# Matching-adjusted Indirect Comparisons of TAR-200 vs. FDA-approved Novel Agents in Bacillus Calmette-Guérin-unresponsive High-risk Non-muscle Invasive Bladder Cancer with Carcinoma in Situ

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## Key Takeaway

TAR-200 demonstrated significantly higher CR rate at any time over FDA-approved novel agents in BCG-unresponsive HR NMIBC with CIS, as well as at first disease assessment compared with NAI + BCG.

## Conclusions

- TAR-200 is a novel iDRS that offers a convenient fixed duration treatment regimen with a low number of doses for patients with BCG-unresponsive HR NMIBC with CIS, without the need for reinduction.
- Given that no head-to-head trials exist in this setting, the MAIC provides scientific information for clinical and reimbursement decision making.
- TAR-200 provides a statistically significant clinical benefit in CR rate at any time vs. pembrolizumab, nadofaragene, and NAI + BCG.
- TAR-200 also provides a significantly higher CR rate at first disease assessment compared with NAI + BCG.

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Disclosures

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- SC, RJ, XL, JH, HS, and SH: employees and stockholders of Johnson & Johnson.
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## Introduction

- TAR-200 is a novel intravesical drug releasing system (iDRS) designed for sustained, local delivery of gemcitabine within the bladder.
- TAR-200 is being investigated in the phase 2b SunRISe-1 study for patients with Bacillus Calmette-Guérin (BCG)-unresponsive high-risk (HR) non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS), with or without papillary tumors, who have refused or are ineligible for radical cystectomy (Cohort 2). TAR-200 has demonstrated a centrally assessed any time complete response (CR) rate of 82.4% in this population.[1]
- The FDA has approved pembrolizumab, nadofaragene firadenovec-vncg (nadofaragene), and nogapendekin alfa inbakicept-pmln in combination with BCG (NAI + BCG) as novel treatment options in this setting.
- In the absence of head-to-head data, matching-adjusted indirect comparisons (MAICs) were conducted to compare the CR rate at any time and at first disease assessment of TAR-200 vs. FDA-approved novel agents.

## Methods

- A systematic literature review identified published data on the comparator regimens in the BCG-unresponsive HR NMIBC with CIS setting.
- The feasibility of conducting MAICs was assessed by reviewing the study and patient characteristics, patient eligibility criteria, outcome definitions, and timepoints of SunRISe-1 and trials of FDA-approved novel agents—KEYNOTE-057,[2,3] CS-003,[4,5] and QUILT 3.032[6,7]— to determine heterogeneity.
- Three unanchored MAICs were conducted using individual patient data (IPD) from SunRISe-1 Cohort 2 and summary-level data from the US prescribing information (USPI) and primary journal publications of the comparators.
- Imbalances in patient characteristics (tumor stage, prior doses of BCG instillation, Eastern Cooperative Oncology Group, age, gender and race) were adjusted by weighting the TAR-200 IPD to match the reported baseline characteristics of the comparator trials.
- Comparative efficacy was estimated for CR rate at any time and at first disease assessment. Relative effects were quantified using rate differences with 95% confidence intervals derived from weighted logistic regression analysis.

## Results

- Dosing regimens, modes of delivery, and definitions of CR varied across the SunRISe-1, KEYNOTE-057, CS-003, and QUILT 3.032 trials (**Table 1**). The SunRISe-1 trial includes a more stringent disease assessment of CR, including required biopsies at weeks 24 and 48, than what is used in the comparator trials. This difference in definitions across trials could not be addressed within the MAIC.

**Table 1: Comparison of treatment characteristics and CR definitions in trials investigating novel agents for the treatment of BCG-unresponsive HR NMIBC with CIS**

| Product | TAR-200 | Pembrolizumab | Nadofaragene | NAI + BCG |
|---|---|---|---|---|
| Trial | SunRISe-1 (Cohort 2)[1] | KEYNOTE-057[2,3] | CS-003[4,5] | QUILT 3.032[6,7] |
| Mode of delivery | Intravesical drug releasing system | IV infusion | Intravesical instillation | Intravesical instillation |
| Dosing regimen | Q3W for the first 6 months; then Q12W for up to 2 years | 200 mg Q3W or 400 mg Q6W for up to 2 years | • 1 induction dose followed by dosing every 3 months for 12 months (4 doses total)<br>• Patients can continue receiving treatment once every 3 months at the discretion of their treating physician | • Induction: QW for 6 consecutive weeks. A second induction may be administered if CR is not achieved at month 3.<br>• Maintenance: QW for 3 weeks. Patients with stable disease receive maintenance dose at months 4, 7, 10, 13, and 19.<br>• For patients with an ongoing CR at month 25 and later, additional maintenance may be administered (QW for 3 weeks at months 25, 31, and 37). |
| Total number of doses | 14 doses over 2 years | 16 or 34 doses over 2 years | • 4 doses in Year 1<br>• Treat to progression thereafter (4 doses/year) | • 21–24 doses over 2 years<br>• 9 additional doses (optional Year 3) |
| Definition of CR | Negative cystoscopy and negative (including atypical) centrally read UC, or positive cystoscopy w/ biopsy-proven benign or low-grade NMIBC and negative (including atypical) centrally read UC at any time, and biopsy at weeks 24 and 48 | Absence of low-grade Ta, HR disease, and progressive disease (central review) by negative results for cystoscopy (with TURBT/biopsies as applicable), UC, and computed tomography urography imaging | Negative results for cystoscopy (with TURBT/biopsies as applicable) and UC | Negative results for cystoscopy (with TURBT/biopsies as applicable) and UC based on investigator assessment of urine cytology, cystoscopy, and local pathology results |
| Timing of CR assessment | Every 12 weeks through Week 99 (Year 2), and then every 24 weeks thereafter through Year 3 | Every 12 weeks for 2 years and then every 24 weeks for 3 years | 3, 6, 9, and 12 months | Every 3 months for up to 2 years |

Abbreviations: BGC = Bacillus Calmette-Guérin; CIS = carcinoma in situ; CR = complete response; HR = high-risk; IV = intravenous; nadofaragene = nadofaragene firadenovec-vncg; NAI + BCG = nogapendekin alfa inbakicept-pmln in combination with Bacillus Calmette-Guérin; NMIBC = non-muscle invasive bladder cancer; Q3W = every 3 weeks; Q6W = every 6 weeks; Q12W = every 12 weeks; QW = weekly; TURBT = transurethral resection of bladder tumor; UC = urine cytology

- Baseline characteristics were similar across all four trials after matching (**Table 2**).

**Table 2: Baseline characteristics of patients in trials investigating novel agents for the treatment of BCG-unresponsive HR NMIBC with CIS**

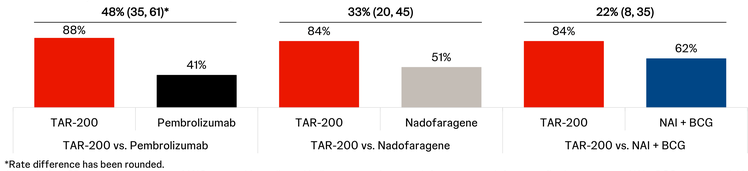
| Variable | Categories | SunRISe-1 (N=85) | KEYNOTE-057 (N=96) | CS-003 (N=98) | QUILT 3.032 (N=77) |
|---|---|---|---|---|---|
| Age in years | Median (Range) | 71 (40–88) | 73 (44–92) | 70 (44–89) | 73 (50–91) |
| Gender | Male % | 80.0 | 84 | 88 | 86 |
| | Female % | 20.0 | 16 | 12 | 14 |
| Race | White % | 87.1 | 67 | 92 | 90 |
| | Non-White % | 12.9 | 33 | 8 | 10 |
| ECOG | 0 % | 91.8 | 73 | 90 | 83 |
| | 1+ % | 8.2 | 27 | 10 | 17 |
| Number of prior BCG instillation | Median | 12 | 12 | 12 | 12 |
| Stage | CIS+T1 % | 10.6 | 13 | 5 | 10 |
| | CIS+Ta % | 22.4 | 25 | 19 | 21 |
| | CIS alone % | 67.1 | 63 | 76 | 69 |

Clinical cut off: March 31, 2025

Abbreviations: BCG = Bacillus Calmette-Guérin; CIS = carcinoma in situ; ECOG = Eastern Cooperative Oncology Group; HR = high-risk; NMIBC = non-muscle invasive bladder cancer; T1 = tumor invades the subepithelial connective tissue; Ta = non-invasive papillary carcinoma

- After adjustment, the three MAICs showed that TAR-200 provides significantly higher CR rate at any time vs. all three FDA-approved novel agents ($P$<0.05 for all comparisons) in the BCG-unresponsive HR NMIBC with CIS setting (**Figure 1**).
  - The greatest incremental difference was observed in the TAR-200 vs. pembrolizumab comparison (+48%).

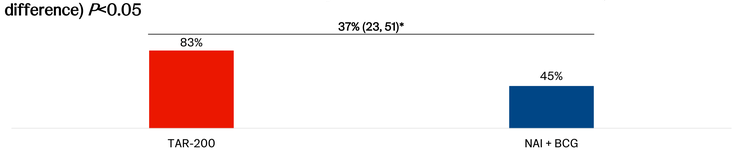
**Figure 1: MAICs of TAR-200 vs. FDA-approved novel agents: adjusted CR at any time (absolute rate differences) $P$<0.05 for all comparisons**




*Rate difference has been rounded.
Abbreviation: CR = complete response; MAICs = matching-adjusted indirect comparisons; nadofaragene = nadofaragene firadenovec-vncg; NAI + BCG = nogapendekin alfa inbakicept-pmln in combination with Bacillus Calmette-Guérin

- Given that reinduction was allowed in QUILT 3.032, an analysis comparing CR rate at first disease assessment of TAR-200 versus NAI + BCG was conducted to assess the impact of reinduction on CR rate (**Figure 2**).
  - Results from this analysis showed that treatment with TAR-200 led to a significantly higher CR rate at first disease assessment compared with NAI + BCG ($P$<0.05) based on calculated data that excluded patients who received a second induction.
  - Calculation for CR at first disease assessment for NAI + BCG:
    - In the USPI, the efficacy results from QUILT 3.032 (n=77) state that 62% achieved CR at any time (n=48 responders). The USPI also states that 31% (n=24) of patients received a second induction course.
    - Chamie et al. 2023[7] also states that 24 patients received reinduction in Cohort A.
    - We can deduce that the 24 reinduced patients are the same across both data sets. Chamie et al. 2023[7] states that of the 24 reinduced patients, 13 achieved CR after reinduction.
    - Triangulating between the sources, we can then calculate from the USPI that 48 total responders – 13 responders after reinduction/77 total patients = 45% of patients achieved CR at first disease assessment.

**Figure 2: MAIC of TAR-200 vs. NAI + BCG: adjusted CR at first disease assessment (absolute rate difference) $P$<0.05**




*Rate difference has been rounded.
Abbreviations: CR = complete response; MAIC = matching-adjusted indirect comparison; NAI + BCG = nogapendekin alfa inbakicept-pmln in combination with Bacillus Calmette-Guérin

## Limitations

- The MAIC methodology can only adjust for observed and reported baseline characteristics. Any confounders not consistently reported or missing across studies may impact internal validity.
- Some differences in study design and outcomes can introduce biases that the MAIC cannot fully address.

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