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Safety and efficacy of Bel-sar (AU-011), a Virus-like-Drug-Conjugate (VDC) in patients with Non-Muscle Invasive Bladder Cancer (NMIBC)

*Max Kates, M.D., Sabine D. Brookman-May, M.D., Joseph McQuaid, M.D., Jennifer Linehan, M.D., Xianne Penny, PhD, , Gautam Jayram, M.D., Piyush Agarwal, M.D., Joseph Jacob, M.D. M.C.R., Gary D. Steinberg, M.D., Neal D. Shore, M.D., and Seth P. Lerner, M.D.**

Johns Hopkins School of Medicine, Baltimore, MD (M.K.); University of Munich, LMU, Munich, Germany (S.B.M.); Aura Biosciences, Boston, MA (S.B.M., X.P., J.M.); John Wayne Cancer institute, Santa Monica, CA (J.L.); Urology Associates of Nashville, Nashville, TN (G.J.); University of Chicago, Chicago, IL (P.K.A.); Rush University, Chicago, IL (G.D.S.); SUNY Upstate Medical University, Syracuse, NY (J.J.); Carolina Urologic Research Center and Genesis Care US, Myrtle Beach, SC (N.D.S.); Baylor College of Medicine, Houston, TX (S.P.L.);

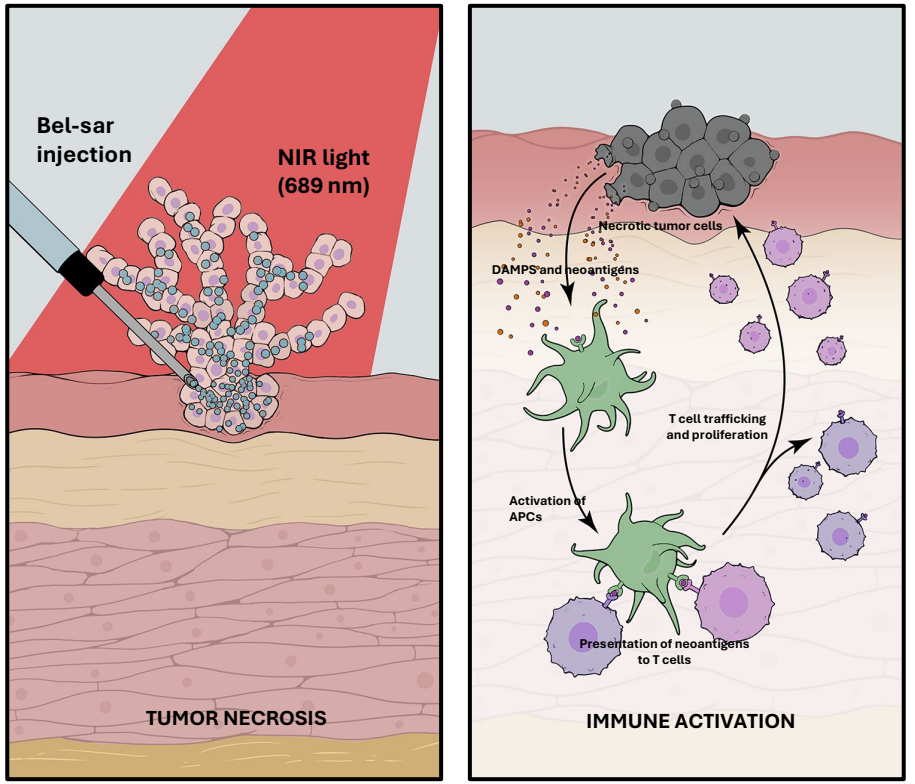
presenting author

Investigational Product Candidates

This presentation discusses product candidates that are under preclinical or clinical evaluation and that have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA) or any other regulatory authority. Until finalized in a clinical study report, clinical trial data presented herein remain subject to adjustment as a result of clinical site audits and other review processes. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied

Background

- Current standard of care for NMIBC leaves a large, unmet medical need:
  - High recurrence rates
  - Need for repeat surgeries and adjuvant treatments
- AU-011 is a focally administered, Virus-like-Drug-Conjugate (VDC) with an **immune-ablative dual mechanism of action:**
  - Selective binding to tumor-expressed heparan sulfate proteoglycans (HSPG)
  - Induction of immediate tumor necrosis after light activation
  - Stimulation of anti-tumor immunity
- AU-011 demonstrated 80% tumor control rate at 12 months in a Phase 2 trial in early-stage choroidal melanoma*



Direct cytotoxic effect + long-term anti-tumor immunity

Local cystoscopic administration of drug with cystoscopy needle

<5 minutes

Laser light activation

<10 minutes total laser time
< 3 min/lesion

Kines RC, et al. *Int J Cancer*. 2016;138(4):901–11. Kines RC, et al. *Mol Cancer Ther*. 2018;17(2):565–74. Kines RC, et al. *Cancer Immunol Res*. 2021;9:693–706.

* Press release announcing Phase 2 end of study results available here: https://ir.aurabiosciences.com/news-releases/news-release-details/aura-biosciences-reports-positive-phase-2-end-study-results

Phase 1 trial of bel-sar for bladder cancer designed to evaluate safety, feasibility, and mechanism of action

Single dose window of opportunity study in NMIBC all-comers

Histopathological assessment completed at time of standard of care TURBT

Part 1 (n=5)

bel-sar alone

Drug only (No light)

Total 100 µg

NMIBC (N=5)

50 µg at tumor base
50 µg within lamina propria

Part 2 (n=~10)

bel-sar + focal light activation

Cohort A: Drug + light

Total 100 µg

NMIBC (N=4)

50 µg at tumor base
50 µg within lamina propria

Cohort B: Drug + light

Total 100 µg

NMIBC (N=3)

100 µg at tumor base

Cohort C: Drug + light

Total 200 µg

NMIBC (N=3)

200 µg at tumor base

Safety Review Board completed after each cohort. Patients followed for safety after TURBT to 56 days.

Study objectives	Safety & dose-limiting toxicity	Feasibility of technique	Focal distribution of bel-sar	Focal necrosis	Markers of immune activation

NMIBC, non-muscle-invasive bladder cancer; **TURBT**, transurethral resection of bladder tumor.
Clinicaltrials.gov identifier: NCT05483868; bel-sar-102.

Efficacy data: Ta Intermediate-Risk NMIBC

4/5 patients demonstrated CR; 5/5 patients with immune response in target tumor

	Patient A1	Patient A3	Patient A4[c]	Patient B2	Patient C1[d]
Screening diagnosis	Multiple (TURBT) Ta low-grade	Multiple Ta low-grade	Multiple Ta low-grade Prior Ta high-grade	Multiple Ta low-grade	Multiple Ta low-grade
Screening AUA risk classification	Intermediate (TURBT)[f]	Intermediate	Intermediate	Intermediate	Intermediate
AU-011 dose/delivery	100 µg IT/IM	100 µg IT/IM	100 µg IT/IM	100 µg IT	200 µg IT
Clinical complete response: Target tumor[a]	✓	✓	✓	-	✓
Clinical complete response: Non-target tumor[a] (bladder urothelial field effect[b])	2/2	1/2	1/1	0/1	0/1
Immune response[e]: Target tumor	✓	✓	✓	✓	✓
Immune response[e]: Non-target tumor	✓	✓	✓	✓	✓
Necrosis	✓	✓	✓	-	-
Visual changes on cystoscopy	✓	✓	-	Tumor Visually Smaller	✓

Cohorts A–C:
Single-dose drug with light activation

[a]For purposes of this analysis, Clinical complete response defined as absence of tumor cells on histopathologic evaluation. [b]Bladder urothelial field effect: absence of tumor cells in non-target lesions. [c]Previously treated tumor demonstrated high-grade disease but pathology at time of treatment revealed low-grade disease in non-target tumor. [d]Local pathology with no evidence of carcinoma in 3/3 target specimens. Central pathology demonstrated single fibrovascular core in 1/3 target specimens consistent with small area of papillary disease of unclear distance from target injection. [e]Immune response is defined by immunocyte infiltration on post-treatment histopathology. [f]Single lesion visualized at screening on office cystoscopy. Multiple lesions subsequently seen with improved visualization at time of TURBT qualifying for intermediate risk classification. **AUA**, American Urological Association; **IM**, intramural; **IT**, intratumoral; **TURBT**, transurethral resection of bladder tumor; **CR,** clinical complete response; **NMIBC**, non-muscle-invasive bladder cancer. Clinicaltrials.gov identifier: NCT05483868; AU-011-102.

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Efficacy data: Ta High-Risk NMIBC

1/5 patients demonstrated CR; 5/5 patients with immune response in target tumor

	Patient A2	Patient B1	Patient B3	Patient C2	Patient C3[d]
Screening diagnosis	Single Ta high-grade	Multiple Ta high-grade	Single Ta high-grade	Multiple Ta high-grade	Multiple Ta low-grade Prior Ta high-grade
Screening AUA risk classification	High	High	High	High	High (BCG Failure)
AU-011 dose/ delivery	100 µg IT/IM	100 µg IT	100 µg IT	200 µg IT	200 µg IT
Clinical complete response: Target tumor[a]	-	-	-	-	✓
Clinical complete response: Non-target tumor[a] (bladder urothelial field effect[b])	NA	0/1	NA	NA	1/3
Immune response[c]: Target tumor	✓	✓	✓	✓	✓
Immune response[c]: Non-target tumor	NA	✓	NA	NA	✓
Necrosis	-	-	-	-	✓
Visual changes on cystoscopy	Tumor Visually Smaller	Tumor Visually Smaller	-	Tumor Visually Smaller	✓

Cohorts A–C:
Single-dose drug with light activation

[a]Clinical complete response defined as absence of tumor cells on histopathologic evaluation. [b]Bladder urothelial field effect: absence of tumor cells in non-target lesions. [c]Immune response is defined by immunocyte infiltration on post-treatment histopathology. [d]Two tumors in target tumor field with 1/2 tumors with clinical complete response. BCG failure qualifying as high risk by AUA criteria. **AUA,** American Urological Association; **BCG**, Bacillus Calmette-Guerin; **IM**, intramural; **IT**, intratumoral; **CR**, clinical complete response. Clinicaltrials.gov identifier: NCT05483868; AU-011-102.

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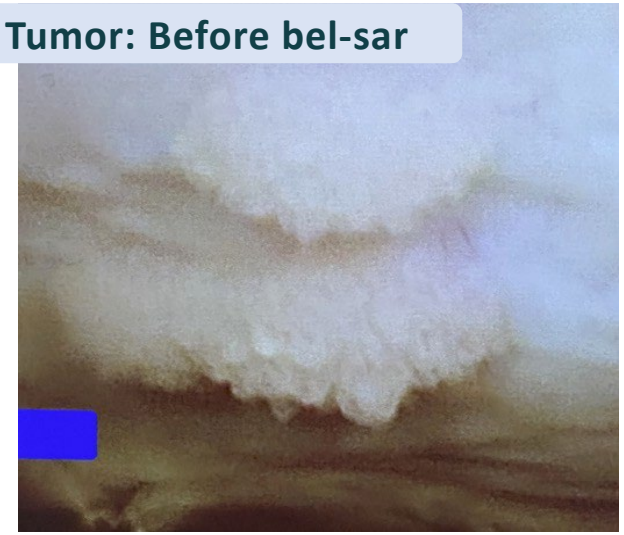
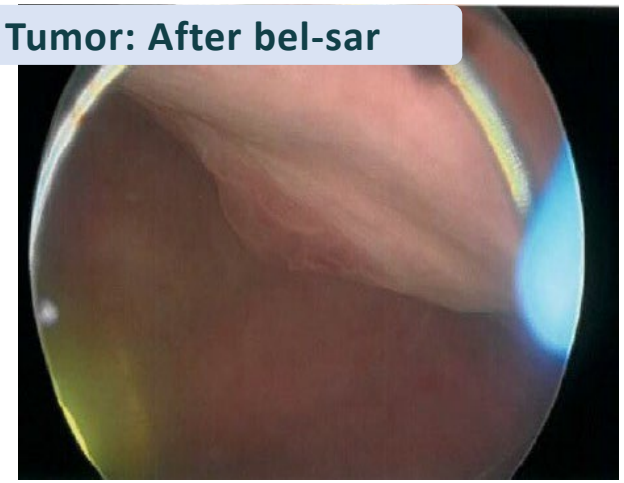
Visual and Immune Response

Patient A3; Intermediate-Risk NMIBC

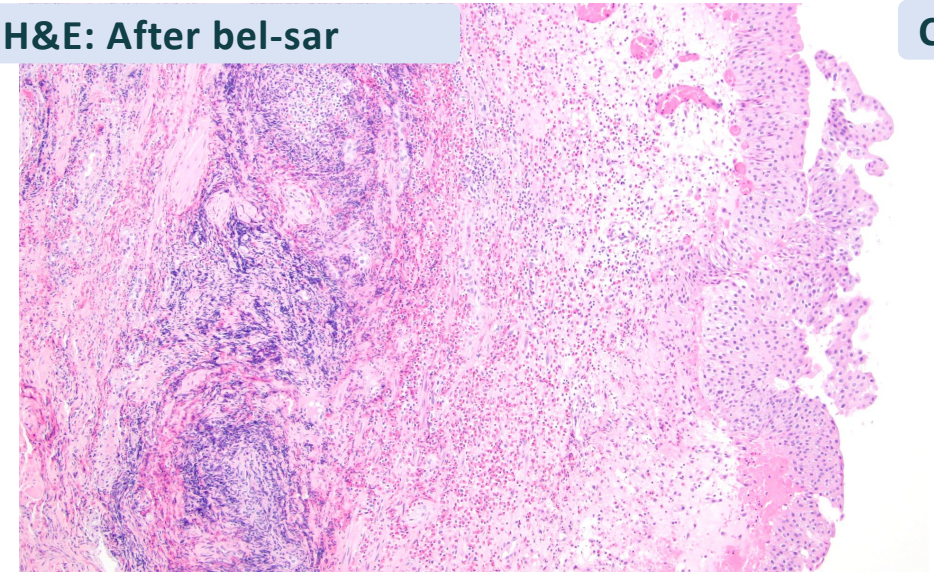
Tumor: Before bel-sar



Tumor: After bel-sar

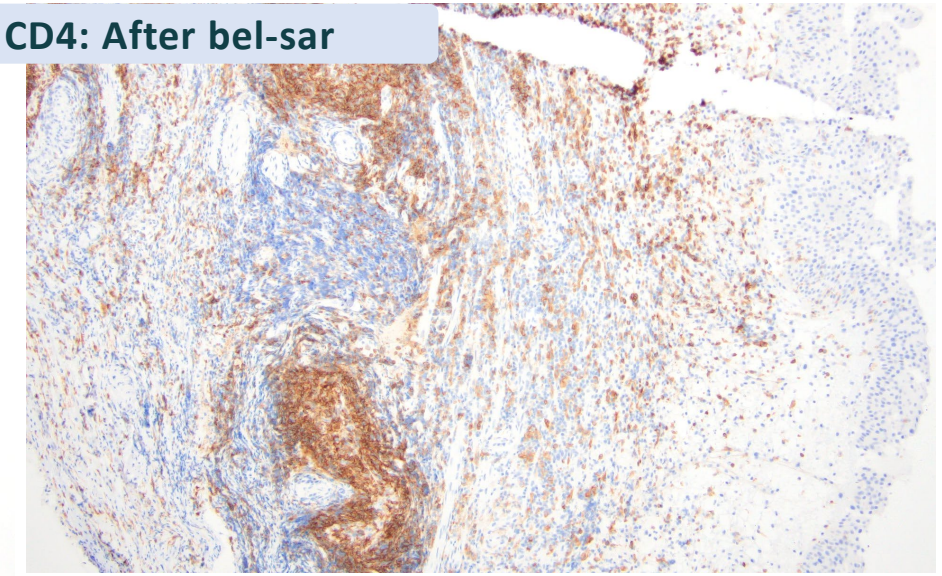


H&E: After bel-sar



Lymphoid follicles were observed, suggesting a strong adaptive immune response.

CD4: After bel-sar



Significant infiltration of CD4+/CD8+ T-cells in both treated and untreated tumors, indicating a **urothelial field effect**.

Mature Tertiary Lymphoid Structures (TLS) in Target (Treated) Lesion:

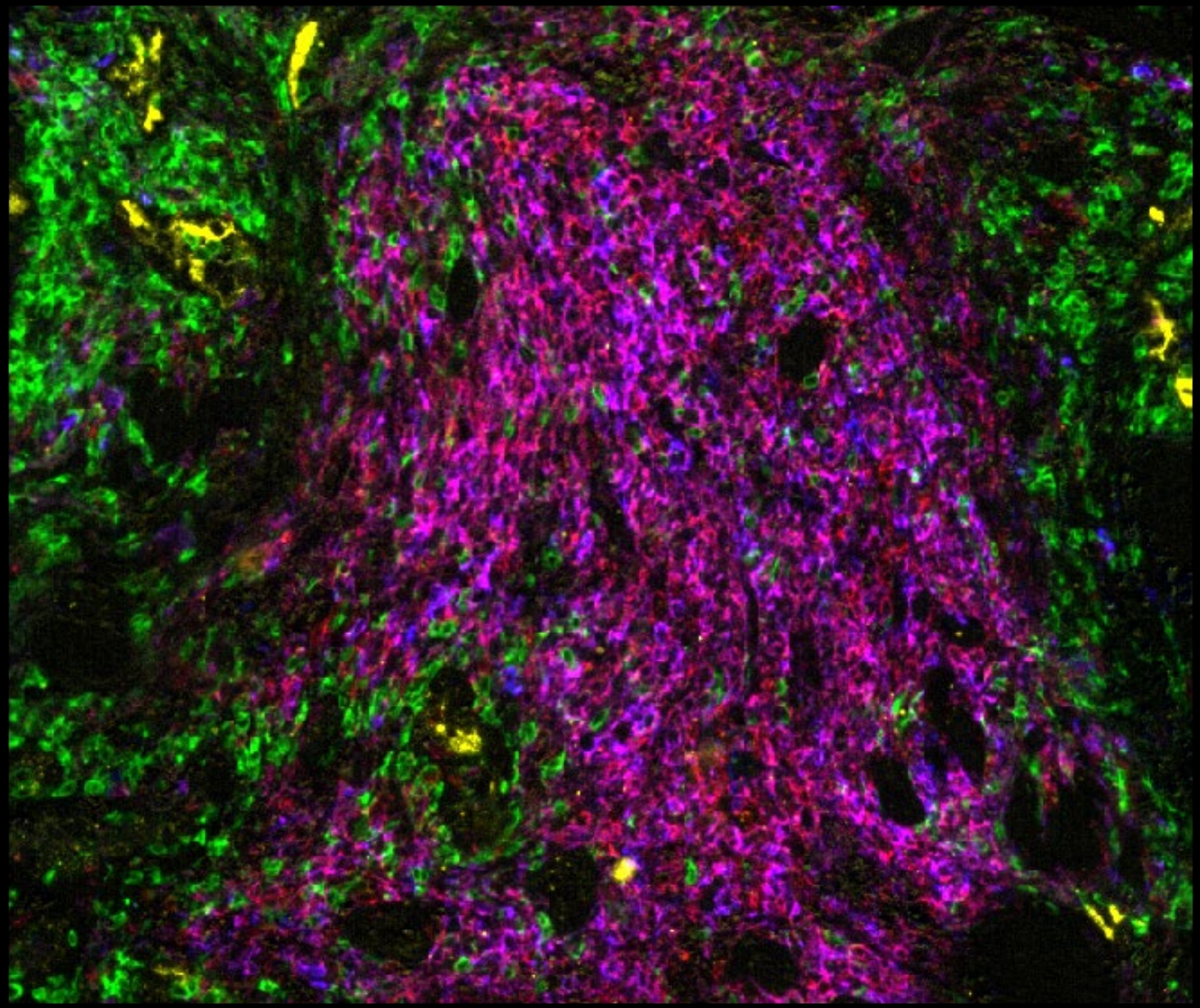
Active Immunosurveillance After Bel-sar Treatment

CD3: T cells

CD20: B cells

CD23: Follicular Dendritic Cells (FDC)
(Found in B cell follicles, only present in mature TLS)

PNAd: Peripheral Node Addressin
(Stains for high endothelial venules, evidence of lymphocyte trafficking from periphery)



Multiplex Immunofluorescence: Patient A3 (Intermediate-Risk NMIBC)

TLS Not Present in Lesion Prior to Treatment

Early Tertiary Lymphoid Structures (TLS) in Distant Non-Target (Non-Treated) Lesion:

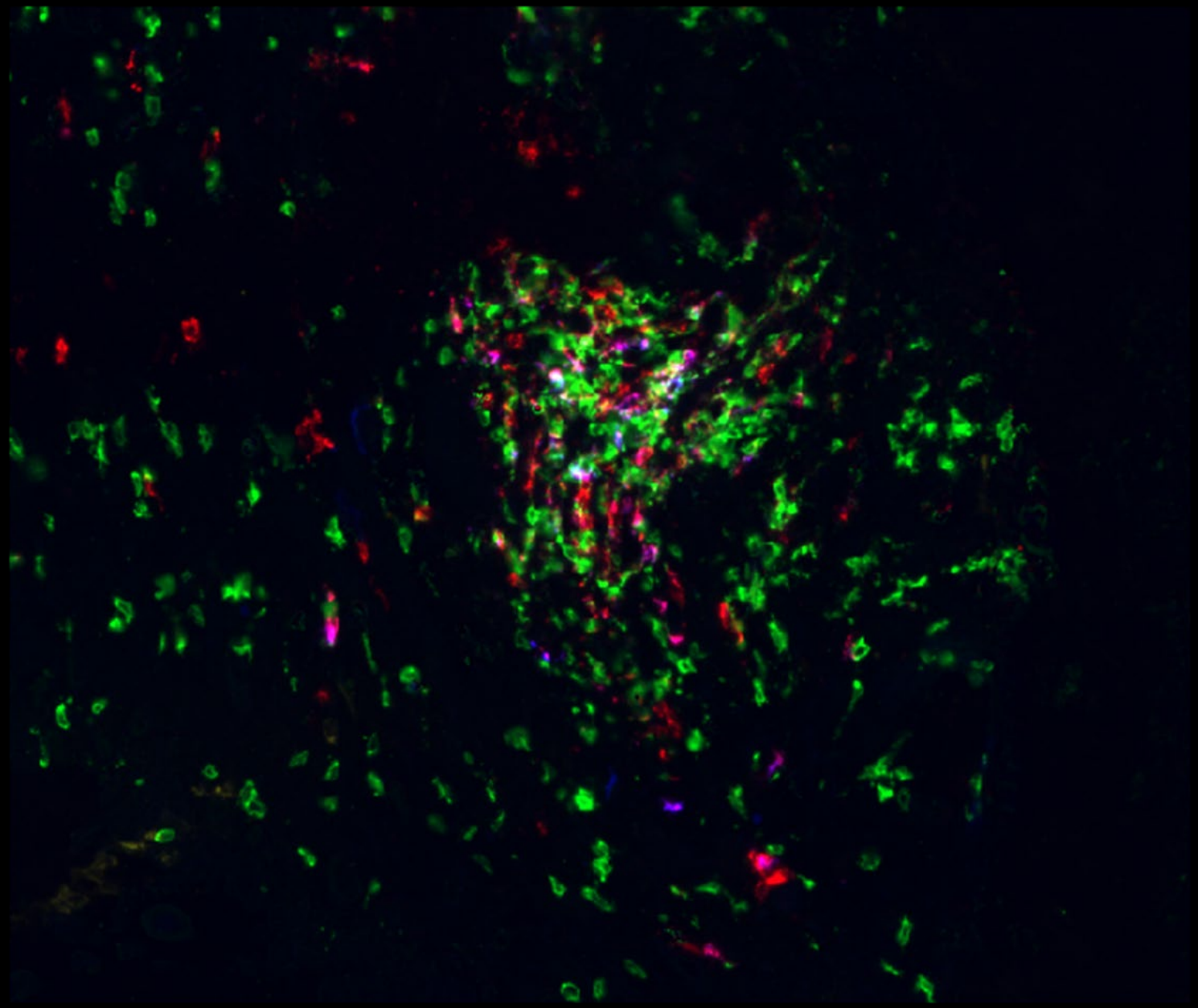
Urothelial Immune Field Effect After Bel-sar Treatment

CD3: T cells

CD20: B cells

CD23: Follicular Dendritic Cells (FDC)
(Found in B cell follicles, only present in mature TLS)

PNAd: Peripheral Node Addressin
(Stains for high endothelial venules, evidence of lymphocyte trafficking from periphery)



Multiplex Immunofluorescence: Patient A3 (Intermediate-Risk NMIBC)

Conclusions

- Dual mechanism of action demonstrated with Virus-like Drug Conjugate:
  - **Tumor cell necrosis with clinical complete response**
  - **Strong local immune response (active immunosurveillance)** with generation of mature TLS
  - Extensive **urothelial field effect** in NMIBC with early TLS visualized in distant, non-treated lesions
- Safety Data:
  - **Only grade 1 drug-related adverse events**
- Biological Activity Data:
  - **IR NMIBC: Clinical Complete Response achieved in 4 out of 5 tumors, and 4 non-target tumors**
  - **HR NMIBC: Tumor shrinkage occurred in 3 out of 5 patients**, although tumor cells remained on pathology; **one complete response in a target tumor**
- Field Effect:
  - Clinical complete response in both treated and non-treated lesions within 7 to 12 days suggests the potential of AU-011 as a promising upfront immune-ablative treatment

IR, intermediate-risk; **HR**, high-risk; **NMIBC**, non-muscle-invasive bladder cancer; **TLS**, teriary lymphoid structure
Clinicaltrials.gov identifier: NCT05483868; AU-011-102.