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ADVANCED-2: Phase 2 Open-label Study to Evaluate Safety and Anti-tumor Activity of Intravesical Instillation of TARA-002 in Adults with High-grade Non-muscle Invasive Bladder Cancer

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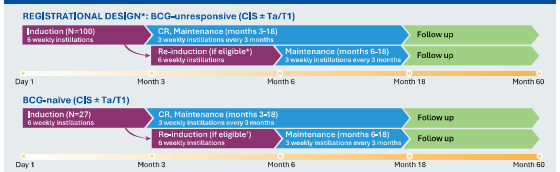
INTRODUCTION

- With the current Bacillus Calmette-Guérin (BCG) shortage and limited effective alternative therapies, there remains a significant unmet need for treatment options for patients with non-muscle invasive bladder cancer (NMIBC).
- TARA-002 is a broad spectrum immune potentiator that elicits a TH1 pro-inflammatory cytokine response.
- TARA-002 is a lyophilized biological preparation for instillation containing cells of *Streptococcus pyogenes* (Group A, type 3) Su strain treated with benzylpenicillin and is being developed for the treatment of high-grade NMIBC.

METHODS

FIGURE 1. ADVANCED-2 STUDY SCHEMA



Abbreviations: BCG = Bacillus Calmette-Guérin; CR = complete response; CIS = carcinoma in situ ; FDA = Food and Drug Administration; HG = high-grade

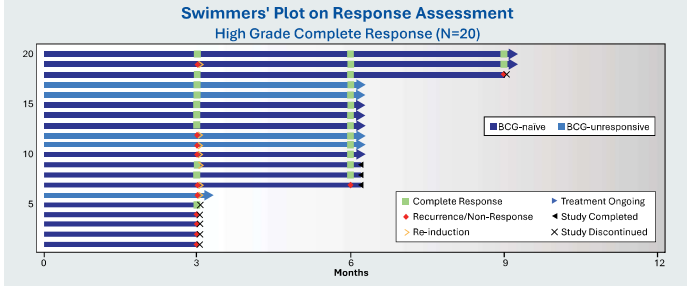
*Aligned with the FDA's 2024 BCG-Unresponsive NMIBC: Developing Drugs and Biologics for Treatment Guidance for Industry. †Residual CIS and/or recurrence of HGTa

- ADVANCED-2 (NCT05951179) is an ongoing, actively enrolling, Phase 2, open-label study to evaluate the safety and efficacy of intravesical instillation of TARA-002 (40 KE) in adults ≥ 18 years with BCG-unresponsive and BCG-naïve (never exposed and those who have not received intravesical BCG for at least 24 months prior to the most recent CIS diagnosis) CIS NMIBC (± Ta/T1) with active disease (**Figure 1**).
- The primary endpoint is high-grade complete response (CR) at any time up to Month 6. Key secondary endpoint is durability of response at Month 12.

Learn more about our study:
NCT05951179
Contact us at **clinicaltrials@protaratx.com** for more information.

RESULTS

FIGURE 2. FIRST RESULTS OF ADVANCED-2: 70% CR AT ANY TIME IN ALL SUBJECTS



Abbreviations: BCG = Bacillus Calmette-Guérin; CR = complete response; CIS = carcinoma in situ

NOTES:

At the time of data cutoff, of the 24 subjects enrolled, 20 subjects were evaluated for high-grade CR at Month 3 and later. Eighteen subjects were evaluated for high-grade CR at Month 6 and 3 subjects at Month 9.

Evaluable subjects include those who had at least one dose of study drug before the response assessment of time point and were discontinued due to diagnosis of progression or treatment failure. Subjects who have not yet completed the visit time point were not included.

Central urine cytology is pending for 3 subjects at Month 6 and 1 subject at Month 9.

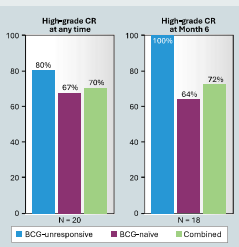
Baseline Characteristics

- All 24 enrolled subjects were white, and the majority were non-Hispanic (96%, 23 of 24) and male (79%, 19 of 24). The median age was 71 years.
- Eastern Cooperative Oncology Group (ECOG) Score was 0 for 75% (18 of 24) of subjects.
- Majority of patients had a baseline diagnosis of CIS only (58%, 14 of 24), and 25% (6 of 24) and 17% (4 of 24) had CIS + Ta and CIS + T1 disease, respectively.

Response Assessment

- The rates of high-grade CR at any time were 70% (14 of 20) overall, 80% (4 of 5) for BCG-unresponsive subjects, and 67% (10 of 15) for BCG-naïve subjects (**Figure 2, Figure 3**).
- The rates of high-grade CR at Month 6 were 72% (13 of 18) overall, 100% (4 of 4) for BCG-unresponsive subjects, and 64% (9 of 14) for BCG-naïve subjects (**Figure 3**).
- 100% (9 of 9) of subjects who were complete responders at Month 3, and continued the study, maintained response through Month 6.
- Of the 5 subjects who did not achieve initial CR and received re-induction, the CR rate at Month 6 was 80% (4 of 5).

FIGURE 3. FIRST RESULTS FROM ADVANCED-2: TARA-002 MONOTHERAPY DEMONSTRATED 72% CR AT 6 MONTHS



	BCG-unresponsive	BCG-naive	Combined
	N = 5	N = 15	N = 20
High-grade CR at any time, n (%)	**4/5 (80.0)**	**10/15 (66.7)**	**14/20 (70.0)**
High-grade CR at Timepoint, n (%)			
Month 6	4/4 (100.0)	9/14 (64.3)	13/18 (72.2)
Month 9	0	2/3 (66.7)	2/3 (66.7)
High-grade CR at any time by Baseline Diagnosis, n (%)			
CIS only	4/5 (80.0)	6/7 (85.7)	10/12 (83.3)
CIS + Ta/T1	0	4/8 (50.0)	4/8 (50.0)
High-grade CR at Month 6 by Baseline Diagnosis, n (%)			
CIS only	4/4 (100.0)	5/6 (83.3)	9/10 (90.0)
CIS + Ta/T1	0	4/8 (50.0)	4/8 (50.0)

Safety

TABLE 1. SUMMARY OF TREATMENT EMERGENT ADVERSE EVENTS IN ALL SUBJECTS

N = 24	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4/5
Subjects with TEAEs, n^ (%)	16 (67)	11 (46)	7 (29)	3 (13)	0
Subjects with Related TEAEs^*, n (%)	6 (25)	6 (25)	0	0	0
Subjects with Serious TEAEs†, n (%)	3 (13)	0	1 (4)	2 (8)	0
Subjects with TEAEs leading to Study Drug Withdrawal, n (%)	0	0	0	0	0

Abbreviations: AE = adverse event; TEAE = treatment emergent AE

^ Subjects may be counted in multiple categories; *TEAEs assessed by the Investigator as study drug related included dysuria, urinary incontinence, fatigue, chills, bladder discomfort, hematuria and micturition urgency. All were Grade 1; †Non-drug related Serious TEAEs included urinary tract infection (UTI; N = 2) and urosepsis (N =1).

- Majority of TEAEs were Grade 1 and transient. No subjects experienced drug-related serious AEs (SAEs) or TEAEs leading to withdrawal or death (**Table 1**).
- Common AEs reflect urinary tract instrumentation effects, such as bladder spasm, burning sensation, and UTI.
- AEs were consistent with the known safety profile of an immune-potentiating drug, such as flu-like symptoms.

CONCLUSIONS

- TARA-002 appears to be well tolerated with encouraging efficacy and durability of response in subjects with high-risk NMIBC with CIS.
- Further study is planned to understand the potential of TARA-002 in both the BCG-naïve and BCG-unresponsive population.

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