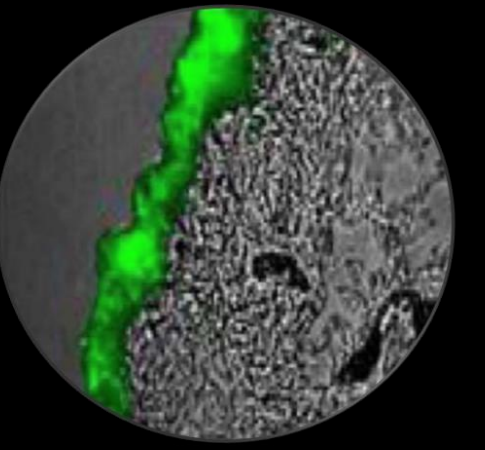


PHASE 1 OUTCOMES OF A NOVEL THIRD GENERATION LIPOSOMAL PACLITAXEL FORMULATION (TSD-001) IN PATIENTS WITH LOW-INTERMEDIATE RISK NON-MUSCLE INVASIVE BLADDER CANCER (NMIBC)



Daniel Huynh MD¹, Rian Dickstein MD², Karl Bean³, Michael G Oefelein MD³,
LIPAC Oncology, LLC



Introduction/Background

The purpose of this study (NCT 03081858) is to report Phase 1 outcomes of a novel liposomal formulation of paclitaxel (TSD-001), specifically designed for intravesical instillation for NMIBC.

Paclitaxel is a first-line/preferred agent and FDA approved for a variety of carcinomas, and is active against metastatic urothelial cancer (40% RR).

TSD-001 (3rd generation liposomal formulation of paclitaxel) is highly active against bladder cancer cells with an $IC_{50} T24 = 4.7$ ng/mL vs 1000 ng/mL for MMC. TSD-001 also demonstrates targeted lethality, with deep penetration into the detrusor and intravesical persistence up to 72 hours.

1. Danny Huynh Urology, Bakersfield, CA
2. Chesapeake Urology, Hanover, MD
3. LIPAC Oncology LLC, Pomona, CA

Methods/Materials

This is the first in human exposure of TSD-001 (IND129419) in patients, after TURBT, with documented low-intermediate risk NMIBC. The study design is prospective, non-randomized and adaptive, in which two cohorts (n=3, subjects each) received six escalating intravesical dose (range, 10-540 mg TSD-001) exposures every 2 weeks until Dose Limiting Toxicity (DLT, G3-4 AEs) is observed. Adverse events (AEs) were classified according the NCI CTCAE version 5.0. Urinary symptom bother was collected using the IPSS and OAB-q instruments. Bioanalytical measurement of paclitaxel urine and plasma concentration was performed using a validated assay. Bladder tumor recurrence was assessed by cystoscopy and biopsy.

Figure 1 OAB-q scores before and at conclusion of exposure

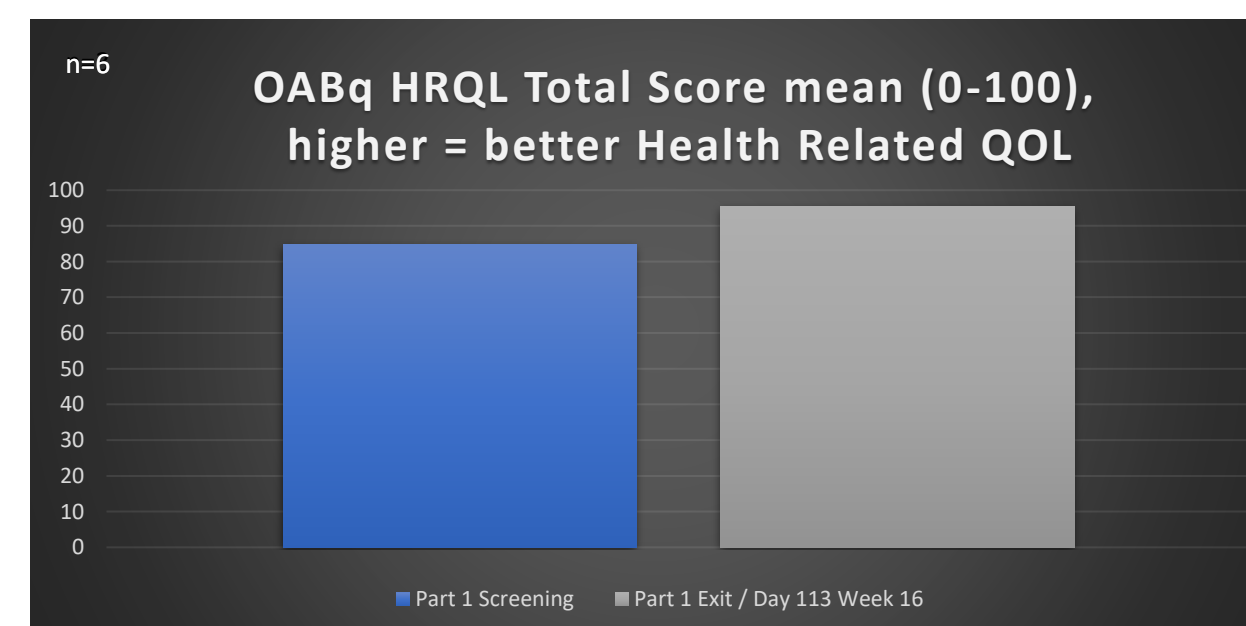


Table 1 Treatment Emergent Adverse Events

TEAE	GRADE	RELATION TO STUDY DRUG	AE DLT
UTI	G 1	Not related	No
UTI	G 2	Possible	No
Worsening constipation	G 1	Not related	No
Bladder calculus	G 1	Not related	No
Post Tx Hematuria	G 1	Not related	No
Fatigue	G 1	Not related	No
Insomnia	G 1	Not related	No
Hypersomnia	G 1	Not related	No

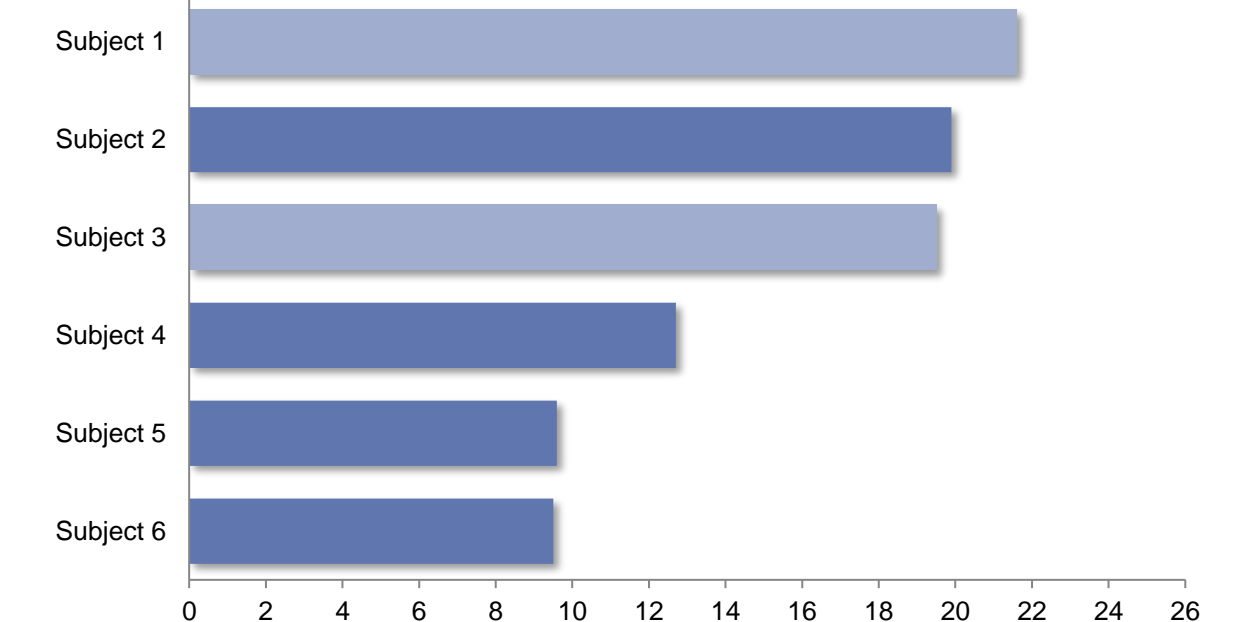
Results

A total of 8 AEs were reported, all of which were G1 or G2 in intensity and none of which met the criteria for DLT (Table 1). There was no change from baseline in the IPSS or OAB-q scores (fig 1). No measurable plasma concentrations of paclitaxel (LLQ <5.0 ng/mL) were reported over all doses (10-150 mg). Urine paclitaxel concentrations demonstrated proportional increase in concentration with increasing dose. No evidence of TCCa clinical recurrence has been identified in the 6 study subjects at a mean follow-up of 15 months (fig 2).

Conclusions

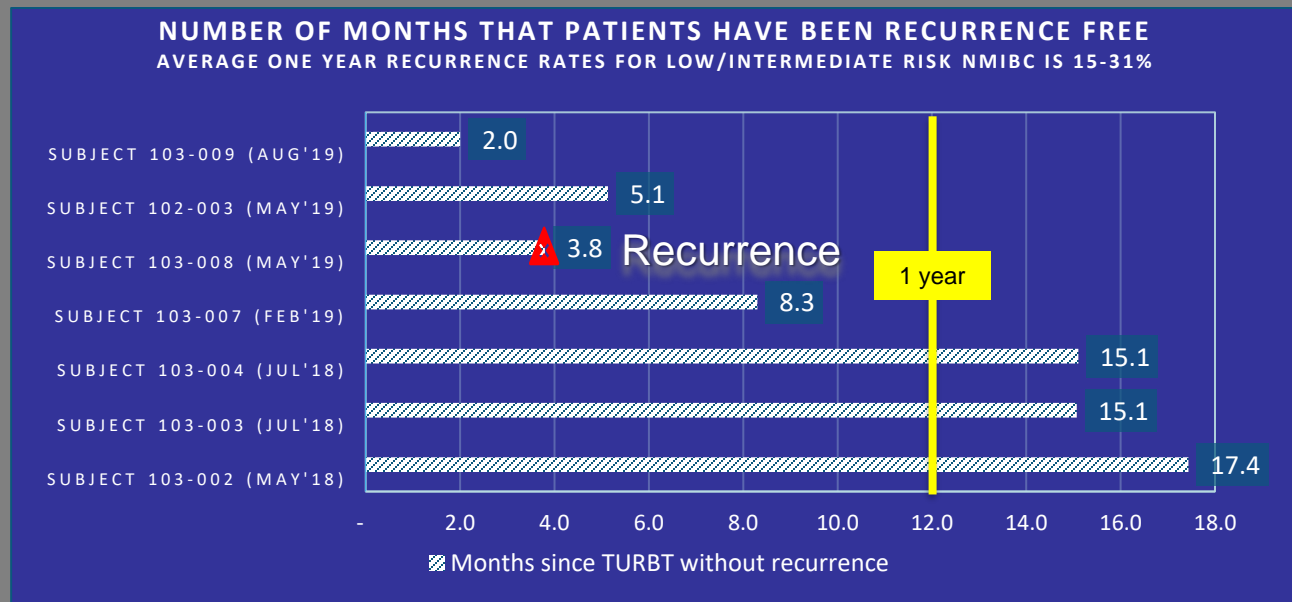
NMIBC patients exposed to escalating TSD-001 dose (10-540 mg paclitaxel) until maximum deliverable dose (540 mg) demonstrated no DLT. Voiding function and bother were unchanged from baseline to completion. There was no evidence of systemic paclitaxel exposure based on a valid bioanalytical assessment. No evidence of clinical recurrence or progression has been observed at a mean follow-up of 15 months. TSD-001 delivers high urinary concentrations of paclitaxel with no measurable systemic exposure, and is very well tolerated in NMIBC patients.

Fig. 2 RFS after TURBT and LiPax Promising Phase 1 Observations



Bibliography

1. Intravesical treatment of bladder cancer: review. *Phar Res* 25:1500-10, 2008
2. Marker lesion experiments in bladder cancer—What have we learned? *J Urology* 2010, 183:1678-85
3. OAB-q 2004 Pfizer
4. Long-Term Survival Outcomes with Intravesical Nanoparticle Albumin-Bound Paclitaxel for Recurrent Nonmuscle Invasive Bladder Cancer after Previous Bacillus Calmette-Guérin Therapy *Urology* 2017



TEAE	GRADE	RELATION TO STUDY DRUG	AE DLT
UTI	G 1	Not related	No
UTI	G 2	Possible	No
Worsening constipation	G 1	Not related	No
Bladder calculus	G 1	Not related	No
Post Tx Hematuria	G 1	Not related	No
Fatigue	G 1	Not related	No
Insomnia	G 1	Not related	No
Hypersomnia	G 1	Not related	No