# Primary Results From the Phase 3 SHINE Study of Ibrutinib in Combination With Bendamustine-Rituximab and R Maintenance as a First-Line Treatment for Older Patients With Mantle-Cell Lymphoma

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## INTRODUCTION

- Older patients with previously untreated mantle cell lymphoma (MCL) are usually treated with chemoimmunotherapy regimens such as bendamustine-rituximab (BR), R-CHOP, or VR-CAP[1-4]
  - BR has become the most commonly used first-line regimen[5]
- BR alone:
  - Improved progression-free survival (PFS) compared with R-CHOP (35 vs 22 months),[6] and has a better safety profile[6,7]
- BR with rituximab (R) maintenance:
  - 2 independent observational studies showed significantly improved PFS with the addition of R maintenance after BR[5,8]
- Ibrutinib, a first-in-class, once-daily, Bruton's tyrosine kinase inhibitor, in combination with BR demonstrated activity in first-line MCL in a phase 1b study[9]

## OBJECTIVES

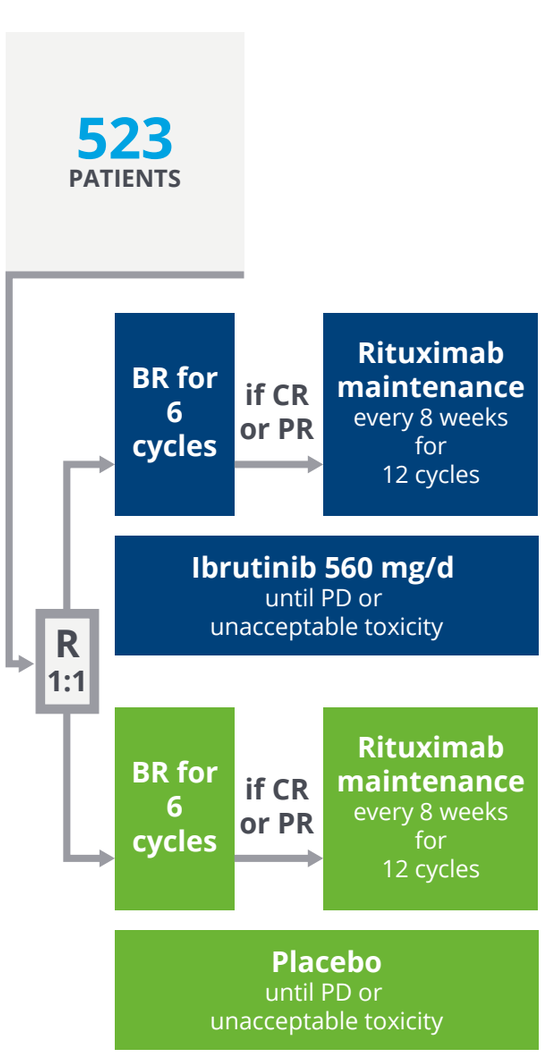
- This randomized, multicenter, double-blind phase 3 study (SHINE; NCT01776840) evaluated ibrutinib plus BR and R maintenance in older patients with untreated MCL

## SHINE STUDY DESIGN

**Patients**
- Previously untreated MCL
- ≥ 65 years of age
- Stage II-IV disease
- No planned stem cell transplant

**Stratification factor**
- Simplified MIPI score (low vs intermediate vs high)

**Enrolled between May 2013 and November 2014 at 183 sites**




**Primary end point:**
- PFS (investigator-assessed) in the ITT population

**Key secondary end points:**
- Overall survival (OS), overall response rate (ORR), time to next treatment (TTNT), and safety

CR, complete response; ITT, intent-to-treat; MIPI, Mantle Cell Lymphoma International Prognostic Index; PD, progressive disease; PR, partial response.

B-CELL MALIGNANCIES

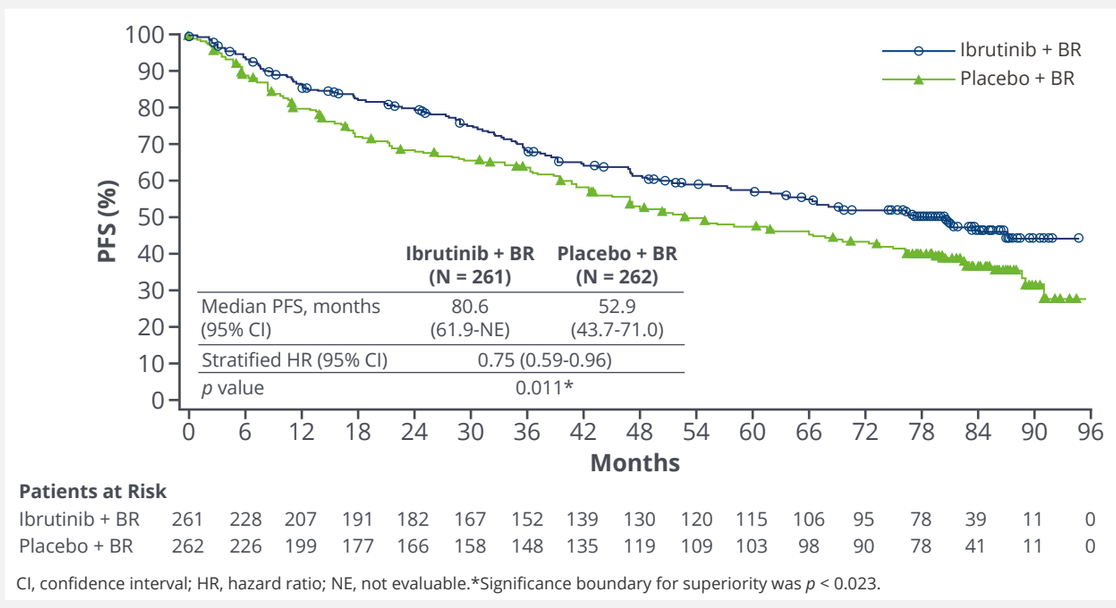
## RESULTS

### Baseline characteristics and median follow-up

- Among the 523 patients, median age was 71 years and 65.6% had low/intermediate simplified MIPI
- At primary analysis, median follow-up was 84.7 months

### Primary end point of improved PFS was met

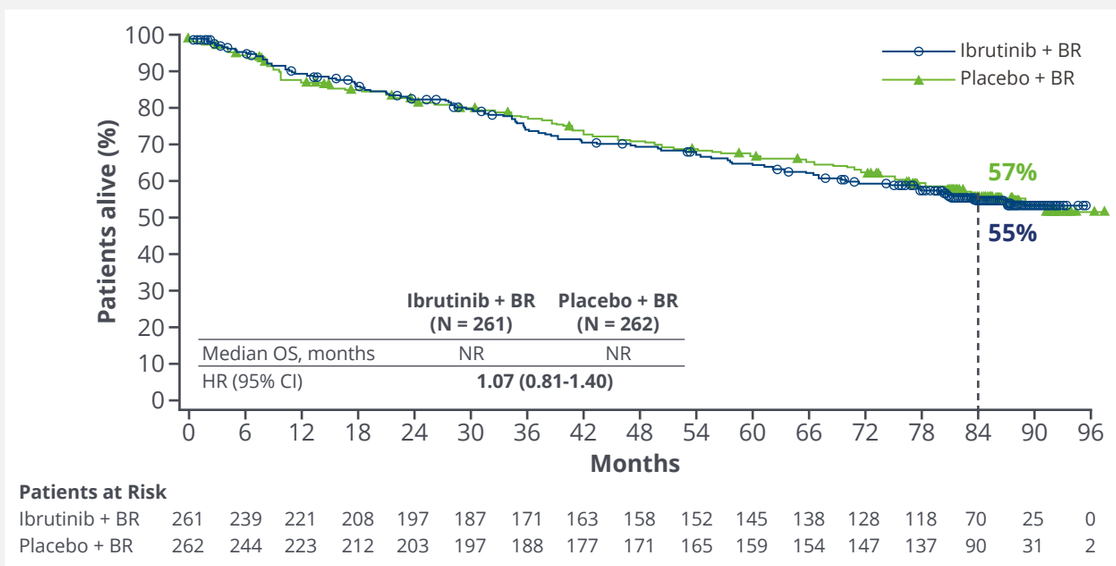
- Ibrutinib plus BR and R maintenance achieved:
  - Significant improvement in median PFS by 2.3 years (6.7 vs 4.4 years)
  - 25% reduction in risk of PD or death (HR 0.75 [95% CI, 0.59-0.96]; $p = 0.011$)




CI, confidence interval; HR, hazard ratio; NE, not evaluable.*Significance boundary for superiority was $p < 0.023$.

### Overall survival

- Median OS was not reached in both arms (HR 1.07; 95% CI, 0.81-1.40)



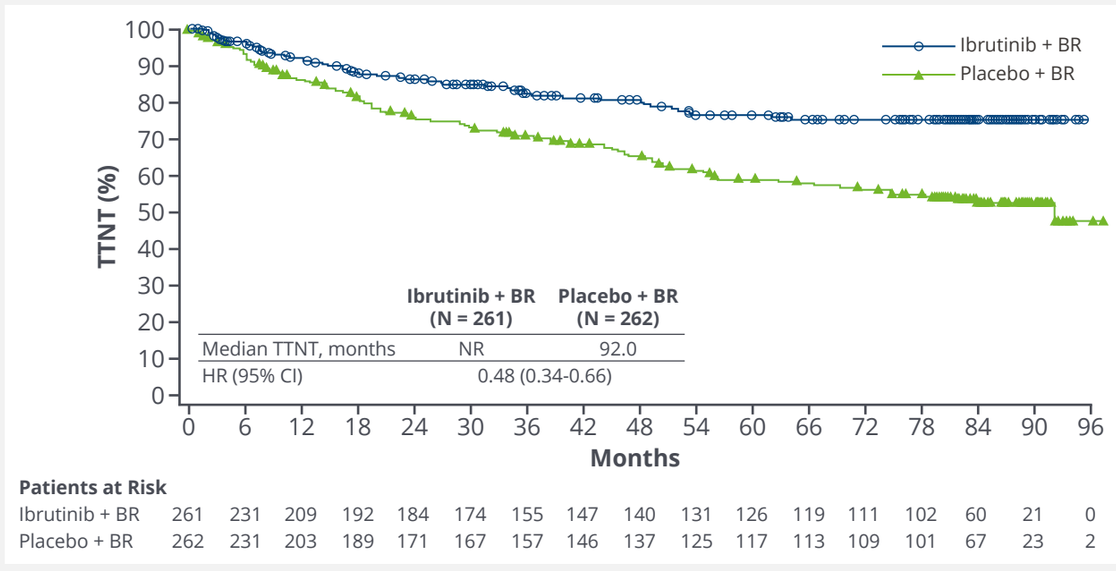

NR, not reached.

### Response rate

- ORR was 89.7% in the ibrutinib plus BR arm and 88.5% in the placebo plus BR arm
- Complete response rate was numerically higher in the ibrutinib plus BR arm (65.5% vs 57.6%; $p = 0.057$)

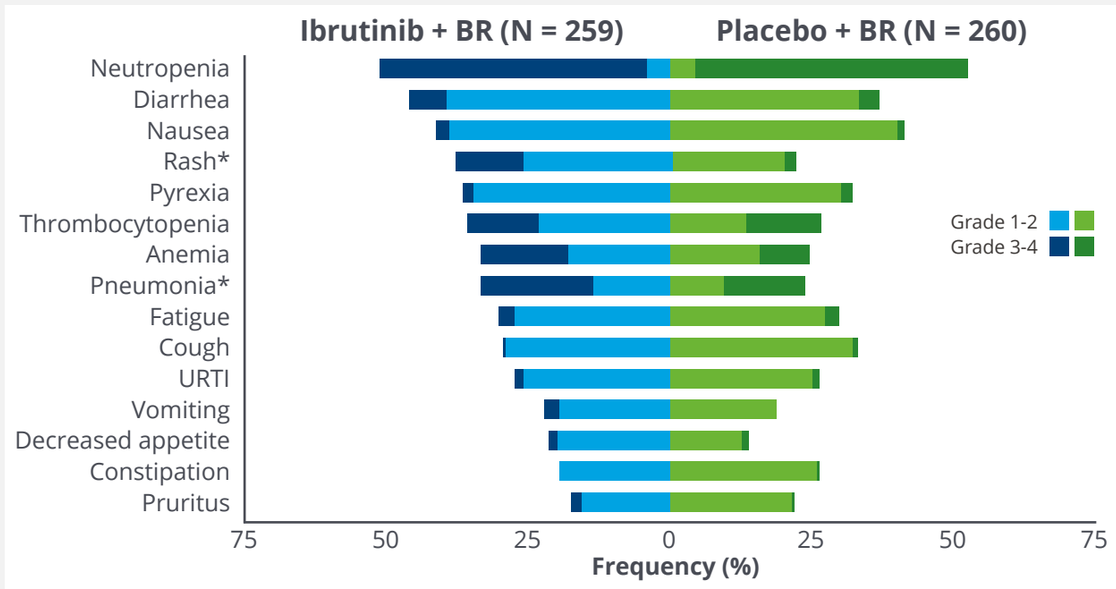
### Time to next treatment

- Median TTNT was longer in the ibrutinib plus BR arm
- Subsequent second-line antilymphoma treatment was initiated in 19.9% of patients in the ibrutinib plus BR arm versus 40.5% of patients in the placebo plus BR arm




### Common treatment-emergent adverse events (≥ 20%)

- Rates of grade 3 or 4 treatment-emergent adverse events were 81.5% and 77.3% in the ibrutinib plus BR and placebo plus BR arms, respectively




URTI, upper respiratory tract infection. *Difference of ≥ 10% in any grade treatment-emergent adverse event.

REFERENCES:

1. Hermine O, et al. *Lancet*. 2016;388:565-575. 2. Le Gouill S, et al. *N Engl J Med*. 2017;377:1250-1260. 3. Robak T, et al. *Leuk Lymphoma*. 2019;60:2622-2634. 4. Monga N, et al. *Crit Rev Oncol Hematol*. 2021;158:103212. 5. Martin P, et al. *J Clin Oncol*. 2021;39(suppl 15):7504. 6. Rummel MJ, et al. *Lancet*. 2013;381:1203-1210. 7. Flinn IW, et al. *J Clin Oncol*. 2019;37:984-991. 8. Hill BT, et al. *Hematol Oncol*. 2019;37:405-407. 9. Maddocks K, et al. *Blood*. 2015;125:242-248.

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## KEY TAKEAWAY

SHINE is the first phase 3 study to show that ibrutinib in combination with chemoimmunotherapy is highly effective in patients with untreated MCL.

## CONCLUSIONS

**Ibrutinib + BR and R maintenance:**

- Median PFS of 6.7 years: a statistically significant and clinically meaningful 2.3-year PFS advantage
- Consistent and expected AEs within the known profiles for ibrutinib and BR
- A new benchmark for first-line treatment of older patients with MCL or those unsuitable for autologous stem cell transplantation

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## DISCLOSURES

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