ZYNLONTA® (loncastuximab tesirine-lpyl) – Use Before or After Hematopoietic Stem Cell Transplant

Summary

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 adult patients (≥ 18 years of age) with relapsed or refractory (R/R) B-Cell Non-Hodgkin Lymphoma (B-NHL).[4]
    - A total of 42 patients (23%) had received prior hematopoietic stem cell transplantation (HSCT) in LOTIS-1, while 12 patients (6.6%) went on to receive HSCT following treatment with ZYNLONTA.[4]
        - Safety and efficacy in these subgroups were not reported.
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which evaluated the efficacy and safety of ZYNLONTA monotherapy in patients with R/R diffuse large B-cell lymphoma (DLBCL) following ≥2 lines of prior systemic therapy.[1]
    - A total of 24 patients (16.6%) patients had received prior HSCT. Twenty-one patients (14%) had autologous HSCT, 2 patients (1%) had allogenic HSCT, and 1 patient (1%) had both autologous and allogenic HSCT.[1]
    - At data cut-off March 01, 2021, the overall response rate (ORR) in the all-treated population was 48.3% (n=70), with a complete response (CR) of 24.8% (n=36) and a partial response (PR) of 23.4% (n=34).[3]
        - In patients who received prior HSCT, the ORR was 58.3% (95% CI: 36.6, 77.9), with a CR of 29.2% (95% CI: 12.6, 51.1).[2]
    - At data cut-off March 01, 2021, 11 patients (7.6%) proceeded to stem cell transplantation as consolidation after responding to ZYNLONTA.[3]

Clinical Data

LOTIS-1 (Phase 1)

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 adult patients (≥ 18 years of age) with R/R B-NHL.[4]
- The study was conducted in two parts, dose-escalation (Part 1) followed by dose-expansion (Part 2). Patients with histologically confirmed R/R B-NHL were enrolled if they had failed or became intolerant to established therapies or if they had no other treatment options available.[4]

Hematopoietic Stem Cell Transplantation Before ZYNLONTA

- A total of 42 patients (23%) received prior HSCT. Table 1 provides additional information regarding those 42 patients. Safety and efficacy in this subgroup were not reported, and no additional information regarding this patient population is available.[4]

Table 1. Patients with Prior Hematopoietic Cell Transplantation in LOTIS-1. Adapted from Data on File, LOTIS-1 Clinical Study Report.[5]

	All Patients with B-NHL (N=183)	Patients with DLBCL (n=139)
Prior Hematopoietic Stem Cell Transplantation, n (%)		
Autologous	31 (16.9)	22 (15.8)
Allogeneic	5 (2.7)	2 (1.4)
Both	4 (2.2)	2 (1.4)
Other[a]	2 (1.1)	1 (0.7)

[a] One patient with DLBCL had a peripheral stem cell harvest transplant and one patient with follicular lymphoma received a double cord transplant; B-NHL=B-cell Non-Hodgkin lymphoma; DLBCL=Diffuse Large B-cell Lymphoma[4]

- In the total population, the ORR in evaluable patients (n=180) was 45.6% (95% CI: 38.1, 53.1), including CR in 48 patients (26.7%) and PR in 34 patients (18.9%).[4]
- The most frequently reported treatment emergent adverse events (TEAEs) were hematologic related which included platelet count decreased in 128 patients (71.1%), neutrophil count decreased in 106 patients (59.2%), anemia in 60 patients (32.8%) and white blood cell (WBC) count decreased in 22 patients (12%).[4]
- Fatigue was the most common non-hematological TEAE in 78 patients (42.6%), followed by nausea in 59 patients (32.2%), peripheral edema in 58 patients (31.7%), and gamma glutamyltransferase (GGT) increased in 57 patients (31.1%).[4]

Hematopoietic Stem Cell Transplantation After ZYNLONTA

- A total of 12 patients (6.6%) received HSCT after ZYNLONTA.[4] Safety and efficacy in these subgroups were not reported. Information regarding the outcomes of these patients is not available.

LOTIS-2 (Phase 2)

- LOTIS-2 was a phase 2, multicenter, open-label single-arm study which evaluated the efficacy and safety of ZYNLONTA used as monotherapy in patients with R/R DLBCL following ≥2 lines of prior systemic therapy.[1]
    - ORR according to the 2014 Lugano classification was the primary endpoint of the study.

Hematopoietic Stem Cell Transplantation Before ZYNLONTA

- A total of 24 patients (16.6%) received prior HSCT.[1] Table 2 below provides a breakdown of the prior HSCT in those 24 patients.

Table 2. Patients Receiving Prior Hematopoietic Stem Cell Transplantation in LOTIS-2. Adapted from Data on File, LOTIS-2 Clinical Study Report.[6]

	All-Treated Population (N=145)
Prior Hematopoietic Stem Cell Transplantation, n (%)	
Autologous	21 (14.5)
Allogeneic	2 (1.4)
Both	1 (0.7)

- At data cut-off March 01, 2021, the ORR in the all-treated population was 48.3% (n=70), with a CR of 24.8% (n=36) and a PR of 23.4% (n=34).[3]

    - In patients who received prior HSCT, the ORR was 58.3% (95% CI: 36.6, 77.9), with a CR of 29.2% (95% CI: 12.6, 51.1).[2]
- Out of 145 patients, 143 patients (98.6%) experienced at least one TEAE.[3]
- The most common (≥10%) Grade ≥3 TEAEs included neutropenia in 38 patients (26.2%), thrombocytopenia in 26 patients (17.9%), increased GGT in 25 patients (17.2%), and anemia in 15 patients (10.3%).[3]

Hematopoietic Stem Cell Transplantation After ZYNLONTA

- At data cut-off March 01, 2021, 11 patients (7.6%) proceeded to stem cell transplantation as consolidation after responding to ZYNLONTA.[3]
    - No efficacy or safety information regarding this updated subset of patients is available.
- Sixty-eight patients (47%) received subsequent therapy following ZYNLONTA treatment, including 9 patients (6%) with subsequent autologous HSCT (5 [3%]) or allogenic HSCT (4 [3%]) as consolidation therapy.[1]
- At data cut off data April 05, 2020, 3 patients (30%) experienced Grade ≥3 AEs following stem cell transplant. AEs reported in this patient population included, acute kidney injury, bronchopulmonary aspergillosis, cardiogenic shock, multiple organ dysfunction syndrome, pulmonary hemorrhage, respiratory failure, sepsis, septic shock (10%, n=1 each).[6]

Literature Search

- A PubMed biomedical literature search conducted on April 17, 2025, yielded no relevant data regarding the use of ZYNLONTA before or after hematopoietic stem cell transplant.

Relevant Prescribing Information

Section 14: Clinical Studies[7]

14.1: Relapsed or Refractory Diffuse Large B-Cell Lymphoma

- Of the 145 patients enrolled, the median age was 66 years (range 23 to 94), 59% male, and 94% had an ECOG performance status of 0 to 1. Race was reported in 97% of patients; of these patients, 90% were White, 3% were Black, and 2% were Asian. The diagnosis was DLBCL not otherwise specified (NOS) in 88% (including 20% with DLBCL arising from low-grade lymphoma), high-grade B-cell lymphoma in 7%. The median number of prior therapies was 3 (range 2 to 7), 63% with refractory disease, 17% with prior stem cell transplant, and 9% with prior chimeric antigen receptor (CAR) T-cell therapy.

References

[1] Caimi PF, Weiyun A, Alderuccio JP, et al. Loncastuximab tesirine in Relapsed or Refractory Diffuse Large B-cell Lymphoma (LOTIS-2): a Multicentre, Open-label, Single-arm, Phase 2 trial. *Lancet Oncol*. 2021 May 11. DOI: 10.1016/S1470-2045(21)00139-X.

[2] Caimi PF, Weiyun A, Alderuccio JP, et al. Loncastuximab tesirine in Relapsed or Refractory Diffuse Large B-cell Lymphoma (LOTIS-2): a Multicentre, Open-label, Single-arm, Phase 2 trial [supplementary appendix]. *Lancet Oncol*. 2021 May 11. DOI: 10.1016/S1470-2045(21)00139-X.

[3] Zinzani PL, Caimi PF, Carlo-Stella C, et al. LOTIS-2 follow-up analysis: Updated results from a Phase 2 study of loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma. Poster presented at: the International Conference on Malignant Lymphoma (ICML) Virtual Congress; June 18–22, 2021; Virtual.

[4] Hamadani M, Radford J, Carlo-Stella C, et al. Final Results of a Phase 1 Study of loncastuximab tesirine in relapsed/refractory B-cell Non-Hodgkin Lymphoma. *Blood*. 2020 Nov 19. DOI: 10.1182/blood.2020007512

[5] Data on File, LOTIS-1 Clinical Study Report. ADC Therapeutics.

[6] Data on File, LOTIS-2 Clinical Study Report. ADC Therapeutics.

[7] ZYNLONTA® (loncastuximab tesirine-lpyl) for injection Prescribing Information, October 2022.

ADC Therapeutics encourages all health care professionals to report any adverse events and product quality complaints to medical information at 855-690-0340. Please consult the ZYNLONTA Prescribing Information.