Activity and safety of first-line treatments for advanced melanoma: a network meta-analysis

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BACKGROUND

Treatment options for advanced melanoma have increased with the Food and Drug Administration (FDA) approval of the anti-LAG3 and anti-PD-1 relatlimab/nivolumab combination. To date, ipilimumab/nivolumab is the benchmark of overall survival (OS), despite a high toxicity profile. Furthermore, in BRAF-mutant patients, BRAF/MEK inhibitors and the atezolizumab/veumurafenib/cobimetinib triplet are also available treatments, making the first-line therapy selection even more complex. To address these issues, we conducted a systematic review and network meta-analysis comparing the activity and safety of ipilimumab/nivolumab with relatlimab/nivolumab and all the other available first-line treatment options in metastatic melanoma.

RESULTS

A total of 9070 patients treated in 18 RCTs of metastatic melanoma were included in the network meta-analysis (Figure 1).

No difference in the risk of disease progression (Figure 2) and response (Figure 3) between ipilimumab/nivolumab and relatlimab/nivolumab was observed (HR=0.99 [95%CI 0.75 – 1.31] and RR=0.99 [95%CI 0.78 – 1.27], respectively). The PD-L1/BRAF/MEK inhibitors triplet and BRAF/MEK inhibitors combinations were superior to ipilimumab/nivolumab in terms of PFS (HR=0.56 [95%CI 0.37 – 0.83] and HR=0.73 [95%CI 0.50 – 1.06], respectively) (Figure 2) and ORR (RR=3.07 [95%CI 1.61 – 5.85] and RR=2.99 [95%CI 1.58 – 5.67], respectively) (Figure 3).

Ipilimumab/nivolumab showed the highest probability to have the highest risk of developing ≥3 TRAEs. Relatlimab/nivolumab trended to a lower risk of ≥3 TRAEs (RR=0.71 [95%CI 0.30 – 1.67]) vs. ipilimumab/nivolumab (Figure 4).

CONCLUSIONS

Relatlimab/nivolumab showed similar PFS and ORR compared to ipilimumab/nivolumab, with a trend for a better safety profile. The triplet combinations were superior to ipilimumab/nivolumab in terms of both PFS and ORR. These results should take into account the absence of a comparison in terms of survival.

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