

Assessing the Impact of Inclusion of Patients with Missing Eastern Cooperative Oncology Group (ECOG) Performance Status in Real-World Outcomes of Third-Line or Later (3L+) Diffuse Large B-Cell Lymphoma (DLBCL)

Objectives



The aim of this study was to evaluate differences in characteristics and real-world overall survival (rwOS) and time to next treatment (rwTTNT) among patients with missing/unknown (M/U) ECOG score compared to patients with known ECOG 0-2 in 3L+ DLBCL.

Conclusions



Median rwOS among ECOG 0-2 and M/U groups was 6.9 (95% CI: 5.8, 9.1) and 10.6 months (95% CI: 7.9, 13.8) over a median follow-up time (reverse KM) of 36.1 (95% CI: 28.0, 41.5) and 17.0 months (95% CI: 15.0, 24.2), respectively.

In this analysis, M/U ECOG score was not associated with worse outcomes, although limitations include differences in follow-up time between groups.

We hypothesize that patients who are sufficiently fit to initiate 3L+ therapy are more likely to have ECOG score 0-2 than ≥ 3 at baseline, despite missingness of ECOG score in the health record. Additional research should assess inclusion of similar cohorts in future clinical trial comparisons.

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Acknowledgments: This study was sponsored by Pfizer.

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Presented at the 2026 ISPOR Conference | May 17-20, 2026 | Philadelphia, PA

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Background

- ECOG performance status is a measurement of a patient's level of functioning, specifically their physical ability and level of daily activity.¹
- Patients with ECOG 0-2 are ambulatory and are generally considered eligible for most treatments, including clinical trial enrollment. Those with ECOG 3+ are considered frail and are not typically eligible for clinical trial participation due to functional status.
- In the real-world setting and in real-world data, ECOG performance status can be missing/unknown (M/U) due to lack of assessment, documentation, or abstraction.
- In many cases, real-world analyses exclude patients with missing ECOG due to inability to confirm functional status. This may result in more restrictive real-world study criteria for clinical trial comparisons, limiting sample size for these analyses.
- This study assessed differences in outcomes among patients with ECOG 0-2 versus M/U in a real-world population similar to the ECHELON-3 trial (NCT04404283).

Results

PATIENTS AND TREATMENT

- Among 476 unique patients qualified for the study and 716 qualifying patient-LOTs, ECOG score was known for 408 qualifying index-LOTs (57%) and was M/U for 308 (43%).
- Patient characteristics were similar between ECOG 0-2 vs. M/U groups and were aligned with expected characteristics of the real-world 3L+ DLBCL population. (**Table 1**)
- Although missingness across variables was slightly greater among the ECOG M/U group, key characteristics were similar between groups except for index LOT initiation year. This may reflect variation in clinical practice patterns over time.
- About half of patients with ECOG 0-2 at baseline and 30.5% of those with ECOG M/U at baseline had ECOG 0-2 at diagnosis. ECOG ≥ 3 was uncommon at diagnosis (ECOG 0-2: 0.7%; M/U: 1.3%).

Table 1. Patient and clinical characteristics

| | ECOG 0-2 N=408 | ECOG M/U N=308 |
|--|-------------------|-------------------|
| Age at Initial Diagnosis, median [IQR] | 64.0 [55.0, 72.0] | 64.0 [54.0, 72.0] |
| Age at Index, median [IQR] | 66.5 [57.0, 75.0] | 66.5 [56.0, 76.0] |
| Sex, n (%) | | |
| Female | 163 (40.0) | 113 (36.7) |
| Male | 245 (60.0) | 195 (63.3) |
| Race, n (%) | | |
| Asian | 13 (3.2) | 13 (4.2) |
| Black or African American | 23 (5.6) | 14 (4.5) |
| White | 290 (71.1) | 208 (67.5) |
| Other | 73 (17.9) | 62 (20.1) |
| Unknown | 9 (2.2) | 11 (3.6) |
| Practice Setting, n (%) | | |
| Academic | 147 (36.0) | 114 (37.0) |
| Community | 261 (64.0) | 194 (63.0) |
| Follow-Up Time from Index (Reverse KM; months), median (95% CI) | 36.1 (28.0, 41.5) | 17.0 (15.0, 24.2) |
| Year of Index, n (%) | | |
| 2017 | 11 (2.7) | 9 (2.9) |
| 2018 | 79 (19.4) | 31 (10.1) |
| 2019 | 81 (19.9) | 45 (14.6) |
| 2020 | 94 (23.0) | 41 (13.3) |
| 2021 | 60 (14.7) | 65 (21.1) |
| 2022 | 41 (10.0) | 62 (20.1) |
| 2023 | 42 (10.3) | 55 (17.9) |
| Stage at Diagnosis by Any Staging System, n (%) | | |
| 1 | 17 (4.2) | 9 (2.9) |
| 2 | 71 (17.4) | 50 (16.2) |
| 3 | 118 (28.9) | 76 (24.7) |
| 4 | 163 (40.0) | 128 (41.6) |
| Unknown | 39 (9.6) | 45 (14.6) |
| Calculated International Prognostic Index (IPI) at Diagnosis, n (%) | | |
| Low Risk (IPI Score 0-1) | 48 (11.8) | 29 (9.4) |
| Low-Intermediate Risk (IPI Score 2) | 63 (15.4) | 27 (8.8) |
| High-Intermediate Risk (IPI Score 3) | 30 (7.4) | 11 (3.6) |
| High Risk (IPI Score 4-5) | 12 (2.9) | 4 (1.3) |
| Unknown | 255 (62.5) | 237 (76.9) |
| ECOG Status at Diagnosis, n (%) | | |
| 0-2 | 209 (51.2) | 94 (30.5) |
| ≥ 3 | 3 (0.7) | 4 (1.3) |
| Unknown | 196 (48.0) | 210 (68.2) |

Methods

- Eligible adult patients who received ≥ 2 prior lines of therapy (LOTs) were identified from COTA's real-world database of curated electronic health records using inclusion/exclusion criteria derived from the ECHELON-3 trial.
- Qualifying patient-LOTs were identified based on the following criteria: 3L+ initiation between October 18, 2017 and December 31, 2023, no ECOG performance status ≥ 3 at baseline, no evidence of solid tumor malignancy two years prior to index LOT, no exclusionary treatment history, and sufficiently precise key study dates (at least month and year precision).
- Multiple index date qualification was used to identify all, first, and last qualifying LOTs.^{2,3,4,5}
- Baseline period was the earlier of 30 days pre-index or end of prior LOT not exceeding -90 to +7 days post-index. rwOS and rwTTNT were estimated by Kaplan-Meier (KM) method and follow-up time by reverse KM.
- A robust variance estimate was used to account for within subject correlation caused by having multiple observations per patient. Mortality data uses health records and obituary sources, validated previously.⁶

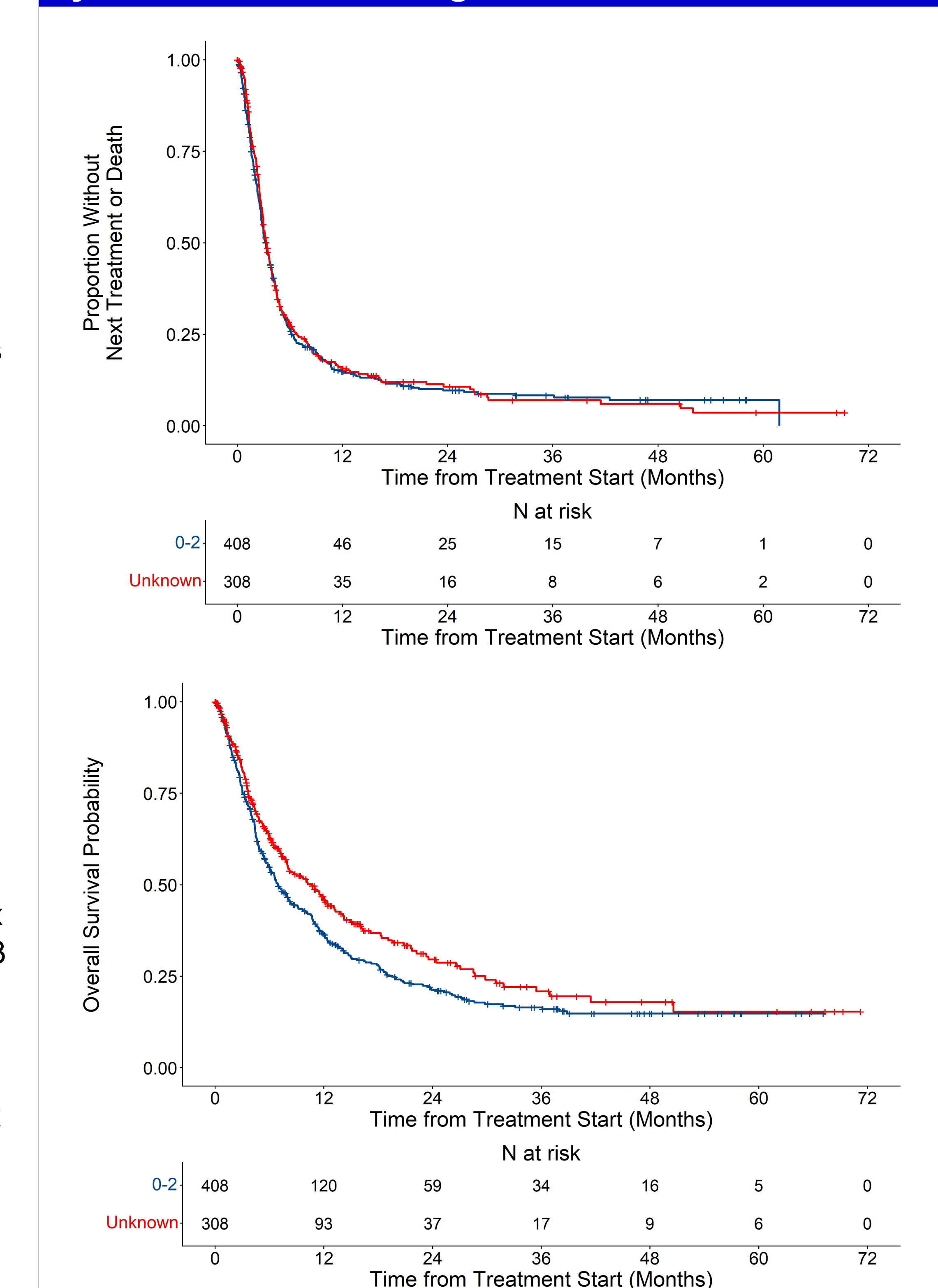
Table 2. Real-world outcomes by ECOG 0-2 vs missing/unknown

| | N | rwTTNT Events | rwTTNT Median (95% CI) | rwOS Events | rwOS Median (95% CI) |
|-----------------------------|-----|------------------|---------------------------|----------------|-------------------------|
| All Qualifying-LOTs | | | | | |
| ECOG 0-2 | 408 | 345 | 3.3 (2.8, 3.7) | 300 | 6.9 (5.8, 9.1) |
| ECOG M/U | 308 | 249 | 3.4 (3.0, 3.8) | 180 | 10.6 (7.9, 13.8) |
| First Qualifying-LOT | | | | | |
| ECOG 0-2 | 263 | 215 | 3.6 (3.0, 4.4) | 183 | 10.1 (7.4, 12.6) |
| ECOG M/U | 213 | 174 | 3.4 (3.0, 4.0) | 116 | 13.3 (10.6, 20.8) |
| Last Qualifying-LOT | | | | | |
| ECOG 0-2 | 271 | 208 | 3.6 (3.1, 4.3) | 185 | 5.2 (4.5, 6.7) |
| ECOG M/U | 205 | 146 | 3.8 (3.3, 4.5) | 114 | 8.2 (5.9, 16.1) |

OUTCOMES

- Median follow-up time (reverse KM) among all qualifying LOTs for the ECOG 0-2 group was 36.1 months (95% CI: 28.0, 41.5) and for the ECOG M/U group was 17.0 months (95% CI: 15.0, 24.2). (**Table 1**)
- Although follow-up time was shorter for ECOG M/U group, median rwTTNT and rwOS were similar among all-qualifying, first-qualifying, and last-qualifying LOTs.
 - Median rwTTNT among all qualifying-LOTs for the ECOG 0-2 group was 3.3 months (95% CI: 2.8, 3.7) and among the ECOG M/U group was 3.4 months (95% CI: 3.0, 3.8). (**Table 2**).
 - There were 480 death events across all qualifying LOTs (ECOG 0-2: 300 death events and ECOG M/U: 180).
 - Among all qualifying-LOTs, median rwOS among the ECOG 0-2 and M/U groups was 6.9 months (95% CI: 5.8, 9.1), and 10.6 months (7.9, 13.8), respectively. (**Table 2 & Figure 1**)
 - Median rwOS among unique patients with ECOG 0-2 and M/U at first-qualifying index date was 10.1 (95% CI: 7.4, 12.6) and 13.3 months (95% CI: 10.6, 20.8), respectively. (**Table 2**)
 - Median rwOS among unique patients with ECOG 0-2 and M/U at last-qualifying index date was 5.2 (95% CI: 4.5, 6.7) and 8.2 months (95% CI: 5.9, 16.1), respectively.
- KM curves by ECOG status among the all qualifying-LOTs groups are presented in **Figure 1**.

Figure 1. Kaplan-Meier curves of rwTTNT and rwOS by ECOG 0-2 vs missing/unknown



ECOG: Eastern Cooperative Oncology Group; KM: Kaplan-Meier; OS: overall survival; rw: real-world; TTNT: time to next treatment