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A phase 3 randomized, open-label study of nivolumab (anti-PD-1; BMS-936558; ONO-4538) versus investigator's choice chemotherapy (ICC) in patients with advanced melanoma after prior anti-CTLA-4 therapy.

SLIDES

Interview with: Prof. Dr. med. Ulrich Keilholz, Direktor des Charité Comprehensive Cancer Center, Berlin, Germany:

Abstract:

Aim: Effective therapies are needed for patients (pts) with melanoma (MEL) who progress on or after anti-CTLA-4 therapy and a BRAF inhibitor. This phase 3 open-label trial evaluated the efficacy of nivolumab, a fully human IgG4 PD-1 immune checkpoint inhibitor antibody, which demonstrated durable antitumor activity and promising overall survival (OS) in phase 1 trials in pretreated patients.

Methods: Pts with metastatic MEL who progressed on or after anti-CTLA-4 therapy (and a BRAF inhibitor if BRAF V600 mutation positive) were randomized 2:1 to receive nivolumab 3 mg/kg IV Q2W (n = 268 treated) or ICC (dacarbazine 1000 mg/m^2 Q3W, or carboplatin AUC 6 + paclitaxel 175 mg/m^2 Q3W; n = 102 treated) until progression or unacceptable toxicity. Pts were stratified by PD-1 ligand expression, BRAF status and best response to prior anti-CTLA-4 therapy. Co-primary endpoints were objective response rate (ORR) by independent radiology review committee (IRC) and OS of nivolumab- versus ICC-treated pts. Response (RECIST 1.1) was assessed 9 W after randomization, followed by Q6W for the first 12 mo and then Q12W.

Results: ORR was assessed as planned in the first 120 nivolumab and 47 ICC pts with follow-up of ≥6 mo. Baseline age, sex and M stage were balanced between arms. Confirmed ORR (IRC) in nivolumab and ICC pts was 32% (95% CI: 24, 41) and 11% (95% CI: 3.5, 23), with median time to response of 2.1 mo (range: 1.6, 7.4) and 3.5 mo (range: 2.1, 6.1), respectively. Reduction of ≥50% in target lesion burden occurred in 82% (31/38) of nivolumab responders and 60% (3/5) of ICC responders. Median duration of response for nivolumab was not reached (range: 1.4 +, 10+ mo) with 36 (95%) pts still in response.

Median duration of response for ICC was 3.6 mo (range: 1.3 + , 3.5) with 4 (80%) pts still in response. Among nivolumab-treated pts, an additional 10 (8.3%) pts had immune-related response patterns observed. Grade 3-4 drug-related adverse events (AEs) were seen in 9.0% and 31% of pts treated with nivolumab and ICC, respectively. Discontinuations due to drug-related AEs, any grade, occurred in 2.2% and 7.8% of treated pts, respectively.

Conclusions: In pts with metastatic MEL who progressed on or after anti-CTLA-4 therapy (and BRAF inhibitors), nivolumab was well tolerated and showed higher ORR as compared with ICC, with durable tumor regression in the majority of responders.

Disclosure: J.S. Weber: Advisory board-BMS, Merck, Genentech, all less than $5000 USD annually Corporate sponsored research-BMS, Merck, Genentech, all to my institution, not me personally; D.R. Minor: I am a speaker for BMS and I own stock in BMS (approx $26,000). I also am a speaker for Glaxo; F.S. Hodi: Consultant, not paid: Bristol-Myers Squibb Corporate-sponsored research: Bristol-Myers Squibb; R. Gutzmer: Consultant: BMS, Merck/MSD, Roche, GSK, Novartis, AlmirallHermal Honoraria: same as above + Janssen, Amgen, Pfizer, Boehringer Ingelheim Corporate-sponsored research: Roche, Novartis, Pfizer, Johnson & Johnson (payment to institution); B. Neyns: Consultant: BMS, GSK, Merck-Serono, Novartis Honoraria: BMS, GSK Research funding: GSK, Pfizer (payment to institution); C. Hoeller: Advisory board: BMS; N.I. Khushalani: Advisory board: Amgen, Genentech, Provectus Speaker's bureau: Prometheus Research funding: BMS, Biovex, Eisai, Genentech, Celgene, Merck, Pfizer, Threshold, and Roche, Allos, and Pfizer for NCCN trials; W.H. Miller: Consultant and Honoraria: BMS, Roche, Novartis, Merck Stock holdings: BMS; J-J. Grob: Advisor: BMS, Roche, GSK, Merck, Celgene; G. Linette: Consultant: BMS, Genentech, Ziopharm Honoraria: Genentech K. Grossmann: Research funding: BMS (payment to institution); J.C. Hassel: Consultant: BMS, GSK Honoraria: BMS, Roche, Amgen, MSD; P. Lorigan: Consultant and honoraria: BMS, Merck, Roche, GSK, Celgene, Novartis, Amgen; M. Maio: Consultant and honoraria: BMS, Roche, MSD, GSK Research funding: BMS, MedImmune (payment to institution); M. Sznol: Consultant: Bristol-Myers Squibb, Genentech/Roche, Amgen, AstraZeneca/MedImmune, Symphogen, Merus, Immune Design, Anaeropharma, Kyowa-Hakko Kirin, Lion Biotechnologies, Nektar, and Seattle Genetics. Other: Haymarket Media; A. Lambert and A. Yang: Employment: Bristol-Myers Squibb Stock holdings: Bristol-Myers Squibb; J. Larkin: Consultant: BMS, Pfizer, Novartis, GSK, MSD, Roche/Genentech (non-remunerated). Research funding: Pfizer, Novartis (payment to institution). All other authors have declared no conflicts of interest.