Columvi® (glofitamab)

Important Safety Information to Minimize the Risk of Tumor Flare and a reminder of Patient Card

For Healthcare Professionals

Important Safety Information

Tumor flare is an important identified risk along with Cytokine Release Syndrome (CRS) and Immune effector Cell-Associated Neurotoxicity Syndrome (ICANS) for Columvi. This guide is intended to provide information about managing the risk of Tumor Flare.

If you are prescribing Columvi, please give a Patient Card completed with relevant contact information to all patients receiving treatment with Columvi, to educate them about the symptoms of CRS and ICANS and the need to seek medical attention immediately if they have any CRS and/or ICANS symptoms. Patients should also be advised to keep the Patient Card with them at all times and show it to any healthcare professional who may treat them.

To obtain copies of the Patient Card, please contact israel.drugsafety@roche.com.

Alert Health Care providers to have on-site immediate access to tocilizumab.

For more information, please refer to Columvi prescribing information on the Ministry of Health website at https://israeldrugs.health.gov.il/#!/byDrug or on Roche website at www.roche.co.il

Explore the Following Sections to Learn More About Managing Tumor Flare:

Contents

1. What is Columvi?

Columvi is a "2:1" T-cell bispecific humanized monoclonal antibody that binds to human CD20 on B cells through two fragment antigen-binding (Fab) domains, and to the human CD3 epsilon subunit (CD3e) of the T-cell receptor (TCR) complex on T cells through a single Fab domain. The molecule is based on the human IgG1 isotype but contains an Fc-part devoid of Fc gamma receptor (FcγR) and complement (C1q) binding.

2. Important identified risks associated with Columvi use

- Cytokine Release Syndrome (CRS)*
- Tumor Flare
- Serious infections
- ICANS*

* The information of the occurrence, prevention and management of CRS and ICANS associated with Columvi is provided in the Columvi prescribing information. The signs/symptoms of CRS and ICANS may not be well understood by patients (please refer to page 2 for the reminder of Patient Card).

3. Guidance on minimising the risk of tumor flare

3.1 What is tumor flare?

Tumor flare is associated with some anti-cancer therapies (e.g., immunomodulating agents, T-cell engaging therapies, checkpoints inhibitors)[1,2,3,4,5], where the mechanism of action that includes redirecting the immune response towards tumor killing results in the activation and trafficking of immune cells to tumor sites. In a relapsed or refractory aggressive NHL population, tumor flare reactions were reported infrequently after immunomodulatory agents [2,3,4,5].

Tumor flare is typically characterized by localized responses, which can manifest as tumor pain, volumetric enlargement of tumor sites, swelling or inflammation, usually in early cycles of treatment. Tumor flare is a phenomenon whereby symptoms present due to effects of influx of immune cells in response to treatment with Columvi. Tumor pseudoprogression is primarily a radiological diagnosis, in contrast to the clinical manifestations that characterise tumor flare (Taleb 2019)[1].

Depending on tumor size and anatomic location, events associated with tumor flare may potentially result in mass effects on surrounding structures that can compromise organ function, e.g., dyspnea as a result of airway compression, pleural or pericardial effusion, and bleeding or perforation if major blood vessels or highly vascularized areas are involved.

3.2 Tumor flare and Columvi

Adverse events of tumor flare involving lymph nodes in the head and neck presenting with pain and involving lymph nodes in the thorax with symptoms of breathlessness due to development of pleural effusion have been reported with Columvi. Most tumor flare events occurred during Cycle 1, and no tumor flare events were reported beyond Cycle 2. The median duration was 3.5 days (range: 1 to 35 days).

3.3 Patient monitoring

Patients with tumors at critical anatomic locations are at most risk of serious sequelae, as tumor flare reactions may affect surrounding structures. Therefore, evaluation of lymphoma distribution is important prior to treatment initiation to anticipate the potential spectrum of clinical manifestations of tumor flare after Columvi administration.

Patients with tumors involving critical anatomic locations (e.g., major vessels, tracheobronchial tree and upper airway, heart and pericardium) should be closely monitored for tumor flare, and prospective preventive or interventional measures may need to be considered or planned prior to dosing.

Proactive monitoring of vital signs, physiological parameters, or implementing prophylactic procedures (e.g., tracheostomy) may be required.

Depending on the clinical manifestation of tumor flare, further medical and/or surgical management may be necessary (e.g., anti-inflammatory agents, airway management, decompression, tracheostomy, stenting, prolonged hospitalization).

Reporting adverse events

Reporting adverse events after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse events.

Side effects can be reported to the Ministry of Health using the online form for reporting side effects that can be found on the homepage of the Ministry of Health website www.health.gov.il or by entering the link: https://sideeffects.health.gov.il/
or to Roche by email to Israel.DrugSafety@roche.com,
Phone: 09-9737722, Fax: 09-9737736.

4. References

1. Taleb BA. Tumour flare reaction in cancer treatments: a comprehensive literature review. Anticancer Drugs 2019;30(9):953-958.
2. Chanan-Khan A, Miller KC, Musial L, et al. Clinical efficacy of lenalidomide in patients with relapsed or refractory chronic lymphocytic leukemia: results of a phase II study. J Clin Oncol 2006; 24:5343–49.
3. Chanan-Khan AA, Whitworth A, Bangia N, et al. Lenalidomide-associated tumor flare reaction is manageable in patients with chronic lymphocytic leukemia. J Clin Oncol 2008;26:4851–52.
4. Chanan-Khan A, Miller KC, Takeshita K et al. Results of a phase 1 clinical trial of thalidomide in combination with fludarabine as initial therapy for patients with treatment-requiring chronic lymphocytic leukemia (CLL). Blood 2005;106:3348–52.
5. Corazzelli G, De Filippi R, Capobianco G, et al. Tumor flare reactions and response to lenalidomide in patients with refractory classic Hodgkin lymphoma. Am J Hematol 2010 Jan;85(1):87+90. doi: 10.1002/ajh.21571. PMID: 20029955.

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