CD20 Expression and Anti-Tumor Activity of Columvi

This article responds to your request for information on Columvi™ (glofitamab) and the need for CD20 expressing B-cells for anti-tumor activity.

In brief

- Columvi is an anti-CD20×CD3 T-cell engaging bispecific antibody that targets CD20 expressing B-cells.
    - Lysis of B-cells by Columvi does not occur in the absence of CD20 expression.
- In the Columvi pivotal study, patients were not screened for CD20 expression.
    - Patients were eligible if they had a diagnosis of a B-cell malignancy associated with CD20 expression.
- In a retrospective study amongst 42 patients with Columvi-refractory B-NHL, Grigg et al. found that only four of the patients were CD20-negative prior to start of Columvi. After treatment with Columvi, 23 patients had PD of which 13 were CD20-negative at the time of relapse.
- There is no recommendation for measuring levels of CD20 expressions prior to administration of Columvi.
    - The potential risks and benefits of treating patients with CD20-negative DLBCL with Columvi should be considered.

Abbreviations

B-NHL=B-cell non-Hodgkin lymphoma
DLBCL=diffuse large B-cell lymphoma
PD=progressive disease
PR=partial response
OS=overall survival

Mechanism of action of Columvi and role of CD20 expression

Columvi is a bispecific monoclonal antibody that binds to[1]

- CD20 expressed on the surface of B cells, and
- CD3 in the T-cell receptor complex expressed on the surface of T cells.

By simultaneous binding to CD20 on the B cell and CD3 on the T cell, Columvi induces[1]

- lysis of CD20-expressing B cells,
- activation and proliferation of T-cells, and
- release of cytokines.

Lysis of B cells mediated by Columvi is CD20-specific and does not occur in the absence of[1]

- CD20 expression, or
- simultaneous binding of T cells to CD20-expressing cells

Anti-tumor activity of Columvi in DLBCL with low CD20 expression

Data from non-clinical studies show[2,3]

- Columvi efficiently killed cell lines expressing very low levels of CD20.
    - Evidence of Columvi's in vitro activity includes lysis of 50% of tumor cells with 0.5% of CD20 receptor occupancy.
- tumor cell killing can efficiently occur in the presence of saturating levels of obinutuzumab, thus supporting the hypothesis that Columvi works effectively under conditions of limited CD20 access.

Anti-tumor activity of Columvi in CD20-negative DLBCL

Experience from clinical trials

There is limited data in patients with CD20-negative DLBCL treated with Columvi.[4] CD20-negative DLBCL is defined as less than 5% of CD20-positive cells in the tumor area.[4]

In the Columvi pivotal study, patients were not prescreened for CD20 expression because[5]

- data from non-clinical studies demonstrated anti-tumor activity of Columvi even with low CD20 expression,[2,3] and
- CD20 is expressed in the majority of B-cell-derived human malignancies.
    - Published reports show that CD20-negative B-cell-derived malignancies are rare.[6]

In the pivotal clinical trial, patients were eligible if they had a diagnosis of a B-cell malignancy associated with CD20 expression. Fresh tumor biopsy or archival tumor tissue samples was mandatory for entry into the study to:

- assess CD20 expression, retrospectively,
- determine prognostic or predictive factors, and
- investigate baseline immune status.[2]

Three patients had CD20-negative disease; all had progressive disease as their best response to Columvi and died during follow-up.[4] The efficacy of Columvi has not been established in patients with CD20-negative disease who have relapsed from prior anti-CD20 therapy.[4]

In the Columvi pivotal study, patients who had progressed after completing treatment with 12 cycles of Columvi were strongly recommended to provide a fresh tumor sample for exploratory assessment of CD20 expression, before receiving retreatment with Columvi.[7]

Case reports and published literature on the use of Columvi in patients with CD20-negative DLBCL

Grigg et al. conducted a single-center retrospective study of 42 patients with aggressive B-NHL who were refractory or relapsed after Columvi therapy to assess post-Columvi treatment outcomes and CD20 status.[8]

Prior to treatment with Columvi, CD20 status was assessed in 32 patients, of which four had CD20-negative disease. In these four patients, two had a PR as their best response to Columvi and two had PD.

After treatment with Columvi, 23 patients had PD. CD20 status was assessed in 22 patients with available biopsies. Thirteen (59%) patients were found CD20-negative, of which

- ten had converted from CD20-positive to CD20 negative,
- two remained persistently CD20-negative, and
- the pretreatment CD20 status of the rest was unknown.

Those who were CD20-negative at relapse

- progressed earlier on Columvi (median PFS 2.5 months vs. 5.5 months; p = 0.4), and
- had shorter median OS from time of progression (4.4 months vs. 10.4 months; p = 0.06).

Of those who progressed after treatment with Columvi, two patients received re-treatment with Columvi. Of these two patients, the non-responder to re-treatment was CD20-negative prior to Columvi re-exposure.

Prescribing considerations for measurement of CD20 expression levels before administering Columvi

There is no recommendation for assessment of CD20 expression prior to Columvi initiation.[1] However, the potential risks and benefits associated with treatment of patients with CD20-negative DLBCL with Columvi should be considered.[4] It is possible that patients with CD20-negative DLBCL may have less benefit compared to patients with CD20-positive DLBCL.[4] The decision to biopsy to assess the presence of CD20 prior to treatment with Columvi is left to the discretion of the healthcare provider.

References

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