Paper 018 3006132 ACTIVITY AND SAFETY OF CRIZOTINIB IN PATIENTS WITH ADVANCED CLEAR CELL SARCOMA (CCSA) WITH MET ALTERATIONS. EUROPEAN ORGANIZATION FOR RESEARCH AND TREATMENT OF CANCER PHASE 2 TRIAL 90101 “CREATE” Patrick Schöffski1 ; Agnieszka Wozniak2 ; Silvia Stacchiotti3 ; Piotr Rutkowski4 ; Jean-Yves Blay5 ; Lars Lindner8 ; Sandra Strauss9 ; Alan Anthoney12; Florence Duffaud14; Stephan Richter13; Raf Sciot6 ; Debiec-Rychter Maria10; Sandrine Marreaud7 ; Laurence Collette7 ; Sebastian Bauer11 1 General Medical Oncology, University Hospitals Leuven, Leuven, Belgium; 2 Department of Oncology, KULeuven, Laboratory of Exerimental Oncology, Leuven, Belgium; 3 Sarcoma Unit, Cancer Medical Department, Fondazione IRCC Istituto Nazionale Tumori, Milan, Italy; 4 Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; 5 Université Claude Bernard Lyon Institute, Centre Léon Bérard, Lyon, France; 6 Department of Pathology, University Hospitals Leuven, Leuven, Belgium; 7 European Organisation for Research and Treatment of Cancer, Brussels, Belgium; 8 Department of Medicine III, University Hospital, LMU Munich, Munich, Germany; 9 Department of Oncology, University College London Hospitals NHS Trust, London, United Kingdom; 10Department of Human Genetics, University Hospitals Leuven, Leuven, Belgium; 11Westdeutsches Tumorzentrum, Universitätsklinikum Essen, Essen, Germany; 12Leeds Institute of Cancer & Pathology, University of Leeds, Leeds, United Kingdom; 13University Cancer Center/Medical Dept, University Hospital Carl Gustav Carus, Dresden, Germany; 14Medical oncology Unit, La Timone University Hospital, Marseille, France

Objective: Clear cell sarcoma (CCSA) is an orphan and very treatment-resistant malignancy characterised by a specific t(12;22) translocation, which leads to rearrangement of the EWSR1 gene and overexpression of MET. We prospectively investigated the efficacy and safety of the MET/ALK/ROS1 tyrosine kinase inhibitor crizotinib in patients with advanced or metastatic CCSA. Methods: Patients with CCSA received oral crizotinib 250 mg twice daily. Primary endpoint was the objective response rate (ORR; RECIST 1.1), secondary endpoints included duration of response, disease control rate (DCR), progression-free survival (PFS), progression-free rate (PFR), overall survival (OS), overall survival rate (OSR), and safety. The study design focused on MET+ disease with documented rearrangement of the EWSR1 gene by fluorescence in situ hybridization (FISH). Results: Among 43 consenting patients with the local diagnosis of CCSA, 36 had centrally confirmed CCSA, 28 of whom were eligible, treated and evaluable. 26/28 patients had MET+ disease, of whom one achieved a confirmed partial response and 17 had stable disease (SD) (ORR 3.8%, 95% CI: 0.1-19.6). Further efficacy endpoints in MET+ CCSA were a DCR of 69.2% (48.2-85.7%), a median PFS of 131 days (49-235), and a median OS of 277 days (232-442). The 3, 6, 12 and 24 month PFR was 53.8% (34.6-73.0), 26.9% (9.8-43.9), 7.7% (1.3-21.7) and 7.7% (1.3-21.7), respectively. Half of the MET+ CCSA cases had a measurable reduction of target lesions. Among two evaluable MET- patients, one had SD and one had progression as best response. The most common treatment-related adverse events were nausea (18/34 [52.9%]), fatigue (17/34 [50.0%]), vomiting (12/34 [35.3%]), diarrhea (11/34 [32.4%]), constipation (9/34 [26.5%] and blurred vision (7/34 [20.6%]). Conclusion: While objective RECIST responses to crizotinib are uncommon in patients with CCSA with rearrangement of the EWSR1 gene, shrinkage of target lesions and disease control was observed in a considerable proportion of patients. The outcome of crizotinib treatment in CCSA is similar to results achieved in soft tissue sarcoma with single-agent doxorubicin in first line or with pazopanib in subsequent lines of treatment. Given the long follow-up in this trial, our series will serve as an important resource for further prospective research in this rare and hard to treat malignancy.