New oncology reimbursements in Belgium

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OVERVIEW OF BELGIAN REIMBURSEMENT NEWS

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ALECTINIB (ALECENSA®)

Alectinib (Alecensa®) was already reimbursed for patients with ALK-positive advanced non-small cell lung cancer (NSCLC) progressing during or after treatment with crizotinib or intolerant to crizotinib.

ALK positivity had to be demonstrated by immunohistochemistry (ICH) and confirmed by fluorescence in situ hybridization (FISH).

Now it will also be reimbursed for previously untreated ALK-positive advanced NSCLC. ALK status shall be demonstrated by at least one validated test: ICH, in situ hybridization (ISH), and/or Next Generation Sequencing (NGS). The test shall be done in a laboratory which can guarantee the validation of the analytical procedures.

Reimbursement shall be requested via the e-health system by a medical oncologist or a pulmonologist with particular competence in oncology.

Approval for first-line treatment is based on the results of the **ALEX** trial in which 303 patients with previously untreated patients ALK-positive NSCLC were randomised to receive either alectinib (600 mg twice daily) or crizotinib (250 mg twice daily). The rate of investigator-assessed progression-free survival (PFS) (primary endpoint) was significantly higher with alectinib than with crizotinib (12-month PFS rate 68.4% [95% CI 61.0-75.9] with alectinib *vs.* 48.7% [95% CI 40.4-56.9] with crizotinib; hazard ratio [HR] for disease progression or death: 0.47 [95% CI 0.34-0.65]; p<0.001); the median PFS with alectinib was not reached as compared with 11.1 months (95% CI 9.1-13.1) with crizotinib. The results for independent review committee (IRC)-assessed PFS were consistent with those for the primary endpoint. Twelve percent of patients in the alectinib group had an event of central nervous (CNS) progression, as compared with 45% of patients in the crizotinib group (cause-specific HR: 0.16; 95% CI 0.10-0.28; p<0.001). The overall response rate (ORR) was 82.9% (95% CI 76.0-88.5) with alectinib *vs.* 75.5% (95% CI 67.8-82.1) with crizotinib (p=0.09). Grade ≥ 3 adverse events (AEs) were less frequent with alectinib (41% *vs.* 50%).

In **J-ALEX**, 207 ALK inhibitor-naive Japanese patients with ALK-positive NSCLC who were chemotherapy-naive or had received one previous chemotherapy regimen, were randomly assigned (1:1) to receive oral alectinib 300 mg twice daily or crizotinib 250 mg twice daily until progressive disease, unacceptable toxicity, death, or withdrawal. The primary endpoint was PFS assessed by an IRC. At the second interim analysis, an independent data monitoring committee (IDMC) determined that the primary endpoint of the study had been met (HR: 0.34 [99.7% CI 0.17-0.71], stratified log-rank p<0.0001) and recommended an immediate release of the data. Median progression-free survival had not yet been reached with alectinib (95% CI 20.3-not estimable [NE]) and was 10·2 months (95 % CI 8.2-12.0) with crizotinib. Grade ≥ 3 AEs occurred at a greater frequency with crizotinib (52% *vs.* 26 %). Dose interruptions due to adverse events were also more prevalent with crizotinib

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and more patients receiving crizotinib discontinued the study drug because of an adverse event.

AVELUMAB (BAVENCIO®)

Avelumab (Bavencio®) is reimbursed when it is administered for an indication mentioned in the summary of product characteristics (SPC); treatment of adult patients with metastatic Merckel Cell Carcinoma (MCC) (monotherapy).
Reimbursement shall be requested via the e-health system by a medical oncologist or a specialist with experience in this indication.
The efficacy and safety of avelumab was investigated in the study EMR100070-003 **(JAVELIN Merkel 200)** with two parts. Part A was a single-arm, multicentre study conducted in patients (N=88) with histologically confirmed metastatic MCC, whose disease had progressed on or after chemotherapy administered for distant metastatic disease.
Part B included patients with histologically confirmed metastatic MCC who were treatment-naïve to systemic therapy in the metastatic setting.
For Part A, the major efficacy outcome measure was confirmed best overall response (BOR). The ORR was 33.0% (95% CI 23.3-43.8). The complete response (CR) and partial response (PR) rates were 11.4% and 21.6%, respectively. The median duration of response (DOR) was not reached (18-NE). Six- and twelve-month PFS rates were 40% (95% CI 29-50) and 30% (95% CI 41-41), respectively. Median OS was 12.9 months (95% CI 7.5-NE).
For Part B, the major efficacy outcome measure was durable response, defined as objective response (complete response (CR) or partial response (PR)) with duration of at least six months.
For Part B, an interim analysis of efficacy was conducted with 39 patients who received at least one dose. The ORR was 62.1% (95% CI 42.3-79.3)(CR: 13.8; PR: 48.3%). Median PFS was 9.1 months (95% CI 1.9-not estimable).

REFERENCE

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RIBOCICLIB (KISQALI®)

Ribociclib (Kisqali®) can be reimbursed in association with a non-steroidal aromatase inhibitor for the treatment of postmenopausal patients with hormone-receptor positive HER-2 negative locally advanced or metastatic breast cancer who received have received adjuvant tamoxifen and who relapsed within twelve months after the end of adjuvant therapy.
Reimbursement shall be requested via the e-health system by a medical oncologist or a specialist with particular competence in oncology and with experience in chemotherapy for breast cancer.
MONALEESA-2 is a randomised, double-blind, placebo-controlled, multicentre phase III clinical study in which 668 patients, who received no prior therapy for advanced disease, were randomized in a 1:1 ratio to receive either ribociclib and letrozole (N=334) or placebo and letrozole (N=334), stratified according to the presence of liver and/or lung metastases. Ribociclib was given orally at a dose of 600 mg daily for 21 consecutive days followed by seven days off treatment in combination with letrozole 2.5 mg once daily for 28 days. Cross-over was not allowed.
The primary endpoint was locally assessed PFS. At the time of the second interim analysis, the median duration of follow-up was 26.4 months. Median PFS was 25.3 months (95% CI 23.0-30.3) for ribociclib plus letrozole and 16.0 months (95% CI 13.4-18.2) for placebo plus letrozole (HR: 0.568; 95% CI 0.457-0.704; log-rank p=9.63x10-8). OS data remain immature, with 116 deaths observed; 50 in the ribociclib arm and 66 in the placebo arm (HR: 0.746; 95% CI 0.517-1.078). The ORR was 42.5% with ribociclib plus letrozole versus 28.7% with placebo plus letrozole. The most common grade >3 AEs (≥5% of the patients in either group) were neutropenia (59.3% in the ribociclib group and 0.9% in the placebo group), leukopenia (21.0% and 0.6%, respectively), hypertension (9.9% and 10.9%), increased alanine aminotransferase level (9.3% and 1.2%), lymphopenia (6.9% and 0.9%), and increased aspartate aminotransferase level (5.7% and 1.2%). Febrile neutropenia occurred in five patients (1.5%) in the ribociclib group and in none in the placebo group. The rates of discontinuation because of AEs were 7.5% and 2.1%, respectively.

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