Quality of life (QoL) in the phase 3 METEOR trial of cabozantinib vs everolimus for advanced renal cell carcinoma (RCC)


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Background: In a randomized Phase 3 trial in advanced RCC after prior VEGFR TKI therapy (Choueiri N Engl J Med 2015, ASCO 2016 abstract 4506) cabozantinib was superior to everolimus in the primary endpoint of PFS (median 7.4 vs 3.8 mo; HR 0.58; p < 0.0001) and significantly improved secondary endpoints of OS (median 21.4 vs 19.3 mo; HR 0.72; p < 0.0001) and ORR (17% vs 3%; p < 0.0001). QoL outcomes were exploratory endpoints.

Methods: 658 patients were randomized 1:1 to receive cabozantinib 60 mg qd (n = 330), or everolimus 10 mg qd (n = 328). QoL questionnaires (Functional Assessment of Cancer Therapy: Kidney Symptom Index [FKSI-19] and EuroQol EQ-5D-5L) were administered on Day 1 (pre-dose), every 4 weeks through W25D1, then every 8 weeks through final tumor assessment. The FKSI-19 has 19 items each scored on a 5-point scale (0-4); a 9-item disease-related symptom index (FKSI-DRS) is then every 8 weeks through final tumor assessment. The FKSI-19 total score was similarly sustained in each arm over time: estimated mean change from BL −3.48 cabozantinib vs −2.21 everolimus (ES (95% CI) −1.60, −0.58; p < 0.0001). Scores at end of treatment (mainly due to progression) were −7 points lower than BL in each arm. On the Treatment Side Effects subscale, diarrhea and nausea were worse for cabozantinib (ES −0.77 and −0.34, respectively), shortness of breath was worse for everolimus (ES +0.30). Diarrhea and nausea are frequent AEs for VEGFR TKIs. No treatment differences were observed for the other three FKSI subscales (DRS-Physical, DRS-Emotional, Function/Well Being) or for the EQ-5D-5L questionnaire. In a post hoc analysis, median time to deterioration (earlier of death, progression, or ≥ 2-point decrease in FKSI-DRS) was longer in the cabozantinib arm (5.5 vs 3.7 mo; p = 0.0001).

Conclusions: Cabozantinib improved PFS, OS, and ORR, and resulted in QoL similar to everolimus in patients with advanced RCC. The benefits of cabozantinib are further supported by a delay of time to deterioration.

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