Real-world Outcomes in Patients with Bacillus Calmette-Guérin (BCG)-unresponsive High-risk Non-muscle Invasive Bladder Cancer with Carcinoma *in Situ* — A Chart Review Study of the American Urological Association's Quality Registry

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Key Takeaway

For patients with HR-NMIBC with CIS who are BCG-unresponsive, there is a significant unmet need for more effective, durable, and innovative bladder-sparing treatment options

Conclusions

Despite IVES chemo being the most used salvage therapy in the US for patients with BCG-unresponsive HR-NMIBC with CIS, this analysis shows that outcomes are suboptimal, with only a small proportion of patients achieving a CR

Among patients who responded, the duration of response was limited, with a median of only 8.8 months

Most patients experience persistent disease, recurrence, progression, or death within a short timeframe with a modest median EFS of 3.75 months

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Poster

https://www.congresshub.com/Oncology/SUO2025/TAR-200/Kulkarni-Real-World

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To learn more about AQUA Registry, visit at https://www.auanet.org/AQUA

Disclosures

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Introduction

- For patients with high-risk non-muscle invasive bladder cancer (HR-NMIBC), Bacillus Calmette-Guérin (BCG) is the standard of care (SOC) treatment[1]
  - However, up to 40% of patients ultimately become unresponsive to BCG, increasing the risk of disease recurrence and progression[2,3]
- Radical cystectomy (RC) is recommended for patients with BCG-unresponsive HR-NMIBC with CIS. However, its invasive nature and quality of life concerns limit its real-world use; intravesical chemotherapy (IVES chemo) is the most used salvage therapy in this setting in the US[4]
- The effectiveness of IVES chemo can be assessed through real-world (RW) studies, which often use treatment duration and healthcare resource utilization as proxies. This approach is commonly adopted due to limited availability of treatment response and recurrence in structured data, such as payer claims and electronic health records (EMR)

Objective

Building on existing data, this study examines the real-world outcomes of IVES chemo in patients with BCG-unresponsive HR-NMIBC with CIS through a retrospective chart review

Methods

Database and study population:

- This analysis used data from patient charts and electronic medical records from the American Urological Association Quality (AQUA) Registry's NMIBC module and linked to Komodo Health claims for comprehensive treatment data
- Adult patients with BCG-unresponsive HR-NMIBC with CIS and initiated an IVES chemo between 2015-2022 were included:
  - BCG-unresponsiveness was defined as having received adequate BCG (≥ 7 doses within 6 months of BCG initiation) and initiated a non-BCG treatment (index date) within 1 year of adequate BCG treatment
  - Index non-BCG treatment is an IVES chemo for this analysis
  - Evidence of CIS/TIS within 180 days before and 30 days after the index date
  - At least 1 all-cause medical record during 12-month post-index

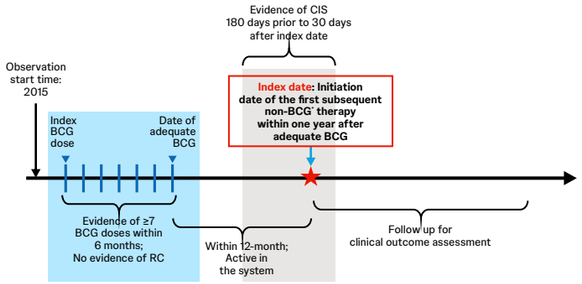
Outcome definitions:

- Complete response (CR): Negative cystoscopy, negative urine cytology or pathology, or physician documentation abstracted from unstructured clinical notes
- Duration of response (DOR): Time from first CR to the earliest of high-risk recurrence, treatment change, progression to MIBC (≥T2) or metastatic disease, or death
- Event-free survival (EFS): Time from IVES chemo initiation to persistent disease at the first disease assessment, high-risk recurrence, progression, subsequent therapy following a cystoscopy/transurethral resection of bladder tumor (TURBT)/biopsy or death
- High-risk recurrence was confirmed by positive TURBT or biopsy with high-grade Ta, any T1, or CIS records from unstructured clinical notes

Descriptive analysis (RW IVES chemo):

- Patient baseline characteristics: Age, sex, race, ethnicity, tumor stage (CIS only or CIS+Papillary), total doses of prior BCG
- RW IVES chemo pattern
- Clinical outcomes of RW IVES chemo: Overall CR, DOR, and EFS

Figure 1: Study design



*For this analysis, we included patients whose index non-BCG treatment is a IVES chemo; BCG=Bacillus Calmette-Guérin; CIS=carcinoma *in situ*; RC=radical cystectomy.

Results

Patient baseline characteristics

- Study included 134 patients with HR-NMIBC CIS who initiated IVES chemo after becoming BCG-unresponsive (**Table 1**)
- Median age: 75 years (range 55–88), male: 82.1%, White: 91.3%; 67.2% of patients had CIS only, while 32.8% had CIS with papillary tumor. The median number of prior BCG doses was 12 (range 7–19) (**Table 1**)
- The most used IVES chemo was mitomycin (36.6%) and gemcitabine (29.9%)

Table 1: Baseline characteristics

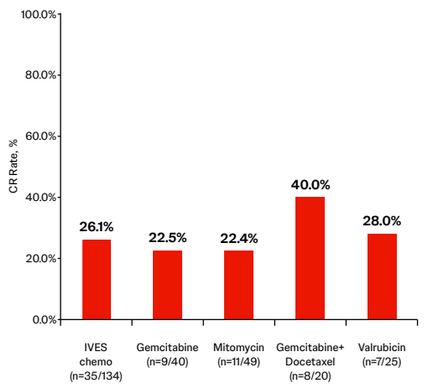
Characteristics	RW IVES chemo (n=134)
Age, median (range)	75 (55–88)
Sex, n (%)	
Male	110 (82.1%)
Female	24 (17.9%)
Race, n (%)*	
White	94 (91.3%)
Black or African American	6 (5.83%)
Asian	1 (1.0%)
Others	2 (1.9%)
Ethnicity, n (%)*	
Not Hispanic or Latino	104 (99.1%)
Hispanic or Latino	1 (1.0%)
Tumor stage, n (%)	
CIS only	90 (67.2%)
CIS + papillary	44 (32.8%)
Total doses of prior BCG, median (range)	12 (7–19)

*% calculated among a subset of patients with race/ethnicity information in the database.
BCG=Bacillus Calmette-Guérin; CIS=carcinoma *in situ*; IVES chemo=intravesical chemotherapy; RW=real world.

CR in patient treated with IVES chemo (Figure 2)

- 26% of patients achieved CR with IVES chemo treatment
- The CR rate for different IVES chemo are as follows:
  - Mitomycin: 22.4% (n=11/49)
  - Gemcitabine: 22.5% (n=9/40)
  - Valrubicin: 28.0% (n=7/25)
  - Gemcitabine+Docetaxel: 40.0% (n=8/20)

Figure 2: Overall CR rate for IVES chemo

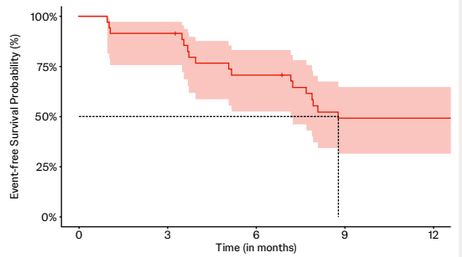


CR=complete response; IVES chemo=intravesical chemotherapy.

DOR in patients who achieved CR with IVES chemo (Figure 3)

- Among patients who responded to IVES chemo (n=35), the median DOR was 8.8 months (95% CI: 7.17–40.60 months)
- 51% of responders experienced high-risk recurrence, treatment change, progression, or death by 9 months

Figure 3: DOR among patients with BCG-unresponsive HR-NMIBC CIS who responded to IVES chemo (n=35)



Time (in months)	0 m	3 m	6 m	9 m	12 m
N at Risk	35	32	24	16	16
Survival Probability	100%	91%	71%	49%	49%

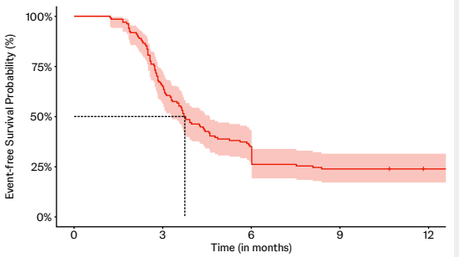
N	Events	Median (months)	0.95 LCL	0.95 UCL
35	25	8.78	7.17	40.60

BCG=Bacillus Calmette-Guérin; CIS=carcinoma *in situ*; DOR=duration of response; HR-NMIBC=high-risk non-muscle invasive bladder cancer; IVES chemo= intravesical chemotherapy; LCL=lower confidence interval limit; m=months; UCL=upper confidence interval limit.

EFS in patients treated with IVES chemo (Figure 4)

- Among all patients treated with IVES chemo (n=134), the median EFS was 3.75 months (95% CI: 3.29–4.57 months)
- 76% of patients experienced an EFS event by 9 months

Figure 4: EFS after initiating IVES chemo in patients with BCG-unresponsive HR-NMIBC CIS (n=134)



Time (in months)	0 m	3 m	6 m	9 m	12 m
N at Risk	134	87	47	32	30
Survival Probability	100%	65%	35%	24%	24%

N	Events	Median (months)	0.95 LCL	0.95 UCL
135	111	3.75	3.29	4.57

BCG=Bacillus Calmette-Guérin; CIS=carcinoma *in situ*; EFS=event free survival; HR-NMIBC=high-risk non-muscle invasive bladder cancer; IVES chemo=intravesical chemotherapy; LCL=lower confidence interval limit; m=months; UCL=upper confidence interval limit

Limitations

- Limitations include small sample size, retrospective study design, absence of central pathology review, and missing or unknown data that may confound results
- The information on patient's non-urological medical care (e.g., comorbidities managed outside of urologic settings) may be incomplete or unavailable, as AQUA Registry primarily collects data from community urologists and other urologic care providers
- Participation in AQUA Registry is voluntary, it may not fully capture the diversity of urologic practices across the U.S., potentially limiting the generalizability of study findings beyond the represented population

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Urothelial Cancer

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