New oncology reimbursements in Belgium

P. Specenier, MD, PhD

OVERVIEW OF BELGIAN REIMBURSEMENT NEWS

(BELG J MED ONCOL 2017;11(5):249-250)

As previously reported, Opdivo® (nivolumab) and Keytruda® (pembrolizumab) are reimbursed for all indications approved by the European Medicine's Agency (EMA).[1,2]

KEYTRUDA® (PEMBROLIZUMAB)

Keytruda® has received a positive opinion by the Committee for Medicinal Products for Human use (CHMP) for the treatment of locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy based on the outcome of **Keynote-045**.[2] Approval by the European Commission (EC) is expected in September 2017. Keytruda will be reimbursed for this indication upon EC approval. In KEYNOTE-045, 542 patients who had received a first line platinum-containing regimen for locally advanced/metastatic disease or as neoadjuvant/adjuvant treatment, with recurrence/progression <12 months following completion of therapy were randomised (1:1) to receive either KEYTRUDA 200 mg every three weeks (n=270) or investigator's choice of chemotherapy (IC) (paclitaxel 175 mg/m², docetaxel 75 mg/m², or vinflunine 320 mg/m², all administered every three weeks). Co-primary endpoints were overall survival (OS) and progression-free survival (PFS). There was no statistically significant difference between pembrolizumab and chemotherapy with respect to PFS. However, OS and objective response rate (ORR) were significantly better with pembrolizumab.

Median OS was 10.3 months (95% confidence interval [CI] 8.0-11.8) with pembrolizumab versus 7.4 months (95% CI 6.1-8.3) with IC, with a hazard ratio (HR) of 0.73 (95% CI 0.59-0.91; p=0.002).[4]

OPDIVO® (NIVOLUMAB)

Recently, Opdivo® (nivolumab) has been approved for the treatment of squamous cell cancer of the head and neck (HNSCC) in adults progressing on or after platinum-based therapy and for the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy.[1]

Approval and reimbursement in HNSCC is based on the results of the **CheckMate 141** trial, in which 361 patients progressing within six months after the last dose of platinum-containing chemotherapy were randomly assigned, in a 2:1 ratio, to receive nivolumab or standard-of-care (SOC) (weekly methotrexate, docetaxel, or cetuximab). OS (primary endpoint) was significantly longer with nivolumab than with SOC with a HR of 0.70 (97.73% CI 0.51-0.96; p=0.01). Median OS was 7.5 months (95% CI 5.5-9.1) in the nivolumab group versus 5.1 months (95% CI 4.0-6.0) with SOC. The ORR was 13.3% (95% CI 9.3- 18.3) with nivolumab versus 5.8% (95% CI 2.4-11.6) with SOC. There was no difference in PFS.[5]

Approval for urothelial carcinoma is based on the outcome of **CheckMate 275**, a phase II, single-arm study, enrolling 270 patients progressing during or following platinum-containing chemotherapy. Confirmed objective response was achieved in 19.6% of patients (95% CI 15.0-24.9). Confirmed objective response rate was 28.4% (95% CI 18-9-39.5) in patients with PD-L1 ≥ 5%, 23.8% (95% CI 16.5-32.3) in patients with PD-L ≥1%, and 16.1% (95% CI 10.5-23.1) in patients with PD-L1 <1%.[6]

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

Please send all correspondence to: T. Feys, MSc, MBA, Ariez International BV, Oude Houtlei 118, 9000 Ghent, Belgium, tel: +32 479 56 78 90, email: t.feys@ariez.com.

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

CYRAMZA® (RAMUCIRUMAB)

Cyramza® (ramucirumab) is a human receptor-targeted antibody that specifically binds VEGF
Receptor 2 and blocks binding of VEGF-A, VEGF-C, and VEGF-D.[7]

In REGARD, 355 patients with locally recurrent and unresectable, or metastatic gastric cancer (including gastro-esophageal junction [GEJ] adenocarcinoma) following platinum- or fluoropyrimidine-containing chemotherapy, were randomly assigned 2:1 to receive best supportive care (BSC) plus either ramucirumab 8 mg/kg or placebo every two weeks. The primary endpoint was OS and secondary endpoints included PFS. OS was statistically significantly improved in patients receiving ramucirumab as compared with patients receiving placebo (HR: 0.776; 95% CI: 0.603 to 0.998; p=0.0473), corresponding to an increase in median OS from 3.8 to 5.2 months. Progression-free survival was also statistically significantly improved in patients receiving ramucirumab (HR 0.483; 95% CI: 0.376 to 0.620; p<0.0001), corresponding to an increase in median PFS from 1.3 to 2.1 months.[8]

RAINBOW, is a global, randomised, double-blind, study of ramucirumab plus paclitaxel versus placebo plus paclitaxel conducted in 665 patients with locally recurrent and unresectable or metastatic gastric cancer (including GEJ adenocarcinoma) following platinum- and fluoropyrimidine-containing chemotherapy, with or without anthracycline. Ramucirumab at 8 mg/kg or placebo was administered on days 1 and 15 of a 28-day cycle. Paclitaxel at 80 mg/m² was administered on days 1, 8, and 15 of each 28-day cycle.[9]

ABRAXANE® (NAB-PACLITAXEL)

Abraxane® (nab-paclitaxel) can be reimbursed when it is used in combination with gemcitabine for the treatment of patients with metastatic pancreatic adenocarcinoma with an ECOG performance status of 0 or 1. In MPACT (Metastatic Pancreatic Adenocarcinoma Clinical trial, 861 patients were randomised to receive nab-paclitaxel 125 mg/m² followed by gemcitabine 1,000 mg/m² given on days 1, 8 and 15 of each 28-day cycle.[10]

Median overall survival (primary endpoint) was 8.5 months (95% CI 7.89, 9.53) with nab-paclitaxel/gemcitabine and 6.7 months (95% CI 6.01, 7.23) with a hazard ratio of 0.72 (95% CI 0.617, 0.835; p<0.0001). Median progression-free survival was 5.5 and 3.7 months, respectively (HR 0.69, p<0.0001). Overall response rate was 23% with the combination and 7% with gemcitabine (p<0.0001).[11]

GARDASIL 9®

Gardasil 9® is reimbursed for female persons between twelve and nineteen years of age. Gardasil 9 is a 9-valent vaccine against HPV types 6, 11, 16, 18, and five additional types (31, 33, 45, 52, and 58). Based on epidemiology studies, Gardasil 9 is anticipated to protect against the HPV types that cause approximately 90% of cervical cancers, >95% of adenocarcinoma in situ (AIS), 75-85% of high-grade cervical intraepithelial neoplasia (CIN 2/3), 85-90% of HPV related vulvar cancers, 90-95% of HPV related high-grade vulvar intraepithelial neoplasia (VIN 2/3), 80-85% of HPV related vaginal cancers, 75-85% of HPV related high-grade vaginal intraepithelial neoplasia (VaIN 2/3), 90-95% of HPV related anal cancer, 85-90% of HPV related high-grade anal intraepithelial neoplasia (AIN2/3), and 90% of genital warts.[12]

REFERENCES

1. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003985/WC500189765.pdf.

2. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003820/WC500190990.pdf.

3. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/003820/smops/Positive/human_smop_001170.jsp&mid=WC0b01ac058001d127.

4. Bellmunt J, et al. Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma. N Engl J Med. 2017; 376(11):1015-26.

5. Ferris RL, et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. N Engl J Med. 2016;375(19):1856-67.

6. Sharma P, et al. Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial. Lancet Oncol. 2017;18(3):312-22.

7. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002829/WC500180724.pdf.

8. Fuchs CS, et al. REGARD Trial Investigators. Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet. 2014;383:31-9.

9. Wilke H, et al. RAINBOW Study Group. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. Lancet Oncol. 2014;15(11):1224-35.

10. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000778/WC500020435.pdf.

11. Von Hoff DD, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med. 2013;369(18):1691-703.