2021 ESMO congress

1040O
Phase II trial of ipilimumab, nivolumab and tocilizumab for unresectable metastatic melanoma

J.S. Weber[1], T. Muramatsu[1], O. Hamid[2], J. Mehnert[1], F.S. Hodi[3], S. Krishnarajapet[1], S. Malatyali[1], E. Buchbinder[3], J. Goldberg[1], R. Sullivan[4], M. Faries[2], I. Mehmi[2]

[1] Perlmutter Cancer Center, Laura and Isaac Perlmutter Cancer Center, New York, NY, USA, [2] At Cedars Sinai, The Angeles Clinic and Research Institute, Los Angeles, CA, USA, [3] Medicine, Dana Farber Cancer Institute, Boston, MA, USA[4] Cancer Center, Massachusetts General Hospital, Boston, MA, USA

Background

Immunotherapy with ipilimumab and nivolumab has response rates of 45-55%, but 50% of patients (pts) suffer grade 3-5 immune-related adverse events. High serum IL-6 is associated with a poor outcome with checkpoint inhibition and with short survival in many cancers. Tocilizumab is a humanized IL-6 receptor blocking antibody approved for several arthritides and cytokine release syndrome. In anecdotal cases it reverses steroid-resistant colitis and other immune toxicities. To assess if tocilizumab could reduce toxicity and/or augment efficacy of checkpoint inhibition, a phase II trial of ipilimumab, nivolumab and tocilizumab was performed. Results from the first stage of the trial are reported.

Methods

In this Simon two-stage design phase II study, eligible pts had untreated unresectable/metastatic melanoma. Adjuvant therapy was permitted. Ipilimumumab at 1 mg/kg, and nivolumab at 3 mg/kg were administered intravenously (IV) every 3 weeks (wks), 4 times during induction, then nivolumab maintenance is given for up to 2 years. Tocilizumab was given at 4 mg/kg every 6 wks IV during the first 24 wks. In stage 1 >/= 11 responses in 18 were required and/or less than 6 pts with grade 3-5 irAEs to proceed to stage 2 to total 67 pts.

Results

Twenty-eight pts have started therapy including 14 men and 14 women with a median age of 67. Twenty had ECOG PS 1, and 8 PS 0. Twenty-four pts had stage IV and 4 stage IIIc/d disease. There were 5 grade 3-4 irAEs with one each with enteritis, colitis and nephritis and two with trasaminitis. At 6 months of median follow up, there are 14 RECIST responses of 20 pts (70% ORR) with at least one evaluation at week 12. Two pts are stable at 18 weeks. No responder or stable pts have progressed. Four pts progressed, and two died. Correlative marker studies by serum Luminex assay showed that higher levels of baseline TNF-alpha were associated with grade 3-4 toxicity, and elevated IL-6/IL-8 and C5a at week 7 were associated with progression.

Conclusions

Flipped dose IPI/NIVO with TOCI has promising anti-tumor activity with a favorable toxicity profile. Incidence of grade 3/4 irAEs was 25%. High baseline TNF-a was associated with grade 3/4 irAEs, and elevated week 7 IL-6/IL-8/C5a were associated with progression. Further correlative studies will be presented.

Clinical trial identification

NCT03999749.

Legal entity responsible for the study

NYU Grossman School of Medicine.

Funding

Bristol-Myers Squibb.

Disclosure

J.S. Weber: Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Invited Speaker: Genentech. O. Hamid: Financial Interests, Personal and Institutional, Invited Speaker: BMS; Financial Interests, Personal and Institutional, Invited Speaker: Genentech. J. Mehnert: Financial Interests, Personal and Institutional, Advisory Board: BMS. F.S. Hodi: Financial Interests, Personal and Institutional, Advisory Board: BMS; Financial Interests, Personal and Institutional, Advisory Board: Genentech. E. Buchbinder: Financial Interests, Personal and Institutional, Advisory Board: BMS; Financial Interests, Personal and Institutional, Advisory Board: Genentech. J. Goldberg: Financial Interests, Institutional, Advisory Board: BMS; Financial Interests, Institutional, Advisory Board: Genentech. R. Sullivan: Financial Interests, Personal and Institutional,

Advisory Board: BMS; Financial Interests, Personal and Institutional, Advisory Board: Genentech. M. Faries: Financial Interests, Personal and Institutional, Advisory Board: BMS; Financial Interests, Personal and Institutional, Advisory Board: Genentech. I. Mehmi: Financial Interests, Personal and Institutional, Advisory Board: BMS; Financial Interests, Personal and Institutional, Advisory Board: Genentech. All other authors have declared no conflicts of interest.