Oligometastatic

Toxicity of L19-Interleukin 2 combined with Stereotactic Body Radiotherapy: A phase I study.

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INTRODUCTION

The immunocytokine L19-IL2 delivers interleukin-2 to the tumour by exploiting the selective L19-dependent binding of extradomain B of fibronectin on tumour blood vessels. In preclinical models, L19-IL2 has been shown to enhance the local and abscopal effects of radiotherapy. The clinical safety of L19-IL2 monotherapy has been established previously. In this study, the safety and tolerability of L19-IL2 following Stereotactic Body Radiotherapy (SBRT) was assessed.

MATERIALS AND METHODS

Patients with oligometastatic solid tumours received radical SBRT to all visible metastases. Within one week following SBRT, intravenous L19-IL2 using a 3+3 dose escalation design was administered. Safety and tolerability were analysed as the primary endpoint using the CTCAE4.03 scoring system, progression-free and overall survival as secondary endpoints.

RESULTS

A total of 6 patients in two L19-IL2 dose levels were included. The 15 Mio International Units (IU) dose level was well tolerated with no dose limiting toxicity. The most frequently reported adverse events were chills, non-infectious fever, fatigue, edema, erythema, pruritus, nausea/vomiting as well as cough and dyspnea. Blood analysis revealed abnormalities in liver function tests, anaemia, hypoalbuminemia, and hypokalaemia. At the second dose level (i.e., 22.5 Mio IU), which is the recommended dose for L19-IL2 monotherapy, all three included patients experienced dose-limiting toxicity, but toxicities recovered without sequelae. We documented two long-term progression-free responders both having non-small cell lung cancer as primary tumour.

CONCLUSION

Based in the results of this phase I clinical trial, the recommended phase II dose for SBRT combined with L19-IL2 is 15 Mio IU. The therapeutic efficacy of this combination is currently being evaluated in the multicentric EU-funded phase II clinical trial, ImmunoSABR.