Phase 2 Study of the Efficacy and Safety of Erdafitinib in Patients With Bacillus Calmette-Guérin (BCG)-Unresponsive, High-Risk Non–Muscle-Invasive Bladder Cancer (HR-NMIBC) With *FGFR3/2* Alterations (*alt*) in THOR-2: Cohort 2 Interim Analysis Results

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INTRODUCTION

- Patients presenting with NMIBC carcinoma in situ (CIS) have a high risk of progression[1,2]
- FGFR inhibition may benefit patients with CIS with *FGFRalt* who are unresponsive to first-line BCG, for whom treatment options, other than radical cystectomy, are limited[3-5]
  - Data are limited in patients with CIS only, but in the broader NMIBC population the prevalence of *FGFR3alt* is up to 80%[6]
- Erdafitinib, an oral selective pan-FGFR tyrosine kinase inhibitor, is approved for locally advanced or metastatic urothelial cancer in adults with susceptible *FGFR3/2alt* who have progressed during or after ≥1 line of platinum-containing chemotherapy[7-9]
- THOR-2 (NCT04172675) is a multicohort phase 2 study of erdafitinib in patients with HR-NMIBC (Figure 1)

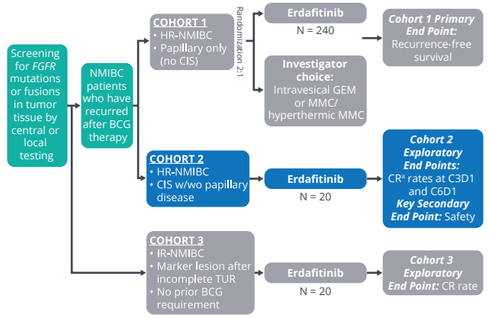
OBJECTIVES

- To report efficacy and safety results from Cohort 2 of the THOR-2 study, an exploratory cohort of patients with BCG-unresponsive CIS with *FGFRalt* with or without papillary disease

METHODS

- Inclusion criteria: age ≥18 years, histologically confirmed, BCG-unresponsive HR-NMIBC with *FGFR3/2alt* (by local/central testing) presenting as CIS, with or without a papillary tumor, and refusal or ineligibility for cystectomy
- Patients received continuous oral erdafitinib 6 mg once daily without uptitration in 28-day cycles (for this patient population, dose was selected to improve tolerability while maintaining activity to prevent disease recurrence)
- Erdafitinib was discontinued if no complete response (CR) was observed within 3 months

FIGURE 1: THOR-2 study design (Cohort 2 presented herein)



Stratifications: Tumor type (Ta vs T1) and type of prior BCG therapy (BCG-unresponsive vs BCG-experienced)

C3D1, Cycle 3 Day 1; C6D1, Cycle 6 Day 1; GEM, gemcitabine; IR, intermediate risk; MMC, mitomycin C; TUR, transurethral resection.
[a]CR was defined as at least 1 of the following: 1) negative cystoscopy and negative (including atypical) urine cytology, or 2) positive cystoscopy with biopsy-proven benign or low-grade NMIBC and negative cytology.

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RESULTS

Patients

- As of the data cutoff (September 2022), 10 patients have received erdafitinib
  - Median follow-up from first dose was 9.2 months and patients received erdafitinib for a median duration of 5.9 months (range, 1.1-17.0)
- Median age was 72 years (range, 52-83) and 90% of patients had CIS (Table 1)

TABLE 1: Baseline and disease characteristics

Characteristic	ITT population, n=10
Age, median (range), years	72 (52-83)
Sex, n (%)	
Male	9 (90)
Female	1 (10)
Race, n (%)	
Asian	2 (20)
Black or African American	1 (10)
White	5 (50)
Unknown	2 (20)
Ethnicity, n (%)	
Not Hispanic or Latino	8 (80)
Unknown	2 (20)
Geographic region, n (%)	
Europe	6 (60)
North America	1 (10)
Rest of the world	3 (30)
Tumor stage, n (%)	
Ta[a]	1 (10)
CIS	9 (90)
Baseline ECOG PS, n (%)	
0	6 (60)
1	4 (40)
FGFR alteration type, n (%)	10 (100)
Specific *FGFR3* mutation	7 (70)
S249C	3 (30)
Y373C	0
R248C	0
G370C	0
Specific gene fusions[b]	

ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intent-to-treat. [a]1 patient with Ta was misenrolled. [b]Gene fusions screened: *FGFR2:BICC1*, *FGFR2:CASP7*, *FGFR3:BAIAP2L1*, *FGFR3:TACC3_V1*, *FGFR3:TACC3_V3*, *FGFR3:TACC3_Other*.

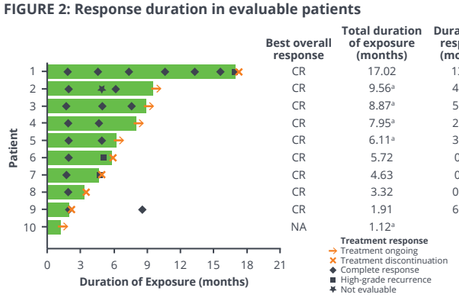
Efficacy

- Among 10 enrolled patients, at first evaluation (C3D1) the CR rate was 100% (9/9 evaluable patients) and at second evaluation (C6D1) it was 75% (6/8 evaluable patients)
  - The median duration of response (DOR) has not yet been reached; 6 of 9 patients' responses are ongoing at data cutoff (Figure 2)

Safety

- Tables 2 and 3 show safety summary and the most common treatment-emergent adverse events (TEAEs) related to treatment, respectively
- Among AEs of special interest, 1 patient (10%) had grade 2 retinal detachment that led to treatment discontinuation and 1 patient (10%) had grade 1 subretinal fluid; both events were resolved

FIGURE 2: Response duration in evaluable patients



[a]Patient is still on treatment. [b]DOR for patient is currently censored.

TABLE 2: Safety summary

TEAE summary	n (%)
TEAEs any grade	10 (100)
Treatment related	10 (100)
Grade ≥3 TEAEs	4 (40)
Treatment related	3 (30)
Serious TEAEs	2 (20)
Treatment related	1 (10)
TEAEs leading to treatment discontinuation	2 (20)
Treatment related	1 (10)
TEAEs leading to dose reduction/interruption[a]	4 (40)/6 (60)

[a]All TEAEs leading to dose reduction/interruption were treatment-related.

TABLE 3: Most common treatment-related TEAEs

TEAE by preferred term	Any grade (≥40%) n (%)	Grade ≥3 (all events) n (%)
Dry mouth	6 (60)	1 (10)
Diarrhea	5 (50)	0
Hyperphosphatemia	5 (50)	0
Dysgeusia	5 (50)	0
Stomatitis	4 (40)	1 (10)
Nail disorder	4 (40)	1 (10)
Dry skin	4 (40)	0
Onychomadesis	–	1 (10)
Acute kidney injury	–	1 (10)
Chronic kidney disease	–	1 (10)
Sepsis	–	1 (10)
Hypotension	–	1 (10)

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Presented at ASCO GU; February 16-18, 2023; San Francisco, CA, USA, and online.

KEY TAKEAWAYS

- CR rates after 3 and 6 treatment cycles were 100% and 75%, respectively, with median DOR not reached, and 6 CRs still ongoing at the last disease evaluation
- Thus far, only 1 serious treatment-related TEAE and 1 treatment-related TEAE leading to discontinuation have been observed

CONCLUSIONS

- Data from Cohort 2 of THOR-2 demonstrate antitumor activity of erdafitinib at C3D1 and C6D1 evaluations in patients with HR-NMIBC with *FGFRalt*; data from THOR-2 Cohorts 1 and 3 will be reported separately
- The study is ongoing, and the observed responses have remained consistent with the current results
- Safety data were consistent with the known safety profile of erdafitinib

ACKNOWLEDGMENTS

This project was funded by Janssen Research & Development. Erdafitinib (JNJ-42756493) was discovered in collaboration with Astex Pharmaceuticals. Medical writing assistance was provided by Ewa Wandzioch, PhD, and was funded by Janssen Global Services, LLC.

DISCLOSURES

James W.F. Catto has served as a consultant or in an advisory role for Astra Zeneca/Medimmune, Janssen, Ferring and Roche; has participated in a speakers' bureau for ASCO, Roche, AstraZeneca/ Medimmune, MSD Oncology, and Nucleix; has received travel and accommodation expenses from European Association of Urology; has received honoraria from Abbott Laboratories; and has received research funding from Roche/Genentech.

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