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SECOMBIT: The best sequential approach with combo immunotherapy [ipilimumab (I) /nivolumab (N)] and combo target therapy [encorafenib (E)/binimetinib (B)] in patients with BRAF mutated metastatic melanoma: A phase II randomized study

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Background

Treatment with targeted therapy (BRAF and MEK inhibitors) and immune-checkpoint inhibitors (anti-CTLA4, anti-PD-1) have improved the outcome of *BRAF-V600* metastatic melanoma patients in first line. Targeted therapy demonstrated higher response rates, which may be limited over time; while the combination I+N is associated with lower but durable response rate. The best sequencing remains an open question. In addition, a short course of targeted therapy switched to I+N at best response is supported by models and may be clinically advantageous. To investigate the best sequential strategy, we started the SECOMBIT study: a randomized three-arm phase 2 study with no formal comparative test (NCT02631447).

Methods

From Nov 2016 to May 2019, 37 sites in 9 countries enrolled 251 patients with untreated, metastatic *BRAFV600*-mutated melanoma. Patients were randomized to Arm A [E+B until PD, followed by I+N until PD], or Arm B (I+N until PD, followed by E+B until PD) or Arm C (E+B for 8 weeks, followed by I+N until PD, followed by E+B until PD). Treatment schedules were: *targeted therapy* - E 450 mg p.o. od + B 45 mg p.o. bid; *immunotherapy* - I 3 mg/kg + N 1 mg/kg Q3w x 4 cycles, followed by N 3 mg/kg Q2w. OS is the primary endpoint of the study. Secondary endpoints include total PFS (TPFS), 2- and 3-year survival rate, best overall response rate, duration of response, biomarkers evaluation.

Results

The study primary endpoint was met in each arm with at least 30 patients alive at 24 months. The median follow-up estimated with the reverse Kaplan-Meier method was 32.2 months (IQR= 27.9-41.6). The median OS was not reached in any of the treatment arms. The survival rate at 2 and 3 years was 65% and 54% in arm A, 73% and 62% in arm B and 69% and 60% in arm C respectively. Total PFS rate at 2 and 3 years was 46% and 41% in arm A, 65% and 53% in arm B, 57% and 54% in arm C.

Conclusions

The OS and TPFS rates at 2 and 3 years showed a better trend in arm B and C. Data continue to be collected to provide additional information on the long-term benefit of the three treatment combinations. The biomarkers analysis is ongoing.

Clinical trial identification

NCT02631447.

Legal entity responsible for the study

Fondazione Melanoma Onlus.

Funding

BMS and Array Biopharma/Pfizer.

Disclosure

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