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Original paper

The 2012 ASCO (American Society of Clinical Oncology) annual meeting has been held once again at the McCormick Conference Center in Chicago, Illinois, where ASCO has booked a 10-year run for the meeting. The meeting was attended by more than 30,000 oncology professionals from around the world. Of more than 4500 abstracts published at the meeting, 310 were related to melanoma. Here we report the results of the most interesting clinical trials presented at the meeting. Apart from updated overall survival (OS) results of a phase 3 study evaluating the efficacy of vemurafenib and some new data on ipilimumab (expanded access program [EAP] and treatment of patients with brain metastases) we report on practice changing trials: a phase 3 (BREAK) trial evaluating efficacy of dabrafenib and a phase 3 study (METRIC) assessing trametinib in the treatment of metastatic melanoma patients. Another encouraging treatment strategy is combination of dabrafenib and trametinib evaluated in a phase I/II study. Results of new immune checkpoint targeting by monoclonal antibody anti-PD1 (BMS-936558) in an early phase trial in monotherapy or in combination with a multipeptide vaccine in metastatic melanoma patients are presented. Also, results of dendritic cell-based vaccine (randomized phase II trial) immunization in patients with high risk resected melanoma are shown. Furthermore, results of other melanoma immunotherapy strategies evaluated in early phase studies are reported.

Key words: melanoma, kinase inhibitors, BRAF inhibitor, MEK inhibitor, immunotherapy, cancer vaccines.

Recent advances in melanoma treatment – American Society of Clinical Oncology (ASCO) 2012 perspective

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Kinase inhibitors

Vemurafenib is a selective BRAF inhibitor. Recently it has been evaluated in metastatic melanoma patients with BRAF V600E mutation after progression of earlier systemic treatment (phase 2 trial BRIM2). Vemurafenib was also tested in a phase 3 trial (BRIM3) in previously untreated patients. The results of these two trials led to its approval by the U.S. Food and Drug Administration (FDA) in August 2011 and the European Medicines Agency (EMA) in February 2012 for the treatment of metastatic melanoma with BRAF mutation. Updated overall survival (OS) results of the BRIM3 study have been presented at the ASCO meeting this year. The overall response rate in patients treated with vemurafenib was 57% [5.6% – complete response (CR), 51.3 – partial response (PR)] compared with 8.6% (1.2% – CR, 7.4% – PR) observed in patients receiving dacarbazine (DTIC). Median progression-free survival (PFS) was also longer in patients treated with the study drug (6.9 vs. 1.6 months; HR 0.38; 95% CI: 0.32–0.46; $p < 0.001$) as well as median OS (13.6 vs. 9.7 months; HR 0.70; 95% CI: 0.57–0.87; $p < 0.001$). In patients treated with vemurafenib, adverse cutaneous skin carcinoma, keratoacanthoma and skin papilloma were noted respectively in 19%, 11% and 28% of patients [1].

James Larkin presented results of an open-label, multicenter safety study of vemurafenib in patients with metastatic melanoma. Of 1964 screened patients, 914 were enrolled in the study and 834 evaluable for toxicity analysis. 70% of patients received prior systemic treatment due to metastatic melanoma (14% – ipilimumab, 2% – MEK and BRAF inhibitors). Adverse events (AEs) were observed in 66% of patients (88% were related to vemurafenib). The most frequently observed any grade AEs were arthralgia (31%), rash (29%), fatigue (22%), photosensitivity (21%) and nausea (15%). Grade 3 and 4 AEs occurred respectively in 33% and 1.9%. The most common were rash (3.6%), arthralgia (3.1%) and cutaneous cell carcinoma/keratoacanthoma (4.3%). In 6% of patients treatment was discontinued due to AEs (mainly arthritis and abdominal pain). At the time of study analysis 302 patients were evaluable for tumor assessment at week 8 of treatment; 61% developed objective responses, and 29% stable disease (SD) [2].

Another active BRAF kinase inhibitor in the treatment of metastatic melanoma patients is dabrafenib (GSK2118436). Results of a randomized, open-label, multicenter phase 3 study (BREAK-3) comparing the efficacy of dabrafenib and DTIC in patients with BRAF V600E mutated metastatic melanoma were presented at the meeting. The study enrolled 250 previously untreated patients. In one study arm patients received oral dabrafenib at a dose of 150 mg twice a day. In the second arm DTIC at a dose of 1000 mg/m^2 was administered in three-week intervals. 31% of patients presented greater than