



Original Articles

Treatment of Newly Diagnosed POEMS Syndrome: Bortezomib or Lenalidomide? Experience from Two Countries

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Supplementary Files

Statement of Ethics. The study protocol was approved by the ethics committee of the participating centers (Türkiye center: Cerrahpaşa Ethics Committee Approval No. 2025/479, date: 04/JUN/2025; Italy center: Comitato Etico Policlinico Gemelli Approval No. 0025195/20).

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the Good Clinical Practice (GCP) guidelines. Due to the retrospective nature of the study, patient consent was obtained in accordance with local ethics committee regulations. All data were anonymized to ensure patient confidentiality, and all investigators provided written statements of adherence to data protection and privacy standards.

Authors' Contribution List

Conception and design: DO, FA, AS

Data collection and curation: DO, FA, TO, GM, ZB, DM, FL, DD

Data analysis and statistical modeling: DO, FA, UY, AS

Drafting of the manuscript: DO, FA, TE, AS

Critical revision of the manuscript: FA, AEE, MCA, ZB, SB, LL

Supervision: SB, LL, AS

Statistical Analysis. Statistical analyses were conducted using Jamovi (version 2.6.44, The Jamovi Project, 2023; <https://www.jamovi.org>) and JASP (version 0.19.3, Jeffreys' Amazing Statistics Program, 2024; <https://jasp-stats.org>). Bayesian survival analyses were performed in R (version 4.5.0, R Foundation for Statistical Computing, Vienna, Austria) using relevant packages (RStan 2.21.8, ggplot2 3.4.0, survminer 0.4.9).

Statistical significance was set at $p \leq 0.05$. Normality of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed variables were presented as mean $\pm$ standard deviation, and non-normally distributed variables as median (range). Categorical variables were summarized as frequencies and percentages. Comparisons between bortezomib- and lenalidomide-treated groups were performed according to the distribution of variables. The Mann–Whitney U test was used for continuous, non-parametric variables. Categorical variables were analyzed using Pearson's chi-square test when expected cell counts were sufficient; otherwise, Fisher's exact test or Fisher–Freeman–Halton test was applied for sparse contingency tables.

Treatment responses were categorized according to the IMWG criteria. Very good partial response (VGPR) and complete response (CR) were combined into a single category representing deep response ($\geq$ VGPR), and response categories were analyzed as an ordinal variable ($\geq$ VGPR > PR > stable disease > progressive disease). Owing to the ordinal nature of the response categories, between-group comparisons were performed using the linear-by-linear association test, while the Fisher–Freeman–Halton exact test was reported as a sensitivity analysis. One patient with missing response data was excluded from this comparison, resulting in 25 evaluable patients.

Owing to the rarity of POEMS syndrome and the limited number of events (five deaths among 26 patients), survival between treatment groups was compared using a Bayesian log-normal accelerated failure time (AFT) model with

weakly informative priors ($\beta \sim \text{Normal}(0, 2.5)$; intercept $\sim \text{Normal}(0, 10)$; $\log(\sigma) \sim \text{Normal}(0, 1)$). The treatment effect is reported as a time ratio (TR), defined as the ratio of model-estimated median survival times (lenalidomide/bortezomib), with 95% credible intervals; a TR below 1 indicates shorter estimated survival with lenalidomide. Posterior probabilities $P(\text{TR} < 1)$ and $P(\text{TR} > 1)$ were computed, and a two-sided p-like value was derived as twice the smaller of the two. Because an AFT coefficient does not translate into a single proportional hazard ratio, hazard-scale inference was obtained from a separate univariable Bayesian Cox proportional hazards model including treatment only. Additional prognostic variables (ASCT and age at diagnosis) were examined in separate univariable Cox models on an exploratory basis; given the number of events, no multivariable model was fitted. In sensitivity analyses, the treatment effect was re-estimated under informative priors reflecting published survival expectations in POEMS syndrome (median overall survival of approximately 165 months and similar 5-year survival across regimens), with the treatment-effect prior centered at the null (Supplementary Table S1). Markov chain Monte Carlo sampling used four chains, and convergence was confirmed with R-hat values and effective sample sizes. Classical Kaplan–Meier curves and the log-rank test were computed for reference. Overall survival was measured from diagnosis; measurement from treatment initiation was examined as a sensitivity analysis and yielded unchanged results.

Supplementary Table S1. Prior sensitivity analyses for the treatment effect on overall survival

Model / prior	Estimate	95% CrI	Posterior probability
AFT, weakly informative (primary)	TR 0.58	0.04–6.81	$P(\text{TR} < 1) = 0.68$
AFT, informative	TR 1.00	0.54–1.85	$P(\text{TR} < 1) = 0.51$
Cox, weakly informative	HR 1.72	0.25–23.02	$P(\text{HR} > 1) = 0.70$
Cox, informative	HR 1.06	0.55–2.04	$P(\text{HR} > 1) = 0.56$

TR: time ratio (AFT scale); HR: hazard ratio (Cox scale); CrI: credible interval. Informative priors reflect published survival expectations in POEMS syndrome (median overall survival of approximately 165 months; similar 5-year survival across regimens), with the treatment-effect prior centered at the null. Conclusions were unchanged across all prior specifications.

Supplementary Table S2. Univariable Bayesian Cox proportional hazards analyses of overall survival

Variable	HR (median)	95% CrI	$P(\text{HR} > 1)$
Treatment (<i>lenalidomide vs bortezomib</i>)	1.74	0.24–21.77	0.70
ASCT	0.23	0.02–1.42	0.07
Age at diagnosis (<i>per 1 SD</i>)	1.45	0.60–4.02	0.78

HR: hazard ratio; CrI: credible interval; ASCT: autologous stem cell transplantation. Each variable was analyzed in a separate univariable model; given only five death events, no multivariable model was fitted and these estimates are exploratory. Age at diagnosis was standardized. Credible intervals including 1 indicate no robust association with survival. Pain at diagnosis was examined but its estimate was too unstable to report.

Supplementary Table S3. Number of patients at risk over follow-up (overall survival, from diagnosis)

Group	0 mo	50 mo	100 mo	150 mo	200 mo
Bortezomib	9	4	1	0	0
Lenalidomide	17	10	4	2	1

mo: months.