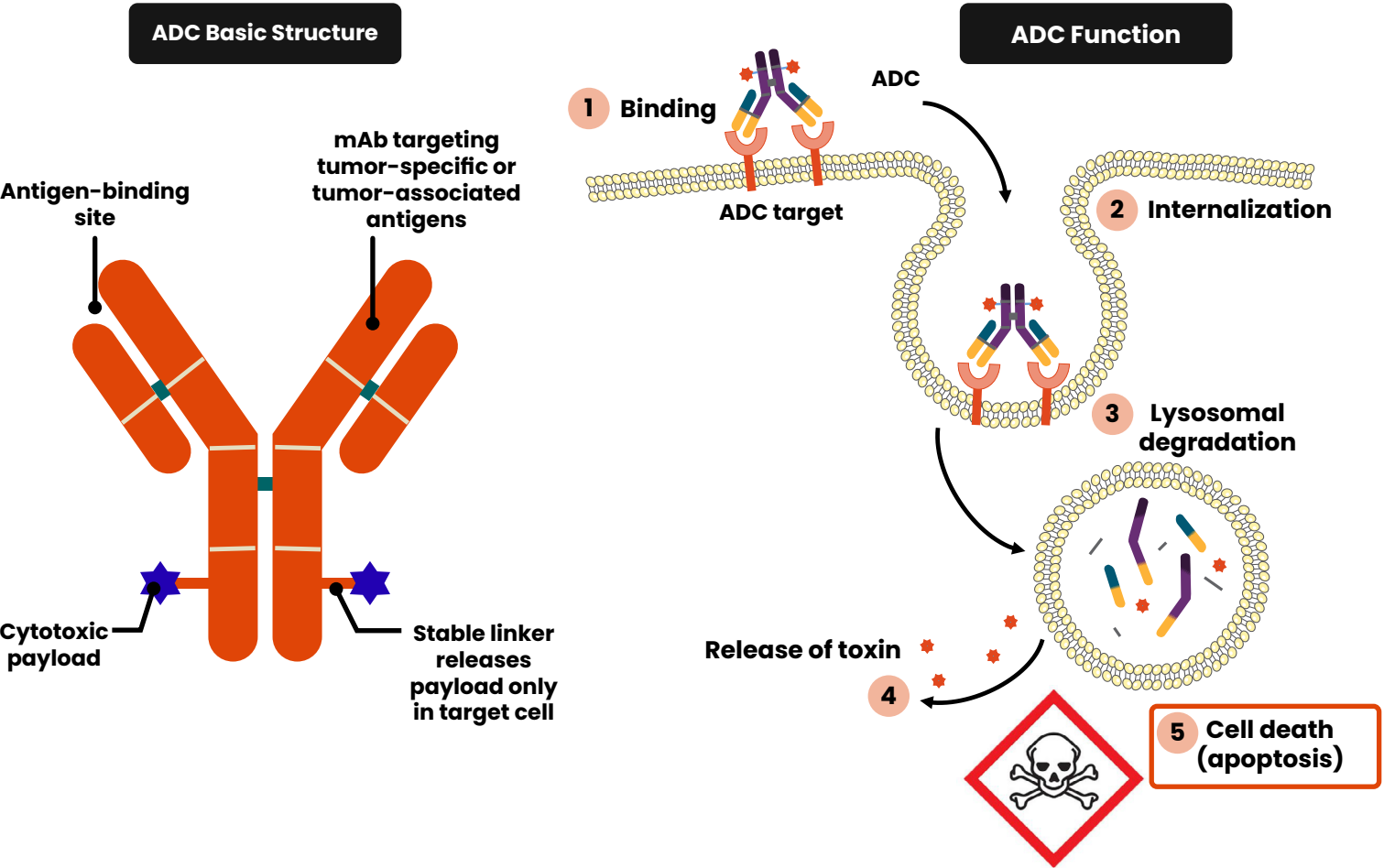


Exploring Novel ADC Treatment Options in R/R DLBCL: A Summary Resource

Mechanism of Action and Molecular Targets¹⁻³

Antibody–drug conjugates (ADC):

- Comprise an antibody directed against a tumor-specific or tumor-associated antigen
- Covalently linked cytotoxic payload
- Upon antibody binding (step 1), the ADC is internalized (step 2), the linker is cleaved (step 3), and the cytotoxic payload is released into the tumor cell (step 4)
- Cytotoxic payload leads to an inhibition of cell division and subsequent cellular apoptosis (step 5)



Approved for R/R DLBCL: Target, Payload, Design

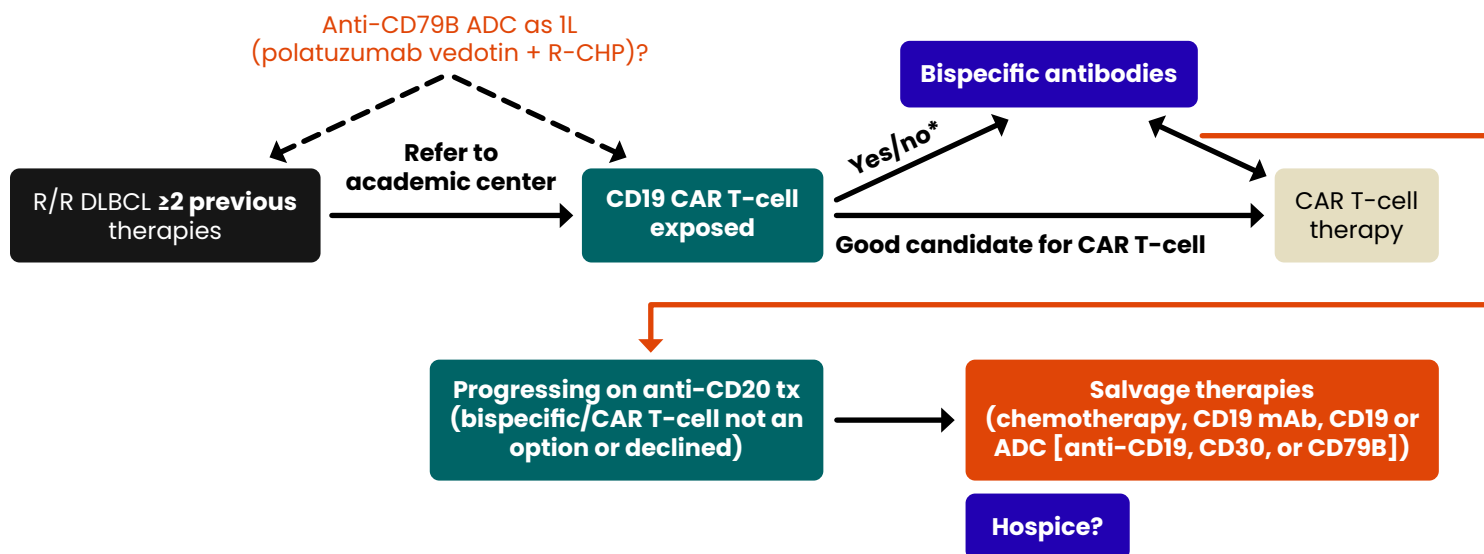
ADC	Target	Payload	Design
Brentuximab vedotin ¹	CD30	MMAE	IgG1 targeting CD30 covalently linked to MMAE, a microtubule-disrupting agent; may also trigger antibody-dependent cellular phagocytosis
Loncastuximab tesirine-lpyl ²	CD19	SG3199	IgG1 targeting CD19; contains a PBD dimer and alkylating agent (SG3199), which binds to the minor groove of DNA forming cytotoxic intrastrand cross-links
Polatuzumab vedotin-piiq ³	CD79B	MMAE	IgG1 monoclonal antibody against CD79B covalently linked to MMAE

FDA-Approved ADCs	Indications and Recommendations
Brentuximab vedotin ¹	FDA-approved indications: - Adult patients with R/R DLBCL NOS, DLBCL arising from indolent lymphoma, after ≥2 of systemic therapy who are not eligible for auto-HSCT or CAR T-cell therapy, in combination with lenalidomide and a rituximab product NCCN® guideline recommend: - Brentuximab vedotin + lenalidomide + rituximab for CD30-positive disease
Loncastuximab tesirine-lpyl ²	FDA-approved indications: - Adults with R/R LBCL after ≥2 lines of systemic therapy, including DLBCL NOS, DLBCL arising from low-grade lymphoma, and high-grade lymphoma NCCN® guideline recommend: - After ≥2 lines of systemic therapy for DLBCL, histologic transformation to DLBCL
Polatuzumab vedotin-piiq ³	FDA-approved indications: - In combination with R-CHP for the treatment of adult patients who have previously untreated DLBCL NOS or high-grade B-cell lymphoma and who have an IPI score ≥2 - In combination with bendamustine and rituximab for adult patients with R/R DLBCL NOS, after ≥2 previous therapies NCCN® guideline recommend: - As second-line therapy for DLBCL ± bendamustine ± rituximab or in combination with mosunetuzumab if not candidates for CAR T-cell therapy

Auto-HSCT, autologous hematopoietic stem cell transplant; NOS, not otherwise specified; R-CHP, rituximab plus cyclophosphamide/doxorubicin/prednisone.

- Tailoring ADC therapy to patients with relapsed or refractory DLBCL is crucial for optimal management of the disease and [mitigating potential adverse effects](#) of treatment.
- Key ADC-related toxicities [to educate patients about](#) and to closely monitor for vary with the specific drug and include peripheral neuropathy, pleural effusion, and skin-related events, which can often be managed with dose holds and dose reductions.

Evolving Treatment Algorithm in DLBCL: Sequence Approved ADCs With Other Available Therapies for DLBCL



*But not a good candidate for CAR T-cell therapy (rapidly progressing disease, comorbidities, patient preference).

References

1. Brentuximab vedotin PI. 2. Loncastuximab tesirine PI. 3. Polatuzumab vedotin PI. 4. National Comprehensive Cancer Network. Clinical practice guidelines in oncology: B-cell lymphomas. v.1.2026. nccn.org.



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