Report TECARTUS® - Brexucabtagene autoleucel

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Brexucabtagene autoleucel **Brand Name:** Tecartus **Originator/licensee:** Kite Pharma EU B.V **Classification:** NI **ATC code:** NA **Orphan Status:** **Eu:** Yes **Us:** Yes **Mechanism of action:** Tecartus, a CD19-directed genetically modified autologous T-cell immunotherapy, binds to CD19 expressing cancer cells and normal B cells. Following anti-CD19 CAR T-cell engagement with CD19 expressing target cells, the CD28 co-stimulatory domain and CD3-zeta signalling domain activate downstream signalling cascades that lead to T-cell activation, proliferation, acquisition of effector functions and secretion of inflammatory cytokines and chemokines. This sequence of events leads to killing of CD19-expressing cells [1].	**Authorized Indication:** **EMA:** Brexucabtagene autoleucel is indicated for the treatment of adult pts 26 years of age and above with relapsed or refractory BCP-ALL [1]. **FDA**: Brexucabtagene autoleucel is indicated for the treatment of adult pts with relapsed or refractory BCP-ALL [2]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 21/07/2022 **FDA M.A. date:** 01/10/2021 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** Yes **-----** **ABBREVIATIONS:** **AE:** Adverse Event **BCP-ALL:** B-cell precursor-Acute Lymphoblastic Leukaemia **CHMP:** Committee for Medicinal Products for Human Use **IV:** Intravenous **NA:** Not Available **PTS:** Patients **SCT:** Stem-Cell Transplantation	**Summary of clinical EFFICACY:** **ZUMA-3 (NCT02614066)** is a phase 2, single-arm, open-label, multicenter trial that evaluated brexucabtagene autoleucel in adults (≥18 years) with relapsed or refractory BCP-ALL. Pts underwent leukapheresis to obtain cells for brexucabtagene autoleucel manufacturing before receiving conditioning chemotherapy (IV fludarabine 25 mg/m² on days −4, −3, and −2; and IV cyclophosphamide 900 mg/m² on day −2). A single brexucabtagene autoleucel infusion was administered at a target dose of 1×10^6 CAR T cells per kg bodyweight on day 0. Pts with a bodyweight >100 kg received a flat dose of 1×10^8 CAR T cells. Prespecified bridging chemotherapy to stabilise the patient's condition during brexucabtagene autoleucel manufacturing was allowed at the physician's discretion. 71 pts were enrolled and underwent leukapheresis. Brexucabtagene autoleucel was successfully manufactured for 65 (92%) pts and administered to 55 (77%). The primary endpoint was the rate of overall complete remission or complete remission with incomplete haematological recovery by central assessment. The primary endpoint was met, with pts (71%; 95% CI 57–82, p<0,0001) reaching complete remission or complete remission with incomplete haematological recovery by central assessment, of whom 31 (56%) had complete remission [3]. **Summary of clinical SAFETY:** All treated pts had at least one AE. The most common AEs of grade 3 or higher were anaemia (27 pts [49%]) and pyrexia (20 pts [36%]). Serious AEs occurred in 41 (75%) pts. Cytokine release syndrome occurred in 49 pts (89%), with grade 3 or 4 cytokine release syndrome occurring in 13 (24%). Neurological events occurred in 33 pts (60%), with events of grade 3 or higher occurring in 14 pts (25%). 20 (36%) treated pts had died as of the data cutoff date, primarily from progressive disease (13 pts [24%]). Six (11%) pts died due to grade 5 AEs other than acute lymphoblastic leukaemia: two related to brexucabtagene autoleucel (brain herniation and septic shock) and four unrelated to the treatment. One patient died due to another reason [3]. **Ongoing studies:** ● ***For the same indication:*** No ● ***For other indications:*** Yes **Discontinued studies (for the same indication):** No **References:** 1. https://www.ema.europa.eu/en/medicines/human/EPAR/tecartus 2. https://www.fda.gov/media/140409/download 3. Shah B.D., Ghobadi A., et al.: KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results of the single-arm, open-label, multicentre ZUMA-3 study. Lancet 2021; 398: 491–502. 4. https://gallery.farmadati.it/ 5. https://www.annalsofoncology.org/article/S0923-7534(19)31639-4/pdf 6. https://www.clinicaltrials.gov/ct2/results?term=Brexucabtagene+autoleucel&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&type=&rslt=&phase=0&phase=1&phase=2&Search=Apply 7. https://adisinsight.springer.com/search	**Cost of therapy:** The ex-factory cost for one infusion of brexucabtagene autoleucel is 360,000.00 € [4]. **Epidemiology:** The estimated overall incidence of ALL and lymphoblastic lymphoma in Europe is 1.28 per 100,000 individuals annually, with significant age-related variations (0.53 at 45–54 years, ~1.0 at 55–74 years and 1.45 at 75–99 years) [5]. ----- **POSSIBLE PLACE IN THERAPY** For the treatment of relapsed or refractory ALL overall evaluation of the clinical situation should take into account the disease-specific factors, patient factors, previous therapy and specific toxicities of prior treatment. Treatment with a curative aim involves achievement of complete remission followed by allogeneic SCT. For BCP-ALL, both blinatumomab and inotuzumab are licensed for the treatment of BCP-ALL. A clinical trial involving immunotherapy with CD19 CAR T-cell therapy is also a possibility. The most commonly used chemotherapy regimens in Europe for relapsed ALL are fludarabine- and anthracycline-containing regimens. Clofarabine-based regimens including cytarabine, cyclophosphamide or etoposide are also commonly used based mostly on data in childhood ALL. Liposomal vincristine is licensed for the treatment of relapsed ALL [5]. **OTHER INDICATIONS IN DEVELOPMENT** Relapsed/Refractory Chronic Lymphocytic Leukemia, Relapsed/Refractory Small Lymphocytic Leukemia, Pediatric and Adolescent Pts With Relapsed/Refractory BCP-ALL or Relapsed/Refractory B-Cell Non-Hodgkin Lymphoma [6]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** / **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION** Tafasitamab, Vodobatinib, Selinexor, Selumetinib [7]. *Service reorganization: Yes *Possible off label use: No

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