2026 ASH Annual Meeting and Exposition
December 12-15, 2026, New Orleans, Louisiana

Sustained benefit of zanubrutinib in relapsed/refractory (R/R) marginal zone lymphoma: MAGNOLIA + LTE1

Authors: Stephen S. Opat,[1] Kim M. Linton,[2] Pamela McKay,[3] Jie Jin,[4] Magdalena Sobieraj-Teague,[5] Peter Browett,[6] Xiaoyan Ke,[7] Fontanet Bijou,[8] Alessandra Tedeschi,[9] Minoru Kanaya,[10] Xin Yan,[11] Jing Rong,[12] Jun Zhang,[13] Jamie Hirata,[13] Judith Trotman[14]

Affiliations: [1]Lymphoma Research Group, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia; [2]Division of Cancer Sciences, Manchester Cancer Research Centre, University of Manchester, Manchester, UK; [3]Beatson West of Scotland Cancer Centre, Glasgow, UK; [4]The First Affiliated Hospital, Zhejiang University College of Medicine, Hangzhou, China; [5]Flinders Medical Centre, Bedford Park, SA, Australia; [6]Auckland City Hospital, Grafton, Auckland, New Zealand; [7]Peking University Third Hospital, Beijing, China; [8]Institut Bergonié, Bordeaux, France; [9]ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy; [10]Department of Hematology, Aiiku Hospital, Sapporo, Japan; [11]BeOne Medicines, Ltd, Shanghai, China; [12]BeOne Medicines, Ltd, Beijing, China; [13]BeOne Medicines, Ltd, San Carlos, CA, USA; [14]Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia

Introduction: We report up to 7 years of follow-up from MAGNOLIA (NCT03846427), an open-label, single-arm, multicenter, phase 2 study of zanubrutinib in patients with R/R marginal zone lymphoma (MZL), and its long-term extension (LTE1; NCT04170283).

Methods: This ad hoc analysis integrated efficacy and safety for patients enrolled in MAGNOLIA and those who rolled over to LTE1. Patients enrolled in LTE1 continued zanubrutinib at the same dose received in MAGNOLIA. Safety was assessed every 3

months, while efficacy was evaluated every 6 months with regular restaging scans at investigators' discretion. All disease progression events were independently confirmed.

Results: Of 68 patients enrolled in the MAGNOLIA study, 66 were efficacy evaluable; 36 patients (52.9%) enrolled in LTE1 (32 [47.1%] continued treatment with zanubrutinib; 4 [5.9%] are in survival follow-up). Baseline characteristics were previously reported (Opat *Blood Adv.* 2023). As of April 1, 2026, with observation (MAGNOLIA + LTE1) up to 7 years (median study follow-up, 35.3 months; range, 1.6-84.3), the overall response rate by investigator was 77.3% (95% CI, 65.3-86.7). With approximately four years of extended follow-up, the complete response (CR) rate increased to 37.9% (95% CI, 26.2-50.7) from 28.8%, with five patients previously assessed with partial response and one patient assessed as a stable disease converting to CR since the study closure of MAGNOLIA. The median time to response remained at 2.99 months. Median duration of response (DOR) was 38.8 months (95% CI, 22.1-not estimable); the DOR rate was 58.4% (95% CI, 43.5-70.6) at 36 months and 47.5% (95% CI, 33.0-60.6) at 60 months. Median progression-free survival (PFS) was 34.3 months (95% CI, 16.5-49.6); the PFS rate was 48.1% (95% CI, 35.4-59.8) at 36 months, 37.8% (95% CI, 25.8-49.7) at 60 months, and 36.1% (95% CI, 24.3-48.0) at 72 months. Median overall survival (OS) was not reached; the OS rate was 74.4% (95% CI, 60.8-83.9) at 60 months and 72.0% (95% CI, 58.0-82.1) at 72 months. In MAGNOLIA + LTE1 (N=68), median treatment exposure was 27.8 months (range, 0.9-82.0); 36 patients (52.9%) were treated with zanubrutinib for >2 years and 24 (35.3%) for >4 years. Serious treatment-emergent adverse events (TEAEs) occurred in 52.9% (n=36) of patients, grade ≥3 TEAEs in 60.3% (n=41), TEAEs leading to treatment discontinuation in 8.8% (n=6), and fatal TEAEs in 8.8% (2.9% were due to COVID-19 pneumonia).

Conclusions: With median study follow-up of 35.3 months and the longest follow-up reaching 7 years, zanubrutinib provided rapid, durable disease control, with sustained efficacy and a consistent safety profile, underscoring its long-term clinical benefit in patients with R/R MZL.