NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®): SECOND-LINE THERAPY FOR R/R DLBCL[1]

R/R DLBCL

Relapsed disease <12 months -OR- Primary refractory disease[1,a]

- Candidates for CAR T-cell therapy → CAR T-cell therapy with bridging therapy as clinically indicated[b]
- Non-candidates for CAR T-cell therapy →
  - Clinical trial
  - **Second-line therapy**
  - Palliative ISRT
  - Best supportive care

Relapsed disease >12 months[1]

- Intention to proceed to transplant → See NCCN Guidelines® for second-line therapy recommendations
- No intention to proceed to transplant →
  - Clinical trial
  - **Second-line therapy**
  - Palliative ISRT
  - Best supportive care

Second-Line Therapy[1,c,f,g]

Relapsed disease <12 months -OR- Primary refractory disease

Non-candidates for CAR T-cell therapy

Preferred regimens
(in alphabetical order)

- Epcoritamab-bysp + GemOx[1,g]
- Glofitamab-gxbm + GemOx[1,g]
- Polatuzumab vedotin-piiq ± bendamustine[h] ± rituximab
- Polatuzumab vedotin-piiq + mosunetuzumab-axgb[1,g]
- **Tafasitamab-cxix**[i] + lenalidomide (excluding primary refractory disease)

Other recommended regimens
(in alphabetical order)

- CEOP ± rituximab
- DHA + platinum (carboplatin, cisplatin, or oxaliplatin) ± rituximab
- ESHAP ± rituximab
- GDP ± rituximab
- GemOx ± rituximab (if unable to receive epcoritamab-bysp or glofitamab-gxbm)
- ICE ± rituximab
- MINE ± rituximab

Useful in certain circumstances

- Brentuximab vedotin for CD30+ disease[j]
- Ibrutinib[r] (non-GCB DLBCL)
- Lenalidomide ± rituximab (non-GCB DLBCL)

Second-Line Therapy[1,c,f,g]

Relapsed disease >12 months

No intention to proceed to transplant

Preferred regimens
(in alphabetical order)

- CAR T-cell therapy (CD19-directed) (with bridging therapy as needed) (if eligible)
  – Lisocabtagene maraleucel
- Epcoritamab-bysp + GemOx[1,g]
- Glofitamab-gxbm + GemOx[1,g] (category 1)
- Polatuzumab vedotin-piiq ± bendamustine[h] ± rituximab
- Polatuzumab vedotin-piiq + mosunetuzumab-axgb[1,g]
- **Tafasitamab-cxix**[i] + lenalidomide

Other recommended regimens
(in alphabetical order)

- CEOP ± rituximab
- GDP ± rituximab
- GemOx ± rituximab (if unable to receive epcoritamab-bysp or glofitamab-gxbm)
- Rituximab

Useful in certain circumstances

- Brentuximab vedotin for CD30+ disease[j]
- Ibrutinib[r] (non-GCB DLBCL)
- Lenalidomide ± rituximab (non-GCB DLBCL)

All recommendations are category 2A unless otherwise indicated.

[a] Management of localized refractory disease is uncertain. RT ± chemoimmunotherapy followed by HDT/ASCR may be an option for some patients. [b] If bridging therapy results in CR or very good PR, proceeding with HDT/ASCR is an appropriate alternative. [c] Inclusion of any anthracycline or anthracenedione in patients with impaired cardiac functioning should have more frequent cardiac monitoring. [d] If additional anthracycline is administered after a full course of therapy, careful cardiac monitoring is essential. Dexrazoxane may be added as a cardioprotectant. [e] Rituximab should be included in second-line therapy if there is relapse after a reasonable remission (>6 mo); however, rituximab can be omitted in patients with primary refractory disease. [f] Refer to package insert for full prescribing information, dose modifications, and monitoring for adverse reactions: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. [g] In the setting of CD20-negative lymphomas, the activity of CD3 x CD20 bispecific antibody therapy is unclear. Rebiopsy to confirm CD20 positivity is recommended prior to initiating CD3 x CD20 bispecific antibody therapy. [h] In patients intended to receive CAR T-cell therapy or CD3 x CD20 bispecific antibody therapy, bendamustine should be used with caution. Delay bendamustine until after CAR-T leukapheresis. [i] It is unclear if tafasitamab-cxix or loncastuximab tesirine-lpyl or if any other CD19-directed therapy would have a negative impact on the efficacy of subsequent anti-CD19 CAR T-cell therapy. [j] Responses with BV have been seen in patients with a low level of CD30 positivity and any level of CD30 positivity is acceptable for the use of BV-based regimens.

ASCR, autologous stem cell rescue; BV, brentuximab vedotin; CAR, chimeric antigen receptor; CBC, complete blood count; CEOP, cyclophosphamide; etoposide, vincristine, prednisone; CR, complete response; DHA, dexamethasone, cytarabine; DLBCL, diffuse large B-cell lymphoma; ESHAP, etoposide, methylprednisolone, cytarabine, cisplatin; GCB, germinal center B-cell–like; GDP, gemcitabine, dexamethasone, carboplatin or cisplatin; GemOx, gemcitabine, oxaliplatin; HDT, high-dose therapy; ICE, ifosfamide, carboplatin, etoposide; ISRT, involved-site radiation therapy; MINE, mesna, ifosfamide, mitoxantrone, etoposide; mo, months; PR, partial response; R/R, relapsed or refractory; RT, radiotherapy.

Learn more about tafasitamab-cxix in R/R DLBCL

Tafasitamab-cxix Indication[2]

MONJUVI is a CD19-directed cytolytic antibody indicated in combination with lenalidomide for the treatment of adult patients with R/R DLBCL not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant (ASCT).

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Please see the Full Prescribing Information, including Warnings & Precautions and Patient Information, for MONJUVI.

Tafasitamab-cxix Warnings and Precautions[2]

Infusion-Related Reactions
MONJUVI can cause infusion-related reactions. Signs and symptoms may include fever, chills, rash, flushing, dyspnea, and hypertension. Premedicate patients prior to starting MONJUVI infusion. Monitor patients frequently during infusion. Based on the severity of the infusion-related reaction, interrupt or discontinue MONJUVI. Institute appropriate medical management.

Myelosuppression
MONJUVI can cause serious or severe myelosuppression, including neutropenia, lymphopenia, thrombocytopenia, and anemia. Monitor CBCs before each treatment cycle and throughout treatment. Monitor patients with neutropenia for signs of infection. Consider granulocyte colony-stimulating factor administration. Withhold MONJUVI based on the severity of the adverse reaction. Refer to the lenalidomide prescribing information for dosage modifications.

Infections
Fatal and serious infections, including opportunistic infections, occurred in patients during treatment with MONJUVI and following the last dose. Monitor patients for signs and symptoms of infection and manage infections as appropriate. Consider infection prophylaxis per institutional guidelines. Consider treatment with subcutaneous or intravenous immunoglobulin (IVIG) as appropriate.

Embryo-Fetal Toxicity
Based on its mechanism of action, MONJUVI may cause fetal B-cell depletion when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with MONJUVI and for 3 months after the last dose. The combination of MONJUVI with lenalidomide is contraindicated in pregnant women because lenalidomide can cause birth defects and death of the unborn child. Refer to the lenalidomide prescribing information on use during pregnancy.

Tafasitamab-cxix Common Adverse Reactions (≥20%)[2]

The most common adverse reactions (≥20%) are neutropenia, respiratory tract infection, fatigue, anemia, diarrhea, thrombocytopenia, cough, pyrexia, peripheral edema, and decreased appetite.