Gemcitabine Intravesical System (Gem-iDRS) Monotherapy in Bacillus Calmette-Guérin–Unresponsive High-Risk Non–Muscle-Invasive Bladder Cancer: Characterization of Recurrence, Progression, and Time to Cystectomy

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Key Takeaway

Recurrence and progression data support Gem-iDRS, which was recently granted FDA approval, as a novel treatment option for patients with BCG-unresponsive CIS with or without papillary disease

Conclusions

- Gem-iDRS monotherapy is associated with a high CR rate and durable responses, with minimal risk of disease progression to a more advanced (T2 or higher) disease stage
- The low rate of RC in Cohort 2 of SunRISe-1 highlights that Gem-iDRS treatment may result in potential delay to RC
- This low rate of progression compares favorably with historical progression rates of ~20% with standard of care in patients with HR NMIBC[6,21]

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Disclosures

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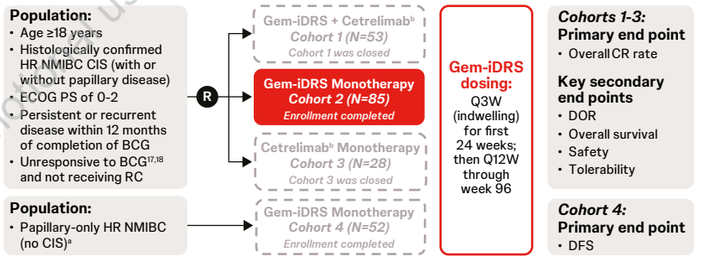
Introduction

- Patients with bacillus Calmette-Guérin (BCG)-unresponsive high-risk non–muscle-invasive bladder cancer (HR NMIBC) have limited bladder-sparing treatment options and are at high risk of disease recurrence and progression[1-7]
- Standard of care for BCG-unresponsive HR NMIBC is radical cystectomy (RC)[1,2]
  - RC is a life-changing operation associated with significant morbidity and mortality rates and negative impact on quality of life[8-10]
- There exists a persistent need for tolerable and effective bladder-sparing therapies for this population
- Gemcitabine intravesical system (Gem-iDRS), previously TAR-200, is a novel intravesical drug-releasing system designed to provide sustained delivery of gemcitabine in the bladder[11-15]
- Gem-iDRS recently received United States Food and Drug Administration (FDA) approval for BCG-unresponsive NMIBC with carcinoma in situ (CIS) with or without papillary tumors based on results from the phase 2b SunRISe-1 study (NCT04640623)[16]
  - We report recurrence, progression, and time to cystectomy analyses in patients receiving Gem-iDRS monotherapy (Cohort 2)

Methods

- SunRISe-1 is ongoing and is assessing Gem-iDRS in patients with BCG-unresponsive HR NMIBC who were ineligible for or refused RC (Figure 1)
- Disease-response assessments included:
  - Cystoscopy and centrally assessed urine cytology every 12 weeks (Q12W) for ≤2 years then every 24 weeks (Q24W) in year 3 until end of study
  - Centrally assessed biopsy at weeks 24 and 48 or as clinically indicated
  - Local imaging Q24W until end of year 3
- Patients with centrally assessed disease recurrence or progression were staged based on tumor, node, metastasis (TNM) classification by the investigator
- Subsequent therapies, including RC, were reported for all patients, as applicable

Figure 1: SunRISe-1 study design (NCT04640623)



CR, complete response; DFS, disease-free survival; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; Q3W, every 3 weeks; R, randomization.
[a]Patients with BCG-unresponsive HR papillary disease–only NMIBC (high-grade Ta, any T1) per protocol amendment 4.
[b]Cetrelimab is an anti–programmed cell death protein 1 (PD-1) antibody[19,20]; cetrelimab dosing was 360 mg intravenously Q3W through month 18.

Results

Patients

- As of March 31, 2025, 85 patients with CIS (median age, 71 years; range, 40-88; concomitant papillary disease, 32.9%) received Gem-iDRS monotherapy (Table 1)

Table 1: Baseline characteristics

Characteristics	Gem-iDRS Monotherapy N=85[a]
Age, yr, median (range)	71 (40-88)
Sex, male, n (%)	68 (80.0)
Race, n (%)	
White	74 (87.1)
Asian	8 (9.4)
Black or African American	2 (2.4)
Not reported/unknown	1 (1.2)
Nicotine use, n (%)	
Current	7 (8.2)
Former	50 (58.8)
Never	28 (32.9)
ECOG PS 0, n (%)	78 (91.8)
Tumor stage, n (%)	
CIS only	57 (67.1)
CIS + papillary disease	28 (32.9)
Total doses of prior BCG, n, median (range)	12 (7-42)
Time from last BCG to CIS diagnosis, mo, median (range)	3.2 (0.1-22)[b]
Reason for not receiving RC, n (%)	
Declined	82 (96.5)
Ineligible	3 (3.5)

[a]Baseline characteristics are shown for all patients who received at least 1 dose of Gem-iDRS in the full analysis set (N=85).
[b]2 patients had >12 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).

Efficacy

- Gem-iDRS monotherapy was associated with an overall centrally assessed CR rate of 82.4%, with 70 of 85 patients achieving CR (Figure 2)
- The median follow-up in all patients was 20.2 months (range, 2-48)
- 37 of 70 responders (52.9%) had a DOR of 12 months or longer (Table 2)
- 37 responders remained in CR at clinical cutoff
  - 33 responses (47.1%) were ongoing with no event as of the clinical cutoff
  - 4 patients were permanently censored due to study discontinuation or receiving subsequent therapy (Table 2)

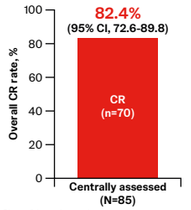
Recurrence and progression

- Overall, 41 of 85 patients (48.2%) had disease persistence, progression, or recurrence (Table 3)
  - 30 (42.9%) were initial responders
- The majority of the 41 patients had persistence or recurrence of HR NMIBC (CIS/Ta/T1)
- Progression to T2 or higher disease (any N+/M+) was observed in 7 of 85 patients (8.2%) (based on local disease evaluation)
  - 5 patients (5.9%) had disease progression within 1 year and 2 (2.4%) after 1 year
  - 1 patient had disease progression to metastatic disease
  - 4 (5.7%) were responders
- There was no observed difference in progression rates based on baseline stage (CIS ±Ta vs T1)
- There were 7 deaths (unrelated to treatment)

Time to RC

- 18 of 85 patients (21.2%) underwent RC
  - 12 (14.1%) were responders
- Median time to cystectomy was not estimable (NE)
- Estimated RC-free rates (Figure 3):
  - 12-month: 86.6% (95% CI, 76.6-92.6)
  - 24-month: 75.5% (95% CI, 63.4-84.1)
- 15 of 18 patients who underwent RC had TNM staging done locally by investigator, and the majority were classified as TIS/CIS (Table 4)

Figure 2 and Table 2: Efficacy outcomes of Gem-iDRS monotherapy in patients with CIS with or without papillary disease



Outcome	Gem-iDRS Monotherapy N=85
Duration of response	
DOR of 12 months or longer, n (%)	37 (52.9)
12-month DOR rate, % (95% CI)[a]	56.2 (43.4-67.1)
Median DOR, months (95% CI)[a]	25.8 (8.3-NE)
Patients with ongoing response, % (n/N)[b]	47.1[c] (33/70)

CI, confidence interval.
[a]Kaplan-Meier estimates.
[b]Response is based on centrally reviewed urine cytology, local cystoscopy, and central biopsy (if available). 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.
[c]37 of 70 responders (52.9%) were censored, including 4 (5.7%) who discontinued the study or started subsequent therapy. 33 (47.1%) patients had an ongoing response with no event at clinical cutoff.

Table 3: Recurrence and progression outcomes of Gem-iDRS monotherapy in patients with CIS with or without papillary disease

Outcome	Gem-iDRS Monotherapy	
	All N=85	Responders n=70
Patients with disease persistence (nonresponders only), recurrence, or progression, n (%)[a]	41 (48.2)	30 (42.9)
HR NMIBC[b]	30 (35.2)	23 (32.9)
Positive cytology only	2 (2.4)	1 (1.4)
CIS and/or Ta only	23 (27.1)	18 (25.7)
T1 (with or without CIS)	5 (5.9)	4 (5.7)
T2 or higher progression	7 (8.2)	4 (5.7)
T2-T4a	5 (5.9)	2 (2.9)
N1	1 (1.2)	1 (1.4)
M1a	1 (1.2)	1 (1.4)
No evidence of disease but positive cytology[c]	4 (4.7)	3 (4.3)

[a]Disease persistence, recurrence, or progression event was based on positive central cytology, high-grade central pathology, or positive imaging. All results based on highest stage from local transurethral resection of bladder tumor results, investigator-assessed clinical stage, and pathologic stage after cystectomy. Patients who discontinued study before disease evaluation are excluded.
[b]Includes patients with high-grade Ta, CIS, or T1 or patients with positive central cytology (n=5) or high-risk NMIBC from central pathology (n=2) but no evidence of high-risk NMIBC by investigator. Note, no cases of low-grade Ta recurrence were reported in Cohort 2.
[c]Patients had positive central cytology or high-grade disease by central pathology but no disease based on local assessment.

Figure 3: Estimated 12- and 24-month RC-free rates

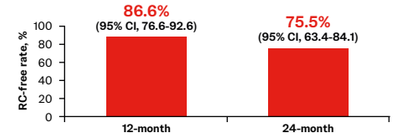


Table 4: Summary of pathology at RC

Outcome	Gem-iDRS Monotherapy N=85
Patients with RC, n (%)	18 (21.2)
Patients with TNM staging[a]	15 (17.6)
TIS/CIS	10 (11.8)
T2	2 (2.4)
T4a	2 (2.4)
M1a	1 (1.2)[b]

[a]All results based on stage from pathologic stage after RC.
[b]Patient also had N+ disease.

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