Benefits of Rituximab Maintenance After First-Line Bendamustine-Rituximab in Mantle Cell Lymphoma: A Meta-Analysis of Clinical Trials and Observational Studies

Julia Wang[1], Dongni Yi[1], Yajuan Gao[1], Robin R. Klebig[1], Jonas Paludo[1], Javier L. Munoz[2], Muhamad Alhaj Moustafa[3], Madiha Iqbal[3], Julio C. Chavez[3], Yucai Wang[1], Jithma P. Abeykoon[1]

[1] Mayo Clinic, Rochester, MN, United States of America; [2] Mayo Clinic, Phoenix, AZ, United States of America; [3] Mayo Clinic, Jacksonville, FL, United States of America

BACKGROUND

- The role of rituximab maintenance therapy following first-line (1L) bendamustine-rituximab (BR) induction in mantle cell lymphoma (MCL) remains controversial.
- The randomized phase 2 MAINTAIN trial (a subgroup analysis within the StiL NHL7-2008 study) showed no significant benefit in progression-free survival (PFS) or overall survival (OS) with rituximab maintenance compared to observation after 1L BR.
- However, several retrospective observational studies and real-world analyses have suggested potential improvements in PFS and/or OS with maintenance rituximab in this setting.
- These conflicting findings highlight the need for a systematic synthesis of available evidence to clarify the clinical benefit of rituximab maintenance after 1L BR in MCL.

OBJECTIVES

- We aimed to evaluate whether rituximab maintenance following 1L BR induction is associated with improved PFS and OS in patients with MCL through a systematic review and meta-analysis of randomized controlled trials (RCTs) and observational studies.

METHODS

- We searched PubMed/MEDLINE, Embase, and abstracts from major hematology/oncology conferences (e.g., ASH, ASCO, EHA) from inception to February 2026 for studies evaluating rituximab maintenance versus no maintenance (observation) after 1L BR in MCL.
- Eligible studies included RCTs and observational cohort/registry studies reporting hazard ratios (HRs) with 95% confidence intervals (CIs) for PFS and/or OS, or data allowing HR estimation. Heterogeneity among studies was assessed with I^2 statistics.
- Pooled HRs with 95% CIs were calculated using the inverse-variance method.
- A random-effects model (DerSimonian-Laird) was employed to account for anticipated heterogeneity between studies.
- A sensitivity analysis with a common-effect (fixed-effect) model was also performed.

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RESULTS

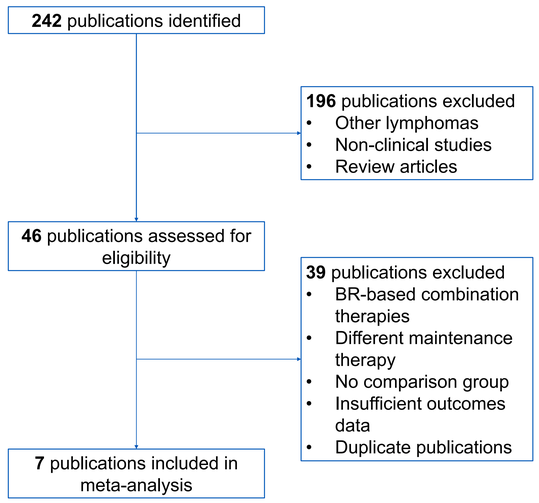

FIGURE 1. Flow diagram of study identification and selection

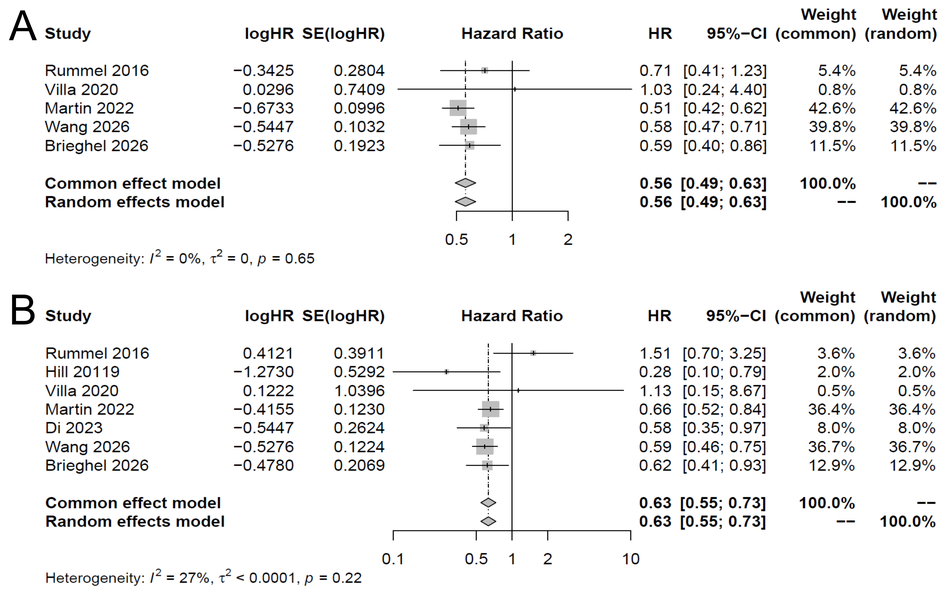

FIGURE 2. Forest plots of (A) PFS and (B) OS with rituximab maintenance versus observation after 1L BR.
Squares represent study-specific estimates, horizontal lines indicate 95% CIs, and diamonds represent pooled estimates.

TABLE 1. Summary of included studies

Study	Study setting	N (total)	n (rituximab maintenance)	n (no rituximab maintenance)	Rituximab maintenance schedule	Median follow-up (years)	PFS: HR (95% CI)	PFS: P value	OS: HR (95% CI)	OS: P value
Rummel et al, 2016 (1)	StiL randomized clinical trial	122	60	62	Every 2 months for 2 years	4.9	0.71 (0.41–1.23)	0.2267	1.51 (0.70–3.25)	0.2974
Hill et al, 2019 (2)	US multicenter retrospective study	135	78	57	Not reported	3.1	–	–	0.28 (0.10–0.79)	0.016
Villa et al, 2020 (3)	British Columbia observational study	190	144	46	Weekly 8 (22%), or every 3 months for 2 years (78%)	3.1	1.03 (0.24–4.40)	0.969	1.13 (0.15–8.67)	0.905
Martin et al, 2022 (4)	US Flatiron database	1106	427	679	Not reported	3.8	0.51 (0.42–0.62)	0.001	0.66 (0.52–0.84)	0.001
Di et al, 2023 (5)	US SEER-Medicare database	198	98	100	Not reported	5.7	–	–	0.58 (0.35–0.97)	–
Wang et al, 2026 (6)	North America multicenter observational study	703	394	309	Most commonly every 2-3 months for 2-3 years	5.8	0.58 (0.48–0.71)	0.001	0.59 (0.46–0.75)	0.001
Brieghel et al, 2026 (7)	Danish National Lymphoma Registry	244	169	75	Not reported	6.1	0.59 (0.40–0.86)	–	0.62 (0.41–0.93)	–

Abbreviations: BR, bendamustine and rituximab; CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

CONCLUSIONS

- This meta-analysis provides evidence that rituximab maintenance after 1L BR induction in MCL is associated with statistically significant improvements in both PFS and OS.
- These results, driven largely by observational data with low-to-moderate heterogeneity, support the incorporation of rituximab maintenance into routine clinical practice and future trial designs for patients with MCL receiving frontline BR.

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CONTACT

Jithma P. Abeykoon, MD

Division of Hematology, Mayo Clinic

Email: Abeykoon.Jithma@mayo.edu