Report AUCATZYL® - Obecabtagene autoleucel

Product & Mechanism of action

Substance: Obecabtagene autoleucel

Brand Name: Aucatzyl

Originator/licensee: Autolus GmbH

Classification: NCE

ATC code: L01XL

Orphan Status:
Eu: Yes
Us: Yes

Mechanism of action: Obe-cel is an autologous immunotherapy consisting of the pt's own T cells engineered to express a chimeric antigen receptor that recognises and binds to CD19 on target cells. This results in activation of the immunological effect of the T-cell releasing inflammatory cytokines and chemokines, leading to killing of CD19-expressing cells [1].

Authorized indications Licensing status

Authorized Indication:
EMA: Obe-cel is indicated for the treatment of adults ≥ 26 years of age and above with R/R B ALL [1].

FDA: Obe-cel is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adults with R/R B ALL [2].

Route of administration: IV

Licensing status
EU CHMP P.O. date: 22/05/2025
FDA M.A. date: 08/11/2024

EU Speed Approval Pathway: No
FDA Speed Approval Pathway: No

ABBREVIATIONS:
AE: Adverse Event
B ALL: B cell precursor acute lymphoblastic leukaemia
CHMP: Committee for Medicinal Products for Human Use
CI: Confidential Interval
CR: Complete Remission
CRi: Complete remission with incomplete hematologic recovery
ECOG: Eastern Cooperative Oncology Group
HR: Hazard Ratio
ICANS: Immune effector cell-associated neurotoxicity syndrome
IV: Intravenously
M.A.: Marketing Authorization
Obe-cel: Obecabtagene autoleucel
PFS: Progression-Free Survival
Ph: Philadelphia chromosome
PI: Proteasome inhibitor
P.O.: Positive Opinion
PS: Performance Status
Pts: Patients
R/R: Relapsed or refractory
SAE: Serious adverse events
SCT: Stem cell transplant
TKI: Tyrosine kinase inhibitor
TRAE: Treatment related AEs
WHO: World Health Organization

Essential therapeutic features

Summary of clinical EFFICACY:
FELIX study (NCT04404660) is an open-label, multi-centre, single-arm, phase Ib/II study in adults with R/R B ALL. The study consists of two phases and includes three pts. cohorts (cohorts A, B, and C). Cohort A in phase II is the pivotal cohort, on which the efficacy of obe-cel is evaluated.
Eligible pts. were ≥ 18 years of age with either primary refractory B ALL, a first relapse, if first remission ≤12 months, R/R disease after two or more lines of systemic therapy, or R/R disease after allogeneic transplant, provided obe-cel infusion occurs ≥3 months after SCT.
Pts had to have an ECOG PS of 0-1 and a disease burden of ≥ 5% blasts in bone marrow at screening. Pts. with Ph+ disease were eligible, if they were intolerant to or had failed two lines of any TKI or one line of second generation TKI, or if TKI therapy is contraindicated.

N=127 pts. received ≥1 infusion of obe-cel, of whom n=94 were enrolled in phase II, cohort A. Obe-cel was administered in a split dose adjusted according to bone marrow burden, following lymphodepletion. Bone marrow assessment was required prior to lymphodepletion to determine the appropriate dose.
The second dose of obe-cel was given only, if no severe or unresolved toxicities were present. A total of 88 of 94 pts. (94%) in cohort 2A received both doses.

The primary end point was overall remission in cohort 2A, defined as CR or complete remission with incomplete hematologic recovery.
The median follow-up in cohort 2A was 20.3 months. Responses are summarized in table 1 [3].

Table 1: Response in Cohort IIA and in All the Pts. Who Received at Least One Infusion of Obe-Cel.

	Phase II, Cohort A (n=94)	All pts. who received an infusion (n=127)
CR or CRi		
No. of pts.	72	99
% (95% CI)	77 (67-85)	78 (70-85)
CR — no. (%)	52 (55)	73 (57)
CRi — no. (%)	20 (21)	26 (20)

Summary of clinical SAFETY:
Cytokine release syndrome has been eveloped in 87 of 127 pts. (68.5%), with events of grade ≥3 in three pts. (2.4%). ICANS has been developed in 29 of 127 pts. (22.8%), with events of grade ≥3 in nine pts. (7.1%). Of these nine pts., five (56%) had more than 75% bone marrow blasts before lymphodepletion and four (44%) had 5 to 75% bone marrow blasts.
Death occurred in 45 pts. (35.4%). In two pts., death was attributable to obe-cel: one pt. died of acute respiratory distress syndrome with ongoing ICANS, and one died of neutropenic sepsis [3].

Ongoing studies:
- ***For the same indication:*** Yes
- ***For other indications:*** No

Discontinued studies (for the same indication): No

References:
[1] https://www.ema.europa.eu/en/medicines/human/EPAR/aucatzyl
[2] https://www.fda.gov/media/183463/download
[3] https://www.nejm.org/doi/full/10.1056/NEJMoa2406526
[4] https://link.springer.com/article/10.1007/s10552-015-0657-6
[5] https://www.orpha.net/en/disease/detail/513
[6] https://www.mdpi.com/2073-4409/14/5/371

NHS impact

Cost of therapy:
Price is not available yet.

Epidemiology:
ALL is a rare haematological malignancy of the bone marrow. The prevalence of ALL is 1-5/10,000. ALL comprises <1% of adult cancers, but represents the most common childhood malignancy, accounting for approximately 25% of cancers and 80% of all leukaemia in children [4,5].

POSSIBLE PLACE IN THERAPY:
First-line treatment typically involves intensive multi-agent chemotherapy protocols.
The treatment of R/R ALL is a challenging area, with allogeneic hematopoietic SCT remaining the only curative option for pts., who experience relapse.
Blinatumomab and inotuzumab ozogamicin are therapeutic alternatives for relapsed pts., but they tend to produce short duration of response. CAR T cell–based therapies are already available [6].

The addition of Obecabtagene autoleucel to these regimens could represent a further opportunity for these pts.

OTHER INDICATIONS IN DEVELOPMENT: -

SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: -

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION: Venetoclax (NCT03808610; NCT03504644); TBI-1501 (NCT03155191); Vyxeos (NCT03575325)

*Service reorganization: No
*Possible off label use: Yes