

## Erdafitinib for locally advanced or metastatic urothelial carcinoma

The recent article by Roubal and colleagues<sup>1</sup> provided a clinical review of erdafitinib for patients with urothelial carcinoma. Although such a review is a valuable resource, we noted errors in descriptions of indication, dosing, efficacy, and safety. Because precise information on new treatments is essential to caring for patients with cancer, herein we provide corrected information for some of the errors and descriptions.

With regard to indication, based on results from the phase 2 BLC2001 study,<sup>2</sup> erdafitinib received accelerated approval from the Food and Drug Administration for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have susceptible *FGFR2* (fibroblast growth factor receptor 2) or *FGFR3* gene alterations and have progressed during or following treatment with at least one line of prior platinum-containing chemotherapy, including within 12 months of treatment with neoadjuvant or adjuvant platinum-containing chemotherapy,<sup>3,4</sup> not just for patients with “advanced urothelial cancer with specific *FGFR* genetic alterations who have received at least one prior platinum-containing regimen,” as noted in the abstract by Roubal and colleagues.

Roubal et al state that “The labeling for erdafitinib includes 3 black-box warnings.” This is incorrect. While there are warnings and precautions for ocular disorders, hyperphosphatemia, and embryo-fetal toxicity included in the US label, these are not the same as black-box warnings.<sup>3,5</sup> There are no black-box warnings in the US label for erdafitinib.<sup>3</sup>

With regard to dosing, the abstract for Roubal et al notes that “current recommended daily dosing is 8 mg, with dose escalation to 9 mg after 14 to 21 days of therapy if tolerated.” This suggests that safety is the only consideration for up-titration, but up-titration is actually based on serum phosphate levels between days 14 and 21 of erdafitinib treatment as well as tolerability. Serum phos-

phate is a pharmacodynamic biomarker to optimize tumor response to erdafitinib; levels of 5.5 mg/dL or higher within the first 3 months have been associated with improved outcomes.<sup>2,6,7</sup>

In addition, Roubal et al state that “no dose adjustments are needed in the presence of kidney or liver disease.” While the prescribing information for erdafitinib notes that there was no clinically meaningful difference in erdafitinib pharmacokinetics in patients with mild renal or hepatic impairment, it also clearly states that pharmacokinetics in patients with severe impairment are unknown.<sup>3</sup>

With regard to efficacy, Roubal et al indicate in the abstract that “patients who received erdafitinib experienced on average 5.5 months of progression-free survival (95% confidence interval [CI], 4.2-6.0 months)”;

however, 5.5 months was actually the median progression-free survival time. Similarly, in the “Clinical efficacy and safety” section, Roubal et al state that “patients remained on treatment an average of 5 cycles (ranging from 1 to 18 cycles) consisting of 28 days.” However, this is a median of 5 cycles rather than the average or mean.

With respect to safety, Roubal et al state that, “Of the 63 patients who experienced central retinopathy as an adverse effect, 60 patients were able to continue with therapy.” However, only 21 patients in the selected erdafitinib regimen had central serous retinopathy (CSR); among these, most cases were grade 1 or 2, and only 3 patients discontinued therapy due to CSR.<sup>2</sup> CSR is typically reversible, and most patients continued erdafitinib after management through dose interruption/reduction.<sup>2</sup> Roubal et al also indicate that eye exams should be performed to “prevent this adverse effect,” but this statement could be misleading. Rather, regular eye exams are performed to detect and treat or manage CSR.<sup>2,3</sup> Most CSR events occurred within 3 months of initiating treatment; incidence after 6 months was minimal.<sup>8</sup>

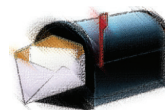
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Minor discrepancies were also noted in reporting of the incidence of adverse events. Roubal et al state that 2% of patients withdrew due to CSR; however, the actual withdrawal rate for CSR was 3% (3 of 99 patients), as cited in both the primary manuscript and prescribing information. Fatigue and dysgeusia were reported as occurring at rates of 21% and 35%, respectively, by Roubal et al, but the actual incidence rates were 32% and 37% in the selected regimen. Finally, Roubal et al note that erdafitinib “also impacts laboratory values including abnormalities in electrolytes and cell counts” and provide percentages for events of all grades. We believe that these percentages could be misleading because most events were grade 1 or 2.<sup>3</sup> Other adverse event data were also described by Roubal et al as “associated with” erdafitinib, suggesting that these events were considered by the physician to be related to treatment. Most phase 2 studies collect data on both treatment-related events that the investigator believes are directly related to therapy and treatment-emergent events, including any event occurring during the treatment period regardless of cause. Treatment-emergent effects may include events related to comorbid medical conditions or disease process in heavily pretreated patients.

We thank Roubal et al for reviewing data from this important study; we thank the editors for their consideration and the opportunity to clarify these points.

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