931TiP PRISM: A randomised phase II trial of nivolumab in combination with alternatively scheduled ipilimumab in first-line treatment of patients with advanced or metastatic renal cell carcinoma

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Background: Initial results from the CheckMate 214 randomised phase III study demonstrate an overall survival advantage for combination ipilimumab plus nivolumab over sunitinib in front-line treatment of patients with intermediate/poor risk metastatic renal cell carcinoma (mRCC). However, the safety profile of nivolumab-plus-ipilimumab could be further optimised: 46% (250/547) of patients experienced a Grade 3-4 adverse reaction (AR), 22% (118/547) discontinued therapy due to ARs and (35%) (152/436) patients needed high dose steroids to resolve immune-mediated ARs. The aim of the PRISM trial is to explore safer and more tolerable scheduling of these agents. We hypothesise that 12-weekly rather than standard 3-weekly dosing of ipilimumab, in combination with nivolumab, will result in lower rates of grade 3-4 ARs whilst maintaining treatment efficacy.

Trial design: PRISM is a multi-centre phase II trial randomising patients (1:2) to nivolumab 3mg/kg combined with ipilimumab 1mg/kg every 3 weeks for 4 doses, followed by nivolumab 240mg flat-dose every 2 weeks (standard arm) versus nivolumab 3mg/kg combined with ipilimumab 1mg/kg at weeks 1, 13, 25 & 37 (4 doses) with single-agent 2-weekly nivolumab 240mg given in intervening weeks (experimental arm). Patients with untreated metastatic clear cell RCC will form the study population and patients with good, intermediate and poor prognosis disease, as per IMDC criteria, are eligible. The primary endpoint of the study is the rate of grade 3 or 4 ARs within the initial 12 months of treatment. Progression-free survival (PFS) at 12 months forms a key secondary endpoint, to exclude the PFS rate of no interest and support further investigation in a subsequent definitive phase III trial. Other secondary endpoints include treatment discontinuation rates, quality of life, overall response rate and duration of response. An exploratory objective is to examine circulating and tissue-based biomarkers of response. The study aims to recruit 189 patients across 15 UK centres over a 2-year period and opened in March 2018. To date, 4 patients have been recruited.

Clinical trial identification: EudraCT: 2017-001476-33.

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