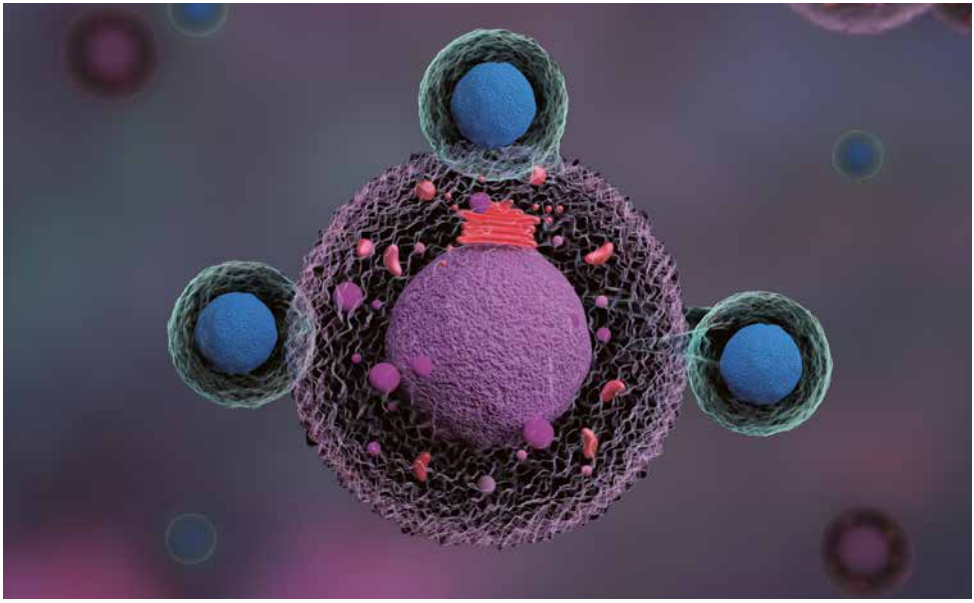
HIRSLANDEN
KLINIK HIRSLANDEN

CAR T-CELL-THERAPIES

FOR THE TREATMENT OF LYMPHOMA

REFERRAL CARD

INFORMATION ON TREATMENT WITH YESCARTA® AND TECARTUS® AND PATIENT CARE



IS YOUR PATIENT SUITABLE FOR CAR T-CELLS?

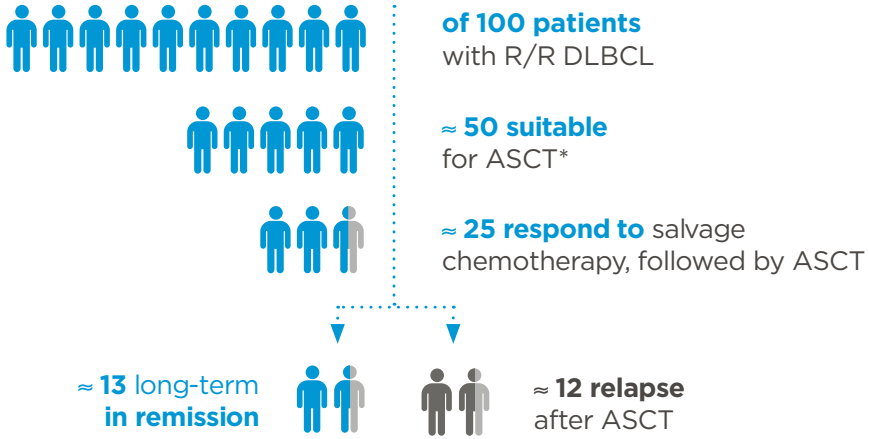
2L R/R DLBCL OR HGBL

Guideline recommendation CAR T-cell therapy from 2L onwards[5]

DLBCL: High medical need in second line

DLBCL patients whose disease is unresponsive to salvage chemotherapy and those patients who are not eligible for high-dose chemotherapy with autologous stem cell transplantation (ASCT) have a poor prognosis to date.[1]

A majority of patients with R/R DLBCL are unable to receive a stem cell transplant or suffer a relapse after transplantation.[1-4]



* Refractory or relapsing patients <12 months: EFS after 3 years = 20%[3]; Relapsing patients >12 months: EFS after 3 years = 45%[3]

Indication YESCARTA® 2L:

YESCARTA® is indicated for the treatment of adult patients with relapsed or refractory **diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL)** that is **refractory to first-line chemoimmunotherapy** or that relapses **within 12 months** of **first-line chemoimmunotherapy.[6]**

Important criteria for patient selection for treatment with YESCARTA® in 2L DLBCL/HGBL:

- ≥18 years[7]
- ECOG 0–1[7]
- Insufficient response in 1L therapy (primary refractory)[7]
- Early relapse (≤12 months) after 1L therapy[7]

Recommendation from the center:

Early contact with the Hirslanden clinic if the patient shows any of the possible indications of early recurrence after 1L therapy:

- ☑ No complete remission after 1L therapy
- ☑ Progressive lymphadenopathy
- ☑ Unexplained cytopenia

When selecting therapy, consider a possible impairment for subsequent CAR T-cell therapy.

ASCT: Autologous stem cell transplantation; DLBCL: diffuse large B-cell lymphoma; EFS: Event Free Survival; R/R: Relapse/Refractory

DLBCL: Diffuse large B-cell lymphoma; ECOG: Eastern Cooperative Oncology Group; HGBL: High-grade B-cell lymphoma

CAR T-CELL THERAPY
IN 2L DLBCL & HGBL

YESCARTA® (axicabtagene ciloleucel) Dispersion for infusion

2L R/R LBCL – ZUMA-7-STUDY

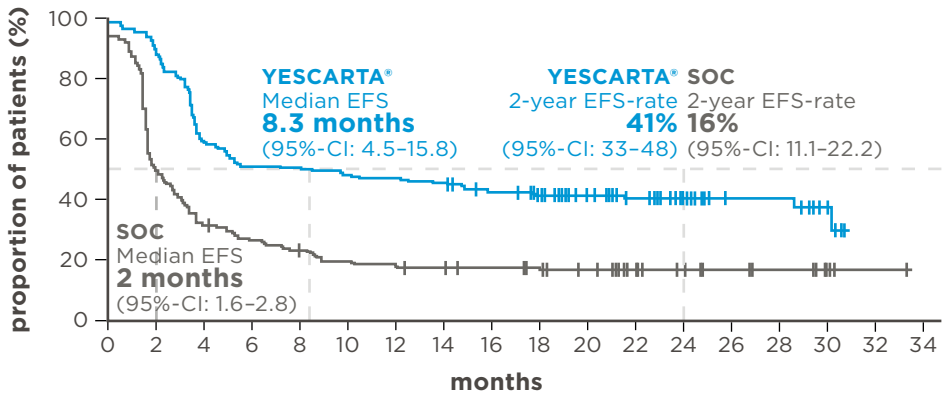
Study design:

Randomized, open-label, multicenter Phase III study of YESCARTA® compared to standard of care (SOC) in the **second-line** setting in adult patients (N=359) with large B-cell lymphoma (LBCL) who were refractory to first-line chemotherapy or relapsed within 12 months.[7]

Study outcomes:

Quadrupled mEFS with YESCARTA® vs. SOCT in 2L[7]

Event-free survival (ITT, n=359)



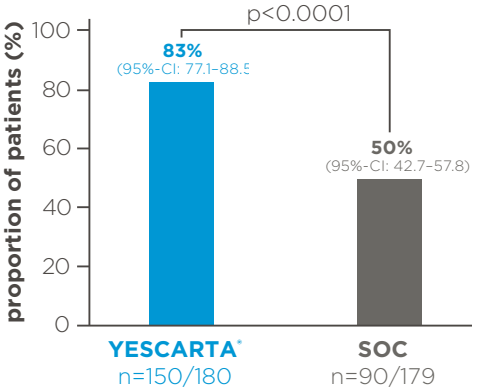
Patients at risk

YESCARTA®	180	163	106	92	91	87	85	82	74	67	52	40	26	12	12	6	
SOC	179	86	54	45	38	32	29	27	25	24	20	12	9	7	6	3	1	0

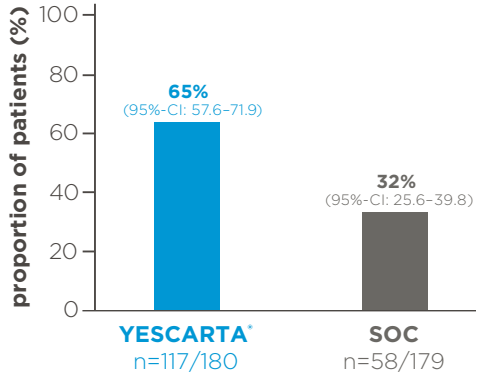
CI: confidence intervall; ITT: Intention-to-treat; mEFS: median event-free survival; SOC: Standard of Care

YESCARTA® doubled the CR vs. SOC[7]

Objective response rate (ORR)



Complete response (CR)



CI: confidence intervall; CR: complete response; ORR: objective response rate; SOC: Standard of Care

CAR T-CELL THERAPY IN 3L DLBCL & PMBCL

YESCARTA® (axicabtagene ciloleucel) Dispersion for infusion

3L R/R DLBCL / PMBCL

Indication YESCARTA® 3L DLBCL/PMBCL:

YESCARTA® is indicated for the treatment of adult patients with **relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL)** after two or more lines of systemic therapy.[6]

Important parameters for patient selection for the treatment of YESCARTA® in 3L DLBCL/PMBCL:

- ≥18 years[8]
- Adequate organ function[8]
- ECOG 0–1[8]
- No uncontrolled infection[6]

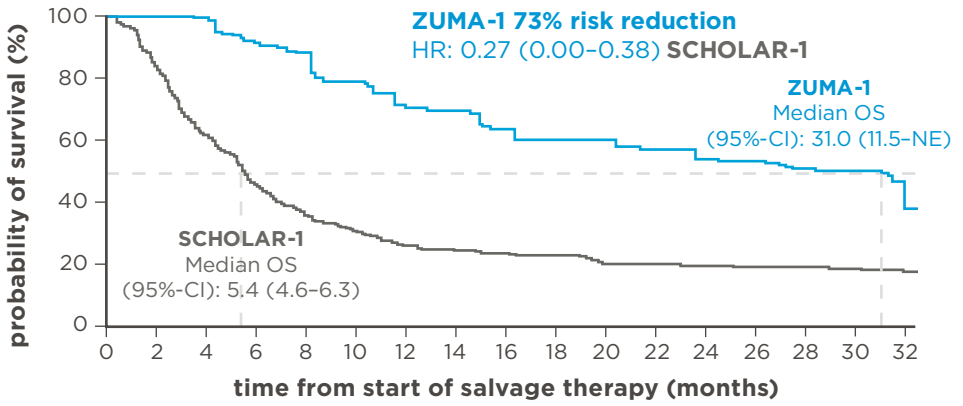
If your patient relapses and is eligible for CAR T-cell therapy, please contact us as soon as possible.

DLBCL: Diffuse large B-cell lymphoma; ECOG: Eastern Cooperative Oncology Group; PMBCL: primary mediastinal large B-cell lymphoma

ZUMA-1 and SCHOLAR-1

YESCARTA® **reduces the risk of death by 73%** compared to conventional therapies[9]

Overal survival (OS)*



adapted from Neelapu SS, et al.[9]

* comparison of confounder-adjusted OS**

ZUMA-1

Progression free survival after 2 years: 72%***,[10]
Overall survival after 5 years: 43%[6]

** Comparison of confounder-adjusted OS. To control for confounding, the treatment-specific survival functions were obtained using augmented inverse-probability weighted complete-case estimators on the primary common support data set for survival (ZUMA-1, N=81; SCHOLAR-1, N=331).

*** in patients with complete remission after 3 months

NE: not evaluable; OS: overall survival

CAR T-CELL THERAPY IN 4L FL

YESCARTA® (axicabtagene ciloleucel) Dispersion for infusion

4L R/R FL

Indication YESCARTA® 4L FL:

YESCARTA® is indicated for the treatment of adult patients with **relapsed or refractory follicular lymphoma (FL)** after three or more lines of systemic therapy.[6]

Important parameters for patient selection for the treatment of YESCARTA® in 4L FL:

- ≥18 years[11]
- Adequate organ function[11]
- ECOG 0–1[11]
- No uncontrolled infection[6]

→ **If your patient relapses and is eligible for CAR T-cell therapy, please contact us as soon as possible.**

FL: follicular lymphoma; ECOG: Eastern Cooperative Oncology Group; R/R: Relapse/Refractory

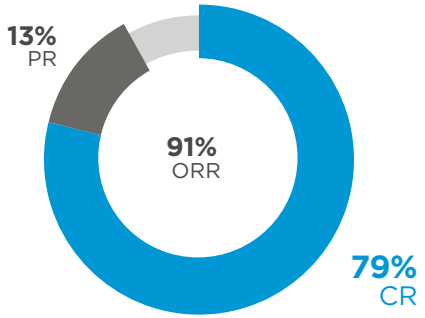
ZUMA-5-STUDY

Study design:

Multicenter, single-arm, open-label phase II study[11]

Study outcomes:

24-month analysis: high response rates in 4L+ patients with r/r FL (n=80)[6]



Durable remissions:

mDOR: 38.6 months (95%-CI: 24.7-NE)[6]

Rate of durable remission
12 months: 78.1% (95%-CI: 66.2–86.2)
18 months: 72.8% (95%-CI: 60.2–82.0)
24 months: 65.4% (95%-CI: 51.2–76.4)

CI: confidence intervall; CR: complete response; FL: follicular lymphoma; mDOR: median duration of response; NE: not evaluable; ORR: objective response rate; PR: partial response

CAR T-CELL THERAPY IN 3L MCL

TECARTUS® (brexucabtagene autoleucel) Dispersion for infusion

3L R/R MCL

Indication TECARTUS® 3L MCL:

TECARTUS® is indicated for the treatment of adult patients with **relapsed or refractory mantle cell lymphoma (MCL)** after two or more lines of systemic therapy including a Bruton tyrosine kinase (BTK) inhibitor.[12]

Important parameters for patient selection for the treatment of TECARTUS® in 3L MCL:

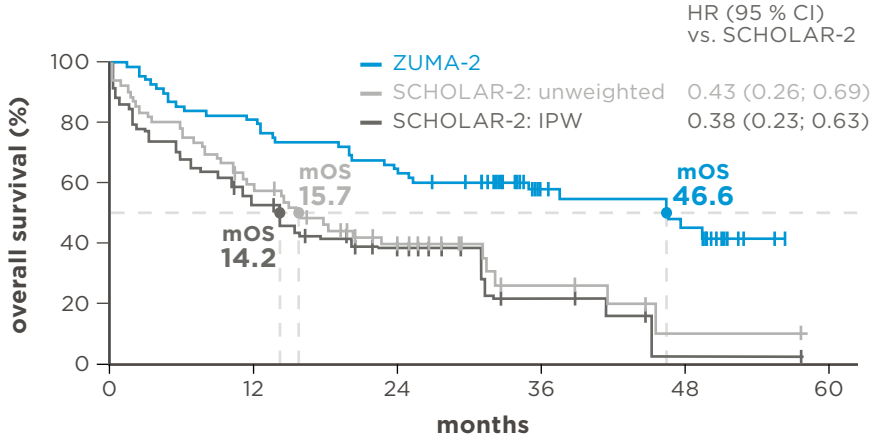
- ≥18 years[13]
- Adequate organ function[13]
- ECOG 0–1[13]
- No uncontrolled infection[12]

If your patient relapses and is eligible for CAR T-cell therapy, please contact us as soon as possible.

MCL: mantle cell lymphoma; R/R: Relapse/Refractory

ZUMA-2 and SCHOLAR-2

Indirect comparison of overall survival in ZUMA-2 and SCHOLAR-2[14]



Kaplan-Meier curves: Indirect comparison of overall survival in ZUMA-2 (registration study) and SCHOLAR-2 (Real-World Standard of Care)

Patients at risk (censored patients)						
ZUMA-2	68 (0)	55 (0)	43 (0)	19 (21)	14 (22)	0 (35)
SCHOLAR-2 unweighted	59 (0)	32 (2)	15 (10)	5 (17)	1 (19)	0 (20)
SCHOLAR-2 IPW	59 (0)	30 (1)	15 (9)	4 (16)	0 (18)	0 (19)

CI: confidence intervall; HR: hazard ratio; IPW: inverse probability weighting; mOS: median overall survival

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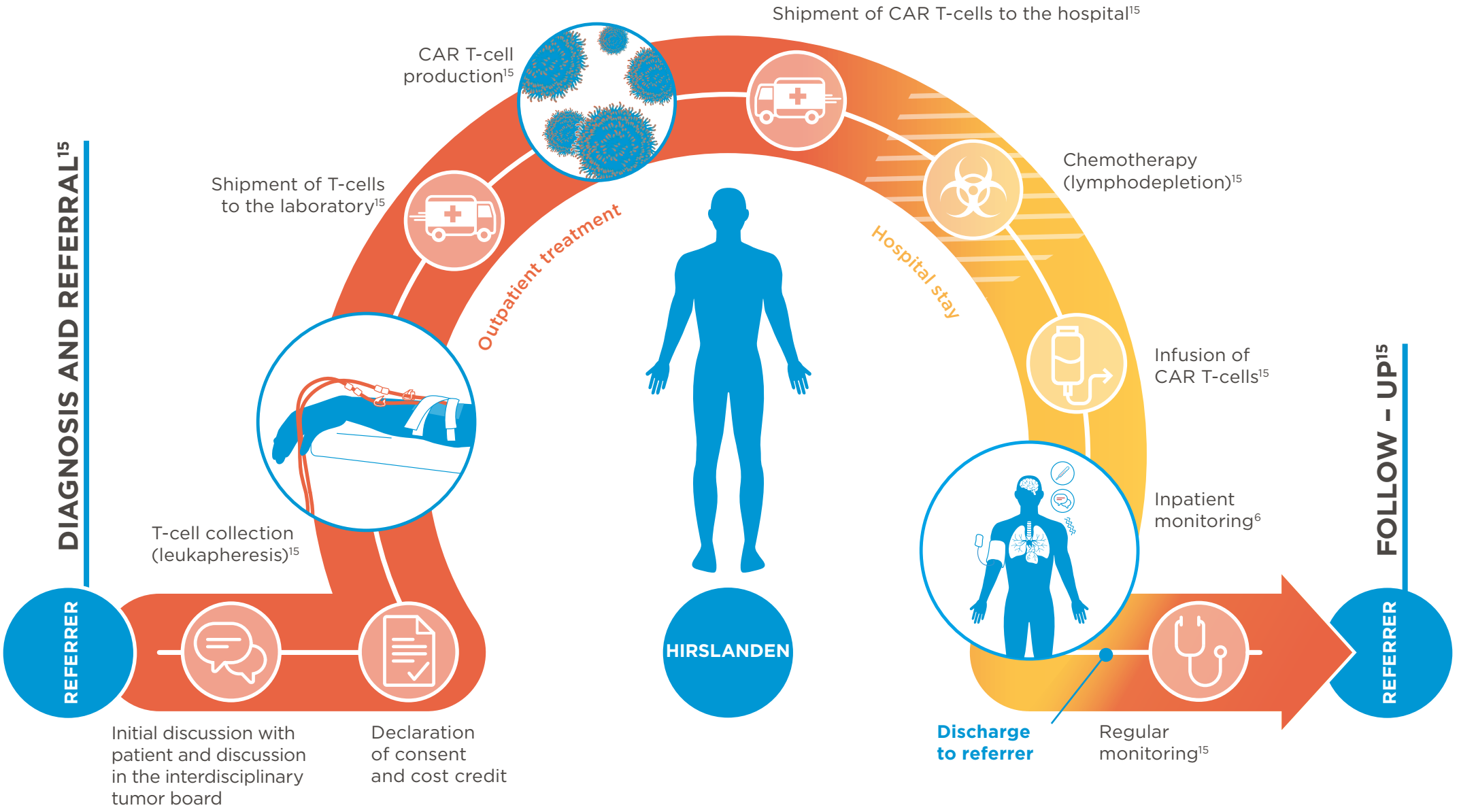
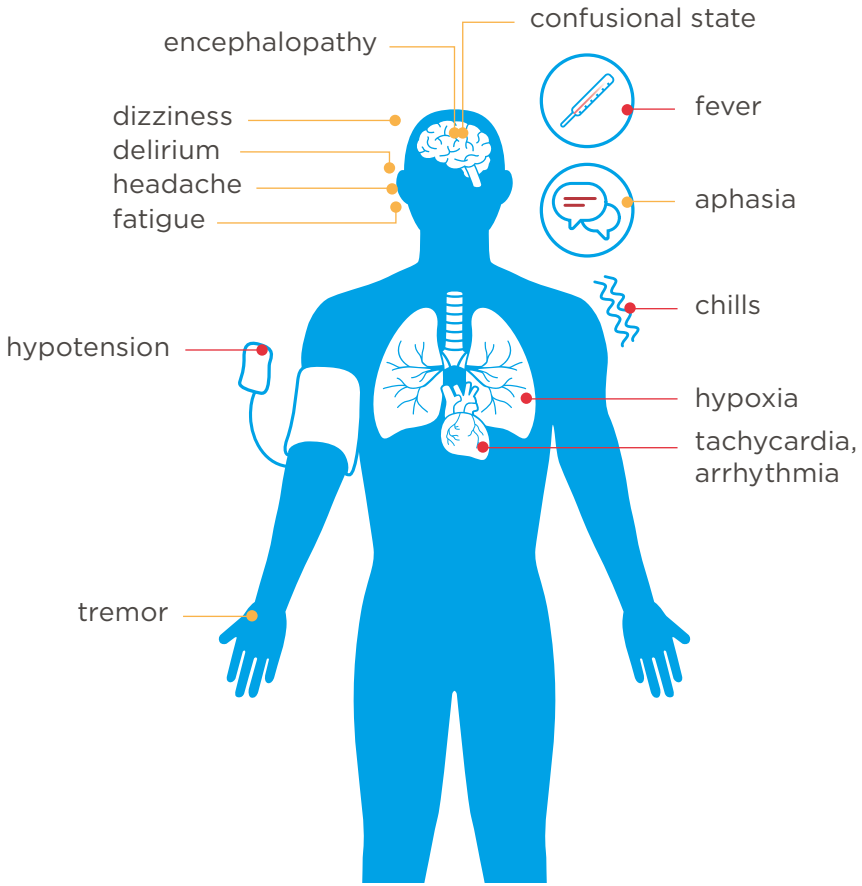
PATIENT CARE



ADVERSE REACTIONS

Some selected adverse reactions to CAR T-cell therapy:[6,12]



● CRS: cytokine release syndrome ● neurological

Not all adverse reactions are presented here. A complete list of adverse reactions can be found in the latest product information for YESCARTA® and TECARTUS®.

REFERENCES

References

1. Friedberg JW. Relapsed/Refractory Diffuse Large B-Cell Lymphoma. Hematology Am Soc Hematol Educ Program 2011;201:498–505. **2.** Westin J & Sehn LH. CAR T Cells as a second-line Therapy for large B-Cell Lymphoma: a Paradigm shift? Blood 2022;139(18):2737–2746. **3.** Gisselbrecht C, et al. Salvage Regimens with autologous Transplantation for relapsed large B-Cell Lymphoma in the Rituximab era. J Clin Oncol 2010;28(27):4184. **4.** Crump M, et al. Randomized Comparison of Gemcitabine, Dexamethasone, and Cisplatin versus Dexamethasone, Cytarabine, and Cisplatin Chemotherapy before Autologous Stem-Cell Transplantation for Relapsed and Refractory aggressive Lymphomas: NCIC-CTG LY.12. J Clin Oncol 2014;32(31):3490-3496. **5.** Onkopedia-Leitlinie, Diffuses grosszelliges B-Zell-Lymphom, Stand Juli 2022, verfügbar unter: https://www.onkopedia.com/de/onkopedia/guidelines/diffuses-grosszelliges-b-zell-lymphom/@@guideline/html/index.html. last viewed: 14.02.2023. **6.** YESCARTA® Product Information, status December 2022; www.swissmedic-info.ch. **7.** Locke FL, et al. Axicabtagene Ciloleucel as Second-Line Therapy for large B-Cell Lymphoma. N Engl J Med 2022;386(7):640–654. **8.** Locke FL, et al. Phase 1 Results of ZUMA-1: A Multicenter Study of KTE-C19 Anti-CD19 CAR-T Cell Therapy in Refractory Aggressive Lymphoma. Mol Ther 2017;25(1):285–295. **9.** Neelapu SS, et al. Comparison of 2-year Outcomes with CAR T Cells (ZUMA-1) vs Salvage Chemotherapy in Refractory large B-Cell Lymphoma. Blood Adv 2021;5(20):4149–4155. **10.** Locke FL, et al. Long-term Safety and Activity of Axicabtagene Ciloleucel in Refractory Large B-Cell Lymphoma (ZUMA-1): a Single-Arm, Multicentre, Phase 1-2 Trial. Lancet Oncol 2019;20(1):31-42 plus Supplement. **11.** Jacobson CA, et al. Axicabtagene Ciloleucel in Relapsed or Refractory indolent Non-Hodgkin Lymphoma (ZUMA-5): a Single-Arm, multicentre, Phase 2 Trial. Lancet Oncol 2022;23(1):91–103. **12.** TECARTUS® Product Information, status January 2023; www.swissmedicinfo.ch. **13.** Wang M, et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med 2020;382(14):1331–1342 (incl. protocol). **14.** Hess G, et al. A Comparison of Overall Survival with Brexucabtagene Autoleucel (Brexu-cel) CAR T-Cell Therapy (ZUMA-2) and Standard of Care (SCHOLAR-2) in Patients with Relapsed/Refractory Mantle Cell Lymphoma (R/R MCL) Previously Treated with a Covalent Bruton Tyrosine Kinase Inhibitor (BTKi). Poster 4627, presented at the 64th ASH annual Meeting, December 10–13 2022, New Orleans, Louisiana; https://ash.confex.com/ash/2022/webprogram/Paper162638.html; zuletzt eingesehen 14.02.2023. **15.** Jacobson CA, et al. Axicabtagene Ciloleucel, an Anti-CD19 Chimeric Antigen Receptor T-Cell Therapy for Relapsed or Refractory Large B-Cell Lymphoma: Practical Implications for the Community Oncologist. The Oncologist 2020;25(1):e138–e146.

The referenced documents can be requested from Gilead Switzerland.

ABRIDGED PRODUCT INFORMATION YESCARTA®

YESCARTA® 0.4 – 2×10⁸ Anti-CD19 CAR T cells, dispersion for infusion
Active substance: Axicabtagene ciloleucel. **COMP:** Autologous T cells which have been transduced with a retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor (CAR), with a target dose of 2×10^6 CAR-positive, viable anti-CD19 T cells/kg body weight. Excipients: CryoStor CS10 (DMSO; Dextran 40), sodium chloride, human serum albumin, 5% DMSO. **IND:** YESCARTA® is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL) that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy, relapsed or refractory (r/r) DLBCL or primary mediastinal large B-cell lymphoma (PMBCL) after two or more lines of systemic therapy and relapsed or refractory follicular lymphoma (FL) after three or more lines of systemic therapy. **POS:** Single infusion bag with $0.4 – 2\times10^8$ anti-CD19 CAR T-cells in approx. 68 ml for a target dose of 2×10^6 anti-CD19 CAR T-cells per kg body weight. **CI:** Hypersensitivity to the active substance, any of the excipients or to any of those substances listed as contraindications in the prescribing information for fludarabine or cyclophosphamide. **PC:** Administration by qualified sites only. Refer to the prescribing information for grading and management guidance for cytokine release syndrome and neurological adverse reactions. In immunosuppressed patients, including patients treated with YESCARTA®, life-threatening and fatal opportunistic infections including disseminated fungal infections and viral reactivation have been reported, therefore take into account in patients with neurological events. **IA:** No studies. **Preg./br.f.:** During preparation for chemotherapy and for at least 6 months after the YESCARTA® infusion, use an effective method of contraception. Infusion of YESCARTA® not recommended for pregnant women. **UE (very common, ≥1/10):** Unspecified pathogen infections, viral infections, bacterial infections, febrile neutropenia, neutropenia, lymphopenia, leukopenia, anaemia, thrombocytopenia, cytokine release syndrome (CRS), immunoglobulins decreased, hyponatraemia, hypophosphataemia, hyperuricemia, appetite decreased, delirium, insomnia, encephalopathy, tremor, headache, dizziness, tachycardia, arrhythmia, hypotension, hypertension, cough, vomiting, diarrhoea, constipation, abdominal pain, nausea, transaminases increased, rash (including rash, application site rash, dermatitis, dermatitis allergic, dermatitis bullous, erythema, pruritus, rash erythematous, rash macular, rash maculo-papular, rash pruritic, rash pustular, Stevens-Johnson syndrome, urticaria) motor dysfunction, musculoskeletal pain, fever, oedema, fatigue, chills. **UE (common, <1/10, ≥1/100):** Fungal infections, coagulopathy, hyperglycaemia, hypokalaemia, hypocalcemia, hypoalbuminaemia, dehydration, weight decreased anxiety, affective disorder, ataxia, seizure, hemiparesis, neuropathy peripheral, myoclonus, cardiac failure, thrombosis, hypoxia, pleural effusion, pulmonary oedema, dyspnoea, rhinorrhoea (including allergic rhinitis), dysphagia, dry mouth, hyperbilirubinaemia, renal impairment, pain, visual impairment **Dispensing category:** A. **Last updated:** December 2022. **MA:** Gilead Sciences Switzerland Sàrl, postal address: General-Guisan-Strasse 8, 6300 Zug. Complete prescribing information available at www.swissmedicinfo.ch. *CH-GS-202301-202212-E*

ABRIDGED PRODUCT INFORMATION TECARTUS®

Abbreviated information for healthcare professionals TECARTUS®
COMP: brexucabtagene autoleucel. **IND:** TECARTUS® is a genetically modified autologous T-cell immunotherapy directed against CD19 and is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after two or more lines of systemic therapy including a Bruton tyrosine kinase (BTK) inhibitor or for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) after two or more systemic therapies. **DOS:** Single infusion bag for autologous and intravenous use only with anti-CD19 CAR T cells in approximately 68 mL for a target dose of 2×10^6 cells/kg body weight for MCL patients and a target dose of 1×10^6 cells/kg body weight for ALL patients. **CI:** Hypersensitivity to the active substance or to any of the excipients. Contraindications of the lymphodepleting chemotherapy must be considered. **W&P:** Administration by qualified treatment centres only. See the information for healthcare professionals for the grading and recommended treatment of cytokine release syndrome and neurological adverse reactions, also known as immune effector cell-associated neurotoxicity syndrome (ICAN). In immunosuppressed patients, life-threatening and fatal opportunistic infections including disseminated fungal infections and viral reactivation have been reported; this should be taken into consideration in patients with neurological events. **IA:** No studies. **P/L:** See the information for healthcare professionals of the relevant chemotherapy for effective contraception during lymphodepleting chemotherapy. Insufficient exposure data to recommend a duration of contraception following TECARTUS®. TECARTUS® is not recommended for women who are pregnant, or for women of childbearing potential not using contraception. **AR (very common, ≥1/10):** Unspecified pathogen infections, bacterial infections, fungal infections, viral infections, leukopenia, neutropenia, lymphopenia, thrombocytopenia, anaemia, febrile neutropenia, cytokine release syndrome, hypogammaglobulinaemia, hypophosphataemia, decreased appetite, hypomagnesaemia, hyperglycaemia, delirium, anxiety, insomnia, encephalopathy, tremor, headache, aphasia, dizziness, neuropathy, tachycardias, bradycardias, hypotension, hypertension, haemorrhage, cough, dyspnoea, pleural effusion, hypoxia, nausea, diarrhoea, constipation, abdominal pain, vomiting, oral pain, alanine aminotransferase increased, blood uric acid increased, hypocalcaemia, aspartate aminotransferase increased, hyponatraemia, direct bilirubin increased, hypokalaemia, rash, skin disorder, muscoloskeletal pain, motor dysfunction, renal insufficiency, oedema, fatigue, pyrexia, pain, chills. **AR (common, <1/10, ≥1/100):** Coagulopathy, hypersensitivity, haemophagocytic lymphohistiocytosis, hypoalbuminaemia, dehydration, seizure, ataxia, increased intracranial pressure, non-ventricular arrhythmias, thrombosis, respiratory failure, pulmonary oedema, dry mouth, dysphagia, bilirubin increased, urine output decreased, visual impairment. **Dispensing category:** A. **MA:** Gilead Sciences Switzerland Sàrl, postal address: General-Guisan-Strasse 8, 6300 Zug. Full information for healthcare professionals published at www.swissmedicinfo.ch. *CH-GS-202301-202301-E*

▼ This medicinal product is subject to additional monitoring. For more information, refer to the information for healthcare professionals for TECARTUS® at www.swissmedicinfo.ch.

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NOTES

CONTACT

Learn more about CAR T-cell therapy via the adjacent QR code.
If you have any questions or referrals relating to cell therapy at Klinik Hirslanden, please contact the medical team of the Medical Programme for Cell Therapy by phone at 044 387 37 80 or by e-mail.

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