

Impact of Dose Reductions on the Efficacy of Erdafitinib in Patients with Advanced or Metastatic Urothelial Carcinoma: A Post-hoc Analysis of the Phase 3 THOR Study Cohort 1 Evaluating Erdafitinib Versus Chemotherapy

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Key Takeaway



In the phase 3 THOR study of patients with advanced or metastatic urothelial carcinoma (Cohort 1), dose reductions of erdafitinib due to treatment-emergent adverse events were common and did not seem to impact efficacy, highlighting the importance of proactive toxicity management to optimize both tolerability and clinical outcomes

Conclusions



Approximately half of patients who received erdafitinib required dose reductions, most commonly due to stomatitis, palmar-plantar erythrodysesthesia, and onycholysis



Baseline characteristics of patients were not remarkably different between the subgroups of patients who had 0 vs 1 vs ≥ 2 dose reductions



Erdafitinib efficacy (OS, PFS, ORR) was sustained overall, even with frequent dose modifications

Introduction

- Erdafitinib, a pan-fibroblast growth receptor (FGFR) inhibitor, is approved for the treatment of patients with unresectable or metastatic urothelial carcinoma (mUC) harboring susceptible *FGFR3* genetic alterations, which progressed on/after ≥ 1 line of a PD-(L)1 inhibitor in the unresectable or metastatic treatment setting¹
- This approval is based on the primary results of the phase 3 THOR study demonstrating significantly longer overall survival (OS) with erdafitinib versus investigator's choice of chemotherapy²
 - At a median follow-up of 15.9 months, median OS was 12.1 months with erdafitinib versus 7.8 months with chemotherapy (hazard ratio [HR], 0.64; 95% CI, 0.47–0.88; $P=0.005$)
- In THOR, dose reductions of erdafitinib were permitted to manage adverse events (AEs)
- Here, we assess the impact of erdafitinib dose reductions on efficacy outcomes in the THOR study

Methods

- THOR was a phase 3, randomized, open-label, global study
- Patients eligible for Cohort 1 were adults ≥ 18 years with advanced or mUC and select *FGFR3/2* alterations; with ECOG performance-status score of ≤ 2 ; and progression during or after 1 or 2 previous systemic therapy that included an anti-PD-(L)1 agent
- Patients were randomized 1:1 to receive erdafitinib (8 mg once daily from Day 1 to Day 14 of Cycle 1, with the option to up-titrate to 9 mg based on serum phosphate levels on Day 14 of Cycle 1) or investigator's choice of chemotherapy (docetaxel or vinflunine; **Figure 1**)
- In this exploratory analysis, OS, progression-free survival (PFS), and objective response rate (ORR) were evaluated by number of erdafitinib dose reductions (0, 1, or ≥ 2)
 - Erdafitinib dose reduction was defined as any decrease from 8 mg to ≤ 6 mg

Figure 1: THOR Cohort 1 study design

Cohort 1

Key Eligibility Criteria

- Age ≥ 18 years
- Metastatic or unresectable UC
- Disease progression
- Prior treatment with anti-PD-(L)1
- 1–2 lines of systemic therapy
- Select *FGFR3/2* alterations (mutations or fusions)
- ECOG PS 0–2

Stratification factors:

- Region (North America vs Europe vs rest of world), ECOG PS (0 or 1 vs 2), and disease distribution (presence vs absence of visceral [lung, liver, or bone] metastases)

ECOG PS, Eastern Cooperative Oncology Group performance status; FGFR, fibroblast growth factor receptor; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; UC, urothelial carcinoma.

Erdafitinib

Once-daily erdafitinib 8 mg with pharmacodynamically guided up-titration to 9 mg

Investigator's choice of chemotherapy

Docetaxel or vinflunine once every 3 weeks

Endpoints

Primary: OS

Key secondary endpoints: PFS, ORR (both investigator-assessed per RECIST v1.1); safety

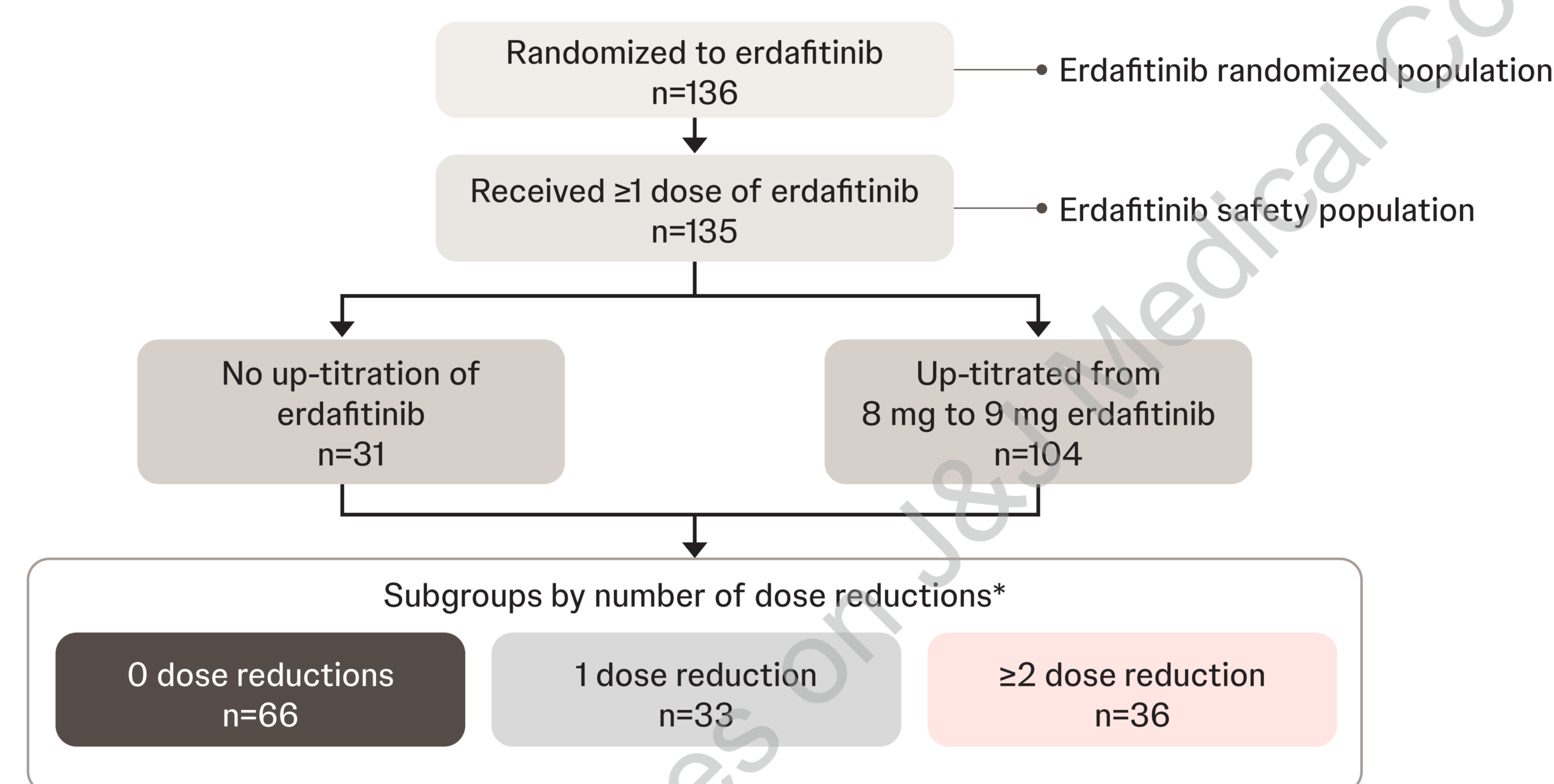
Treat until disease progression or unacceptable toxicity

Results

Patient disposition

- All results are based on the clinical cutoff used in the primary analyses (January 15, 2023)³
- Among 136 patients in THOR Cohort 1 who were randomized to erdafitinib, 66 (48.5%) had no dose reductions, 33 (24.3%) had 1 dose reduction, 36 (26.5%) had ≥ 2 reductions (**Figure 2**)
 - Of 104 patients who up-titrated, 25 (24.0%) had 1 reduction; 22 (21.2%) had ≥ 2 reductions
 - Of 31 patients with no up-titration, 8 (25.8%) had 1 reduction and 14 (45.2%) had ≥ 2 reductions

Figure 2: Disposition of patients included in subgroup analyses by dose reductions



*De-escalation from 9 mg to 8 mg not included.

Baseline characteristics

- Demographic and baseline clinical characteristics were not remarkably different between the subgroups of patients with 0, 1, or ≥ 2 erdafitinib dose reductions (**Table 1**)

Table 1: Baseline characteristics by number of erdafitinib dose reductions

Characteristics	Number of dose reductions		
	0 (n=66)	1 (n=33)	≥ 2 (n=36)
Age, median (range), years	65.0 (34–84)	65.0 (32–85)	69.5 (50–81)
Age, n (%)			
<65 years	32 (48.5)	16 (48.5)	11 (30.6)
65–69 years	13 (19.7)	9 (27.3)	7 (19.4)
70–74 years	9 (13.6)	1 (3.0)	11 (30.6)
≥ 75 years	12 (18.2)	7 (21.2)	7 (19.4)
Female, n (%)	17 (25.8)	12 (36.4)	11 (30.6)
Race, n (%)			
Asian	13 (19.7)	11 (33.3)	13 (36.1)
White	45 (68.2)	17 (51.5)	18 (50.0)
Not reported	8 (12.1)	5 (15.2)	5 (13.9)
Primary tumor location, n (%)			
Lower tract	51 (77.3)	22 (66.7)	21 (58.3)
Upper tract	15 (22.7)	11 (33.3)	15 (41.7)
Visceral metastases, n (%)			
Present	51 (77.3)	24 (72.7)	25 (69.4)
Absent	15 (22.7)	9 (27.3)	11 (30.6)
PD-(L)1 status, n/total (%)			
CPS ≥ 10	5/46 (10.9)	0/22 (0)	2/27 (7.4)
CPS <10	41/46 (89.1)	22/22 (100)	25/27 (92.6)
Previous lines of systemic therapy, n (%)			
1	24 (36.4)	11 (33.3)	10 (27.8)
2	42 (63.6)	22 (66.7)	25 (69.4)
3	0	0	1 (2.8)

CPS, combined positive score; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1.

References

- Balversa[®] (erdafitinib). Summary of Product Characteristics. Accessed August 2025.
- Lloriot Y, et al. *N Engl J Med* 2023;389:1961-1971.

Efficacy outcomes by number of erdafitinib dose reductions

- At a median follow-up of 15.9 months (erdafitinib: 18.0 months, chemotherapy: 14.9 months), median OS in the overall group of patients randomized to erdafitinib (n=136) was 12.1 months vs 7.8 months in the chemotherapy group
 - Median PFS was 5.6 months with erdafitinib vs 2.7 months with chemotherapy
 - Unconfirmed ORR was 45.6% with erdafitinib vs 11.5% with chemotherapy; confirmed ORR was 35.3% vs 8.5%, respectively
- OS, PFS, and ORR outcomes in erdafitinib patient subgroups by number of dose reductions (0, 1, or ≥ 2) were consistent with those in the erdafitinib all randomized population (**Table 2**, **Table 3**)

Table 2: OS and PFS by number of erdafitinib dose reductions

	Erdafitinib randomized population (n=136)	Erdafitinib safety population Number of dose reductions		
		0 (n=66)	1 (n=33)	≥ 2 (n=36)
Overall Survival				
Median (95% CI), mo	12.1 (10.3, 16.4)	10.0 (8.1, 10.9)	10.3 (8.5, 16.8)	23.2 (18.2, NE)
6-mo rate (95% CI), %	85 (77, 90)	77 (63, 86)	87 (69, 95)	97 (81, 100)
12-mo rate (95% CI), %	51 (41, 60)	36 (23, 50)	43 (24, 60)	81 (63, 91)
PFS				
Median (95% CI), mo	5.6 (4.4, 5.7)	4.2 (2.8, 5.4)	5.6 (4.0, 5.9)	10.8 (5.8, 13.7)
6-mo rate (95% CI), %	37 (28, 46)	20 (10, 32)	31 (15, 49)	68 (50, 81)
12-mo rate (95% CI), %	17 (10, 25)	7 (2, 16)	10 (1, 32)	34 (18, 51)

Mo, months; OS, overall survival; PFS, progression-free survival.

Table 3: Objective responses by number of erdafitinib dose reductions (unconfirmed)

n (%)	Erdafitinib randomized population (n=136)	Erdafitinib safety population Number of dose reductions		
		0 (n=66)	1 (n=33)	≥ 2 (n=36)
ORR	62 (45.6)	22 (33.3)	17 (51.5)	23 (63.9)
Best overall response				
Complete response	9 (6.6)	0	4 (12.1)	5 (13.9)
Partial response	53 (39.0)	22 (33.3)	13 (39.4)	18 (50.0)
Stable disease	50 (36.8)	24 (36.4)	14 (42.4)	12 (33.3)
Progressive disease	14 (10.3)	11 (16.7)	2 (6.1)	1 (2.8)
Not evaluable	10 (7.4)	9 (13.6)	0	0
Disease control rate ^a	112 (82.4)	46 (69.7)	31 (93.9)	35 (97.2)

ORR, objective response rate; ^aComplete response + partial response + stable disease.

Adverse events

- The most common treatment-emergent AEs (TEAEs) leading to erdafitinib dose reductions were stomatitis, palmar-plantar erythrodysesthesia, and onycholysis (**Table 4**)

Exposure

- Duration of erdafitinib treatment in patients who had any dose reduction was comparable to those in the overall erdafitinib safety population
 - Mean (standard deviation [SD]) days of exposure was 283.8 (219.16) days and 206.8 (193.93) days, respectively

Table 4: TEAEs leading to dose reduction of erdafitinib with incidence $\geq 10\%$

n (%)	Number of dose reductions	
	1 (n=33)	≥ 2 (n=36)
Stomatitis	7 (21.2)	12 (33.3)
Palmar-plantar erythrodysesthesia	2 (6.1)	10 (27.8)
Onycholysis	5 (15.2)	7 (19.4)
Onychomadesis	4 (12.1)	5 (13.9)
Diarrhea	3 (9.1)	5 (13.9)
Dry mouth	2 (6.1)	4 (11.1)
Hyperphosphatemia	2 (6.1)	4 (11.1)

AE, adverse event; TEAE, treatment-emergent adverse event. ^aOne of these 33 participants is not included in this analysis as they did not meet the criterion for dose reduction based on the exposure data. However, the AE data indicate that the participant had a dose reduction due to an AE.



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Poster

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