Myelosuppression

Incidence and Management

THERAPEUTICS

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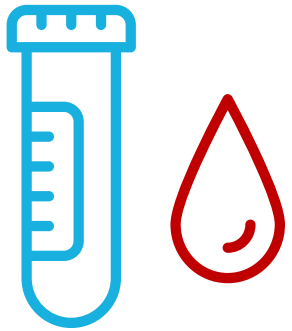
Objectives

Myelosuppression

- Review the incidence, onset, duration, and dose management for myelosuppression in the LOTIS-2 study
- Review the prescribing information recommendations for loncastuximab tesirine (Lonca) and discuss adverse event management for myelosuppression



REFERENCES

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Indication and Usage

Indication for Loncastuximab Tesirine

Loncastuximab tesirine is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma.

This indication is approved under accelerated approval based on overall response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Warnings and Precautions

Myelosuppression Warning From the Lonca Prescribing Information

Treatment with loncastuximab tesirine can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia. Grades 3 or 4 neutropenia occurred in 32%, thrombocytopenia in 20%, and anemia in 12% of patients. Grade 4 neutropenia occurred in 21% and thrombocytopenia in 7% of patients. Febrile neutropenia occurred in 3% of patients.

Monitor complete blood counts throughout treatment. Cytopenias may require interruption, dose reduction, or discontinuation of loncastuximab tesirine. Consider prophylactic granulocyte colony-stimulating factor administration as applicable.

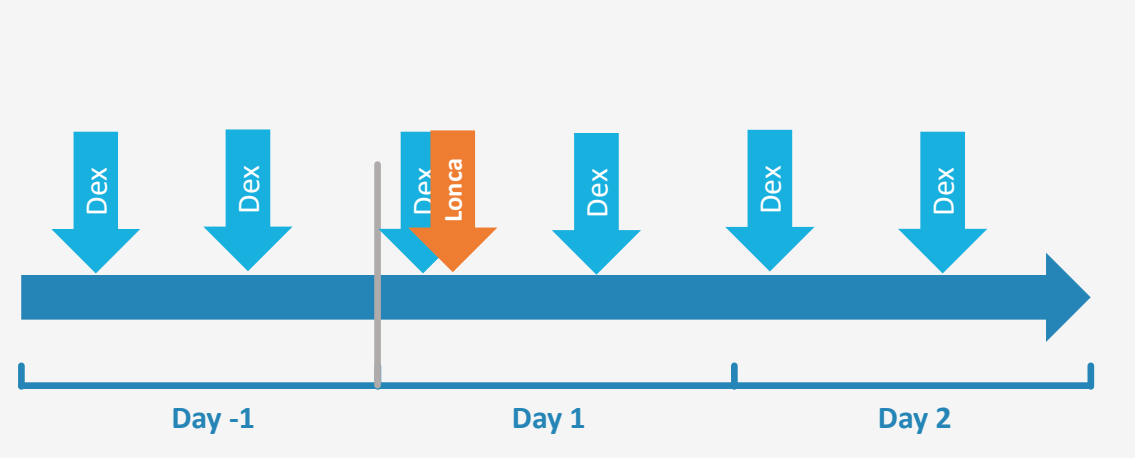
REFERENCES

Premedication Recommendation

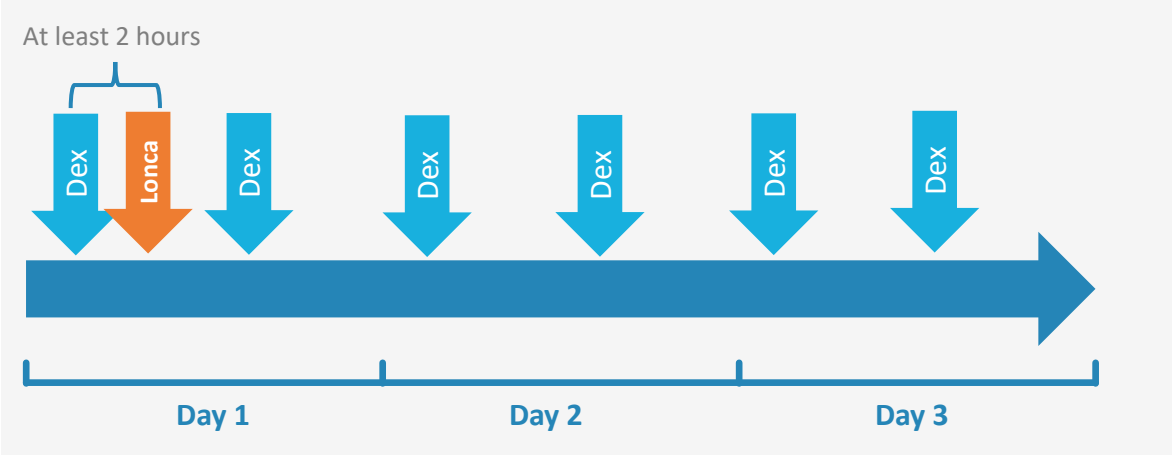
- The loncastuximab tesirine prescribing information recommends dexamethasone premedication[1]
- The loncastuximab tesirine prescribing information also states to consider prophylactic granulocyte colony-stimulating factor administration as applicable[1]

Dexamethasone Premedication Administration

If dexamethasone administration begins the day before Lonca:



If dexamethasone administration does not begin the day before Lonca:



REFERENCES

Incidence, Onset, Duration, and Dose Modification for Neutropenia (LOTIS-2)

All-Treated Population (N=145)[a,b]

Neutropenia

	Incidence	Onset (median)	Duration[c] (median)
Any Grade	**53.8%** (n=78)	**22 Days** Range: 1–232	**22 Days** Range: 1–133
Grade ≥3	**29.7%** (n=43)	**36 Days** Range: 6–232	**10 Days** Range: 1–110

Dose Modification Due to Neutropenia, Subset of Patients With Neutropenia (n=78)[a]

Delayed	Reduced	Discontinued
23.1% (n=18)	**0% (n=0)**	**1.3% (n=1)**

Febrile neutropenia:

In the LOTIS-2 trial, the incidence of Grades 3 or 4 febrile neutropenia was 3.4% (n=5).

- In the LOTIS-2 trial, grade ≥3 neutropenia typically occurred within the first two treatment cycles
- Neutropenia was generally manageable with dose delays and resulted in dose reductions or discontinuations in <5% of patients

[a]Data cutoff: April 6, 2020. Post hoc analysis.

[b]Incidence of hematologic abnormalities was based on laboratory reporting, while dose modifications, time to onset, and duration were based on adverse event reporting.

[c]Missing end dates were imputed using the date of new anticancer therapy (NAT) for patients who received NAT or end of study (EOS) or data cutoff date for patients who did not receive NAT for the calculation of the duration of adverse events. Partial end dates were imputed using the last month or day of a month bounded by EOS. Grade ≥3 duration calculated at the time of first occurrence to until adverse event resolved to grade ≤2.

REFERENCES

Incidence, Onset, Duration, and Dose Modification for Thrombocytopenia (LOTIS-2)

All-Treated Population (N=145)[a,b]

Thrombocytopenia

	Incidence	Onset (median)	Duration[c] (median)
Any Grade	**66.2%** (n=96)	**15 Days** Range: 1–281	**31.5 Days** Range: 5–368
Grade ≥3	**17.9%** (n=26)	**29 Days** Range: 9–281	**23 Days** Range: 1–195

Dose Modification Due to Thrombocytopenia, Subset of Patients With Thrombocytopenia (n=96)[a]

Delayed	Reduced	Discontinued
13.5% (n=13)	**1% (n=1)**	**2.1% (n=2)**

- In the LOTIS-2 trial, grade ≥3 thrombocytopenia typically occurred within the first two treatment cycles
- Thrombocytopenia was generally manageable with dose delays and resulted in dose reductions or discontinuations in <5% of patients

[a]Data cutoff: April 6, 2020. Post hoc analysis.

[b]Incidence of hematologic abnormalities was based on laboratory reporting, while dose modifications, time to onset, and duration were based on adverse event reporting.

[c]Missing end dates were imputed using the date of new anticancer therapy (NAT) for patients who received NAT or end of study (EOS) or data cutoff date for patients who did not receive NAT for the calculation of the duration of adverse events. Partial end dates were imputed using the last month or day of a month bounded by EOS. Grade ≥3 duration calculated at the time of first occurrence to until adverse event resolved to grade ≤2.

REFERENCES

Incidence, Onset, Duration, and Dose Modification for Anemia (LOTIS-2)

All-Treated Population (N=145)[a,b]

Anemia

	Incidence	Onset (median)	Duration[c] (median)
Any Grade	**93.8%** (n=136)	**17 Days** Range: 1–84	**42 Days** Range: 2–525
Grade ≥3	**11.0%** (n=16)	**22 Days** Range: 6–92	**4 Days** Range: 1–103

Dose Modification Due to Anemia, Subset of Patients With Anemia (n=136)[a]

Delayed	Reduced	Discontinued
2.9% **(n=4)**	**0%** **(n=0)**	**0%** **(n=0)**

- In the LOTIS-2 trial, grade ≥3 anemia typically occurred within the first two treatment cycles
- Anemia was generally manageable with dose delays and did not result in dose reductions or discontinuations

[a]Data cutoff: April 6, 2020. Post hoc analysis.

[b]Incidence of hematologic abnormalities was based on laboratory reporting, while dose modifications, time to onset, and duration were based on adverse event reporting.

[c]Missing end dates were imputed using the date of new anticancer therapy (NAT) for patients who received NAT or end of study (EOS) or data cutoff date for patients who did not receive NAT for the calculation of the duration of adverse events. Partial end dates were imputed using the last month or day of a month bounded by EOS. Grade ≥3 duration calculated at the time of first occurrence to until adverse event resolved to grade ≤2.

REFERENCES

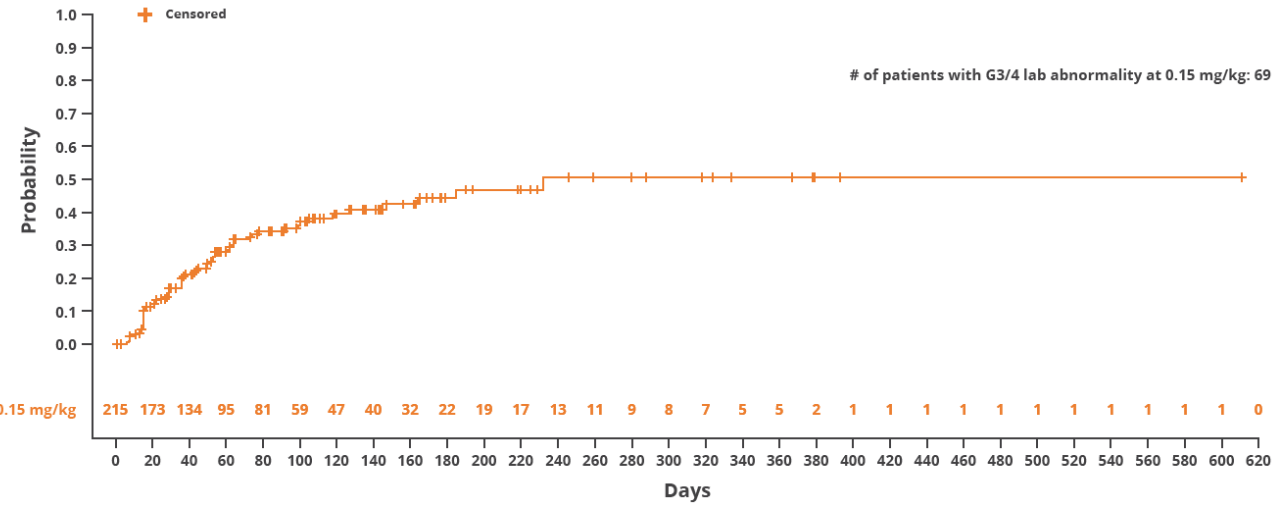
Pooled Analysis from LOTIS-1 and LOTIS-2: Time to Onset of Grade 3/4 Events[1,a-c]

- 215 patients received at least one dose of Lonca (0.15 mg/kg) in LOTIS-1 (n=70) or LOTIS-2 (n=145) and were included[a-c]
- Grade ≥3 neutropenia, thrombocytopenia, and anemia occurred in 32.1% (n=69), 20% (n=43), and 12.6% (n=27) of patients, respectively. Febrile neutropenia occurred in 3.3% (n=7) of patients
  - Most patients with grade 3/4 neutropenia experienced onset in the first 4 months
  - Most patients with grade 3/4 thrombocytopenia or anemia experienced onset in the first 2 months

Thrombocytopenia

Anemia

Time to onset of Grade 3/4 Neutropenia



[a]Data cutoff: March 1, 2021. Post hoc analysis.

[b]Time to event analyses were performed for grade 3/4 neutropenia, thrombocytopenia, and anemia. Analyses were performed if a minimum of 20 patients had an event in at least one dose group. Analyses assessed time to first onset of grade 3/4 anemia, neutropenia, and thrombocytopenia.

[c]The incidence of hematologic abnormalities was based on laboratory reporting, whereas dose modification was based on adverse event reporting.

REFERENCES

Pooled Analysis from LOTIS-1 and LOTIS-2: Incidence and Management of Myelosuppression[1,a-c]

- <10% of patients who developed grade ≥3 neutropenia had neutropenia at baseline, whereas more than half of patients who developed grade ≥3 thrombocytopenia or anemia had grade 1 or 2 thrombocytopenia or anemia at baseline
- Neutrophil growth factors were administered to 33.5% (n=72) of patients: prophylactically to 15.3% (n=33) of patients and as treatment in 26.0% (n=56) of patients
- No new safety signals were identified

	Baseline, n (%)	Patients with a maximum post-baseline of Grade ≥3
Neutropenia	Grade 0	63 (29.3)
	Grade 1	3 (1.4)
	Grade 2	3 (1.4)
	Grade 3	0
	Grade 4	0

Thrombocytopenia

Anemia

Dose Modification Due to Grade ≥3 Myelosuppression

	Delayed	Reduced	Discontinued
Neutropenia	10.2% (n=22)	0.5% (n=1)	0.5% (n=1)
Thrombocytopenia	8.4% (n=18)	0.5% (n=1)	2.3% (n=5)
Anemia	1.4% (n=3)	0	0
Febrile neutropenia	0.5% (n=1)	0	0

[a]Data cutoff: March 1, 2021. Post hoc analysis.

[b]Safety analyses were conducted in the all-treated population, who received ≥1 dose of Lonca.

[c]The incidence of hematologic abnormalities was based on laboratory reporting, whereas dose modification was based on adverse event reporting.

REFERENCES

Dose Modification Recommendation

Dose Modification Recommendation in the Lonca Prescribing Information

	Severity[1,2]	Withhold Lonca Until
Neutropenia	Absolute neutrophil count $<1 \times 10^9$/L	Neutrophil count returns to $\geq 1 \times 10^9$/L
Thrombocytopenia	Platelet count <50,000/mcL	Platelet count returns to ≥50,000/mcL
Other Adverse Reactions	Grade ≥3	Toxicity resolves to grade ≤1

If dosing is delayed by more than 3 weeks due to toxicity related to loncastuximab tesirine, reduce subsequent doses by 50%. If toxicity reoccurs following dose reduction, consider discontinuation.[1]

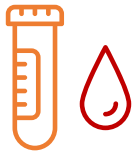
REFERENCES

Management of Myelosuppression

Management of Myelosuppression in Patients Treated With Lonca

Patient counseling in Lonca prescribing information

Advise patients to immediately contact their healthcare provider for a fever of ≥100.4°F (38°C) or signs or symptoms of bruising or bleeding. Advise patients of the need for periodic monitoring of blood counts.[1]



Eligibility in the LOTIS-2 study

To be eligible for treatment with Lonca in LOTIS-2, patients were required to have an ANC ≥1.0 × 10^9/L while off of growth factors for ≥72 hours and a platelet count ≥75 × 10^9/L without transfusion in the prior 7 days.[2]

Growth Factors for the Management of Neutropenia

In LOTIS-2 (N=145), 29.0% (n=42) of patients received growth factors for neutropenia at the discretion of the investigator that aligned with protocols at the clinical site.[3]

Growth Factor Use for Neutropenia[3,a]	
Treatment	**22.8% (n=33)**
Prophylaxis	**13.8% (n=20)**

Number of Times Growth Factor Was Used[3,a]	
1	9.7% (n=14)
2	9.0% (n=13)
3	2.1% (n=3)
>3	8.3% (n=12)

[a]Data cutoff: April 6, 2020. Post hoc analysis.

REFERENCES

Summary

- The Lonca prescribing information includes a warning for myelosuppression; treatment with Lonca can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia[1]
- The Lonca prescribing information states to consider prophylactic granulocyte colony-stimulating factor administration as applicable[1]
- In the LOTIS-2 trial (N=145), grade ≥3 neutropenia, thrombocytopenia, and anemia occurred in 29.7%, 17.9%, and 11% of patients, respectively, and febrile neutropenia occurred in 3.4% of patients[2]
- In the LOTIS-2 trial, most myelosuppression events were manageable with dose delays and resulted in dose reduction or treatment discontinuation of Lonca in <5% of patients[2]
  - The majority of patients did not require growth factors for the management of neutropenia[2]