TREMELIMUMAB FOR PATIENTS WITH CHEMOTHERAPY-RESISTANT ADVANCED MALIGNANT MESOTHELIOMA: AN OPEN-LABEL, SINGLE-ARM, PHASE 2 TRIAL.

ABSTRACT

Monoclonal antibodies to cytotoxic T-lymphocyte antigen 4 (CTLA4) have therapeutic activity in different tumour types. We aimed to investigate the efficacy, safety, and immunological activity of the anti-CTLA4 monoclonal antibody, tremelimumab, in advanced malignant mesothelioma.

In our open-label, single-arm, phase 2 study, we enrolled patients aged 18 years or older with measurable, unresectable malignant mesothelioma and progressive disease after a first-line platinum-based regimen. Eligible patients had to have a life expectancy of 3 months or more, an Eastern Cooperative Oncology Group performance status of 2 or less, and no history of autoimmune disease. Patients received tremelimumab 15 mg/kg intravenously once every 90 days until progressive disease or severe toxicity. The primary endpoint was the proportion of patients who achieved an objective response (complete or partial response), with a target response rate of 17% according to the modified Response Evaluation Criteria in Solid Tumors (RECIST) for pleural malignant mesothelioma or standard RECIST 1.0 for peritoneal malignant mesothelioma. Analyses were done according to intention to treat. This trial is registered with EudraCT, number 2008-005171-95, and ClinicalTrials.gov, number NCT01649024.

Between May 27, 2009, and Jan 10, 2012, we enrolled 29 patients. All patients received at least one dose of tremelimumab (median two doses, range one to nine). No patients had a complete response and two patients (7%) had a durable partial response (one lasting 6 months and one lasting 18 months); one partial response occurred after initial progressive disease. Thus, the study did not reach its primary endpoint. However, we noted disease control in nine (31%) patients and a median progression-free survival of 6·2 months (95% CI 1·3-11·1) and a median overall survival of 10·7 months (0·0-21·9). 27 patients (93%) had at least one grade 1-2 treatment-emergent adverse event (mainly cutaneous rash, pruritus, colitis, or diarrhoea), and four patients (14%) had at least one grade 3-4 treatment-emergent adverse event (two gastrointestinal, one neurological, two hepatic, and one pancreatic).

Although the effect size was small in our phase 2 trial, tremelimumab seemed to have encouraging clinical activity and an acceptable safety and tolerability profile in previously treated patients with advanced malignant mesothelioma.

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ABSTRACT

Il CTLA4 è un anticorpo monoclonare contro l'antigene 4 del linfocita T citotossico ed è stato studiato per la sua attività terapeutica in differenti tipologie di tumore.
Lo scopo di questo studio era quello di valutare l'efficacia, la tollerabilità e l'attività immunologica dell'anticorpo monoclonare anti-CTLA4: il tremalimumab nei pazienti affetti da mesotelioma pleurico maligno.
In questo studio i pazienti che ricevettero il Tremalimumab furono valutati per le risposte al trattamento: non ci furono risposte complete e solo il 7% (2 pazienti) ebbe una risposta parziale duratura.
Tuttavia i ricercatori notarono un controllo della malattia nel 31% dei casi, con una sopravvivenza libera da malattia di 6.2 mesi e una sopravvivenza mediana globale di 10.7 mesi.
Dunque, in pazienti affetti da mesotelioma pleurico maligno precedentemente trattati, il Tremalimumab sembrerebbe avere un'incoraggiante attività clinica ed un'accettabile tollerabilità e sicurezza nella somministrazione.

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