New oncology reimbursements in Belgium

P. Specenier, MD, PhD

OVERVIEW OF BELGIAN REIMBURSEMENT NEWS

(BELG J MED ONCOL 2018;12(6):301-302)

ALECTINIB (ALECENSA®)

Alectinib (Alecensa®) is reimbursed as first-line treatment for patients with ALK-positive Non-Small Cell Lung Cancer (NSCLC). ALK-positivity should be demonstrated by at least one for lung cancer validated test, including ICH, NGS, ISH. A tabulated summary of the evidence on ALK inhibitors in NSCLC can be found in this issue. In the ALEX study, 303 treatment-naïve ALK-positive NSCLC patients were randomly assigned to receive alectinib 600 mg BID or crizotinib 250 mg BID.[1] Investigator-assessed progression-free survival (PFS; primary endpoint) was significantly longer with alectinib. Median PFS was not estimable (NE) (95% confidence interval [CI] 17.7-NE) with alectinib versus 11.1 months (95% CI 9.1-13.1) with crizotinib, with a hazard ratio (HR) of 0.47 (95 % CI 0.34-0.65); p<0.0001.

As we reported earlier in this journal, anti-PD-(L)-1 checkpoint inhibitors are reimbursed immediately for each indication upon approval by the European Medicines Agency (EMA).

NIVOLUMAB (OPDIVO®)

Nivolumab (Opdivo®) has been recently approved as monotherapy for the adjuvant treatment of adults with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection. This approval is based on the outcome of the phase III double-blind CheckMate-238 trial in which 906 patients with stages IIIB, IIIC, and IV completely resected melanoma were randomised 1:1 to nivolumab, 3 mg/kg every two weeks, or to ipilimumab, 10 mg/kg every three weeks for four doses, followed by 10 mg/kg every twelve weeks.[2] Treatment was administered for a period up to one year, or until disease recurrence, a report of unacceptable toxic effects, or withdrawal of consent. The primary end point was recurrence-free survival (RFS) in the intention-to-treat (ITT) population. At a minimum follow-up of eighteen months, the twelve-month rate of RFS was 70.5% (95% CI 66.1 -74.5) in the nivolumab group and 60.8% (95% CI 56.0-65.2) in the ipilimumab group (HR 0.65; 97.56% CI 0.51-0.83; p<0.001). Treatment-related grade 3 or 4 adverse events were reported in 14.4% of the patients in the nivolumab group and in 45.9% of those in the ipilimumab group; treatment was discontinued because of any adverse event in 9.7% and 42.6% of the patients, respectively. Two deaths (0.4%) related to toxic effects were reported in the ipilimumab group more than 100 days after treatment.

PEMBROLIZUMAB (KEYTRUDA®)

Pembrolizumab (Keytruda®) has been approved, in combination with pemetrexed and platinum chemotherapy, for the first-line treatment of metastatic non-squamous NSCLC in adults whose tumours have no EGFR or ALK positive mutations, and as monotherapy for the treatment of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) in adults whose tumours express PD-L1 with a ≥ 50% TPS and progressing on or after platinum-containing chemotherapy. KEYNOTE-189 is a double-blind, phase III trial,

Department of Oncology, University Hospital Antwerp, Edegem, Belgium.

Please send all correspondence to: P. Specenier, MD, PhD, Antwerp University Hospital, Department of Oncology, Wilrijkstraat 10, 2650 Edegem, Belgium, tel: +32 3 8214014, email: pol.specenier@uza.be.

Conflict of interest: The author has nothing to disclose and indicates no potential conflict of interest.

in which 616 patients with metastatic non-squamous NSCLC without sensitising EGFR or ALK mutations who had received no previous treatment for metastatic disease were randomly assigned 2:1 to receive pemetrexed and a platinum-based drug plus either 200 mg of pembrolizumab or placebo every three weeks for four cycles, followed by pembrolizumab or placebo for up to a total of 35 cycles plus pemetrexed maintenance therapy.[3] Crossover to pembrolizumab monotherapy was permitted among the patients in the placebo-combination group who had verified disease progression. The primary end points were overall survival and progression-free survival, as assessed by blinded, independent central radiologic review. After a median follow-up of 10.5 months, the estimated rate of overall survival (OS) at twelve months was 69.2% (95% CI 64.1-73.8) in the pembrolizumab-combination group versus 49.4% (95% CI 42.1-56.2) in the placebo-combination group (HR 0.49; 95% CI 0.38-0.64; p<0.001). Improvement in OS was seen across all PD-L1 categories that were evaluated. Median PFS was 8.8 months (95% CI 7.6-9.2) in the pembrolizumab-combination group and 4.9 months (95% CI, 4.7-5.5) in the placebo-combination group (HR 0.52; 95% CI 0.43-0.64; p<0.001). Adverse events of grade 3 or higher occurred in 67.2% of the patients in the pembrolizumab-combination group and in 65.8% of those in the placebo-combination group.

In KEYNOTE-040, 495 HNSCC patients who progressed after platinum-containing chemotherapy for recurrent/metastatic disease or who presented recurrence or progression within three to six months of multimodal therapy using platinum, were randomised 1:1 to receive pembrolizumab 200 mg every three weeks or standard of care (SOC) (docetaxel, methotrexate, or cetuximab).[4] The trial failed to improve OS in the ITT population (primary endpoint). The median OS was 8.4 months (95% CI 6.5-9.4) with pembrolizumab versus 7.1 months (95% CI 5.9-8.1) with SOC; HR 0.81 (95% 0.66-0.99); p=0.0204 (whereas a HR of 0.8 and a p value of 0.175 was required for statistical significance due to multiplicity). However, in patients with PD-L1 TPS ≥50%, OS was significantly improved with pembrolizumab with a median OS of 11.6 months (95% CI 8.3-19.5) with pembrolizumab versus 7.9 months (95% CI 4.8-9.3) with SOC; HR 0.57 (95% CI 0.35-0.82;); p=0.0017.

In patients with locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy and receive pembrolizumab as first line treatment, its used is now restricted to patients whose tumours express PD-L1 with a combined positive score (CPS) ≥10.

ATEZOLIZUMAB (TECENTRIQ®)

Likewise, atezolizumab (Tecentriq®), when administered as first-line treatment in patients with locally advanced or metastatic urothelial carcinoma who are considered cisplatin ineligible, its use is restricted to patients whose tumours have a PD-L1 expression ≥5%.

These restrictions do not apply to patients who received prior platinum containing chemotherapy.

LIPEGFILGRASTIM (LONQUEX®)

Since August 1st, 2018, new reimbursement criteria are available for lipegfilgrastim (Lonquex®). Lonquex is now reimbursed if administered, under the supervision of a centre for oncology and/or haematology, to reduce the incidence and duration of febrile neutropenia (FN) in patients treated with cytotoxic chemotherapy for malignancy (except chronic myeloid leukaemia and myelodysplastic syndromes), in each of the following situations:

1. For Primary Prevention of FN: a. Cytotoxic chemotherapy with a FN risk ≥ 20%. b. Cytotoxic chemotherapy with a FN risk > 10% and patient and tumour-related factors significantly increase the risk of FN. c. Use of dose-dense or dose-intense chemotherapy regimens. d. To avoid the need for dose reduction and/or dose delay, particularly with curative treatment or with first-line treatment of metastatic disease.
2. For Treatment and Secondary Prevention of FN: Either a neutropenia that is lower than 500/mm³ and more than 38 °C fever. Either a neutropenia that is lower than 500/mm³ for at least five days.

The reimbursement of lonquex is allowed on the basis of an electronic request via the eHealth platform.

REFERENCES

1. Peters S, et al. Alectinib versus Crizotinib in Untreated ALK-Positive Non-Small-Cell Lung Cancer. N Engl J Med. 2017;377(9):829-38.

2. Weber J, et al. Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma. N Engl J Med. 2017;377(19):1824-35.

3. Gandhi L, et al. Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. N Engl J Med. 2018;378(22):2078-92.

4. Cohen EE, et al. Pembrolizumab versus standard of care for recurrent or metastatic head and neck squamous cell carcinoma: Phase 3 KEYNOTE-040 trial. LBA45_PR ESMO Congress 2017.