CONTINUOUS INFUSION OF CILENGITIDE WITH RADIO-CHEMOTHERAPY IN STAGE III NSCLC: A PHASE I STUDY


1Dpt de Radiothérapie, Institut Universitaire du Cancer-Oncopole, Toulouse, FRANCE
2Thoracic Oncology, CHU Toulouse - Hôpital Larrey, Toulouse, FRANCE
3Unité d’oncologie Thoracique, Larrey Hospital, Toulouse, FRANCE
4Bureau des Essais Cliniques, Institut Universitaire du Cancer-Oncopole, Toulouse, FRANCE
5Medical Oncology Dpt, Institut Universitaire du Cancer-Oncopole, Toulouse, FRANCE
6Department of Thoracic Oncology, Hôpital de Larrey, Toulouse, FRANCE

Aim: We have shown that αvβ3 integrins control radioresistance, hypoxia and angiogenesis and that co-expression of FGF-2 and αvβ3 integrins in the tumors of patients treated with exclusive radio-chemotherapy for stage III non-small lung carcinoma (NSCLC), was associated with a worse local control, suggesting that inhibition of αvβ3 integrin could induce a radiosensitization of such tumours. We designed a phase I trial associating the specific αvβ3/αvβ5 integrin inhibitor cilengitide with radio-chemotherapy in patients with stage III NSCLC.

Methods: A standard 3 + 3 dose escalation design was used. Cilengitide was given in continuous infusion starting 2 weeks before and then during the whole course of the radio-chemotherapy (66 Gy combined with a Platine-Navelbine regimen), and then at a dose of 2000 mg twice a week in association with chemotherapy. Planned Cilengitide continuous infusion dose levels were 12, 18, 27 and 40 mg/h. PET-FDG and CT scan were performed before and then after the first two weeks of Cilengitide administration and then 2 months after the end of radio-chemotherapy. Patients were followed by CT scan. Toxicity for DLT was assessed during combined treatment and until 1 month after. Clinical response on CT scan and TEP was evaluated according to RECIST and PERCIST criteria.

Results: Fourteen patients were included between March 2010 and July 2013. Eleven patients were evaluable for DLT. No DLT was observed at level 0, 1 and 2. One DLT, a tracheo-bronchial fistula was reported at the 40 mg/h dose. No relevant adverse event related to Cilengitide (grade 1 and one grade 2) was observed on the whole population. Among 11 patients evaluable for efficacy, 9 patients presented a partial response and 2 a stable disease. At 6 months after the end of radio-chemotherapy, 2 patients presented a progressive disease. At PET evaluation 2 months after radio-chemotherapy, 4 patients had a complete response and 4 patients had a partial response.

Conclusions: Cilengitide given continuously with radio-chemotherapy was well tolerated and shows encouraging clinical results, suggesting that targeting αvβ3 integrin continuously during radio-chemotherapy in NSCLC is a promising approach to treat this disease.

Disclosure: E.L. Cohen-Jonathan Moyal: E Moyal has been member of an advisory board for Merck KGaA and received a funding grant from Merck KGaA for research. All other authors have declared no conflicts of interest.