# TAR-200 +/- Cetrelimab and Cetrelimab Alone in Patients With Bacillus Calmette-Guérin–Unresponsive High-Risk Non–Muscle-Invasive Bladder Cancer: Updated Results From SunRISe-1

**Michiel S van der Heijden[1], Giuseppe Simone[2], Martin Bögemann[3], Evanguelos Xylinas[4], Mathieu Roumiguié[5], Felix Guerrero-Ramos[6], Andrea Necchi[7], Siamak Daneshmand[8], Charles Van Praet[9], Philipp Spiegelhalder[10], Karel Decaestecker[11], Harm Arentsen[12], Daniel Zainfeld[13], Shalaka Hampras[14], Christopher J Cutie[15], Hussein Sweiti[16], Katharine Stromberg[14], Jason Martin[17], Abhijit Shukla[15], Joseph M Jacob[18]**

[1]Department of Medical Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; [2]Department of Urology, 'Regina Elena' National Cancer Institute, Rome, Italy; [3]Department of Urology, Münster University Hospital, Münster, Germany; [4]Department of Urology, Bichat-Claude Bernard Hospital, Assistance Publique-Hôpitaux de Paris, Université de Paris Cité, Paris, France; [5]Department of Urology, Toulouse Hospital, Toulouse, France; [6]University Hospital 12 de Octubre, Madrid, Spain; [7]IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy; [8]Department of Urology, University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [9]Department of Urology, ERN Accredited Center, Ghent University Hospital, Ghent, Belgium; [10]Urologie Neandertal, Gemeinschaftspraxis für Urologie, Mettmann, Germany; [11]Department of Urology, AZ Maria Middelares, Ghent, Belgium; [12]AZ Sint-Jan Hospital Brugge-Oostende, Bruges, Belgium; [13]Urology San Antonio, San Antonio, TX, USA; [14]Janssen Research & Development, Raritan, NJ, USA; [15]Janssen Research & Development, Lexington, MA, USA; [16]Janssen Research & Development, Spring House, PA, USA; [17]Janssen Research & Development, High Wycombe, UK; [18]Department of Urology, Upstate Medical University, Syracuse, NY, USA

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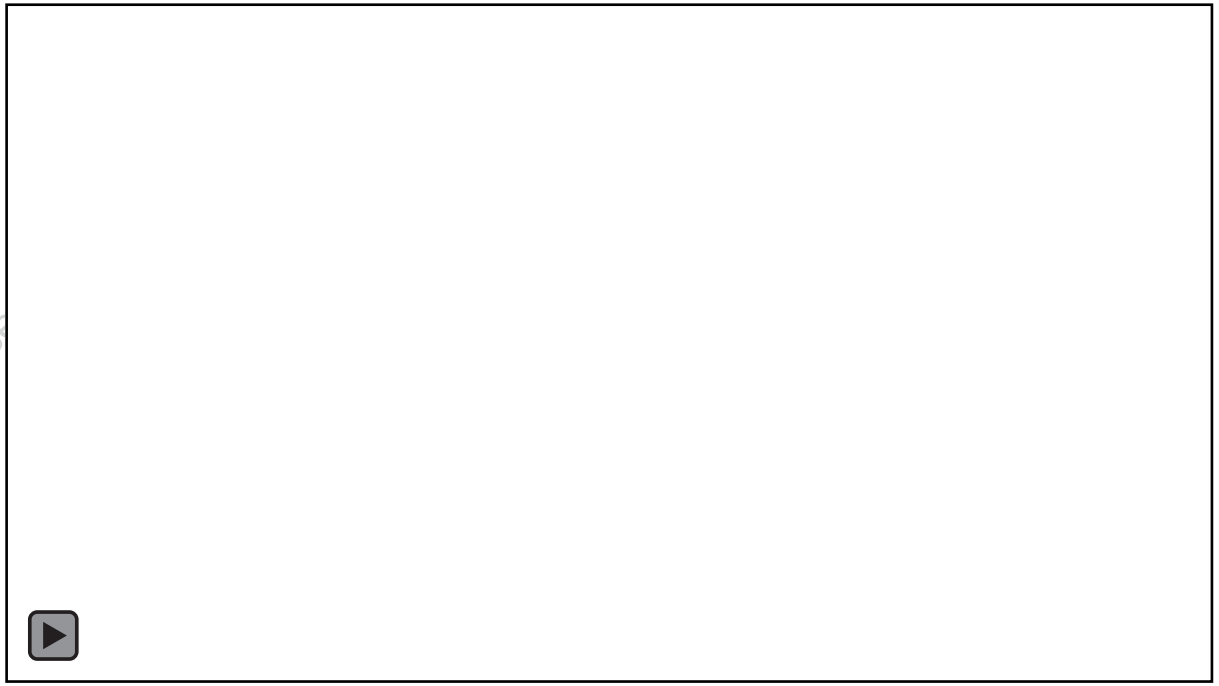
# TAR-200, Cetrelimab, and Addressing Unmet Needs in Patients With HR NMIBC Unresponsive to BCG Treatment

- Standard of care for BCG-unresponsive HR NMIBC is RC[1,2]
  - RC is a life-changing operation associated with considerable morbidity and impact on QoL and a 90-day mortality risk of up to 8%[3]
  - Many patients are unable or unwilling to undergo RC[2]
- Limited US FDA-approved treatment options are available to treat BCG-unresponsive HR NMIBC CIS; 12-month CR rates are:
  - 19% with pembrolizumab[4]
  - 23% with nadofaragene firadenovec[5]
  - 45% with nogapendekin alfa inbakicept + BCG[6]
- Cetrelimab is an anti–PD-1 agent with an efficacy and safety profile consistent with approved anti–PD-1 agents[7,8]

**TAR-200 is a novel gemcitabine intravesical releasing system designed for sustained, local delivery of chemotherapy in the bladder[9-11]**



TAR-200, which has been granted FDA Breakthrough Therapy designation, is placed using a urinary placement catheter in a **2- to 3-minute office procedure**



BCG, bacillus Calmette-Guérin; CIS, carcinoma in situ; CR, complete response; HR, high-risk; NMIBC, non–muscle-invasive bladder cancer; PD-1, programmed cell death protein 1; QoL, quality of life; RC, radical cystectomy; US FDA, United States Food and Drug Administration.

1. Holzbeierlein JM, et al. *J Urol.* 2024;211:533-538. 2. EAU. Available at: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Non-muscle-Invasive-Bladder-Cancer-2023_2023-03-10-101110_jued.pdf. 3. Marqueen KE, et al. *JNCI Cancer Spectr.* 2018;2:pky075. 4. Balar AJ, et al. *Lancet Oncol.* 2021;22:919-930. 5. ADSTILADRIN® (nadofaragene firadenovec-vncg) [prescribing information]. Kastrup, Denmark: Ferring Pharmaceuticals; 2024. 6. Chamie K, et al. *NEJM Evid.* 2023;2(1):EVIDoa2200167. 7. DeAngelis N, et al. *Cancer Chemother Pharmacol.* 2022;89:515-527. 8. Felip E, et al. *Cancer Chemother Pharmacol.* 2022;89:499-514. 9. Daneshmand S, et al. *Urol Oncol.* 2022;40:344.e1-344.e9. 10. Tyson MD, et al. *J Urol.* 2023:209:890-900. 11. van Valenberg FJP, et al. *Eur Urol Open Sci.* 2024;62:8-15.



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# SunRISe-1 Is an Ongoing Open-Label Phase 2b Study

NCT04640623

**Population:**
- Aged ≥18 years
- Histologically confirmed HR NMIBC CIS (with or without papillary disease)
- ECOG PS of 0-2
- Persistent or recurrent disease within 12 months of completion of BCG
- Unresponsive to BCG[1,2] and not receiving RC

R

**TAR-200 + Cetrelimab[b]**
***Cohort 1* (N=53)**
*Cohort 1 was closed*

**TAR-200 Monotherapy**
***Cohort 2* (N=85)**
*Enrollment completed*

**Cetrelimab[b] Monotherapy**
***Cohort 3* (N=28)**
*Cohort 3 was closed*

**Population:**
- Papillary-only HR NMIBC (no CIS)[a]

**TAR-200 Monotherapy**
***Cohort 4* (N=52)**
*Enrollment completed*

**TAR-200 dosing:**
Q3W (indwelling) for the first 24 weeks; then Q12W through Week 96

***Cohorts 1-3:***
**Primary end point**
- Overall CR rate

**Key secondary end points**
- Duration of response
- Overall survival
- Safety
- Tolerability

***Cohort 4:***
**Primary end point**
- DFS rate at 12 months

- Response is determined by quarterly cystoscopy, quarterly central cytology, central pathology at Weeks 24 and 48, and local imaging Q24W
- The study protocol did not allow re-induction for nonresponders, consistent with US FDA guidance[2]
- As of June 2023, Cohorts 1 and 3 were closed for enrollment, and Cohort 2 enrollment continued to achieve N≈80, per protocol amendment
- ***Here we report results from* TAR-200 + cetrelimab *(Cohort 1),* TAR-200 monotherapy *(Cohort 2), and* cetrelimab monotherapy *(Cohort 3) of SunRISe-1***

The clinical data cutoff was May 13, 2024.
DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; Q3W, every 3 weeks; Q12W, every 12 weeks; Q24W, every 24 weeks; R, randomization.
[a]Patients with BCG-unresponsive papillary-only HR NMIBC (high-grade Ta, any T1) per protocol amendment 4.
[b]Cetrelimab dosing was Q3W through Week 78.
1. Lerner SP, et al. *Urol Oncol*. 2009;27:155-159. 2. US Food and Drug Administration. Available at: https://www.fda.gov/media/101468/download.





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# SunRISe-1 Cohorts 1, 2, and 3: Patient Characteristics

| Characteristics | TAR-200 + Cetrelimab *Cohort 1* (N=53)[a] | TAR-200 Monotherapy *Cohort 2* (N=85)[a] | Cetrelimab Monotherapy *Cohort 3* (N=28)[a] |
|---|---|---|---|
| Age, years, median (range) | 76.0 (45-85) | 71.0 (40-88) | 69.5 (51-88) |
| Sex, male, % | 83.0 | 80.0 | 75.0 |
| Race, % | | | |
| White | 60.4 | 72.9 | 85.7 |
| Asian | 13.2 | 9.4 | 3.6 |
| Black or African American | 1.9 | 2.4 | 0 |
| Not reported/ unknown | 24.5 | 15.3 | 10.7 |
| Nicotine use, % | | | |
| Current | 13.2 | 9.4 | 25.0 |
| Former | 41.5 | 57.6 | 46.4 |
| Never | 45.3 | 32.9 | 28.6 |

| Characteristics | TAR-200 + Cetrelimab *Cohort 1* (N=53)[a] | TAR-200 Monotherapy *Cohort 2* (N=85)[a] | Cetrelimab Monotherapy *Cohort 3* (N=28)[a] |
|---|---|---|---|
| ECOG PS 0, % | 86.8 | 91.8 | 92.9 |
| Tumor stage, % | | | |
| CIS only | 73.6 | 67.1 | 66.7[b] |
| CIS + papillary disease | 26.4 | 32.9 | 33.3[b] |
| Total doses of prior BCG, n, median (range) | 12 (2-35) | 12 (7-42) | 12 (7-30) |
| Time from last BCG to CIS diagnosis, months, median (range) | 3.7 (0-11) | 3.4 (0-22)[c] | 3.2 (0-11) |
| Reason for not receiving radical cystectomy, % | | | |
| Declined | 96.2 | 96.5 | 100 |
| Ineligible | 3.8 | 3.5 | 0 |

[a]Patient characteristics are shown for all patients who received at least 1 dose of study drug in the full analysis set of each cohort, Cohort 1 (N=53), Cohort 2 (N=85), and Cohort 3 (N=28).
[b]N=27; data were unavailable for 1 patient at the clinical cutoff.
[c]1 patient had 22.4 months from last BCG dose to CIS diagnosis (protocol deviation); all other patients had ≤12 months from last BCG dose to CIS diagnosis (per protocol).





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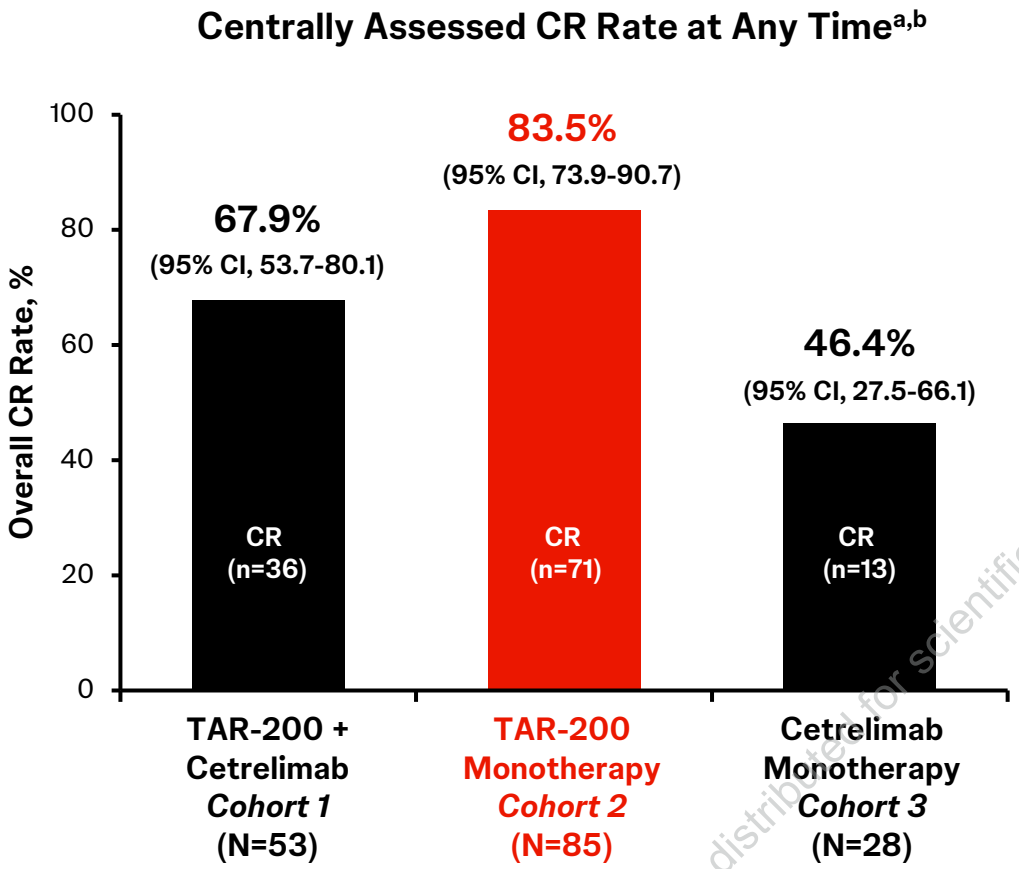
# SunRISe-1 Cohorts 1, 2, and 3: Response Rate and Duration




| | TAR-200 + Cetrelimab *Cohort 1* (N=53) | TAR-200 Monotherapy *Cohort 2* (N=85) | Cetrelimab Monotherapy *Cohort 3* (N=28) |
|---|---|---|---|
| Estimated 12-month CR rate[c], % (95% CI) | **56.7** (41.2-69.6) | **57.4** (40.6-71.0) | **22.8** (8.6-41.1) |
| Estimated 12-month DOR rate[c], % (95% CI) | **75.9** (57.5-87.2) | **65.7** (45.2-80.1) | **48.5** (17.9-73.7) |
| Median follow-up in responders, months (range) | **21.8** (9.2-35.9) | **9.2** (3.7-36.6) | **18.2** (11.3-33.1) |
| Patients remaining in response, % (n/N) | **75.0** (27/36) | **81.6** (58/71) | **53.8** (7/13) |



CI, confidence interval. DOR, duration of response.
[a]Response is based on centrally reviewed urine cytology, local cystoscopy, and central biopsy (if available). CRs do not have to be confirmed. A CR is defined as having a negative cystoscopy and negative (including atypical) centrally read urine cytology, or positive cystoscopy with biopsy-proven benign or low-grade NMIBC and negative (including atypical) centrally read cytology at any time point.
[b]Investigator-assessed CR rates: Cohort 1, 83.0% (95% CI, 70.2-91.9); Cohort 2, 85.9% (95% CI, 76.6-92.5); Cohort 3, 53.6% (95% CI, 33.9-72.5).
[c]Kaplan-Meier estimate.



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# SunRISe-1 Cohorts 1, 2, and 3: Safety Profile

- Overall, most AEs were grade 1 or 2
- Higher rates of grade ≥3 TRAEs were observed with the combination regimen (35.8%) than with TAR-200 (9.4%) or cetrelimab (7.1%) monotherapy
- Patients with serious TRAEs:
  - ***Cohort 1:*** TAR-200 + cetrelimab, 13.2%
  - ***Cohort 2:*** TAR-200, 5.9%
  - ***Cohort 3:*** Cetrelimab, 3.6%
- Rates of discontinuation due to TRAEs:
  - ***Cohort 1:*** TAR-200, 26.4%; cetrelimab, 22.6%[a]
  - ***Cohort 2:*** TAR-200, 5.9%[b]
  - ***Cohort 3:*** Cetrelimab, 7.1%[c]
- No treatment-related deaths were reported

| Patients with events, n (%) | TAR-200 + Cetrelimab *Cohort 1* (N=53)[d] | TAR-200 Monotherapy *Cohort 2* (N=85)[d] | Cetrelimab Monotherapy *Cohort 3* (N=28)[d] |
|---|---|---|---|
| ≥1 TRAEs of any grade | 49 (92.5) | 71 (83.5) | 14 (50.0) |
| Most frequent TRAEs of any grade[e] | | | |
| Pollakiuria | 16 (30.2) | 33 (38.8) | 0 |
| Dysuria | 16 (30.2) | 30 (35.3) | 0 |
| Hematuria | 11 (20.8) | 12 (14.1) | 0 |
| UTI | 11 (20.8) | 17 (20.0) | 0 |
| Pruritus | 7 (13.2) | 1 (1.2) | 3 (10.7) |
| Hypothyroidism | 4 (7.5) | 0 | 3 (10.7) |

| Patients with events, n (%) | TAR-200 + Cetrelimab *Cohort 1* (N=53)[d] | TAR-200 Monotherapy *Cohort 2* (N=85)[d] | Cetrelimab Monotherapy *Cohort 3* (N=28)[d] |
|---|---|---|---|
| ≥1 TRAEs of grade ≥3 | 19 (35.8) | 8 (9.4) | 2 (7.1)[f] |
| Most frequent TRAEs grade ≥3[g] | | | |
| UTI | 2 (3.8) | 1 (1.2) | 0 |
| AST increased | 2 (3.8) | 0 | 0 |
| Urinary tract pain | 1 (1.9) | 3 (3.5) | 0 |

AE, adverse event; AST, aspartate aminotransferase; TRAE, treatment-related adverse event; UTI, urinary tract infection.
[a]The most frequent TRAEs leading to discontinuation in Cohort 1 were bladder pain (n=6), pollakiuria (n=3), bladder irritation (n=2), bladder spasm (n=2), urinary incontinence (n=2), arthritis (n=2), pelvic pain (n=2), and pneumonitis (n=2). Note, patients who discontinued may have had ≥1 TRAE.
[b]TRAEs leading to discontinuation in Cohort 2 were noninfective cystitis (n=3), dysuria (n=1), pollakiuria (n=1), and urinary retention (n=1). Note, patients who discontinued may have had ≥1 TRAE.
[c]TRAEs leading to discontinuation in Cohort 3 were neutropenia (n=1) and myopericarditis (n=1).
[d]Safety data are shown for all patients who received at least 1 dose of study drug in the full analysis set of each cohort, Cohort 1 (N=53), Cohort 2 (N=85), and Cohort 3 (N=28).
[e]TRAEs of any grade by preferred term are listed if they were reported in ≥20% of patients in Cohorts 1 and 2 or in ≥10% of patients in Cohort 3.
[f]TRAEs of grade ≥3 in Cohort 3 were hyperglycemia (n=1), neutropenia (n=1), and myopericarditis (n=1). Note, patients may have had ≥1 TRAE.
[g]TRAEs of grade ≥3 by preferred term are listed if they were reported in ≥2 patients in any cohort.





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# Conclusions: SunRISe-1 Cohorts 1, 2, and 3

- **TAR-200 monotherapy** provides ***the highest single-agent CR rate*** (**84%**) in patients with BCG-unresponsive HR NMIBC, based on published data, without the need for re-induction[1-4]
  - Responses to TAR-200 monotherapy are highly durable; 82% of patients remain in response after median follow-up of 9.2 months
  - TAR-200 monotherapy was well tolerated, with few grade ≥3 TRAEs or TRAEs leading to discontinuation
- **Cetrelimab monotherapy** provided a CR rate comparable to other anti-PD-(L)1 agents[1,2]
- SunRISe-1 results indicate a ***more favorable risk-benefit profile*** for **TAR-200 monotherapy** compared with **TAR-200 + cetrelimab** or **cetrelimab monotherapy** in BCG-unresponsive HR NMIBC
- Results from SunRISe-1 Cohorts 1, 2, and 3 support the prioritized development of TAR-200 monotherapy in patients with BCG-unresponsive HR NMIBC



1. Balar AJ, et al. *Lancet Oncol.* 2021;22:919-930. 2. Black PC, et al. *Eur Urol.* 2023;84:536-544. 3. ADSTILADRIN® (nadofaragene firadenovec-vncg) [prescribing information]. Kastrup, Denmark: Ferring Pharmaceuticals; 2024. 4. Tyson MD, et al. *J Urol.* 2024;211(5S2):e1.



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https://www.congresshub.com/Oncology/ESMO2024/TAR-200/Heijden



**Ongoing studies of TAR-200:**

- **SunRISe-1**
  BCG-unresponsive HR NMIBC
  (cohorts 1-3: CIS; cohort 4: papillary only)
  NCT04640623
  ***Presented here***
- **SunRISe-2**
  RC-ineligible/-refusing MIBC
  NCT04658862
- **SunRISe-3**
  BCG-naive HR NMIBC
  NCT05714202
- **SunRISe-4** ▷
  Neoadjuvant MIBC
  NCT04919512
- **SunRISe-5**
  Papillary-only, BCG-exposed,
  RC-ineligible/refusing, recurrent HR NMIBC
  NCT06211764

▷ **SunRISe-4 Interim Analysis Results**
*Andrea Necchi, et al. Abstract LBA84*
*Proffered Paper Session 2 GU, non-prostate*
Monday, 16 Sep 2024; 08:30, Sevilla Auditorium – Hall 2


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