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ADVANCED-1

Phase 1a/b Safety Study of Intravesical Instillation of TARA-002 in Adults with High-grade Non-muscle Invasive Bladder Cancer

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INTRODUCTION

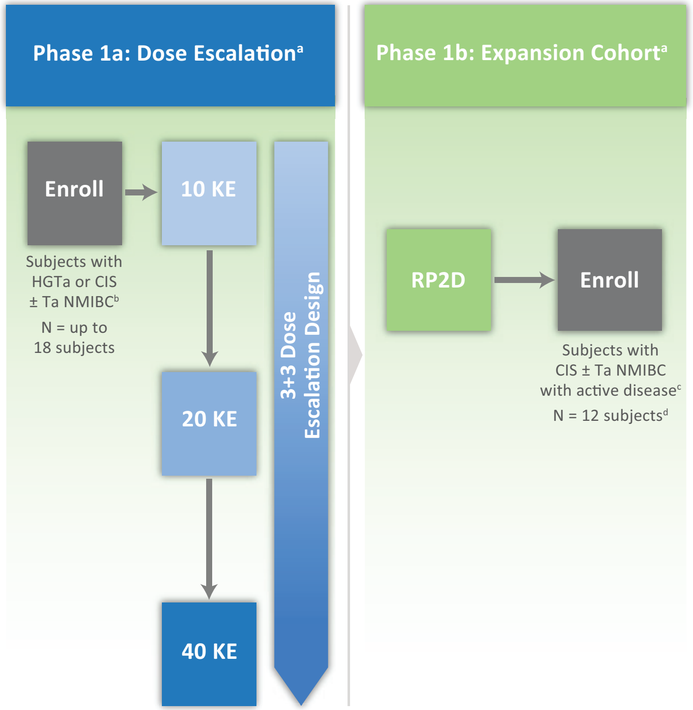
- Bladder cancer is the most common malignancy involving the urinary system, resulting in approximately 18,000 deaths each year in the United States (US)[1]
- Approximately 70% of new urothelial bladder cancer cases are classified as non-muscle invasive bladder cancer (NMIBC)[2,3]
- With the current Bacillus Calmette-Guérin (BCG) shortage and limited effective alternative therapies, there continues to be a significant unmet need for treatment options for patients with NMIBC
- TARA-002 is being developed for the treatment of high-grade (HG) NMIBC
- TARA-002 is a lyophilized biological preparation for instillation containing cells of *Streptococcus pyogenes* (Group A, type 3) Su strain treated with benzylpenicillin
- TARA-002 is manufactured using the same master cell bank as OK-432 (Picibanil®)
- OK-432 is approved in Japan and Taiwan for the treatment of several oncology indications
- Nonclinical toxicology studies with TARA-002 support the starting dose for the planned Phase 1a/b study

CURRENT ENROLLMENT STATUS

- Study started in March 2022
- Phase 1a is currently open for enrollment
- **ClinicalTrials.gov Identifier**: NCT05085977, NCT05085990

METHODS

FIGURE 1. PHASE 1 DOSE FINDING, OPEN-LABEL STUDY WITH EXPANSION EVALUATING INTRAVESICAL TARA-002 IN ADULTS WITH HIGH-GRADE NMIBC



Abbreviations: BCG, Bacillus Calmette-Guérin; CIS, carcinoma in situ; HGTa, high-grade Ta; ICF, Informed Consent Form; KE, Klinische Einheit; MTD, maximum tolerated dose; NMIBC, non-muscle invasive bladder cancer; RP2D, recommended Phase 2 dose.

[a]Subjects will receive weekly intravesical doses of TARA-002 instillation for 6 weeks.

[b]Subjects with HGTa or CIS ± Ta NMIBC who are unable to obtain intravesical BCG, received ≥ 1 dose of intravesical BCG, or received ≥ 1 dose of intravesical chemotherapy.

[c]Defined as disease present at last cystoscopic evaluation prior to signing ICF during the dose expansion phase.

[d]Subjects enrolled in the dose expansion phase will not include subjects previously enrolled and treated in the dose escalation phase.

- ADVANCED-1 is a Phase 1a/b, dose finding, open-label study of intravesical instillation of TARA-002 in adults with HG NMIBC (**Figure 1**)
- During the study, eligible subjects will receive weekly intravesical doses of TARA-002 instillation for 6 weeks
- The overall study duration for each subject includes 28 days of screening period, 6-week treatment period, and 6-week follow-up period
- The study includes a dose escalation phase (Phase 1a) and a dose expansion phase (Phase 1b; **Figure 1**)
- During the dose escalation phase (1a), up to 18 subjects with HGTa or CIS (± Ta) NMIBC with active disease are enrolled
  - Up to 3 dose levels are tested sequentially with 6 weekly intravesical doses, starting with the lowest dose using a 3+3 design in a dose escalation manner (**Figure 1**)
  - The dose escalation phase (1a) will conclude once the maximum tolerated dose (MTD) has been established or if the maximum feasible dose is reached without any safety concerns
- At the established recommended Phase 2 dose (RP2D), the dose expansion phase (1b) will enroll approximately 12 new subjects with CIS (± Ta) NMIBC with active disease

STUDY OBJECTIVES/ENDPOINTS

- The purpose of this study is to evaluate the safety and toxicity of TARA-002, to establish the MTD and RP2D in the treatment of subjects with HGTa or CIS NMIBC during the dose escalation phase (1a), and to further assess the safety and preliminary efficacy of TARA-002 in the treatment of subjects with CIS NMIBC with active disease during the dose expansion phase (1b)
- **Primary Objective**: To evaluate the safety and tolerability of TARA-002
  - Dose Escalation Phase (1a) Primary Endpoints:
    - Incidence of dose limiting toxicity (DLT) adverse events (AEs) in subjects with HGTa or CIS NMIBC
    - MTD and RP2D of TARA-002 in subjects with HGTa or CIS NMIBC
  - Dose Expansion Phase (1b) 1b Primary Endpoint:
    - Incidence of AEs in subjects with CIS NMIBC with active disease

ELIGIBILITY

Key Inclusion Criteria

- Male or female subjects 18 years of age or older at the time of signing the informed consent
- Subjects who have voluntarily given written informed consent after the nature of the study has been explained according to applicable requirements prior to study entry
- Subjects with a histologically confirmed, HGTa or CIS urothelial cell carcinoma of the bladder
- Subjects who are treatment naïve and unable to obtain intravesical BCG for the treatment of NMIBC, have received at least one dose of intravesical BCG, or at least one dose of intravesical chemotherapy

Key Exclusion Criteria

- Penicillin allergy (subjects with a questionable history of allergy to penicillin or no history of penicillin use will undergo sensitivity testing prior to inclusion in the study)
- Concomitant prostatic or upper tract urothelial involvement
- Nodal and metastatic disease are excluded if they existed at any time
- Bladder cancer stage ≥ T1
- Bladder cancer stage CIS with concomitant T1

REFERENCES

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3. Babjuk M, et al. *Eur Urol*. 2019;76(5): 639-657.

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