TAR-200 Plus Cetrelimab or Cetrelimab Alone as Neoadjuvant Therapy in Patients With Muscle-Invasive Bladder Cancer Who Are Ineligible for or Refuse Neoadjuvant Cisplatin-Based Chemotherapy: Interim Analysis of SunRISe-4

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Unmet Need in Patients With MIBC

- Standard of care for MIBC (T2-T4a N0M0) includes RC with or without NAC[1]
  - However, up to 50% of patients with MIBC are ineligible for NAC[2,3]
  - Approximately 50% of patients experience recurrence within 2 years after undergoing RC, and 5-year survival after RC is ~50%[4-6]
- In patients with MIBC undergoing RC, pathologic stage is a prognostic factor for survival[5-8]
  - pCR rates with RC alone, with NAC, and with neoadjuvant checkpoint inhibitors are 10-15%, ~30%, and 31-39%, respectively[7-13]
  - pCR in patients who have received neoadjuvant chemotherapy therapy is associated with a 55% lower risk of death and an 81% lower risk of recurrence compared with patients with residual disease[8]
- There is a high unmet need for effective and more tolerable treatment options for patients with MIBC who are candidates for RC but not candidates for or who refuse NAC

MIBC, muscle-invasive bladder cancer; NAC, neoadjuvant cisplatin-based chemotherapy; pCR, pathologic complete response rate; RC, radical cystectomy.

1. Scarpato KR, et al. *Res Rep Urol.* 2015;7:143-151. 2. Thompson RH, et al. *BJU Int.* 2014;113:E17–E21. 3. Jiang DM, et al. *Nat Rev Urol.* 2021;18:104-114. 4. Li G, et al. *Clin Invest Med.* 2017;40:E81-E94. 5. Stein JP, et al. *J Clin Oncol.* 2001;19:666-675. 6. Madersbacher S, et al. *J Clin Oncol.* 2003;21:690-696. 7. Isbarn H, et al. *J Urol.* 2009;182:459-465. 8. Petrelli F, et al. *Eur Urol.* 2014;65:350-357. 9. Bandini M, et al. *Ann Oncol.* 2020;31:1755–1763. 10. Powles T, et al. *Nat Med.* 2019;25:1706–1714. 11. Szabados B, et al. *Eur Urol.* 2022;82:212–222. 12. Grossman HB, et al. *N Engl J Med.* 2003;349:859-866. 13. Necchi A, et al. *JAMA Oncol.* 2023;9:1447-1454.

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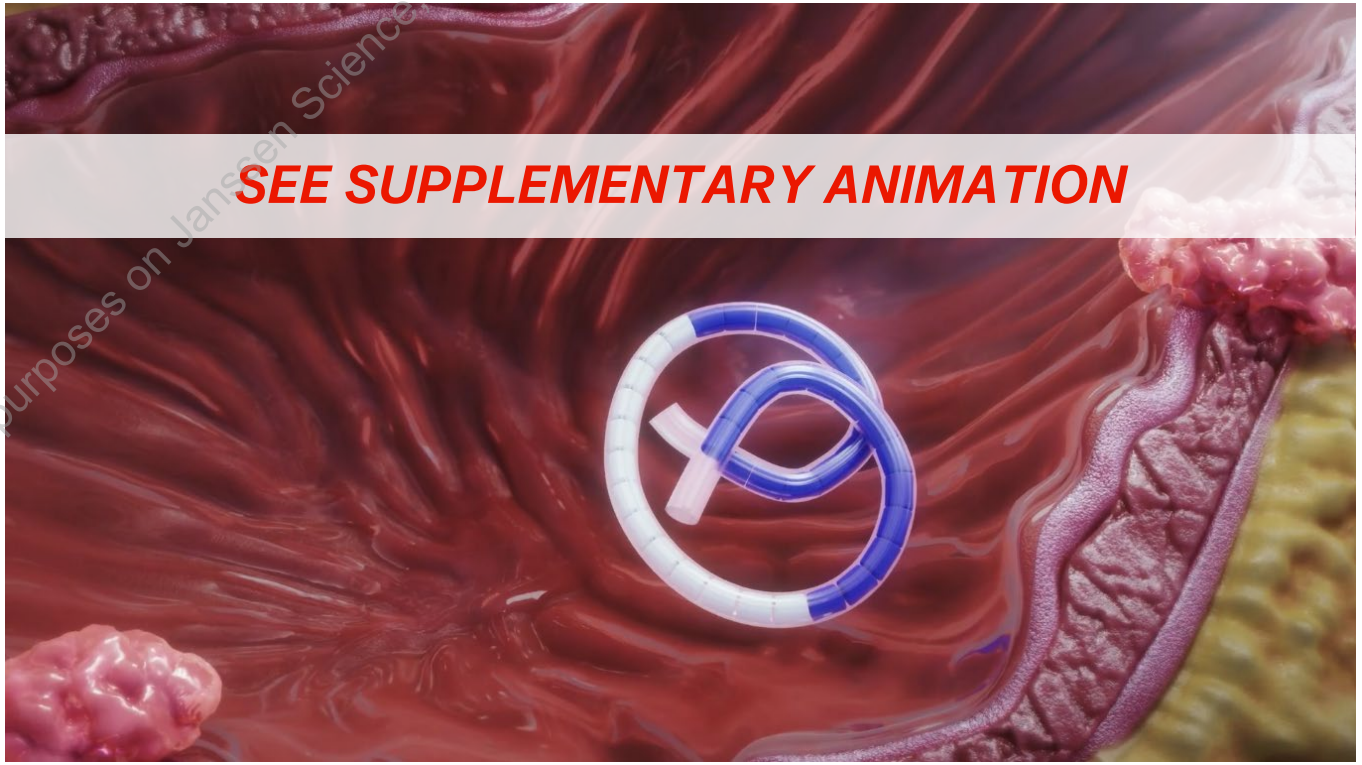
TAR-200 Is a Gemcitabine Intravesical Releasing System Designed to Provide Sustained Gemcitabine Within the Bladder

- Phase 1 studies show clinical activity for TAR-200 in patients with MIBC[1,2]
- Cetrelimab is an anti–PD-1 agent[3,4]
- SunRISe-4 (NCT04919512) is an ongoing randomized phase 2 study assessing the efficacy and safety of neoadjuvant **TAR-200 + cetrelimab** or **cetrelimab monotherapy** in patients with MIBC scheduled for RC who are ineligible for or refuse NAC

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



PD-1, programmed death 1.

1. Daneshmand S, et al. *Urol Oncol.* 2022;40:344.e1-344.e9. 2. Tyson MD, et al. *J Urol.* 2023:209:890-900. 3. DeAngelis N, et al. *Cancer Chemother Pharmacol.* 2022;89:515-527. 4. Felip E, et al. *Cancer Chemother Pharmacol.* 2022;89:499-514.

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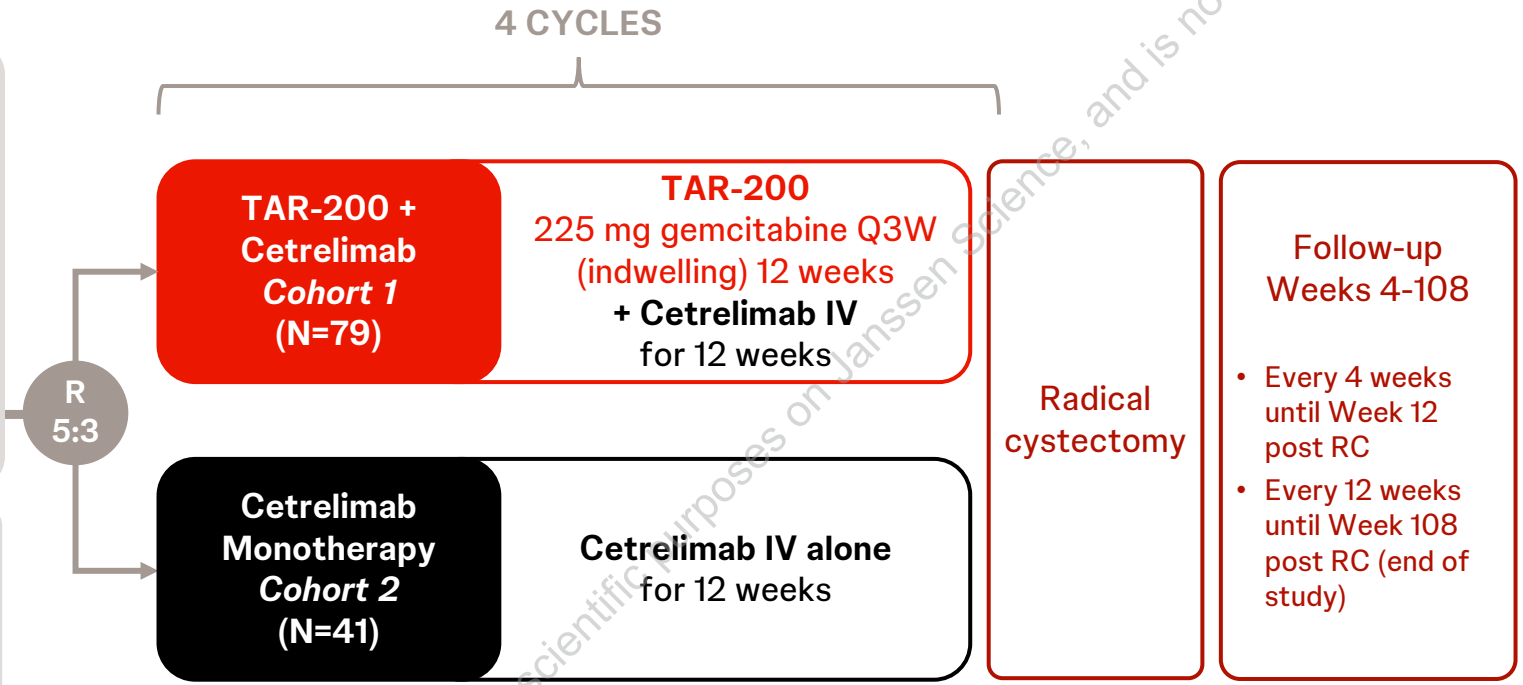
SunRISe-4: Phase 2b Study of Neoadjuvant TAR-200 + Cetrelimab in Patients With MIBC (cT2-T4a N0M0)

Population:
- Aged ≥18 years
- Histologically confirmed cT2-T4a N0M0 MIBC (absence of nodal or metastatic disease at screening)
- Predominant UC histology
- ECOG PS of 0-1
- Ineligible or refusing NAC
- Scheduled for RC

Stratification:
- Visible residual disease at TURBT: complete vs incomplete (≤3 cm)
- Tumor stage at MIBC diagnosis: cT2 vs cT3-4a



Primary end point
- Pathologic CR rate (ypT0N0)

Secondary end points
- Recurrence-free survival
- Safety

Exploratory end points
- Pathologic OR rate (≤ypT1N0)
- Overall survival
- Time to symptomatic progression
- Quality of life according to FACT-BI
- Pharmacokinetics
- Biomarker analysis

NCT04919512

- Sample size: N=160
- For this interim analysis, the clinical data cutoff was May 31, 2024

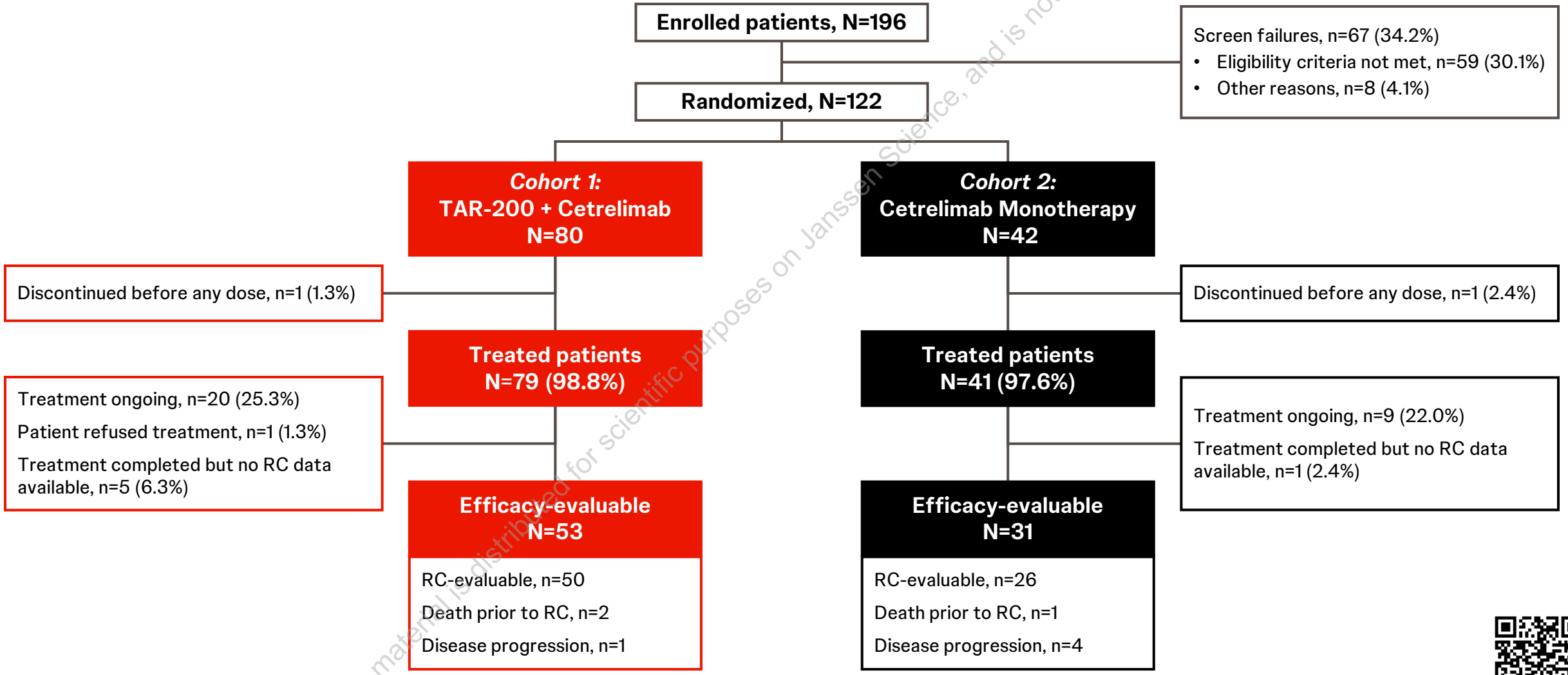
CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; FACT-BI, Functional Assessment of Cancer Therapy–Bladder; IV, intravenous; OR, overall response; Q3W, every 3 weeks; R, randomization; TURBT, transurethral resection of bladder tumor; UC, urothelial carcinoma.

Statistical Plan

Objectives	To determine the antitumor effects of TAR-200 + IV cetrelimab and IV cetrelimab alone and to demonstrate the ***contribution of components*** of TAR-200 and cetrelimab
Hypothesis	A ***side-by-side descriptive*** summary of efficacy will illustrate the contribution of TAR-200 to the efficacy of the combination therapy[a]
Interim Analysis 2	After ~80 participants (~50 in Cohort 1 and ~30 in Cohort 2) complete the RC Results of **interim analysis 2** are presented here
Analysis Populations	***Safety:*** All patients who receive at least 1 dose of any study treatment ***Efficacy evaluable:*** All patients who have adequate RC results or who have radiographic progression or death before RC

[a]No formal statistical hypothesis testing will be conducted to compare cohorts. *Sample size:* Assuming a pCR rate of 40% for TAR-200 + cetrelimab (Cohort 1), 100 patients will provide greater than 90% probability to have the lower limit of the 80% credible interval exceeding 20% pCR rate (or approximately 80% probability of exceeding 30% pCR rate). Assuming a pCR rate of 30% for cetrelimab monotherapy (Cohort 2), 60 participants will provide approximately 65% probability to have the lower limit of the 80% credible interval exceeding 20% pCR rate.

SunRISe-4: Patient Disposition



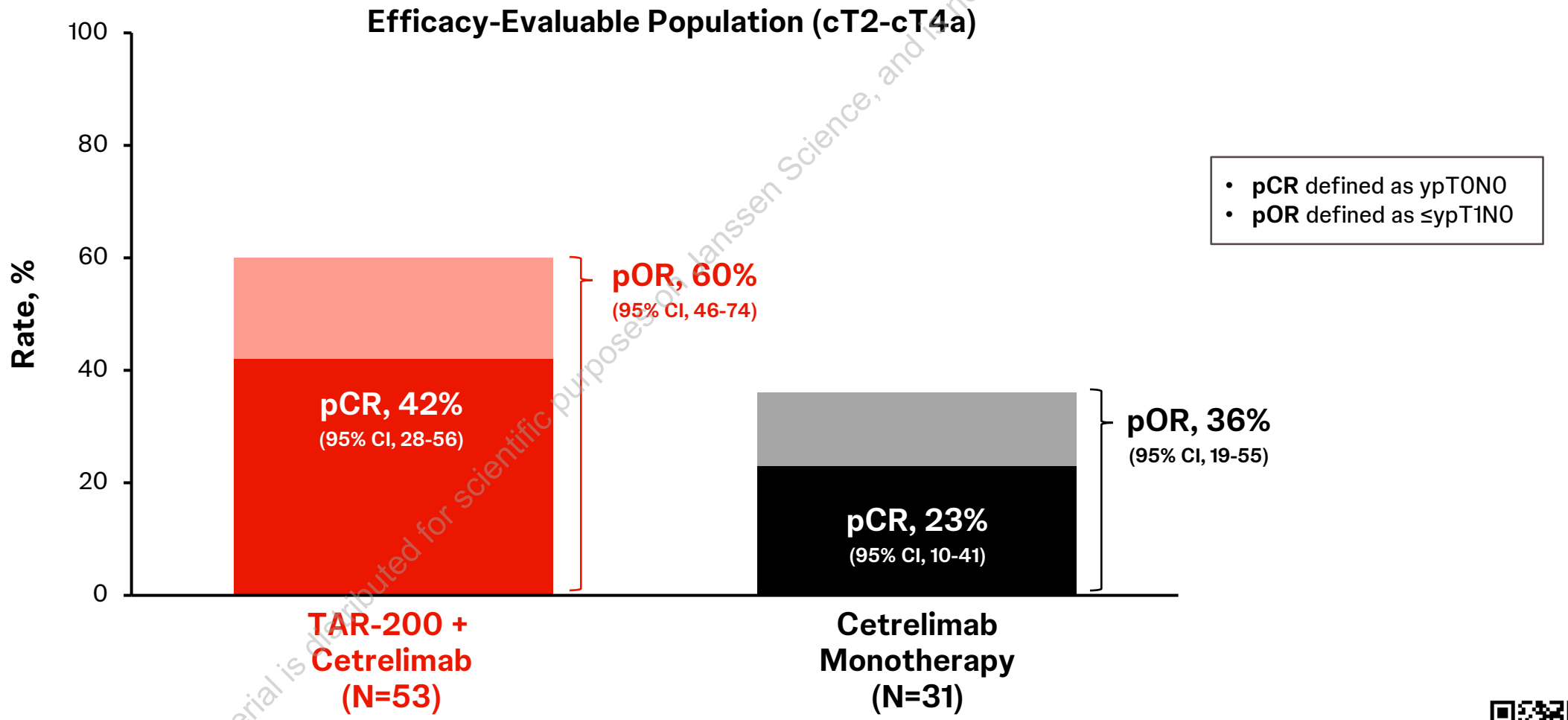
Study start date was July 7, 2022.

SunRISe-4: Baseline Characteristics

Characteristic	TAR-200 + Cetrelimab (N=79)	Cetrelimab Monotherapy (N=41)
Age, median (range), y	74.0 (54-85)	68.0 (48-80)
Sex, male, n (%)	68 (86.1)	34 (82.9)
Race, n (%)		
White	52 (65.8)	29 (70.7)
Asian	18 (22.8)	10 (24.4)
Other	9 (11.4)	2 (4.9)
Region, n (%)		
America	29 (36.7)	12 (29.3)
Asia	19 (24.1)	11 (26.8)
Western Europe	31 (39.2)	18 (43.9)
Nicotine use history, n (%)		
Current	20 (25.3)	11 (26.8)
Former	39 (49.3)	22 (53.7)
Never	20 (25.3)	8 (19.5)

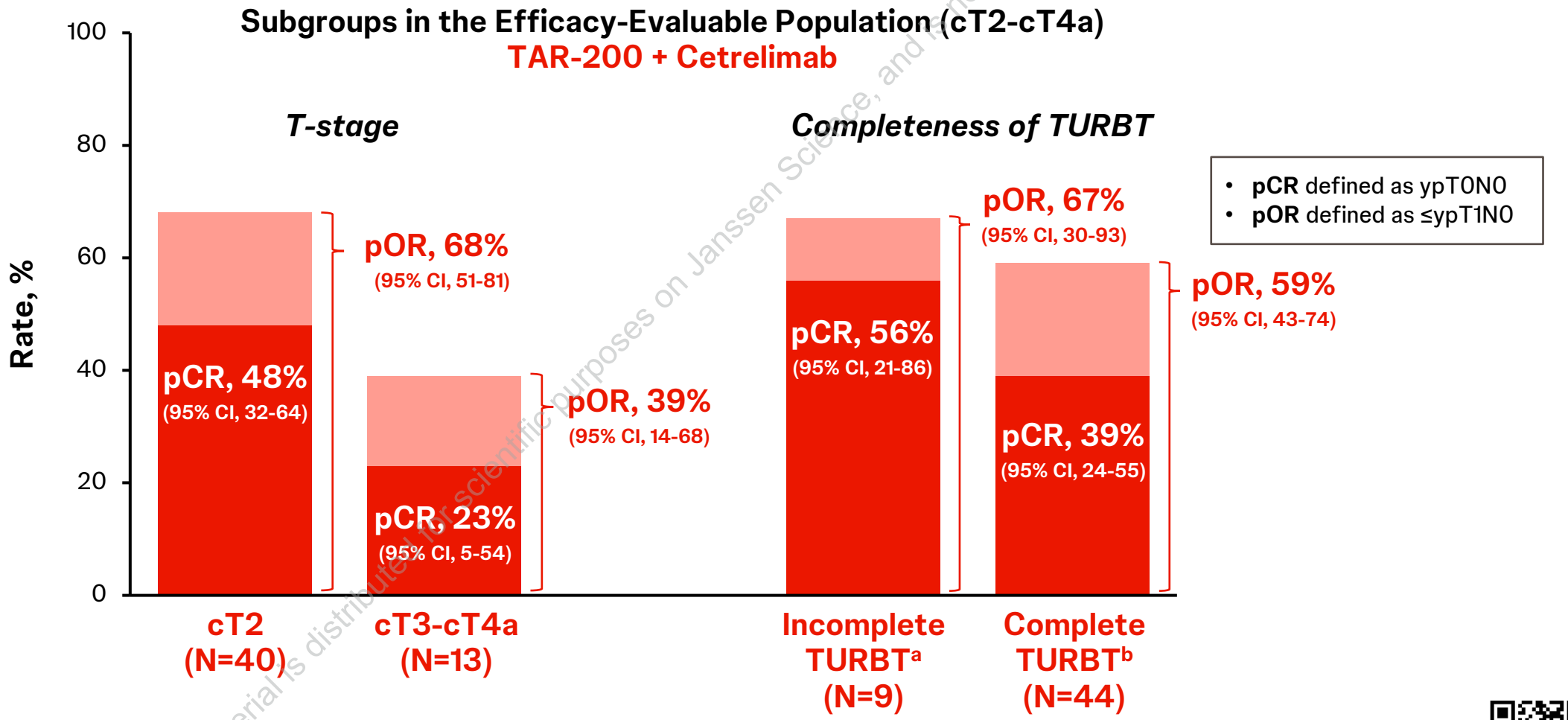
Characteristic	TAR-200 + Cetrelimab (N=79)	Cetrelimab Monotherapy (N=41)
ECOG PS 1, n (%)	14 (17.7)	10 (24.4)
NAC, n (%)		
Ineligible	31 (39.2)	15 (36.6)
Refusing	48 (60.8)	26 (63.4)
Residual disease (visibly incomplete TURBT), n (%)	16 (20.3)	6 (14.6)
Tumor stage, n (%)		
cT2	62 (78.5)	35 (85.4)
cT3-4a	17 (21.5)	6 (14.6)
UC with variant histology, n (%)	16 (20.3)	11 (26.8)
Prior intravesical therapy, n (%)	10 (12.7)	8 (19.5)

Neoadjuvant TAR-200 + Cetrelimab Showed Higher pCR and pOR Rates Than Cetrelimab Monotherapy



Clinical data cutoff was May 31, 2024.
CI, confidence interval; pOR, pathologic overall response.

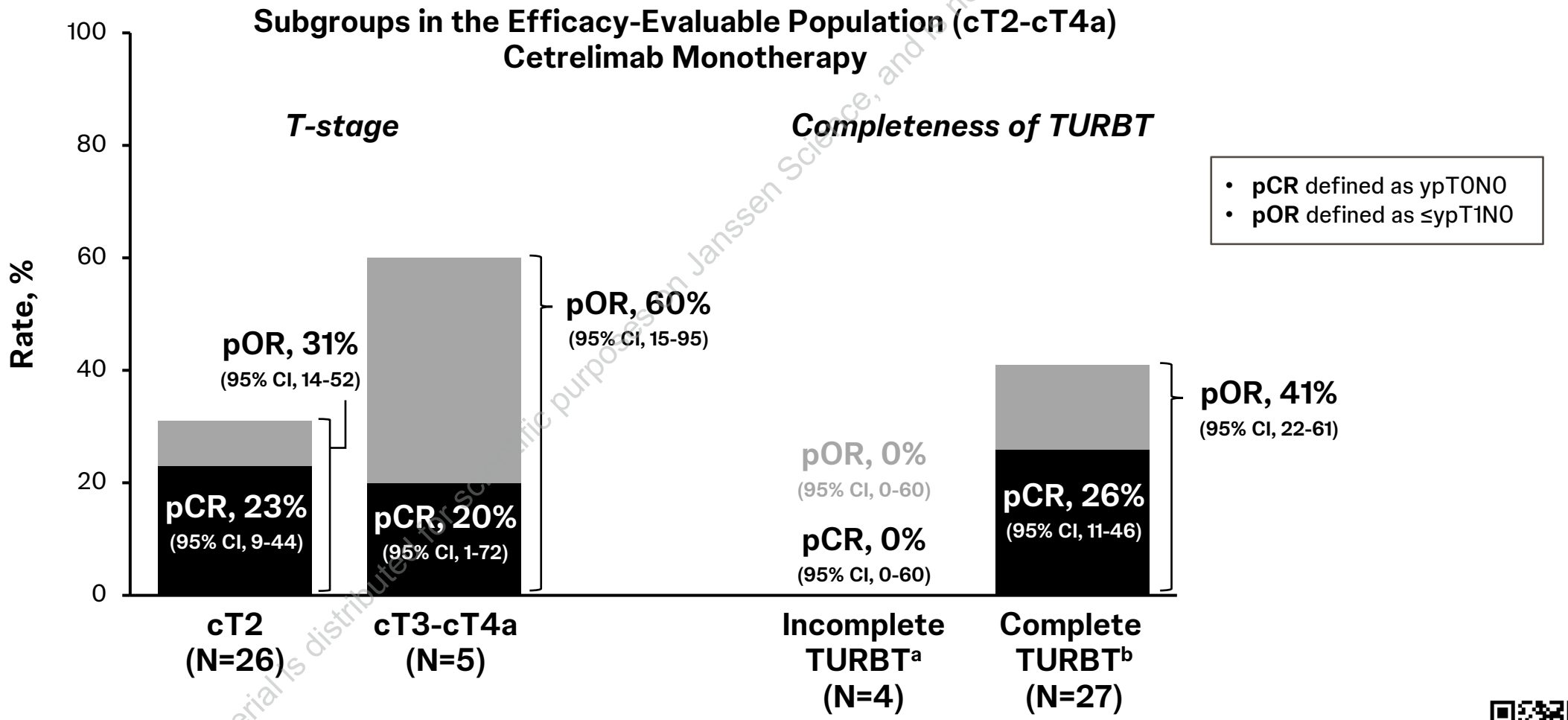
Efficacy by Clinical Stage and Completeness of TURBT in the TAR-200 + Cetrelimab Cohort



Clinical data cutoff was May 31, 2024.

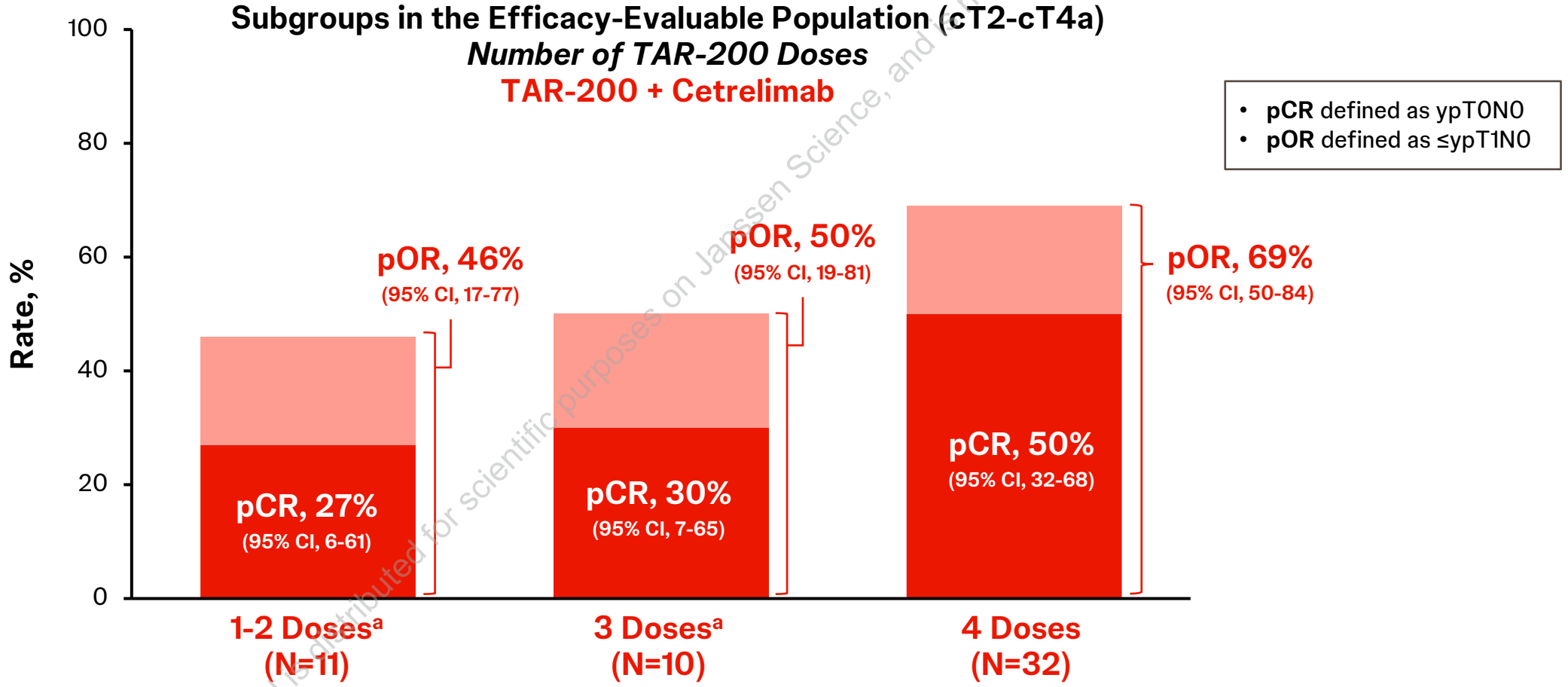
[a]Patients with visibly incomplete resection (≤3 cm) at TURBT. [b]Patients with visibly complete resection at TURBT.

Efficacy by Clinical Stage and Completeness of TURBT in the Cetrelimab Monotherapy Cohort



Clinical data cutoff was May 31, 2024.
[a]Patients with visibly incomplete resection (≤3 cm) at TURBT. [b]Patients with visibly complete resection at TURBT.

Efficacy by TAR-200 Dose Exposure



Clinical data cutoff was May 31, 2024.

[a]Patients with ≤3 doses of TAR-200 may have missed or skipped a dose without discontinuing treatment or may have discontinued treatment due to treatment-related adverse events or for any other reason.

Most Frequent Treatment-Related Adverse Events With TAR-200 + Cetrelimab Were Grade 1-2 Urinary Events

- Immune-related AEs of grade ≥3
  - **TAR-200 + Cetrelimab:** 6.3% of patients
  - **Cetrelimab Monotherapy:** 4.9% of patients
- Median time to RC
  - **TAR-200 + Cetrelimab:** 13.7 weeks
  - **Cetrelimab Monotherapy:** 12.6 weeks

Patients With ≥1 Event, n (%)[a]	TAR-200 + Cetrelimab (N=79)	Cetrelimab Monotherapy (N=41)
≥1 TRAE (any grade)[b]	57 (72.2)	18 (43.9)
Dysuria	22 (27.8)	22 (18.3)
Pollakiuria	22 (27.8)	22 (18.3)
Micturition urgency	12 (15.2)	12 (10.0)
Hematuria	11 (13.9)	11 (9.2)
Serious TRAEs	9 (11.4)	1 (2.4)
TRAEs grade ≥3	9 (11.4)	2 (4.9)
TRAEs leading to discontinuation	10 (12.7)	0
TRAEs leading to TAR-200 discontinuation[c]	7 (8.9)	–
TRAEs leading to cetrelimab discontinuation[d]	6 (7.6)	0
TRAEs leading to death	0	1 (2.4)[e]

AE, adverse event; TRAE, treatment-related adverse event; CTCAE, Common Terminology Criteria for Adverse Events.
[a]Median follow-up (post RC) was 10.2 weeks. AEs were reported using CTCAE v5.0.
[b]TRAEs occurring in ≥10% of patients in either treatment group are listed.
[c]Most frequent TRAE leading to TAR-200 discontinuation was pollakiuria (n=2).
[d]No TRAE led to cetrelimab discontinuation in ≥2 patients.
[e]TRAE leading to death was reported as hyperglycemic, hyperosmolar nonketotic syndrome (n=1).

SunRISe-4: Conclusions

- The combination of neoadjuvant **TAR-200 + cetrelimab** showed pCR and pOR rates of **42%** and **60%**, respectively, in patients with MIBC
  - In the cT2 subgroup, **48%** of patients treated with TAR-200 + cetrelimab achieved pCR, and **68%** were downstaged to ≤T1 at RC
- **Cetrelimab monotherapy** provided pCR and pOR rates of **23%** and **35%**, respectively
- **TAR-200 + cetrelimab** had a manageable safety profile in the neoadjuvant setting
  - Most TRAEs with TAR-200 + cetrelimab were low grade
  - The rate of discontinuations due to TRAEs was low at **13%**

SunRISe-4 demonstrates for the first time a benefit of the addition of TAR-200, an intravesical targeted releasing system, to checkpoint inhibition as neoadjuvant treatment in patients with MIBC

Acknowledgments

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

Ongoing studies of TAR-200:

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

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