SunRISe-1: Phase 2b Study of TAR-200 in Combination With Cetrelimab, TAR-200 Alone, or Cetrelimab Alone in Participants With High-Risk Non-Muscle-Invasive Bladder Cancer Unresponsive to Intravesical Bacillus Calmette-Guérin Who Are Ineligible for or Elected Not to Undergo Radical Cystectomy

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INTRODUCTION

- Non-muscle-invasive bladder cancer (NMIBC) has a wide range of disease severity (≈70% of patients present with pathological stage Ta, ≈20% present with T1, and ≈10% present with carcinoma in situ).[1]
- Standard therapy is generally complete transurethral resection of bladder tumor (TURBT), followed by adjuvant treatment tailored to individual risk.
- Additional treatments for high-risk NMIBC include bacillus Calmette-Guérin (BCG) immunotherapy, intravesical chemotherapy, or radical cystectomy (RC).[2,3]
- Treatment options are limited for patients unresponsive to BCG who are ineligible for or elect not to undergo RC.[4,5]
- TAR-200 is a novel, intravesical drug delivery system (Figure 1) that enables sustained release of gemcitabine into the bladder, which increases dwell time of local drug concentration.[6]
- Cetrelimab (JNJ-63723283) is an investigational, fully human immunoglobulin G4 (IgG4) kappa monoclonal antibody that targets the programmed cell death protein-1 (PD-1) receptor, blocking signaling from both programmed death ligand-1 and -2 (PD-L1 and PD-L2).[7]

FIGURE 1: TAR-200 allows continuous local delivery of gemcitabine to tumors within the bladder

OBJECTIVE

- To evaluate the overall complete response (CR) rate in participants treated with TAR-200 in combination with cetrelimab (Cohort 1), TAR-200 alone (Cohort 2), or cetrelimab alone (Cohort 3) with carcinoma in situ (CIS), with or without concomitant high-grade Ta or T1 papillary disease.

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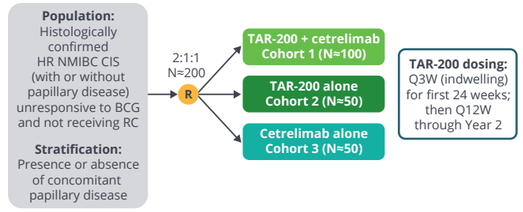
METHODS

FIGURE 2: SunRISe-1 phase 2b study design



HR, high risk; Q3W, every 3 weeks; Q12W, every 12 weeks; R, randomization.

TABLE 1: Study end points

Primary end point	
Overall CR rate	Defined as the proportion of participants without high-grade disease assessed by cystoscopy and biopsy and centrally read urine cytology at any time point
Secondary end points	
• Duration of CR (remain free of recurrence/progression of high-grade disease 12 months after CR)	
• Overall survival	
• Gemcitabine, and its metabolite 2'2'-difluorodeoxyuridine (dFdU), concentration in urine and plasma	
• Serum concentration and incidence of anti-cetrelimab antibodies	
• Health-related quality of life (EORTC QLQ-C30 and EORTC QLQ-NMIBC24)	
• Safety and tolerability	

EORTC QLQ, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire.

Disease assessments

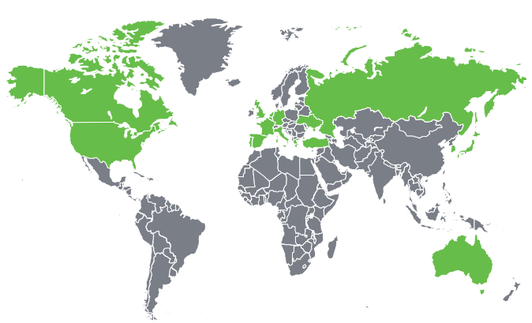
- Cystoscopy, urine cytology, computed tomography/magnetic resonance imaging (CT/MRI) scan with contrast, and TURBT at baseline;
- Cystoscopy and centrally read urine cytology Q12W through Year 2, every 24 weeks (Q24W) thereafter through Year 3, in accordance with institutional standard of care, and collected at 6-month intervals during Year 4 and Year 5;
- TURBT at Week 24 and Week 48 and performed at any time clinically indicated;
- CT/MRI scan with contrast Q24W through Year 3.

TABLE 2: Key eligibility criteria

Key inclusion criteria	Key exclusion criteria
Age ≥ 18 years with histologically confirmed diagnosis of persistent or recurrent high-risk, non-muscle-invasive urothelial CIS (Tis) with or without papillary disease (T1, high-grade Ta)[a]	Histologically confirmed, muscle-invasive, locally advanced, nonresectable, or metastatic urothelial carcinoma
Ineligible for or have elected not to undergo RC	Concurrent extravesical non-muscle-invasive transitional cell carcinoma of the urothelium
BCG-unresponsive high-risk NMIBC after treatment with adequate BCG therapy[b]	Prior therapy with anti-PD-1 agent, anti-PD-L1 agent, or agent targeting another inhibitory T cell receptor
Eastern Cooperative Oncology Group performance status 0, 1, or 2	
Normal thyroid function and adequate bone marrow, liver, and renal function (creatinine clearance > 40 mL/min)	

[a]Visible papillary disease must be fully resected prior to randomization (residual Tis acceptable) and documented at screening cystoscopy. [b]Minimum of 5 of 6 doses of an induction course (adequate induction) plus 2 of 3 doses of a maintenance course, or 2 of 6 doses of a second induction course.

FIGURE 3: SunRISe-1 study is enrolling at ≈165 sites in 17 countries



- The SunRISe-1 study enrollment initiated in January 2021 and is expected to reach primary completion on October 24, 2024.
- This study is not restricted to PD-L1-positive patients.

KEY TAKEAWAY

Study results will be used to evaluate efficacy and safety data for TAR-200 plus cetrelimab, TAR-200 alone, and cetrelimab alone in the treatment of high-risk NMIBC for patients unresponsive to BCG who are ineligible for or elected not to undergo RC.

The SunRISe-1 study opened in January 2021 and is enrolling participants at ≈165 study locations worldwide; currently, the study is active in 13 countries with 60 participants enrolled as of July 18, 2022.

REGISTRATION

This ongoing study is registered at Clinicaltrials.gov: NCT04640623

CONTACT INFORMATION

For more information on qualification and enrollment in SunRISe-1, please contact Shalaka Hampras, MBBS, MPH, PhD, Study Responsible Physician, SHampras@its.jnj.com

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DISCLOSURE

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