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SAFETY INFORMATION FROM THE PIVOTAL TRIAL OF COLUMVI™ (glofitamab-gxbm) IN 3L+ PATIENTS WITH DLBCL, NOS AND LBCL ARISING FROM FL

3L+=third-line and subsequent therapy; DLBCL, NOS=diffuse large B-cell lymphoma, not otherwise specified; FL=follicular lymphoma; LBCL=large B-cell lymphoma.

Please see Important Safety Information throughout and full Prescribing Information provided with this presentation.

INDICATIONS AND USAGE AND DISCLAIMER

- COLUMVI (glofitamab-gxbm) is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) or large B-cell lymphoma (LBCL) arising from follicular lymphoma, after two or more lines of systemic therapy
- This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)

Please see Important Safety Information and BOXED WARNING throughout and full Prescribing Information provided with this presentation.

BOXED WARNING: Cytokine Release Syndrome (CRS), including serious or fatal reactions, can occur in patients receiving COLUMVI. Premedicate before each dose, and initiate treatment with the COLUMVI step-up dosing schedule to reduce the risk of CRS. Withhold COLUMVI until CRS resolves or permanently discontinue based on severity.

Please Note: For FDA approved products, please consult the product's full prescribing information for a complete discussion of risks and benefits of the product(s) for its approved indication(s).

The information we provide may additionally include relevant references to non-Genentech product information derived from publicly available sources.

BOXED WARNING & WARNINGS AND PRECAUTIONS

WARNING: CYTOKINE RELEASE SYNDROME

See full prescribing information for complete boxed warning

Cytokine Release Syndrome (CRS), including serious or fatal reactions, can occur in patients receiving COLUMVI. Premedicate before each dose, and initiate treatment with the COLUMVI step-up dosing schedule to reduce the risk of CRS. Withhold COLUMVI until CRS resolves or permanently discontinue based on severity. (2.1, 2.2, 2.3, 2.4, 5.1)

- **Neurologic Toxicity:** Can cause serious neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). Monitor for neurologic toxicity; withhold or permanently discontinue based on severity. (5.2)
- **Serious Infections:** Can cause serious or fatal infections. Monitor patients for signs and symptoms of infection and treat appropriately. (5.3)
- **Tumor Flare:** Can cause serious tumor flare reactions. Monitor patients at risk for complications of tumor flare. (5.4)
- **Embryo-Fetal Toxicity:** May cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception. (5.5, 8.1, 8.3)

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NP30179: PHASE 1/2, OPEN-LABEL, MULTICENTER, MULTICOHORT TRIAL OF COLUMVI (glofitamab-gxbm) FOR PATIENTS WITH R/R DLBCL AFTER ≥2 PRIOR LINES OF THERAPY[1,2]

DLBCL Cohort Key Eligibility Criteria

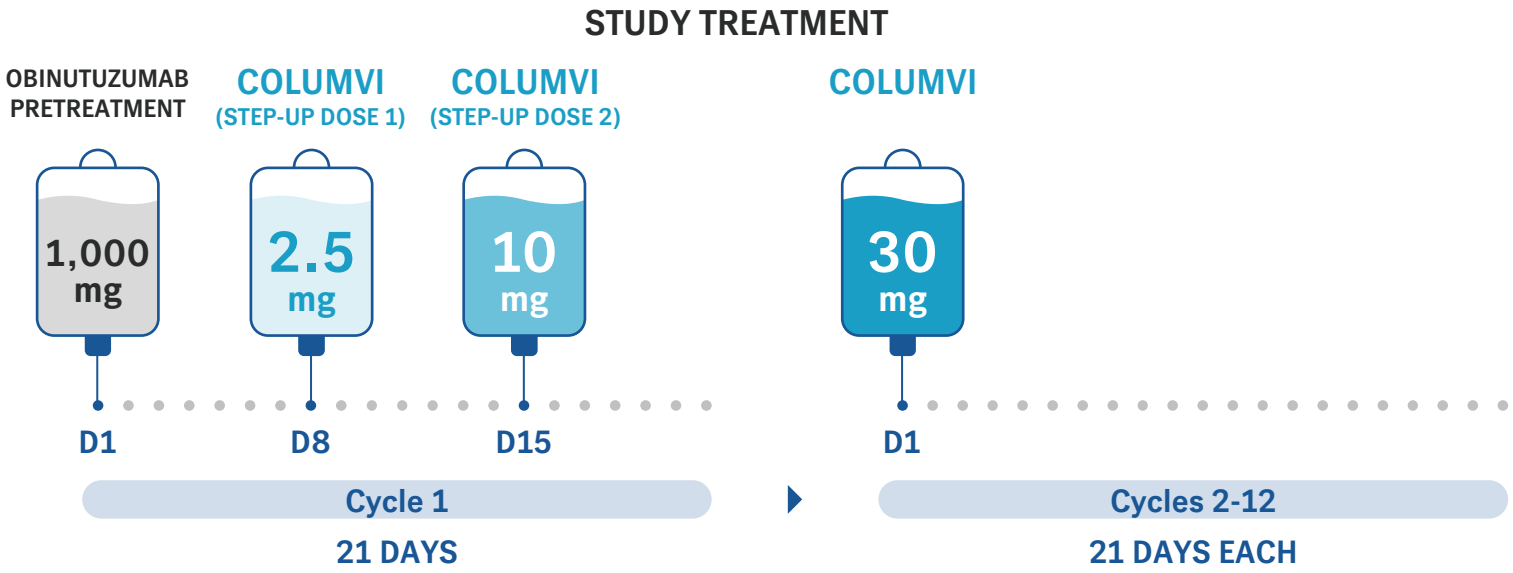
- DLBCL NOS, transformed FL, HGBCL, or PMBCL
- ECOG PS 0-1
- ≥2 prior regimens, including:
  - anti-CD20 antibody
  - anthracycline

Primary Endpoint

- CR (best response) rate by IRC*

Key Secondary Endpoints

- ORR*†
- DOCR*†
- DOR*†



- **COLUMVI was administered as a fixed-duration treatment (12 cycles) with Cycle 1 step-up dosing to mitigate the risk of CRS**
- **Obinutuzumab pretreatment was administered on C1D1 (7 days prior to COLUMVI initiation) to deplete circulating and lymphoid tissue B cells**
- **Patients should be hospitalized during and for 24 hours after completion of step-up dose 1 (2.5 mg dose on C1D8)**
- **Patients who experienced any grade CRS during step-up dose 1 should be hospitalized during and for 24 hours after completion of step-up dose 2 (10 mg on C1D15). CRS with step-up dose 2 can occur in patients who did not experience CRS with step-up dose 1**
- **For subsequent doses, patients who experienced Grade ≥2 CRS with their previous infusion should be hospitalized during and for 24 hours after the completion of the next COLUMVI infusion**

*By PET-CT (Lugano criteria).[3] †By IRC and investigator.
C=cycle; CR=complete response; CRS=cytokine release syndrome; CT=computed topography; D=day; DLBCL=diffuse large B-cell lymphoma; DoCR=duration of complete response; DoR=duration of response; ECOG PS=Eastern Cooperative Oncology Group performance status; FL=follicular lymphoma; IRC=independent review committee; NOS=not otherwise specified; ORR=objective response rate; PET=positron emission tomography; PMBCL=primary mediastinal B-cell lymphoma.
1. Dickinson MJ et al. N Engl J Med. 2022;387(24):2220-2231. 2. COLUMVI [prescribing information]. South San Francisco, CA: Genentech, Inc. 2023. 3. Cheson BD et al. J Clin Oncol. 2014;32(27):3059-68.

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SAFETY RESULTS[1,2]

N (%)	N=145
Adverse Reactions	143 (98.6%)
Grade 3-4 Adverse Reactions	85 (58.6%)
Serious Adverse Reactions	70 (48%)*
Fatal Adverse Reactions	8 (5.5%)†
Adverse Reactions Leading to Permanent Discontinuation of COLUMVI	10 (7%)‡
Adverse Reactions Leading to Dose Interruptions of COLUMVI	27 (19%)§

*Serious adverse reactions in ≥2% of patients included CRS, COVID-19 infection, sepsis, and tumor flare. †COVID-19 infection (n=5; 3.4%), sepsis (n=2; 1.4%), and delirium (n=1; 0.6%). ‡Includes infection, delirium, neutropenia, and CRS.
§Most frequently (≥2%) from neutropenia and thrombocytopenia.
1. COLUMVI [prescribing information]. South San Francisco, CA: Genentech, Inc. 2023. 2. Genentech Data on File.

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SAFETY RESULTS (CONTINUED)[1]

Select Adverse Reactions (≥10%) in Patients Treated with COLUMVI

	N=145	
	All grades	Grade 3 or 4
Immune system disorders		
Cytokine release syndrome	70%	4.1%
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain*	21%	2.1%
General disorders		
Fatigue†	20%	1.4%
Pyrexia	16%	0
Edema‡	10%	0
Skin and subcutaneous tissue disorders		
Rash§	20%	1.4%
Gastrointestinal disorders		
Constipation	14%	0
Diarrhea	14%	0
Nausea	10%	0
Abdominal Pain‖	10%	0
Neoplasms		
Tumor Flare	12%	2.8%
Neurologic Disorders		
Headache	10%	0

Select Laboratory Abnormalities (≥20%) That Worsened from Baseline in Patients Treated with COLUMVI¶‖

	All grades	Grade 3 or 4
Hematology		
Lymphocytes decreased	90%	83%
Hemoglobin decreased	72%	8%
Neutrophils decreased	56%	26%#
Platelets decreased	56%	8%
Chemistry		
Fibrinogen decreased	84%	21%
Phosphate decreased	69%	28%
Sodium decreased	49%	7%
Calcium decreased	48%	2.1%
Gamma-glutamyl transferase increased	33%	9%
Potassium decreased	32%	6%
Uric acid increased	23%	23%

Clinically relevant adverse reactions occurring in <10% of patients who received COLUMVI included infusion-related reaction, peripheral neuropathy, pneumonia, mental status changes, vomiting, tumor lysis syndrome, febrile neutropenia, upper respiratory tract infection, sepsis, herpes zoster infection, gastrointestinal hemorrhage, tremor, and myelitis.

The Select Adverse Reactions table includes a combination of grouped and ungrouped terms. Adverse reactions were graded using NCI CTCAE version 4.03, with the exception of CRS, which was graded per ASTCT consensus criteria in most cases.

*Includes musculoskeletal pain, back pain, bone pain, flank pain, myalgia, neck pain, and pain in extremity. †Includes fatigue and asthenia. ‡Includes edema, edema peripheral, swelling face, and face edema. §Includes rash, rash pruritic, rash maculo-papular, dermatitis, dermatitis acneiform, dermatitis exfoliative, erythema, palmar erythema, pruritus, and rash erythematous. ‖Includes abdominal pain, abdominal discomfort, and abdominal pain upper. ¶The denominator used to calculate the rate varied from 137 to 145 based on the number of patients with a baseline value and at least one post-treatment value. #Grade 4 neutrophil decrease occurred in 9% of patients.

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OTHER ADVERSE EVENTS OF INTEREST[1,2]

N (%)	N=145
Infections and infestations (all grades)	57 (39.3%)
Grade 3–4	15 (10.3%)*
Grade 5	7 (4.8%)*
Neutropenia (all grades)	55 (37.9%)
Grade ≥3	39 (26.9%)
Febrile neutropenia (all grades)	5 (3.4%)
Grade ≥3	5 (3.4%)

N (%)	N=145
Tumor flare events (all grades)	17 (11.7%)
Grade ≥3	4 (2.8%)
Neurologic toxicity (all grades)	58 (40.0%)†
Grade ≥3	3 (2.1%)‡
ICANS	7 (4.8%)
Grade ≥3	2 (1.4%)

*Grade 3 or higher infections reported in ≥2% of patients were COVID-19 infection (6%), including COVID-19 pneumonia, and sepsis (4.1%). †The most frequent neurologic toxicities of any grade were headache (10%), peripheral neuropathy (8%), dizziness or vertigo (7%), and mental status changes (4.8%, including confusional state, cognitive disorder, disorientation, somnolence, and delirium). ‡Grade 3 or higher neurologic adverse reactions occurred in 2.1% of patients and included somnolence, delirium, and myelitis.

CTCAE=Common Terminology Criteria for Adverse Events; ICANS=immune effector cell-associated neurotoxicity syndrome.

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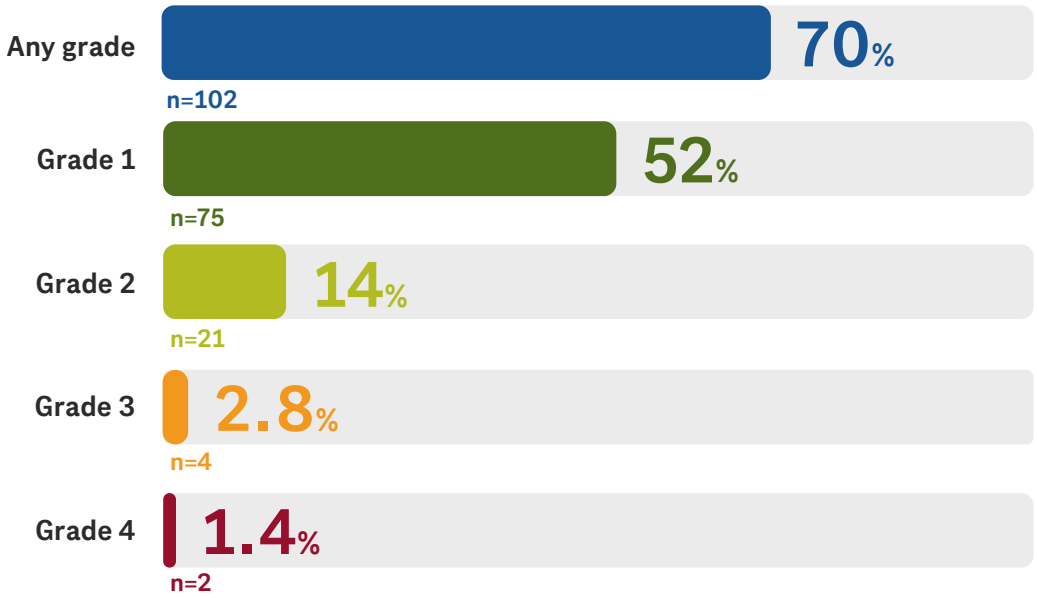
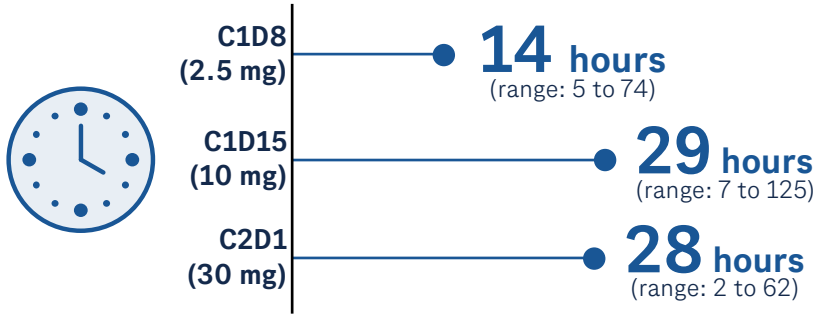
CYTOKINE RELEASE SYNDROME PROFILE

Incidence of CRS*[1,2]
N=145

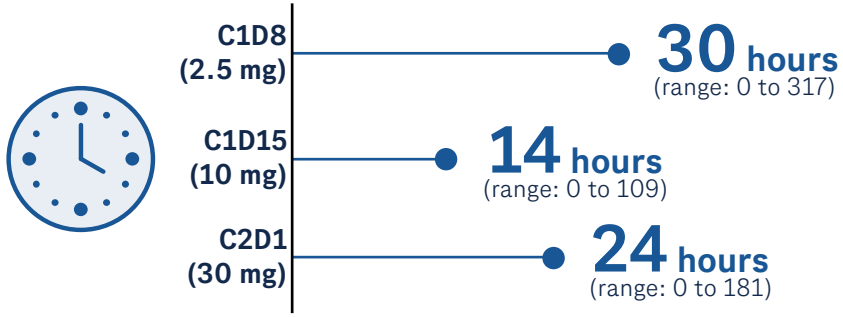


CRS was predominantly Grade 1 and 2

Median Time to CRS Onset From Start of Infusion[1,2]



Median CRS Duration[2]



*Graded per ASTCT consensus criteria in most cases.
ASTCT=American Society for Transplantation and Cellular Therapy; C1D8=Cycle 1, Day 8; C1D15=Cycle 1, Day 15; C2D1=Cycle 2, Day 1.
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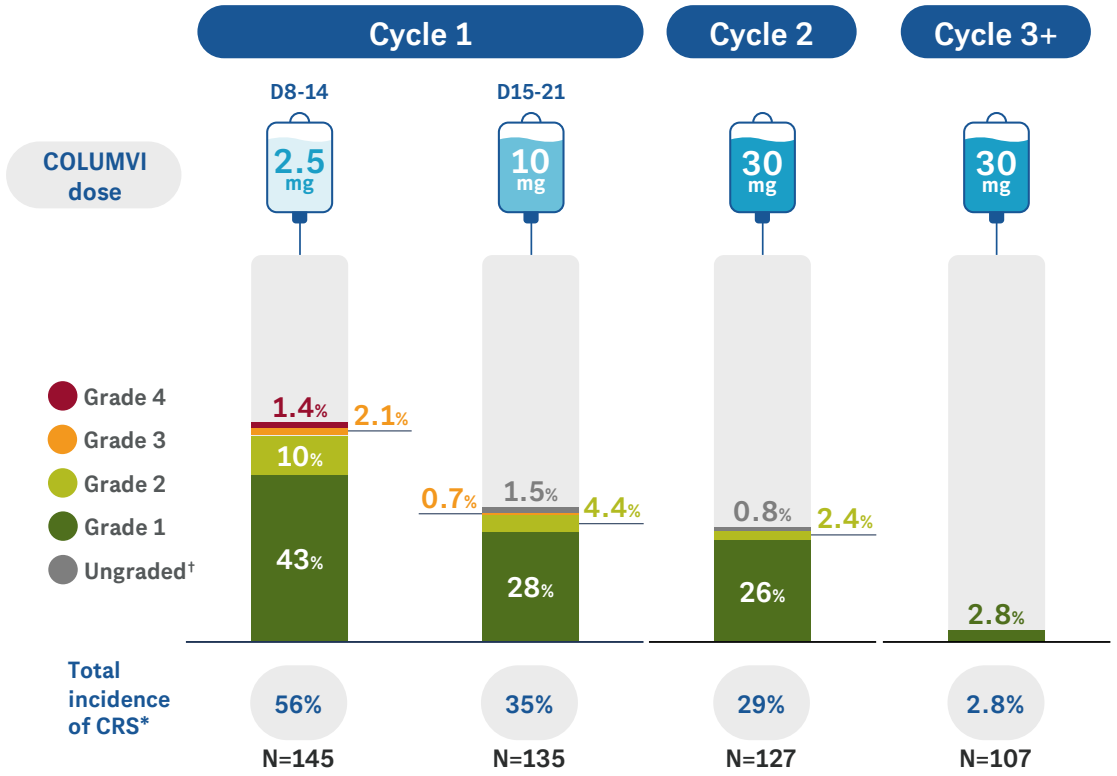
CYTOKINE RELEASE SYNDROME BY CYCLE[1,2]*



- Recurrent CRS occurred in 34% of all patients
- CRS can first occur with the 10 mg dose
  - Of 135 patients treated with the 10 mg dose of COLUMVI, 15 patients (11%) experienced their first CRS event with the 10 mg dose, of which 13 events were Grade 1, 1 event was Grade 2, and 1 event was Grade 3

CRS occurred predominantly in Cycles 1 and 2 and most events occurred after the C1D8 dose (the first dose of COLUMVI 2.5 mg)

*Graded per ASTCT consensus criteria in most cases. †ASTCT grading unavailable for ungraded events.

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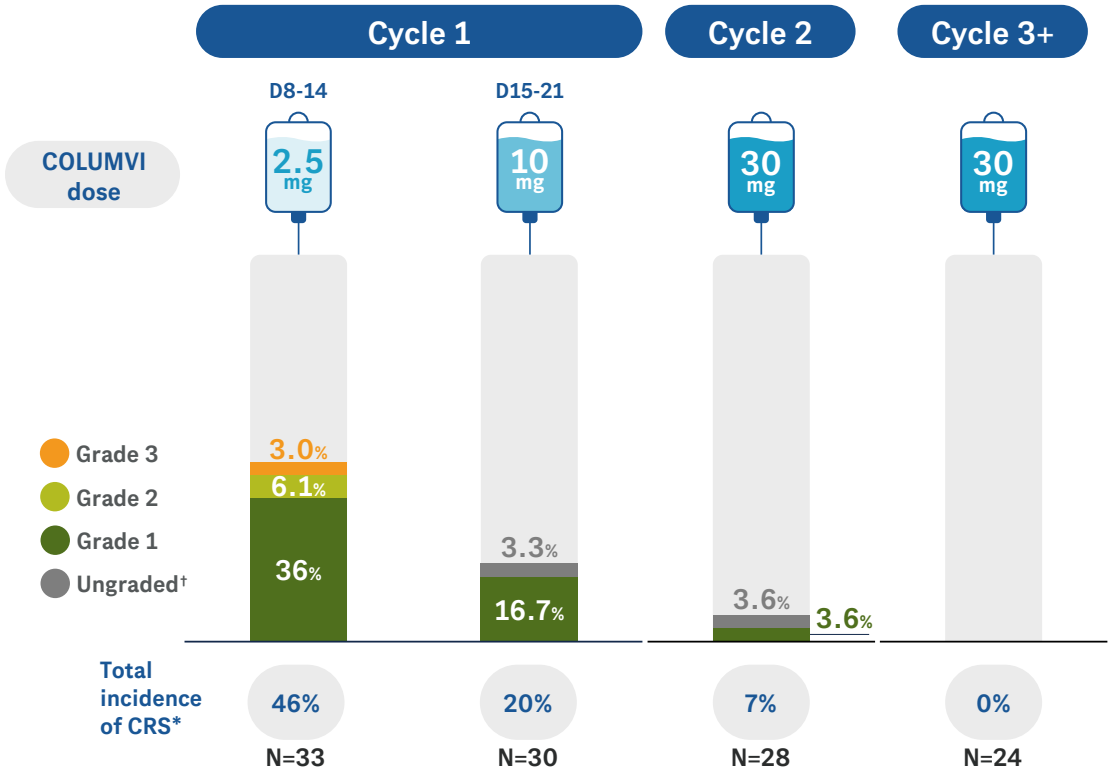
CRS BY CYCLE IN PATIENTS WHO RECEIVED DEXAMETHASONE PREMEDICATION[1]



Limitations: No formal inference may be drawn from this data set

*Graded per ASTCT consensus criteria in most cases. †ASTCT grading unavailable for ungraded events.
1. Genentech Data on File.

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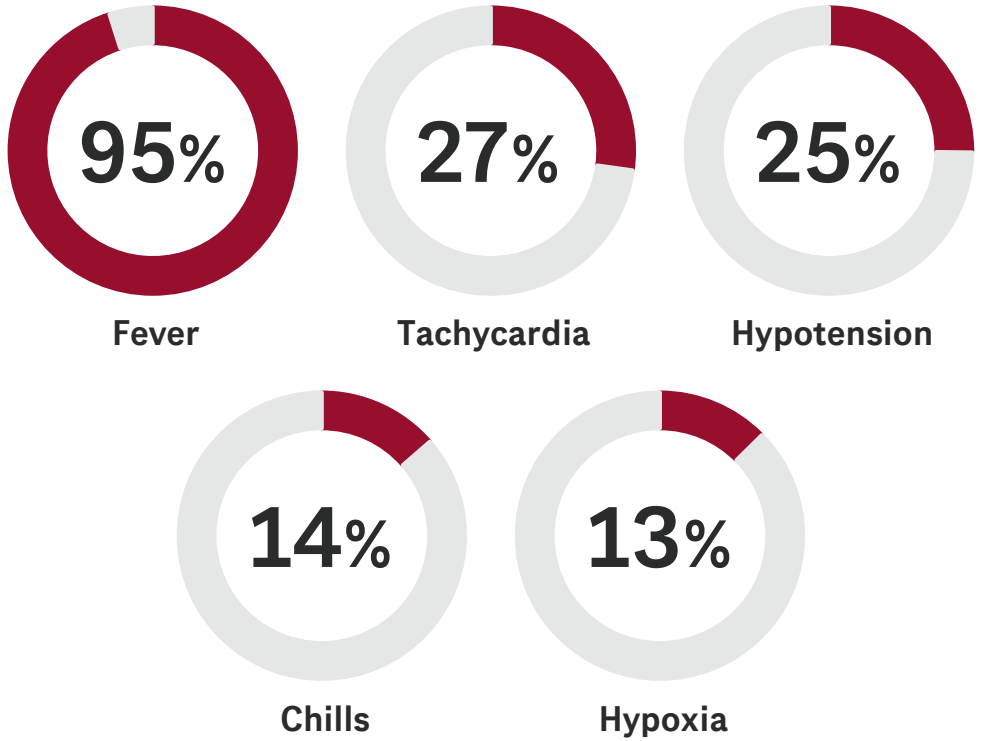
MOST COMMON SYMPTOMS OF PATIENTS WHO EXPERIENCED CRS[1,2]



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MONITORING FOR CYTOKINE RELEASE SYNDROME[1]

- Administer the COLUMVI infusions intravenously in a healthcare setting with immediate access to medical support to manage CRS, including severe CRS
- For the first COLUMVI step-up dose (2.5 mg on Cycle 1 Day 8), patients should be hospitalized during and for 24 hours after completion of the COLUMVI infusion
- Patients who experienced any grade CRS during step-up dose 1 should be hospitalized during and for 24 hours after completion of step-up dose 2 (10 mg on Cycle 1 Day 15). CRS with step-up dose 2 can occur in patients who did not experience CRS with step-up dose 1
- For subsequent infusions (30 mg on Day 1 of Cycle 2 or subsequent cycles), patients who experienced Grade ≥2 CRS with their previous infusion should be hospitalized during and for 24 hours after completion of the next COLUMVI infusion
- For monitoring after delayed or missed doses of COLUMVI, follow the recommendations in Table 2 of the COLUMVI Prescribing Information

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CRS MANAGEMENT PER ASTCT 2019 GRADING CRITERIA IN THE COLUMVI (glofitamab-gxbm) USPI[1]

Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension.

If CRS is suspected, withhold COLUMVI and manage according to the recommendations below and current practice guidelines. Administer supportive care for CRS, which may include intensive care for severe or life-threatening cases.

Grade and Presenting Symptoms*	Actions	For Next COLUMVI Dose
Grade 1 **Temperature ≥100.4°F (38°C)†**	• Withhold COLUMVI and manage per current practice guidelines – If symptoms resolve, restart infusion at a slower rate‡	• Ensure CRS symptoms are resolved for at least 72 hours before next dose§ • Consider slower infusion rate for next dose
Grade 2 **Temperature ≥100.4°F (38°C)† with:** Hypotension not requiring vasopressors and/or hypoxia requiring low-flow oxygen‖ by nasal cannula or blow-by	• Withhold COLUMVI and manage per current practice guidelines – If symptoms resolve, restart infusion at a slower rate‡	• Ensure CRS symptoms are resolved for at least 72 hours before next dose§ • For the next dose, consider a slower infusion rate, monitor more frequently, and consider hospitalization • For recurrent Grade 2 CRS, manage per Grade 3 CRS

*American Society for Transplantation and Cellular Therapy (ASTCT) 2019 consensus grading criteria. †Premedication may mask fever. Therefore, if clinical presentation is consistent with CRS, follow these management guidelines. ‡Duration of infusion may be extended up to 8 hours, as appropriate for that cycle (see Table 1 of the COLUMVI PI). §Refer to Table 2 of the COLUMVI PI for information on restarting COLUMVI after dose delays. ‖Low-flow oxygen defined as oxygen delivered at <6 L/minute, high-flow oxygen defined as oxygen delivered at ≥6 L/minute.

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CRS MANAGEMENT PER ASTCT 2019 GRADING CRITERIA IN THE COLUMVI (glofitamab-gxbm) USPI[1]

Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension.

If CRS is suspected, withhold COLUMVI and manage according to the recommendations below and current practice guidelines. Administer supportive care for CRS, which may include intensive care for severe or life-threatening cases.

Grade and Presenting Symptoms*	Actions	For Next COLUMVI Dose
Grade 3 **Temperature ≥100.4°F (38°C)† with:** Hypotension requiring vasopressor (with or without vasopressin) and/or hypoxia requiring high-flow oxygen‖ by nasal cannula, face mask, non-rebreather mask, or Venturi mask	• Withhold COLUMVI and manage per current practice guidelines, which may include intensive care	• Ensure CRS symptoms are resolved for at least 72 hour before next dose§ • Hospitalize for the next dose, monitor more frequently, and consider a slower infusion rate‡ • For recurrent Grade 3 CRS, permanently discontinue COLUMVI
Grade 4 **Temperature ≥100.4°F (38°C)† with:** Hypotension requiring multiple vasopressors (excluding vasopressin) and/or hypoxia requiring oxygen by positive pressure (e.g., CPAP, BiPAP, intubation, and mechanical ventilation)	• Permanently discontinue COLUMVI and manage per current practice guidelines, which may include intensive care	

*American Society for Transplantation and Cellular Therapy (ASTCT) 2019 consensus grading criteria. †Premedication may mask fever. Therefore, if clinical presentation is consistent with CRS, follow these management guidelines. ‡Duration of infusion may be extended up to 8 hours, as appropriate for that cycle (see Table 1 of the COLUMVI PI). §Refer to Table 2 of the COLUMVI PI for information on restarting COLUMVI after dose delays. ‖Low-flow oxygen defined as oxygen delivered at <6 L/minute, high-flow oxygen defined as oxygen delivered at ≥6 L/minute.

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NEUROLOGIC TOXICITY (INCLUDING ICANS) MANAGEMENT IN THE COLUMVI (glofitamab-gxbm) USPI[1]

At the first sign of neurologic toxicity, including ICANS, consider neurology evaluation and withholding COLUMVI based on the type and severity of neurotoxicity. Rule out other causes of neurologic symptoms. Provide supportive therapy, which may include intensive care.

Severity*†	Actions
Grade 1	• Continue COLUMVI and monitor neurologic toxicity symptoms • If ICANS, manage per current practice guidelines
Grade 2	• Withhold COLUMVI until neurologic toxicity symptoms improve to Grade 1 or baseline‡§ • Provide supportive therapy and consider neurologic evaluation • If ICANS, manage per current practice guidelines
Grade 3	• Withhold COLUMVI until neurologic toxicity symptoms improve to Grade 1 or baseline for at least 7 days§‖ • For Grade 3 neurologic events lasting more than 7 days, consider permanently discontinuing COLUMVI • Provide supportive therapy and consider neurology evaluation • If ICANS, manage per current practice guidelines
Grade 4	• Permanently discontinue COLUMVI • Provide supportive therapy, which may include intensive care, and consider neurology evaluation • If ICANS, manage per current practice guidelines

*Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03. †Based on ASTCT 2019 grading for ICANS. ‡Consider the type of neurologic toxicity before deciding to withhold COLUMVI. §See Section 2.2 Dosage and Administration of COLUMVI Prescribing Information on restarting COLUMVI after dose delays. ‖Evaluate benefit-risk before restarting COLUMVI.

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