

**Primary endpoint:** Investigator-assessed failure-free survival.

**Secondary endpoint:** OS; PFS; DoR; CRR; ORR; conversion rate of PR to CR after induction end.

**Eligibility:** Previously untreated patients with histologically confirmed mantle cell lymphoma; aged 18–65 years; Ann Arbor stage II–IV; eligible for auto-HSCT; ECOG PS ≤2; ≥1 measurable lesion.

TRIAL DESIGN Randomized 1:1:1

Group A (n = 288)

immunochemotherapy + auto-HSCT

Group I (n = 290)

immunochemotherapy + ibrutinib


Group A + I (n = 292)

immunochemotherapy + ibrutinib + auto-HSCT

Induction immunochemotherapy consisted of 6 alternating cycles of:

R-CHOP (cycles 1, 3, and 5):		
Rituximab	375 mg/m <sup>2</sup>	Day 0 or 1
Cyclophosphamide	750 mg/m <sup>2</sup>	Day 1
Doxorubicin	50 mg/m <sup>2</sup>	Day 1
Vincristine	1.4 mg/m <sup>2</sup>	Day 1
Prednisone	100 mg	Days 1–5

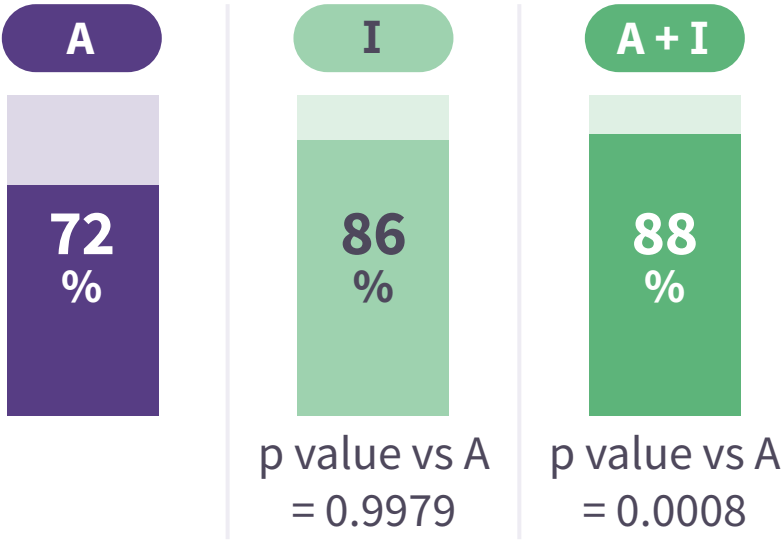
R-DHAP/R-DHAOx (cycles 2, 4, and 6):		
Rituximab	375 mg/m <sup>2</sup>	Day 0 or 1
Dexamethasone	40 mg/m <sup>2</sup>	Day 1
Cytarabine	2×2 g/m <sup>2</sup>	Days 1–4
Cisplatin or oxaliplatin	100 mg/m <sup>2</sup>	Day 2
	130 mg/m <sup>2</sup>	Day 1

 Ibrutinib | 560 mg

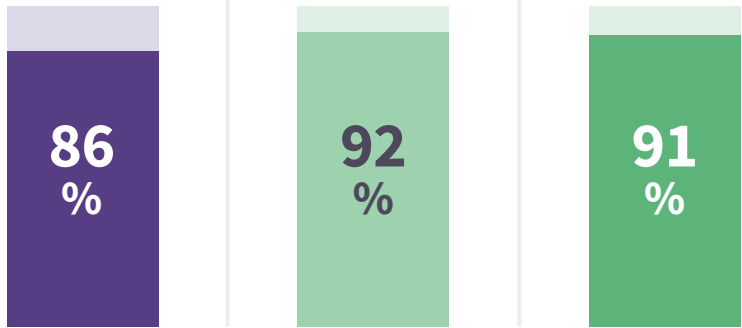
Days 1–19 of R-CHOP and as daily maintenance therapy for 2 years in patients who were failure-free after induction.

EFFICACY

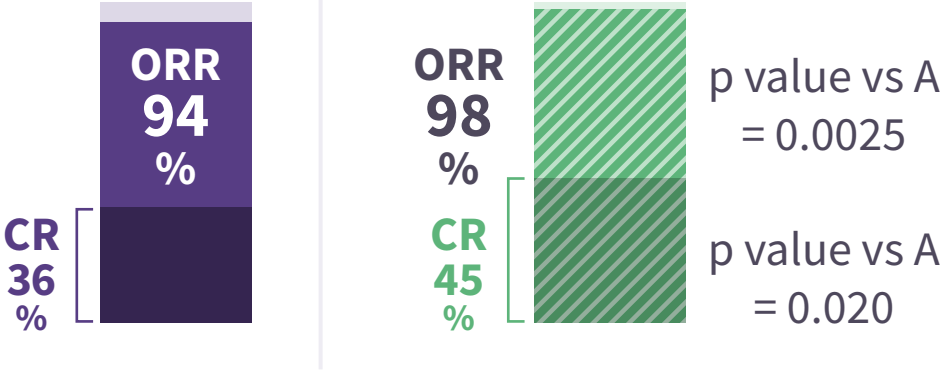
3-year failure-free survival



3-year overall survival

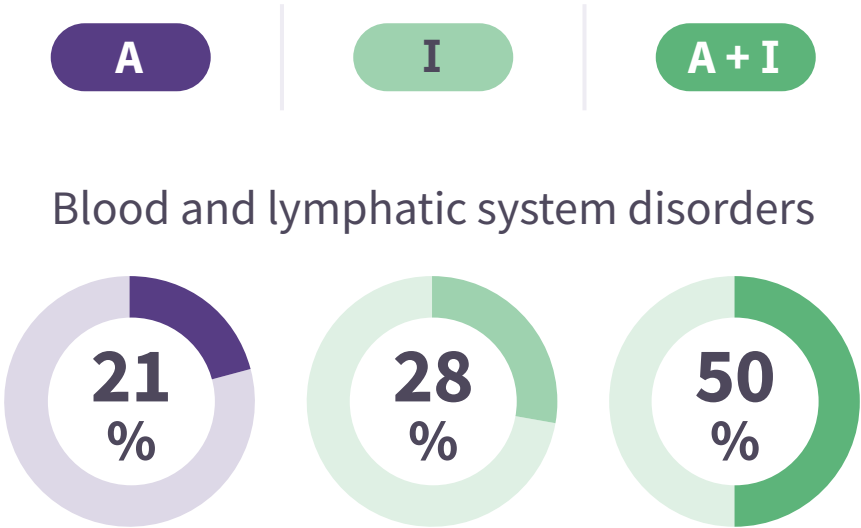


Response rates

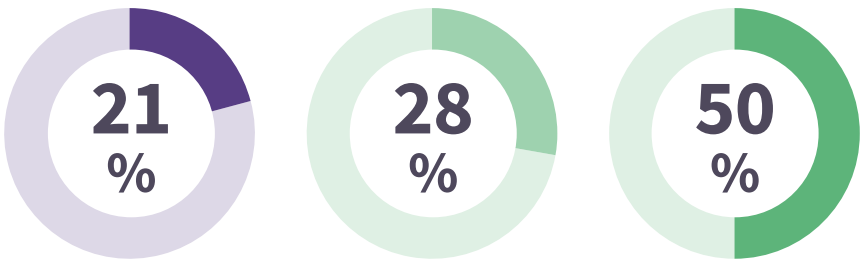


SAFETY

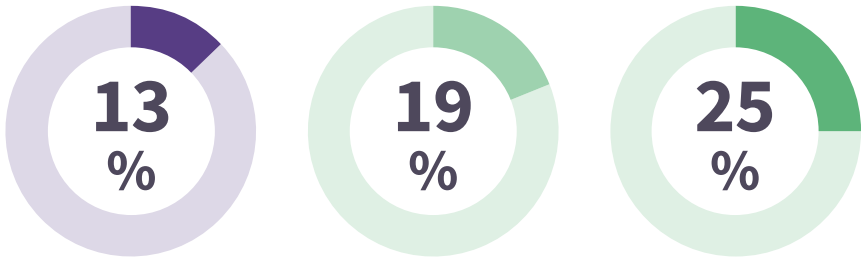
Grade 3–5 AEs during maintenance or follow-up



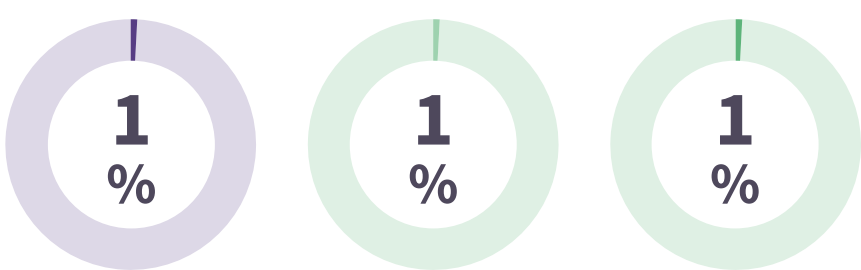
Blood and lymphatic system disorders



Infections and infestations



Fatal infections



The addition of ibrutinib to immunochemotherapy improved outcomes in younger patients with mantle cell lymphoma; however, toxicity was increased when ibrutinib was given after auto-HSCT.

**Abbreviations:** AE, adverse event; Ara-c, cytarabine; auto-HSCT, autologous hematopoietic stem cell transplantation; CR, complete remission; CRR, complete response rate; DoR, duration of remission; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial remission; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; R-DHAOx, rituximab, dexamethasone, cytarabine, oxaliplatin; R-DHAP, rituximab, dexamethasone, cytarabine, cisplatin.

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