HTA Austria
Austrian Institute for
Health Technology Assessment
GmbH

Dorocubicel + unexpanded CD34- cells (Zemcelpro) for the treatment of haematological malignancies in adults

HTA-Appendix

Final Appendix

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1 Introduction

1.1 Disease background

Table 1-1: Overview of guidelines for specific diseases

Disease	Guideline/Title	Reference
Acute myeloid leukaemia	ESMO/Acute myeloid leukaemia in adult patients: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up Onkopedia/Akute Myeloische Leukämie (AML)	[1] [2]
Chronic myeloid leukaemia	ESMO/Chronic myeloid leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up Onkopedia/Chronische Myeloische Leukämie (CML)	[3] [4]
Lymphoma	ESMO/Lymphomas: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up Onkopedia/ Hodgkin Lymphom	[5] [6]
Mulitple myeloma	ESMO/Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up Onkopedia/ Multiples Myelom	[7] [8]
Myelodysplastic syndromes	ESMO/Myelodysplastic syndromes: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up Onkopedia/Myelodysplastic Neoplasms	[9] [10]
Myeloproliferative neoplasms	ESMO/Philadelphia chromosome-negative chronic myeloproliferative neoplasms: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up Onkopedia/ Myeloproliferative Neoplasien (MPN) (früher: Chronische Myeloproliferative Erkrankungen (CMPE))	[11] [12]

Abbreviations: AML…acute myeloid leukaemia, CML…chronic myeloid leukaemia, CMPE…chronic myeloproliferative diseases, EHA…European Hematology Association, ESMO…European Society For Medical Oncology, MPN…myeloproliferative neoplasm

1.2 Standard of care

Table 1-2: Results from the transplant report [13]

Indication	Allogeneic		Autologous		Total SCT	CAR T
	1st SCT	2nd/3rd SCT	1st SCT	2nd/3rd SCT		
AML & related precursor neoplasms including mixed phenotype AL	115	6	0	0	121	0
Precursor Lymphoid Neoplasms	35	6	0	0	41	4
Total acute leukaemia	**150**	**12**	**0**	**0**	**162**	**4**
CML	4	0	0	0	4	0
CLL/PLL/Richter	1	0	0	0	1	0
Total chronic leukaemia	**5**	**0**	**0**	**0**	**5**	**0**
NHL/ undiff.	12	0	57	3	72	83

HL	1	0	15	0	16	0
Total lymphoma	**13**	**0**	**72**	**3**	**88**	**83**
Myeloma	0	0	180	44	224	57
Others	2	0	14	1	17	5
Total plasma cell diseases	**2**	**0**	**194**	**45**	**241**	**62**
Total solid tumours	**1**	**0**	**17**	**7**	**25**	**0**
MPN/MDS	**55**	**5**	**0**	**0**	**60**	**0**
Other diseases	**25**	**2**	**1**	**0**	**28**	**1**
Total allogeneic and autologous SCT	**251**	**19**	**284**	**55**	**609**	**150**

Abbreviations: AL…acute leukaemia, AML…acute myeloid leukaemia, CAR…chimeric antigen receptor, CLL…chronic lymphatic leukaemia, CML…chronic myeloid leukaemia, HL…Hodgkin lymphoma, NHL…Non-Hodgkin lymphoma, MDS…myelodysplastic syndrome, MPN…myeloproliferative neoplasm, PLL…prolymphozytic leukaemia, SCT…stem cell transplantation

Management of cord blood (CB)

Cord blood (CB) cells for allogeneic use are collected in more than 160 public CB banks worldwide, with more than 800,000 CB units being available for transplantation [14]. The following steps are included in the collection and storage of CB:

Before delivery:

- Provision of information on CB donation
- Consent from parents
- Assessment of donor eligibility
- Testing of maternal blood for infectious disease markers

Collection:

- Collection of CB in utero (before the placenta is delivered) or ex utero (after the placenta is delivered)
- Labour characteristics are noted (including description of incidences like fever or other complications, drugs administered, etc.)
- Local storage after collection
- Transportation to the processing centre

Storage:

- Cryopreservation within 48 hours after collection in the processing laboratory
- Many CB banks are now committed to processing and storing only those CB units with high TNC (e.g., >150 × 10^7 TNC or higher)
- Volume reduction (centrifugation)

Table 1-3: Selection criteria for cord blood [14]

Initial selection of a single CBU:
a) HLA matching of the recipient and CBU
b) CBU cell dose (TNC ± CD34+) at cryopreservation
c) Patient's diagnosis (malignant versus nonmalignant)
d) Avoiding CBU containing Ag that matches the specificity of any pretransplant donor-specific anti-HLA Ab in the recipient
HLA matching should be based upon allelic typing for HLA-A, HLA-B, HLA-C, and HLA-DRB1 for single CBT
1. Select an HLA-matched (8/8) CBU. TNC dose should be $>3 \times 10^7$ /kg
2. If an HLA-matched (8/8) CBU is unavailable, select a CBU matched at 7/8 HLA loci. HLA-A or HLA-B mismatches are preferable to HLA-DRB1 mismatches. TNC dose should be $>3 \times 10^7$ /kg for 5–7/8 matched units
3. If a CBU matched at 8/8 or 7/8 HLA loci is unavailable, consider a CBU matched at 5 or 6/8 HLA loci. Avoid mismatches in HLA-DRB1
4. If CBU 4/8 matched, CBU may rarely be considered as a single CB graft if no other option is available. TNC dose should be $>5 \times 10^7$ /kg for 4/8 matched units
5. CBU 3/8 HLA-matched CBU is not recommended
Other criteria: nucleated cell dose, CD34+ cell dose, AB0 compatibility

Abbreviations: CB…cord blood, CBU…cord blood unit, HLA…human leukocyte antigen, TNC…total nucleated cell count

Note: This table presents cord blood unit selection criteria based on the EBMT Handbook, which serves as the primary European guideline and was recommended by clinical experts. However, specific selection criteria may vary between individual countries and transplant centers.

1.3 Medicinal product under evaluation

No additional tables or figures are provided for this chapter.

2 Scope of assessment

No additional tables or figures are provided for this chapter.

3 Methods

Guiding questions based on the EUnetHTA core model [15]

Table 3-1: Health problem and current use

Element ID	Research question
A0001	For which health conditions, and for what purposes, is the technology used?
A0002	What is the disease or health condition in the scope of this assessment?
A0025	How is the disease or health condition currently managed according to published guidelines and in practice?
A0007	What is the target population in this assessment?
A0023	How many people belong to the target population?

Table 3-2: Description of the technology

Element ID	Research question
B0001	What is the technology and the comparator(s)?
A0020	For which indications has the technology received marketing authorisation or CE marking?
B0003	What is the phase of development and implementation of the technology and the comparator(s)?
B0004	Who administers the technology and the comparators and in what context and level of care are they provided?
B0008	What kind of special premises are needed to use the technology and the comparator(s)?
B0009	What supplies are needed to use the technology and the comparator(s)?
A0021	What is the reimbursement status of the technology?
A0018	What are the other typical or common alternatives to the current technology?
A0022	Who manufactures the technology?

Table 3-3: Clinical effectiveness

Element ID	Research question
D0001	What is the expected beneficial effect of the technology on mortality?
D0005	How does the technology affect symptoms and findings (severity, frequency) of the disease or health condition?
D0006	How does the technology affect progression (or recurrence) of the disease or health condition?
D0011	What is the effect of the technology on patients' body functions?
D0016	How does the use of technology affect activities of daily living?
D0012	What is the effect of the technology on generic health-related quality of life?
D0013	What is the effect of the technology on disease-specific quality of life?

Table 3-4: Safety

Element ID	Research question
C0008	How safe is the technology in comparison to the comparator(s)?
C0005	What are the susceptible patient groups that are more likely to be harmed through the use of the technology?
B0010	What kind of data/records and/or registry is needed to monitor the use of the technology and the comparator?

Table 3-5: Economic aspects

Element ID	Research question
E0001	What types of resources are used when delivering the assessed technology and its comparators (resource-use identification)?
A0002	What amounts of resources are used when delivering the assessed technology and its comparators (resource-use measurement)?
E0009	What were the measured and/or estimated costs of the assessed technology and its comparator(s)?
E0010	What are the uncertainties surrounding the costs and economic evaluation(s) of the technology and its comparator(s)?
E0013	What methodological assumptions were made in relation to the technology and its comparator(s)?

Table 3-6: Organisational, ethical, and social aspects

Element ID	Research question
G0002	What kind of involvement has to be mobilised for patients/participants and important others and/or caregivers?
G0101	What are the processes ensuring access to the new technology for patients/participants?
H0200	What are the experiences of living with the condition?
H0100	What expectations and wishes do patients have with regard to the technology and what do they expect to gain from the technology?
H0006	How do patients perceive the technology under assessment?
H0002	What is the burden on caregivers?
F0010	What are the known and estimated benefits and harms for patients when implementing or not implementing the technology?
F0104	Are there any ethical obstacles for evidence generation regarding the benefits and harms of the intervention?
H0012	Are there factors that could prevent a group or person from gaining access to the technology?

3.1 Search strategy

3.1.1 Cochrane

Date of search: 16.09.2025	
ID	**Search**
#1	(dorocubicel*) (Word variations have been searched)
#2	(zemcelpro*) (Word variations have been searched)
#3	("ect 001") (Word variations have been searched)
#4	("ect 001 cb") (Word variations have been searched)
#5	("ect 001 um 171") (Word variations have been searched)
#6	("ect 001cb") (Word variations have been searched)
#7	(ect001*) (Word variations have been searched)
#8	("ect001 um171") (Word variations have been searched)
#9	(ect001cb) (Word variations have been searched)
#10	("cord blood expanded") (Word variations have been searched)
#11	(UM171*) (Word variations have been searched)
#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
#13	((clinicaltrials OR trialsearch OR ANZCTR OR ensaiosclinicos OR Actrn OR chictr OR cris OR ctri OR registroclinico OR clinicaltrialsregister OR DRKS OR IRCT OR Isrctn OR rctportal OR JapicCTI OR JMACCT OR jRCT OR JPRN OR Nct OR UMIN OR trialregister OR PACTR OR R.B.R.OR REPEC OR SLCTR OR Tcr)):so
#14	#12 NOT #13

3.1.2 Embase

Date of search: 16.09.2025		
Number	**Search**	**Results**
#15	#13 NOT #14	179
#14	'clinical trial':dtype	533,362
#13	1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	185
#12	um171	159
#11	'cord blood expanded'	7
#10	'ect001cb'	4
#9	'ect001 um171'	0
#8	'ect001'	2
#7	'ect 001cb'	0
#6	'ect 001 um 171'	0
#5	'ect 001 cb'	0
#4	'ect 001'	10
#3	dorocubicel*	101
#2	'dorocubicel'/exp	101
#1	zemcelpro*	0

3.1.3 International HTA database

Date of search: 17.09.2025	
Search step	**Search query, "Hits", "Search At"**
9	(UM171*) OR ("cord blood expanded") OR (ect001cb) OR (ect001*) OR ("ect 001cb") OR ("ect 001") OR (zemcelpro*) OR (dorocubicel*),"0","2025-09-17T08:57:16.000000Z"
8	UM171*,"0","2025-09-17T08:52:00.000000Z"
7	"cord blood expanded","0","2025-09-17T08:50:49.000000Z"
6	ect001cb,"0","2025-09-17T08:49:04.000000Z"
5	ect001*,"0","2025-09-17T08:48:41.000000Z"
4	"ect 001cb","0","2025-09-17T08:48:26.000000Z"
3	"ect 001","0","2025-09-17T08:48:03.000000Z"
2	zemcelpro*,"0","2025-09-17T08:45:59.000000Z"
1	dorocubicel*,"0","2025-09-17T08:45:37.000000Z"

3.1.4 Medline

Date of search: 16.09.2025	
1	dorocubicel.mp. (0)
2	zemcelpro.mp. (0)
3	"ect 001".mp. (0)
4	"ect-001 cb".mp. (0)
5	"ect 001 cb".mp. (0)
6	"ect 001 um 171".mp. (0)
7	ect 001cb.mp. (0)
8	ect001cb.mp. (0)
9	cord blood expanded.mp. (3)
10	UM171*.mp. (67)
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 (70)
12	remove duplicates from 11 (70)

3.2 Study selection – PRISMA flow chart

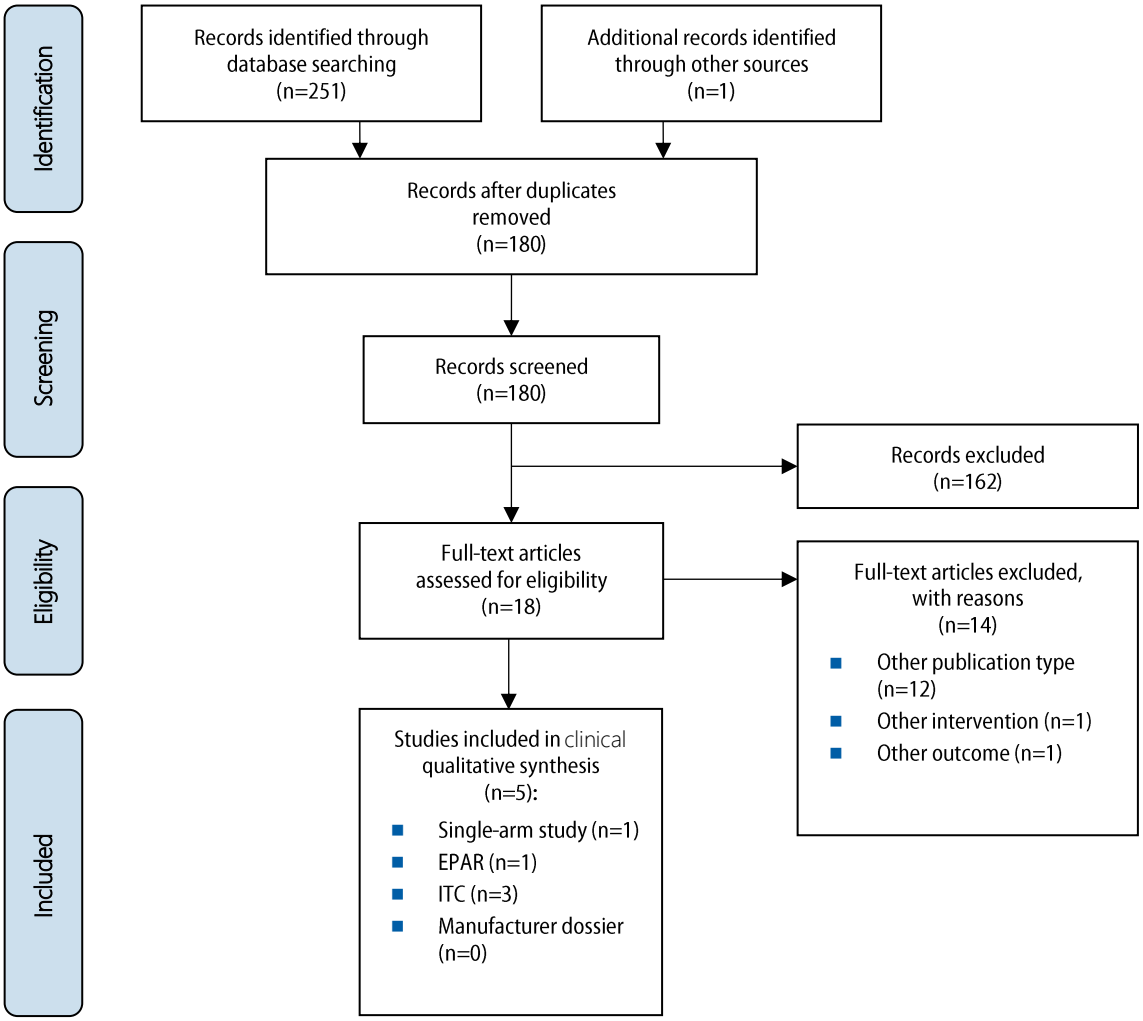

Figure 3-1: Flow chart of study selection (PRISMA Flow Diagram)

Note: The systematic literature search did not identify any economic model for Zemcelpro.

Abbreviations: EPAR…European public assessment report, ITC…indirect treatment comparison, n…number

3.3 Organisational, ethical and social assessment

3.3.1 Structured patient questionnaire

Table 3-1: Questions for patients diagnosed with haematological malignancies

Questions for patients	
Question 1	In welcher Rolle füllen Sie den Fragebogen aus? ■ Einzelne/r Patient:in ■ Angehörige ■ Andere
Question 2	In welchem Land befindet sich Ihr Hauptwohnsitz?
Question 3	Sind Sie Mitglied einer Patient:innenorganisation? Wenn ja: ■ Bei welcher Patient:innenorganisation sind Sie Mitglied? ■ Welche Erkrankung/en wird/werden von der Patient:innenorganisation vertreten? ■ Welche Rolle haben Sie in der Patient:innenorganisation?
Question 4a	Wie lautet die Diagnose?
Question 4b	In welchem Stadium befindet sich die Erkrankung? Wie würden Sie den Schweregrad aktuell einschätzen?
Question 4c	Welche Symptome haben Sie/haben Ihre Angehöriger/Ihr Angehöriger derzeit?
Question 4d	Krankheitsgeschichte: ■ Seit wann leben Sie/Ihre Angehörige/Ihr Angehöriger mit der Erkrankung? Wann wurde sie diagnostiziert? ■ Bitte beschreiben Sie die Behandlungsgeschichte: Wie wurde die Erkrankung festgestellt? Welche Behandlungen wurden bisher durchgeführt?
Question 4e	Zusätzliche Information, die Ihrer Meinung nach für den HTA-Bericht hilfreich wäre.
Question 5	Falls zutreffend, wie sind Sie an Informationen zu den Erfahrungen von Patient:innen gelangt? ■ Persönliche Erfahrungen ■ Erlebnisse von Patient:innen
Question 6	Was beeinflusst die Erkrankung Ihr tägliches Leben (bzw. das Leben einer Patient/ eines Patienten)?
Question 7	Nur für Patient:innen: Welche Auswirkungen hat die Erkrankung auf Ihr familiäres und soziales Umfeld?
Question 8	Nur für Angehörige: Wie wirkt sich die Erkrankung auf das familiäre und soziale Umfeld aus?
Question 9	Wie geht es Ihnen/Ihre Angehörigen/Ihnen mit der derzeit angewandten Therapie? Falls keine spezifische Therapie zur Verfügung steht, geben Sie das bitte an.
Question 10	Kennen Sie das Medikament Zemcelpro?
Question 11a	Was würden Sie/Ihre Angehörige/Ihr Angehöriger im Allgemeinen von einer neuen Therapie erwarten?
Question 11b	Welche Bedenken haben Sie gegenüber dem neuen Medikament?
Question 12	Für Personen, die Erfahrung mit Zemcelpro im Rahmen von klinischen Studien haben: Welche Auswirkungen hatte/hat es auf Ihr Leben (positive und negative Auswirkungen)?
Question 13	Bitte geben Sie alles an, was Ihrer Meinung nach für die Bewertung des Arzneimittels durch das zuständige HTA-Team wissenswert sein könnte (z.B. ethische oder soziale Aspekte).
Question 14	Bitte fassen Sie die aus Ihrer Sicht wichtigsten Punkte in maximal fünf Aussagen zusammen. Beispiel: ■ Die größten Herausforderungen eines Lebens mit Blutkrebs sind … ■ Die derzeitigen Therapien/Gesundheitsinterventionen sind ungeeignet, weil … ■ Die Patient:innen erwarten sich von einer neuen Therapie vor allem …

Abbreviations: HTA…health technology assessment

3.3.2 Consultations with clinical experts

Table 3-2: Questions for clinical experts

Questions about the population	
Question 1	Was sind die häufigsten Indikationen für eine allogene Stammzelltransplantation bei Erwachsenen in Österreich?
Question 2	Welche Spender werden bei Erwachsenen in Österreich am häufigsten verwendet?
Question 3	Welche Quellen für hämatopoetische Stammzellen werden in Österreich verwendet?
Question 4	Wie viele Patient:innen in Österreich für Zemcelpro möglich/relevant?
Questions about the intervention	
Question 5	Welche zusätzlichen logistischen Anforderungen entstehen für Transplantationszentren?
Question 6	Welche Aufgaben übernimmt der Hersteller?
Question 7	Was bleibt in der Verantwortung der Transplantationszentren?
Question 8	Zusätzlicher Aufwand für Auswahl und Verfügbarkeit CBU?
Question 9	Zusätzliche Voruntersuchungen notwendig vor Zemcelpro? Welche?
Question 10	Zusätzliche Vorbehandlungen notwendig vor Zemcelpro? Ändert sich zum Beispiel myeloablative Konditionierung oder GVHD-Prophylaxe?
Question 11	Benötigt es zusätzliche Folgetherapien nach Zemcelpro (unter anderem G-CSF)?
Question 12	Wie lange sind Patient:innen insgesamt stationär (3-4 Wochen)? Länger als bei einer allogenen Stammzelltransplantation?
Question 13	Welche Prozesse ändern sich mit der Verwendung von Zemcelpro und damit einhergehende Kosten?
Questions about the comparator	
Question 14	Welche Therapien stehen für Patient:innen mit malignen hämatologischen Erkrankungen zur Verfügung, wenn kein Spender verfügbar ist? Wo werden diese Patient:innen derzeit behandelt?
Question 15	Stellt Zemcelpro einen Ersatz für eine andere Therapie dar oder eine neue Option für diese Patient:innengruppe? Wird CBU dadurch zunehmen?
Question 16	Was wäre aus Ihrer Sicht die relevante Vergleichstherapie?
Question 17	Stellen CAR-T-Zellen eine Alternative zur allogenen Stammzelltransplantation und Zemcelpro dar? Wenn ja, in welchen Indikationen?
Questions about the outcome	
Question 18	Welche sind die (3-5) zentralen Endpunkte für die Beurteilung der Wirksamkeit und Sicherheit von Zemcelpro?
Further Questions	
Question 19	Gibt es in Österreich allogene Nabelschnurblutbanken?
Question 20	Welche Leitlinien sind für Österreich relevant?
Question 21	Welche Register sind in Österreich relevant?
Question 22	Sind die Ergebnisse der ECT-001-CB.002 und ECT-001-CB.004 klinisch relevant?
Question 23	Ist das Sicherheitsprofil von Zemcelpro im Vergleich zu anderen Transplantaten eher günstig oder ungünstig?
Question 24	Wie lassen sich diese Ergebnisse mit den Ergebnissen anderer allogener Stammzelltransplantationen vergleichen?
Question 25	Vergleichsweiser Zusatznutzen: Zemcelpro vs. allogener Stammzelltransplantation Zuordnung der Kategorie 4: gleicher oder ähnlicher medizinisch-therapeutischer Zusatznutzen. Stimmen Sie dieser Einstufung basierend auf diesen Ergebnissen zu oder sind auch andere Endpunkte relevant?
Question 26	Vergleichsweiser Zusatznutzen: Zemcelpro vs. allogener Stammzelltransplantation mit MMUD Zuordnung der Kategorie 4: gleicher oder ähnlicher medizinisch-therapeutischer Zusatznutzen. Stimmen Sie dieser Einstufung basierend auf diesen Ergebnissen zu oder sind auch andere Endpunkte relevant?
Question 27	Vergleichsweiser Zusatznutzen. Zemcelpro vs. allogener Stammzelltransplantation mit Haplo Zuordnung der Kategorie 3: moderater medizinisch-therapeutischer Zusatznutzen. Stimmen Sie dieser Einstufung zu oder eher gleicher Nutzen: keine Langzeitdaten zu Zemcelpro, keine direkten Vergleiche, Präferenz in der Praxis: Zemcelpro oder Haplo?

Question 28	LKF-Pauschale für Stammzelltransplantation für 90 Tage: Follow-up-Behandlungen und Rehospitalisierungen inkludiert?
Question 29	Relevante zusätzliche Kosten zu berücksichtigen?
Question 30	Weite indikationsbezogene Anwendungskriterien, die nicht im EPAR geregelt sind, zum Beispiel: ■ Was bedeutet in der österreichischen Praxis „keine geeigneten Spenderzellen"? In welchen Fällen würden CBU oder Zemcelpro eingesetzt werden, zum Beispiel, bei Patient:innen mit anderer Herkunft oder wenn doppelt CBU notwendig ist? Relevante Formulierung für Anewndungskriterien? ■ Für die Anwendung von Patient:innen unter 18 und über 65 Jahre liegen keine Daten zur Wirksamkeit und Sicherheit vor – Einschätzung zu einer Altersbegrenzung? ■ Zemcelpro als zweite allogene Stammzelltransplantation möglich= ■ Weitere?
Question 31	45 Tage: Vorteil oder Nachteil für die Praxis?
Question 32	Einschätzung des administrativen Aufwands?

Abbreviations: CBU…cord blood unit, GVHD…graft versus host disease, G-CSF…granulocyte colony-stimulating factor, Haplo…haploid, LKF…leistungsorientierte Krankenanstaltenfinanzierung, MMUD…mismatched unrelated donor

4 Clinical effectiveness and safety

4.1 Characteristics of included studies

Table 4-1: Eligibility criteria of the ECT-001-CB.001 study [16]

Inclusion criteria	Exclusion criteria
■ Underlying haematological malignancy, excluding primary myelofibrosis[1] requiring an unrelated donor allo-HSCT (as defined by the transplant centre), but the patient lacks an 8/8 HLA identical donor, or the disease requires an urgent transplant and cannot wait the required time to identify an unrelated donor. ■ The status of the patient must meet centre eligibility criteria for unrelated donor transplantation. ■ 3-64 years old (paediatric patients will become eligible only after 5 adult patients have been enrolled in the study and received the UM171 expanded product). ■ Weight ≥ 12kg ■ Availability of at least 2 UCBs with HLA match ≥ 4/6 and ≥4/8, and meeting the following requirements: ■ CB to be expanded (numbers are pre-freeze): • Cohort 1: CD34+ cell count 1.0-4.9 x 105/kg and TNC ≥ 2.0 x 107/kg, • Cohort 2: CD34+ cell count 0.5-4.9 x 105/kg and TNC ≥ 1.5 x 107/kg • Cohort 3: CD34+ cell count 0.25-4.9 x 105/kg and TNC ≥ 1.25 x 107/kg ■ Non-expanded CB/back-up cord (numbers are pre freeze): TNC count ≥ 2.0 x 10^7/kg with $CD34^+$ min of 1.5 x 10^5/kg or minimum of 1.5 x 10^7 TNC/kg with 1.7 x 10^5 CD34+ cells/kg. ■ Karnofsky score ≥ 70% • Bilirubin < 2 x ULN unless felt to be related to Gilbert's disease or haemolysis; AST and ALT ≤ 2.5 x ULN; alkaline phosphatase ≤ 5 x ULN. • Measured or estimated creatinine clearance ≥ 60 ml/min/1.73 m^2. • Left ventricular ejection fraction > 40%. • FVC, forced expiratory volume in 1 second (FEV1), and diffusing capacity corrected for haemoglobin (DLCOc) ≥ 50% of predicted. • Signed written informed consent (parents or legal guardians for minor patients). • Female patients of childbearing potential must have a negative serum pregnancy test within 7 days of enrolment.	■ Primary myelofibrosis never treated with chemotherapy. ■ Any haematologic disease never treated with chemotherapy and planned conditioning regimen does not include 12 Gy TBI. ■ Allogeneic myeloablative transplant within 12 months. ■ Allo-HSCT within 6 months. ■ Uncontrolled infection. ■ Presence of a malignancy other than the one for which the UCB transplant is being performed, and the expected survival related to the malignancy is estimated to be less than 75% at 5 years. ■ HIV positivity. ■ Hepatitis B or C infection with measurable viral load. ■ Liver cirrhosis. ■ Availability of CB with ≥ 5 x 10^5/kg CD34+ cells at cryopreservation. ■ Pregnancy, breastfeeding or unwillingness to use appropriate contraception. ■ Participation in a trial with an investigational agent within 30 days before entry in the study. ■ Patient is unable to give informed consent or unable to comply with the treatment protocol, including appropriate supportive care, follow-up, and tests. ■ Availability of a 6/6 matched related donor. ■ Any abnormal condition or laboratory result that, in the opinion of the PI, is capable of altering the patient's condition or study outcome.

[1] If the patient was diagnosed with primary myelofibrosis, but has progressed to leukaemia or pre-leukaemic state, the patient may become eligible depending on BM results before transplant and presence of splenomegaly. PI approval is necessary for the patient to be included in the clinical trial.

Abbreviations: allo-HSCT…allogeneic haematopoietic stem cell transplantation, ALT…alanine aminotransferase, AST…aspartate aminotransferase, BM…bone marrow, CB…cord blood, CB…ucord blood unit, CD34+…cluster of differentiation 34 positive, DLCOc…diffusing capacity corrected for haemoglobin, FEV1…forced expiratory volume in one second, FVC…forced vital capacity, HIV…human immunodeficiency virus, HLA…human leukocyte antigen , PI…principal investigator, TBI… total body irradiation, TNC…total nucleated cells, ULN…upper limit of normal

Table 4-2: Eligibility criteria of the ECT-001-CB.002 and ECT-001-CB.004 studies [17]

Inclusion criteria	Exclusion criteria
■ 18-70 years ■ High-risk acute leukaemia/myelodysplasia • AML: Primary induction failure, chemorefractory relapse, post-transplant relapse, high-risk CR1 (any adverse genetic abnormality as defined by ELN excluding FLT3 mutation, secondary or therapy related AMLY excluding good risk genetic abnormalities as defined by ELN or any other poor risk feature known to be associated with a PFS or DFS ≤40% at 2 years after conventional transplantation), CR2 (excluding good risk genetic abnormalities defined by ELN), ≥CR3 • ALL: Primary induction failure, chemorefractory relapse, post-transplant relapse, high-risk ALL in CR1 (Philadelphia-like ALL or any other poor risk feature known to be associated with a PFS or DFS ≤40% at 2 years after conventional transplantation), ≥CR2, MRD+ within 1 month of start of conditioning regimen • MDS: Post-transplant relapse, ≥10% blasts within 1 month of start of conditioning regimen, very poor cytogenetics (>3 abnormalities), poor risk feature known to be associated with a PFS or DFS ≤40% at 2 years after conventional transplantation, TP53 mutation, ≥40 years with RAS/JAK2 mutation, CMML with HCT-specific CPSS score high or intermediate, stable disease after 6 cycles of azacitidine (or another demethylating agent), progressive disease while on azacitidine (or another demthylating agent) ■ KPS ≥70% ■ Adequate organ function ■ Adequate comorbidity ■ CB unit for expansion + back-up unit (≥4/6 or ≥4/8 HLA match) ■ CD34+ >0.5×10^5/kg, TNC >1.5×10^7/kg ■ Informed consent	■ Patients never treated with cytotoxic chemotherapy. ■ Planned regimen without 12Gy TBI. ■ Allogeneic myeloablative or autologous HSCT <6 months. ■ Planned use of antithymocyte globulin in conditioning regime. ■ Planned use of HLA-matched CB (8/8), HLA antibodies against expanded CB. ■ Uncontrolled infection ■ Malignancy other than indication <75% estimated 5-year survival. ■ Seropositivity for HIV, hepatitis B/c with measurable viral load. ■ Liver cirrhosis ■ Active CNS involvement, chloroma >2 cm. ■ ≥50% blasts in marrow <1 month prior to conditioning, peripheral blasts >1000/mm^3 ■ Trial participation with investigational agents within 30 days. ■ Pregnancy ■ Unwillingness to use contraception

Abbreviations: ALL…acute lymphoblastic leukaemia, allo-HSCT…allogeneic haematopoietic stem cell transplantation, AML…acute myeloid leukaemia, CB…cord blood, CD34+…cluster of differentiation 34 positive, CMML…chronic myelomonocytic leukaemia, CNS…central nervous system, CPSS…CMML-specific prognostic scoring system, CR...complete remission, DFS…disease-free survival, ELN…European Leukemia Net, FLT3…FMS-like tyrosine kinase 3, Gy…Gray, HLA…human leukocyte antigen, HSCT…haematopoietic stem cell transplantation, JAK2…janus kinase 2, KPS…Karnofsky performance status, MDS…myelodysplastic syndrome, mm…millimetre, MRD…minimal residual disease, PFS…progression-free survival, RAS…rat sarcoma, TBI…total body irradiation, TNC…total nucleated cells, TP53…tumour protein 53

Table 4-3: Eligibility criteria of the ECT-001-CB.003 [18]

Inclusion criteria	Exclusion criteria
■ 18–65 years ■ Newly diagnosed MM according to the International Myeloma Working Group criteria, with measurable disease and at least one of the following: • t(4;14), t(14;16), t(14;20), del(17p13), chromosome 1 abnormalities with ISS II or III; • Revised-ISS 3 • Primary plasma cell leukaemia • Refractory to first-line triplet Bortezomib-based induction treatment • ≥ 2 cytogenetic abnormalities as defined above, regardless of ISS stage ■ Received a first-line triplet Bortezomib-induction regimen for a minimum of 4 cycles with achievement of at least partial response; or received a double or triplet Lenalidomide-based second-line induction treatment with at least partial response for patients refractory to Bortezomib in first-line. ■ Received high-dose Melphalan ≥ 140 mg/m^2 followed by ASCT. ■ Availability of a CB with an HLA match ≥ 5/8 and < 8/8 meeting the following requirements: CD34+ cell count ≥ 0.5 x 105/kg and nucleated cell count >= 1.5 x 107/kg.	■ Having previously received two ASCT. ■ Having previously received autologous-allogeneic tandem transplantation. ■ Having received more than 4 months of maintenance with Lenalidomide or Bortezomib after ASCT. ■ KPS < 70% or HCT-CI > 3 ■ Bilirubin > 2 x ULN unless felt to be related to Gilbert's disease or haemolysis; AST and ALT > 2.5 x ULN; alkaline phosphatase > 5 x ULN; liver cirrhosis. ■ Non-secretory disease or non-measurable disease in serum or urine at the time of diagnosis. ■ Uncontrolled infection. ■ Active infection with any of the following viruses: HIV, HTLV-1 or 2, hepatitis B or C. ■ Presence of another malignancy with an expected survival estimated < 75% at 5 years. ■ Suspicion of cardiac amyloidosis. ■ Current history of drug and/or alcohol abuse. ■ Availability of a matched sibling donor. ■ Pregnancy, breastfeeding or unwillingness to use appropriate contraception. ■ Participation in a trial with an investigational agent within 30 days before entry in the study. ■ Patient unable to give informed consent or unable to comply with the treatment protocol, including appropriate supportive care, follow-up and tests. ■ Any abnormal condition or laboratory result that is considered by the PI capable of altering the patient's condition or study outcome

Abbreviations: ALT…alanine aminotransferase, ASCT…autologous stem cell transplantation, AST…aspartate aminotransferase, CB…cord blood, CD34+…cluster of differentiation 34 positive, HCT-CI…haematopoietic cell transplantation-comorbidity index, HIV…human immunodeficiency virus, HLA…human leukocyte antigen, HTLV…human T cell lymphotropic virus, ISS…international staging system, KPS…Karnofsky performance status, MM…multiple myeloma, PI…principal investigator, ULN…upper limit of normal

Table 4-4: Eligibility criteria of the ECT-001-CB.007 [19]

Inclusion criteria	Exclusion criteria
■ AML ■ Chemo-refractory relapse (MRD+) ■ Primary induction failure (no CR or CRi after >= 2 courses of intensive induction therapy): < 30% blasts in evaluable marrow. ■ Relapse after previous allogeneic (or autologous) transplant (>4 months) ■ Secondary or therapy-related MDS/AML ■ Poor response to induction (5-30% blasts) or MDR+ after induction ■ MDS ■ Relapse after allogeneic or autologous transplant (>4 months) ■ ≥10 % blasts within 30 days of start of conditioning regimen ■ Poor and very poor cytogenetic abnormalities ■ Chronic myelogenous leukaemia: Patients who progressed to blast crisis ■ Mixed phenotype acute leukaemia: MRD+ or relapse after previous transplant (>4 months). ■ JMML ■ Availability of 2 ≥ 4/8 HLA matched CBU (allele level: A, B, C and DRB1) ■ Cord to be expanded: CD34+ cell count ≥ 0.5 x 10^5/kg and TNC ≥ 1.5 x 10^7/kg (pre-cryo) ■ Back up cord: Pre-freeze TNC ≥ 2 x 10^7/kg with CD34+ cells ≥ 1.5 x 10^5/kg. If a single cord does not meet this criterion, 2 backup cords will be an acceptable alternative, with a minimum for each of 1.5 x 10^7 TNC/kg with 1.0 x 10^5 CD34+/kg. Another acceptable HSC backup source could be a haploidentical with medical clearance before starting the conditioning regimen. ■ Lansky / Karnofsky >60% ■ Bilirubin < 2 x ULN unless felt to be related to Gilbert's disease or hemolysis; AST and ALT < 3 x ULN; alkaline phosphatase < 5 x ULN ■ Estimated or measured creatinine clearance ≥ 50ml/min/1.73m2 ■ Left ventricular ejection fraction of ≥ 40% ■ Signed written informed consent ■ Female patients of childbearing potential must have a negative serum pregnancy test within 7 days of enrolment and must be willing to use an effective contraceptive method while enrolled in the study.	■ Previous allogeneic transplantation within 4 months. ■ Uncontrolled infection. ■ Presence of other malignancy other than the one for which the CB transplant is being performed, with an expected survival to be less than 75% at 5 years ■ Seropositive for HIV ■ Hepatitis B and C infection with measurable viral load. ■ Liver cirrhosis ■ Active CNS disease ■ Chloroma > 2cm ■ >30% blasts in marrow in evaluable marrow sample ■ Pregnancy, breastfeeding, or unwillingness to use appropriate contraception. ■ Participation in a trial with an investigational agent within 30days prior to entry in the study. ■ Any abnormal condition or lab result that is considered by the PI capable or altering patient's condition or study outcome.

Abbreviations: ALT…alanine aminotransferase, AML…acute myeloid leukaemia, AST…aspartate aminotransferase, CB…cord blood, CBU…cord blood unit, CD34+…cluster of differentiation 34 positive, CNS…central nervous system, CR…complete remission, CRi…complete remission with incomplete blood count recovery, HIV…human immunodeficiency virus, HLA…human leukocyte antigen, HSC…haematopoietic stem cell, JMML…juvenile myelomonocytic leukaemia, MDS…myelodysplastic syndrome, MRD…minimal residual disease, n…number, PI…principal investigator, TNC…total nucleated cell, ULN…upper limit of normal

4.1.1 Study population

Table 4-5: Key baseline demographics of the ECT-001-CB.001 study [16]

Parameter	ECT-001-CB.001
N	22
Age [years], median (range)	45 (19-63)
Sex [f/m] (%)	
Male	14 (64%)
Female	8 (36%)
Previous allogeneic treatment	5 (23%)
Disease type (n[%])	
ALL	7 (32%)*
AML	8 (36%)*
MDS	1 (5%)*
Multiple myeloma	0
Various	6 (27%)*
Disease status (n [%])	
Acute leukaemia in first CR	8 (36%)
Acute leukaemia in second CR	4 (18%)
Acute leukaemia not in CR	3 (14%)
Myelodysplastic syndrome or myeloproliferative disease	2 (9%)
Aggressive non-Hodgkin lymphoma not in complete or partial remission	2 (9%)
Non-Hodgkin lymphoma in partial or complete remission	2 (9%)
Low-grade non-Hodgkin lymphoma or CLL	1 (5%)

*Notes: * Calculated based on the supplementary information [16]*

Abbreviations: ALL…acute lymphoblastic leukaemia, AML…acute myeloid leukaemia, CLL…chronic lymphocytic leukaemia, CR…complete remission, f…female, FAS…full analysis set, m…male, MDS…myelodysplastic syndrome, n…number, NA…not available

4.1.2 Outcomes

Table 4-6: Definition of efficacy outcomes [16, 17]

Outcomes	Definition
Overall survival (OS)	OS is defined as the time of transplant until death from any cause or last follow-up.
Non-relapse mortality (NRM)	NRM is defined as death due to any cause other than malignant relapse occurring after the commencement of the conditioning regimen that could be related to the transplantation procedure. If the participant received another stem cell source as treatment for graft failure, NRM was considered as death at any time unrelated to relapse until 4 months post second transplant. If death occurs ≥ 4 months after the 2nd transplant from a transplant-related complication, it was not considered NRM related to the trial.
Progression-free survival (PFS)	PFS is defined as the time of transplant until relapse/progression, death or last follow-up.
Neutrophil engraftment	Neutrophil engraftment is defined as the time from transplant and first day of three consecutive days with absolute neutrophil count (ANC) ≥ 0.5 x 10^9/L.
Platelet engraftment	Platelet engraftment is defined as the time between transplant and first day of a sustained platelet count ≥ 20 x 10^9/L with no platelet transfusion in the preceding 7 days.
Graft versus host disease-free relapse-free survival (GRFS)	GRFS is defined as the absence of grade 3-4 acute GVHD, moderate or severe chronic GVHD, relapse/progression, death or last follow-up.
Chronic graft versus host disease-free and relapse-free survival (CRFS)	CRFS is defined as the absence of moderate to severe chronic GvHD, relapse or progression, death or last follow-up.
Transplant-related mortality (TRM)	TRM is defined as any death of any cause other than malignant relapse, occurring after the commencement of conditioning regimen that could be related to the transplantation procedure. It obviously excludes non-related deaths such as accidents. Incidence of TRM was monitored throughout the study and in particular at 100 days, 1, 2, and 3 years post-transplantation. If it exceeded 30% at day 100, stopping rules may be applied that could prematurely terminate the trial. If the patient received another stem cell source as treatment for graft failure, TRM would be considered as death at any time unrelated to relapse until 4 months post-second transplant. If death occurred≥4 months after the second transplant from a transplant-related complication, it would not be considered TRM related to the trial.

Abbreviations: *ANC…absolute neutrophil count, CRFS…chronic graft versus host disease-free and relapse-free survival, GRFS…graft versus host disease-free and relapse-free survival, GVHD…graft versus host disease, NRM…non-relapse mortality, OS…overall survival, PFS…progression-free survival, TRM…transplant-related mortality*

4.2 Results on effectiveness and safety

4.2.1 Clinical efficacy outcomes

Table 4-7: Efficacy endpoints of the ECT-001-CB.001 study [20]

Efficacy endpoints		ECT-001-CB.001 (n=22)
OS, Kaplan-Meier estimates (95% CI) - 12 months		86.4% (73-100)
OS, median		NR
OS, Kaplan-Meier estimates (95% CI) - 24 months		72.7% (56-94)
NRM, cumulative incidence (95%CI) - 12 months		4.5% (0-14)
NRM, cumulative incidence (95%CI) - 24 months		4.5% (0-14)
PFS, Kaplan-Meier estimates (95% CI) - 12 months		72.7% (56-94)
PFS, median		NR
PFS, Kaplan-Meier estimates (95% CI) - 24 months		72.7% (56-94)
QoL		NR
Neutrophil engraftment	Evaluable patients, n	22
	Median time to neutrophil engraftment (days), median (range) for patients who have reached neutrophil engraftment	18 (10-30)
	Median time to neutrophil engraftment (days), median (range) for all patients	NR
	Proportion achieving neutrophil engraftment by day 42, n (%)	22 (100%)
Platelet engraftment	Evaluable patients, n	22
	Median time to platelet engraftment (days), median (range) for patients who have reached platelet engraftment	42 (27-63)
	Median time to platelet engraftment (days), median (range) for all patients	NR
	Proportion achieving platelet engraftment by day 100, n (%)	21 (95.5%)
Acute GVHD grade III-IV at 12 months, cumulative incidence (95%CI)		9.1% (0-21)
Moderate to severe chronic GVHD at 24 months, cumulative incidence (95%CI)		NR
GRFS, Kaplan-Meier estimates (95% CI) - 12 months		63.6% (46-87)
GRFS, Kaplan-Meier estimates (95% CI) - 24 months		59.1% (42-84)
CRFS, Kaplan-Meier estimates (95% CI) - 12 months		72.7% (56-94)
CRFS, Kaplan-Meier estimates (95% CI) - 24 months		68.2% (51-91)
QoL		Not reported

Abbreviations: *CI…confidence interval, CRFS…chronic graft versus host disease-free and relapse-free survival, GRFS…graft versus host disease-free and relapse-free survival, GVHD…graft versus host disease, n…number, NR…not reached, NRM…non-relapse mortality, OS…overall survival, PFS…progression-free survival, QoL…quality of life*

4.2.2 Safety outcomes

Table 4-8: AEs (grade ≥3) after Zemcelpro administration of frequency ≥5% by maximal toxicity grade [20]

AEs	SAS (N=116)

	Grade 3	Grade 4	Grade 5	All grades
Number of participants with any AEs, n(%)	27 (23.3%)	71 (61.2%)	17 (14.7%)	115 (99.1%)
Neutropenia	5 (4.3%)	70 (60.3%)	0 (0.0%)	75 (64.7%)
Thrombocytopenia	0 (0.0%)	74 (63.8%)	0 (0.0%)	74 (63.8%)
Leukopenia	0 (0.0%)	73 (62.9%)	0 (0.0%)	73 (62.9%)
Lymphopenia	1 (0.9%)	70 (60.3%)	0 (0.0%)	71 (61.2%)
Anaemia	62 (53.4%)	4 (3.4%)	0 (0.0%)	66 (56.9%)
Hypertension	44 (37.9%)	0 (0.0%)	0 (0.0%)	44 (37.9%)
Febrile neutropenia	41 (35.3%)	0 (0.0%)	0 (0.0%)	41 (35.3%)
Hyperglycaemia	34 (29.3%)	0 (0.0%)	0 (0.0%)	34 (29.3%)
Decreased appetite	33 (28.4%)	0 (0.0%)	0 (0.0%)	33 (28.4%)
Nausea	29 (25.0%)	0 (0.0%)	0 (0.0%)	29 (25.0%)
aGVHD	23 (19.8%)	2 (1.7%)	2 (1.7%)	27 (23.3%)
Hypogammaglobulinaemia	22 (19.0%)	0 (0.0%)	0 (0.0%)	22 (19.0%)
Pneumonia	20 (17.2%)	1 (0.9%)	1 (0.9%)	22 (19.0%)
Diarrhoea	20 (17.2%)	0 (0.0%)	0 (0.0%)	20 (17.2%)
Sepsis	16 (13.8%)	2 (1.7%)	2 (1.7%)	20 (17.2%)
Mucosal inflammation	19 (16.4%)	0 (0.0%)	0 (0.0%)	19 (16.4%)
Hypervolaemia	16 (13.8%)	0 (0.0%)	0 (0.0%)	16 (13.8%)
Stomatitis	16 (13.8%)	0 (0.0%)	0 (0.0%)	16 (13.8%)
ALT increased	13 (11.2%)	1 (0.9%)	0 (0.0%)	14 (12.1%)
Engraftment Syndrome	11 (9.5%)	2 (1.7%)	0 (0.0%)	13 (11.2%)
Hypokalaemia	13 (11.2%)	0 (0.0%)	0 (0.0%)	13 (11.2%)
Pyrexia	13 (11.2%)	0 (0.0%)	0 (0.0%)	13 (11.2%)
Acute kidney injury	12 (10.3%)	0 (0.0%)	0 (0.0%)	12 (10.3%)
Hypophosphataemia	12 (10.3%)	0 (0.0%)	0 (0.0%)	12 (10.3%)
Rash maculo-papular	12 (10.3%)	0 (0.0%)	0 (0.0%)	12 (10.3%)
Blood creatinine increased	11 (9.5%)	0 (0.0%)	0 (0.0%)	11 (9.5%)
CD4 lymphocytes decreased	9 (7.6%)	2 (1.7%)	0 (0.0%)	11 (9.5%)
EBV infection reactivation	10 (8.6%)	0 (0.0%)	0 (0.0%)	10 (8.6%)
Bacteraemia	10 (8.6%)	0 (0.0%)	0 (0.0%)	10 (8.6%)
Coronavirus infections	9 (7.8%)	0 (0.0%)	1 (0.9%)	10 (8.6%)
Device-related infection	9 (7.8%)	0 (0.0%)	0 (0.0%)	9 (7.8%)
Headache	9 (7.8%)	0 (0.0%)	0 (0.0%)	9 (7.8%)
Hypomagnesaemia	9 (7.8%)	0 (0.0%)	0 (0.0%)	9 (7.8%)
Clostridium difficile colitis	8 (6.9%)	0 (0.0%)	0 (0.0%)	8 (6.9%)
Fatigue	7 (6.0%)	0 (0.0%)	0 (0.0%)	7 (6.0%)
Epstein-Barr viraemia	7 (6.0%)	0 (0.0%)	0 (0.0%)	7 (6.0%)
Hyponatraemia	5 (4.3%)	0 (0.0%)	1 (0.9%)	6 (5.2%)
Transplant failure	0 (0.0%)	6 (5.2%)	0 (0.0%)	6 (5.2%)
Syncope	6 (5.2%)	0 (0.0%)	0 (0.0%)	6 (5.2%)

Notes: AEs were classified into AEs using MedDRA Version 23.1 (or later). aGVHD defined as per CTCAE.

Abbreviations: AE…adverse event, aGVHD…acute graft versus host disease, ALT…alanine aminotransferase, CD4…cluster of differentiation, EBV…Epstein-Barr virus, SAS…safety analysis set

Table 4-9: Adverse drug reactions (grade ≥3) after Zemcelpro administration of frequency ≥5% by maximal toxicity grade [20]

ADR	SAS (N=116)			
	Grade 3	**Grade 4**	**Grade 5**	**All grades**
Number of participants with any ADRs, n (%)	37 (31.9%)	57 (49.1%)	9 (7.8%)	103 (88.8%)
Lymphopenia	5 (4.3%)	49 (42.2%)	0 (0.0%)	54 (46.6%)
Anaemia	50 (43.1%)	1 (0.9%)	0 (0.0%)	51 (44.0%)
Neutropenia	8 (6.9%)	33 (28.4%)	0 (0.0%)	41 (35.3%)
Thrombocytopenia	2 (1.7%)	35 (30.2%)	0 (0.0%)	37 (31.9%)
Leukopenia	2 (1.7%)	32 (27.6%)	0 (0.0%)	34 (29.3%)
AGVHD	22 (19.0%)	2 (1.7%)	2 (1.7%)	26 (22.4%)
Hypogammaglobulinemia	21 (18.1%)	0 (0.0%)	0 (0.0%)	21 (18.1%)
Febrile neutropenia	18 (15.5%)	0 (0.0%)	0 (0.0%)	18 (15.5%)
Hypertension	15 (12.9%)	0 (0.0%)	0 (0.0%)	15 (12.9%)
Engraftment syndrome	11 (9.5%)	2 (1.7%)	0 (0.0%)	13 (11.2%)
Pneumonia	11 (9.5%)	1 (0.9%)	1 (0.9%)	13 (11.2%)
CD4 lymphocytes decreased	9 (7.8%)	2 (1.7%)	0 (0.0%)	11 (9.5%)
EBV infection reactivation	10 (8.6%)	0 (0.0%)	0 (0.0%)	10 (8.6%)
Decreased Appetite	10 (8.6%)	0 (0.0%)	0 (0.0%)	10 (8.6%)
Diarrhoea	10 (8.6%)	0 (0.0%)	0 (0.0%)	10 (8.6%)
Nausea	10 (8.6%)	0 (0.0%)	0 (0.0%)	10 (8.6%)
Rash maculo-papular	9 (7.8%)	0 (0.0%)	0 (0.0%)	9 (7.8%)
Sepsis	6 (5.2%)	1 (0.9%)	1 (0.9%)	8 (6.9%)
Epstein-Barr viraemia	6 (5.2%)	0 (0.0%)	0 (0.0%)	6 (5.2%)
Pyrexia	6 (5.2%)	0 (0.0%)	0 (0.0%)	6 (5.2%)

Notes: ADRs were classified using MedDRA Version 23.1 (or later).

Abbreviations: ADR…adverse drug reaction, aGVHD…acute graft versus host disease, CD4…cluster of differentiation 4, EBV…Epstein-Barr virus, SAS…safety analysis set

Table 4-10: Non-relapse-related deaths among the SAS population [20]

Deaths	SAS (n=116)
	N (%)
Infections and infestations	8 (6.9)
Sepsis	2 (1.7)
Septic shock	2 (1.7)
Citrobacter sepsis	1 (0.9)
Coronavirus infection	1 (0.9)
Enterococcal infection	1 (0.9)
Metapneumovirus infection	1 (0.9)
Pneumocystis jirovecii pneumonia	1 (0.9)
Pneumonia	1 (0.9)
Respiratory, thoracic and mediastinal disorders	6 (5.2)
Pulmonary alveolar haemorrhage	2 (1.7)
Idiopathic pneumonia syndrome	1 (0.9)
Organising pneumonia	1 (0.9)
Pulmonary hypertension	1 (0.9)
Immune system disorders	2 (1.7)
aGVHD	2 (1.7)
General disorders	1 (0.9)
Multiple organ dysfunction syndrome	1 (0.9)

Abbreviations: aGVHD…acute graft versus host disease, n…number

4.3 Quality of evidence

No additional tables or figures are provided for this chapter.

4.4 Indirect treatment comparison

Table 4-11: Engraftment outcomes for Zemcelpro compared to six control groups from Cohen et al. (2025) study [22]

Group		Days to neutrophil engraftment Median (95% CI) *
CB	Zemcelpro (n=19)	18 (12-20)
	CB (n=36)	22 (17-32)
	P-value	0.0009
10/10 MUD PBSC	Zemcelpro (n=21)	18 (13-22.5)
	MUD PBSC (n=59)	17 (14-21)
	P-value	0.94
10/10 MUD BM	Zemcelpro (n=17)	18 (13-22.5)
	MUD BM (n=31)	23 (19.5-27.5)
	P-value	0.014
9/10 UD	Zemcelpro (n=21)	18 (13-22.5)
	9/10 UD (n=61)	17 (14-21)
	P-value	0.98
Haplo	Zemcelpro (n=20)	18 (12-20)
	Haplo (n=59)	19 (17-23)
	P-value	0.09
MSD	Zemcelpro (n=21)	18 (13-22.5)
	MSD (n=61)	18 (15-21)
	P-value	0.83

*Notes: * Only patients who achieved an absolute neutrophil count > 500/μL.*

Abbreviations: BM…bone marrow, CB…cord blood, CI…confidence interval, Haplo…haploidentical, MSD…matched sibling donor, MUD…matched unrelated donor, n…number, PBSC…peripheral blood stem cells, UD…unrelated donor

Table 4-12:Clinical outcomes of Zemcelpro compared to six other stem cell sources from Cohen et al. (2025) study [22]

Outcomes	Time	N at risk Zemcelpro/ EBMT	Zemcelpro, % (95 % CI)	EBMT cohorts, % (95% CI)	HR (95% CI) Zemcelpro vs. EBMT	P value
CB						
AGVHD (grade 2-4)	D 180	19/35	63.2 (36.3-81.2)	54.3 (36.2-69.3)	1.01 (0.45-2.28)	0.97
AGVHD (grade 3-4)	D 180	19/35	10.5 (1.7-29.1)	17.1 (6.8-31.4)		0.52
CGVHD	2 years	19/33	21.1 (6.2-41.9)	32.5 (16.5-49.6)	0.58 (0.17-1.9)	0.37
CGVHD (severe or extensive)*	2 years	19/33	0	16.3 (5.7-31.7)		0.07
Relapse	2 years	19/36	26.3 (9.2-47.4)	17.6 (6.9-32.2)	1.4 (0.4-4.92)	0.6
NRM	2 years	19/36	5.3 (0.3-22)	22.2 (10.3-37)	0.22 (0.02-2.08)	0.19
PFS	2 years	19/36	68.4 (42.8-84.4)	60.2 (42.1-74.3)	0.74 (0.29-1.91)	0.53
OS	2 years	19/36	68.4 (42.8-84.4)	66.3 (48.3-79.3)	0.83 (0.32-2.15)	0.7
GRFS	1 year	19/35	62 (36.3-79.8)	57.1 (39.3-71.5)	0.55 (0.23-1.31)	0.18
GRFS	2 years	19/35	62 (36.3-79.8)	40.6 (23.9-56.7)		
10/10 MUD PBSC						
AGVHD (grade 2-4)	D 180	21/55	71.4 (45.2-86.7)	41.8 (28.6-54.5)	1.59 (0.9-2.79)	0.11
AGVHD (grade 3-4)	D 180	21/55	10.5 (1.7-29.1)	16.4 (8-27.3)		0.46
CGVHD	2 years	21/47	23.8 (8.2-43.8)	35.8 (21.3-50.5)	0.5 (0.21-1.21)	0.13
CGVHD (severe or extensive)*	2 years	21/44	0%	16 (6.3-29.8)		0.04
Relapse	2 years	21/59	23.8 (8.3-43.7)	33.1 (20.7-45.9)	0.6 (0.23-1.56)	0.29
NRM	2 years	21/59	4.8 (0.3-20.2)	16.6 (8-27.9)	0.25 (0.03-2.47)	0.24
PFS	2 years	21/59	71.4 (47.2-86)	50.3 (36.1-63)	0.49 (0.19-1.27)	0.14
OS	2 years	21/59	71.4 (47.2-86)	54 (39.2-66.7)	0.51 (0.21-1.28)	0.15
GRFS	1 year	21/59	71.4 (47.2-86)	40.9 (27.7-53.6)	0.4 (0.17-0.95)	0.037
GRFS	2 years	21/59	65.8 (41.2-82)	34.1 (21.6-47.1)		
10/10 MUD BM						
AGVHD (grade 2-4)	D 180	17/30	64.7 (35.6-83.2)	26.7 (12.4-43.3)	2.87 (1.33-6.18)	0.007
AGVHD (grade 3-4)	D 180	17/30	11.8 (1.8-32)	10 (2.5-23.9)		0.85

CGVHD	2 years	17/25	17.6 (4-39.3)	40 (20.6-58.8]	0.36 (0.08-1.5)	0.16
CGVHD (severe or extensive)*	2 years	17/24	0	30.6 (12.9-50.4)		0.015
Relapse	2 years	17/31	29.4 (10.2-51.9)	23.5 (10.1-40.1)	1.21 (0.39-3.73)	0.74
NRM	2 years	17/31	5.9 (0.3-24.2)	24 (10.2-40.9)	0.24 (0.03-1.65)	0.15
PFS	2 years	17/31	64.7 (37.7-82.3)	52.5 (33.1-68.7)	0.72 (0.31-1.67)	0.45
OS	2 years	17/31	64.7 (37.7-82.3)	59.1 (39.2-74.5)	0.81 (0.38-1.7)	0.57
GRFS	1 year	17/31	57.4 (30.6-77)	41.9 (24.7-58.3)	0.57 (0.27-1.21)	0.14
GRFS	2 years	17/31	57.4 (32.5-77.8)	34.6 (18.5-51.3)		
9/10 UD						
AGVHD (grade 2-4)	D 180	21/59	71.4 (45.2-86.7)	37.4 (25.1-49.6)	2.2 (1.18-4.11)	0.013
AGVHD (grade 3-4)	D180	21/59	9.5 (1.5-26.7)	17 (8.7-27.7)		0.41
CGVHD	2 years	21/50	23.8 (8.2-43.8)	38.1 (24.1-51.9)	0.38 (0.13-1.1)	0.075
CGVHD (severe or extensive)*	2 years	21/50	0	7.3 (2.3-16.2)		0.21
Relapse	2 years	21/62	23.8 (8.3-43.7)	31.2 (19.6-43.6)	0.58 (0.18-1.81)	0.35
NRM	2 years	21/61	4.8 (0.3-20.2)	25.4 (15-37.1)	0.16 (0.02-1.19)	0.073
PFS	2 years	21/61	71.4 (47.2-86)	43.2 (30.1-55.6)	0.39 (0.14-1.07)	0.068
OS	2 years	21/61	71.4 (47.2-86)	53.8 (39.7-65.9)	0.48 (0.18-1.3)	0.15
GRFS	1 year	21/61	65.8 (41.2-82)	38.4 (26.1-50.6)	0.4 (0.16-0.98)	0.046
GRFS	2 years	21/61	65.8 (41.2-82)	36.5 (24.3-48.7)		
Haplo						
AGVHD (grade 2-4)	D 180	20/56	65 (38.7-82.2)	30.4 (18.8-42.7)	2.3 (1.18-4.46)	0.014
AGVHD (grade 3-4)	D 180	20/56	5 (0.3-21.1)	8.9 (3.2-18.2)		0.6
CGVHD	2 years	20/52	20 (5.9-40.1)	28.9 (16.8-42.1)	0.52 (0.14-1.92)	0.33
CGVHD (severe or extensive)*	2 years	20/51	0	12.5 (4.9-23.7)		0.10
Relapse	2 years	20/59	25 (8.7-45.5)	27.4 (16.2-39.9)	0.74 (0.26-2.1)	0.57
NRM	2 years	20/59	5 (0.3-21.1)	31.3 (19.2-44)	0.13 (0.02-1.06)	0.056
PFS	2 years	20/59	70 (45.1-85.3)	41.3 (27.9-54.3)	0.42 (0.19-0.95)	0.038

OS	2 years	20/59	70 (45.1-85.3)	44.3 (30.4-57.2)	0.41 (0.19-0.92)	0.03
GRFS	1 year	20/59	65 (40.3-81.5)	45.2 (31.9-57.7)	0.45 (0.2-1)	0.049
GRFS	2 years	20/59	65 (40.3-81.5)	36.4 (23.6-49.3)		
MSD						
AGVHD (grade 2-4)	D 180	21/57	71.4 (45.2-86.7)	29.8 (18.5-42)	2.83 (1.54-5.21)	0.0008
AGVHD (grade 3-4)	D 180	21/57	9.5 (1.5-26.7)	15.8% [7.7-26.5]		0.49
CGVHD	2 years	21/49	23.8 (8.2-43.8)	41 (26.5-55)	0.46 (0.15-1.39)	0.17
CGVHD (severe or extensive)*	2 years	21/46	0	26.9 (15.1-40)		0.01
Relapse	2 years	21/61	23.8 (8.3-43.7)	41.9 (28.8-54.4)	0.49 (0.2-1.18)	0.11
NRM	2 years	21/61	4.8 (0.3-20.2)	9.1 (3.3-18.7)	0.44 (0.11-1.77)	0.25
PFS	2 years	21/61	71.4 (47.2-86)	49 (35.4-61.3)	0.48 (0.21-1.09)	0.08
OS	2 years	21/61	71.4 (47.2-86)	56.5 (42.2-68.5)	0.57 (0.28-1.18)	0.13
GRFS	1 year	21/61	65.8 (41.2-82)	35.4 (23.2-47.9)	0.37 (0.16-0.82)	0.014
GRFS	2 years	21/61	65.8 (41.2-82)	29.5 (18.1-41.8)		

*Note: * The p-value was based on the Gray test as the Cox model (with cluster) cannot be used, as there is no event in the Zemcelpro group.*

Abbreviations: AGVHD…acute graft versus host disease, BM…bone marrow, CB…cord blood, CGVHD…chronic graft versus host disease, CI…confidence interval, D…day, EBMT…European Society for Blood and Marrow Transplantation, GRFS…graft-versus-host disease-free and relapse-free survival, Haplo…haploidentical, HR…hazard ratio, MSD…matched sibling donor, MUD…matched unrelated donor, N…number, NRM…non-relapse mortality, OS…overall survival, P…probability value, PBSC…peripheral blood stem cells, PFS…progression-free survival, UD…unrelated donor, vs…versus

Table 4-13: Univariate analysis of Zemcelpro cohort compared with CB and MUD PBSC controls in Cohen et al. (2023) [21]

Outcomes	Zemcelpro		CB		P Zemcelpro vs. CB	MUD PBSC		P Zemcelpro vs. PBSC
	N	**Prob % (95% CI)**	**N**	**Prob % (95% CI)**		**N**	**Prob % (95% CI)**	
NRM	22		67			69		
1 year	17	4.5 (0.0-17.3)	36	30.0 (19.6-41.6)	<0.01	40	17.5 (9.4-27.4)	0.05
2 years	17	4.5 (0.0-17.3)	24	30.0 (19.6-41.6)	<0.01	25	19.4 (10.8-29.9)	0.03
PFS	22		67			69		
1 year	16	72.7 (52.7-88.8)	35	54.7 (42.7-66.5)	0.11	39	57.8 (45.9-69.1)	0.18
2 years	16	72.7 (52.7-88.8)	23	45.6 (33.5-58.0)	0.02	24	45.4 (33.3-57.7)	0.02
OS	22		67			70		
1 year	19	86.4 (69.3-97.2)	40	62.4 (50.5-73.6)	0.01	47	69.4 (58.0-79.7)	0.06
2 years	16	72.7 (52.7-88.8)	27	53.6 (41.3-65.7)	0.09	33	59.2 (47.1-70.8)	0.23
GRFS	22		66			69		
1 year	14	63.6 (42.9-82)	25	39.3 (27.9-51.3)	0.04	16	24.0 (14.7-34.8)	<0.01
2 years	14	63.6 (42.9-82)	14	27.9 (17.3-39.9)	<0.01	7	16.0 (7.9-26.3)	<0.01
aGVHD (grade 2-4)	22							
100 d	9	59.1 (37.5-79)	24	45.1(33.2-57.2)	0.26	34	50 (38.3-61.7)	0.47
1 year	6	63.6 (42-82.7)	18	48.2 (36.2-60.3)	0.21	25	51.6 (39.8-63.3)	0.33
2 years	4	63.6 (42-82.7)	11	48.2 (36.2-60.3)	0.21	20	51.6 (39.8-63.3)	0.33
aGVHD (grade 3-4)	22		67			70		
D 100	21	4.5 (0.0-17.3)	43	15.1 (7.5-24.8)	0.10	49	28.6 (18.6-39.7)	<0.01
1 year	18	9.1 (0.8-24.7)	35	16.70 (8.7-26.2)	0.33	39	30.1 (19.9-41.4)	0.01
2 years	15	9.1 (0.8-24.7)	23	16.7 (8.7-26.2)	0.33	30	30.1 (19.9-41.4)	0.01
CGVHD	22		66			70		
1 year	17	13.6 (2.6-31.2)	26	22.6 (13.0-33.9)	0.33	20	49 (37-61.1)	<0.01
2 years	14	13.6 (2.6-31.2)	18	24.8 (14.6-36.6)	0.24	10	55.2 (42.6-67.5)	<0.01
Neutrophil engraft-ment	22		64			70		
Median d (range)	22	18 (10-30)	57	21 (8-53)	<0.01	68	13 (9-24)	<0.01
D 30	2	100 (31-100)	10	79.7 (68.8-88.7)	<0.01	2	97.1 (90.9-99.9)	0.22
D 42	2	100 (31-100)	4	87.5 (77.9-94.6)	<0.01	1	97.1 (90.9-99.9)	0.22

D 100	2	100 (31-100)	1	89.1 (79.8-95.7)	<0.01	1	97.1 (90.9-99.9)	0.22
Platelet recovery	22		65			70		
Median d (range)	21	42 (27-62)	50	42 (1-180)	0.84	68	18 (1-48)	<0.01
D 30	22	4.5 (0-17.3)	58	6.2 (1.6-13.3)	0.77	12	82.9 (73-90.8)	<0.01
D 42	12	54.5 (33.2-75)	35	40 (28.4-52.2)	0.25	3	94.3 (87.1-98.7)	<0.01
D 100	1	95.5 (75.5-100)	5	76.9 (65.3-86.7)	0.03	1	97.1 (90.2-100)	0.81
Graft failure								
D 42	22	0	59	5.1 (0-10.7)	0.28	68	0	NE

Abbreviations: AGVHD…acute graft versus host disease, CB…cord blood, CGVHD…chronic graft versus host disease, CI…confidence interval, d…days, GRFS…graft versus host disease-free and relapse-free survival, GVHD…graft versus host disease, MUD…matched unrelated donor, n…number, NE…not estimable, NRM…non-relapse mortality, OS…overall survival, P…p-value, PBSC…peripheral blood stem cell, PFS…progression-free survival, Prob…probability, vs…versus

Table 4-14: Baseline demographics of the post-hoc analyses described in the ECT-001-CB.001 study [16]

Baseline demographics of the post-hoc analyses				
Parameter	UM171 CB cohort (n=22)	CB control (n=20)	BM cohort (n=12)	PBSC cohort (n=25)
Follow-up time, median (months, IQR)	18 (12-22)	50 (43-54)	16 (15-22)	17 (13-21)
Age [years], median (range)	45 (19-63)	47 (24-57)	50 (23-60)	52 (20-64)
Sex [f/m] (%)				
Female	8 (36%)	NA	NA	NA
Male	14 (64%)	NA	NA	NA
Previous allogeneic transplant	5 (23%)	1 (5%)	0	0
Median HCTCI score (IQR)	2 (0-3)	2 (0-3)	2 (0-2)	1 (0-2)
Patients with HCTCI score ≥3 (n [%])	8 (36%)	5/17 (29%)	2 (17%)	5 (20%)
Karnofsky performance score (n [%])				
90-100	9 (41%)	14 (70%)	6 (50%)	9 (36%)
≤ 80	13 (59%)	6 (30%)	6 (50%)	15 (60%)
Conditioning regimen (n [%])				
Cyclophosphamide, 12 Gy total body irradiation, fludarabine	8 (36%)	6 (30%)	0	0
Cyclophosphamide, thiotepa, 4 Gy total body irradiation	14 (64%)	14 (70%)	0	0
Cyclophosphamide, 12 Gy total body irradiation	0	0	5 (42%)	9 (36%)
Cyclophosphamide, busulfan	0	0	7 (58%)	16 (64%)
Anti-thymocyte globulin in preparative regimen	0	0	4 (33%)	12 (48%)
Stem cell source				
CB	22 (100%)	20 (100%)	0	0
Matched related donor	0	0	1 (8%)	13 (52%)
Matched unrelated donor	0	0	11 (92%)	12 (48%)
Disease status (n [%])				
Acute leukaemia in first CR	8 (36%)	5 (25%)	5 (42%)	17 (68%)
Acute leukaemia in second CR	4 (18%)	7 (35%)	0	3 (12%)
Acute leukaemia not in CR	3 (14%)	1 (5%)	1 (8%)	0
Myelodysplastic syndrome or myeloproliferative disease	2 (9%)	1 (5%)	4 (33%)	5 (20%)
Aggressive non-Hodgkin lymphoma not in complete or partial remission	2 (9%)	3 (15%)	0	0
Non-Hodgkin lymphoma in partial or complete remission	2 (9%)	1 (5%)	1 (8%)	0
Low-grade non-Hodgkin lymphoma or CLL	1 (5%)	2 (10%)	0	0
Multiple myeloma	0	0	1 (8%)	0

Abbreviations: BM…bone marrow, CB…cord blood, CLL…chronic lymphocytic leukaemia, CR…complete remission, f…female, Gy…Gray, HCTCI…haematopoietic cell transplantation comorbidity index, IQR…interquartile range, m…male, n…number, NA…not available, PBSC…peripheral blood stem cell

5 Price comparisons, treatment costs and budget impact

5.1 Parmacoeconomic model(s)

5.1.1 Submitted pharmaco-economic model

The marketing authorisation holder did not submit a pharmacoeconomic model.

5.1.2 Economic evaluation based on pharmacoeconomic models

No pharmacoeconomic evaluation could be identified for Zemcelpro.

5.2 Budget impact analysis

5.2.1 Budget impact analysis submitted by the manufacturer

The marketing authorisation holder did not submit a pharmacoeconomic model.

5.2.2 Austrian cost analysis (self-calculated)

There are no additional tables for the cost analysis.

6 Extended perspectives

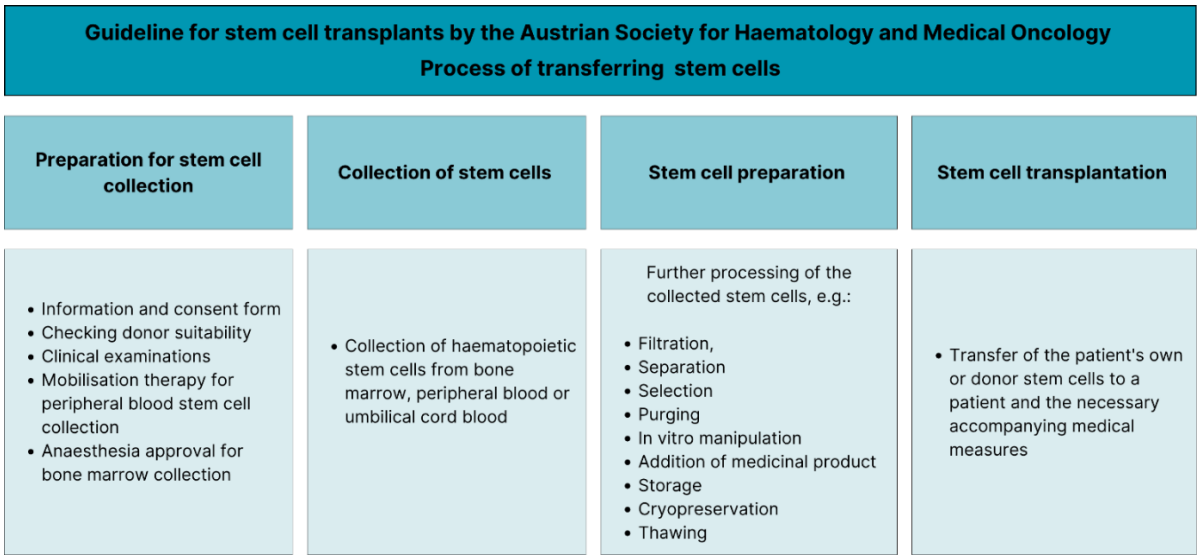

Figure 6-1: Process of transferring stem cells

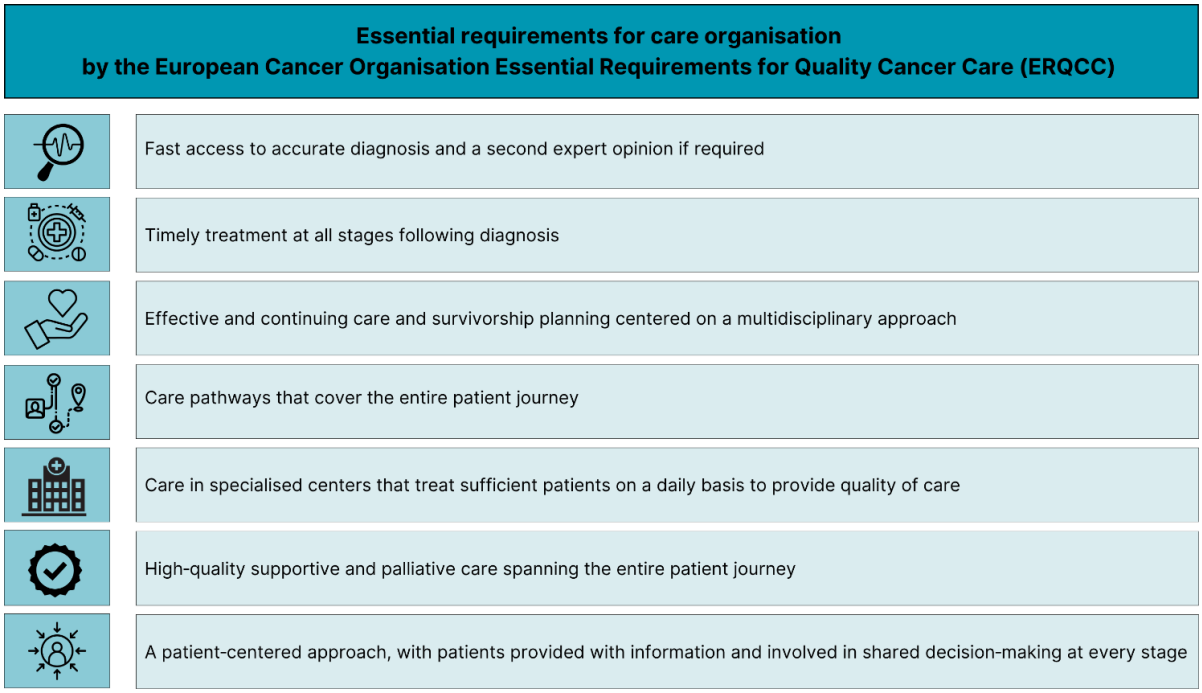

Figure 6-2: Recommendations for the organisation of care in patients with haematological malignancies by the European Cancer Organisation Essential Requirements for Quality Cancer Care (ERQCC) [23]
Abbreviations: ERQCC…essential requirements for quality cancer care

7 Development costs and public contributions

Table 7-1: Financing/patent deals/licensing/funding rounds of all companies involved in the development of Zemcelpro

Type of information	Details on collaboration, financing, and public funding	Year	Amount (in USD)	Funders/ Investors/ Acquiror	Source
ExCellThera/ Cordex Biologics					
Public funding	A Phase 1 Study of ECT-001 Expanded Cord Blood and Myeloablative Regimen with Reduced Toxicity in Patients with Severe Sickle Cell Disease.	2020	$600,000	California Institute for Regenerative Medicine (CIRM)	https://www.cirm.ca.gov/our-progress/awards/phase-1-study-ect-001-expanded-cord-blood-and-myeloablative-regimen-reduced-toxicity-patients-severe-sickle-cell-disease
Public funding	ExCellThera : six million to protect a Quebec biotech firm	2020	CAN$6,000,000	Quebec	https://www.lapresse.ca/affaires/2020-02-11/excellthera-six-millions-pour-proteger-une-biotech-quebecoise
Public funding	ExCellThera to establish stem cell bioproduction facility thanks to the Government of Canada support	2020	CAN$4,000,000	Government	https://www.canada.ca/en/economic-development-quebec-regions/news/2020/11/excellthera-to-establish-stem-cell-bioproduction-facility-creating-up-to-150-jobs-thanks-to-government-of-canada-support.html
Public funding	IRICoR makes an additional investment in ExCellThera	2020	n.a.	IRICoR	https://www.newswire.ca/news-releases/iricor-makes-additional-investment-in-excellthera-867688738.html?utm_source=chatgpt.com
Public funding	ExCellThera is CCRM's first spin-off, brought into the world via a partnership between CCRM and the Institute for Research in Immunology and Cancer Commercialisation of Research (IRICoR).	2021	n.a.	IRICoR	https://www.signalsblog.ca/catching-up-with-excellthera-and-co-founder-guy-sauvageau
Licensing	Excellthera today announced that it has entered into a licensing agreement with Astellas Pharma Inc. through its US subsidiary, Astellas Institute for Regenerative Medicine, for the in vitro use of the UM171 compound and certain other molecules in the field of pluripotent stem cells (PSCs) and PSC-derived cells.	n.a.	n.a.	Astellas Pharma	https://www.globenewswire.com/news-release/2021/07/13/2261937/0/en/ExCellThera-and-Astellas-enter-into-a-license-for-the-use-of-molecule-UM171-in-the-field-of-pluripotent-stem-cells.html
Collab-oration	2021 agreement with Ossium Health to combine their stem cell technologies for treating blood cancers and improving organ tolerance.	2021	n.a.	Ossium Health	https://www.globenewswire.com/news-release/2021/04/21/2214107/0/en/Excellthera-and-Ossium-Health-Announce-a-Collaboration-to-Advance-Their-Technologies-and-Platforms-to-Improve-Human-Health.html

University of Montreal					
Basic research	HOXB4 Is An Activator of HSC Self-Renewal/ HOXB4 Is An Activator of HSC Self-Renewal (PI Guy Sauvgeau)	2004-2009	$1,961,033	National Heart, Lung, and Blood Institute	https://reporter.nih.gov/search/y7LcpoYsn0KbjTb7oiEsaw/project-details/6928369
Basic research	Grant for the Institute for Research in Immunology and Cancer CECR in Therapeutics Discovery under the program Centres of Excellence for Commercialisation and Research - Group	2007	CAN$ 2,836,000.00	Natural Sciences and Engineering Research Council of Canada	https://www.nserc-crsng.gc.ca/ase-oro/Details-Detailles_eng.asp?id=366697
Basic research	Funding awarded to the "Interrogating and implementing Omics for precision medicine in acute myeloid leukaemia" project led by Guy Sauvageau and Josée Hébert	2018	$12.8 million	Genome Canada	https://www.iric.ca/en/about/news/2018/04/25/guy-sauvageau-and-josee-hebert-winners-of-the-2017-genome-canada-genomics-and-precision-health-competition https://genomecanada.ca/project/interrogating-and-implementing-omics-precision-medicine-acute-myeloid-leukemia/
Basic funding	Innovative Chemogenomic Tools to Improve Outcome in Acute Myeloid Leukaemia	2012-2013	n.a.	Genome Canada	https://genomecanada.ca/project/innovative-chemogenomic-tools-improve-outcome-acute-myeloid-leukemia/
Clinical Research Institute Of Montreal					
Basic research	HOXB4-- A Hemopoietic Stem Cell 'Expanding' Factor (PI Guy Sauvgeau)	2001-2003	$600,000	National Heart, Lung, and Blood Institute	https://reporter.nih.gov/search/y7LcpoYsn0KbjTb7oiEsaw/projects

Abbreviations: PI…Principal Investigator, IRICoR…Institute for Research in Immunology and Cancer Commercialization of Research, CIRM…California Institute for Regenerative Medicine, PSCs…pluripotent stem cells

Table 7-2: Search terms used to identify the development history and public contributions of Zemcelpro

Database/ News outlet/ clinical trial registry/ funding website	Search terms used	Relevant information found (yes/no)	Search period	Type of information extracted
https://www.ema.europa.eu/en/medicines	Zemcelpro	yes	Earliest mention – 08/2025	Active substance, Medical specialty, Pharmacotherapeutic group, Therapeutic area, Class, Orphan designation, Categorization, Additional monitoring, Conditional approval, Accelerated assessment, PRIME: priority medicines, Marketing authorization issued
https://adisinsight.springer.com/		yes		Alternative names
https://pubmed.ncbi.nlm.nih.gov/	ExCellThera Cordex Biologics ECT 001 ECT-001-CB UM 171 cell therapy – ExCellThera UM171-Expanded Cord Blood Transplantation allogeneic human umbilical cord blood expanded with um-171 cord blood expanded with um-171 dbd2hm3i4v ect-001-cb Guy Sauvgeau Anne Marinier Zemcelpro dorocubicel CD34- cells IRIC Josée Hébert University of Montreal Hôpital Maisonneuve Rosemont IRICoR	yes		Development history
https://clinicaltrials.gov/		yes		Clinical trials
https://euclinicaltrials.eu/		yes		
https://eudract.ema.europa.eu/		yes		
https://trialsearch.who.int/		yes		
https://cordis.europa.eu/		yes		
https://reporter.nih.gov/		yes		Basic research. Authors selected based on literature found on PubMed
https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm		no		Patent information and associated references
https://competition-cases.ec.europa.eu/search		no		Funding amounts
https://www.ihi.europa.eu/		no		
https://eismea.ec.europa.eu/index_en		no		
https://eit.europa.eu/		no		
https://eic.ec.europa.eu/index_en		no		
https://www.eib.org/en/index		no		
https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls_en		no		
https://www.sbir.gov/		no		Project funding for companies involved in the development
https://www.nsf.gov/		no		

https://www.ukri.org/		no		SME, national, regional, local, international, supranational funding
https://foerderportal.bund.de/		no		
https://www.health-holland.com/		no		
https://www.bpifrance.com/		no		
https://www.inserm.fr/en/home/		no		
https://innovationsfonden.dk/da		no		
https://lundbeckfonden.com/en		no		
https://www.ucc.ie/en/apc/		no		
https://www.amractionfund.com/about		no		
https://www.gatesfoundation.org/		no		
https://genomecanada.ca/		yes		
https://www.google.com/		yes		Patent information
https://www.forbes.com/		no		n.a.
https://www.reuters.com/		no		
https://www.science.org/		no		
https://www.cafepharma.com/		no		Collaborations, funding, financing, Series A-C funding, patent information, acquisitions
https://www.livescience.com/		no		
https://www.biospace.com/		no		
https://www.bioworld.com/		no		
https://www.biopharmadive.com/		no		
https://pharmaphorum.com/		no		
https://pharmatimes.com/		no		
https://pharmafile.com/		no		
https://www.fiercepharma.com/		no		
https://www.fiercebiotech.com		no		
https://www.biocentury.com		no		
https://www.businesswire.com/		no		
https://www.businessinsider.com/		no		
https://www.statnews.com/		no		
https://finance.yahoo.com		no		
https://www.globenewswire.com		yes		
https://www.sec.gov/		no		
https://www.lapresse.ca		yes		
https://www.newswire.ca/		yes		

8 Landscape overview

8.1 Ongoing studies on Zemcelpro

Table 8-1: List of ongoing studies with Zemcelpro [24]

Title	Trial ID	Other IDs	Phase	Status	Estimated study completion date	Sponsor
US Study of UM171-Expanded CB in Patients With High Risk Leukemia/Myelodysplasia	NCT04103879	ECT-001-CB.004	2	Active, not recruiting	02/2026	ExCell-Thera inc.
UM171 Expanded Cord Blood In Patients With High-Risk Acute Leukemia/Myelodysplasia	NCT03913026	ECT-001-CB.002	2	Active, not recruiting	10/2027	Ciusss de L'Est de l'Île de Montréal
US Study of ECT-001-CB in Pediatric and Young Adult Patients With High-Risk Myeloid Malignancies	NCT04990323	ECT-001-CB.007	1/2	Re-cruiting	06/2027	ExCell-Thera inc.
ECT-001 (UM171) Expanded Cord Blood Transplant to Treat High-risk Multiple Myeloma	NCT03441958	ECT-001-CB-003, HMR007	1/2	Active, not recruiting	10/2025	Ciusss de L'Est de l'Île de Montréal

Abbreviations: NCT…National Clinical Trial, US…United States

8.2 Specific obligations for Zemcelpro post-authorisation

No additional tables or figures are provided for this chapter.

8.3 Treatments in development

Table 8- 1: Landscape overview for Haematological malignancy requiring stem cell transplants

Indication	Active ingredient	NCT Number	Originator	Developer	Estimated EC decision
Orca-t					
Orca-t in combination with tacrolimus for treatment of advanced Haematological malignancy in adults and elderly patients undergoing	Orca-t in combination with tacrolimus	NCT05316701 NCT04013685	Orca Bio	Orca Bio	Jan 2027

Indication	Active ingredient	NCT Number	Originator	Developer	Estimated EC decision
myeloablative allogenic hematopoietic cell transplantation from an HLA-matched donor					
Smart101					
Smart101 monotherapy for treatment of Haematological malignancy in adults and the elderly with left ventricular ejection fraction of ≥40% and after haploidentical hematopoietic stem cell transplantation with post-transplant cyclophosphamide	Smart101	NCT05768035	Smart Immune	Smart Immune	Jun 2029

Abbreviations: NCT…National Clinical Trial

9 Discussion

Table 9-1: Summary table characterising the applicability of the included studies [20]

Domain	Description of the applicability of evidence	
	Pivotal FAS	**SAS**
Population	The pivotal FAS comprised a subset of 25 patients (infused: 24) aged 24-64 years (median: 47 years) from studies ECT-001-CB.002 and ECT-001-CB.004, who received a myeloablative conditioning regimen and were then intended to be transplanted with cryopreserved Zemcelpro derived from expansion of a small CB unit (defined as containing $<1.5 \times 10^5$ CD34+ cells/kg or $<2.5 \times 10^7$ TNC/kg pre-cryopreservation). Approximately 28% had received prior allogeneic transplant. All patients were classified as having high-risk or very high-risk acute leukaemia/myelodysplasia.	The SAS population comprised 116 patients aged 1-66 years (median: 44 years) from studies ECT-001-CB-001, ECT-001-CB.002, ECT-001-CB.003, ECT-001-CB.004 + ECT-001-CB.007. Approximately 26.4% had received prior allogeneic transplant. The underlying disease was predominantly AML (43.1%), ALL (24.1%), MM (15.5%), and MDS (12.1%). Patients received various conditioning regimens (high, intermediate, and low).
	Applicability: This represents a heterogeneous high-risk population with haematological malignancies and limited treatment options. The SAS population is considerably more heterogeneous than the pivotal FAS (which focused on high/very high-risk acute leukaemias/MDS with myeloablative conditioning only). This broader population provides additional safety data but limits direct applicability to the approved indication. Furthermore, the applicability to the Austrian population with various haematological malignancies is unclear.	
Intervention	The intervention consisted of doroubicel and unexpanded CD34-cells. Patients received Zemcelpro following myeloablative conditioning.	The intervention consisted of dorocubicel and unexpanded CD34-cells following myeloablative conditioning. 70.7% of patients received cryopreserved product and 29.3% fresh product.
	Applicability: According to the manufacturer, the manufacturing success rate (96%) is high. However, the duration of the production of Zemcelpro (time from selected CBU by transplant centre to delivery of finished product to transplant centre) is long (approx. 45 days [25]).	
Comparators	The studies ECT-001-CB.002 and ECT-001-CB.004 were phase 2, single-arm, open-label studies without randomised control groups.	All five studies were phase 1/2 or phase 2, single-arm, open-label studies without randomised control groups.
	Applicability: The absence of a randomised comparator arm represents a significant limitation for assessing relative efficacy compared to the current SoC. It should be noted that in Austrian clinical practice, other stem cell transplant options (matched unrelated donors, haploidentical transplantation) represent the primary alternative when matched related donors are unavailable, with unmanipulated CB less commonly used.	
Outcomes	■ OS: 66% (95% CI: 49-82) at 12 months, 51.4% (95% CI: 32-82) at 24 months ■ NRM: 21.2% (95% CI: 4-38) at 12 months; 21.2% (95% CI: 4-38) at 24 months ■ PFS: 52.8% (95% CI: 36-78) at 12 months; 45.3% (95% CI: 28-74) at 24 months ■ Time to neutrophil engraftment: median 20 days (range 10-39) ■ Time to platelet engraftment: median 40 days (range 29-175) ■ Proportion reaching neutrophil engraftment by day 42: 84% (21/25 patients) ■ Proportion reaching platelet engraftment by day 100: 19 (79.2%) ■ CRFS: 45.2% (95% CI: 29-71) at 12 months; 30.2% (95% CI: 15-62) at 24 months	■ OS: NR ■ NRM: 12.1% ■ PFS: NR ■ Time to neutrophil engraftment: NR ■ Time to platelet engraftment: NR ■ Proportion reaching neutrophil engraftment by day 42: NR ■ Proportion reaching platelet engraftment by day 100: NR ■ CRFS: NR ■ GRFS: NR ■ TRM: 12.9%

Domain	Description of the applicability of evidence	
	■ GRFS: 29.1% (95% CI: 15-55) at 12 months; no data available past 21 months ■ TRM: 21.2% (95% CI: 4-38) at 12 and 24 months	
	Applicability: The pivotal FAS shows high rates of OS and PFS, as well as low rates of NRM, relapse and moderate-to-severe chronic GVHD. However, the small patient size resulted in a wide CI. Furthermore, patient-reported outcomes, including QoL measures, were not reported. Additionally, long-term follow-up data are limited. Therefore, a comprehensive assessment of sustained efficacy and late-onset toxicities is required and is expected to be delivered as a part of specific obligations for the conditional marketing authorisation.	
Setting	The studies were conducted at multiple centres: ■ ECT-001-CB.002: 1 centre in Canada; ■ ECT-001-CB.004: 2 centres in the USA and 1 centre in the Netherlands. All centres were experienced transplant facilities. Treatment required inpatient management with specialised CB expansion and transplantation capabilities. The median initial hospitalisation was 34 days (range 16-130). ICU admission rate was 7.1% during initial hospitalisation. Re-hospitalisation within the first 100 days occurred in 43.4% of patients.	The studies were conducted at multiple centres: ■ ECT-001-CB.001: 2 centres in Canada; ■ ECT-001-CB.002: 1 centres in Canada; ■ ECT-001-CB.003: 1 centre in Canada; ■ ECT-001-CB.004: 2 centres in the USA and 1 centre in the Netherlands; ■ ECT-001-CB.007: 1 centre in the USA
	Applicability: Austria has established HSCT centres, suggesting existing infrastructure that could potentially accommodate Zemcelpro administration. However, several logistical challenges must be addressed: The transplant centre selects a suitable CBU, which then needs to be transported to the manufacturer in Canada for processing. After manufacturing is complete, the final product is transported back to the transplant centre for infusion.	

Abbreviations: BM…bone marrow, CB…cord blood, CBU…cord blood unit, CD34+…cluster of differentiation 34 positive, CI…confidence interval, CLL…chronic lymphocytic leukaemia, CRFS…chronic graft versus host disease-free relapse-free survival, FAS…full analysis set, GRFS…graft versus host disease-free relapse-free survival, HCTCI…haematopoietic cell transplantation comorbidity index, HLA…human leukoocyte antigen, HSCT…haematopoietic stem cell transplantation, ICU…intensive care unit, IQR…interquartile range, n…number, MM…multiple myeloma, NR…not reported, NRM…non-relapse mortality, OS…overall survival, PFS…progression-free survival, QoL…quality of life, TNC…total nucleated cells, TRM…transplant-related mortality, USA…United States of America

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List of abbreviations

AE ..... *adverse event*
ADR ..... *adverse drug reaction*
AGVHD ..... *acute graft versus host disease*
ALL ..... *acute lymphoblastic leukaemia*
Allo-HSCT ..... *allogeneic haematopoietic stem cell transplantation*
ALT ..... *alanine transaminase*
AML ..... *acute myeloid leukaemia*
ANC ..... *absolute neutrophil count*
ASCT ..... *autologous stem cell transplantation*
AST ..... *aspartate aminotransferase*
BM ..... *bone marrow*
CB ..... *cord blood*
CBU ..... *cord blood unit*
CD34+ *CD34-positive*
CGVHD ..... *chronic graft versus host disease*
CI ..... *confidence interval*
CIBMTR ..... *Center for International Blood and Marrow Transplant Research*
CLL ..... *chronic lymphocytic leukaemia*
CML ..... *chronic myeloid leukaemia*
CMML ..... *chronic myelomonocytic leukaemia F*
CNS ..... *central nervous system*
CPSS ..... *CMML-specifc prognostic scoring system*
CR ..... *complete remission*
CRi ..... *complete remission with incomplete blood count recovery*
CRFS ..... *chronic graft versus host disease-free and relapse-free survival*
DFS ..... *disease-free survival*
DLCOc ..... *diffusing capacity corrected for haemoglobin*
ELN ..... *European LeukemiaNet*
EBV ..... *Epstein-Barr virus*
FAS ..... *full analysis set*
FEV1 ..... *forced expiratory volume in 1 second*
FLT3 ..... *FMS-like tyrosine kinase 3*
FVC ..... *forced vital capacity*
GRFS ..... *graft versus host disease-free and relapse-free survival*
GVHD ..... *graft versus host disease*
Gy ..... *Gray*
G-CSF ..... *granulocyte colony-stimulating factor*
HTA ..... *health technology assessment*
HCT-CI ..... *haematopoietic cell transplantation comorbidity index*
ISS ..... *international staging system*
ITC ..... *indirect treatment comparison*
JAK ..... *Janus kinase*
JMML ..... *juvenile myelomonocytic leukaemia*
KPS ..... *Karnofsky performance score*
MDS ..... *myelodysplastic syndromes*
MM ..... *millimetre*
MRD ..... *minimal residual disease*
MSD ..... *matched sibling donor*
MUD ..... *matched unrelated donor*
NCCN ..... *National Comprehensive Cancer Network*
N ..... *number*
NA ..... *not available*
NRM ..... *non-relapse mortality*
OS ..... *overall survival*
PBSC ..... *peripheral blood stem cells*
PFS ..... *progression-free survival*
PI ..... *principal investigator*
QoL ..... *quality of life*
RAS ..... *rat sarcoma*
SAS ..... *safety analysis set*
TBI ..... *total body irradiation*
TNC ..... *total nucleated cells*

TP53 ..... tumour protein 53

TRM ..... transplant-related mortality

ULN ..... upper limit of normal

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