TAR-210 Erdafitinib Intravesical Delivery System in Non–Muscle-Invasive Bladder Cancer With Select *FGFR* Alterations: Updated First-in-Human Results

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Presented by A Vilaseca at the 119th AUA Annual Meeting; May 3-6, 2024; San Antonio, TX, USA

Disclosures

- A Vilaseca has received consulting/advisory fees from Accord, Astellas, Bayer, and Janssen, and travel support from Astellas, Janssen, and Recordati

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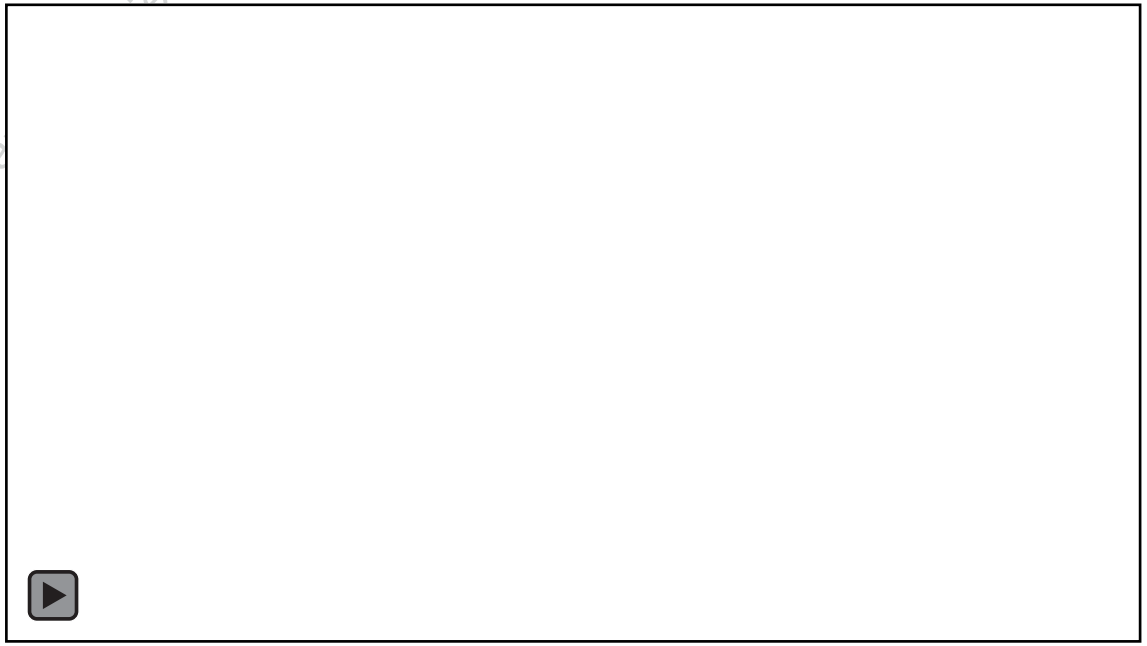
TAR-210 Is Designed to Deliver Sustained Local Delivery of Erdafitinib, a Pan-FGFR Inhibitor, Throughout 3 Months in the Bladder

- Despite available treatment options for patients with NMIBC, recurrence rates remain high, underscoring the need for effective therapies[1]
- Activating *FGFR* alterations are prevalent in 50-80% of patients with NMIBC and may function as oncogenic drivers[2-4]
- Erdafitinib is a selective pan-FGFR tyrosine kinase inhibitor[5]
  - Erdafitinib has regulatory approval in the United States to treat patients with locally advanced or mUC with susceptible *FGFR3* alterations following at least 1 prior systemic treatment, with additional approvals across geographies[6-9]

TAR-210 is a novel targeted releasing system designed for sustained local delivery of erdafitinib over 3 months in the bladder



TAR-210 is inserted into the bladder through a dedicated urinary placement catheter and removed via cystoscopy.

FGFR, fibroblast growth factor receptor; mUC, metastatic urothelial carcinoma; NMIBC, non–muscle-invasive bladder cancer.

1. Ritch CR, et al. *J Urol.* 2020;203:505-511. 2. Hernández S, et al. *J Clin Oncol.* 2008;24:3664-3671. 3. Knowles MA, Hurst CD. *Nat Rev Cancer.* 2014;15:25-41. 4. Khalid S, et al. *Eur Urol Open Sci.* 2020;21:61-68. 5. Perera TPS, et al. *Mol Cancer Ther.* 2017;16:1010-1020. 6. BALVERSA® (erdafitinib) [package insert]. Horsham, PA: Janssen Products, LP; 2024. 7. Loriot Y, et al. *N Engl J Med.* 2019;381:338-348. 8. Siefker-Radtke AO, et al. *Lancet Oncol.* 2022;23:248-258. 9. Loriot Y, et al. *N Engl J Med.* 2023;21:1961-1971.

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TAR-210 First-in-Human Phase 1: Cohorts 1 and 3

Study Design

NCT05316155

Molecular Eligibility

FGFR alterations:

- Flexible molecular eligibility strategy used
  - Local or central fresh/ archival **tissue-based** testing by NGS or PCR

—or—

  - Central **urine cell-free DNA** NGS testing

HR NMIBC (Cohort 1)

- Recurrent, high-grade Ta/T1, papillary only, no CIS
- BCG-experienced and not undergoing radical cystectomy
- TURBT with complete resection of all visible disease prior to treatment

IR NMIBC (Cohort 3)

- Recurrent, history of low-grade only Ta/T1 disease
- **Visible target lesions** prior to treatment (chemoablation design)

Part 1: Dose Escalation

BOIN[1,2]

- **TAR-210-D** ~4 mg/day
- **TAR-210-B** ~2 mg/day

- Placement every 3 months

Part 2: Dose Expansion

- Expansion of both dose levels

Response assessed every 3 months with continued treatment for up to 1 year if recurrence free (Cohort 1) or complete response (Cohort 3).

Clinical cutoff date: **March 22, 2024**.

BCG, bacillus Calmette-Guérin; BOIN, Bayesian optimization interval; CIS, carcinoma in situ; HR, high risk; IR, intermediate risk; NGS, next-generation sequencing; PCR, polymerase chain reaction; PK, pharmacokinetics; TURBT, transurethral resection of bladder tumor.

1. Liu S, Yuan Y. *J R Stat Soc Ser C Appl Stat.* 2015;64:507-523. 2. Yuan Y, et al. *Clin Cancer Res.* 2016;22:4291-4301.

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TAR-210 First-in-Human Phase 1: Patient Characteristics

Characteristic	Cohort 1 HR NMIBC (N=21)	Cohort 3 IR NMIBC (N=43)
Age, years, median (range)	73 (62-90)	67 (41-89)
Gender, male, %	71	79
Race, %		
White	81	60
Asian	19	40
ECOG performance status, %		
0	62	79
1	24	14
2	14	7

Characteristic	Cohort 1 HR NMIBC (N=21)	Cohort 3 IR NMIBC (N=43)
Tumor stage, %		
Ta	76	95[a]
T1	24	5[a]
Multiple tumors, %	43	43[a]
Prior BCG, %	100	21
Prior intravesical chemotherapy, %	10	51
Prior TURBT and tumor ablative procedures, median (range)[b]	4 (1-12)	2 (1-14)
FGFR alterations, %		
FGFR3 mutations	90	95
FGFR3 gene fusions	10	5

ECOG, Eastern Cooperative Oncology Group.
[a]N=42. [b]Prior cancer-related surgery/procedure of interest were counted only once on a given date and includes the following procedures: fulguration, cauterization, and laser photoablation.

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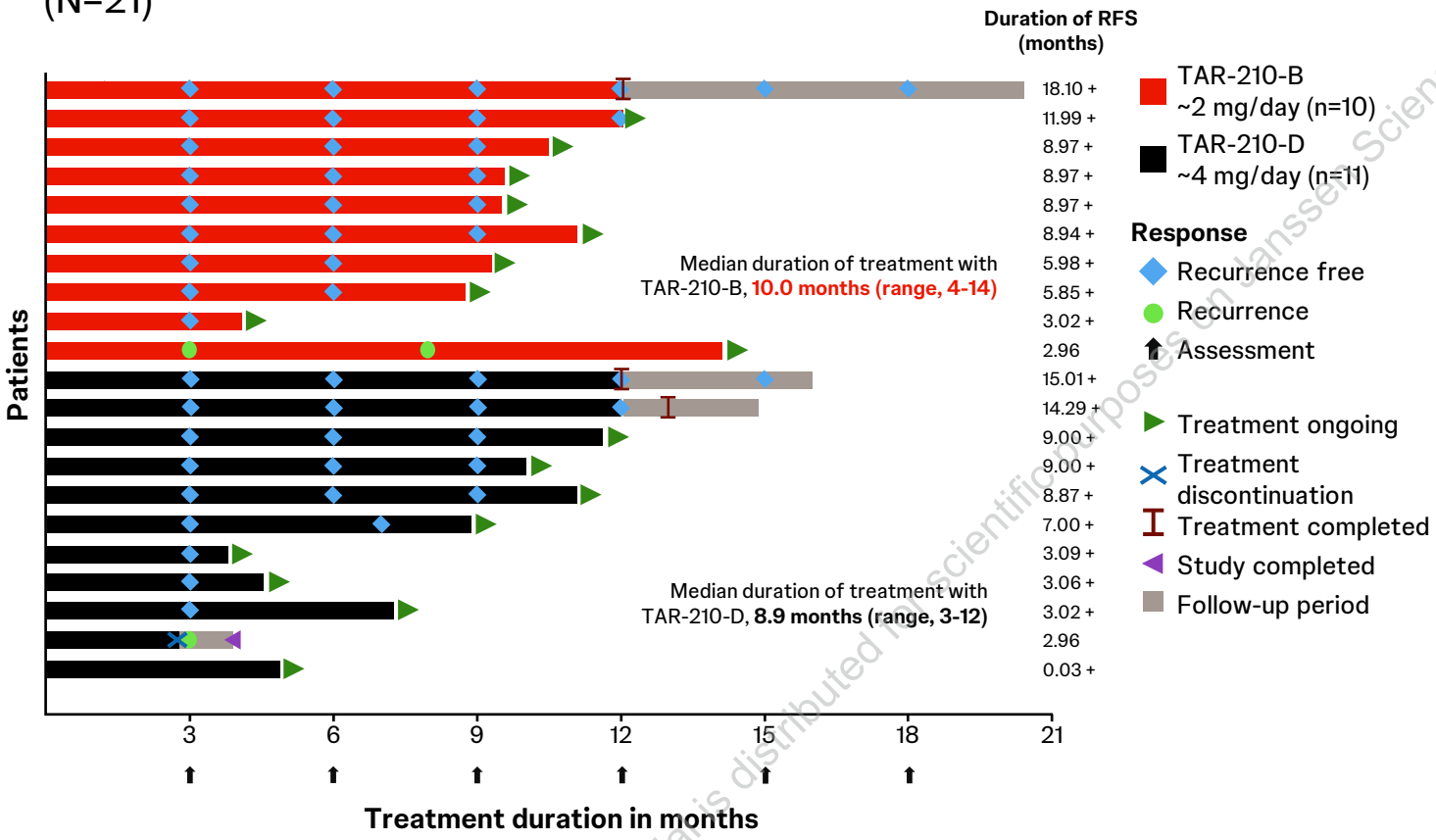
TAR-210 HR NMIBC (Cohort 1): Results

HR NMIBC With *FGFR* Alterations (Cohort 1)
(N=21)



- **90% estimated 12-month RFS rate[a]** (n=21)
  - Median RFS was not estimable
  - 2 of 21 patients have recurred
  - Median duration of follow-up 8.9 months
- No difference observed in RFS between the TAR-210 dose levels

+ Indicates patient was censored; CI, confidence interval; CR, complete response; NE, non-estimable; RFS, recurrence-free survival.
[a]All treated patients were efficacy evaluable. RFS was estimated using the Kaplan-Meier method.

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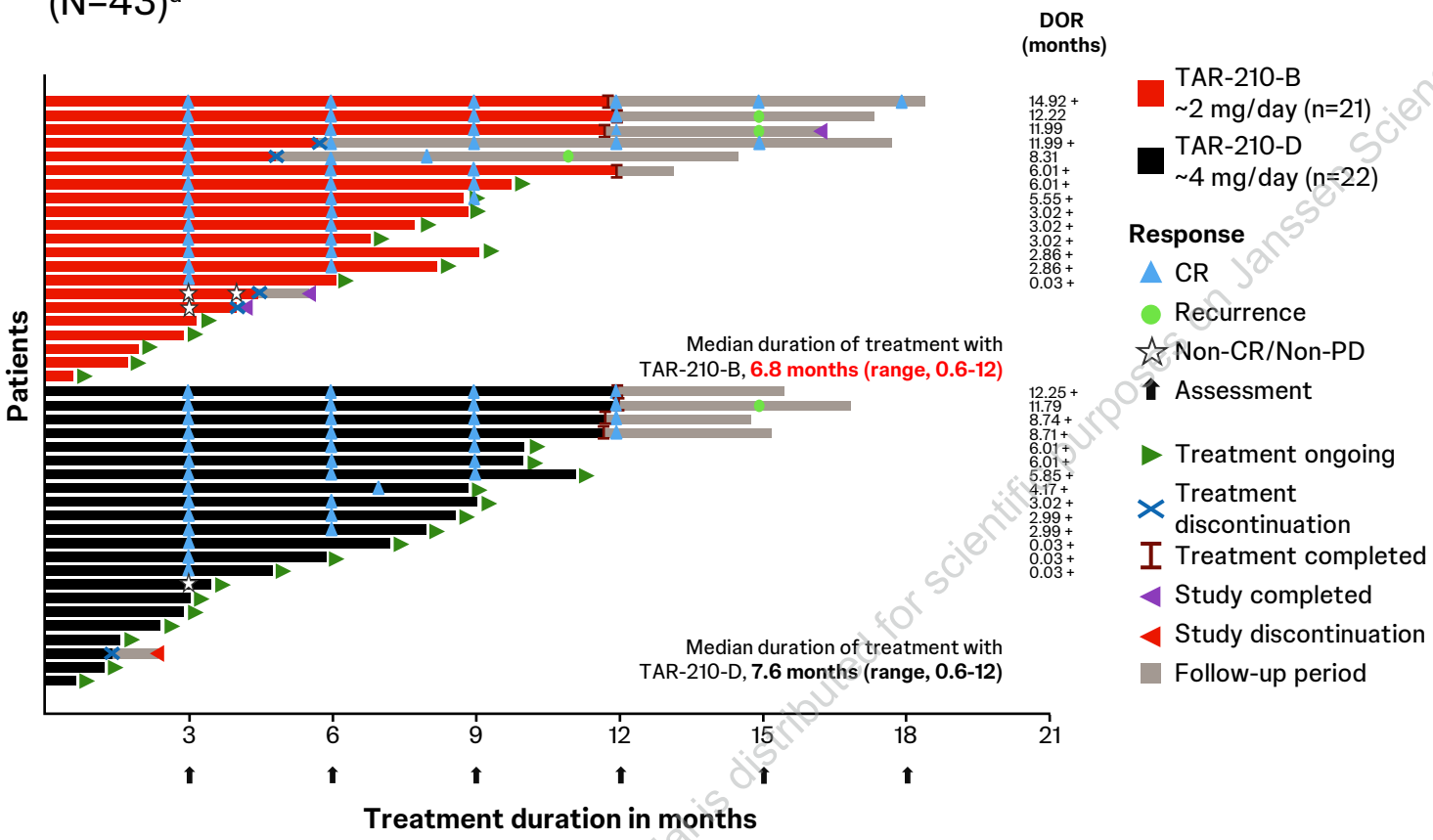
TAR-210 IR NMIBC (Cohort 3): Results

IR NMIBC With *FGFR* Alterations (Cohort 3)
(N=43)[a]



- Overall, 31 patients were evaluable for response[b]
- **90% CR rate,** with 28/31 patients achieving a CR at Week 12
  - Overall, **100% of patients achieved a clinical response**; 3 patients had a non-CR/non-PD response
- Consistent CR rate across both doses
- 86% (24/28) of CRs are ongoing at time of clinical cutoff

Durable response rate at specific landmarks[c]	% (95% CI)
6 months	100 (100-100)
9 months	89 (43-98)

+ Indicates patient was censored; DOR, duration of response; PD, progressive disease.
[a]43 patients were treated; 31 patients were efficacy evaluable for CR and DOR. [b]Efficacy evaluable patients were those having at least one disease evaluation or discontinuing treatment prior to their first disease evaluation for either PD or recurrence. [c]DOR was estimated using the Kaplan-Meier method.

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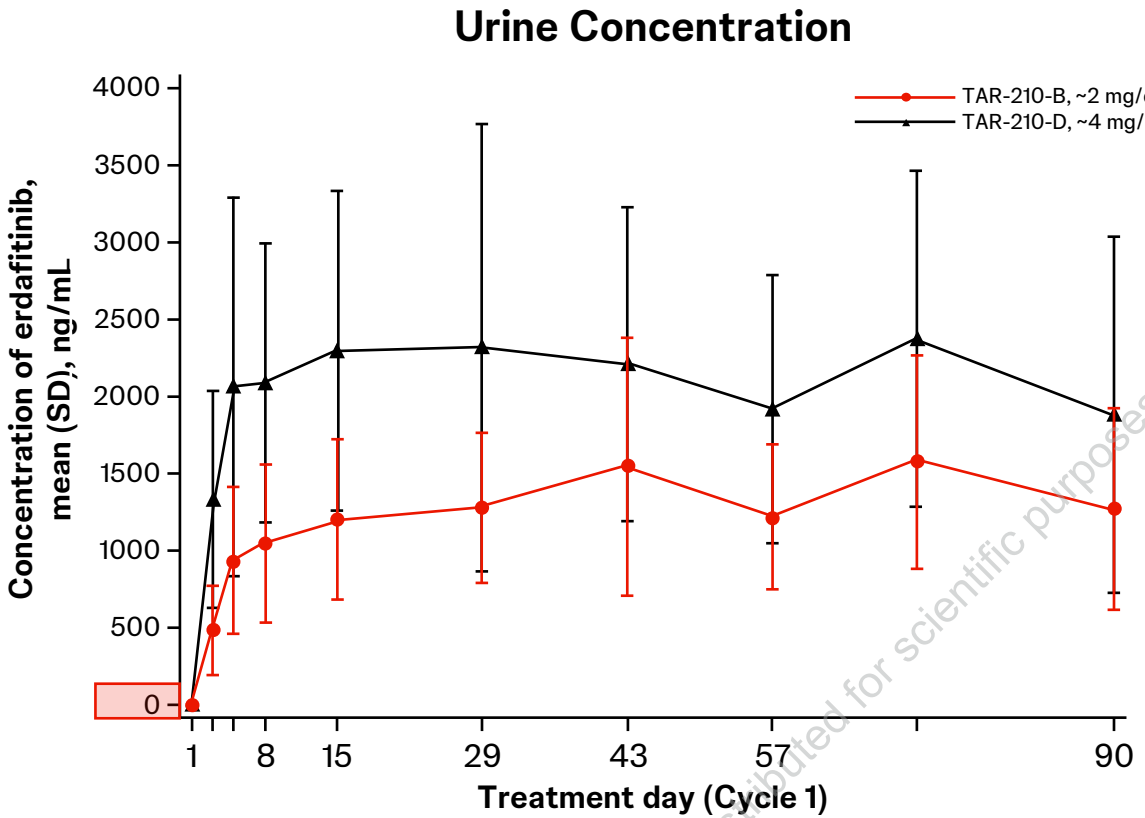
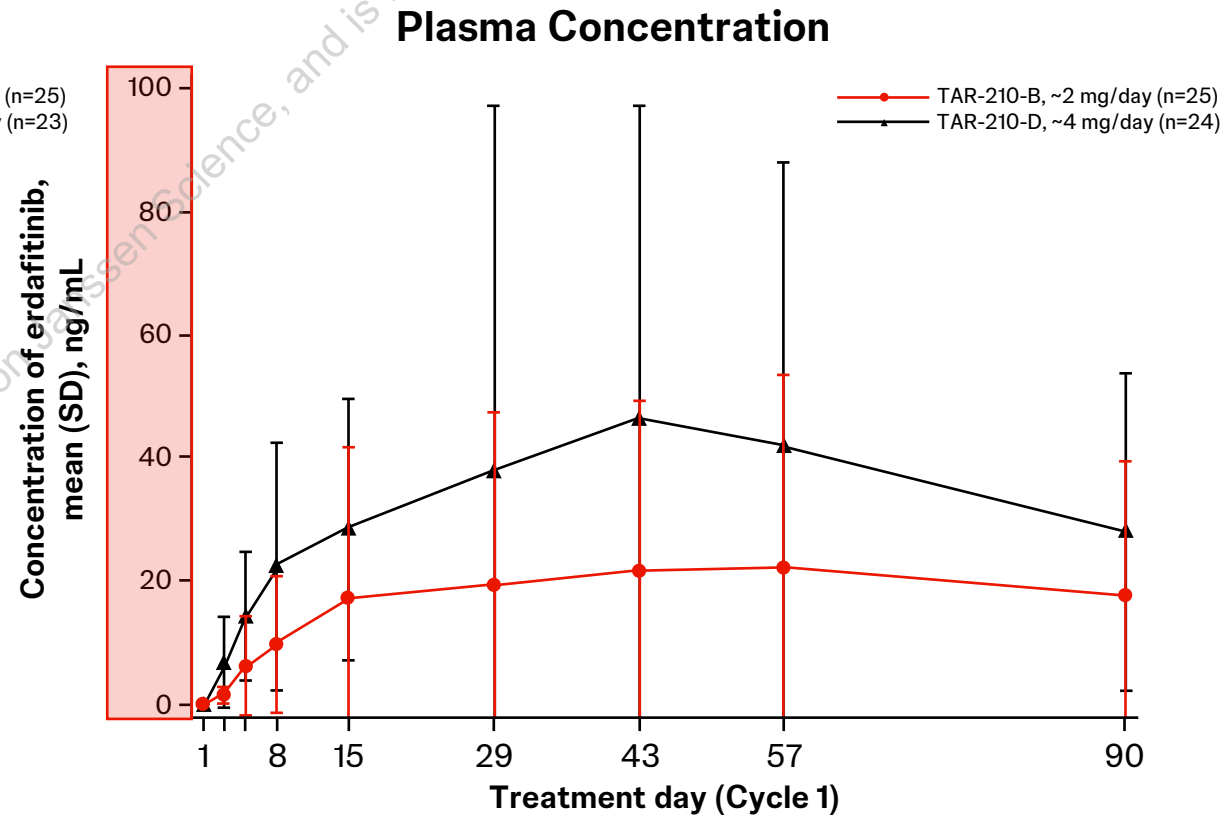
TAR-210 Provided Sustained Erdafitinib Concentrations in Urine With Very Low Plasma Concentrations





- No hyperphosphatemia was reported, consistent with the very low plasma concentrations observed with TAR-210
- Mean plasma erdafitinib concentrations were >50× lower than mean urine concentrations

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Safety and Tolerability of TAR-210 in HR NMIBC (Cohort 1) and IR NMIBC (Cohort 3)

- The majority of AEs were grade 1/2 lower urinary tract AEs
- Few patients discontinued due to AEs
  - 2 patients (3%) discontinued due to TRAEs of low-grade urinary symptoms
- 2 patients had serious TRAEs with pyelonephritis and sepsis or UTI and sepsis, respectively
  - Both events resolved with antibiotics and patients were able to continue TAR-210
- No dose-limiting toxicities were identified

Patients with events, n (%)	HR NMIBC (Cohort 1)		IR NMIBC (Cohort 3)		All patients (N=64)
	TAR-210-B ~2 mg/day (n=10)	TAR-210-D ~4 mg/day (n=11)	TAR-210-B ~2 mg/day (n=21)	TAR-210-D ~4 mg/day (n=22)	
≥1 AE	10 (100)	9 (82)	20 (95)	15 (68)	54 (84)
≥1 TRAE[a]	9 (90)	5 (55)	9 (43)	6 (27)	30 (47)
Hematuria	5 (50)	2 (18)	7 (33)	4 (18)	18 (28)
Dysuria	4 (40)	2 (18)	4 (19)	2 (9)	12 (19)
Micturition urgency	2 (20)	1 (9)	5 (24)	0	8 (13)
UTI	0	1 (9)	3 (14)	1 (5)	5 (8)
Urethral pain	1 (10)	1 (9)	1 (5)	0	3 (5)
Cystitis noninfective	0	0	1 (5)	1 (5)	2 (3)
≥1 TRAE of grade ≥2	3 (30)	3 (27)	6 (29)	2 (9)	14 (22)

AE, adverse event; TRAE, treatment-related adverse event; UTI, urinary tract infection.
[a]Listed are AEs related to TAR-210 by preferred term that were reported in >1 patient in either cohort.

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Conclusions: First-in-Human TAR-210 in HR and IR NMIBC

- TAR-210 shows **promising clinical activity** in patients with *FGFR*-altered HR and IR NMIBC
  - In BCG-experienced HR NMIBC (Cohort 1), estimated 12-month RFS rate was **90% (95% CI, 66-97)**
    - With 2 recurrence events and a median follow-up of 8.9 months, the median RFS was not reached
  - In IR NMIBC (Cohort 3), **90% (95% CI, 74-98)** of patients achieved a CR at Week 12
    - 86% of CRs are ongoing at time of clinical cutoff
- TAR-210 provided high erdafitinib concentrations in urine with very low plasma concentrations, **limiting systemic toxicities**
  - Oral erdafitinib-associated eye and skin toxicities and hyperphosphatemia were not observed
- **The majority of TRAEs were grade 1 or 2** lower urinary tract AEs, with low rates of treatment discontinuation (3%) due to TRAEs

Based on these first-in-human results, the phase 3 MoonRISe-1 study in *FGFR*-altered intermediate-risk NMIBC has been initiated
(Li R, et al. *Presented in the Learning Lab this morning*)

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Acknowledgments

https://www.congresshub.com/Oncology/AUA2024/TAR-210/Vilaseca
The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

- We thank the patients who participated in the study, their families, and the investigators and clinical research staff from the study centers

- This study was sponsored by Janssen Research & Development LLC, a Johnson & Johnson company

- Erdafitinib was discovered in collaboration with Astex Pharmaceuticals

- Editorial support was provided by Nicolisha Narainpersad, PhD, of Parexel and funded by Janssen Global Services, LLC