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# Ongoing Phase 3 waveLINE-010 Study of Zilovertamab Vedotin Plus R-CHP Versus R-CHOP in Participants With Untreated Diffuse Large B-Cell Lymphoma

Russell Gollard[1]; Jessica Flynn[2]; Nishitha Reddy[2]; Rushdia Z. Yusuf[2]; Anas Al-Janadi[3]

[1]Optum Care Cancer Care, Las Vegas, NV, USA; [2]Merck & Co., Inc., Rahway, NJ, USA; [3]Corewell Health, Grand Rapids, MI, USA

## Background

- Despite recent advances in the treatment of diffuse large B-cell lymphoma (DLBCL), 5-year survival rates range from 53% to 70%[1,2]
- Modest improvements have been made in the standard-of-care treatment of DLBCL, in which rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) immunochemotherapy has been used in the first-line setting[3]
- Zilovertamab vedotin, a receptor tyrosine kinase-like orphan receptor (ROR1)–targeting antibody-drug conjugate with a monomethyl auristatin E payload, has shown promising efficacy in patients with DLBCL[4,5]
- The randomized, open-label, phase 3 waveLINE-010 study (NCT06717347) will evaluate the efficacy and safety of zilovertamab vedotin in combination with rituximab plus cyclophosphamide, doxorubicin, and prednisone (R-CHP) versus R-CHOP in participants with untreated DLBCL

## Objectives

### Primary

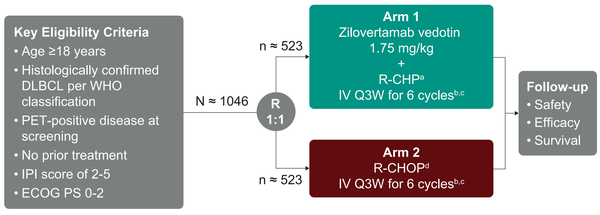
- To evaluate progression-free survival (PFS) per Lugano criteria by blinded independent central review (BICR) of zilovertamab vedotin in combination with R-CHP versus R-CHOP

### Secondary

- To evaluate the following in participants treated with zilovertamab vedotin in combination with R-CHP versus R-CHOP
  - Complete response (CR) rate at end of treatment (EOT) per Lugano criteria by BICR
  - Overall survival (OS)
  - Event-free survival (EFS) per Lugano criteria by BICR
  - Duration of CR
  - Safety and tolerability
  - Changes from baseline in health-related quality-of-life assessments

## Methods

### Study design




**Stratification factors**

- 3 geographic regions (Western Europe, the United States, Canada, and Australia vs Asia vs rest of world)
- IPI score (2 vs 3-5)
- Bulk (<7.5 cm vs ≥7.5 cm)

ECOG PS, Eastern Cooperative Oncology Group performance status; IPI, International Prognostic Index; IV, intravenously; PET, positron emission tomography; Q3W, every 3 weeks; R, randomized; WHO, World Health Organization.
[a]Rituximab 375 mg/m² plus cyclophosphamide 750 mg/m², doxorubicin 50 mg/m², and prednisone 100 mg/day.
[b]Prednisone will be administered per approved product label on days 1 and 5 Q3W.
[c]Participants with high-grade DLBCL, with an IPI score of 3-5, will receive 2 additional cycles of rituximab 375 mg/m² IV Q3W (or biosimilar).
[d]Rituximab 375 mg/m² plus cyclophosphamide 750 mg/m², doxorubicin 50 mg/m², vincristine 1.4 mg/m², and prednisone 100 mg/day.

### Participant eligibility criteria

#### Key inclusion criteria

- Age ≥18 years
- Histologically confirmed DLBCL per WHO classification of neoplasms of the hematopoietic and lymphoid tissues, including but not limited to
  - DLBCL, NOS
  - DLBCL leg type
  - Epstein-Barr virus–positive DLBCL
  - T-cell histiocytic-rich DLBCL
- PET-positive disease at screening (4-5 on the Lugano 5-point scale)
- No prior treatment for DLBCL
- IPI score of 2-5[a]
- ECOG PS score of 0-2 within 7 days of randomization[b]
- Adequate organ function

#### Key exclusion criteria

- History of transformation of indolent disease to DLBCL
- Diagnosis of primary mediastinal B-cell lymphoma or gray zone lymphoma
- Ann Arbor stage I DLBCL
- Clinically significant (active) cardiovascular disease
- Clinically significant pericardial or pleural effusion
- Ongoing grade >1 peripheral neuropathy
- A demyelinating form of Charcot-Marie-Tooth disease
- HIV and history of Kaposi sarcoma and/or multicentric Castleman disease
- Ongoing corticosteroid therapy (exceeding 30 mg daily of prednisone equivalent)
- Known additional malignancy that is progressing or has required active treatment within the past 2 years
- Known active central nervous system lymphoma
- Active autoimmune disease that has required systemic treatment in the past 2 years
- Active infection requiring systemic therapy
- Concurrent active hepatitis B or C virus infection
- History of allogeneic tissue/solid organ transplant

NOS, not otherwise specified.
[a]Participants with an IPI score of 2 will be capped at 30% per arm.
[b]Participants with an ECOG PS score of 2 will be capped at 20% per arm.

### Assessments and follow-up

| Assessment | Detail |
|---|---|
| Response | • Response assessments (CT scans/FDG-PET) will be performed after day 1 of cycle 4 but before day 1 of cycle 5, and then at 12 weeks after cycle 4 scan (EOT assessment)<br>• Follow-up assessments will be completed every 24 weeks for 2 years from EOT assessment, then every year for 3 years (total of 5 years) |
| AEs | • AEs will be monitored and assessed by investigators throughout the study and for 30 days after the last dose of study treatment (90 days for serious AEs, or 30 days if new anticancer therapy is initiated)<br>• AEs will be graded according to National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0 |
| PROs | • PRO measures will be administered before dosing on day 1 of every cycle, at the EOT visit, and at the 30-day safety follow-up visit |

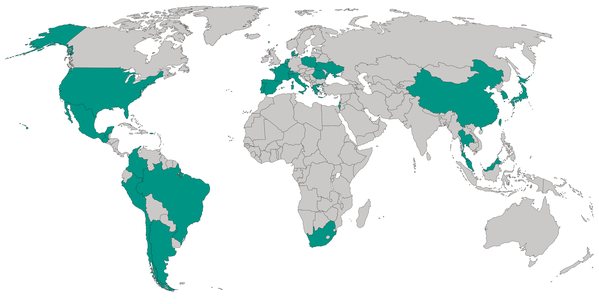
AE, adverse event; CT, computed tomography; FDG-PET, fluorodeoxyglucose positron emission tomography; PRO, patient-reported outcome.

### Analyses

| Analysis | Detail |
|---|---|
| Efficacy | • Efficacy analyses will be conducted in the intention-to-treat population, which consists of all randomly assigned participants<br>• PFS, OS, and EFS will be estimated using the Kaplan-Meier method. The hazard ratio and its 95% CI will be estimated using a stratified Cox proportional hazards model using the Efron method of tie handling<br>• CR rate at EOT will be compared between treatment groups using the Miettinen and Nurminen method, and point estimates and 95% CIs will be calculated using the exact binomial method |
| Safety | • Safety analyses will be conducted in the all-participants-as-treated population, which will consist of all participants who receive ≥1 dose of study treatment<br>• Safety will be summarized descriptively |
| PROs | • PROs will be assessed in all randomly assigned participants who have ≥1 PRO assessment available for the specific end point and have received ≥1 dose of study treatment |

## Status

### Sites of participant enrollment for waveLINE-010 (green)



### References

1. Crump M et al. *Blood.* 2017;130:1800-1808.
2. Garg M et al. *Blood.* 2022;140:12106-12107.
3. Ohmachi K et al. *Blood Adv.* 2021;5:984-993.
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### Contact information

Contact the author at russell.gollard1@optum.com for questions and comments.

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