IP50-01

Comparative Effectiveness of Gemcitabine Intravesical System vs Real-World Intravesical Chemotherapy in BCG-Unresponsive High-Risk Non–Muscle-Invasive Bladder Cancer With Carcinoma in Situ: An Indirect Treatment Comparison Using an External Control Group

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Key Takeaway

Gem-iDRS was associated with significantly higher any time CR rate and lower risk of persistent disease, recurrence, progression, or death compared with RW IVEC in patients with BCG-unresponsive high-risk NMIBC with CIS

Conclusions

- This ITC demonstrates that gem-iDRS was associated with a significantly higher any time CR rate compared with that of RW IVECs in patients with BCG-unresponsive high-risk NMIBC with CIS
- Gem-iDRS was associated with a lower risk of persistent disease, high-risk recurrence, progression, or death vs RW IVECs
- When compared to RW gem monotherapy, gem-iDRS demonstrated a significant improvement in any time CR rate and EFS, highlighting the value of prolonged local release of gem delivered via the gem-iDRS
- Gem-iDRS offer valuable clinical advantages as a bladder-preserving treatment for patients with BCG-unresponsive high-risk NMIBC with CIS

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Introduction

- Radical cystectomy (RC) is the recommended treatment for Bacillus Calmette-Guérin (BCG)-unresponsive high-risk non-muscle-invasive bladder cancer (high-risk NMIBC) with carcinoma in situ (CIS).[1,2] However, it is infrequently performed due to invasiveness and quality-of-life concerns; intravesical chemotherapy (IVEC) remains the most used salvage therapy[3,4]
- Gemcitabine intravesical system (gem-iDRS) enables sustained gemcitabine (gem) delivery to the bladder. In the phase 2b SunRISe-1 study, gem-iDRS achieved 82.4% complete response (CR) with a median response duration of 25.8 months[5]
- Based on SunRISe-1 findings, the United States Food and Drug Administration approved gem-iDRS in September 2025 for the treatment of BCG-unresponsive high-risk NMIBC with CIS.[6] Since direct comparison studies of gem-iDRS and IVEC are lacking,[7] an indirect treatment comparison (ITC) was performed to assess the relative effectiveness of these treatments

Objective

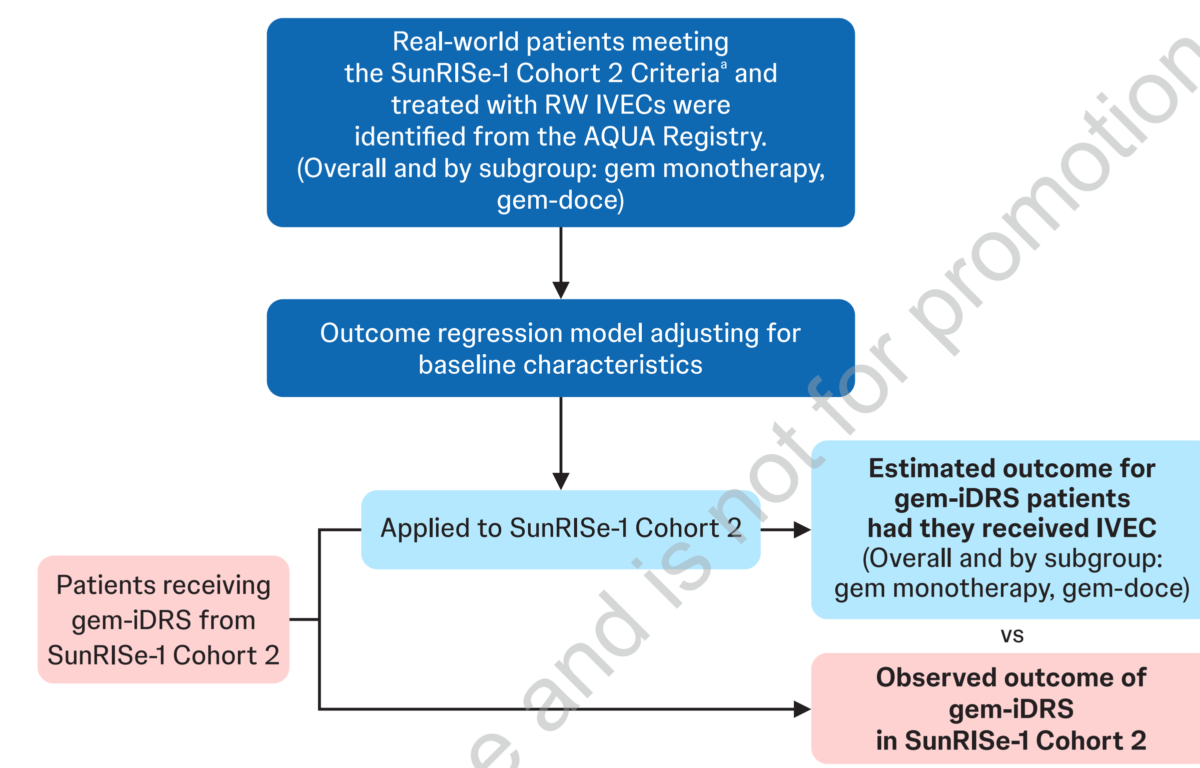
- **To explore the relative effectiveness of gem-iDRS vs RW IVECs, including gem monotherapy and gemcitabine-docetaxel (gem-doce), using a hypothesis-generating ITC in patients with BCG-unresponsive high-risk NMIBC with CIS**

Methods

Study populations and data sources

- Gem-iDRS: Patient-level data from SunRISe-1 Cohort 2; data cutoff March 2025, n=85
- RW comparator: Chart-reviewed patients with high-risk NMIBC with CIS treated with IVEC from the American Urological Association Quality (AQUA) Registry, linked to Komodo Health claims (data cutoff December 2024; n=134)
  - Patients were identified based on receipt of adequate BCG (≥7 doses within 6 months) between 2015–2022 and initiation of IVEC within 1 year of adequate BCG for CIS recurrence
- Eligibility criteria and index date were aligned between the SunRISe-1 Cohort 2 and RW cohorts where corresponding variables were available in the AQUA registry

Figure 1: Study schema for the g-formula-based approach



[a]Based of variables that were available in AQUA registry. AQUA, American Urological Association Quality Registry; gem-doce, gemcitabine-docetaxel; gem-iDRS, gemcitabine intravesical system; IVEC, intravesical chemotherapy; RW, real-world.

Endpoints

- RW endpoints were aligned with SunRISe-1 study definitions where corresponding variables were available in the AQUA Registry
- CR: Normal cystoscopy, negative urine cytology or pathology, or physician documentation abstracted from unstructured clinical notes
- Event-free survival (EFS): Time from treatment initiation to persistent disease at first assessment, high-risk recurrence, progression (≥T2 and/or metastasis), or death
  - Recurrence confirmed by positive TURBT (transurethral resection of bladder tumor) or biopsy with high-grade Ta, any T1 or CIS records from unstructured clinical notes.

Statistical analyses

- Baseline characteristics summarized descriptively
- Confounding adjustment using g-formula approach (**Figure 1**)
- Covariates were identified through systematic literature review and expert opinion, and included age, tumor stage (CIS only vs. CIS + papillary), and number of prior BCG doses
- CR: Odds ratios (ORs) estimated using logistic regression
- EFS: Hazard ratios (HRs) estimated using Cox regression
- Sensitivity analyses using inverse probability treatment weighting (IPTW)
- Analyses conducted using an intent-to-treat (ITT) approach

Subgroup analyses

- Gem-iDRS vs gem monotherapy
- Gem-iDRS vs gem-doce

Results

Patient characteristics

- Baseline characteristics were similar across the gem-iDRS and RW IVECs cohorts (**Table 1**)
  - Majority of patients were male
  - Majority of patients had CIS only tumors
  - Patients received a median of 12 prior doses of BCG
- The median follow-up time was 20.2 months for gem-iDRS SunRISe-1 Cohort 2, and 31.0 months for RW IVEC

Table 1: Baseline characteristics of patients (Unadjusted)

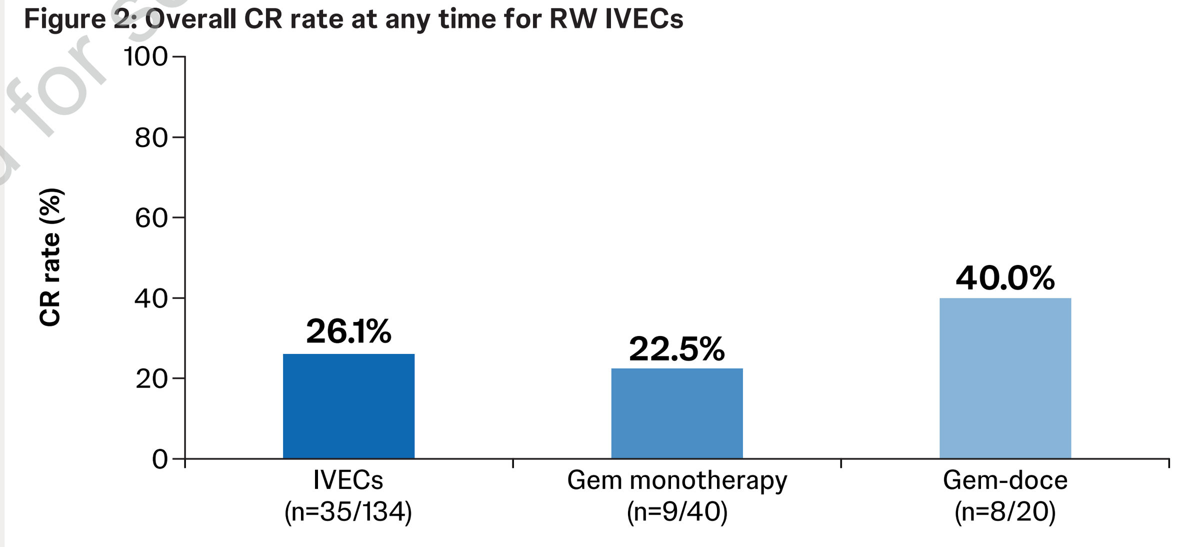
Characteristic	Gem-iDRS SunRISe-1 Cohort 2 (n=85)	AQUA IVEC (n=134)	AQUA gem monotherapy (n=40)	AQUA gem-doce (n=20)
Age, years, median (range)	71 (40–88)	75 (55–88)	77.5 (55–88)	75 (63–83)
Sex, Male	68 (80.0)	110 (82.0)	35 (87.5)	14 (70.0)
Race[a]				
White	74 (88.1)	94 (91.3)	28 (90.3)	16 (100)
Black or African American	2 (2.4)	6 (5.8)	1 (3.2)	-
Asian	8 (9.5)	1 (1.0)	1 (3.2)	-
Others	-	2 (1.9)	1 (3.2)	-
Ethnicity[b]				
Not Hispanic or Latino	76 (90.5)	104 (99.0)	32 (100)	17 (100)
Hispanic or Latino	8 (9.5)	1 (1.0)	-	-
Tumor stage				
CIS only	57 (67.1)	90 (67.2)	21 (52.5)	12 (60.0)
CIS + papillary	28 (32.9)	44 (32.8)	19 (47.5)	8 (40.0)
Total doses of prior BCG	12 (7–42)	12 (7–19)	12 (7–18)	12 (7–15)

Data presented as n (%) or median (range).
[a]n (%) calculated based on 103 patients with race information in AQUA. [b]n (%) calculated based on 105 patients with ethnicity information in AQUA.
AQUA, American Urological Association Quality Registry; BCG, Bacillus Calmette-Guérin; CIS, carcinoma in situ; gem-doce, gemcitabine-docetaxel; gem-iDRS, gemcitabine intravesical system; IVEC, intravesical chemotherapy.

Overall CR at any time

- The overall CR rate for all RW IVECs was 26% (**Figure 2**)

Figure 2: Overall CR rate at any time for RW IVECs

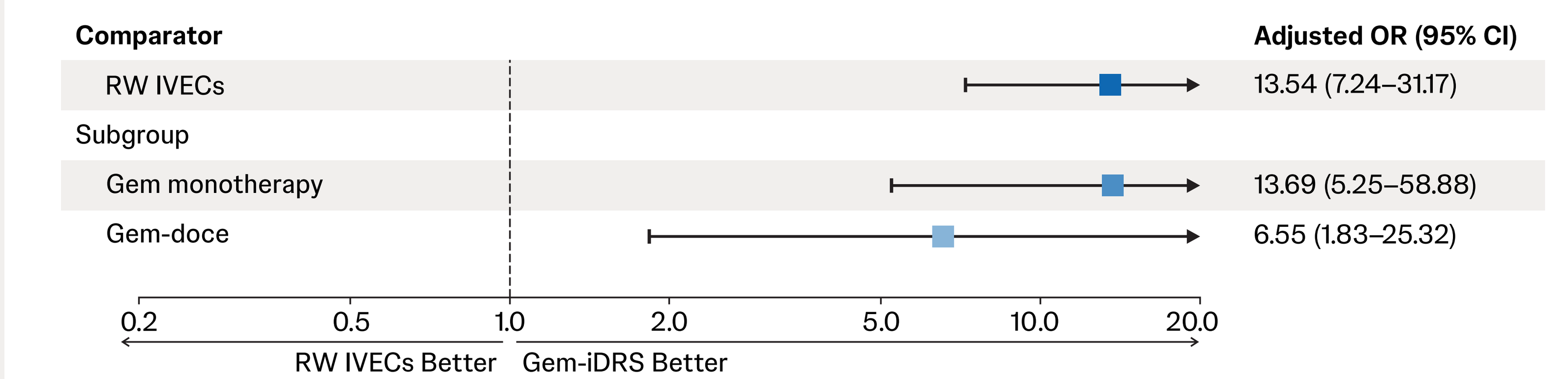


AQUA, American Urological Association Quality Registry; CR, complete response; gem-doce, gem, gemcitabine; gemcitabine-docetaxel; IVEC, intravesical chemotherapy; RW, real-world.

Overall CR at any time in gem-iDRS vs IVEC

- Patients treated with gem-iDRS had significantly higher odds of achieving CR compared with RW IVECs in patients with BCG-unresponsive high-risk NMIBC with CIS (**Figure 3**)
  - ~14 times higher odds to achieve CR vs RW IVEC
  - ~14 times higher odds to achieve CR vs gem monotherapy
  - ~7 times higher odds to achieve CR vs gem-doce
- Results were consistent after IPTW adjustment

Figure 3: Adjusted odds ratios of overall CR at any time with gem-iDRS vs RW IVECs

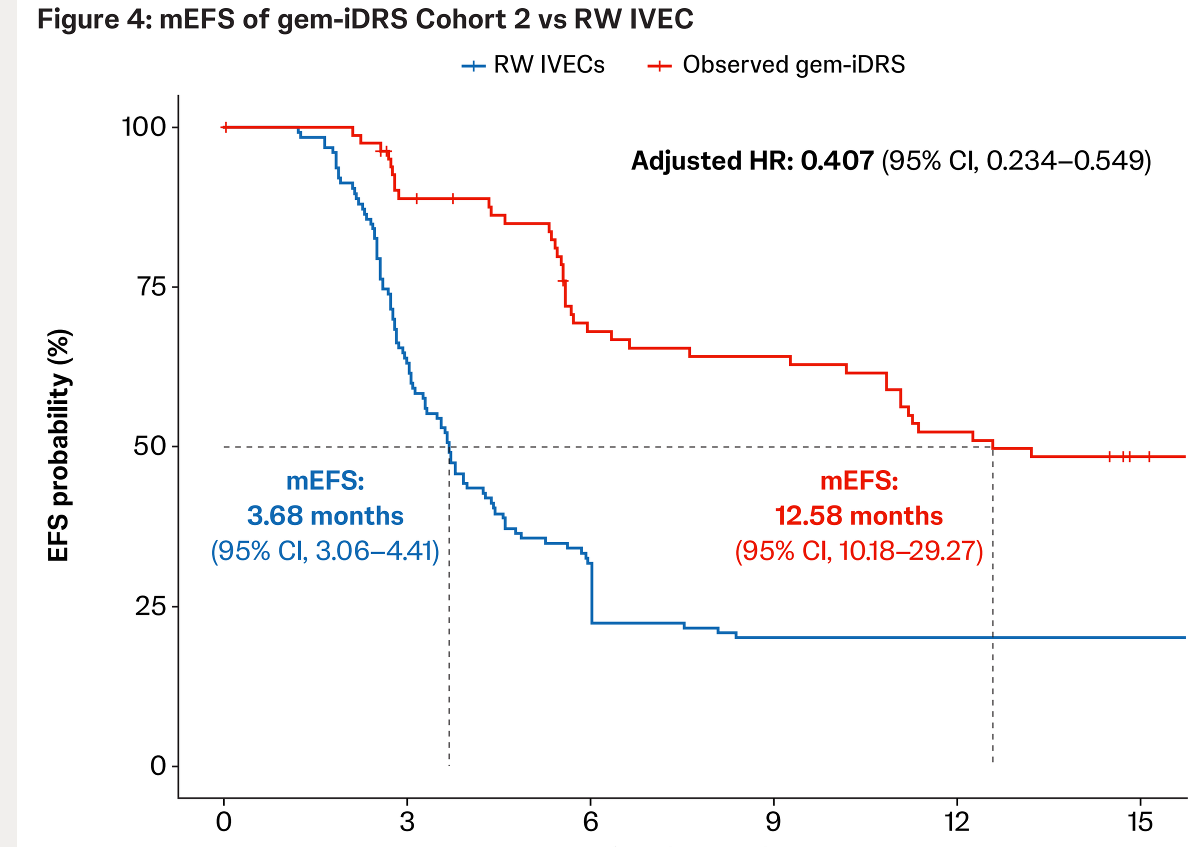


CI, confidence interval; CR, complete response; gem-doce, gemcitabine-docetaxel; gem-iDRS, gemcitabine intravesical system; IVEC, intravesical chemotherapy; OR, odds ratio; RW, real-world.

EFS of gem-iDRS vs RW IVEC

- Gem-iDRS provides longer median EFS vs RW IVECs (12.6 vs 3.7 months)
- Gem-iDRS reduces the risk of persistent disease, high-risk recurrence, progression, or death by 59% compared to RW IVECs in patients with BCG-unresponsive high-risk NMIBC with CIS (HR: 0.41; 95% CI, 0.23–0.55, **Figure 4**)
- After IPTW adjustment, gem-iDRS was associated with a **~57.3%** reduction in the risk of high-risk recurrence, progression, or death compared to RW IVECs (HR: 0.43; 95% CI, 0.30–0.61)

Figure 4: mEFS of gem-iDRS Cohort 2 vs RW IVEC

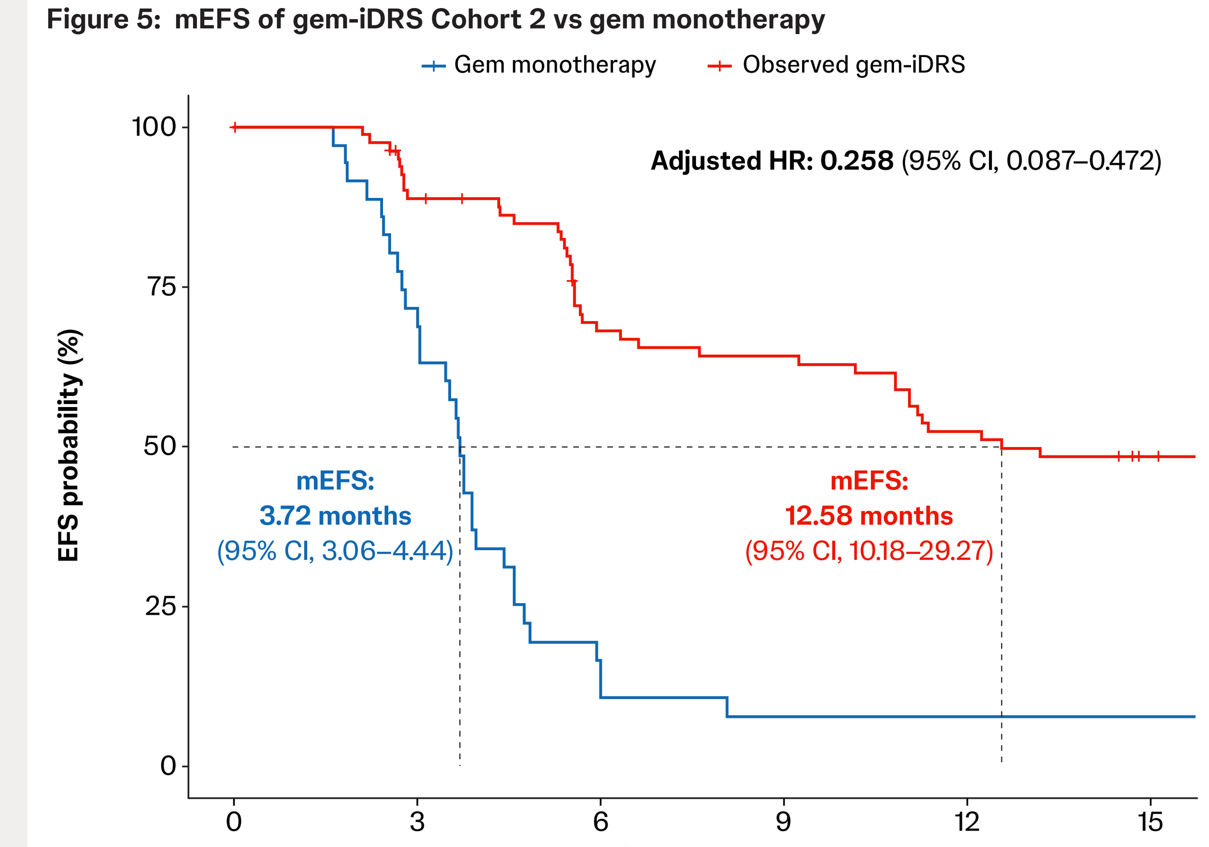


CI, confidence interval; EFS, event-free survival; mEFS, median event-free survival; HR, hazard ratio; gem-iDRS, gemcitabine intravesical system; IVEC, intravesical chemotherapy; RW, real-world.

EFS of gem-iDRS vs RW gem monotherapy and gem-doce

- Gem-iDRS reduces the risk of high-risk recurrence, progression, or death by 74% compared to gem monotherapy. Median EFS: 12.6 vs 3.7 months (HR: 0.26; 95% CI, 0.09–0.47, **Figure 5**)
- The median EFS of gem-doce was 4.0 months. Sample size was too small for statistical comparison versus gem-iDRS

Figure 5: mEFS of gem-iDRS Cohort 2 vs gem monotherapy



CI, confidence interval; EFS, event-free survival; mEFS, median event-free survival; HR, hazard ratio; gem-iDRS, gemcitabine intravesical system.

Limitations

- Although the indirect comparison reached statistical significance, a relatively small retrospective sample of patients contributed to the estimate, resulting in potential imprecision and increased uncertainty that may affect the robustness of the findings
- Possible selection bias and residual confounding due to unmeasured, imperfectly measured, or missing data
- Use of an ITT approach that may bias against the RW comparator cohort
- Generalizability may be limited, given the AQUA Registry's practice distribution being mostly in the community setting

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