Intravesical Photo Dynamic Therapy for BCG-Unresponsive NMIBC CIS Patients - Phase II Clinical Study Interim Analysis

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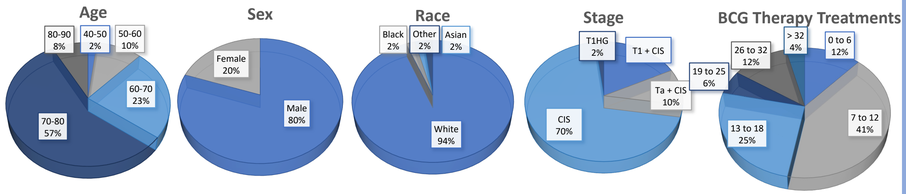
Introduction

Novel therapies are required for Bacillus Calmette-Guerin (BCG)-Unresponsive, high-risk Non-Muscle Invasive Bladder Cancer (NMIBC). We report the interim results of a Phase II Clinical Study of Intravesical Photo Dynamic Therapy (PDT) in patients with BCG-Unresponsive Carcinoma In-Situ (CIS) with or without resected Ta / T1 papillary disease.

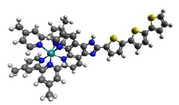
Methods

- Out of a planned 125 patients, 51 patients have been enrolled and treated.
- Study Treatments (Day 0) – intravesical instillation of the the Ruthenium-based photosensitizer TLD-1433 (0.70 mg/cm^2) followed by activation with a 520 nm intravesical laser under general anesthesia (Study Device TLC-3200) to a total of 90 J/cm^2 of laser light).
- An additional Study Treatment was delivered on Day 180 in the absence of progressive disease.

Patient Demographics



Study Drug (TLD-1433)



Study Device (TLC-3200)

Laser Emitter

Laser Detector

Objectives (In compliance with FDA's 2018 Guidance to Industry)

- Primary – Efficacy (Complete Response (CR), at any point in time)
- Secondary - Duration of Efficacy (CR at 12 months, post initial CR)
- Tertiary - Safety (Incidence and severity of Adverse Events, Grade 4 or higher directly related to Study Drug and/or Study Device that do not resolve within 450 days post treatment)

Notes

- The data analysis is interim in nature and represents the clinical data accrued to date.
- This clinical data includes 3 patients treated at the Therapeutic Dose in the Phase Ib clinical study. [1]
- Patients with a negative cystoscopy and positive urine cytology were defined as Indeterminate Response (IR), as these patients remain under investigation for lower and/or upper tract urothelial carcinoma. Total Response Rate (**TRR**) is defined as CR Rate (**CRR**) + IR Rate (**IRR**).

Results

Interim analyses include 43 patients evaluated at the 90 day assessment and 29 patients evaluated at the 450 day assessment. Data for the primary and secondary outcomes are listed in the table:

Assessment Day	90	%	180	%	270	%	360	%	450	%
Complete Response ("CR")	23	53%	17	45%	15	41%	10	29%	8	28%
Indeterminate Response ("IR")	6	14%	9	24%	7	19%	5	15%	3	10%
Total Response (CR and PR)	29	67%	26	69%	22	60%	15	44%	11	38%
Evaluable Patients	43		38		37		34		29	

The interim clinical data demonstrates a 90 day CR of 53% and a sustained duration of response at 360 and 450 days of 29% and 28%, respectively.

There have been eight Serious Adverse Events ("**SAEs**") identified (2 Grade II (tachycardia, hematuria), 3 Grade III (acute kidney injury, cellulitis), 2 Grade IV (urosepsis, depression/anxiety) and 1 Grade V). None of the SAEs were deemed to be directly related to the Study Drug or Study Device according to the Data Safety Monitoring Board.

Early results show a complete response rate in 53% of patients evaluated at 90 days and 28% of patients evaluated at 450 days

Based on the clinical data collected to date, PDT represents a viable treatment option with an acceptable safety profile

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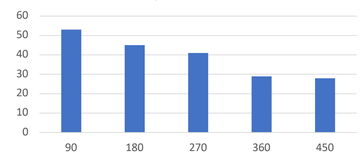
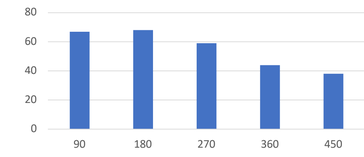
[1] Kulkarni et al. A Phase 1b Clinical Study of Intravesical Photodynamic Therapy in Patients with Bacillus Calmette-Guérin–unresponsive Non–muscle-invasive Bladder Cancer. European Urology Open Science Volume 41, July 2022, Pages 105-111. https://www.sciencedirect.com/science/article/pii/S2666168322005900

[2] Seymour GJ, Walsh MD, Lavin MF, Strutton G, Gardiner RA. Transferrin receptor expression by human bladder transitional cell carcinomas. Urol Res. 1987;15(6):341-4. doi: 10.1007/BF00265663. PMID: 3324443.

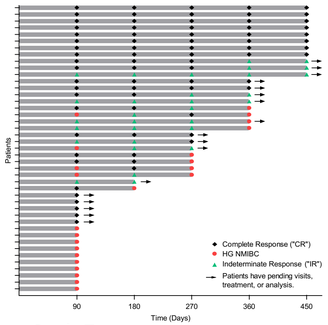
Complete Response Rate ("CRR") (4Q2022)



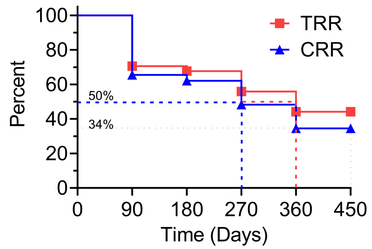
Total Response Rate ("TRR") (4Q2022)



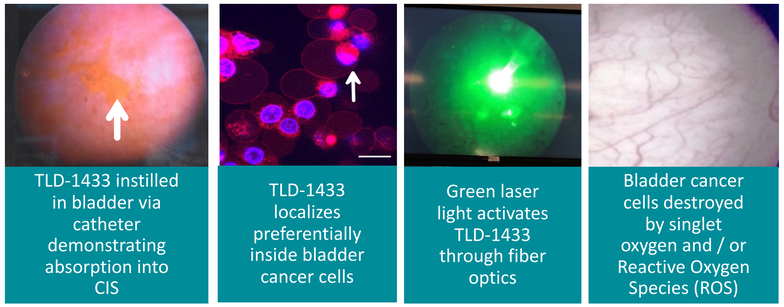
Patient Response



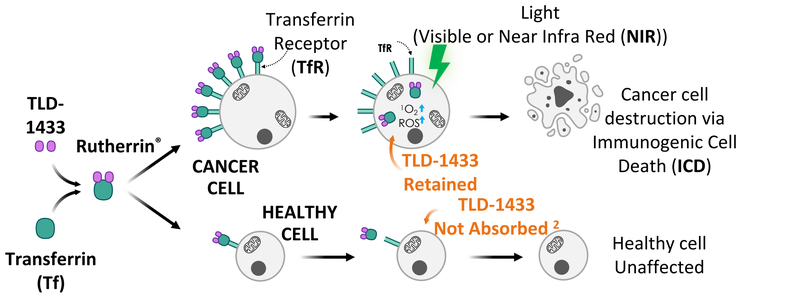
Kaplan Meier Curve



Study Treatment



Mechanism of Action



Future Directions for Research

- Completion of the Phase II NMIBC Clinical Study
- Clinical development of an injectable form of TLD-1433 (TLD-1433 + transferrin = Rutherrin®) to be administered intravenously for absorption into Non-Small Cell Lung Cancer (NSCLC) and GlioBlastoma Multiforme (GBM), then activated with X-ray radiation.