TECARTUS™ (brexucabtagene autoleucel): Cessation of Prior Therapies

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The following information regarding the ZUMA-2 study and timing of cessation of prior therapies is provided below as a professional courtesy in response to your unsolicited request.

Summary

Cessation of Therapies Prior to Leukapheresis

- Prior systemic therapy/Bruton's tyrosine kinase (BTK) inhibitor (ibrutinib or acalabrutinib):
  - At least 2 weeks or 5 half-lives (whichever is shorter) must have elapsed prior to the scheduled date for leukapheresis (exception: systemic inhibitory/stimulatory immune checkpoint therapy [at least 3 half-lives]).[1,2]
- Prior radiation therapy:
  - At least 2 weeks or 5 half-lives (whichever is shorter) must have elapsed prior to the scheduled date for leukapheresis.[3]
- Prior corticosteroid (>5 mg/day of prednisone or equivalent) or immunosuppressive therapy:
  - Must be avoided for 7 days prior to leukapheresis and 5 days prior to TECARTUS administration unless used for bridging therapy.[3]

Cessation of Bridging Therapy Prior to Conditioning Chemotherapy and TECARTUS Infusion

- Bridging therapy with either a corticosteroid or ibrutinib (or acalabrutinib):
  - Must be administered after leukapheresis and completed at least 5 days prior to initiating conditioning chemotherapy.[3]

The full indication, important safety information, and boxed warnings are available at:
https://www.gilead.com/-/media/files/pdfs/medicines/oncology/tecartus/tecartus-pi.pdf

BACKGROUND

ZUMA-2 Study

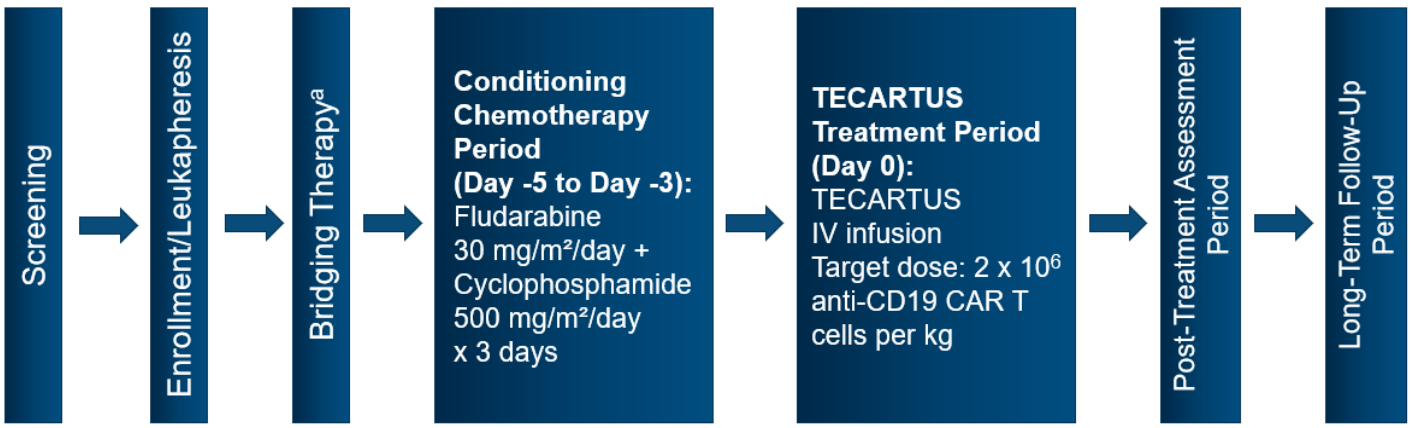
Study design

ZUMA-2 (NCT02601313) was a phase 2, single-group, open-label, multi-center study that evaluated the efficacy and safety of TECARTUS in adult patients with relapsed or refractory mantle-cell lymphoma (MCL) (Figure 1). Key eligibility criteria included histologically confirmed MCL disease that was relapsed or refractory to up to 5 previous therapies, which must have included anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 monoclonal antibody, and BTK inhibitor therapy with ibrutinib or acalabrutinib. However, patients were not required to be refractory to BTK inhibitor therapy, and BTK inhibitor therapy was not required to be the last line of therapy prior to study entry.[1]

Treatment process

Patients underwent leukapheresis to obtain peripheral blood mononuclear cells (PBMC) for the manufacture of TECARTUS.[1,3] Conditioning chemotherapy was administered on Days -5, -4, and -3 prior to TECARTUS infusion (Day 0), and consisted of fludarabine 30 mg/m^2/day and cyclophosphamide 500 mg/m^2/day.[1] On Day 0, after patients were hospitalized, they received a single IV infusion of TECARTUS at a target dose of 2 x 10^6 anti-CD19 chimeric antigen receptor (CAR) T cells per kilogram of body weight (up to a maximum of 2 x 10^8 cells).[1,3] At investigator's discretion and after discussion with the medical monitor, bridging therapy was considered for any patient, particularly those with high disease burden at screening.[1,3] In patients who had high disease burden, bridging therapy was allowed at the investigator's discretion. When administered, bridging therapy occurred after leukapheresis, must have been completed at least 5 days prior to initiation of conditioning chemotherapy, and could include dexamethasone or equivalent glucocorticoid, ibrutinib or acalabrutinib, or a combination of glucocorticoid plus ibrutinib or acalabrutinib.[1,3] Patients who received bridging therapy were required to undergo a repeat positron-emission tomography-computed tomography (PET-CT) to assess disease status and establish a new baseline prior to receiving conditioning chemotherapy and subsequent TECARTUS infusion.[1]

Figure *1*. ZUMA-2 Study Design[3]



[a]Bridging therapy is allowed with (1) dexamethasone oral or IV 20–40 mg (or equivalent) for 1–4 days, (2) ibrutinib oral 560 mg daily (or most recent dose if there had been a dose adjustment), or (3) acalabrutinib oral 100 mg every 12 hours or most recent dose if there had been a dose adjustment. Corticosteroid choice and dose may be adjusted for age/comorbidities or per local or institutional guidelines.

Cessation of Therapies Prior to Leukapheresis

Prior Systemic Therapy or BTK Inhibitor

At least 2 weeks or 5 half-lives, whichever is shorter, must have elapsed since any prior systemic therapy or BTK inhibitor (ibrutinib or acalabrutinib) at the time the patient is planned for leukapheresis, except for systemic inhibitory/stimulatory immune checkpoint therapy. At least 3 half-lives must have elapsed from any prior systemic inhibitory/stimulatory immune checkpoint molecule therapy (eg, ipilimumab, nivolumab, pembrolizumab, atezolizumab, OX40 agonists, 4-1BB agonists) at the time the patient is planned for leukapheresis.[2]

Prior Radiation Therapy

At least 2 weeks or 5 half-lives, whichever is shorter, must have elapsed between any prior radiation therapy and the scheduled date for leukapheresis.[3]

Prior Corticosteroid and Immunosuppressive Therapy

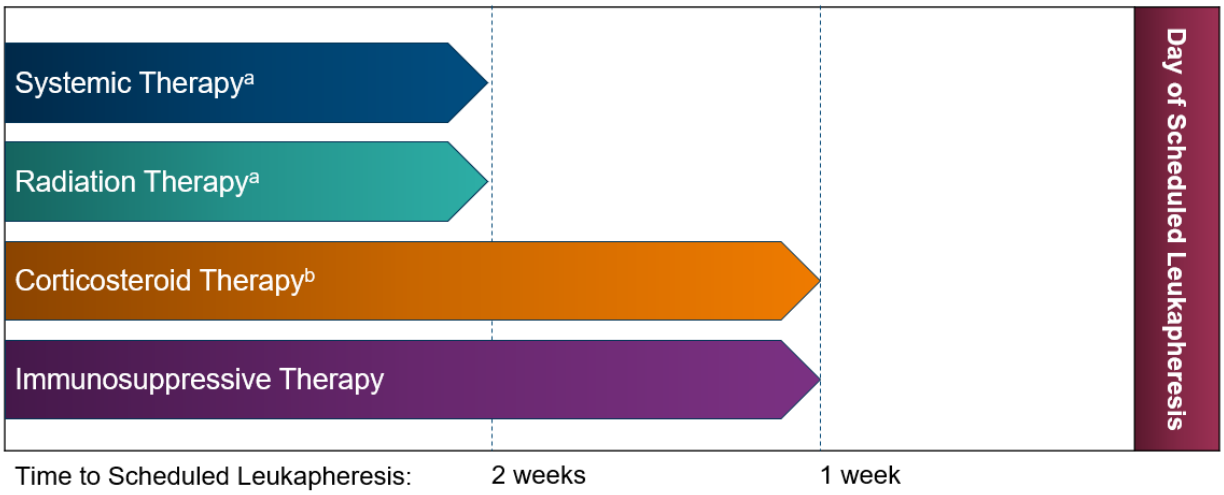
Corticosteroid therapy (at a pharmacologic dose of >5 mg/day of prednisone or equivalent dose of another corticosteroid) and other immunosuppressive drugs must be avoided for 7 days prior to leukapheresis and 5 days prior to TECARTUS administration unless used for bridging therapy.[3]

Additional Considerations

Toxicities due to prior therapy must be stable and recovered to ≤Grade 1 (except for clinical non-significant toxicities such as alopecia) prior to TECARTUS administration.[3]

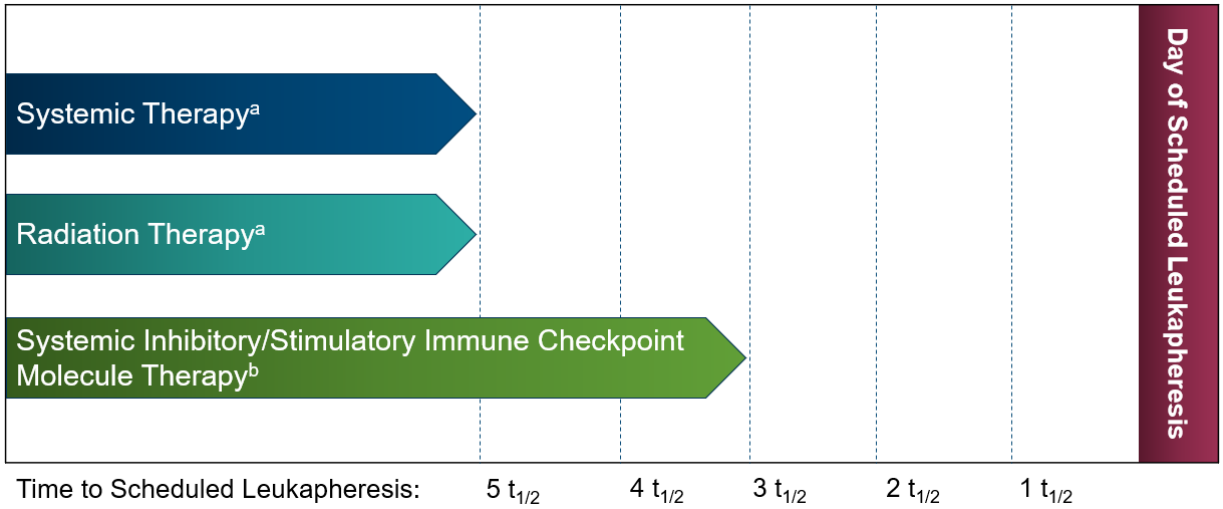
The suggested timing of cessation of therapies prior to leukapheresis is further illustrated in Figures 2 and 3.

Figure 2. Timing (Weeks) of Cessation of Therapies Prior to Leukapheresis (ZUMA-2)[2,3]



[a]At least 2 weeks or 5 half-lives, whichever is shorter, must have elapsed since any prior systemic therapy (except for systemic inhibitory/stimulatory immune checkpoint molecule therapy) or radiation therapy (see Figure 3 below).
[b]>5 mg/day of prednisone (or equivalent doses of other corticosteroids).

Figure 3. Timing (Half-Lives) of Cessation of Therapies Prior to Leukapheresis (ZUMA-2)[2,3]

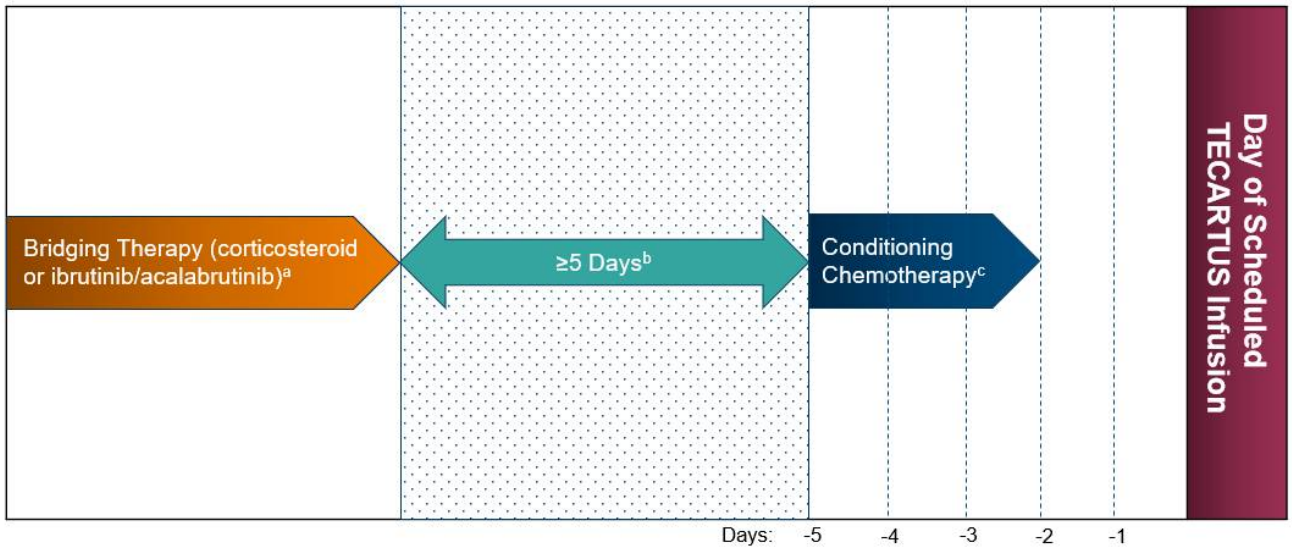


[a]At least 2 weeks or 5 half-lives, whichever is shorter, must have elapsed since any prior systemic therapy or radiation therapy (see Figure 2 above).
[b]eg, ipilimumab, nivolumab, pembrolizumab, atezolizumab, OX40 agonists, 4-1BB agonists.

Cessation of Bridging Therapy Prior to Conditioning Chemotherapy and TECARTUS Infusion

Bridging therapy was allowed at the investigator's discretion and could consist of (1) dexamethasone oral or IV 20–40 mg (or equivalent) daily for 1–4 days, (2) ibrutinib oral 560 mg daily (or most recent dose if there had been a dose adjustment), or (3) acalabrutinib oral 100 mg every 12 hours or most recent dose if there had been a dose adjustment. Corticosteroid choice and dose may be adjusted for age/comorbidities or per local or institutional guidelines. Bridging therapy was administered after leukapheresis and must have been completed at least 5 days prior to initiating conditioning chemotherapy (Figure 4). If bridging therapy is administered, disease state baseline must be reassessed with a repeated PET-CT scan (and bone marrow aspirate/biopsy, if applicable) prior to the start of conditioning chemotherapy.[1,3]

Figure 4. Timing of Cessation of Bridging Therapy After Leukapheresis and Prior to Conditioning Chemotherapy and TECARTUS Infusion (ZUMA-2)[1,3]



[a]Bridging therapy (if applicable) was allowed with (1) dexamethasone oral or IV 20–40 mg (or equivalent) for 1–4 days, (2) ibrutinib oral 560 mg daily (or most recent dose if there had been a dose adjustment), or (3) acalabrutinib oral 100 mg every 12 hours or most recent dose if there had been a dose adjustment. Corticosteroid choice and dose may be adjusted for age/comorbidities or per local or institutional guidelines.
[b]Bridging therapy (if applicable) must have been completed at least 5 days prior to the start of conditioning chemotherapy.
[c]Conditioning chemotherapy consisted of fludarabine 30 mg/m^2 and cyclophosphamide 500 mg/m^2 administered on Day -5, Day -4, and Day -3 prior to TECARCUS infusion.

References

1. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-cell therapy in relapsed or refractory mantle-cell lymphoma. *N Engl J Med*. 2020;382(14):1331-1342. https://pubmed.ncbi.nlm.nih.gov/32242358
2. Supplement to: Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-cell therapy in relapsed or refractory mantle-cell lymphoma. *N Engl J Med*. 2020;382:1331-1342.
3. Protocol for: Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-cell therapy in relapsed or refractory mantle-cell lymphoma. N Engl J Med. 2020;382:1331-1342.

Product Label

For the full indication, important safety information, and Boxed Warning(s), please refer to the TECARTUS US Prescribing Information available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/tecartus/tecartus-pi.pdf.

Follow Up

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