TPS8122 **Poster Session**

Phase II study of pembrolizumab in combination with cisplatin or carboplatin and pemetrexed as induction chemoimmunotherapy in resectable epithelioid and biphasic pleural mesothelioma (CHIMERA study).

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Background: Pleural mesothelioma (PM) is a rare cancer related to asbestos exposure, marked by complex histopathological diagnosis and dismal prognosis. Patients' survival is strongly influenced by the histological subtype and by the eligibility to a multimodal approach, which is reserved to very selected patients. Platinum-pemetrexed chemo-regimen or the immunotherapy combination ipilimumab+nivolumab are the available first-line treatment options for unresectable PM patients. In this setting, pembrolizumab in combination with platinum-pemetrexed showed an improved overall and progression free survival (IND227/Keynote483 trial). In patients with resectable PM, the multimodality approach with platinum-pemetrexed chemotherapy and surgery is usually preferred, achieving pathological complete response (pCR) in 5% of cases. To date, the role of perioperative immunotherapy for PM has not yet been extensively investigated. **Methods:** This is a phase II single arm trial enrolling patients with resectable PM from 8 high volume Italian centers, with 18 months of enrollment and 12 months of follow-up. Inclusion criteria will be the histologically confirmed diagnosis of surgical resectable stage I-IIIA treatment-naïve epithelioid/biphasic PM. Patients will receive 3 cycles of pembrolizumab 200 mg plus cisplatin (75 mg/sm) or carboplatin (AUC 5) and pemetrexed (500 mg/sm) every 3 weeks. The surgical procedure of pleurectomy/decortication will be centralized in 2 centers and will be performed within 6 weeks after the last neoadjuvant cycle. The adjuvant treatment will start within 10 weeks from surgery and will be based on 14 cycles of pembrolizumab 200 mg every 3 weeks. The primary endpoint will be the pCR; secondary endpoints will include: major pathological response, objective response rate, event free survival, OS, surgery feasibility, safety. Translational analysis on tissue and blood samples will also be performed. In order to investigate an improvement of pCR from 5% to 18%, 36 patients and a minimum number of 4 pCR are needed to verify this hypothesis with a least 80% power and a probability of type I error of 0.05. Considering a 10% patients dropped-out because of disease progression precluding surgery, a total number of 40 patients will be included in the study. The trial is currently ongoing since November 2024; 5 patients have been enrolled so far. This is the first clinical trial assessing the activity and safety of pembrolizumab in combination with platinum-pemetrexed for resectable PM patients. Clinical trial information: NCT06155279. Research Sponsor: MSD.