HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
21 SEPTEMBER 2022

The legally binding text is the original French opinion version

Inotuzumab ozogamicin
BESPONSA 1 mg, powder for concentrate for solution for infusion

Reassessment

Key points

Approval of reimbursement only for the treatment of adult patients with relapsed or refractory Philadelphia chromosome-negative (Phi-), CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL).
Actual clinical benefit is now deemed to be substantial (previously it was low) in this indication.

Therapeutic improvement?

No improvement in relation to chemotherapy.

Role in therapeutic strategy?

In adult patients with relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL) with Philadelphia chromosome negative (Phi-), the treatment options (in addition to BESPONSA (inotuzumab ozogamicin)) are:

- further induction polychemotherapy (may or may not be similar to first line, conventional or clofarabine-based) followed by consolidation with allogeneic HSCT if a second complete remission is achieved, and if eligible,
- BLINCYTO (blinatumomab) in adult patients with CD 19 positive relapsed or refractory Philadelphia chromosome negative B-cell precursor ALL,
- KYMRIAH (tisagenlecleucel) in children and young adults (up to and including 25 years of age) with B-cell ALL that is refractory, in relapsed post-transplant or in second or later relapse,
- palliative supportive care.

Role of the medicinal product

BESPONSA (inotuzumab ozogamicin) is a treatment option for adult patients with acute relapsed or refractory Philadelphia chromosome-negative (Phi-), CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL).
Given the lack of direct comparative data (concurrent development) or indirect comparative data of an acceptable methodological quality, its role vis-à-vis BLINCYTO (blinatumomab) and KYMRIAH (tisagenlecleucel) cannot be specified.

COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Phi- B-cell precursor acute lymphoblastic leukaemia is a severe malignant haemopathy characterised by a monoclonal proliferation of poorly differentiated lymphoid hematopoietic precursors that are blocked at an early stage and unable to complete their maturation. This leads to the progressive invasion of bone marrow, blood and even certain organs. It is a life-threatening disease in the short term.

◗ The proprietary medicinal product BESPONSA (inotuzumab ozogamicine) is a curative medicinal product.

◗ The efficacy/adverse-effect ratio remains poorly defined, given that efficacy has only been demonstrated in terms of complete remission with a significant effect size, but without evidence of efficacy in terms of overall survival and with a safety profile marked by a more frequent occurrence of VOD/SOS. However, the preliminary data on use in France is considered satisfactory in view of the medical need and the available alternatives (**expert opinion**).

◗ Therapeutic alternatives are available.

◗ BESPONSA (inotuzumab ozogamicin) is a treatment option for adult patients with relapsed or refractory Philadelphia chromosome negative (Phi-), CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL).

Public health benefit

Considering:

- the severity of relapsed or refractory B-cell precursor acute lymphoblastic leukaemia,
- its low incidence (about 800 new cases per year),
- the partially met medical need,
- the lack of response to the need identified on the basis of the available data (improvement in complete remission, no demonstrated impact on overall survival and quality of life),
- the lack of sufficient data to enable an assessment of its additional impact on the care pathway,

BESPONSA (inotuzumab ozogamicine) is not likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the actual clinical benefit of BESPONSA (inotuzumab ozogamicin) is substantial in relapsed or refractory Philadelphia chromosome negative (Phi-), CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL).

The Committee approves the continued inclusion in the list of proprietary medicinal products approved for community use in the indication for the treatment of adult patients with relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL), (Philadelphia chromosome negative (Phi-)).

Clinical Added Value

Considering:

- **the evidence of the superiority of BESPONSA (inotuzumab ozogamicin) in relation to chemotherapy concerning the complete remission (CR) rate, or complete remission with incomplete haematologic recovery (CRi), with a point-estimated absolute difference of 51% (CI 97.5% [38-64]), considered as clinically relevant, in a randomised, open-label, phase III study;**
- **the lack of evidence of an increase in overall survival;**
- **the lack of formal conclusions that can be drawn from the quality-of-life results;**
- **the more frequent occurrence of occlusive venoocclusive disease/sinusoidal obstruction syndrome;**
- **higher 100-day post-transplant mortality than with chemotherapy;**

the Committee deems that BESPONSA (inotuzumab ozogamicin) provides no clinical added value (CAV V) compared to standard chemotherapy in adult patients with relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL) (with Philadelphia chromosome negative (Phi-)).