

154P Renal toxicity from platinum/pemetrexed and pembrolizumab in the era of combination therapy

D. Dumoulin¹, S. Visser², R. Cornelissen³, J.G. Aerts¹

¹Pulmonology, Erasmus MC Cancer Institute, Rotterdam, Netherlands, ²Internal Medicine, Amphia Ziekenhuis-location Molengracht, Breda, Netherlands, ³Erasmus University Medical Center, Rotterdam, Netherlands

Background: Recently, the phase 3 keynote-189 trial showed that in previously untreated patients with advanced non-squamous NSCLC without targetable mutations, the progression-free and overall survival were significantly longer with addition of pembrolizumab to chemotherapy than with chemotherapy alone. Both chemotherapy and pembrolizumab can give renal toxicity, which can be a major challenge in the clinical setting.

Methods: In a prospective multicenter observational real-life cohort study [Visser Eur Respir J 2018], we evaluated the incidence of acute/chronic kidney disease (AKD/CKD), its related treatment discontinuation frequency and associated clinical variables with AKD in patients with stage IIIB/IV NSCLC treated with platinum/pemetrexed. In addition, the Keynote 189 toxicity data was used for the combination treatment. We thereafter reviewed literature to generate an algorithm for diagnosis and treatment in increased creatinine levels.

Results: 149 patients received pemetrexed platinum, of whom 44 patients (30%) continued maintenance. During induction therapy 48 patients (50%) treated with cisplatin/pemetrexed developed AKD and 15 patients (29%) treated with carboplatin/pemetrexed. During maintenance 13 patients (30%) developed AKD, leading to CKD and treatment discontinuation in eight patients (62%). In the Keynote 189 trial combining pembrolizumab with chemotherapy, nephritis has been reported in 1,7% of patients in any grade (1,5% grade 3-4). However, when looking at an increased blood creatinine in the group that was treated with carboplatin, a total of 12,2% of patients showed any increase (0,7% grade 3-4).

Conclusions: Increased blood creatinine levels from pemetrexed and pembrolizumab is a common entity, probably more common in a real-life setting. This elevation is clinically challenging in a population that receives three agents that can cause a creatinine increase. Currently, there are no markers to distinguish between renal failure due to chemotherapy of immunotherapy. We will present an algorithm based on current knowledge for clinicians as guidance for renal dysfunction in patients treated with chemotherapy and pd-(L)1 checkpoint inhibitors.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: D. Dumoulin: Speakers fee: BMS, Roche, Pfizer, Novartis. R. Cornelissen: Consultancy: Roche, Boehringer Ingelheim, BMS, MSD; Speakers fee: Roche, Pfizer, Boehringer Ingelheim, Novartis, BMS. J.G. Aerts: Advisory boards: BMS, Boehringer Ingelheim, MSD, AstraZeneca, Eli Lilly, Takeda, Ampera; Stock owner: Ampera B.V. All other authors have declared no conflicts of interest.