Columvi and Use in Central Nervous System Lymphoma

This article responds to your request for information on the use of Columvi™ (glofitamab) in patients with CNS lymphoma. This response was developed according to the principles of evidence-based medicine and contains information from published literature including data from case series, retrospective studies, and single case reports.

Roche does not have any recommendations for using Columvi to treat patients with CNS lymphoma. Any decision on using Columvi for the treatment of CNS lymphoma will be at the discretion of the treating physician taking into consideration individual risk-benefit.

In brief

- The efficacy and safety of the use of Columvi in CNS lymphoma has not been established.
    - In the Columvi pivotal clinical trial, patients with current or past history of CNS lymphoma were excluded.
- There is limited information on the use of Columvi in patients with CNS lymphoma.
    - In a case series of four CNS lymphoma patients, Columvi partially penetrated the blood brain barrier and induced clinical and radiographic responses at an average CSF concentration of only 0.1-0.4% of that in the peripheral blood.
    - In a retrospective study of patients with relapsed/refractory B-cell lymphomas, four patients with CNS involvement did not experience a positive response with Columvi monotherapy and had rapid systemic progression. However, no additional neurological toxicities were noted during treatment with Columvi.

Abbreviations

CAR-T = chimeric antigen receptor T-cell

CNS = central nervous system

CSF = cerebrospinal fluid

DLBCL = diffuse large B-cell lymphoma

MRI = magnetic resonance imaging

PET/CT = positron emission tomography/ computed tomography

R/R = relapsed/refractory

Experience from clinical trials

The efficacy and safety of the use of Columvi in CNS lymphoma has not been established. In the Columvi pivotal clinical trial, patients with current or past history of CNS lymphoma were excluded because the ability of Columvi to penetrate the CNS is unknown.[1,2]

Published reports on the use of Columvi in patients with CNS lymphoma

Godfrey et al. reported a case series of four CD20 positive R/R DLBCL patients with secondary CNS involvement treated with Columvi.[3] Patients received a median number of 6.5 (range 2-8) cycles of Columvi, using standard step-up dosing. Two patients received obinutuzumab pre-treatment while two patients did not due to rapidly progressing disease.

Columvi was detected in the CSF of all four patients in concentrations that were sufficient to drive T cell activation and cytotoxicity against CD20 positive lymphoma cells ex vivo.[3] In one patient who had lymphoma involving the CSF, the on-treatment CSF sample showed more than 12-fold increase in the number of CSF leukocytes and a substantial relative decrease in lymphoma cells compared to the pre-treatment sample, which suggested Columvi robustly redirected immune cells to the tumour site in this patient. Although three patients showed radiographic and clinical improvement, contribution of Columvi to the patients' clinical response could not be definitively assessed due to the low number of patients and use of concomitant therapies in some cases.

The authors concluded that Columvi partially penetrates the blood brain barrier and can induce clinical and radiographic responses in patients with CNS lymphoma.[3] As the average CSF concentration of Columvi was only 0.1-0.4% of that in the peripheral blood, these data indicate only low-levels of Columvi are needed in the CSF to elicit responses in CNS lymphoma.

Hsu et al. conducted a retrospective study amongst patients with R/R B-cell lymphomas who had at least three prior lines of therapy and then received Columvi treatment.[4] Among the four patients who had CNS involvement, no additional neurological toxicities were noted during treatment with Columvi. However, none of these patients experienced a positive response to Columvi; all had rapid systemic progression despite the salvage therapy.

Heini et al. reported the case of a 60-year-old patient treated with Columvi after CNS relapse of mantle cell lymphoma following third-line CAR-T treatment.[5] After Columvi administration, a more than 20-fold increase in CAR-T DNA was observed and the patient showed continuous improvement of motoric weakness and regained self-independency. An MRI scan two months after the first Columvi infusion confirmed an objective response. Columvi treatment was tolerated without relevant side effects. The patient completed all 12 planned cycles of Columvi and was alive and without clinical progression at the last follow-up. After the initial peak, CAR-T copy numbers quantified from peripheral blood slowly decreased to pre-Columvi levels.

References

1. A Dose Escalation Study of Glofitamab (RO7082859) as a Single Agent and in Combination With Obinutuzumab, Administered After a Fixed, Single Pre-Treatment Dose of Obinutuzumab in Participants With Relapsed/Refractory B-Cell Non-Hodgkin's Lymphoma. Available at https://clinicaltrials.gov/study/NCT03075696. Accessed on April 13, 2024.

2. Roche Internal Safety Document (Accessed on 13 April 2024)).

3. Godfrey JK, Gao L, Shouse G, et al. Glofitamab stimulates immune cell infiltration of CNS tumors and induces clinical responses in secondary CNS lymphoma. Blood 2024;https://www.ncbi.nlm.nih.gov/pubmed/38484137

4. Hsu YT, Wu SJ, Kao HW, et al. Glofitamab as a salvage treatment for B-cell lymphomas in the real world: A multicenter study in Taiwan. Cancer 2024;https://www.ncbi.nlm.nih.gov/pubmed/38306242

5. Heini AD, Bacher U, Porret N, et al. Experiences with Glofitamab Administration following CAR T Therapy in Patients with Relapsed Mantle Cell Lymphoma. Cells 2022;11:https://www.ncbi.nlm.nih.gov/pubmed/36078155