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Outcomes of Cretostimogene Grenadenorepvec in Heavily Pre-Treated and Second-Line High-Risk BCG-Unresponsive Non-Muscle Invasive Bladder Cancer with Carcinoma in Situ: Analysis from BOND-003 Cohort C

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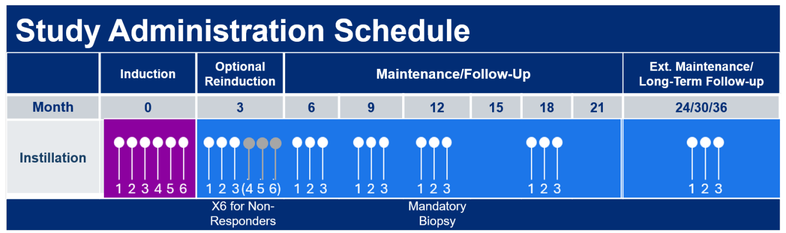
BACKGROUND

- Considerable unmet need exists for effective, well-tolerated bladder-sparing treatment options for patients with HR BCG-UR NMIBC with CIS[1]
- Patients who progress despite BCG and an additional intervening therapy represent a distinctly difficult-to-treat population
- Cretostimogene grenadenorepvec is an oncolytic immunotherapy with dual mechanisms of action, selectively replicating in and lysing cancer cells while amplifying anti-tumor immune response
- BOND-003 is a pivotal Phase 3 trial designed to evaluate cretostimogene in patients with BCG-UR NMIBC
- We report Cohort C efficacy and safety, with subgroup analyses of patients in heavily pre-treated population subgroups.

METHODS

- Eligible patients had HR BCG-UR NMIBC with CIS +/- Ta/T1
- Subgroups identified based on prior treatment exposure prior to BOND-003 enrollment:
  - –Second-Line: patients diagnosed with BCG-UR who received an additional therapy after adequate BCG
  - –Prior Intervening Chemotherapy: adjuvant IVE chemotherapy before or after adequate BCG
- Response assessments: serial cystoscopy, urine cytology, CT urogram/MRU, mandatory mapping biopsy
- All responses centrally confirmed; Primary endpoint: CR at any time

Study Administration Schedule



BOND-003 COHORT C

Strong Efficacy in Heavily Pre-Treated and Second Line Population

Well-Tolerated Safety Profile

RESULTS

Efficacy Evaluable Population

- 110 efficacy evaluable patients
- Majority male (74%), white (62%), >65 years old (83%)
- Median follow-up: 25.8 months; CR rate at any time: 75.5% (83/110)

Safety Profile

Preferred Term (MedDRA v.26.1)	Cretostimogene (n=112)	
	Any Grade (%)	Grade ≥3
Patients with ≥1 TRAE	71 (63.4%)	0 (0)
Treatment-Related AE reported in >20% patients		
Bladder Spasm	28 (25%)	0 (0)
Pollakiuria	25 (22.3%)	0 (0)
Urgency	23 (20.5%)	0 (0)

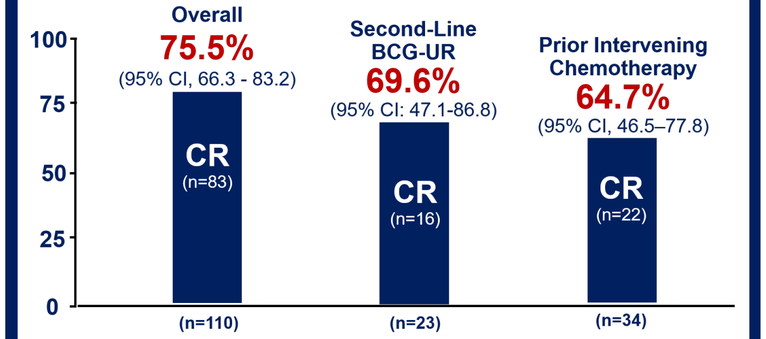
- Most AEs Grade 1-2; median 1-day (IQR 0-7 days) time to TRAE resolution
- High Tx Compliance- no tx-related discontinuations; few missed (1.8%) or delayed (7.1%) doses

Abbreviations: AE: adverse event; ASCO: American Society of Clinical Oncology; AUA: American Urological Association; BCG: Bacillus Calmette-Guérin; CFS: cystectomy-free survival; CIS: carcinoma in situ; CR: complete response; DOR: duration of response; HG: high grade; HR: high-risk; IVE: intravesical; NMIBC: non-muscle invasive bladder cancer; RC: radical cystectomy; SUO: Society of Urologic Oncology; TRAE: treatment-related adverse event; UR: unresponsive; UTUC: upper tract urothelial carcinoma; MIBC: muscle-invasive bladder cancer

Second Line and Prior Intervening Chemotherapy

- 23/110 (21%) patients: Second-Line BCG-UR
  - CR rate at any time: 69.6% (16/23)
- 34/110 (31%) patients Prior Intervening Chemotherapy, with
  - ≥1 course of IVE gemcitabine (11/34; 32%)
  - IVE gemcitabine-docetaxel (16/34; 47%)
  - CR rate at any time: 64.7% (22/34)

Complete Response Rate at Any Time (%)



DISCUSSION

- This analysis focuses on two challenging HR subgroups: Second-Line BCG-UR disease, an indication recently recognized by the FDA,[3] and a broader population of heavily-pretreated patients
- Cretostimogene demonstrated strong CR rates in both heavily pretreated subgroups, supporting its potential as a bladder-sparing option even in heavily pre-treated NMIBC populations
- These findings may reflect cretostimogene's dual mechanism of action which selectively targets cancer cells, in contrast to the non-specific mechanisms of BCG and chemotherapy

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References: 1 NCCN Bladder Cancer Guidelines; 2026, **2** AUA/SUO NMIBC Guidelines; 2024; **3** Remalda Therapeutics, Inc. Press Release, Jan 12, 2026

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Phase 3 Cretostimogene Monotherapy for High-Risk BCG-Unresponsive NMIBC with CIS

BOND-003 COHORT C

FDA Fast Track Designation

FDA Breakthrough Therapy Designation

HR BCG-Unresponsive NMIBC

Cretostimogene Grenadenorepvec
Single-Arm, Open-Label, IVE Administration

Primary Endpoint:
CR at Any Time

Population

- Enrollment complete (n=112)
- Pathologically confirmed High-Risk BCG-Unresponsive NMIBC with CIS +/- Ta/T1
- All Ta/T1 disease resected prior to treatment
- Mandatory biopsies at 12-month assessment[1]

Study Design / Regimen

Induction Course:
Weekly x 6

Second Induction[1]:
Weekly x 6 for non-responders

Maintenance Course:
Weekly x 3 Q3M for Year 1
Weekly x 3 Q6M for Year 2-3

Additional Endpoints

- CR at 12-months
- DoR
- RFS
- PFS
- Cystectomy-Free Survival
- Safety

NCT04452591

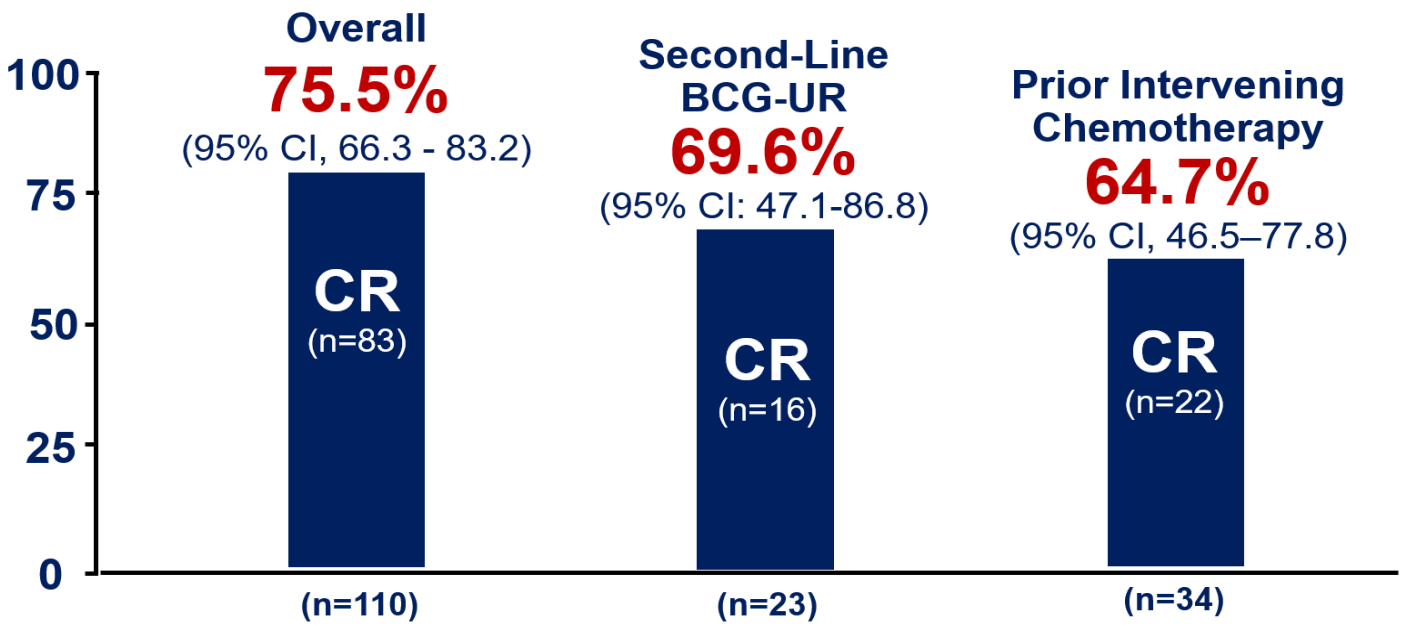
CIS = Carcinoma in situ. RFS = recurrence free survival. PFS = progression free survival.
Note: Patients undergo urine cytology and cystoscopy every 3 months for first 2 years, as well as mandatory bladder mapping at month 12.
[1] All patients required to undergo mandatory, systematic bladder mapping of 5 locations, biopsy of the prostatic urethra, and upper tract imaging to confirm CR.
[2] Second induction course of weekly x 6 for non-responders at month 3.

BOND-003 COHORT C

THE LANCET Oncology

Strong Efficacy in Heavily Pre-Treated and Second-line Disease

Complete Response Rate at Any Time (%)



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BCG= Bacillus Calmette-Guérin; BCG-UR= BCG-unresponsive; CI= confidence interval; CIS= carcinoma in situ; CR= complete response; HR= high-risk; IVE= intravesical; NMIBC= non-muscle invasive bladder cancer
All responses centrally confirmed; primary endpoint: CR at any time. Second-Line: patients diagnosed with BCG-UR who received an additional therapy after adequate BCG. Prior Intervening Chemotherapy: adjuvant IVE chemotherapy before or after adequate BCG.

Key Takeaways

- This analysis focuses on two challenging HR subgroups: Second-Line BCG-UR disease, an indication recently recognized by the FDA, and a broader population of heavily-pretreated patients
- **Cretostimogene demonstrated strong CR rates in both heavily pretreated subgroups**, supporting its potential as a bladder-sparing option even in heavily pre-treated NMIBC populations
- These findings may reflect cretostimogene's dual mechanism of action which selectively targets cancer cells, in contrast to the non-specific mechanisms of BCG and chemotherapy