Poster MCL-575

Updated Results From the Phase 3 ECHO Trial of Bendamustine-Rituximab With or Without Acalabrutinib in Patients With Previously Untreated Mantle Cell Lymphoma: 50 Months of Follow-up

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Objective

- To present updated efficacy and safety data from ECHO with an additional year of follow-up (median time on study: 51.9 months) and explore the impact of treatment sequencing after ABR/PBR in 1L MCL

Conclusions

- At a longer follow-up (median 60.8 months), ABR further improved PFS vs PBR
- OS, both in the intent-to-treat population and after pre-specified censoring of COVID-19 deaths, remained consistent with the previous analysis
- 1L ABR provided a 24% reduction in risk of initiating 3L therapies or death (TTNT2)
- Grade ≥3 AEs remained consistent with longer follow-up and the safety profile remains favorable with no new signals
- These results emphasize the benefits of acalabrutinib plus BR as a 1L treatment approach, improving PFS and delaying need of subsequent therapies in patients with TN MCL
- Collectively, our data demonstrated that concurrent acalabrutinib plus BR as triple front-line therapy is preferable to sequential therapy with BR followed by a BTK inhibitor

Plain language summary

Why did we perform this research?

- Mantle cell lymphoma, or MCL, is a rare type of blood cancer that affects white blood cells and is largely considered incurable.
- In a phase 3 clinical trial (the ECHO study), the regimen of acalabrutinib added to the 2-drug chemoimmunotherapy regimen bendamustine-rituximab was more effective compared to bendamustine-rituximab without acalabrutinib.
- This research provides updated data from the ECHO trial including 1 additional year of follow-up and also examines how receiving acalabrutinib plus bendamustine-rituximab as a first treatment can reduce a patient's chances of requiring future subsequent treatments for their disease.

How did we perform this research?

- Updated data from the phase 3 ECHO study were used to see how the safety and efficacy of acalabrutinib plus bendamustine-rituximab changed with 1 additional year of study follow-up.

What were the findings of this research?

- Initial treatment using acalabrutinib plus bendamustine-rituximab resulted in a reduced risk of patients needing a second or third round of therapy and increased the length of time until the third round of therapy was required, compared with starting therapy with bendamustine-rituximab without acalabrutinib.
- The study showed that continued treatment with acalabrutinib plus bendamustine-rituximab maintained efficacy and did not show any cumulative safety concerns with longer-term exposure to treatment.

What are the implications of this research?

- The results suggest that for newly diagnosed patients, starting with acalabrutinib plus bendamustine-rituximab is better at delaying the need for a subsequent therapy than bendamustine-rituximab without acalabrutinib, given the reduction in risk of needing a third round of therapy.

Where can I access more information?

- Information about the medicine(s) being used in this study and the people who are participating can be found here: https://clinicaltrials.gov/study/NCT02972840

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Presented at the 14th Annual Meeting of the Society of Hematologic Oncology (SOHO 2026); September 9–12, 2026; Houston, Texas, by Victoria Otero

Poster

Supplementary material

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of these materials.

Presented at the 14th Annual Meeting of the Society of Hematologic Oncology (SOHO 2026); September 9–12, 2026; Houston, Texas
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Introduction

- The introduction of combination therapy with the BTKi acalabrutinib plus bendamustine and rituximab (ABR) for 1L MCL is reshaping the sequencing of later lines of therapy
- In the primary analysis of the phase 3 ECHO trial (NCT02972840) in patients aged ≥65 years with TN MCL, PFS was significantly improved with ABR vs PBR (median time on study 44.9 months)[1]

Methods

- ECHO methodology and primary results were published previously[1]
- Updated efficacy (including PFS and OS) and safety data are reported based on 1 additional year of follow-up after the primary analysis (**Figure 1**)
  - Median follow-up was 60.8 months (range, 0–88.5) per reverse K-M for PFS
  - Median time on study was 51.9 months (range, 0.03–93.04) for all other outcomes
- TTNT2 was assessed in a post hoc analysis
  - As PFS2 data were not collected in the ECHO trial, TTNT2 was used as a surrogate endpoint[2]
  - TTNT2 was defined as the time from randomization to ***either*** the start of 3L antilymphoma treatment after discontinuation of randomized treatment ***or*** death

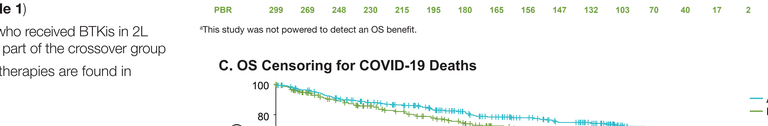
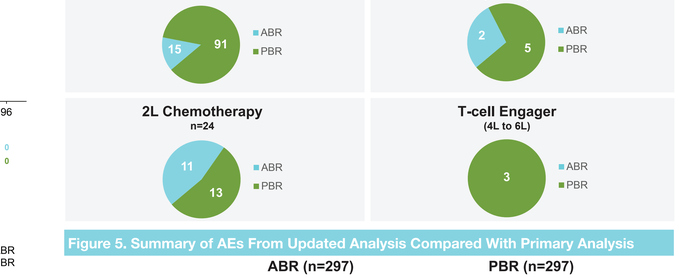


Figure 1. ECHO Study Design



[a]Bendamustine 90 mg/m^2 on days 1 and 2. [b]Rituximab 375 mg/m^2 on day 1.

Results

Patients

- In total, 598 patients were randomized to the ABR (n=299) or PBR arms (n=299)[1]

Updated Efficacy Analysis

- At 60.8 months of follow-up, PFS further improved with ABR vs PBR compared with the primary analysis (**Figure 2A**)
- PFS risk reduction with ABR vs PBR increased from 27% (primary analysis) to 32% (updated analysis)
- Median PFS was longer with ABR vs PBR (6 years vs 4 years)
- OS results were consistent with the previous analysis (**Figure 2B**)
- Although the study was not powered for OS, results were consistent with those reported previously; maturity (number of patients with event) at this timepoint remained low (~38%)
- Censoring beyond median time on study of 52 months was high
- Prespecified OS analysis censoring for COVID-19 deaths showed a similar trend as the primary analysis (**Figure 2C**)

TTNT2 and Subsequent Therapies

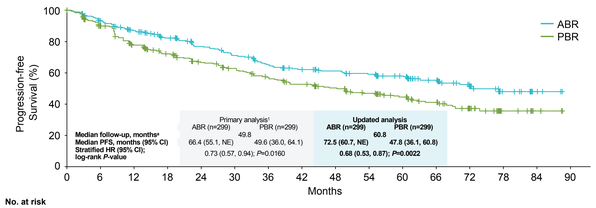
- ABR lowered the risk of needing 3L therapy (TTNT2) by 24% compared with PBR (**Figure 3**)
- At 48 months, the percentage of patients who had not yet initiated 3L therapy or had not died was 67.6% for ABR vs 59.2% for PBR
- Need for subsequent anticancer therapy was 3-fold higher with PBR, at 11% (33/299 patients) with ABR vs 33% (100/299 patients) with PBR (**Table 1**)
- 57 of 79 patients in the PBR arm who received BTKis in 2L received acalabrutinib on study as part of the crossover group
- Additional details on subsequent therapies are found in **Figure 4**

Updated Safety Analysis

- The safety profile remains favorable and similar between arms with longer follow-up, with no new signals despite continuous acalabrutinib therapy in the ABR arm (**Figure 5**)
- In the ABR arm, 1 new case of grade ≥3 atrial fibrillation was reported (primary analysis, 4.0%; updated analysis, 4.4%)
- In the PBR arm, 1 new case of ventricular tachyarrhythmia was reported (primary analysis, 2.4%; updated analysis, 3.0%)
- The total incidence of grade ≥3 cardiac events remained the same for PBR (6.1%) and included 1 new case for ABR (primary analysis, 7.7%; updated analysis, 8.1%)
- The cumulative event rate of grade ≥3 AEs overall was comparable between treatment arms (**Figure 6**)

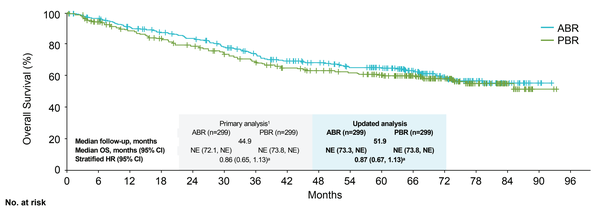
Figure 2. (A) PFS, (B) OS, and (C) OS Censoring for COVID-19 Deaths From Updated Analysis Compared With Primary Analysis

A. PFS



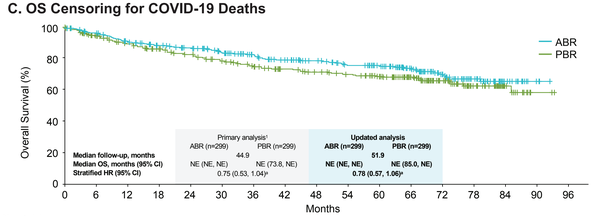
[a]Median follow-up for PFS estimated using the reverse K-M method.

B. OS



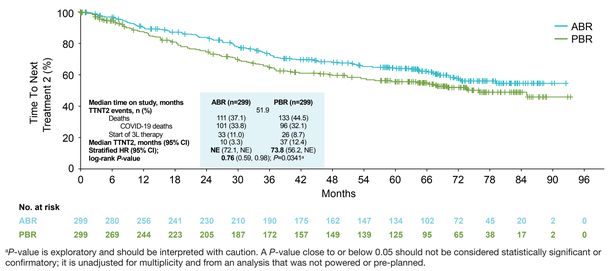
[a]This study was not powered to detect an OS benefit.

C. OS Censoring for COVID-19 Deaths



[a]This study was not powered to detect an OS benefit.

Figure 3. TTNT2



[a]P-value is exploratory and should be interpreted with caution. A P-value close to or below 0.05 should not be considered statistically significant or confirmatory; it is unadjusted for multiplicity and from an analysis that was not powered or pre-planned.

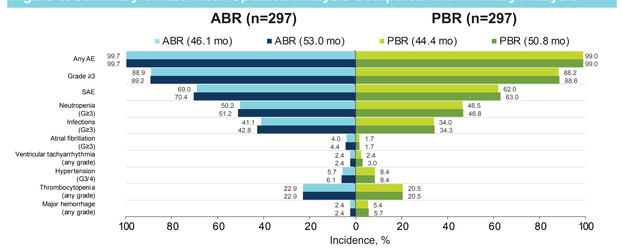
Table 1. Subsequent Anticancer Therapies

Number of Patients	ABR (n=299)	PBR (n=299)
≥1 subsequent anticancer therapy	33	100
2L anticancer therapy[a,b]	33	100
BTKi	12	79
Chemotherapy	11	13
Non-BTKi targeted therapy[c]	9	6[e]
Others[d]	1	3[e]
3L anticancer therapy[a,b]	10	37
BTKi	3	7
Chemotherapy	4	19
Non-BTKi targeted therapy[c]	3	11
4L+ anticancer therapy[a,b]	3	14
BTKi	0	5
Chemotherapy	2	7
Non-BTKi targeted therapy[c]	1	7

[a]A patient receiving multiple subsequent anticancer therapies in the same category is counted only once in the corresponding category.
[b]A patient receiving subsequent anticancer therapies in multiple categories is counted once in all categories.
[c]Targeted therapy includes all other non-BTKi targeted therapies, including CAR-T (ABR, n=2; PBR, n=5) and T-cell engager therapy (PBR, n=3).
[d][e]"Others" category included radiotherapy and Chinese medicine. "Others" category not included under 3L and 4L+ lines due to 0 applicable patients.
[e]One patient received both targeted therapy (sonrotoclax) and other (radiotherapy) therapy.

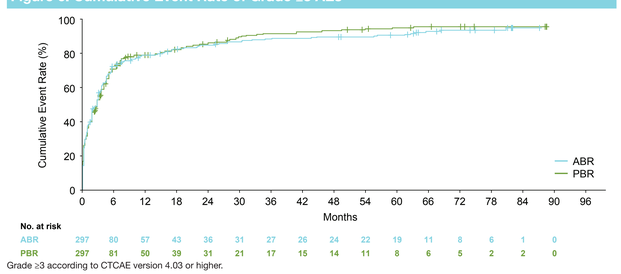
Figure 4. Details on Subsequent Therapies

Figure 5. Summary of AEs From Updated Analysis Compared With Primary Analysis



Median time on study was based on full analysis set (n=299 for both arms); AE incidences are from the safety analysis set (n=297).

Figure 6. Cumulative Event Rate of Grade ≥3 AEs



Grade ≥3 according to CTCAE version 4.03 or higher.

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Abbreviations

1L, first-line; 2L, second line; 3L, third-line; 4L+, fourth-line or greater; ABR, acalabrutinib plus bendamustine-rituximab; AE, adverse event; BID, twice daily; BR, bendamustine-rituximab; BTK, Bruton tyrosine kinase; BTKi, Bruton tyrosine kinase inhibitor; CAR-T, chimeric antigen receptor T-cell therapy; CI, confidence interval; CTCAE, Common Terminology Criteria for Adverse Events; DCO, data cutoff; ECI, event of clinical interest; ECOG PS, Eastern Cooperative Oncology Group performance status; G, grade; HR, hazard ratio; K-M, Kaplan-Meier; MCL, mantle cell lymphoma; NE, not estimable; ORR, overall response rate; OS, overall survival; PBR, placebo plus bendamustine-rituximab; PD, progressive disease; PFS, progression-free survival; PFS2, time to second disease progression; PO, orally; PR, partial response; SAE, serious adverse event; SCT, stem cell therapy; sMIPI, simplified MCL International Prognostic Index; TN, treatment naive; TTNT2, time to second subsequent treatment

References

1. Wang M, et al. *J Clin Oncol*. 2025;43:2276-84.
2. European Medicines Agency (Committee for Medicinal Products for Human Use). Guideline on the evaluation of anticancer medicinal products in man (EMA/CHMP/205/95 Rev.5). 2017.