

# Neoadjuvant Gemcitabine Intravesical System (Gem-iDRS) Plus Cetrelimab or Cetrelimab Alone in Patients With Muscle-Invasive Bladder Cancer Ineligible for/Refusing Neoadjuvant Cisplatin-Based Chemotherapy: Updated Perioperative Outcomes From SunRISe-4

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### Key Takeaway

Surgical outcomes data from SunRISe-4 support the safety and tolerability of gem-iDRS plus cetrelimab as neoadjuvant treatment to improve oncological outcomes for patients with MIBC who are ineligible for or refuse NAC

### Conclusions

In patients with MIBC who were ineligible for or refused NAC, neoadjuvant gem-iDRS plus cetrelimab was not associated with declines in overall health, delays to RC, or significant increase in 30- and 90-day post-RC morbidity or mortality

Addition of gem-iDRS to the checkpoint inhibitor cetrelimab did not worsen safety and post-RC morbidity compared with cetrelimab alone

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**Acknowledgments**  
We thank the patients who participated in the study, their families, and the investigators and clinical research staff from the study centers. Editorial support was provided by Priya Talluri, MSc, of Parexel, and funded by Johnson & Johnson. This study is sponsored by Johnson & Johnson.

**Disclosures**  
SP Psutka has received consulting/advisory fees from CG Oncology, EnGene, Janssen, Medtronic, and Merck; and has received honoraria from AstraZeneca

## Introduction

- Standard of care for muscle-invasive bladder cancer (MIBC) involves radical cystectomy (RC) with neoadjuvant cisplatin-based chemotherapy (NAC), which has demonstrated increased survival benefit versus RC only<sup>1-3</sup>
  - Up to 50% of patients with MIBC are ineligible for NAC<sup>4,5</sup>
  - NAC is associated with decreased general health status and lean muscle mass, increased asthenia and gastrointestinal toxicities, and a delay in time to RC<sup>5-9</sup>
  - About 2-3% and 3-8% of patients experience mortality 30 and 90 days after RC, respectively<sup>10</sup>
- Available treatment options are limited for patients who are ineligible for or refuse NAC<sup>11</sup>
  - Therefore, there is a high unmet need for effective neoadjuvant treatments that maintain overall health and do not delay or complicate planned RC for comorbid patients with MIBC
- Gemcitabine intravesical system (gem-iDRS), previously TAR-200, is a novel intravesical drug-releasing system designed to provide prolonged delivery of gemcitabine in the bladder<sup>12-14</sup>

- In the randomized phase 2 SunRISe-4 study, neoadjuvant gem-iDRS + cetrelimab showed a high pathologic complete response, pathologic overall response, and 1-year recurrence-free survival in patients with MIBC who are ineligible for or refuse NAC<sup>11</sup>
  - We evaluated pre- and post-RC surgical, laboratory, and safety outcomes with neoadjuvant gem-iDRS plus cetrelimab versus cetrelimab alone, including clinical declines, delay to RC, and perioperative complications

## Methods

- SunRISe-4 enrolled patients with histologically confirmed cT2-T4a NOMO MIBC who were ineligible for or refused NAC and were scheduled for RC (Figure 1)
- Patients were randomized 5:3 to receive gem-iDRS plus cetrelimab (Cohort 1) or cetrelimab alone (Cohort 2) every 3 weeks (Q3W) for 12 weeks, followed by RC (protocol-specified RC window: 11-15 weeks)
- Perioperative outcomes include change during treatment in key indicators including ECOG PS (baseline, Weeks 6 and 36) and major laboratory values (baseline to Week 12), time to RC, and 30- and 90-day post-RC morbidity and mortality

## Results

### Patients

- As of clinical cutoff (May 9, 2025), 101 patients were treated in Cohort 1 and 58 in Cohort 2; 88 and 46 patients, respectively, had undergone RC (Figure 1)
- Demographics and baseline disease characteristics for patients receiving RC were balanced across treatment cohorts (Table 1)

Table 1: Baseline characteristics

Characteristics	Gem-iDRS + cetrelimab N=88	Cetrelimab monotherapy N=46
Age, years, median (IQR)	74 (54-85)	69 (43-82)
Sex, male, n (%)	73 (83.0)	37 (80.4)
Race, n (%)		
White	63 (71.6)	35 (76.1)
Asian	17 (19.3)	8 (17.4)
Other/Multiple/Not reported	8 (9.1)	3 (6.5)
Nicotine use, n (%)		
Current	23 (26.1)	11 (23.9)
Former	47 (53.4)	27 (58.7)
Never	1 (1.1)	0
Unknown	17 (19.3)	8 (17.4)
ECOG performance status 0, n (%)	74 (84.1)	36 (78.3)
Tumor stage, n (%)		
cT2	71 (80.7)	38 (82.6)
cT3-4a	17 (19.3)	8 (17.4)
Residual disease (visibly incomplete), n (%)	19 (21.6)	3 (6.5)
Urothelial carcinoma with variant histology, n (%)	20 (22.7)	13 (28.3)
Neoadjuvant chemotherapy, n (%)		
Ineligible	40 (45.5)	20 (43.5)
Refused	48 (54.5)	26 (56.5)
Prior intravesical therapy, n (%)	8 (9.1)	7 (15.2)

IQR, interquartile range.

### Surgical approach

- Surgical approach was per physician preference
- Ileal conduit was the most frequently used type of urinary diversion in either cohort (79.5% in Cohort 1 and 76.1% in Cohort 2; Table 2)

### Change from baseline to RC in ECOG PS and major laboratory values

- ECOG PS was preserved in the majority of patients in both cohorts (Table 3)
- No clinically significant changes in body mass index, albumin, creatinine, or hemoglobin were reported during the neoadjuvant period (Table 3)

### Time to RC

- Most patients had RC within the protocol-specified window (85.2% in Cohort 1 and 84.8% in Cohort 2; Table 4)
- Median time from neoadjuvant therapy initiation to RC within protocol-specified window was 13.6 weeks (range, 11.3-17.1) in Cohort 1 and 13.0 weeks (range, 9.6-15.7) in Cohort 2
- Among 11 patients who had RC after the protocol-specified window, only 1 RC was delayed because of an adverse event during neoadjuvant treatment (grade 2 hematuria in the cetrelimab monotherapy cohort) (Table 4)

### Post-RC morbidity and mortality (RC evaluable set)

- Post-RC mortality rates at 30 and 90 days were 1.3% and 2.9% (Cohort 1), and 4.8% and 6.3% (Cohort 2), respectively (all unrelated to treatment), consistent with historical data<sup>15-17</sup> (Table 5)

Table 2: Surgical approach

Patients, n (%)	Gem-iDRS + cetrelimab N=88	Cetrelimab monotherapy N=46
Method of RC		
Robotic	55 (62.5)	18 (39.1)
Open	23 (26.1)	21 (45.7)
Laparoscopic	10 (11.4)	7 (15.2)
Type of urinary diversion*		
Incontinent diversions		
Ileal conduit (including Bricker, Bricker type, and urostomy)	70 (79.5)	35 (76.1)
Ureterocutaneostomy	1 (1.1)	0
Continent diversions		
Neobladder	11 (12.6)	10 (21.7)
Continent pouch	5 (5.7)	1 (2.2)
Margins assessed		
Yes	88 (100.0)	46 (100)

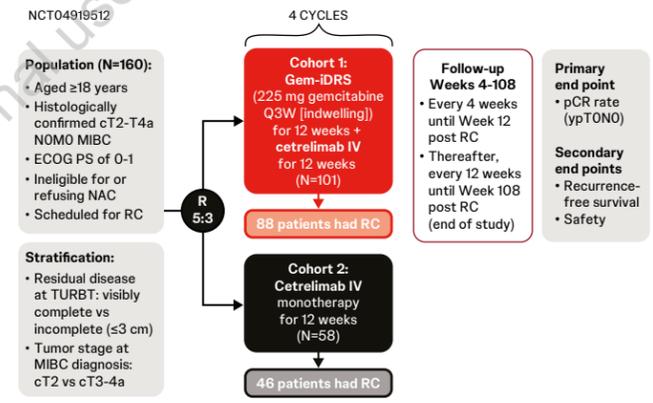
\*For gem-iDRS + cetrelimab, type of urinary diversion was captured for 87 patients.

Table 3: Change from baseline to RC in ECOG PS and major laboratory values

	Gem-iDRS + cetrelimab	Cetrelimab monotherapy
No ECOG PS worsening <sup>a</sup> , n/N (%)	80/95 (84.2)	48/55 (87.3)
Change from baseline to last recorded value prior to RC, median (range)		
BMI <sup>b</sup> , kg/m <sup>2</sup>	-0.3 (-3.6 to 2.6)	0.1 (-3.7 to 2.0)
Albumin <sup>c</sup> , g/L	-1.3 (-25.0 to 4.8)	-1.0 (-14.0 to 9.0)
Creatinine <sup>c</sup> , mg/dL	0.0 (-0.3 to 1.8)	0.1 (-0.8 to 1.1)
Hemoglobin <sup>c</sup> , g/dL	-0.2 (-4.9 to 6.8)	-0.3 (-4.1 to 2.7)

<sup>a</sup>ECOG PS at baseline and Week 6.  
<sup>b</sup>n=87 and n=46 for gem-iDRS + cetrelimab and cetrelimab monotherapy cohorts, respectively.  
<sup>c</sup>n=86 and n=46 for gem-iDRS + cetrelimab and cetrelimab monotherapy cohorts, respectively.

Figure 1: SunRISe-4 study design



ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; pCR, pathologic complete response; TURBT, transurethral resection of bladder tumor.

Table 4: Time to cystectomy

	Gem-iDRS + cetrelimab N=88	Cetrelimab monotherapy N=46
Within protocol-specified window, n (%)	75 (85.2)	39 (84.8)
Median time to RC, weeks (range)	13.6 (11.3-17.1)	13.0 (9.6-15.7)
Before protocol-specified window, n (%)	8 (9.1)	1 (2.2)
Median time to RC, weeks (range)	9.4 (2.6-11.0)	12.7 (12.7-12.7)
Investigator decision, n (%)	2 (2.3)	1 (2.2)
Other, n (%)	2 (2.3)	0
Symptomatic progression, n (%)	2 (2.3)	0
Local progression, n (%)	1 (1.1)	0
Patient decision, n (%)	1 (1.1)	0
After protocol-specific window, n (%)	5 (5.7)	6 (13.0)
Median time to RC, weeks (range)	18.4 (16.0-19.4)	16.5 (12.4-19.0)
Other, n (%)	2 (2.3)	3 (6.5)
Investigator decision, n (%)	1 (1.1)	2 (4.3)
Patient decision, n (%)	2 (2.3)	0
Hematuria, n (%)	0	1 (2.2)

Table 5: Safety outcomes within 30 and 90 days post RC (RC evaluable set)

Patients with ≥1 event	Within 30 days post RC			Within 90 days post RC		
	Overall (N=118) <sup>a</sup>	Gem-iDRS + cetrelimab (n=76)	Cetrelimab monotherapy (n=42)	Overall (N=100) <sup>a</sup>	Gem-iDRS + cetrelimab (n=68)	Cetrelimab monotherapy (n=32)
n (%)						
Post-RC morbidity						
≥1 TEAE any grade	93 (78.8)	62 (81.6)	31 (73.8)	86 (86.0)	58 (85.3)	28 (87.5)
Serious TEAE	46 (39.0)	32 (42.1)	14 (33.3)	49 (49.0)	37 (54.4)	12 (37.5)
Grade ≥3 TEAE	54 (45.8)	38 (50.0)	16 (38.1)	55 (55.0)	40 (58.8)	15 (46.9)
Post-RC mortality <sup>b</sup>						
Any cause	3 (2.5)	1 (1.3) <sup>c</sup>	2 (4.8) <sup>d</sup>	4 (4.0)	2 (2.9) <sup>e</sup>	2 (6.3)

<sup>a</sup>Number of patients who reached 30 or 90 days post RC and with at least 1 TEAE occurring within 30 or 90 days post RC.  
<sup>b</sup>No deaths that occurred within 30 and 90 days post RC were related to neoadjuvant treatment with gem-iDRS or cetrelimab.  
<sup>c</sup>Due to hypoxia.  
<sup>d</sup>Due to peritonitis and cardiac arrest in 1 patient each.  
<sup>e</sup>Due to hypoxia and cardio-respiratory arrest in 1 patient each.  
TEAE, treatment-emergent adverse event.

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