PhALLCON trial responder analysis: Ponatinib superior to imatinib in newly-diagnosed Ph+ ALL

KEY TAKEAWAYS

- The Phase 3 PhALLCON trial demonstrated that ponatinib, combined with reduced-intensity chemotherapy, was **superior to imatinib in newly diagnosed Ph+ ALL**
- In-depth responder analysis of the PhALLCON trail showed that ponatinib resulted in **higher rates of MRD negativity, longer PFS, and reduced rates of allo-SCT** compared with imatinib

Ponatinib is a third-generation *BCR::ABL1* tyrosine kinase inhibitor (TKI). The US FDA approved ponatinib plus chemotherapy in March 2024 for the treatment of adults with newly-diagnosed Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL), based on the results of PhALLCON trial. In-depth responder analysis of the trial showed that treatment with ponatinib led to **higher rates of measurable residual disease (MRD) negativity** and **longer progression-free survival (PFS)** compared with imatinib.

In the PhALLCON trial, patients were randomized to receive:

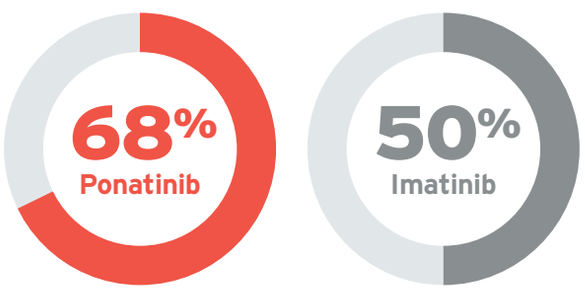
- Ponatinib 30 mg once daily with a dose reduction of 15 mg once daily + reduced intensity chemotherapy (RIC)
- Imatinib 600 mg once daily + RIC

The analysis investigated and compared rates of MRD negativity, PFS and allogeneic stem cell transplant (allo-SCT) between patients receiving ponatinib and imatinib

Ponatinib N = 154 VS **Imatinib N = 78**

Substantially higher rates of MRD negativity with ponatinib vs imatinib

MRD negativity



PFS more than doubled with ponatinib vs imatinib

PFS	**20.2 months** Ponatinib	**7.5 months** Imatinib

Reduced transplantation with ponatinib vs imatinib

Patients receiving allo-SCT overall	**36%** Ponatinib	**47%** Imatinib
Patients with MRD negativity receiving allo-SCT	**32%** Ponatinib + RIC	**56%** Imatinib + RIC

WHAT DOES THIS MEAN FOR PATIENTS?

PhALLCON is the first global Phase III randomized trial to compare two TKIs in adults with newly-diagnosed Ph+ ALL. It found that **ponatinib, combined with reduced-intensity chemotherapy, was superior to imatinib.** Consequently, the US FDA approved ponatinib plus chemotherapy in March 2024 for treating adults with newly diagnosed Ph+ ALL.

The analysis of the PhALLCON trial presented at EHA 2024 showed that ponatinib achieved higher rates of MRD negativity and **more than doubled PFS compared with imatinib**. Additionally, fewer patients on ponatinib required stem cell transplants, and the safety profiles of both drugs were comparable. These results suggest that ponatinib could be a more effective frontline treatment option for patients with Ph+ ALL.

Reference: *Ribera J-M, et al. Adverse prognostic impact of secondary-type mutations in ELN 2022 favorable risk acute myeloid leukemia. Presented at the 29th European Hematology Association (EHA) Congress, Madrid. June 13-16, 2024. Abstract #S115.*

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