HIRSLANDEN
KLINIK HIRSLANDEN

CAR T CELL THERAPY

for the treatment of multiple myeloma

BROCHURE FOR REFERRING PHYSICIANS

INFORMATION ON THE THERAPY WITH ABECMA® AND PATIENT CARE

IS YOUR PATIENT ELIGIBLE FOR CAR T CELL THERAPY?

TREATMENT OF MULTIPLE MYELOMA WITH ABECMA® (IDECABTAGENE VICLEUCEL)

A genetically modified autologous T cell immunotherapy consisting of T cells transduced with a lentiviral vector (LVV) encoding a chimeric antigen receptor (CAR) that recognises the B cell maturation antigen.[1]

ABECMA® (idecabtagene vicleucel) is indicated for the treatment of adult patients with relapsed and refractory multiple myeloma who:

- have received two previous therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and have demonstrated disease progression on or within 60 days after the last therapy.[1]
- have received at least three previous lines of therapy, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy.[1]

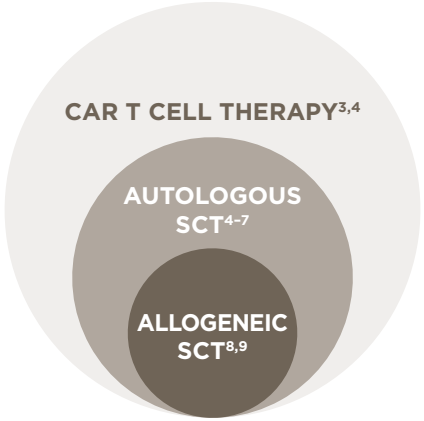
THE ONLY CAR T CELL THERAPY AUTHORISED IN SWITZERLAND IN RRMM WITH RWD FOR > 1 YEAR[1,15]

WHEN IS MY PATIENT ELIGIBLE FOR TREATMENT WITH ABECMA®?

CAR T therapy can also be considered for patients who are not eligible for stem cell transplant (SCT).[9,10]

PATIENT CHARACTERISTICS:[1]

PREVIOUS TREATMENT WITH IMID, PI AND ANTI-CD38 MAB



- ☑ No upper age limit
- ☑ Chemosensitive or chemorefractory
- ☑ Clinically fit
  e.g. good performance status and adequate organ function (kidney, liver, lung and heart function)
- ☑ Eligible or ineligible for SCT*[1]

ORGAN FUNCTION:[1]

ADEQUATE ORGAN FUNCTION (KIDNEY, LIVER, LUNG AND HEART FUNCTION)

* It is not recommended that patients receive ABECMA® within 4 months after an allogeneic SCT, as there is a potential risk of aggravated graft-versus-host disease (GvHD). Leukapheresis for the manufacture of ABECMA® should be performed no earlier than 12 weeks after an allogeneic SCT.[1]

SCT: Stem cell transplant

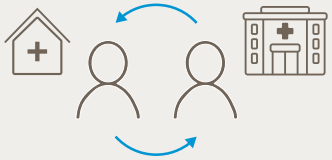
WHEN IS THE RIGHT TIME TO PLAN TREATMENT WITH ABECMA®?

"CAR T cell therapy is an innovative immunotherapy which draws on the body's own defence cells. Planning the treatment is complex and should take place as early as possible in the course of treatment to ensure good outcome prospects."

Prof. Dr. med. Christoph Renner, Klinik Hirslanden, Zurich

Why is early identification of eligible patients so important?

- The treatment outcome worsens with each further relapse and the treatment urgency increases after each further treatment.[16]
- Early planning and good collaboration between referring physicians and the Klinik Hirslanden may have a positive effect on treatment success.[17,18]
- CAR T cell therapy should be planned early, so that leukapheresis can be performed as soon as possible to gain time.



Early collaboration with the Klinik Hirslanden is crucial, e.g. for answering the following questions:

- ☑ Is the patient eligible for CAR T cell therapy?
- ☑ What bridging therapy may be needed?
- ☑ When should cytotoxic T cell therapy be avoided?*
- ☑ Evaluate whether myeloma therapy is needed until leukapheresis.

* Certain treatments (e.g. alkylating agents) can impair the manufacturing success of CAR T cell therapy, as they inhibit the production of healthy T cells.[11,19]

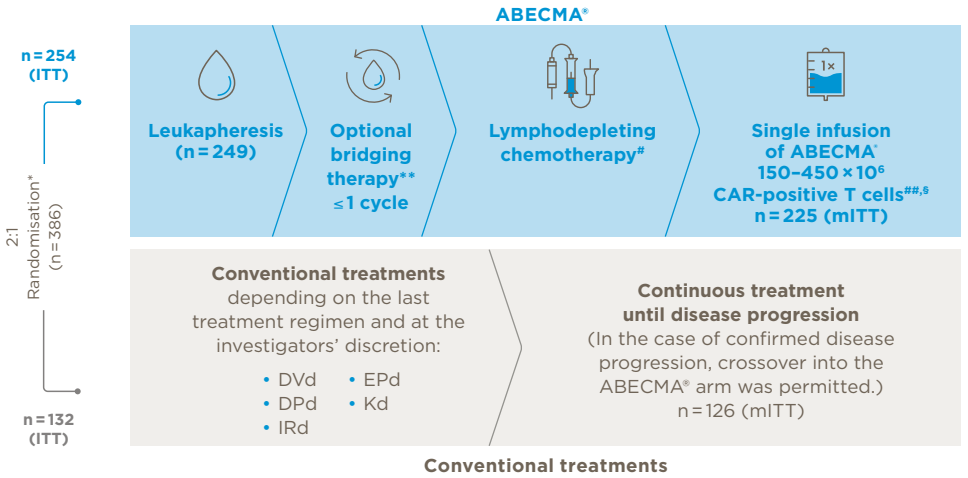
WHY CAR T THERAPY IN RRMM?

KARMMA-3: RANDOMISED PHASE III STUDY WITH ABECMA®[2]

TRIPLE CLASS-EXPOSED PATIENTS

INCLUSION CRITERIA (N = 254)

- Adults with rrMM
- 2–4 previous treatments
- Previously treated with:
  - IMiD*
  - Proteasome inhibitor
  - Anti-CD38 antibody
- Refractory to the last treatment
- ECOG PS 0–1

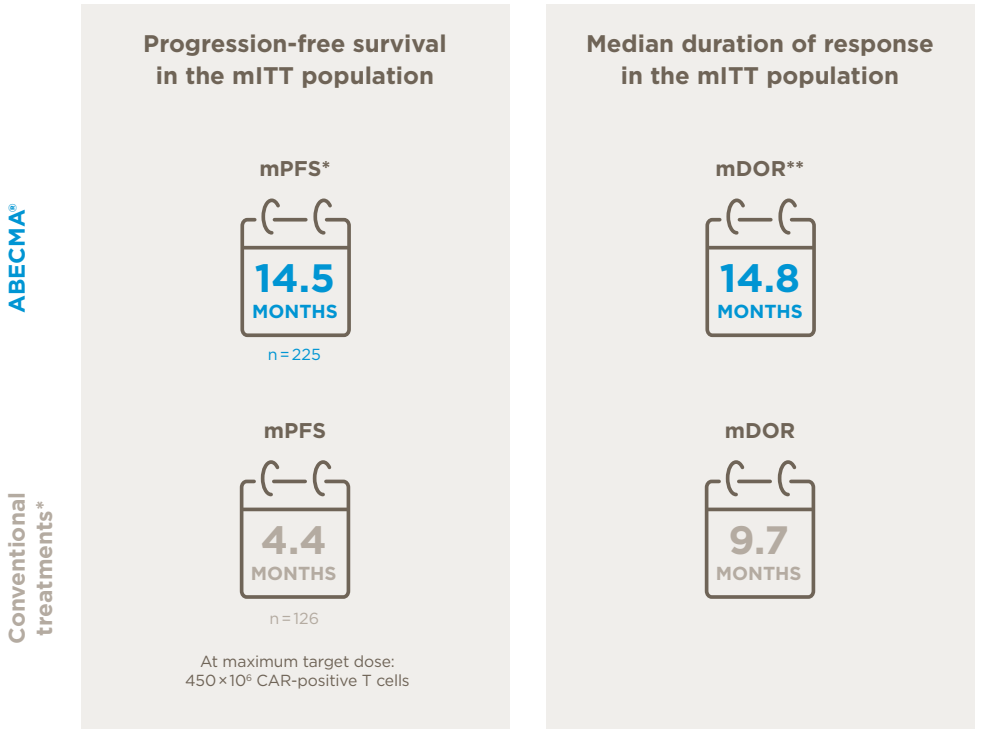


END POINTS

- Primary: PFS§§
- Secondary (selection): ORR, OS, CR, DOR, TTR, tolerance, quality of life

* Stratification by age (< 65 versus ≥ 65 years), number of previous anti-myeloma treatments (2 versus 3 or 4) and presence of a high-risk cytogenetic profile [translocations/deletions t(4;14), t(14;16) or del(17p)].
** Bridging therapy with up to 1 cycle of DPd, DVd, IRd, Kd or EPd, depending on the last anti-myeloma treatment, was permitted for disease control between leukapheresis and up to 14 days before the start of lymphodepleting chemotherapy.
# 3 days of cyclophosphamide 300 mg/m² IV and fludarabine 30 mg/m² IV; ABECMA® infusion 2 days after completion of the lymphodepleting chemotherapy.
The dose of 150 × 10⁶ CAR-positive T cells is not part of the permitted dose range.
§ The median KarMMa-3 dosage was 445.3 × 10⁶ CAR-positive T cells (range: 174.9 to 529.0 × 10⁶ CAR-positive T cells).
§§ Assessment of the mITT population by an independent review committee (IRC) according to the International Myeloma Working Group (IMWG) criteria.

PROFOUND AND SUSTAINED RESPONSE WITH ABECMA® VERSUS CONVENTIONAL TREATMENTS (MITT)[20]



The mITT population of KarMMa-3 (n = 351) is defined as the group of all randomised patients who received the study treatment to which they were randomly assigned (mITT population = safety population).

* mPFS: Median progression-free survival.
** mDOR: Median duration of response.

OVERVIEW OF SAFETY PROFILE[1,2,#]

The typical CAR T side effects cytokine release syndrome (CRS) and neurotoxicity (NT) were mild and resolved rapidly in most cases.[1,2,*]

CRS

4%

(n = 9)

Severity grade ≥3
Grade 5 CRS in 1% (n = 2)
All grades of CRS in 88% (n = 197)

Median time to onset

1 DAY

Time range:
1 to 14 days

Median time to resolution

3.5 DAYS

Time range:
1 to 51 days

No delayed neurotoxicity occurred in the KarMMa-3 study[1,2,*]

NT

3%

(n = 7)

Severity grade ≥3
No grade 5 NT
All grades of NT in 15% (n = 34)

Median time to onset

3 DAYS

Time range:
up to 317 days**

Median time to resolution

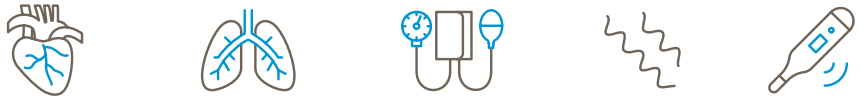
2 DAYS

Time range:
1 to 37 days

* Data refer to the safety population in KarMMa-3 (mITT population, n = 225).
** One patient developed encephalopathy on Day 317, which, in the opinion of the investigators, was not related to the ABECMA® treatment but to a worsening of pneumonia and Clostridium difficile colitis. The next longest time to occurrence of NT was 46 days.
# You can obtain more information on possible side effects from the detailed medicinal product information for healthcare professionals for ABECMA® at www.swissmedicinfo.ch.

COMMON ADVERSE REACTIONS AND SYMPTOMS OF CAR T THERAPY[13,14,*]

CYTOKINE RELEASE SYNDROME (CRS)



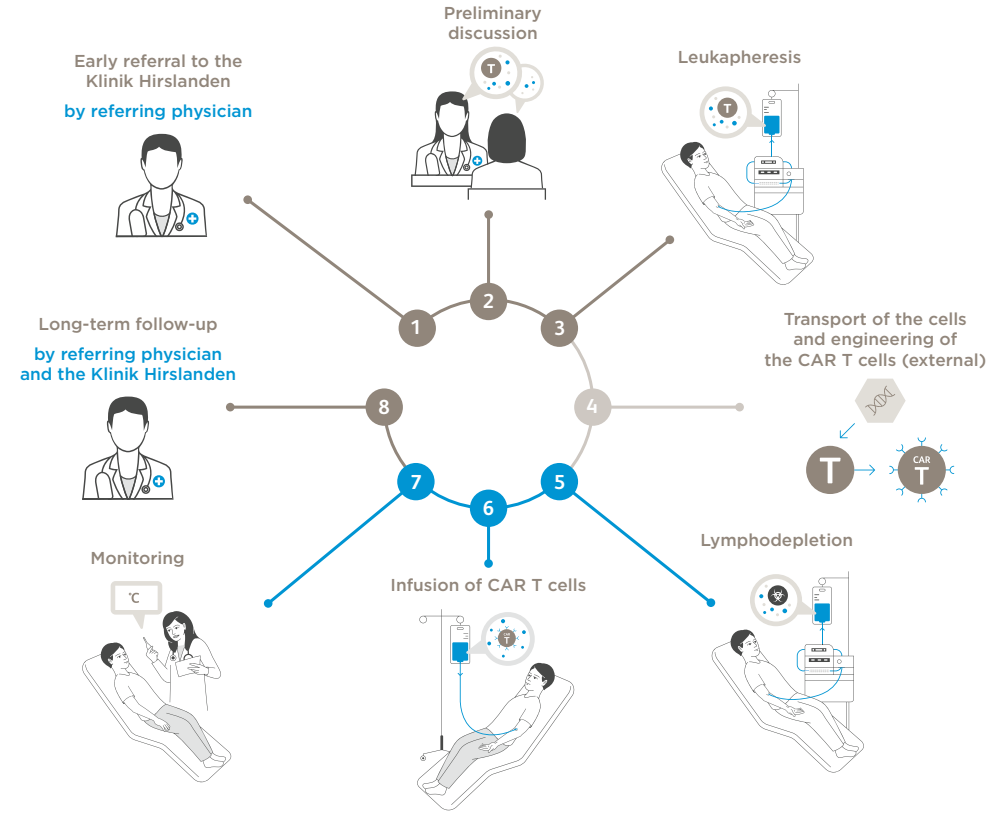
Tachycardia, arrhythmia | **Hypoxia** | **Hypotension** | **Chills** | **Fever**

NEUROTOXICITY (NT)

Encephalopathy | **Dizziness, delirium, headache** | **Aphasia** | **Fatigue**

* Not an exhaustive list of CRS and NT symptoms.

PROCEDURE AND CARE DURING CAR T THERAPY IN THE KLINIK HIRSLANDEN[1,12]



outpatient

inpatient

REFERENCES, SUCCINCT STATEMENT

1. Product Information of ABECMA®, version april 2024, www.swissmedicinfo.ch. **2.** Rodriguez-Otero P et al. Ide-cel or standard regimens in relapsed and refractory multiple myeloma. N Engl J Med. 2023 Mar 16;388(11):1002–1014. May;9(5):1225. **3.** Hayden PJ, Sirait T, Koster L, et al. An international survey on the management of patients receiving CAR T-cell therapy for haematological malignancies on behalf of the Chronic Malignancies Working Party of EBMT. Curr Res Transl Med. 2019 Jun;67:79–88. **4.** Gisselbrecht C, Glass B, Mounier N, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. J Clin Oncol. 2010 Sep;28(27):4184–4190. **5.** Gisselbrecht C, Van Den Neste E. How I manage patients with relapsed/refractory diffuse large B cell lymphoma. Br J Haematol. 2018 Sep;182(5):633–643. **6.** Al Hamed R, Bazarbachi AH, Malard F, et al. Current status of autologous stem cell transplantation for multiple myeloma. Blood Cancer J. 2019 Apr;9(4):44. **7.** Belotti A, Ribolla R, Cancelli V, et al. Transplant eligibility in elderly multiple myeloma patients: prospective external validation of the international myeloma working group frailty score and comparison with clinical judgment and other comorbidity scores in unselected patients aged 65–75 years. Am J Hematol. 2020 Jul;95(7):759–765. **8.** Luoma S, Silvennoinen R, Rauhala A, et al. Long-term outcome after allogeneic stem cell transplantation in multiple myeloma. Annals of Hematology. 2021 Apr;100:1553–1567. **9.** Chavez JC, Bachmeier C, Kharfan-Dabaja MA. CAR T-cell therapy for B-cell lymphomas: clinical trial results of available products. Ther Adv Hematol. 2019 Apr;10:1–20. **10.** Munshi NC, Anderson LD, Shah N, et al. Idecabtagene vicleucel in relapsed and refractory multiple myeloma. N Engl J Med. 2021 Feb;25;384(8):705–716. **11.** Rytlewski J, Fuller J, Mertz DR, et al. Correlative analysis to define patient profiles associated with manufacturing and clinical endpoints in relapsed/refractory multiple myeloma (RRMM) patients treated with idecabtagene vicleucel (ide-cel; bb2121), an anti-BCMA CAR T cell therapy. J Clin Oncol 40. 2022 Jun; suppl 16; abstr 8021. **12.** Maus MV, Levine BL. Chimeric antigen receptor T-cell therapy for the community oncologist. Oncologist. 2016 May;21:608–617. **13.** Shimabukuro-Vornhagen A, Gödel P, Subklewe M, et al. Cytokine release syndrome. J Immunother Cancer. 2018 Jun;6(1):56. **14.** Lee DW, Santomasso BD, Locke FL, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. Biol Blood Marrow Transplant. 2019 Apr;25(4):625–638. **15.** Driessen C, Baur K, Heim D, et al. A national platform and scoring system allocates CAR-T treatment slots for multiple myeloma to patients with high likelihood to reach complete remission. Presented at the 65th Annual ASH Meeting and Exposition. San Diego, CA and online; Dec 9–12, 2023. Abstract 4701. **16.** McMillan A et al. Post relapse survival rates in diffuse large B-cell lymphoma. Blood. 2016 Dec 2;128(22):4204. **17.** https://touchoncology.com/education/car-t-in-clinical-practice-navigating-the-patient-journey-from-referral to-long-term-follow-up/ – last request: 25.02.2024. **18.** Porter DL et al. CAR T therapy referral for diffuse large B cell lymphoma (DLBCL) by U. S. community Hematology / Oncology (cH / O) practices: perceptions and patterns. Blood. 2021;138(Supplement 1):4977. **19.** Korell F et al. Current challenges in providing good leukapheresis products for manufacturing of CAR-T cells for patients with relapsed/refractory NHL or ALL. Cells. 2020 May;9(5):1225. **20.** Manier S et al. Idecabtagene vicleucel versus standard regimens in patients with triple-class–exposed relapsed and refractory multiple myeloma: a KarMMa-3 analysis in the modified intention-to-treat (mITT) population. Poster presentation International Myeloma Society (IMS) Annual Meeting 2023; 27.–30.09.2023; Athens, Greece; Poster P-032. **Literature on request.**

ABECMA® (idecabtagene vicleucel) ▼ This medicinal product is subject to additional monitoring. For more information, please refer to the Summary of Product Characteristics for ABECMA® at www.swissmedicinfo.ch. I: In adults with relapsed and refractory multiple myeloma who have received at least two prior lines of therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression during or within 60 days after the last therapy; or who have received at least three prior lines of therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy. **D:** as a single infusion with a target dose of 420×10^6 CAR-positive viable T cells (range 260 to 500×10^6 CAR-positive viable T cells) under the direction and supervision of a trained physician at a qualified treatment centre. **CI:** hypersensitivity to active substances/excipients. Also note contraindications for lymphodepleting chemotherapy. **W&P:** cytokine release syndrome (CRS) and neurological toxicities with life-threatening reactions have occurred after treatment with ABECMA®. Patients must be monitored daily in a qualified facility for 10 days after infusion. Two doses of tocilizumab and access to another dose within 8 h need to be available. Parkinsonism with reported symptoms such as tremor, dysphasia, bradykinesia and parkinsonian-like reflexes occurred. Allergic reactions and virus reactivations (CMV and HBV) may occur. Severe infections and febrile neutropenia have been observed. Risk of prolonged cytopenia and hypogammaglobulinemia. Patients may develop secondary malignancies. No administration to patients with active infections or inflammatory diseases. Vaccination with live viral vaccines should be avoided 6 weeks before treatment. Patients should not be treated with ABECMA® within 4 months after allogeneic stem cell transplantation either (risk of increased GvHD). The donation of blood, organs, tissues and cells is prohibited. **IA:** no interaction studies have been conducted. **AE:** infections, decreased blood cell count, disseminated intravascular coagulation, hypogammaglobulinemia, CRS, haemophagocytic lymphohistiocytosis, electrolyte disorders, decreased appetite, insomnia, delirium, headache, encephalopathy, dizziness, tremor, motor dysfunction, aphasia, ataxia, hemiparesis, seizure, tachycardia, atrial fibrillation, hypotension, hypertension, cough, dyspnoea, hypoxia, pulmonary oedema, diarrhoea, nausea, constipation, vomiting, gastrointestinal bleeding, arthralgia, myalgia, fatigue, pyrexia, oedema, chills, asthenia, AP increased, AST increased, ALT increased, CRP increased. **PF:** one or more infusion bags containing a total cell dispersion of 260 to 500×10^6 CAR-positive viable T cells. **Detailed information:** Information for Healthcare Professionals at www.swissmedicinfo.ch. **MAH:** Bristol-Myers Squibb SA, CH-Steinhausen. Version 02/2024.

08/2024 • 2012-CH-2400028

CONTACT

Find out more about CAR T cell therapy using the QR code. For questions and referrals regarding cell therapy at the Klinik Hirslanden, the team of physicians involved in the medical programme for cell therapy would be pleased to help you by phone at +41 (0)44 387 37 80 or by email.

Prof. Dr. med. Christoph Renner

Specialist for: Haematology, General Internal Medicine, Medical Oncology

christoph.renner@kho.ch

PD Dr. med. Panagiotis Samaras

Specialist for: Medical Oncology, General Internal Medicine

panagiotis.samaras@kho.ch

PD Dr. med. Karin Hohloch

Specialist for: General Internal Medicine, Medical Oncology and Haematology

karin.hohloch@kho.ch

Associate Professor (UNIC) Dr. med. Ulf Petrausch

Specialist for: Medical Oncology, General Internal Medicine, Allergology and Clinical Immunology

ulf.petrausch@ozh.ch

in cooperation with:

HIRSLANDEN
KLINIK HIRSLANDEN

Bristol Myers Squibb®