TAR-200 in Patients With Bacillus Calmette–Guérin-Unresponsive High-Risk Non–Muscle-Invasive Bladder Cancer: Results From SunRISe-1 Study

Joseph M Jacob[1], Andrea Necchi[2], Siamak Daneshmand[3], Giuseppe Simone[4], Evanguelos Xylinas[5], David S Morris[6], Philipp Spiegelhalder[7], Daniel Zainfeld[8], Taek Won Kang[9], Justin T Matulay[10], Laurence H Belkoff[11], Karel Decaestecker[12], Harm Arentsen[13], Shalaka Hampras[14], Christopher J Cutie[15], Hussein Sweiti[16], Katharine Stromberg[14], Jason Martin[17], Abhijit Shukla[15], Michiel S van der Heijden[18]

[1]Upstate Medical University, Syracuse, NY, USA; [2]IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy; [3]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [4]"Regina Elena" National Cancer Institute, Rome, Italy; [5]Bichat-Claude Bernard Hospital, Assistance Publique-Hôpitaux de Paris, Université de Paris Cité, Paris, France; [6]Urology Associates, Nashville, TN, USA; [7]Urologie Neandertal, Gemeinschaftspraxis für Urologie, Mettmann, Germany; [8]Urology San Antonio, San Antonio, TX, USA; [9]Chonnam National University Medical School, Chonnam National University Hospital, Gwangju, South Korea; [10]Atrium Health Levine Cancer Institute, Charlotte, NC, USA; [11]MidLantic Urology/Solaris Health, Bala Cynwyd, PA, USA; [12]AZ Maria Middelares, Ghent, Belgium; [13]AZ Sint-Jan Hospital Brugge-Oostende, Bruges, Belgium; [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]Netherlands Cancer Institute, Amsterdam, Netherlands

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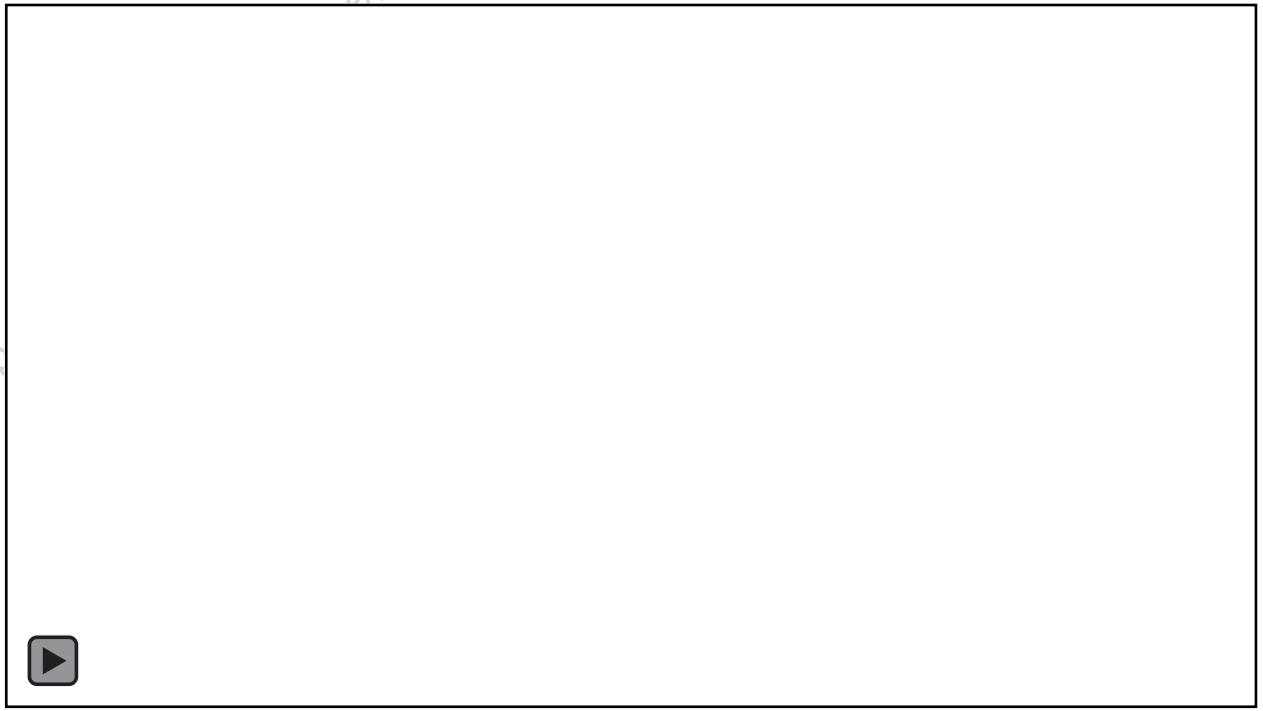
TAR-200 and Addressing Unmet Needs in Patients With HR NMIBC Unresponsive to BCG Treatment

- Standard of care for BCG-unresponsive HR NMIBC is radical cystectomy (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 treatment options are available to treat BCG-unresponsive HR NMIBC CIS; 12-month CR rates are:
  - 19% with pembrolizumab[4]
  - 15% with atezolizumab[5]
  - 23% with nadofaragene firadenovec[6]

TAR-200 is a novel targeted releasing system designed for sustained, local delivery of gemcitabine in the bladder[7,8]



TAR-200 is placed using a urinary placement catheter in a **2-3 minute office procedure.**

BCG, bacillus Calmette–Guérin; CIS, carcinoma in situ; CR, complete response; HR, high-risk; NMIBC, non–muscle-invasive bladder cancer; QoL, quality of life; RC, radical cystectomy.

1. NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer. Version 2. 2024. 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. Black PC, et al. *Eur Urol.* 2023;84:536-544. 6. ADSTILADRIN® (nadofaragene firadenovec-vncg) [prescribing information]. Kastrup, Denmark: Ferring Pharmaceuticals; 2022. 7. Daneshmand S, et al. *Urol Oncol.* 2022;40:344.e1-344.e9. 8. Tyson MD, et al. *J Urol.* 2023:209:890-900.

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

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

2:1:1
N≈200

R

- **TAR-200 + cetrelimab[b] Cohort 1 (N=55)[c]** — *Cohort 1 was closed*
- **TAR-200 alone Cohort 2 (N=85)** — *Enrollment completed*
- **Cetrelimab[b] alone Cohort 3 (N=28)[d]** — *Cohort 3 was closed*

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

- **TAR-200 alone Cohort 4 (N≈50)** — *Enrollment was closed*

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, and central pathology at Weeks 24 and 48 and as clinically indicated[e]
- The study protocol did not allow re-induction for nonresponders, consistent with US FDA guidance[2]
- Here we report updated results from the **TAR-200 monotherapy cohort (Cohort 2)** of SunRISe-1

The clinical data cutoff was January 2, 2024.
CR, complete response; DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; Q3W, every 3 weeks; Q12W, every 12 weeks; R, randomization; US FDA, United States Food and Drug Administration.
[a]Patients with BCG-unresponsive papillary-only HR NMIBC (high-grade Ta, any T1) per protocol amendment 4. [b]Cetrelimab is an anti-programmed cell death-1[3,4]; cetrelimab dosing was through Week 78. [c]55 patients were randomized and 53 were treated in Cohort 1. [d]28 patients were randomized and treated in Cohort 3. [e]Imaging (CT/MRI) was performed every 24 weeks through Year 3.
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. 3. DeAngelis N, et al. *Cancer Chemother Pharmacol.* 2022;89:515-527. 4. Felip E, et al. *Cancer Chemother Pharmacol.* 2022;89:499-514.

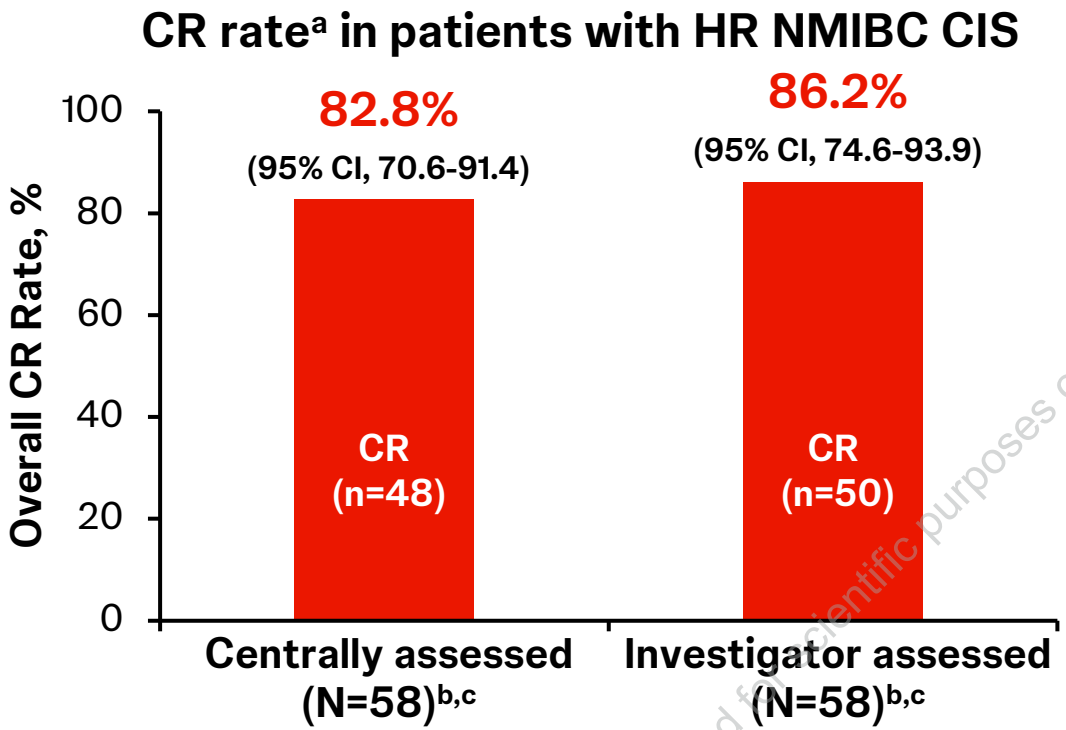
Patient Characteristics in the TAR-200 Monotherapy Cohort

Characteristics	TAR-200 (N=85)[a]
Age, years, median (range)	71 (40-88)
Sex, male, %	80.0
Race, %	
White	72.9
Asian	9.4
Black or African American	2.4
Not reported/unknown	15.3
Nicotine use, %	
Current	9.4
Former	57.6
Never	32.9

Characteristics	TAR-200 (N=85)[a]
ECOG PS 0, %	91.8
Tumor stage, %	
CIS only	67.1
CIS + papillary disease	32.9
Total doses of prior BCG, n, median (range)	12 (7-42)
Time from last BCG to CIS diagnosis, months, median (range)	3.4 (0-22)[b]
Reason for not receiving RC, %	
Declined	96.5
Ineligible	3.5

[a]Patient characteristics are shown for all patients who received at least one dose of TAR-200 in the full analysis set (N=85). [b]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).

TAR-200 Monotherapy: High CR Rate With Rapid Onset



Landmark time	Overall CR rate, % (95% CI)
6 months	**75.7** (59.1, 86.3)
12 months	**61.9** (41.4, 77.1)

CR rate based on Kaplan-Meier estimate.

- High rate of CR was consistent between centrally and investigator-assessed response
- Onset of response was rapid, with 47 of 48 (98%) CRs achieved at the first disease assessment at Week 12

CI, confidence interval.
[a]Overall CR rate is based on CR at any time. [b]The efficacy analysis was performed on all treated patients who had active disease at baseline and adequate disease assessment postbaseline, or who progressed, died, had been withdrawn from treatment due to the recurrence of high-risk or progressive disease, or discontinued the study (N=58). 2 patients discontinued the study before having a disease evaluation but were included in the denominator of the evaluation of CR rate. [c]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.

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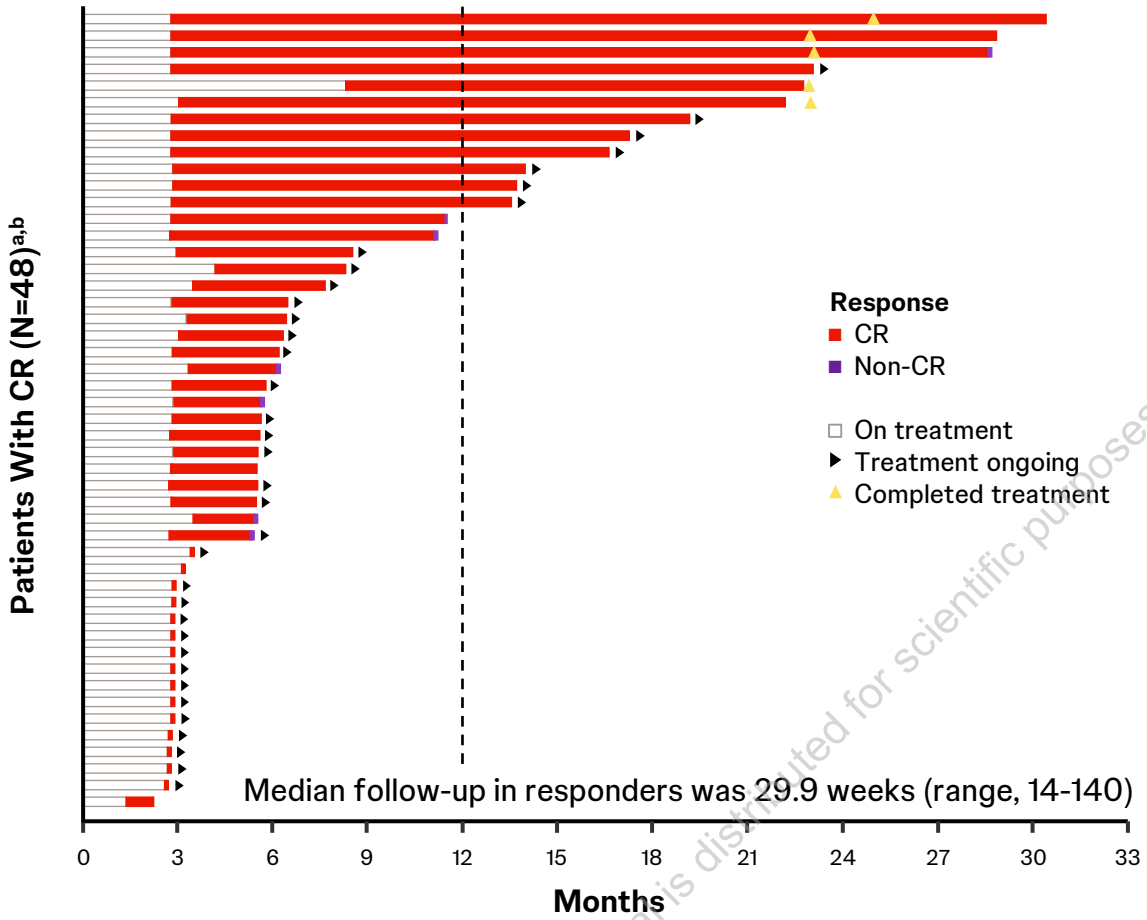
TAR-200 Monotherapy Was Associated With a Durable Response



- 41 of 48 (85%) responses were ongoing at clinical cutoff, with 4 of 5 (80%) who completed 2-year treatment remaining in response
- None of the responders progressed to MIBC or metastatic disease
- 1 of 48 (2.1%) responders underwent RC
- Kaplan–Meier estimates for DOR:
  - 6-month DOR rate: 87.0% (95% CI, 69.0-94.9)
  - 12-month DOR rate: 74.6% (95% CI, 49.8-88.4)
  - 18-month DOR rate: 74.6% (95% CI, 49.8-88.4)

MIBC, muscle-invasive bladder cancer.
[a]The efficacy analysis was performed on all treated patients who had active disease at baseline and adequate disease assessment postbaseline, or who progressed, died, had been withdrawn from treatment due to the recurrence of high-risk or progressive disease, or discontinued the study. Response duration shown for patients with CR (N=48). [b]A CR is defined as having a negative cystoscopy and negative (including atypical) centrally read urine cytology or a positive cystoscopy with biopsy-proven benign or low-grade NMIBC and negative (including atypical) centrally read cytology at any time point.

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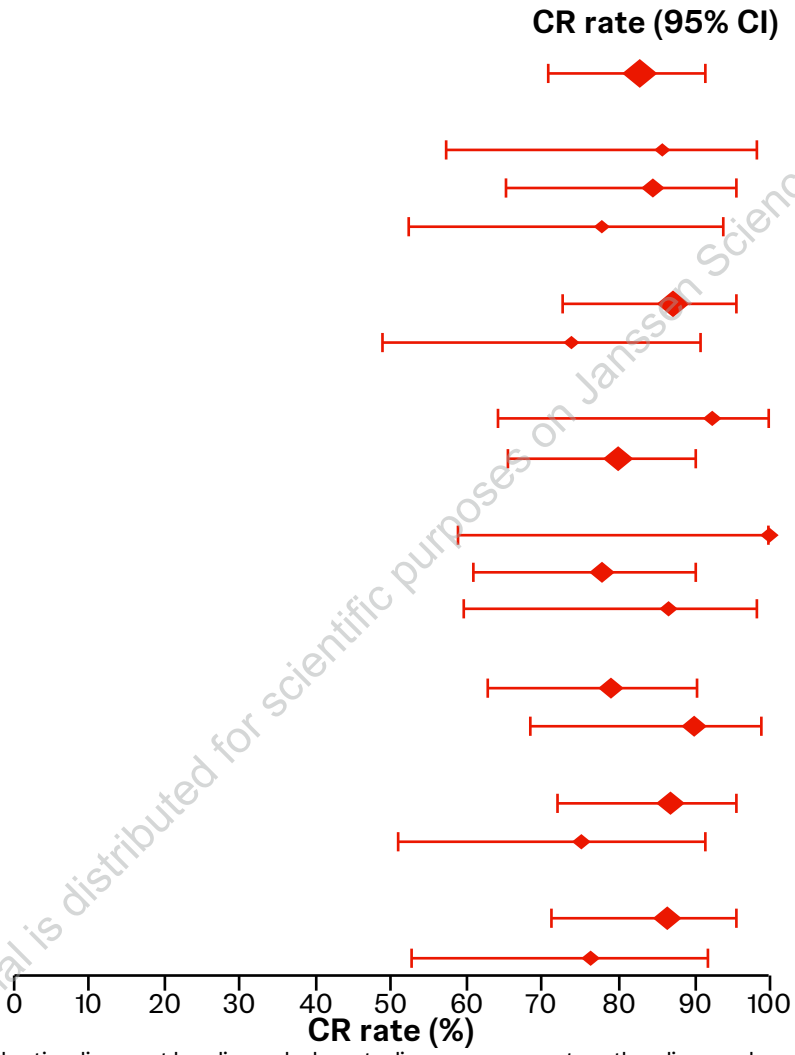
TAR-200 Monotherapy CR Rate Consistent Across Patient Subgroups



	CR rate (95% CI)	CR rate, % (n/N)	95% CI, %
Overall[a]		82.8 (48/58)	70.6-91.4
Age group, years			
<65		85.7 (12/14)	57.2-98.2
65 to <75		84.6 (22/26)	65.1-95.6
≥75		77.8 (14/18)	52.4-93.6
Race			
White		87.2 (34/39)	72.6-95.7
Other		73.7 (14/19)	48.8-90.9
Sex			
Female		92.3 (12/13)	64.0-99.8
Male		80.0 (36/45)	65.4-90.4
Region			
Asia Pacific		100 (7/7)	59.0-100
Europe		77.8 (28/36)	60.8-89.9
North America		86.7 (13/15)	59.5-98.3
Tumor stage			
CIS only		78.9 (30/38)	62.7-90.4
CIS with papillary disease		90.0 (18/20)	68.3-98.8
Prior BCG strain			
BCG Tice		86.8 (33/38)	71.9-95.6
Other		75.0 (15/20)	50.9-91.3
Nicotine use			
Current/former		86.5 (32/37)	71.2-95.5
Never		76.2 (16/21)	52.8-91.8

[a]The efficacy analysis was performed on all treated patients who had active disease at baseline and adequate disease assessment postbaseline, or who progressed, died, had been withdrawn from treatment due to the recurrence of high-risk or progressive disease, or discontinued the study (N=58).

TAR-200 Monotherapy Safety Profile

- Most AEs were grade 1 or 2, with onset within 12 weeks of treatment initiation
  - However, resolution of most AEs was within 2 weeks
- 61 patients (71.8%) had ≥1 treatment-related AEs[a,b]
- 4 patients (4.7%) had ≥1 serious treatment-related AEs
- 7 patients (8.2%) had grade 3 treatment-related AEs
- Few patients (n=4; 4.7%) discontinued treatment due to AEs[c]
- No treatment-related deaths were reported

Characteristics	TAR-200 (N=85)[d]	
	Any grade	Grade ≥3
≥1 AE	73 (85.9)	19 (22.4)
≥1 treatment-related AEs[a,b,e]	61 (71.8)	7 (8.2)
Pollakiuria	30 (35.3)	0
Dysuria	25 (29.4)	1 (1.2)
Micturition urgency	13 (15.3)	0
Urinary tract infection	13 (15.3)	1 (1.2)
Hematuria	8 (9.4)	0
Noninfective cystitis	7 (8.2)	0
Urinary tract pain	6 (7.1)	2 (2.4)
Bladder pain	3 (3.5)	1 (1.2)
Urinary retention	2 (2.4)	1 (1.2)
Renal impairment	1 (1.2)	1 (1.2)
Urosepsis	1 (1.2)	1 (1.2)

AE, adverse event.
[a]Number of patients who experienced AEs related to TAR-200, the insertion procedure, removal procedure, or urinary placement catheter that led to discontinuation of TAR-200. [b]An AE was categorized as related if the investigator determined that there was a possible, probable, or causal relationship between the AE and TAR-200 or the insertion or removal procedure or urinary placement catheter. [c]Treatment-related AEs leading to discontinuation were noninfective cystitis (n=3), dysuria (n=1), and pollakiuria (n=1). [d]Safety is shown for all patients who received at least 1 dose of TAR-200 in the safety analysis set (N=85). [e]Treatment-related AEs by preferred term of any grade were reported in ≥5% of patients, and all treatment-related AEs by preferred term of grade ≥3 are listed.

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Conclusions: TAR-200 Monotherapy Cohort From SunRISe-1

- **TAR-200 monotherapy provides a high rate of CR with rapid onset of response** in patients with BCG-unresponsive HR NMIBC
  - 98% of CRs achieved at 12 weeks
  - 82.8% CR rate via central review and 86.2% CR rate via investigator assessment
  - The CR rates at 6 and 12 months were estimated to be 75.7% and 61.9%, respectively
- **TAR-200 responses were durable**
  - 85% of responders are ongoing, with a median follow-up of 30 weeks
  - 1-year DOR rate was 74.6% (95% CI, 49.8-88.4) based on Kaplan–Meier estimate
  - 5 patients have completed 2 years of treatment; 4 of these patients remain in CR
  - None of the responders progressed to MIBC or metastatic disease
  - 1 of 48 (2.1%) responders has undergone RC
- **Most AEs** were **grade 1 or 2**, and there were **few treatment discontinuations** due to AEs

TAR-200, which is administered in a 2-3 minute in-office procedure, has been granted FDA Breakthrough Therapy designation

Acknowledgments

https://www.congresshub.com/Oncology/AUA2024/TAR-200/Jacob
The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Ongoing studies of TAR-200:

- **SunRISe-1**
  BCG-unresponsive HR NMIBC
  (Cohorts 1-3: CIS; Cohort 4: papillary only)
  NCT04640623
  Cohort 2 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

▷ *Additional AUA 2024 presentations on TAR-200:*
Clinical Trials in Progress, Bladder Cancer
Sunday, May 5, 2024; 10:00 AM-12:00 PM; Learning Lab

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