MCL-339

# GLOBRYTE: A Phase III, Open-label, Multicenter, Randomized Trial Evaluating Glofitamab Monotherapy in Patients With Relapsed or Refractory Mantle Cell Lymphoma

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## Summary

GLOBRYTE is a Phase III, open-label, multicenter, randomized, controlled trial in patients with relapsed/refractory (R/R) mantle cell lymphoma (MCL)

Patients will receive either fixed-duration glofitamab monotherapy or investigator's (INV) choice of rituximab + bendamustine (BR) or rituximab + lenalidomide (R-Len)

The primary objective is to evaluate the efficacy of glofitamab monotherapy compared with INV choice of BR or R-Len with respect to progression-free survival (PFS)

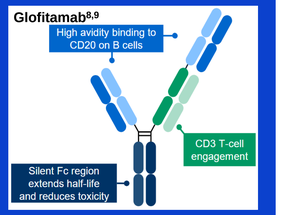
GLOBRYTE will enroll approximately 182 patients with R/R MCL from an estimated 77 sites in the Asia-Pacific region, Europe and the USA

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## Background

- R/R MCL is an aggressive disease with a lack of curative treatments and a poor prognosis, particularly for patients progressing on Bruton tyrosine kinase inhibitors (BTKi)[1–3]
- Current options for MCL after ≥1 prior therapies (including a BTKi) include:
  - Chimeric antigen receptor (CAR) T-cell therapy brexucabtagene autoleucel, which has high response rates but the potential for severe toxicities[4,5]
  - Pirtobrutinib, which is a reversible and non-covalent BTKi that is FDA-approved for R/R MCL, has an overall response rate (ORR) and complete response (CR) rate of <60% and <20%, respectively[6,7]
- Alternative therapies are urgently needed to improve outcomes in R/R MCL[2]
- Glofitamab is a CD20xCD3 bispecific antibody with a 2:1 format that engages and redirects T-cells to eliminate B cells[8,9]




## Phase I/II results for glofitamab in R/R MCL, with a fixed treatment duration, showed high response rates and durable responses, with manageable and mostly low-grade cytokine release syndrome (CRS)

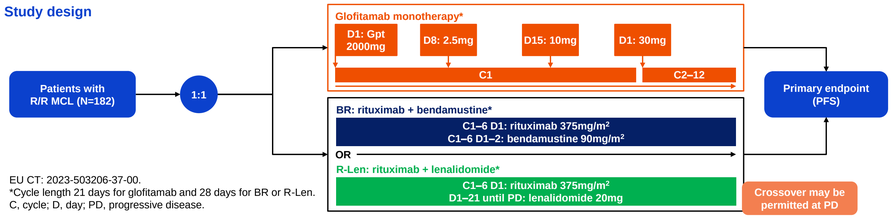
- Fixed-duration glofitamab monotherapy was administered with step-up dosing and obinutuzumab pretreatment (Gpt; 1000 or 2000mg), to mitigate the risk of CRS[10]

| Efficacy results | Safety results |
|---|---|
| • High response rate (84% ORR; 73% CR)<br>• Median DoCR was 10.0 (95% CI: 4.9–NE) months and 74.1% (20/27) of patients who achieved a CR remained in remission at data cut-off* | • Manageable, mostly low-grade CRS in heavily pretreated patients with R/R MCL (N=37) most of whom had failed prior BTKi therapy |

*Note that these results are not yet stable and could vary in the future as many patients were still on treatment at the time of the data cut-off and so the median duration of follow-up was relatively short. CI, confidence interval; DoCR, duration of complete response; NE, not estimable.

## GLOBRYTE (NCT06084936) is a Phase III, open-label, multicenter, randomized, controlled trial in R/R MCL

### Study design




EU CT: 2023-503206-37-00.
*Cycle length 21 days for glofitamab and 28 days for BR or R-Len.
C, cycle; D, day; PD, progressive disease.

### Key eligibility criteria

| Inclusion criteria | Exclusion criteria |
|---|---|
| • Aged ≥18 years<br>• Histologically confirmed MCL with documentation of either overexpression of cyclin D1 or the presence of t(11:14)<br>• R/R MCL; measurable disease<br>• ECOG performance status 0–2<br>• ≥1 prior line of systemic therapy including BTKi and another option (e.g. anti-CD20 monoclonal antibody, chemotherapy, or targeted agent such as bortezomib)<br>• Life expectancy ≥12 weeks<br>• Confirmed availability of tumor biopsy tissue (pre-treatment or recent archival specimen) | • Leukemic, non-nodal MCL<br>• Prior CAR T-cell therapy or treatment with glofitamab or other CD20xCD3 bispecific antibodies<br>• Primary/secondary CNS lymphoma, or history of CNS lymphoma or other malignancies*<br>• Current or prior CNS disease (including epilepsy or CNS vasculitis; stroke or transient ischemic attack within the past 2 years)<br>• Significant CV disease (New York Heart Association Class III or IV cardiac disease/Objective Assessment Class C or D), MI within the last 6 months, unstable arrhythmias, or unstable angina<br>• Known active infection at time of enrollment |

*Except for curatively-treated basal or squamous cell skin cancer, *in-situ* cervical cancer, low-grade early prostate cancer, or any other malignancy treated with curative intent and in remission for ≥2 years. CNS, central nervous system; CV, cardiovascular; ECOG, Eastern Cooperative Oncology Group; MI, myocardial infarction.

## Treatment

- Eligible patients will be randomly assigned
- Patients will receive glofitamab for a fixed-duration of 12 cycles, unless PD or unacceptable toxicity occurs earlier. BR will be administered for 6 cycles and R-Len until PD
- Crossover to glofitamab may be permitted if PD is confirmed radiologically by the INV

## Study objectives

**Primary objective**

To evaluate the efficacy of glofitamab monotherapy compared with INV choice of BR or R-Len with respect to PFS

**Primary efficacy endpoint**

PFS determined by BIRC

| Secondary efficacy endpoints | Safety endpoints |
|---|---|
| INV-assessed PFS | Incidence and severity of AEs:<br>• Vital signs<br>• Laboratory test results |
| | **Exploratory/other endpoints** |
| OS | Evaluation of prognostic biomarkers and their association with response, including high risk factors (i.e. high Ki67, TP53 alterations) |
| | Evaluation of MRD response and its relationship with clinical outcome |
| BIRC- and INV-assessed<br>• CR<br>• ORR<br>• DoR/DoCR | Immunogenicity against glofitamab |
| | Pharmacokinetics |
| | Health-related quality of life including:<br>• Time to deterioration in physical functioning or fatigue (10-point decrease in score vs baseline) on the EORTC QLQ-C30<br>• Change in lymphoma symptoms on the FACT-Lym questionnaire |

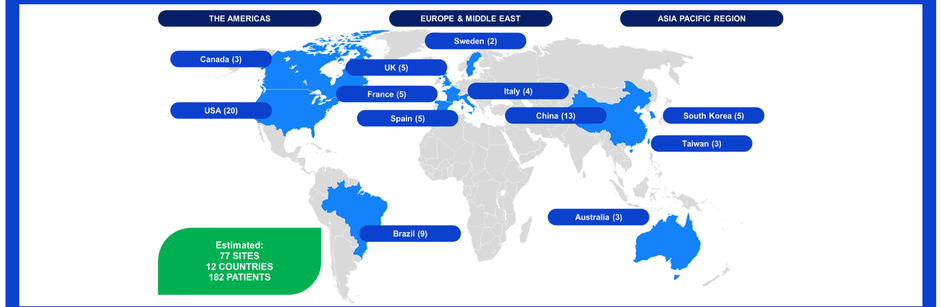
PFS and tumor responses will be determined according to 2014 Lugano Response Criteria for MCL.[11]
AE, adverse event; BIRC, blinded independent review committee; DoR, duration of response; EORTC QLQ-C30, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30; FACT-Lym, Functional Assessment of Cancer Therapy – Lymphoma; MRD, minimal residual disease; OS, overall survival.

### Statistical methods

- Stratified hazard ratios with 95% CIs will be calculated for PFS and OS, and odds ratios (95% CI) will be calculated for differences in CR rate and ORR between treatment arms
- Treatment comparisons will be made with a 2-sided, 0.05 level, stratified log-rank test

## Enrollment sites

- An estimated 77 sites will enroll approximately 182 patients with R/R MCL in the Asia-Pacific region, Europe and the USA
- The study has commenced recruitment




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**Disclosures**

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