LymphomaHub

DLBCL, FL

Polatuzumab or pinatuzumab vedotin plus rituximab for R/R NHL: Results from the ROMULUS phase II trial

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On 29 March 2019, Frank Morschhauser from the CHRU of Lille University, Lille, FR and colleagues, published in the *Lancet Haematology* results from the phase II clinical trial ROMULUS (NCT01691898). This multicenter, open-label, randomized study compared the efficacy of polatuzumab vedotin plus rituximab (R-pola) to pinatuzumab vedotin plus rituximab (R-pina) in patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) or R/R follicular lymphoma (FL). The primary endpoints of the trial were safety, tolerability, and anti-tumor response.

Study design & baseline characteristics

- N = 123 patients with R/R NHL:
  - DLBCL: n = 81 patients
  - FL (Grade 1–3a): n = 42 patients
- Patients were randomly 1:1 assigned to either:
  - R-pola (n = 49; [DLBCL, n = 39; FL, n = 20]):
    - R: 375 mg/m^2 intravenously
    - Pola: 2.4 mg/kg intravenously
    - Treatment was received every 21 days until disease progression (PD) or unacceptable toxicity up to one year
  - R-pina (n = 63 [DLBCL, n = 42; FL, n = 21]):
    - R: 375 mg/m^2 intravenously
    - Pina: 2.4 mg/kg intravenously
    - Treatment was received every 21 days until disease progression (PD) or unacceptable toxicity up to one year
  - DLBCL patients received a median of seven cycles of R-pina and a median of six cycles of R-pola
  - FL patients received a median of seven cycles of R-pina and a median of ten and a half cycles of R-pola
  - Patients with sufficient recovery from any treatment-emergent toxicity from the initial regimen (pina or pola) were eligible to receive crossover treatment consisting of the alternative alone or combined with rituximab, as per the intention-to-treat principle. Safety and efficacy endpoints were reported for the original treatment each patient received

Key findings

DLBCL patients

- Objective overall response (ORR):
  - R-pina (n = 42): 60% (95% CI, 43–74)
  - R-pola (n = 39): 54% (95% CI, 37–70)
- Complete response (CR):
  - R-pina (n = 42): 26% (95% CI, 14–42)
  - R-pola (n = 39): 21% (95% CI, 9–36)
- Median progression-free survival (PFS):
  - R-pina (n = 42): 5.4 months (95% CI, 3.9–6)
  - R-pola (n = 39): 5.6 months (95% CI, 4.3–8
- Median duration of response (DoR):
  - R-pina (n = 42): 6.2 months (95% CI,3.6–4)
  - R-pola (n = 39): 13.4 months (95% CI, 6.5–2)
- Median overall survival (OS):
  - R-pina (n = 42): 16.5 months (95% CI, 7.5–5)
  - R-pola (n = 39): 20.1 months (95% CI, 10.4–6)
- Median OS among patients who were refractory to their previous therapy:
  - R-pina (n = 42): 11.9 months (95% CI, 6.3–0)
  - R-pola (n = 39): 11.7 months (95% CI, 5.3–9)

FL patients

- ORR:
  - R-pina (n = 21): 62% (95% CI, 38–82)
  - R-pola (n = 20): 70% (95% CI, 46–88)
- CR:
  - R-pina (n = 21): 5% (95% CI, 0.1–24)
  - R-pola (n = 20): 45% (95% CI, 23–68)
- Median PFS:
  - R-pina (n = 21): 12.7 months (95% CI, 8.9–5)
  - R-pola (n = 20): 15.3 months (95% CI, 12.2–1)
- Median DoR:
  - R-pina (n = 21): 6.5 months (95% CI,6.0–1)
  - R-pola (n = 20): 9.4 months (95% CI, 7.2–not estimable)

- Median OS:
  - R-pina (n = 21): not reached
  - R-pola (n = 20): not reached

Full cohort

- Two-year OS among all patients (DLBCL + FL):
- R-pina: 90.5% (95% CI, 77.9–100.0)
- R-pola: 87.8% (95% CI, 72.0–100.0)
- Six patients with PD received crossover treatment with R-pina or R-pola accordingly (5 DLBCL, 1 FL):
  - Five out of six PD patients progressed further after crossover
  - One patient died after receiving one cycle of crossover treatment

Safety

- The most common treatment-emergent adverse events (TEAEs) for both R-pina and R-pola groups were:
  - Fatigue
  - Diarrhea
  - Peripheral neuropathy
  - Nausea
  - Neutropenia
- Pina was discontinued in 79% of patients with DLBCL and in 91% of patients with FL
- Pola was discontinued in 80% of patients with DLBCL and in 85% of patients with FL
- The most common reasons for treatment discontinuation were PD (38%) in patients with DLBCL and AEs (62%) in patients with FL
- Neutropenia was the most common Grade 3–4 AE and led to treatment discontinuation in only one patient treated with R-pina in each of the DLBCL and FL patient groups
- Febrile neutropenia was reported in 2% of DLBCL patients in the R-pina group (Grade 4) and in 5% of DLBCL patients in the R-pola group (Grade 3). It was also reported in 5% of FL patients in the R-pina arm (Grade 3)

Conclusions

- R-pina and R-pola are potential treatment options for patients with R/R DLBCL or R/R FL
- Pola is currently under further investigation for NHL due to its longer DoR when compared to pina, and overall benefit–risk of R-pola

References

1. Morschhauser F. *et al.* Polatuzumab vedotin or pinatuzumab vedotin plus rituximab in patients with relapsed or refractory non-Hodgkin lymphoma: final results from a phase 2 randomised study (ROMULUS). *Lancet Haematol*. 2019 Mar 29. pii: S2352-3026(19)30026-2. DOI: 10.1016/S2352-3026(19)30026-2 [Epub ahead of print].
