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Lung & Brain

Pembrolizumab for management of patients with NSCLC and brain metastases: long-term results and biomarker analysis from a non-randomised, open-label, phase 2 trial.

Goldberg SB, Schalper KA, Gettinger SN, Mahajan A, Herbst RS, Chiang AC, Lilenbaum R, Wilson FH, Omay SB, Yu JB, Jilaveanu L, Tran T, Pavlik K, Rowen E, Gerrish H, Komlo A, Gupta R, Wyatt H, Ribeiro M, Kluger Y, Zhou G, Wei W, Chiang VL, Kluger HM.

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BACKGROUND:

We did a phase 2 trial of pembrolizumab in patients with non-small-cell lung cancer (NSCLC) or melanoma with untreated brain metastases to determine the activity of PD-1 blockade in the central nervous system. Interim results were previously published, and we now report an updated analysis of the full NSCLC cohort.

METHODS:

This was an open-label, phase 2 study of patients from the Yale Cancer Center (CT, USA). Eligible patients were at least 18 years of age with stage IV NSCLC with at least one brain metastasis 5-20 mm in size, not previously treated or progressing after previous radiotherapy, no neurological symptoms or corticosteroid requirement, and Eastern Cooperative Oncology Group performance status less than two. Modified Response Evaluation Criteria in Solid Tumours (mRECIST) criteria was used to evaluate central nervous system (CNS) disease; systemic disease was not required for participation. Patients were treated with pembrolizumab 10 mg/kg intravenously every two weeks. Patients were in two cohorts: cohort 1 was for those with PD-L1 expression of at least 1% and cohort 2 was patients with PD-L1 less than 1% or unevaluable. The primary endpoint was the proportion of patients achieving a brain metastasis response (partial response or complete response, according to mRECIST). All treated patients were analysed for response and safety endpoints. This study is closed to accrual and is registered with ClinicalTrials.gov, NCT02085070.

FINDINGS:

Between 31 March 2014 and 21 May 2018, 42 patients were treated. Median follow-up was 8.3 months (IQR 4.5-26.2). 11 (29.7% [95% CI 15.9-47.0]) of 37 patients in cohort 1 had a brain metastasis response. There were no responses in cohort 2. Grade 3-4 adverse events related to treatment included two patients with pneumonitis, and one each with constitutional symptoms, colitis, adrenal insufficiency, hyperglycaemia, and hypokalaemia. Treatment-related serious adverse events occurred in six (14%) of 42 patients and were pneumonitis (n=2), acute kidney injury, colitis, hypokalaemia, and adrenal insufficiency (n=1 each). There were no treatment-related deaths.

INTERPRETATION:

Pembrolizumab has activity in brain metastases from NSCLC with PD-L1 expression of at least 1% and is safe in selected patients with untreated brain metastases. Further investigation of immunotherapy in patients with CNS disease from NSCLC is warranted.