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Urine-Based Molecular Testing Identifies *FGFR* Alteration–Positive Patients for Treatment With TAR-210

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Key Takeaway

Patients with *FGFR*-altered NMIBC were successfully identified using urine testing during recruitment in the first-in-human clinical study of TAR-210, a novel erdafitinib intravesical system that provides locally sustained release of erdafitinib in the bladder

Conclusions

Urine testing for *FGFR*alt allowed identification of additional patients with NMIBC. This is particularly valuable when a result could not be obtained from the tissue sample submitted in parallel

Rates of *FGFR*alts, overall and specific type of alt, identified in urine were generally comparable with those of *FGFR*alts identified in tissue

All patients identified through urine samples were recurrence free (HR NMIBC) or achieved a complete response (IR NMIBC) at the data cutoff

These findings support the use of urine testing during patient selection in the recently initiated phase 3 study (MoonRISe-1, NCT06319820)

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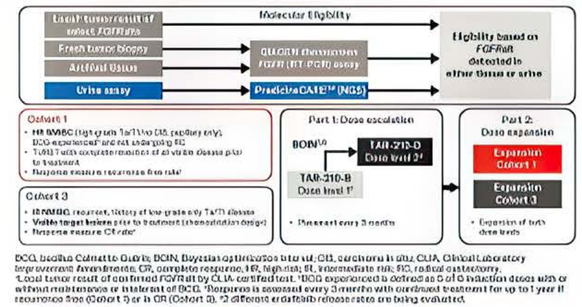
Introduction

- Between 50% and 80% of patients with non–muscle-invasive bladder cancer (NMIBC) have alterations in fibroblast growth factor receptor (*FGFR*) genes that may be oncogenic drivers in bladder cancer[1-3]
- Erdafitinib is a selective pan-FGFR tyrosine kinase inhibitor[4] approved for the treatment of patients with locally advanced or metastatic urothelial cancer with susceptible *FGFR* alterations (*FGFR*alt) after ≥1 prior systemic treatment[5]
- TAR-210 is a novel erdafitinib intravesical releasing system that provides local, sustained delivery of erdafitinib within the bladder[6]
  - TAR-210 is being evaluated in a first-in-human clinical study (NCT05316155) in patients with early-stage bladder cancer whose tumors harbor select *FGFR*alts[6] (Figure 1)
- Effective identification of NMIBC with select *FGFR*alts may be hindered by limited tumor material for tissue-based tests
  - To overcome this challenge, a urine-based assay was implemented alongside the molecular screening strategy for tissue samples
  - Here we report early results of *FGFR*alt detection via the urine assay for patient selection

Methods

- Bladder tumor samples were tested via QIAGEN *therascreen*® FGFR reverse transcription polymerase chain reaction (RT-PCR) assay and urine samples via PredicineCARE™ next-generation sequencing (NGS) assay (152 gene panel including *FGFR1-4*)
- Detection of select *FGFR*alts by either test was sufficient for molecular eligibility

Figure 1: First-in-human TAR-210 study design



BCG, Bacillus Calmette-Guérin; BOIN, Bayesian optimization interval; CIS, carcinoma in situ; CLIA, Clinical Laboratory Improvement Amendments; CR, complete response; HR, high risk; IR, intermediate risk; RC, radical cystectomy. †Local tumor result of confirmed FGFRalt by CLIA-certified test. ‡BCG experienced is defined as ≥ 5 of 6 induction doses with or without maintenance or intolerant of BCG. §Response is assessed every 3 months with continued treatment for up to 1 year if recurrence free (Cohort 1) or in CR (Cohort 3). *2 different erdafitinib release rates are being evaluated.

Results

Detection of *FGFR*alts in Tissue and Urine During Screening

- Overall, the *FGFR*alt+ rate and frequency of type of alteration identified by urine were generally comparable with those identified in tissue (Table 1)
  - In Cohort 1, 36.5% of tissue and 32.3% of urine samples yielded an *FGFR*alt+ result
  - In Cohort 3, 71.8% of tissue and 55.1% of urine samples yielded an *FGFR*alt+ result
  - The most prevalent *FGFR*alt detected across both cohorts and sample types was *FGFR3* S249C

Table 1: *FGFR*alts detected by tissue and urine testing in screened patients in Cohort 1 and Cohort 3

Patients With *FGFR*alts, n (%)	Cohort 1 HR NMIBC		Cohort 3 IR NMIBC	
Number of samples that yielded an *FGFR*alt test result	Tissue (n=63)	Urine (n=65)	Tissue (n=103)	Urine (n=89)
*FGFR*alt+ (within samples that yielded a result), n (%)	23 (36.5)	21 (32.3)	74 (71.8)	49 (55.1)
Number of samples with single *FGFR*alts detected	n=23	n=19	n=69	n=46
Single *FGFR*alts detected, n (%)				
FGFR3 S249C	17 (73.9)	12 (57.1)	33 (44.6)	26 (51.0)
FGFR3 R248C	2 (8.7)	0	8 (10.8)	5 (10.2)
FGFR3 Y373C	2 (8.7)	5 (23.8)	24 (32.4)	13 (26.5)
FGFR3 G370C	0	0	3 (4.1)	0
FGFR3 S371C	0	1 (4.8)	0	1 (2.0)
FGFR3-TACC3 (fusion)	2 (8.7)	1 (4.8)	1 (1.4)	2 (4.1)
Number of samples with multiple *FGFR*alts detected	n=0	n=2	n=5	n=3
Multiple *FGFR*alts detected, n (%)				
S249C & Y373C	0	1 (4.8)	2 (2.7)	0
R248C & Y373C	0	0	1 (1.4)	0
S249C & G370C	0	0	1 (1.4)	0
R248C & S249C & Y373C	0	0	1 (1.4)	0
S249C & R248C	0	0	0	1 (2.0)
S249C & M238I	0	0	0	1 (2.0)
S249C & S371C	0	0	0	1 (2.0)
S249C & L324V	0	1 (4.8)	0	0

Baseline Characteristics of Enrolled Patients

- At the March 22, 2024, data cutoff, 21 patients with HR NMIBC and 43 patients with IR NMIBC had been treated with TAR-210 in Cohort 1 and Cohort 3, respectively (Table 2)

Table 2: Baseline demographic and disease characteristics of patients in Cohort 1 and Cohort 3

Characteristic, n (%)*	Cohort 1 HR NMIBC (N=21)	Cohort 3 IR NMIBC (N=43)
Age, median (range), y	73.0 (62-90)	67.0 (41-89)
Sex, male	15 (71.4)	34 (79.1)
Race		
White	17 (81.0)	26 (60.5)
Asian	4 (19.0)	17 (39.5)
Tumor grade		
N	21	42
High grade	21 (100)	0
Low grade	0	42 (100)
ECOG PS		
0	13 (61.9)	34 (79.1)
1	5 (23.8)	6 (14.0)
2	3 (14.3)	3 (7.0)
Tumor stage at baseline†		
Ta	16 (76.2)	40 (95.2)
T1	5 (23.8)	2 (4.8)
Multiple tumors‡	9 (42.9)	18 (42.8)
Prior BCG	21 (100.0)	9 (20.9)
Prior intravesical therapy	2 (9.5)	22 (51.2)
Prior TURBT and tumor ablative procedures, median (range)	4 (1-12)	2 (1-14)

ECOG PS, Eastern Cooperative Oncology Group performance status; TURBT, transurethral resection of bladder tumor.
*Unless otherwise stated. †Cohort 3 n=42; data were unavailable for 1 patient at the dataset cutoff.

Efficacy of TAR-210 by Enrolled Sample Type

- As of March 22, 2024, a total of 21 patients with HR NMIBC and 31 with IR NMIBC were efficacy evaluable
  - Among those enrolled, 28.6% with HR NMIBC and 29.0% with IR NMIBC were enrolled based on urine samples only (Figure 2)
- All 6 patients (100%) with HR NMIBC enrolled by urine samples only were recurrence free at data cutoff; 85.7% enrolled based on tissue samples only were recurrence free (Figure 3)
- All 9 patients (100%) with IR NMIBC enrolled by urine samples only had a CR at the first disease evaluation at 3 months; 92.9% enrolled based on tissue samples had CR (Figure 4)

Figure 2: Urine testing complements tissue testing for enrollment among patients in Cohort 1 and efficacy-evaluable patients in Cohort 3

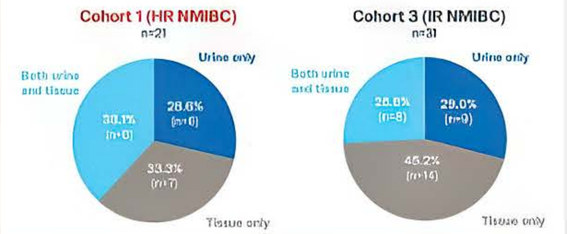
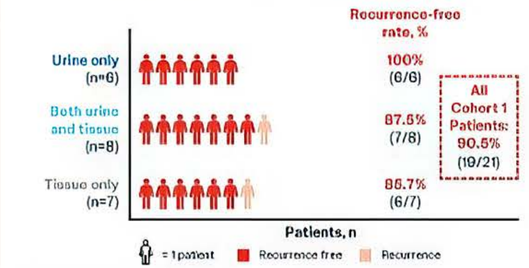
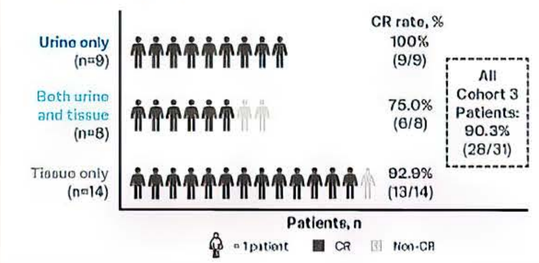


Figure 3: Proportion of patients with HR NMIBC (Cohort 1) who were recurrence free by enrolled sample type[a]



[a]All treated patients were efficacy evaluable.

Figure 4: Proportion of patients with IR NMIBC (Cohort 3) with CR at 3-month evaluation by enrolled sample type[a]



[a]Efficacy-evaluable patients were those having at least 1 disease evaluation or discontinuing treatment prior to their first disease evaluation for other progressive disease or recurrence.

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