Polivy and Pretreatment Testing of CD79b Receptor Status

This article responds to your request for information on the need for testing of CD79b receptor status before starting treatment with Polivy® (polatuzumab vedotin).

Consult your local prescribing information for product use instructions. Any actions beyond the approved label information are the responsibility of the user.

In brief

- There is no recommendation about IHC testing of CD79b receptor status before starting treatment with Polivy.
- Evidence from clinical trials and in vitro studies suggest that IHC testing of CD79b receptor status before starting treatment with Polivy is not mandatory or necessary.

Abbreviations

DLBCL=diffuse large B-cell lymphomas
IHC=immunohistochemical
OS=overall survival
PFS=progression-free survival
R/R=relapsed/refractory
STEP=Subgroup Treatment Effect Pattern

CD79b receptor

The CD79b receptor is a cell surface component of the B cell receptor. CD79b is expressed only on

- normal cells within B cell lines other than plasma cells, and
- malignant B cells.

CD79b is expressed in > 95% of DLBCL.[1]

Role of CD79b in the mechanism of action of Polivy

Polivy is an antibody-drug conjugate that binds with CD79b to get rapidly internalized within the B cell. Lysosomal proteases then cleaves the linker to deliver the cytotoxic agent within the B cell.[1]

Testing for CD79b receptor before Polivy treatment

Roche has no recommendation on IHC testing of CD79b receptor status before starting treatment with Polivy.[2]

Evidence from clinical trials and in vitro studies, suggest that IHC testing of CD79b receptor status before starting treatment with Polivy is not necessary and should not be mandatory.[3-5]

Effect of CD79b receptor status on Polivy activity

GO29365 study analysis

The GO29365 pivotal study investigated the potential effect of the following on the activity of Polivy

- the presence or absence of CD79b, and
- different levels of CD79b expression.[3]

CD79b receptor status was determined in 83 patients by 1) IHC assay and 2) RNA measurement. Of the 83 patient samples stained

- 80 (96.4%) had detectable CD79b by IHC assay, and
- all showed measurable expression of CD79b by RNA assessments, including three that were negative by IHC.[3]

The study used the STEP plot approach to evaluate the relationship between CD79b expression and Polivy treatment effect in the patients with R/R DLBCL. No relationship was observed between levels of CD79b expression and clinical outcome for both response rate and time-to-event clinical end points, including PFS and OS.[3]

ROMULUS study analysis

The Phase 2 ROMULUS trial performed a retrospective biomarker analysis on tumor samples at baseline from patients who received Polivy with rituximab, to correlate the activity of Polivy with biomarkers in R/R DLBCL and follicular lymphoma.[4] CD79b was expressed across B-cell malignancies. While a majority of samples expressed high levels of CD79b, even minimal expression was sufficient for the activity of Polivy. Polivy also showed activity independent of subtype.

In vitro and Phase 1 study analysis

Pfeifer et.al., analyzed the activity of Polivy in different molecular subtypes of DLBCL both in vitro and in early clinical trials. Polivy induced cytotoxicity in models with and without mutations in the signaling molecule CD79B.[5]

References

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3. Sehn L, Herrera A, Flowers C, et al. Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma. J Clin Oncol 2020;38:155-165. https://www.ncbi.nlm.nih.gov/pubmed/31693429

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5. Pfeifer M, Zheng B, Erdmann T, et al. Anti-CD22 and anti-CD79B antibody drug conjugates are active in different molecular diffuse large B-cell lymphoma subtypes. Leukemia 2015;29:1578-86. https://www.ncbi.nlm.nih.gov/pubmed/25708834