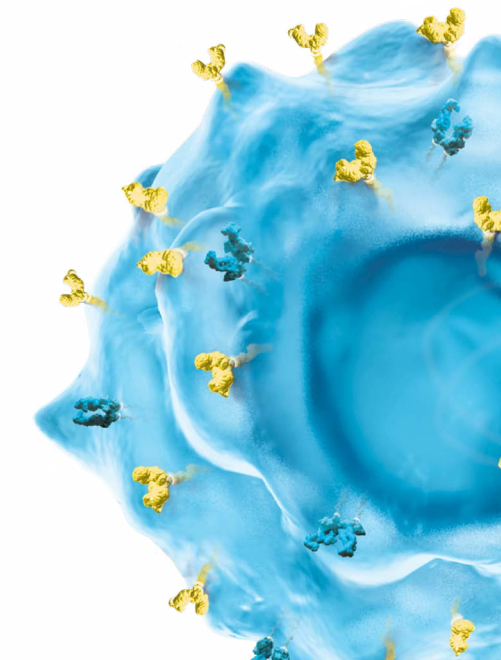
HIRSLANDEN
KLINIK HIRSLANDEN

CAR T CELL THERAPY

for the treatment of recurrent/refractory (r/r) aggressive B-cell non-Hodgkin lymphoma as of 2L*

BROCHURE FOR REFERRING PHYSICIANS

INFORMATION ON THE THERAPY WITH BREYANZI® AND PATIENT CARE



* For more extensive information on this indication, please see page 3 of this brochure

IS YOUR PATIENT ELIGIBLE FOR CAR T CELL THERAPY?

TREATMENT OF R/R AGGRESSIVE B-CELL NON-HODGKIN LYMPHOMA (B-CELL NHL) AS OF 2L* WITH BREYANZI® (LISOCABTAGENE MARALEUCEL)

BREYANZI® is a CD19-directed genetically modified autologous T cell immuno-therapy comprised of chimeric antigen receptor (CAR)-positive, viable T-cells (comprising CD8+ and CD4+ cell components).[1]

* BREYANZI® is indicated for the treatment of adult patients with:

- diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma (HGBCL), or primary mediastinal large B-cell lymphoma (PMBCL) that is refractory to first-line chemoimmunotherapy or relapses within 12 months of first-line chemoimmunotherapy,[1]
- relapsed or refractory (r/r) DLBCL, HGBCL or PMBCL after two or more lines of systemic therapy.[1]

Highly efficacious anti-CD19 CAR T cell therapy with well controllable safety profile for the treatment of r/r B-cell-NHL patients as of 2L[1–4*]

MANY PATIENTS WITH R/R AGGRESSIVE B-CELL NHL MAY BENEFIT FROM CAR T CELL THERAPY[1]

AUTOLOGOUS SCT*

ALLOGENIC SCT*

- Younger, fitter patients[14]
- Fewer comorbidities

CAR T CELL THERAPY USING BREYANZI®

- No age limit (≥18 years)
- Chemosensitive + chemorefractory
- ECOG 0–2**
- After autologous/allogenic SCT or without preceding SCT
- Can also be used in patients with moderate impairmentof cardiac, hepatic and renal function***
- Possible even for secondary CNS lymphomas***

Patients may be eligible for CAR T cell therapy even if they are ineligible for haematopoietic stem cell transplantation.

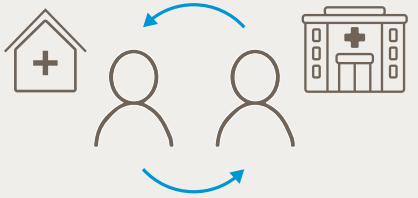
* SCT: Stem cell transplant.
** TRANSCEND-NHL-001 study: ECOG ≤2 during pre-screening.[3]
TRANSFORM study: ECOG ≤1 during pre-screening.[2]
*** Patients with mild/moderate impairment of cardiac, hepatic and renal function, as well as with secondary CNS lymphomas, were included in the TRANSCEND-NHL-001 and TRANSFORM studies.[2,3]

PATIENTS BENEFIT FROM EARLY PLANNING OF CAR T CELL THERAPY

Treatment outcomes worsen with each subsequent recurrence and therapeutic urgency increases after each subsequent treatment.[5]

Early planning and good collaboration between referring and treating doctors may have a positive effect on treatment success.[6,7]

CAR T cell therapy should be planned early so that leukapheresis can be performed as soon as possible to gain time.



Decide together

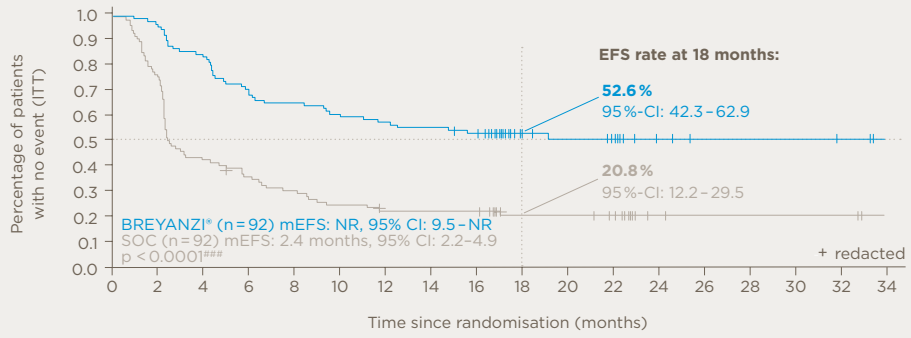
- whether or not the patient is eligible for CAR T cell therapy
- whether and what type of bridging therapy is required
- when cytotoxic T-cell therapy should be avoided

BREYANZI® – EFFICACY OUTCOMES IN 2L (TRANSFORM)[2]

TRANSFORM is a global, randomised, open-label phase 3 pivotal study for direct comparison of BREYANZI® vs. Standard Of Care (SOC) in 2L-LBCL patients who were eligible for ASCT and who relapsed or became refractory to first-line chemoimmunotherapy within 12 months after its completion.[2]

BREYANZI® IN 2L – SIGNIFICANT SUPERIORITY COMPARED TO SOC AFTER ONLY A SINGLE INFUSION[#,##,2]

Primary endpoint: Event-free survival (EFS)[#]



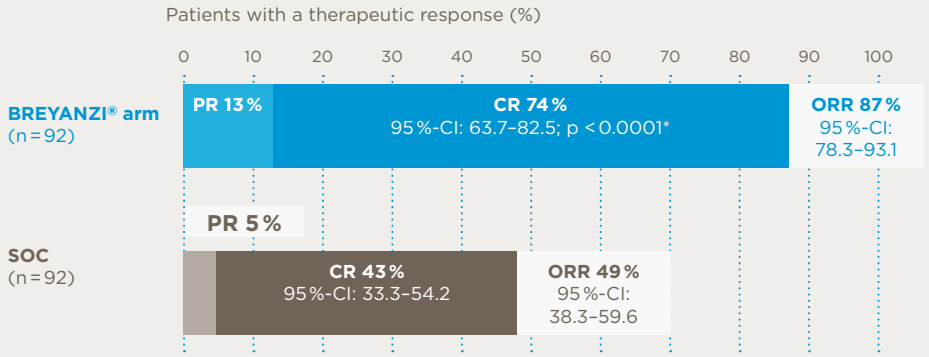
Patients at risk

BREYANZI®	92	87	76	62	59	55	52	48	45	24	20	17	5	3	3	3	3	0
SOC	92	66	39	32	27	22	19	19	19	12	12	10	3	2	2	2	2	0

Cited with adjustments from [2]

HIGH RESPONSE RATE DURING TREATMENT WITH BREYANZI® – A BENEFIT OF 30% COMPARED TO SOC[2]

Secondary endpoint: Complete response (CR)



Cited with adjustments from [2]

* The p value was compared with the level of significance of 0.021 that was prespecified for the primary analysis.[2]

\# Event-free survival (EFS) is defined as the time from randomisation to death from any cause, PD, non-achievement of CR or PR within 9 weeks after randomisation, or the start of antineoplastic therapy due to efficacy concerns, whichever occurs first.[2]

Determined by the Independent Review Committee (IRC) using the Lugano classification.[15]

The EFS was not formally reinvestigated at the time of the primary analysis.[2,3]

BREYANZI® – GOOD RESPONSE IN 2L ACROSS DIFFERENT SUBGROUPS (TRANSFORM)[2]

A RESPONSE TO THERAPY WAS ALSO OBSERVED IN ALL INVESTIGATED SUBGROUPS, INCL. PATIENTS WITH THE FOLLOWING CHARACTERISTICS:*

- NHL histology types (DLBCL NOS de novo, DLBCL, HGBCL, PMBCL)
- Relapsed after or refractory to the previous treatment
- High tumour burden**
- < 65 and ≥ 65 years
- ECOG PS (during screening) 0, 1
- sAAIPI: 0 or 1; 2 or 3
- Secondary CNS lymphoma

* Other subgroups with a response to therapy in the TRANSCEND NHL 001 study of BREYANZI® in 3L were patients receiving bridging therapy, patients with secondary CNS lymphoma and patients with comorbidities, such as renal failure (creatinine clearance < 60 mL/min), lactate dehydrogenase ≥ 500 U/L and heart failure (LVEF < 50 %).[3]

** i. e., the total product diameter ≥ 50 cm^2.

OTHER SELECTED SECONDARY ENDPOINTS[2]

The mPFS in patients treated with BREYANZI® was significantly# superior to SOC at a median follow-up of 17.5 months. OS tended to be numerically favourable in patients treated with BREYANZI®.[2]

Parameter	BREYANZI®	SOC
mPFS, months (95 % CI)#,##	NR (12.6–NR)	6.2 (4.3–8.6)
PFS rate at 18 months, % (95 % CI)	58.2 (47.7–68.7)	28.8 (17.7–40.0)
mOS, months (95 % CI)###	NR (29.5–NR)	29.9 (17.9–NR)
OS rate at 18 months, % (95 % CI)	73.1 (63.9–82.3)	60.6 (50.2–71.1)
mOS, adjusted for crossover effect, months (95 % CI)###	NR (29.5–NR)	NR (8.1–NR)
OS rate at 18 months, adjusted for crossover effect, % (95 % CI)####	73.1 (63.9–82.3)	54.1 (43.1–65.2)

\# $p < 0.0001$. The p value was compared with the level of significance of 0.021 that was prespecified for the primary analysis.[2]

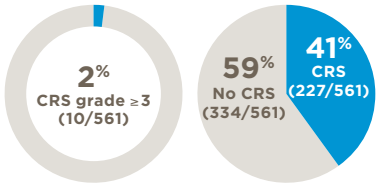
PFS is defined as the time from randomisation to death from any cause or PD, whichever occurs first.[2]

OS is defined as the time from randomisation to death from any cause.[2]

Crossover from the SOC arm to the BREYANZI® arm was allowed if no complete or partial response was achieved after three cycles of immunochemotherapy, or the disease progressed at any point in time, or a new antineoplastic therapy had to be initiated because no complete response had been achieved 18 weeks after randomisation.[2,3]

SELECTED ADVERSE REACTIONS TO BREYANZI® THERAPY (POOLED DATA)[1,#]

CYTOKINE RELEASE SYNDROME (CRS) OCCURRED IN 41% OF PATIENTS[*,**,##]



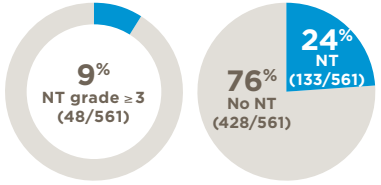
Median time to

onset	resolution
4 days	5 days
Range: 1–63 days	Range: 1–17 days

No grade 5 events occurred.

After BREYANZI® infusion, 21% (116/561) of patients received tocilizumab and/or a corticosteroid to treat CRS. The breakdown showed that 10% (55/561) received only tocilizumab, 9% (53/561) received tocilizumab and a corticosteroid and 1% (8/561) received only corticosteroids.[1]

NEUROTOXICITY (NT) OCCURRED IN 24% OF PATIENTS[*,**,##]



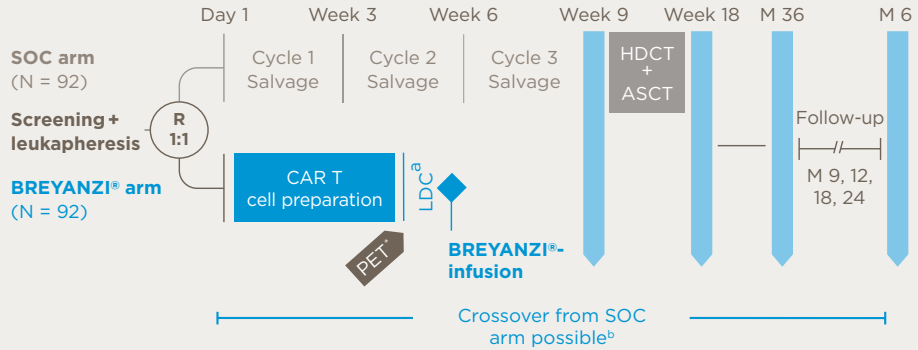
Median time to

onset	resolution
8 days	8 days
Range: 1–66 days	Range: 1–89 days

No grade 5 events occurred.

TRANSFORM (PHASE 3 PIVOTAL STUDY): STUDY DESIGN, ENDPOINTS AND PARAMETERS[2]

Study design[2]



Standard of Care (SOC) comprised three cycles of immunochemotherapy followed by an HDCT and ASCT in patients who achieved CR or PR after salvage chemotherapy.[2]

Endpoints

Primary:
- Event-free survival (EFS)**

Secondary (selection):
- Complete response (CR)
- Duration of response (DOR)
- Overall survival (OS)
- Progression-Free Survival (PFS)

Study parameters

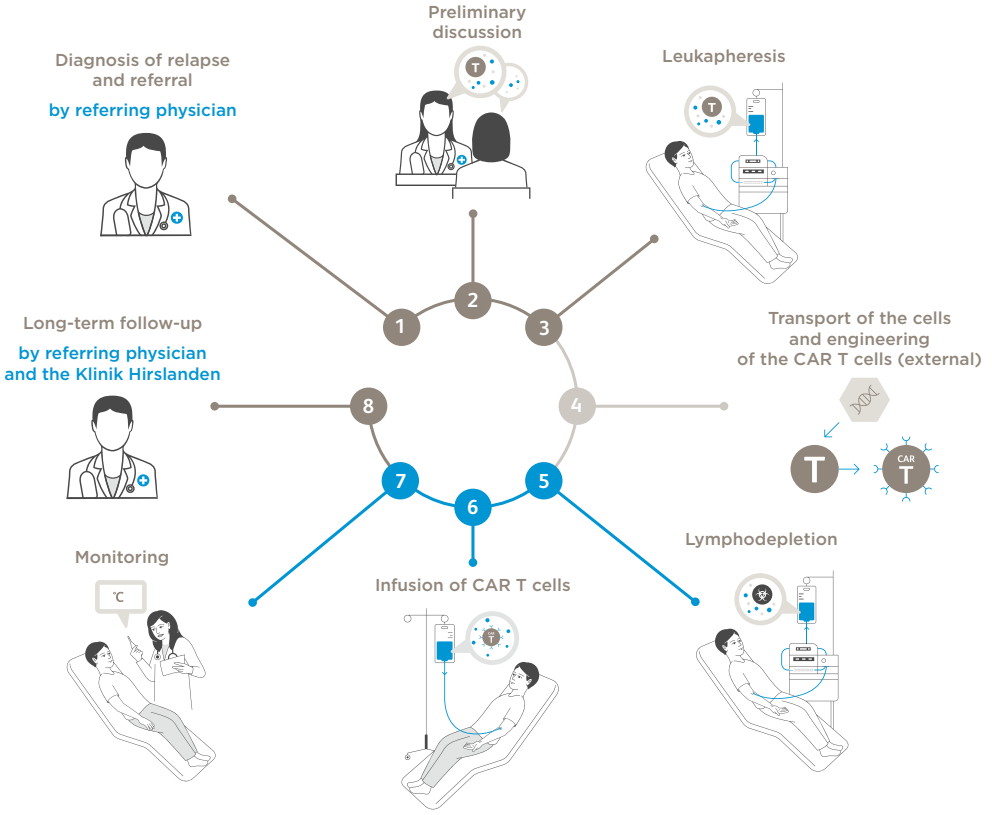
- Crossover from SOC to BREYANZI® study arm possible[b]
- Bridging chemotherapy was permissible in the BREYANZI® study arm
- Median follow-up to time of the primary analysis: 17.5 months[2]

ASCT: Autologous stem cell transplant; **HDCT:** High-dose chemotherapy; **LDC:** Lymphodepleting chemotherapy.

\# You can obtain more information on potential adverse reactions from the Product Information on BREYANZI® at www.swissmedicinfo.ch.
All severities.
* Safety Set with no crossover from SOC to BREYANZI®.
** CRS was assessed using the criteria reported by Lee 201419.
*** Defined as an investigator-identified neurological BREYANZI®-related adverse event, assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.20

* Positron emission tomography (only for patients who received bridging chemotherapy).
** Event-free survival (EFS) is defined as the time from randomisation to death from any cause, PD, non-achievement of CR or PR within 9 weeks after randomisation, or the start of antineoplastic therapy due to efficacy concerns, whichever occurs first.[2,3]
a LDC comprises fludarabine 30 mg/m²/day and cyclophosphamide 300 mg/m²/day over three days.[2,3]
b Crossover from the SOC arm to the BREYANZI® arm was allowed if no complete or partial response was achieved after three cycles of immunochemotherapy, or the disease progressed at any point in time, or a new antineoplastic therapy had to be initiated because no complete response had been achieved 18 weeks after randomisation.[2,3]

PROCEDURE AND CARE DURING CAR T THERAPY IN THE KLINIK HIRSLANDEN[1,8,9]



outpatient

inpatient

BREYANZI® – A CHANCE FOR LASTING REMISSION FOR PATIENTS WITH R/R NHL*,1–3

A CD19-directed CAR T cell therapy comprised of CD8+ and CD4+ cell components[1]

Superior efficacy to SOC in 2L[#,1,2]**
EFS | CR | PFS

Long persistence of CAR T cells
BREYANZI® detectable in peripheral blood for up to 24 months[##,1]

Authorised for an extensive patient cohort as 2L or greater*,[2]
DLBCL | HGBCL | PMBCL

Impressive, easily monitored safety profile[###,1]

	Grade ≥ 3	Grade 5			Grade ≥ 3	Grade 5
CRS	2 %	0 %	|	NT	9 %	0 %

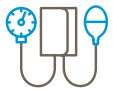
* For more extensive information on this indication, please see page 3 of this brochure.
** Salvage chemotherapy followed by HDCT and ASCT.
# $p < 0.0001$ compared to SOC for EFS, CR and PFS.[1,2]
data from the TRANSCEND-NHL-001 study.[1]
pooled data.

COMMON ADVERSE REACTIONS AND SYMPTOMS OF CAR T THERAPY

CYTOKINE RELEASE SYNDROME (CRS)[19,20]*

Tachycardia, arrhythmia

Hypoxia



Hypotension

Chills

Fever

NEUROTOXICITY (NT)[19,20]*

Encephalopathy

Dizziness, delirium, headache

Aphasia

Fatigue

* Not an exhaustive list of CRS and NT symptoms.

REFERENCES, SUCCINCT STATEMENT

1. Product Information of BREYANZI®, version may 2024, www.swissmedicinfo.ch. **2.** Abramson JS et al. Lisocabtagene maraleucel as second-line therapy for large B-cell lymphoma: primary analysis of phase 3 TRANSFORM study. Blood. 2023;141(14):1675–1684;(Data and supplement). **3.** Abramson JS et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. Lancet. 2020 Sep 19;396(10254):839–852. **4.** Kamdar M et al. Lisocabtagene maraleucel versus standard of care with salvage chemotherapy followed by autologous stem cell transplantation as second-line treatment in patients with relapsed or refractory large B-cell lymphoma (TRANSFORM): results from an interim analysis of an open-label, randomised, phase 3 trial. Lancet. 2022; 399(10343): 2294–2308. **5.** McMillan A et al. Post relapse survival rates in diffuse large B-cell lymphoma. Blood. 2016 Dec 2;128(22):4204. **6.** https://touchoncology.com/education/car-t-in-clinical-practice-navigating-the-patient-journey-from-referral-tolong-term-follow-up/ – last request: 14.03.2023. **7.** 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. **8.** Product Information of ABECMA®, version April 2024, www.swissmedicinfo.ch. **9.** Maus MV, Levine BL. Chimeric antigen receptor T-cell therapy for the community oncologist. Oncologist. 2016 May;21:608-617. **10.** Shimabukuro-Vornhagen A et al. Cytokine release syndrome. J Immunother Cancer. 2018 Jun;6(1):56. **11.** Lee DW 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. **12.** Turtle CJ et al. CD19 CAR-T cells of defined CD4+:CD8+ composition in adult B cell ALL patients. J Clin Invest. 2016 Jun 1;126(6):2123–2138. **13.** Lee DH et al. Improved expansion and function of CAR T cell products from cultures Initiated at defined CD4:CD8 ratios. Blood. 2018 Nov 29;132(Supplement 1):3334. **14.** 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. **15.** Cheson BD et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol 2014; 32(27): 3059–68. **16.** Swerdlow SH et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016; 127(20): 2375–90. **17.** Shah NN et al. CD4/CD8 T-cell selection affects chimeric antigen receptor (CAR) T-cell potency and toxicity: updated results from a phase I anti-CD22 CAR T-cell trial. J Clin Oncol. 2020 Jun 10;38(17):1938–1950. **18.** Gardner RA et al. Intent-to-treat leukemia remission by CD19 CAR T cells of defined formulation and dose in children and young adults. Blood. 2017 Jun 22;129(25):3322–3331. **19.** Lee DW et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood. 2014 Jul 10;124(2):188–195. **20.** https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/ – last request: 05.10.2023. **Literature on request.**

BREYANZI® (lisocabtagene maraleucel) ▼ This medicinal product is subject to additional monitoring. For more information, please refer to the Information for healthcare professionals for BREYANZI® at www.swissmedicinfo.ch. I: in adults with diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma (HGBCL), or primary mediastinal large B-cell lymphoma (PMBCL) that is refractory to first-line chemoimmunotherapy or relapses within 12 months of first-line chemoimmunotherapy; or with relapsed or refractory (r/r) DLBCL, HGBCL or PMBCL after two or more lines of systemic therapy. **D:** the target dose is 100×10^6 CAR-positive viable T cells (consisting of a 1:1 target ratio of CD8+ and CD4+ cell components) within a range of 44 to 120×10^6 CAR-positive viable T cells. To be administered under the direction and supervision of a trained physician at a qualified treatment center. **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 BREYANZI®. Patients should be monitored daily for at least the first week after the infusion. Two doses of tocilizumab and access to another dose within 8h need to be available. Allergic reactions and virus reactivations (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. There are no data on the use of BREYANZI® in primary CNS lymphomas, heart lymphomas and CD19-negative DLBCL. Treatment with BREYANZI® may lead to tumor lysis syndrome (TLS). The lentivirus used to make BREYANZI® may give false positive results for some HIV nucleic acid tests. Vaccination with live viral vaccines should be avoided 6 weeks before treatment. The donation of blood, organs, tissues and cells is prohibited. **IA:** No interaction studies have been conducted. Theoretical risk that anti-EGFR monoclonal antibodies could reduce the number of BREYANZI® cells and thus decrease their benefit, as a shortened EGFR is expressed on CAR T cells. **AE:** infections, decreased blood cell count, hypofibrinogenemia, CRS, hypogammaglobulinaemia, hypophosphataemia, insomnia, anxiety, delirium, headache, encephalopathy, dizziness, tremor, aphasia, peripheral neuropathy, visual disturbances, ataxia, dysgeusia, cerebellar syndrome, cerebrovascular disease, seizure, tachycardia, arrhythmia, hypotension, hypertension, thrombosis, cough, dyspnoea, pleural effusion, hypoxia, nausea, constipation, diarrhoea, abdominal pain, vomiting, gastrointestinal bleeding, rash, acute kidney injury, fatigue, pyrexia, oedema, chills, infusion-related reactions. **P:** BREYANZI® is available in cryopreservation vials. Each vial contains 4.6 ml of cell dispersion (separate CD8+ and CD4+ cell components) (A). **Detailed information:** Information for Healthcare Professionals at www.swissmedicinfo.ch. **MAH:** Bristol-Myers Squibb SA, Hinterbergstrasse 16, 6312 Steinhausen. Version 09/2023.

06/2024 • 2009-CH-2400001

in cooperation with:

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Bristol Myers Squibb™

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.

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