immune response will be assessed histologically

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