LONG-TERM SURVIVAL OF PATIENTS WITH ADVANCED MELANOMA IN PHASE 2 STUDY OF NIVOLUMAB (ANTI-PD-1; ONO-4538/BMS-936558)

Y. Kiyohara1, H. Tahara2, H. Uhara3, Y. Moroi4, N. Yamazaki5
1Dermatology Division, Shizuoka Cancer Center, Shizuoka, JAPAN
2Department of Surgery and Bioengineering, Advanced Clinical Research Center Institute of Medical Science, The University of Tokyo, Tokyo, JAPAN
3Department of Dermatology, University of Shinshu, Nagano, JAPAN
4Department of Dermatology, Graduate School of Medical Science, Kyushu University, Fukuoka, JAPAN
5Department of Dermatologic Oncology, National Cancer Center Hospital, Tokyo, JAPAN

Aim: We report updated survival and clinical activity of nivolumab, a fully human IgG4 programmed cell death-1 (PD-1) immune checkpoint inhibitor antibody, in a phase 2 study (ONO-4538-02) of previously treated Japanese patients (pts) with advanced melanoma (MEL).

Methods: Nivolumab (2 mg/kg IV Q3W) was given to pts until unacceptable toxicity, disease progression or complete response. Clinical responses were assessed by investigators according to RECIST 1.1 and immune-related response criteria.

Results: 35 MEL pts were treated with nivolumab and responses and safety were evaluated. The ORR and immune-related ORR were 22.9% (8/35 pts) and 28.6% (10/35 pts), respectively. The median duration of response and the median PFS were 127.5 days and 169 days, respectively. The median overall survival was 18.2 month at present. Drug-related AEs were observed in 85.7% of patients, including elevation of C-reactive protein, lactate dehydrogenase, aspartate aminotransferase, and GGTL, and decreasing of free triiodothyronine, pruritus, malaise, nausea and decreased appetite. Grade (G) 3 hepatitis and G2 pneumonitis were occurred in 2 and 1 pts, respectively. Psoriasis arthropica was reported in 1 pt. G3/4 drug-related AEs were reported in 25.7% of pts. No G3/4 pneumonitis or drug-related deaths were reported. Flow cytometric analysis of PBMCs in patients treated with nivolumab revealed that the number of PD-1-positive CD4 and CD8 T cells decreased from the baseline. Induction of chemokine CXCL9 in the serum at day 43 or the end of treatment phase was observed. The pts are still being followed up in order to assess OS and PFS.

Conclusions: These results demonstrated that the Japanese patients treated with nivolumab showed durable response with a favorable long-term safety profile which was similar to preceding/ongoing clinical studies of nivolumab in Caucasian pts. This study continues as of April 2014, and will further assess the efficacy and safety of nivolumab for MEL pts.

Disclosure: Y. Kiyohara: I have provided the study sponsor with scientific advice and have received consultancy fees as members of the lead investigator for the phase 2 (ONO-4538-02) study; H. Tahara: I have provided the study sponsor with scientific advice and have received consultancy fees as members of the lead investigator for the phase 2 (ONO-4538-02) study; H. Uhara: I have provided the study sponsor with scientific advice and have received consultancy fees as members of the lead investigator for the phase 2 (ONO-4538-02) study; Y. Moroi: I have provided the study sponsor with scientific advice and have received consultancy fees as members of the lead investigator for the phase 2 (ONO-4538-02) study; N. Yamazaki: I have provided the study sponsor with scientific advice and have received consultancy fees as members of the lead investigator for the phase 2 (ONO-4538-02) study.