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ORIGINAL ARTICLE

Erdafitinib in BCG-treated high-risk non-muscle-invasive bladder cancer

J. W. F. Catto[1,2*], B. Tran[3], M. Rouprêt[4], J. E. Gschwend[5], Y. Loriot[6], H. Nishiyama[7], J. P. Redorta[8], S. Daneshmand[9], S. A. Hussain[1,2], H. J. Cutuli[10], G. Procopio[11], V. Guadalupi[11], N. Vasdev[12,13], V. Naini[14], L. Crow[15], S. Triantos[15], M. Baig[15] & G. Steinberg[16], for the THOR-2 Cohort 1 Investigators[†]

[1]Department of Oncology and Metabolism, University of Sheffield, Sheffield; [2]Sheffield Teaching Hospitals NHS Trust, Sheffield, UK; [3]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; [4]Department of Urology, GRC 5 Predictive Onco-Uro, Hôpital Pitié-Salpêtrière, Sorbonne University, Paris, France; [5]Department of Urology, School of Medicine and Health, Technical University of Munich, Munich, Germany; [6]Department of Cancer Medicine, INSERM U981, Gustave Roussy, Université Paris-Saclay, Villejuif, France; [7]Department of Urology, Institute of Medicine, University of Tsukuba, Tsukuba, Japan; [8]Department of Urology, Fundació Puigvert, Universitat Autònoma de Barcelona, Barcelona, Spain; [9]Department of Urology, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, USA; [10]Uro-oncology and Research Unit, Sirio Libanes Hospital, Buenos Aires, Argentina; [11]Oncologia Medica Genitourinaria, Fondazione IRCCS Istituto Nazionale Tumori Milano, Milan, Italy; [12]Hertfordshire and Bedfordshire Urological Cancer Centre, Lister Hospital, East and North Herts NHS Trust, Stevenage; [13]School of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK; [14]Janssen Research & Development, San Diego; [15]Janssen Research & Development, Spring House; [16]Department of Urology, Rush University Medical Center, Chicago, USA

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Background: Treatment options are limited for patients with high-risk non-muscle-invasive bladder cancer (NMIBC) with disease recurrence after bacillus Calmette—Guérin (BCG) treatment and who are ineligible for/refuse radical cystectomy. *FGFR* alterations are commonly detected in NMIBC. We evaluated the activity of oral erdafitinib, a selective pan-fibroblast growth factor receptor (FGFR) tyrosine kinase inhibitor, versus intravesical chemotherapy in patients with high-risk NMIBC and select *FGFR3/2* alterations following recurrence after BCG treatment.

Patients and methods: Patients aged ≥18 years with recurrent, BCG-treated, papillary-only high-risk NMIBC (high-grade Ta/T1) and select *FGFR* alterations refusing or ineligible for radical cystectomy were randomized to 6 mg daily oral erdafitinib or investigator's choice of intravesical chemotherapy (mitomycin C or gemcitabine). The primary endpoint was recurrence-free survival (RFS). The key secondary endpoint was safety.

Results: Study enrollment was discontinued due to slow accrual. Seventy-three patients were randomized 2 : 1 to erdafitinib ($n = 49$) and chemotherapy ($n = 24$). Median follow-up for RFS was 13.4 months for both groups. Median RFS was not reached for erdafitinib [95% confidence interval (CI) 16.9 months-not estimable] and was 11.6 months (95% CI 6.4-20.1 months) for chemotherapy, with an estimated hazard ratio of 0.28 (95% CI 0.1-0.6; nominal P value = 0.0008). In this population, safety results were generally consistent with known profiles for erdafitinib and chemotherapy.

Conclusions: Erdafitinib prolonged RFS compared with intravesical chemotherapy in patients with papillary-only, high-risk NMIBC harboring *FGFR* alterations who had disease recurrence after BCG therapy and refused or were ineligible for radical cystectomy.

Key words: erdafitinib, FGFR, intravesical chemotherapy, non-muscle-invasive bladder cancer, recurrence-free survival, safety

INTRODUCTION

The standard of care for patients with high-risk, papillary, non-muscle-invasive bladder cancer (NMIBC) is complete transurethral resection of papillary tumor followed by intravesical bacillus Calmette—Guérin (BCG) treatment.[1-3] Even after adequate BCG treatment, however, recurrence is frequent (12%-78%) and progression rates are high (up to 46%).[4-6]

Radical cystectomy is considered the standard of care for patients with high-risk NMIBC who have recurrence after BCG treatment.[1-3] It is associated, however, with high morbidity (>60% of patients develop complications),[7] mortality (perioperative mortality rate, 2%),[8] significant impact on health-related quality of life, and persistent functional impairments, including the likely need for an ileal conduit.[9,10] Additionally, many patients are ineligible for radical cystectomy because of advanced age, frailty, comorbidities, and complication risks.[11,12]

*Correspondence to: Prof. James W. F. Catto, Department of Oncology and Metabolism, University of Sheffield, GU19, G Floor, The Medical School, Sheffield, UK. Tel: +44-114-215-9002

E-mail: j.catto@sheffield.ac.uk (J. W. F. Catto).

†THOR-2 Cohort 1 Investigators are listed in the Supplementary Appendix, available at https://doi.org/10.1016/j.annonc.2023.09.3116.

Consequently, there remains a high unmet need in the high-risk NMIBC population with recurrence after BCG treatment and who are ineligible for or refuse radical cystectomy, as treatment options are limited. Pembrolizumab is approved for BCG-refractory carcinoma *in situ* (CIS).[13] To date, however, there are no approved targeted therapies for the BCG-treated high-risk papillary NMIBC population.[1,2]

Fibroblast growth factor receptor (*FGFR3/2*) gene alterations (mutations and fusions) are found in 60%-70% of individuals with low-risk NMIBC[14] and in 31% or more of those with high-risk papillary NMIBC,[15-17] and may function as oncogenic drivers.[17] Erdafitinib is an oral selective pan-fibroblast growth factor receptor (FGFR) tyrosine kinase inhibitor.[18] On the basis of results from the phase II BLC2001 trial, erdafitinib was granted accelerated approval in the United States and 18 other countries to treat adults with locally advanced or metastatic urothelial carcinoma with susceptible *FGFR3/2* alterations that has progressed after platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.[19-21] More recently, a phase III randomized clinical trial demonstrated superior median overall survival for erdafitinib versus standard chemotherapy in patients with *FGFR*-altered advanced urothelial carcinoma after prior checkpoint inhibitor treatment.[22]

THOR-2 (clinical trial number NCT04172675) is a randomized, multicohort phase II trial of erdafitinib in patients with NMIBC. Cohort 1 assessed whether erdafitinib improved recurrence-free survival (RFS) over intravesical chemotherapy in patients with recurrent, BCG-treated, papillary-only, high-risk NMIBC harboring select *FGFR3/2* alterations who refused or were ineligible for radical cystectomy. Cohorts 2 and 3 were exploratory, enrolled patients with BCG-unresponsive CIS with/without papillary disease and patients with intermediate-risk NMIBC, respectively, and will be reported separately.

METHODS

Study design and oversight

This ongoing study, including 150 sites in 17 countries, was designed by the sponsor, Janssen Research & Development. The study was conducted in accordance with current Good Clinical Practice guidelines of the International Conference on Harmonisation, applicable regulatory and country-specific requirements, and the principles of the Declaration of Helsinki, and was approved by review boards at all participating institutions. Written informed consent was provided by all patients.

An independent data monitoring committee was commissioned by the sponsor to review safety data at 6-month intervals and make recommendations regarding study conduct. Data captured by study site personnel were used to prepare case report forms in a database system managed by the sponsor.

Patients

Eligible patients were adults with histologically confirmed recurrent, BCG-treated, papillary-only high-risk NMIBC (high-grade Ta/T1) and select *FGFR3/2* alterations, an Eastern Cooperative Oncology Group performance status score of 0 or 1, adequate organ function, and either refused or were ineligible for radical cystectomy. Patients had transurethral resection of all visible papillary tumors before study entry. Central laboratory testing or local tissue-based historical testing was used to confirm molecular eligibility. Patients were required to have at least one of the following *FGFR3* gene mutations: R248C, S249C, G370C, Y373C, or at least one of the following *FGFR2* or *FGFR3* gene fusions: *FGFR2-BICC1*, *FGFR2-CASP7*, *FGFR3-TACC3*, *FGFR3-BAIAP2L1*. Additionally, patients had to be BCG-unresponsive or BCG-experienced. BCG-unresponsive was defined as experiencing recurrent high-grade Ta/T1 disease within 6 months of completion of adequate BCG therapy, or T1 high-grade at the first disease assessment following an induction BCG course. BCG-experienced was defined as reporting recurrent high-grade Ta/T1 disease within 12 months of completion of BCG therapy (expanded definitions are in Supplementary Table S1, available at https://doi.org/10.1016/j.annonc.2023.09.3116). Exclusion criteria included previous treatment with an FGFR inhibitor and active malignancies other than NMIBC.

Cohort 1 was designed to enroll ∼240 patients, but enrollment for this study was terminated in December 2022 due to poor accrual. Reasons for slow accrual included the COVID-19 pandemic, intermittent global shortage of BCG leading to patients not receiving adequate BCG as defined in protocol, limited tumor tissue availability in the NMIBC population resulting in molecular testing challenges, and concern from urologists and patients about potential systemic toxicities.

Treatment

Patients were randomized 2 : 1 to receive oral erdafitinib or investigator's choice of intravesical chemotherapy (Supplementary Figure S1, available at https://doi.org/10.1016/j.annonc.2023.09.3116). Erdafitinib dosing was 6 mg daily without uptitration in 28-day cycles for a maximum of 2 years. Initially, patients received erdafitinib 8 mg daily with individualized uptitration. The independent data monitoring committee reviewed safety data from the first four patients treated with erdafitinib and recommended changing the dose to 6 mg daily, without uptitration, aiming to improve tolerability and maintain activity while preventing early treatment discontinuation. Intravesical chemotherapy comprised instillations of mitomycin C/hyperthermic mitomycin C 40 mg or gemcitabine 2000 mg once weekly for at least four induction doses followed by monthly maintenance for at least 6 months. Additional doses of intravesical chemotherapy were allowed per local standard of care. Gemcitabine and mitomycin C were selected as comparators to erdafitinib in this setting based

on treatment guidelines and clinical data.[1,23,24] Patients with confirmed high-risk recurrence in the chemotherapy group were allowed to cross over to erdafitinib. Randomization was stratified by tumor stage (Ta versus T1) and type of prior BCG therapy (BCG-unresponsive versus BCG-experienced). Due to termination of cohort 1 enrollment and the smaller than planned sample size, however, the primary analysis was unstratified for RFS.

Endpoints

The primary endpoint was RFS, defined as the time from randomization to reappearance of histologically proven high-risk disease (high-grade Ta/T1 or CIS) or death. Secondary and exploratory endpoints included RFS rate at 6 and 12 months, safety, time to progression, overall survival, and time to cystectomy. Efficacy endpoints of time to progression, time to cystectomy, and overall survival were not assessed due to insufficient number of observed events at clinical cut-off.

Assessments

Disease response was assessed by cystoscopy, bladder mapping (if prior history of CIS), urine cytology, and a computed tomography/magnetic resonance imaging urogram. Cystoscopy was carried out at cycle 3 day 1, then every 12 weeks for up to 2 years of treatment and thereafter every 24 weeks for an additional 2 years or until high-risk disease recurrence or progression. Adverse events were recorded from date of informed consent through end of the 30-day safety follow-up period and graded using the National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0. Ophthalmologic examinations (including optical coherence tomography and Amsler grid test) were carried out at screening and at prespecified timepoints during treatment.

Statistical analysis

Cohort 1 was designed to enroll ∼240 patients (randomized 2 : 1) with the primary efficacy analysis planned when ∼160 RFS events were observed. This assumed statistically a 67% improvement in median RFS for the erdafitinib group over the chemotherapy group (i.e. hazard ratio of 0.60 for erdafitinib relative to chemotherapy and increased median RFS from 6 months to 10 months). Due to termination of cohort 1 enrollment and the resulting sample size of 73 patients, however, the statistical analysis plan was amended to remove all prespecified hypothesis testing. All reported *P* values are nominal. Descriptive subgroup analyses were conducted, but with no adjustment for multiplicity. The 95% confidence intervals (CIs) are presented but should not be used in place of a hypothesis test.

RESULTS

Patients

Of a total of 1092 patients screened for molecular eligibility in cohort 1, 882 (81%) had adequate tumor samples for testing, and 336 had *FGFR* alterations (positivity rate, 38%; Supplementary Table S2, available at https://doi.org/10.1016/j.annonc.2023.09.3116). Patients were screened and enrolled in cohort 1 between 6 July 2020, and 15 November 2022. At clinical cut-off of 27 June 2023, 73 patients were randomized in cohort 1: 49 to erdafitinib and 24 to chemotherapy (Figure 1). One patient in the chemotherapy group was randomized but never treated due to treatment refusal and was excluded from the safety population. At clinical cut-off, one patient (2%) in the erdafitinib group and seven (29%) in the chemotherapy group had completed study treatment; 28 patients (57%) in the erdafitinib group and 14 (58%) in the chemotherapy group had discontinued study treatment. The most frequent reasons for discontinuation were adverse events in the erdafitinib group and high-risk recurrent disease in the chemotherapy group. Baseline demographics and clinical characteristics were generally balanced between treatment groups (Table 1 and Supplementary Table S2, available at https://doi.org/10.1016/j.annonc.2023.09.3116). There were only two black patients enrolled, likely due to limited enrollment in the United States (Supplementary Table S3, available at https://doi.org/ 10.1016/j.annonc.2023.09.3116). At baseline, 57% and 58% of patients were BCG-unresponsive and 59% and 58% had tumor stage Ta in the erdafitinib and chemotherapy groups, respectively. Ninety-four percent of patients in cohort 1 had *FGFR3* mutations and 10% had *FGFR* gene fusions; *FGFR3*-S249C mutation was the most prevalent alteration, followed by *FGFR3*-Y373C mutation (Supplementary Table S4, available at https://doi.org/10.1016/j.annonc.2023.09.3116).

Efficacy

The median follow-up for RFS was 13.4 months in both treatment groups. At clinical cut-off, 25 total RFS events had occurred (11, erdafitinib; 14, chemotherapy). The Kaplan—Meier estimate of median RFS (95% CI) was not reached in the erdafitinib group (16.9 months to non-estimable) and was 11.6 months (6.4-20.1 months) in the chemotherapy group (Figure 2A and Table 2), with a hazard ratio of 0.28 (95% CI 0.1-0.6) based on a Cox proportional hazards model (nominal two-sided log-rank test *P* value = 0.0008). The 6- and 12-month RFS rates (95% CI) were 96% (83.7% to 98.9%) and 77% (60.0% to 87.4%) for erdafitinib versus 73% (50.1% to 87.1%) and 41% (18.9% to 61.7%) for chemotherapy, respectively.

Nine patients (38%) crossed over from chemotherapy to receive erdafitinib. The observed RFS benefit for erdafitinib was generally consistent across subgroups based on prior BCG therapy (BCG-experienced versus BCG-unresponsive) and tumor stage (Ta versus T1) (Figure 2B and Supplementary Table S5, available at https://doi.org/10.1016/j.annonc.2023.09.3116).

Safety

The safety analysis set comprised 72 patients, 49 in the erdafitinib group and 23 in the chemotherapy group, who

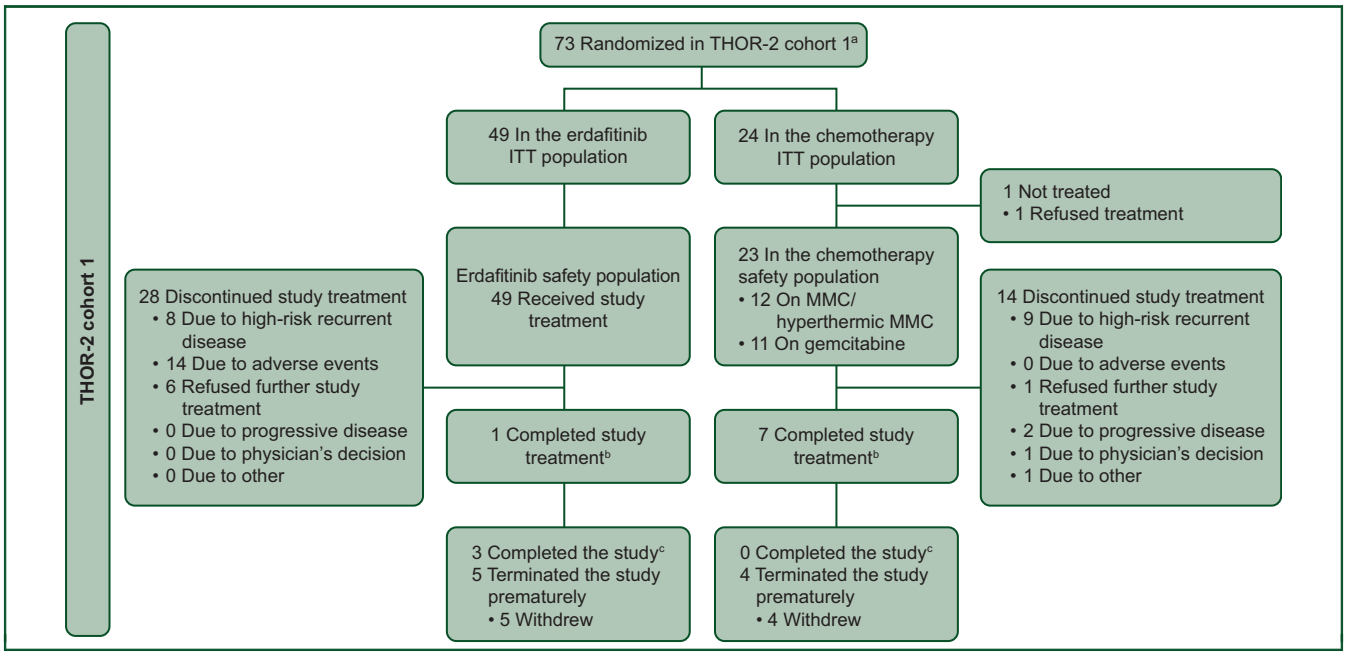

Figure 1. CONSORT diagram. THOR-2 cohort 1 study and treatment disposition.
ITT, intent-to-treat; MMC, mitomycin C.
[a]For patients who cross over from chemotherapy to erdafitinib treatment, this figure summarizes disposition before crossover.
[b]A patient was considered to have completed the study if he or she had died before the end of the study, had not been lost to follow-up, or had not withdrawn consent for study participation before the end of the study.
[c]A patient was considered as having completed treatment if he or she had completed 2 years of erdafitinib or had completed a maximum duration (minimum of at least 7 months) per local standard of care for gemcitabine or mitomycin C.

received at least one dose of study treatment. The median duration of exposure was 9.0 months (range 1.0-23.1 months) with erdafitinib and 6.4 months (range 1.1-14.2 months) with chemotherapy.

Adverse events of any cause were reported in 100% and 83% of patients in the erdafitinib and chemotherapy groups, respectively, as shown in Table 3 (overall safety in Supplementary Table S6, available at https://doi.org/10.1016/j.annonc.2023.09.3116). The most frequent grade $\geq$3 treatment-related adverse events were stomatitis (10%), nail dystrophy (4%), and glossitis (4%) in the erdafitinib group and alanine aminotransferase increased (4%) in the chemotherapy group (Supplementary Table S7, available at https://doi.org/10.1016/j.annonc.2023.09.3116). Serious adverse events occurred in 11 (22%) and three (13%) patients in the erdafitinib and chemotherapy groups, respectively (Supplementary Table S8, available at https://doi.org/10.1016/j.annonc.2023.09.3116).

No treatment-emergent adverse events that led to death were reported. Three deaths occurred in the erdafitinib group after treatment discontinuation, two due to disease progression (395 and 249 days after discontinuation) and one due to secondary malignancy (recurrence of diffuse large B-cell lymphoma); all three were deemed unrelated to treatment.

Adverse events of any cause led to treatment discontinuation in 14 patients (29%) in the erdafitinib group and no patients in the chemotherapy group (Supplementary Table S9, available at https://doi.org/10.1016/j.annonc.2023.09.3116). The most frequent adverse event leading to erdafitinib discontinuation was stomatitis (6%).

Adverse events of interest based on the known safety profile of erdafitinib included nail disorders (78%), hyperphosphatemia (74%), eye disorders (excluding central serous retinopathy, 59%), skin disorders (51%), dry mouth (47%), mucositis (41%), and central serous retinopathy (39%) (Supplementary Table S10, available at https://doi.org/10.1016/j.annonc.2023.09.3116). Most central serous retinopathy adverse events were either grade 1 or 2; two patients in the erdafitinib group reported grade 3 events (at clinical cut-off, events had resolved in one patient and were resolving in the other). Central serous retinopathy events (central serous chorioretinopathy, detachment of macular retinal pigment epithelium, maculopathy, and macular detachment) led to treatment discontinuation in six patients.

DISCUSSION

A high unmet need continues to exist for patients with high-risk NMIBC and recurrence after BCG treatment who refuse or are ineligible for radical cystectomy. In this population, *FGFR3* alterations are highly prevalent (43%-57%).[25,26] The THOR-2 randomized trial represents an innovative application of precision medicine in the management of NMIBC, exploring FGFR inhibition as a treatment option for this disease. Furthermore, this study gained alignment with the Food and Drug Administration (FDA) on a new definition for BCG-experienced disease in this patient population that can be utilized in clinical trials, providing clear definitions for patients who may have been impacted by BCG shortages.

Table 1. Demographics and disease characteristics of patients at baseline

Characteristic[a]	Erdafitinib (*N* = 49)	Chemotherapy (*N* = 24)
Median age (range), years	69 (37-86)	68 (39-85)
Sex		
Male	37 (76)	19 (79)
Female	12 (25)	5 (21)
Race		
White	27 (55)	12 (50)
Asian	14 (29)	7 (29)
Black	1 (2)	1 (4)
Unknown	1 (2)	1 (4)
Not reported	6 (12)	3 (13)
Ethnicity		
Hispanic or Latino	9 (18)	5 (21)
Not Hispanic or Latino	32 (65)	15 (63)
Not reported	5 (10)	3 (13)
Unknown	3 (6)	1 (4)
Geographic region		
North America	6 (12)	0
Europe	20 (41)	11 (46)
Asia	14 (29)	7 (29)
South America	9 (18)	6 (25)
Prior BCG therapy		
Unresponsive	28 (57)	14 (58)
Experienced	21 (43)	10 (42)
ECOG performance status[b]		
0	39 (80)	20 (83)
1	10 (20)	4 (17)
Tumor stage		
Ta	29 (59)	14 (58)
T1	20 (41)	10 (42)
FGFR alterations[c,d]		
FGFR3 mutations	46 (94)	22 (96)
FGFR gene fusions	6 (12)	1 (4)

Data are *n* (%) except where noted.
BCG, bacillus Calmette—Guérin; ECOG, Eastern Cooperative Oncology Group.
[a]*N* for each parameter reflects non-missing values. Percentages are calculated with the number of patients in each treatment group with available data as denominator.
[b]Scores on the ECOG scale range from 0 (no disability) to 5 (death).
[c]One patient was found to have a false-positive QIAGEN test and received chemotherapy.
[d]Patients could have both *FGFR3* mutations and gene fusions.

At median follow-up of 13.4 months, median RFS was not reached in the erdafitinib group and was 11.6 months in the chemotherapy group, resulting in a hazard ratio of 0.28. The observed hazard ratio reflects prolonged RFS for erdafitinib treatment compared with standard of care chemotherapy in patients with papillary-only high-risk NMIBC with select *FGFR* alterations and disease recurrence after BCG therapy who either refused or were ineligible for radical cystectomy. The RFS curves show a clear, early separation supporting an early clinical benefit, with continued separation of curves over longer follow-up. By ~15 months, the RFS curves show sustained disease control with erdafitinib. Notably, the RFS benefit of erdafitinib over chemotherapy was consistent across subgroups assessed, including prior BCG therapy (BCG-experienced versus BCG-unresponsive) and tumor stage (Ta versus T1). These phase II results demonstrate the clinical benefit of erdafitinib compared with intravesical chemotherapy in patients with papillary-only high-risk NMIBC harboring *FGFR* alterations who had disease recurrence after BCG therapy.

In this patient population, the safety results were consistent with the known safety profiles for erdafitinib and intravesical chemotherapy, with no new safety signals observed. The higher rates of adverse events and grade ≥3 treatment-related adverse events noted with erdafitinib were consistent with the on-target effect of FGFR inhibition, mechanism of action, and systemic exposure to erdafitinib. Most adverse events in the erdafitinib group were grade 1 or 2 and were managed with dose reductions and interruptions. Discontinuation due to treatment-related adverse events was more frequent with erdafitinib (29%) compared with intravesical chemotherapy (0%). No treatment-related deaths were reported in either group; however, three deaths unrelated to treatment occurred after discontinuation in the erdafitinib group.

Of note, central serous retinopathy events, a known class effect of FGFR inhibitors, were more frequent in the erdafitinib group in this study (at 6 mg daily) than previously reported for erdafitinib at 8 mg with uptitration in patients with locally advanced or metastatic urothelial cancer (39% versus 27%),[21] possibly as a result of proactive surveillance with optical coherence tomography regardless of symptoms and longer duration of treatment in this study. Most events of central serous retinopathy had resolved at the time of the clinical cut-off.

The rate of erdafitinib discontinuation in this NMIBC population was higher than in previously reported clinical studies of erdafitinib in patients with locally advanced or metastatic urothelial cancer (29% versus 16%),[21] highlighting the lower tolerance to adverse events in the localized disease setting of NMIBC compared with metastatic urothelial cancer and the challenges associated with managing NMIBC with systemic therapies.[27] Treatment discontinuation rates of 16%-29% due to systemic toxicity have been reported in patients with NMIBC.[28,29] Despite the rate of erdafitinib treatment discontinuation and high rate of dose reductions and interruptions, however, clear reduction in recurrence of disease was observed with erdafitinib in this patient population, suggesting early and sustained therapeutic benefit of erdafitinib.

Of the first four patients treated with 8 mg daily erdafitinib with uptitration to 9 mg, three interrupted erdafitinib for grade 2 toxicities and two of those discontinued erdafitinib (one for grade 2 toxicity), highlighting the low acceptability of systemic toxicity in patients with NMIBC. The 6 mg dose of erdafitinib (without uptitration), which is lower than the approved starting dose for metastatic disease,[19] had previously demonstrated antitumor activity in patients with metastatic disease in the 6 mg dose cohort of the BLC2001 trial ($n = 78$; objective response rate, 35%).[20] The 6 mg dose in this study resulted in manageable toxicity with preserved efficacy, with a median duration of treatment of 9.0 months for erdafitinib. In the metastatic setting, antitumor activity was observed with erdafitinib at the 6 mg

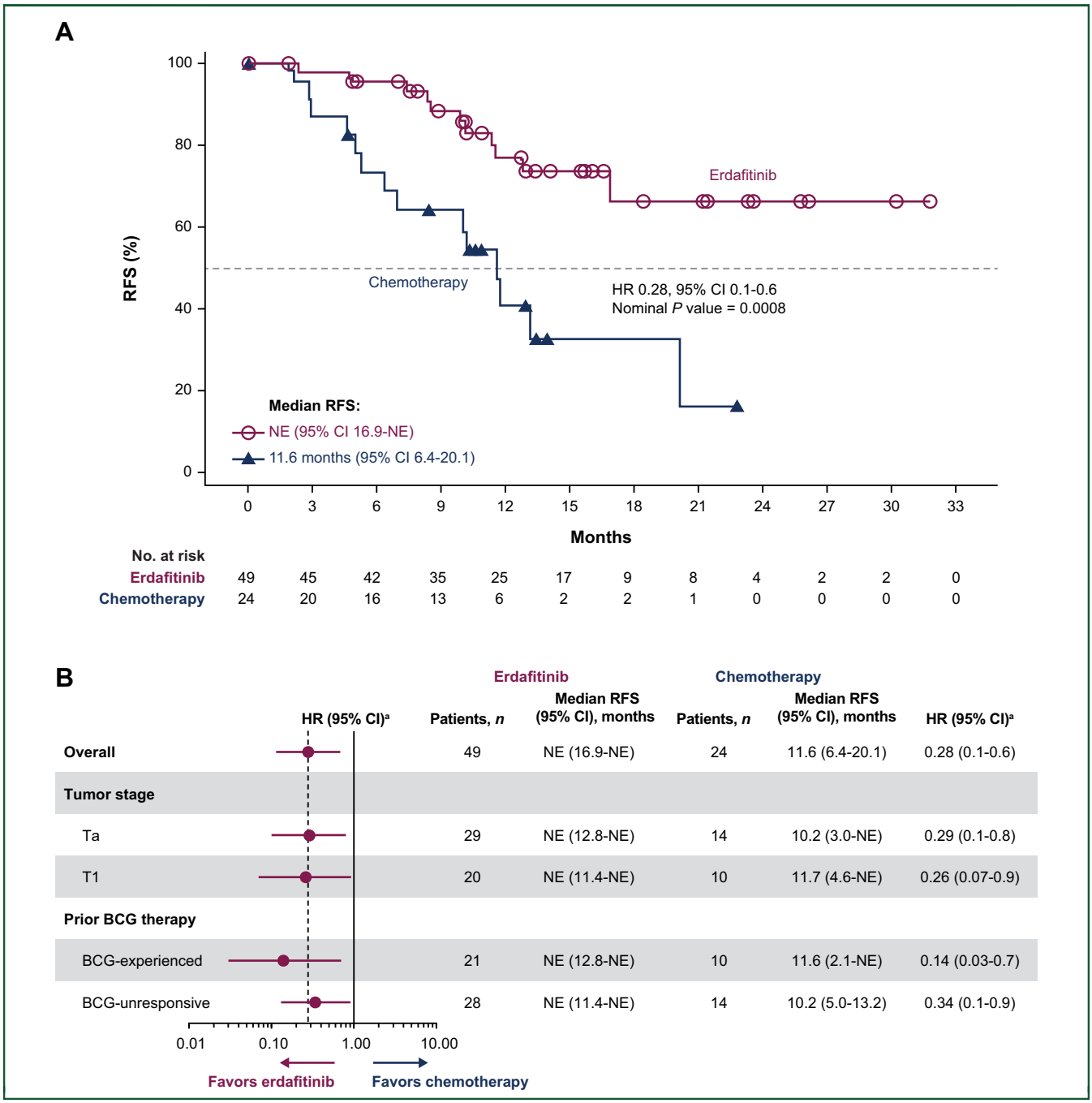

Figure 2. Recurrence-free survival. Kaplan–Meier estimate of recurrence-free survival by treatment group (panel A). Recurrence-free survival in subgroups (panel B). Subgroups were based on prior BCG therapy (BCG-experienced versus BCG-unresponsive) and tumor stage (Ta versus T1).
BCG, bacillus Calmette–Guérin; CI, confidence interval; HR, hazard ratio; NE, non-estimable; RFS, recurrence-free survival.
[a]Hazard ratio and 95% CI were estimated using a stratified Cox proportional hazards regression model. A hazard ratio <1 indicates longer recurrence-free survival time in erdafitinib group compared with chemotherapy (gemcitabine or mitomycin) group.

dose ($n = 78$; objective response rate, 35%), and the median treatment duration for erdafitinib 8 mg with uptitration was 5.3 months.[20]

Given the observed antitumor activity of erdafitinib and the tolerability challenges noted in this study, local delivery that reduces systemic toxicities represents an opportunity to change the treatment landscape for patients with NMIBC and *FGFR* alterations. Accordingly, a first-in-human study (NCT05316155) evaluating the novel intravesical drug delivery system, TAR-210, designed to provide sustained, local release of erdafitinib within the bladder while limiting systemic exposure, is ongoing.

In conclusion, our findings demonstrate that oral erdafitinib reduced the rate of recurrence or death over intravesical chemotherapy in patients with high-risk resected papillary Ta/T1 NMIBC harboring *FGFR* mutations or fusions with recurrence after BCG treatment and who refused or were ineligible for radical cystectomy. Erdafitinib tolerability

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Table 2. Recurrence-free survival—unstratified analysis

Recurrence-free survival[a]	Erdafitinib (*N* = 49)	Chemotherapy (*N* = 24)
Number of events, *n* (%)	11 (22)	14 (58)
Number of censored, *n* (%)	38 (78)	10 (42)
Study cut-off	33 (87)	7 (70)
Subsequent anticancer therapy	1 (3)	2 (20)
Withdrawal of consent	4 (11)	1 (10)
Kaplan—Meier estimates, months		
25% Percentile (95% CI)	12.8 (8.5-NE)	5.3 (2.1-10.2)
Median (95% CI)	NE (16.9-NE)	11.6 (6.4-20.1)
75% Percentile (95% CI)	NE (NE-NE)	20.1 (11.6-NE)
Min, max	(0.0+, 31.8+)	(0.0+, 22.8+)
HR (95% CI)[b]	0.28 (0.13-0.62)	
Nominal *P* value[c]	0.0008	
6-Month survival rate (95% CI), %	96 (84-99)	73 (50-87)
12-Month survival rate (95% CI), %	77 (60-87)	41 (19-62)
24-Month survival rate (95% CI), %	66 (44-81)	NE (NE-NE)

CI, confidence interval; HR, hazard ratio; NE, non-estimable; RFS, recurrence-free survival.

[a]RFS in months was calculated as (date of RFS event or censoring − date of randomization + 1)/(365.25/12). If the patient was recurrence-free and alive or had unknown status at the cut-off date of assessment, RFS was censored at the date of last tumor assessment. Patients without post-baseline disease assessment were censored at date of randomization. Patients who withdrew consent before RFS event were censored at the last tumor assessment. Patients who were lost to follow-up were censored at the last tumor assessment before they were lost to follow-up. Patients who started subsequent anticancer therapies without RFS event were censored at the last disease assessment before the start of subsequent anticancer therapies.

[b]HR and 95% CI were estimated using a stratified Cox proportional hazards regression model. A hazard ratio of <1 indicates longer RFS time in erdafitinib group compared with the chemotherapy (gemcitabine or mitomycin) group.

[c]*P* value comparing RFS between treatment groups was based on an unstratified log-rank test.

was manageable in this patient population. Additional studies with larger patient populations and longer follow-up may be warranted.

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DISCLOSURE

JWFC has received consulting fees from AstraZeneca, Ferring, Ipsen, Roche, and Janssen; has received speaker fees from Bristol Myers Squibb, Pfizer, Merck Sharp & Dohme (MSD), Janssen, Astellas, Nucleix, and Roche; has received honoraria for membership in advisory boards from Ferring, Roche, Gilead, Photocure, Pfizer, Bristol Myers Squibb, QED Therapeutics, and Janssen; and has received research funding from Roche. BT has served as a consultant for Amgen, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Ipsen, IQVIA, Janssen-Cilag, MSD Oncology, Novartis, Pfizer/EMD Serono, Roche Molecular Diagnostics, Sanofi, and Tolmar; has received honoraria from Amgen, Astellas Pharma, Bayer, Bristol Myers Squibb, Janssen, Janssen-Cilag, Sanofi, Tolmar, and Pfizer; has received research funding (institutional) from Amgen, Astellas, AstraZeneca, Bayer Pharma, Genentech, Janssen-Cilag, and Pfizer; and has received research funding (personal) from

Table 3. Treatment-emergent adverse events in the safety population[a]

Adverse event[b]	Erdafitinib (*N* = 49)				Chemotherapy (*N* = 23)			
	Any grade	Grade 1	Grade 2	Grade ≥3	Any grade	Grade 1	Grade 2	Grade ≥3
Any adverse event	49 (100)				19 (83)			
Hyperphosphatemia	36 (74)	29 (59)	7 (14)	0	0	0	0	0
Diarrhea	27 (55)	17 (35)	9 (18)	1 (2)	3 (13)	2 (9)	1 (4)	0
Dry mouth	23 (47)	15 (31)	8 (16)	0	0	0	0	0
Stomatitis	20 (41)	7 (14)	8 (16)	5 (10)	0	0	0	0
Nail dystrophy	15 (31)	3 (6)	10 (20)	2 (4)	0	0	0	0
Dry skin	11 (22)	10 (20)	1 (2)	0	0	0	0	0
Dry eye	11 (22)	7 (14)	4 (8)	0	0	0	0	0
Dysgeusia	11 (22)	7 (14)	4 (8)	0	0	0	0	0
Constipation	10 (20)	7 (14)	2 (4)	1 (2)	1 (4)	1 (4)	0	0
Decreased appetite	10 (20)	9 (18)	1 (2)	0	0	0	0	0
Central serous chorioretinopathy	10 (20)	5 (10)	5 (10)	0	0	0	0	0
Alopecia	9 (18)	7 (14)	2 (4)	0	0	0	0	0
Onycholysis	9 (18)	2 (4)	7 (14)	0	0	0	0	0
Urinary tract infection	9 (18)	0	9 (18)	0	4 (17)	2 (9)	2 (9)	0
Fatigue	9 (18)	7 (14)	2 (4)	0	1 (4)	1 (4)	0	0
Hematuria	1 (2)	1 (2)	0	0	4 (17)	2 (9)	2 (9)	0

Data are *n* (%).

[a]Listed are adverse events of any cause by preferred term and worst toxicity grade that were reported in >15% of the patients in either treatment group. For patients who cross over from chemotherapy to erdafitinib treatment, this table summarizes adverse events before crossover.

[b]Patients are counted only once for any given event, regardless of the number of times they experienced the event. The event experienced by the patient with the worst toxicity is used. If a patient has missing toxicity for a specific adverse event, the patient is only counted in the total column for that adverse event. Adverse events are coded using MedDRA Version 26.0.

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DATA SHARING

Janssen Pharmaceutical Companies of Johnson & Johnson's data sharing policy is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for study data access can be submitted through the Yale Open Data Access (YODA) Project site at http://yoda.yale.edu.

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