

Partial Response or Better at 6 Months Is Not a Prognostic Indicator of Progression-Free Survival in Waldenström Macroglobulinemia Treated With Zanubrutinib: a Post Hoc Analysis of the ASPEN Study

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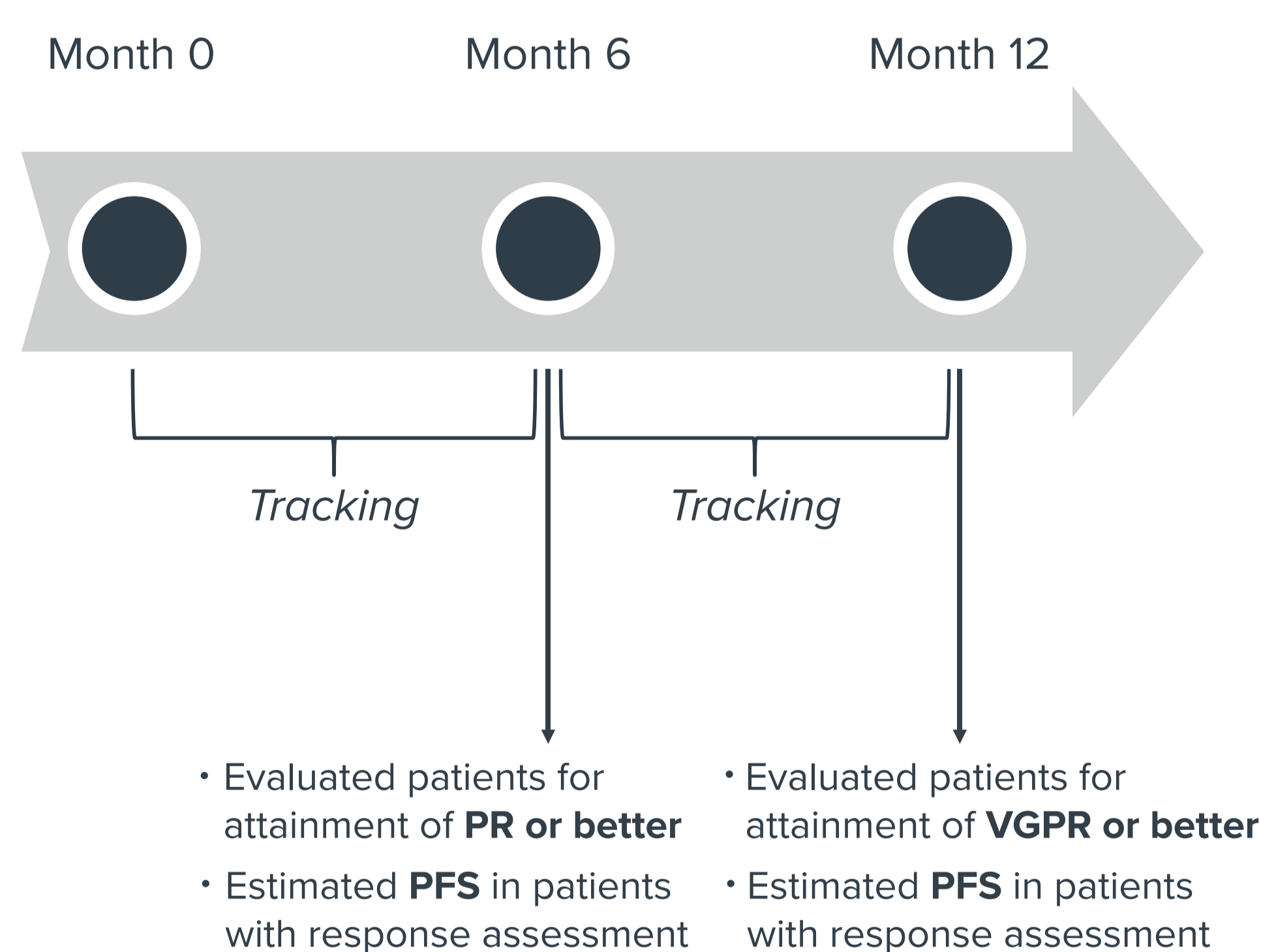
INTRODUCTION

- Attaining partial response (PR) or better at 6 months was associated with superior progression-free survival (PFS) in patients with Waldenström macroglobulinemia (WM) treated with ibrutinib (IBR) monotherapy¹
- This post hoc analysis of the ASPEN study aimed to evaluate the PFS prognostic value of attaining PR or better at 6 months in patients with WM treated with zanubrutinib (ZANU), a second-generation Bruton tyrosine kinase inhibitor (BTKi) with more selectivity and sustained occupancy than IBR
- The PFS prognostic value of very good partial response (VGPR) or better at 12 months was also evaluated

METHODS

- The methodology for the ASPEN study has been described previously²
- This post hoc analysis evaluated the attainment of PR or better at 6 months and VGPR at 12 months from therapy initiation (Figure 1)
- Responses were assessed based on the 11th International Workshop on WM (IWWM-11) criteria which rely on categorical decreases in IgM alone for PR and VGPR attainment³
- Since 2 analyses were done using the same dataset, P values <.025 were considered statistically significant

Figure 1. Post Hoc Analysis Assessment Timeline



PFS, progression-free survival; PR, partial response; VGPR, very good partial response.

RESULTS

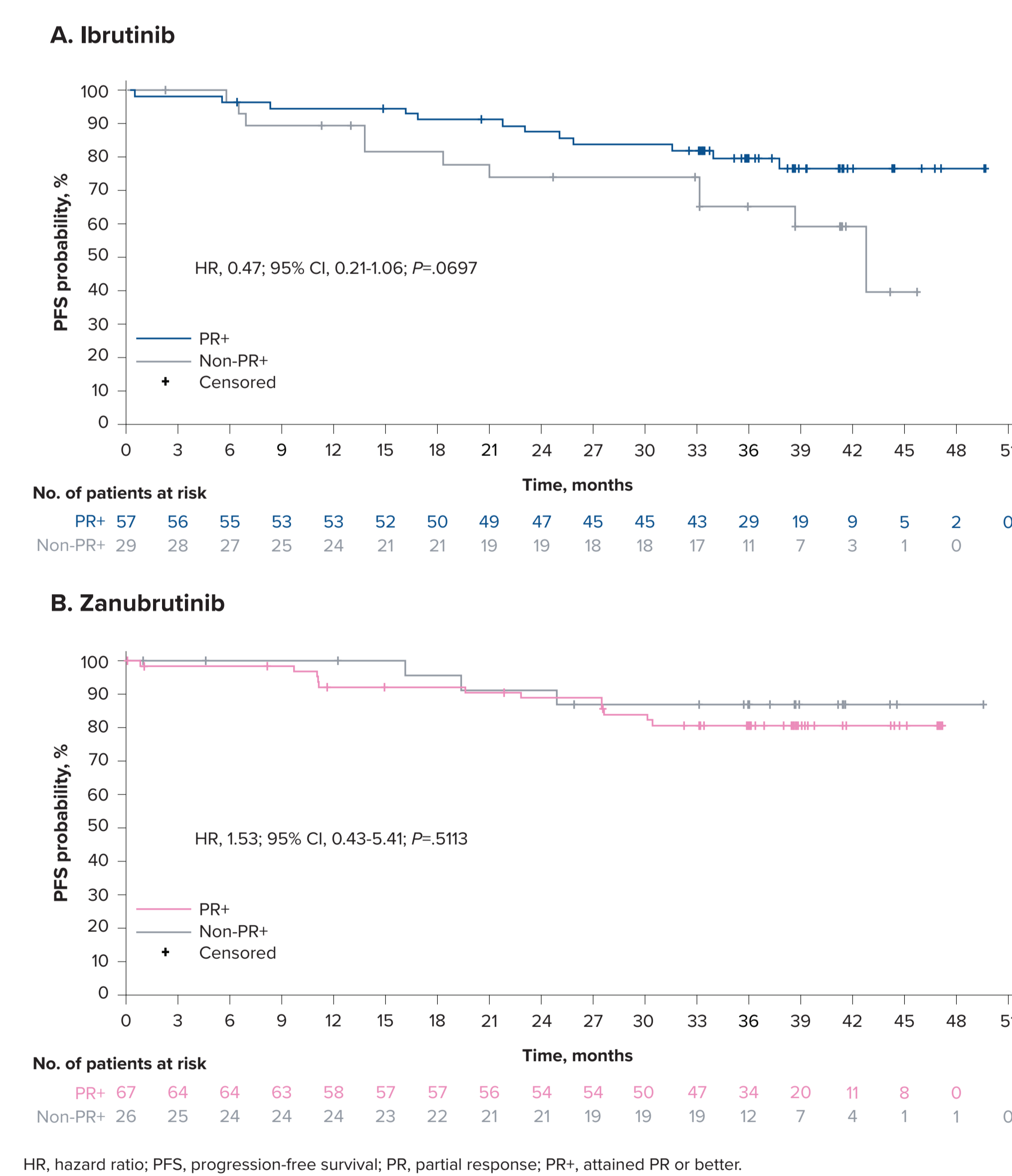
- As previously reported, there were generally no differences in baseline characteristics observed between the 2 arms; there was a higher proportion of patients with age >75 years and CXCR4^{MUT} disease in the ZANU arm⁴
- Response rates that were available at 6 and 12 months are shown in Table 1; data from the long-term follow-up analysis⁴ are also included for comparison

Table 1. Response Rates

	IBR	ZANU
LTFU response rates, n/N (%)^{4,a}		
VGPR or better	26/99 (26.3)	37/102 (36.3)
PR or better	83/99 (83.8)	87/102 (85.3)
Response rates at 6 months, n/N (%)		
VGPR or better	8/86 (9.3)	16/93 (17.2)
PR or better	57/86 (66.3)	67/93 (72.0)
Response rates at 12 months, n/N (%)		
VGPR or better	11/81 (13.6)	22/85 (25.9)
PR or better	59/81 (72.8)	63/85 (74.1)

IBR, ibrutinib; IWWM-11, 11th International Workshop on Waldenström macroglobulinemia LTFU, long-term follow-up; PR, partial response; VGPR, very good partial response; ZANU, zanubrutinib.
^aThe LTFU analysis of the ASPEN trial at the median follow-up of 44.4 months.⁴The response rates have been adjusted based on the IWWM-11 response criteria.³

Figure 2. PFS in Patients Who Attained PR or Better at 6 Months After Treatment Initiation



HR, hazard ratio; PFS, progression-free survival; PR, partial response; PR+, attained PR or better.

- PR or better at 6 months was associated with favorable PFS in patients with WM treated with IBR (Figure 2A)
- The PFS in patients with WM treated with ZANU was similar between those who did and did not attain PR or better at 6 months (Figure 2B)

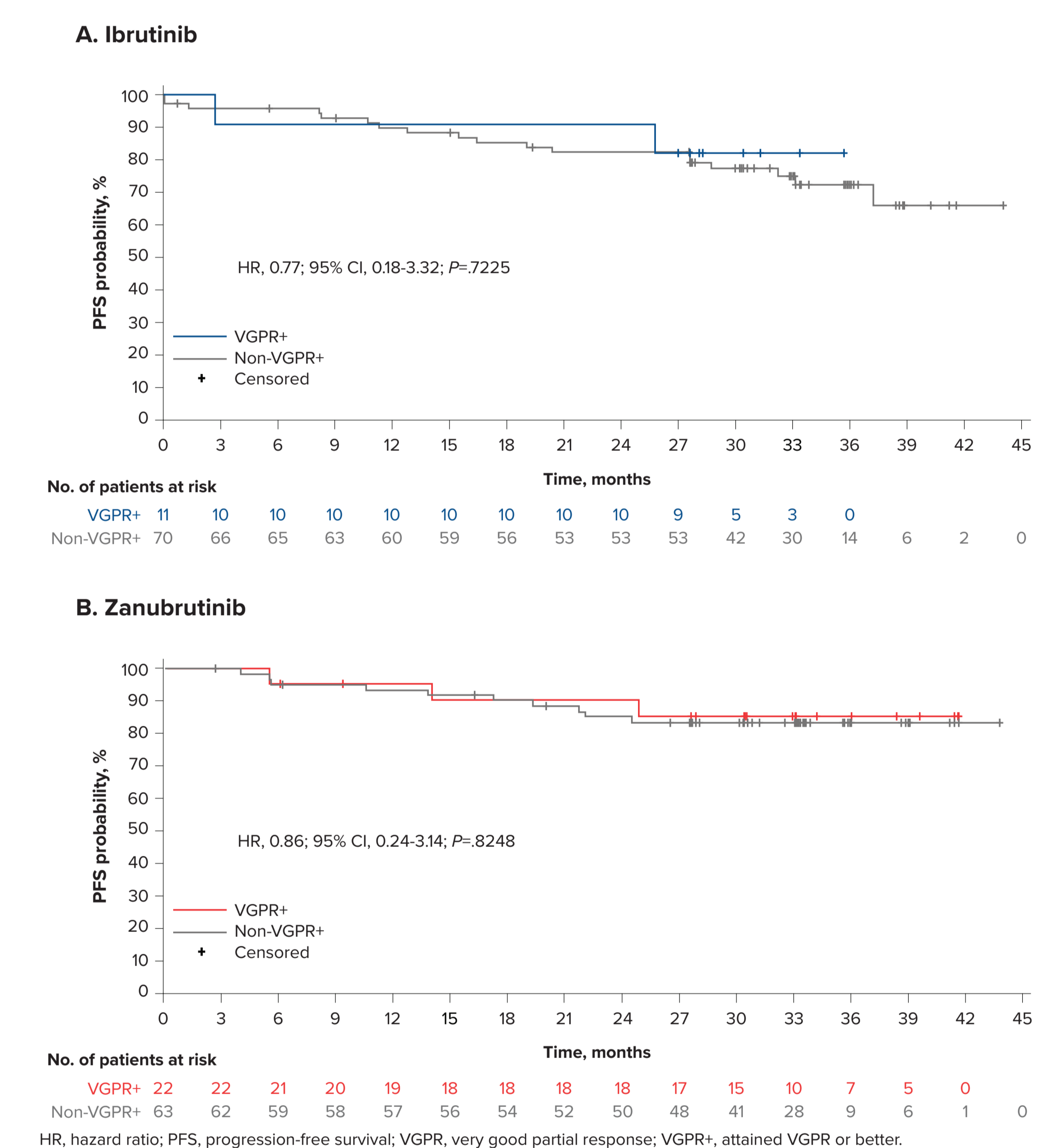
PFS event-free rates

- The 3-year landmark PFS event-free rates from the 6-month mark with ZANU (81% among those who attained PR at 6 months; 87% among those who did not attain PR at 6 months) were consistently similar to the rate in IBR-treated patients with PR or better at 6 months (80%)
- In contrast, the event-free rate was lower (65%) in patients treated with IBR who did not attain PR or better at 6 months

CONCLUSIONS

- Results of the ASPEN trial provide additional support for PR or better at 6 months as a positive prognostic factor for PFS in patients with WM treated with IBR
- PFS in ZANU-treated patients, whether or not they attained PR or better at 6 months, was similar to PFS in IBR-treated patients with PR or better at 6 months

Figure 3. PFS in Patients Who Attained VGPR or Better at 12 Months From Treatment Initiation



- Patients treated with IBR (Figure 3A) or ZANU (Figure 3B) had similar PFS rates regardless of whether they attained VGPR or better at 12 months

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DISCLOSURES

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