The real-world impact of cancer immunotherapy on the survival of patients with metastatic melanoma

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Background: Between 2010 and 2015, pivotal trials with strict enrolment criteria led to the approval of several new immunotherapies for metastatic melanoma (MM). We sought to determine the impact of these treatments in the “real-world” of a population-based study.

Methods: The Danish MM database contains data on the entire unsellected population diagnosed with MM within a nationwide area. To evaluate the impact of novel treatments, all 843 MM cases (excluding ocular) diagnosed in the three non-consecutive years marked by major changes in the availability of 1st line treatments (2012: i.v. IL-2 and BRAFi; 2014: anti-CTLA-4; 2016: anti-PD-1 and MEKi) were retrieved. Patients were grouped into “trial-like” and “trial-excluded” based on seven predefined eligibility criteria used in all MM registration immunotherapy clinical trials, including CNS metastases and PS ≥ 2.

Results: The baseline characteristics of patients diagnosed in 2012, 2014 and 2016 were similar. In the “trial-like” population (39% of all MM), the median overall survival (OS) was not yet reached in the 2016 group versus 18.8 months in 2014 (hazard ratio [HR] for death 0.52, 95% CI 0.36-0.75; p = 0.0005) and 16.5 months in 2012 (HR 0.41, 95% CI 0.27-0.62; p < 0.0001). In the “trial-excluded” population (61% of all MM), 75% of patients had known CNS metastases and/or PS ≥ 2. Here, the median OS was improved to 6.9 months in the 2016 group versus 5.2 months in 2014 (HR 0.66, 95% CI 0.52-0.84; p = 0.0007) and 4.3 months in 2012 (HR 0.65, 95% CI 0.52-0.83; p = 0.0005). To isolate the effects of immunotherapy, the BRAF wild-type population of 2014 and 2016 was analyzed. Here, “trial-like” patients diagnosed in 2016 had an improved overall survival (median OS not reached in 2016 vs 13.3 months in 2014, HR 0.33, 95% CI 0.20-0.55; p < 0.0001), while “trial-excluded” patients had a 1-year improved survival rate in 2016 (35.9% vs 18.8% in 2014, p = 0.0153).

Conclusions: The introduction of modern treatments has led to an improved survival of real world patients with MM, regardless of their eligibility to clinical trials and BRAF status. These data support indirectly the application of modern treatments, including anti-PD-1, to patient populations which are not represented in pivotal trials.

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Immuno-oncology (IO) has changed treatment (Tx) landscape of non-small cell lung cancer, NSCLC. A meta-analysis was performed on the primary outcome of overall survival (OS) for advanced NSCLC. For frontline NSCLC patients, multiple immune checkpoint inhibitors (ICI) were compared, treating 1st line patients with traditional chemotherapy.

We conducted an independent review for the RCTs evaluating ICIs in frontline NSCLC. All ICIs tested were compared to single-agent chemotherapy (CT) and each other. Network estimates of effects on OS showed the superiority of nivolumab over all other treatments (HR 1.78, 95%CI 0.72-4.39; ipilimumab 1.82, 95%CI 1.35-2.47) and platinum doublet chemotherapy (HR 1.72, 95%CI 1.31-2.26). pembrolizumab was superior to ipilimumab (HR 1.71, 95%CI 1.19-2.46) with 27% of patients achieving complete response (CR). The superiority of pembrolizumab was also observed when compared to nivolumab (HR 1.39, 95%CI 1.02-1.90).

Patients who received nivolumab in earlier line and who get greater benefit to nivolumab treatment given after nivolumab. Secondary endpoints were response rate (RR) to nivolumab and general patient characteristics.

In the current UK treatment landscape for stage IIIb/IV NSCLC, only 73% of patients were treated with IO Tx in 1L. A high proportion of 1L patients is still treated with traditional chemotherapy. 30% of patients were treated with IO Tx in 1L. A high proportion of 1L patients is still treated with traditional chemotherapy.

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