Grupo Português Génito - Urinário

GPGU – NOTÍCIAS

Crizotinib achieves long-lasting disease control in advanced papillary renal-cell carcinoma type 1 patients with MET mutations or amplification. EORTC 90101 CREATE trial

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Abstract

Purpose

Papillary renal-cell carcinoma type 1 (PRCC1) is associated with MET gene alterations. Our phase II trial prospectively assessed the efficacy and safety of crizotinib in patients with advanced/metastatic PRCC1 with or without MET mutations (MET+ and MET−).

Experimental design

Eligible patients with reference pathology-confirmed PRCC1 received 250 mg oral crizotinib twice daily. Patients were attributed to MET+/MET− sub-cohorts by the sequencing of exons 16–19 of the MET gene in tumour tissue. The primary end-point was objective response rate (ORR). If at least two of the first 12 eligible and evaluable MET+ patients achieved a confirmed partial response (PR) or complete response (CR) (in accordance with the Response Evaluation Criteria in Solid Tumours, version 1.1), a maximum of 35 patients were enrolled. Secondary end-points included duration of response (DOR), disease control rate (DCR), progression-free survival (PFS), PFS rate (PFSR), overall survival (OS) and safety.

Results

Forty-one patients provided consent, of whom 23 were eligible, treated and evaluable. In four MET+ patients, two achieved PR and one had stable disease (SD) (ORR 50%; 95% confidence interval [CI]: 6.8–93.2), DOR was 21.8 and 37.3 months, 1-year PFSR: 75.0% (95% CI: 12.8–96.1) and 1-year OS: 75.0% (95% CI: 12.8–96.1). Among 16 MET− patients, one achieved a PR lasting more than 9.9 months and 11 had SD (ORR: 6.3%; 95% CI: 0.2–30.2), 1-year PFSR: 27.3% (95% CI: 8.5–50.4) and 1-year OS: 71.8% (95% CI: 41.1–88.4). Among three patients with unknown MET status (MET?) due to technical failure, one achieved PR lasting more than 6.9 months, and one had SD (ORR 33.3%, 95% CI: 0.8–90.6), 1-year PFSR: 66.7% (95% CI: 5.4–94.5) and 1-year OS: 100%. MET amplification was found post hoc in one MET+ patient (PR, DOR: 37.3 months), and one MET− case who had SD. Common treatment-related adverse events were oedema (47.8%), fatigue (47.8%), nausea (39.1%), diarrhoea (39.1%) and blurred vision (34.8%).

Conclusion

Crizotinib is active and well tolerated in advanced, metastatic PRCC1, achieving objective responses and long-lasting disease control in patients with MET mutations or amplification. Sporadic, durable responses are also seen in MET− and MET? cases, suggesting the presence of other alterations of MET or alternative pathways