# Patient-reported Outcomes in Adults With Newly Diagnosed Ph+ Acute Lymphoblastic Leukemia Treated With Ponatinib or Imatinib in Combination With Reduced-Intensity Chemotherapy: Results From the Phase III PhALLCON Study

POSTER # ALL-442

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## Background

- Ponatinib is a potent, pan-BCR::ABL1 tyrosine kinase inhibitor approved by the US FDA as a frontline treatment for Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL), in combination with chemotherapy.[1]
- In the randomized, phase III PhALLCON trial (NCT03589326), ponatinib demonstrated a favorable clinical profile versus imatinib in adults with newly diagnosed Ph+ ALL, when combined with reduced-intensity chemotherapy:
  - Higher percentage of patients achieving minimal residual disease-negative complete remission at the end of induction (EOI; 34% vs 17%)[2]
  - Comparable safety profile
- However, health-related quality of life (HRQoL) data are needed to evaluate the treatment effect of ponatinib from the patient perspective.

## Objective

- To compare the effect of ponatinib versus imatinib on patient-reported outcome (PRO) endpoints in PhALLCON

## Methods

- Adults (age ≥18 years) with newly diagnosed Ph+ ALL were randomized 2:1 to ponatinib or imatinib plus reduced-intensity chemotherapy through induction (cycles 1-3), consolidation (cycles 4-9), and maintenance (cycles 10-20) phases in 28-day cycles, followed by single-agent ponatinib or imatinib after cycle 20.
- PROs were assessed as exploratory endpoints with the Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu) and EQ-5D-5L.
  - Assessment visits: baseline; cycle 1 day 1 (C1D1), C4D1, C7D1, C10D1, C13D1, C16D1, C19D1, C21D1, and every 6 cycles thereafter; and the end of treatment (EOT)
- Six primary domains of interest were preselected based on their clinical relevance and importance to the target population[3,4]: FACT-General (FACT-G) physical well-being (PWB), FACT-Leu "additional concerns" subscale (FACT-LeuS), FACT-G total score (TS), FACT-Leu trial outcome index (TOI), FACT-Leu TS, and EQ-5D-5L visual analog scale (EQ-VAS).
- PRO-evaluable population: patients with ≥1 PRO assessment
- Comparative assessments between arms followed the guidance from the ICH E9(R1) estimand framework.[5]
  - Least squares (LS) mean changes from baseline to the end of induction (EOI) and the end of consolidation (EOC) were analyzed using analysis of covariance (ANCOVA).
  - Hazard ratios (HRs) for time to confirmed improvement or deterioration from baseline were estimated using stratified Cox proportional hazards models.
    - Confirmed improvement/deterioration was defined as meaningful improvement/deterioration exceeding the threshold at ≥2 consecutive assessments.
- Overall treatment tolerability was assessed using the FACT-G Item GP5 ("I am bothered by side effects of treatment").
- The meaningfulness of within-patient changes, within-group changes, and between-group differences was interpreted based on published thresholds for each PRO domain.[6,7]

## Results

### Baseline characteristics

- The PRO-evaluable population included 238 patients (159 ponatinib, 79 imatinib), with a median follow-up of 20.1 months (range 17.8–23.1) at data cutoff (Aug 12, 2022).
- Baseline patient characteristics were comparable between arms.
- Patients had a mean age of 51 years, with 54% being female.
- Most patients (68%) were White and 13% were Asian.

### Baseline PRO scores

- Baseline PRO scores (**Table 1**) were comparable between arms.
- Patients had worse PRO scores compared with the reference populations (**Table 1**).

### Changes from baseline to EOI

- Differences in LS mean changes from baseline to EOI were significant and in favor of ponatinib over imatinib for four of the six primary domains of interest: FACT-G PWB, FACT-LeuS, FACT-Leu TOI, and FACT-Leu TS (**Table 2**).
  - Differences between arms exceeded the minimal important difference thresholds for FACT-LeuS, FACT-Leu TOI, and FACT-Leu TS.

### Changes from baseline to EOC

- Differences in LS mean changes from baseline to EOC significantly favored ponatinib over imatinib across all six primary domains (**Table 2**).
  - The differences were meaningful for all domains but FACT-LeuS.

**Table 1. Baseline PRO scores**

| PRO domain | Mean (SD) | | Reference population norm |
|---|---|---|---|
| | Ponatinib | Imatinib | |
| FACT-Leu | n = 150 | n = 74 | |
| FACT-G PWB | 21.9 (5.0) | 22.5 (4.6) | 24.8 |
| FACT-LeuS | 49.1 (10.2) | 50.2 (9.2) | - |
| FACT-Leu TOI | 85.8 (18.9) | 88.8 (17.3) | - |
| FACT-G TS | 77.0 (16.3) | 79.0 (15.7) | 85.5 |
| FACT-Leu TS | 126.1 (24.8) | 129.2 (22.9) | - |
| EQ-5D-5L | n = 154 | n = 76 | |
| EQ-VAS | 71.2 (19.7) | 72.7 (18.3) | 82.5 |

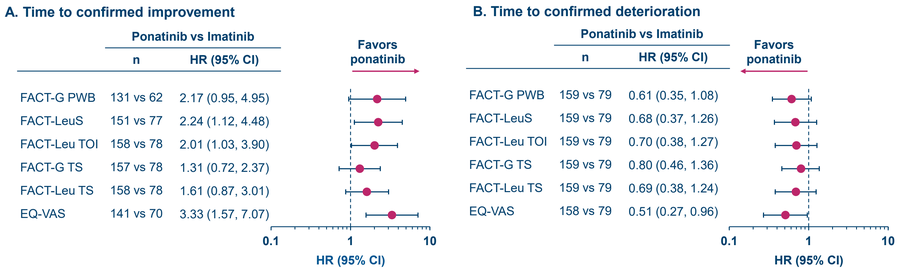
Norm scores were derived from the Austrian general population (FACT-Leu)[8] and the UK general population (EQ-VAS),[9] and were reweighted by the age and sex distributions of the PRO-evaluable population. A lower PRO score indicates worse HRQoL. EQ-VAS, EQ-5D-5L visual analog scale; FACT, Functional Assessment of Cancer Therapy; FACT-G, FACT-General; FACT-Leu, FACT-Leukemia; HRQoL, health-related quality of life; LeuS, "additional concerns" leukemia subscale; PRO, patient-reported outcome; PWB, physical well-being; SD, standard deviation; TOI, trial outcome index; TS, total score.

**Table 2. LS mean changes from baseline**

| PRO domain | LS mean change from baseline (95% CI) | | Difference in LS mean change from baseline (95% CI) | MID |
|---|---|---|---|---|
| | Ponatinib | Imatinib | | |
| **Baseline to EOI** | | | | |
| FACT-Leu | n = 125 | n = 63[a] | | |
| FACT-G PWB | -0.30 (-1.08, 0.47) | -1.85[b] (-2.95, -0.75) | 1.55[b] (0.20, 2.89) | 2 |
| FACT-LeuS | 2.30[b] (0.94, 3.66) | -2.14[b] (-4.07, -0.21) | **4.44[b] (2.08, 6.80)** | 4 |
| FACT-Leu TOI | 2.10 (-0.50, 4.70) | -4.11[b] (-7.84, -0.38) | **6.21[b] (1.67, 10.75)** | 5 |
| FACT-G TS | -1.16 (-3.36, 1.05) | -2.88 (-6.04, 0.29) | 1.72 (-2.13, 5.58) | 3 |
| FACT-Leu TS | 1.17 (-2.07, 4.41) | -5.14[b] (-9.79, -0.49) | **6.31[b] (0.65, 11.98)** | 6 |
| EQ-5D-5L | n = 127 | n = 66 | | |
| EQ-VAS | 0.95 (-1.95, 3.86) | -1.89 (-5.97, 2.18) | 2.85 (-2.14, 7.83) | 7 |
| **Baseline to EOC** | | | | |
| FACT-Leu | n = 101 | n = 53[c] | | |
| FACT-G PWB | 0.44 (-0.48, 1.36) | -2.51[b] (-3.78, -1.23) | **2.94[b] (1.37, 4.51)** | 2 |
| FACT-LeuS | 1.47 (-0.18, 3.11) | -1.66 (-3.91, 0.60) | 3.12[b] (0.33, 5.92) | 4 |
| FACT-Leu TOI | 2.27 (-0.81, 5.35) | -4.98[b] (-9.25, -0.71) | **7.25[b] (1.98, 12.52)** | 5 |
| FACT-G TS | -0.30 (-2.95, 2.35) | -5.52[b] (-9.19, -1.86) | **5.23[b] (0.71, 9.74)** | 3 |
| FACT-Leu TS | 1.27 (-2.67, 5.20) | -7.00[b] (-12.44, -1.55) | **8.26[b] (1.54, 14.98)** | 6 |
| EQ-5D-5L | n = 103 | n = 59 | | |
| EQ-VAS | 5.30[b] (1.85, 8.75) | -2.49 (-7.07, 2.09) | **7.79[b] (2.05, 13.52)** | 7 |

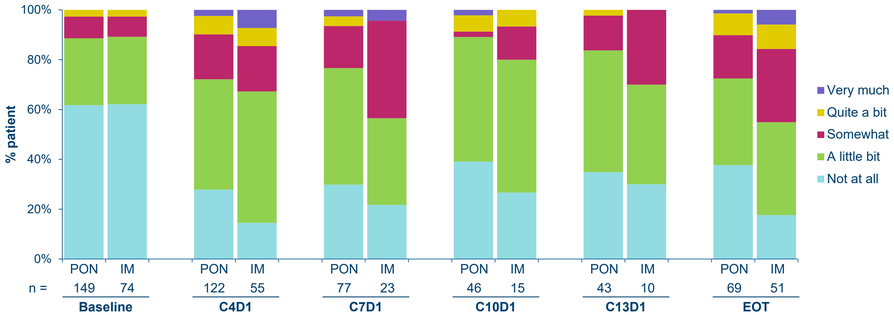
Differences exceeding the between-group MID thresholds are bolded. CI, confidence interval; EOC, end of consolidation; EOI, end of induction; EQ-VAS, EQ-5D-5L visual analogue scale; FACT, Functional Assessment of Cancer Therapy; FACT-G, FACT-General; FACT-Leu, FACT-Leukemia; LeuS, "additional concerns" leukemia subscale; MID, minimal important difference; PRO, patient-reported outcome; PWB, physical well-being; TOI, trial outcome index; TS, total score. [a]n = 62 for FACT-Leu TOI, FACT-G TS, FACT-Leu TS. [b]Nominal P<0.05 for within-group change from baseline or between-group difference in change from baseline. [c]n = 54 for FACT-LeuS.

**Figure 1. HR for time to confirmed improvement/deterioration**




n represents the number of patients who were eligible for the analysis at baseline; patients whose baseline scores precluded them from achieving meaningful improvement or deterioration were excluded from the respective analysis. CI, confidence interval; EQ-VAS, EQ-5D-5L visual analogue scale; FACT-G, FACT-General; FACT-Leu, Functional Assessment of Cancer Therapy-Leukemia; HR, hazard ratio; LeuS, "additional concerns" leukemia subscale; PWB, physical well-being; TOI, trial outcome index; TS, total score.

**Figure 2. Distribution of the responses to the FACT-GP5 item ("I am bothered by side effects of treatment")**




C, cycle; D, day; EOT, end of treatment; FACT-GP5, Functional Assessment of Cancer Therapy-General item GP5; IM, imatinib; PON, ponatinib.

### Time to confirmed improvement/deterioration

- The time to achieve confirmed improvement was shorter with ponatinib versus imatinib for FACT-LeuS, FACT-Leu TOI, and EQ-VAS (**Figure 1**).
- Patients were at significantly lower risk of experiencing confirmed deterioration with ponatinib versus imatinib for EQ-VAS (**Figure 1**).

### Treatment tolerability

- Across post-baseline visits, patients on ponatinib vs imatinib were less bothered by treatment side effects, as measured using the FACT-GP5 item (**Figure 2**).

## Conclusions

- The present analysis showed that ponatinib was associated with significant and meaningful improvement in leukemia-specific symptoms and overall quality of life as compared with imatinib in patients with newly diagnosed Ph+ ALL.
- Overall treatment tolerability, as measured by the FACT-GP5, was more favorable with ponatinib versus imatinib.
- These PRO findings lend further support to the use of ponatinib in combination with reduced-intensity chemotherapy as a frontline treatment for Ph+ ALL.

### References

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### Acknowledgments

This study was sponsored by Takeda Development Center Americas, Inc. Medical writing and editorial assistance was provided by Hui Zhang, PhD, and Stephen Gilliver, PhD, of Evidera PPD, and was funded by Takeda.

### Disclosures

**AA** and **DR** are employees of Takeda, which funded this study. **LS** and **SG** are employees of Evidera, which was paid by Takeda for work relating to this study. **IA** has received honoraria from Takeda, Amgen, Pfizer, Jazz, and Sobi; served as a consultant or advisor for Takeda, Amgen, Pfizer, Jazz, and Sobi; served on a speakers bureau for Pfizer; and received research funding from AbbVie and MacroGenics. **PM** has served as a consultant or advisor for Takeda, Daiichi Sankyo, and BMS; served on the speakers bureau for Servier; and received research funding from AbbVie, Takeda, Daiichi Sankyo, Novartis, and Servier. **PV** has served as a consultant or advisor for Blueprint Medicines, AbbVie, Amgen, Cogent Biosciences, Incyte, CTI BioPharma, Daiichi Sankyo, GSK, Karyopharm, Novartis, Pfizer, Genentech, Servier, Stemline, and Morphosys. **VR** has served as a consultant or advisor for Pfizer, Takeda, AbbVie, Astellas, KITE, and Amgen. **CP** has served as a consultant or advisor for AbbVie, Astellas, Novartis, BMS, Menarini Stemline, Blueprint Medicines, Incyte, GSK, Amgen, Pfizer, and Janssen; and received personal fees from Astellas, Novartis, Pfizer, and Amgen. **JTL** has served as a consultant or advisor for Adaptive Biotechnologies, Kite/Gilead, Pfizer, and Takeda; and received payment for travel, accommodations, and expenses from Adaptive Biotechnologies. **MRB** has no conflicts of interest to declare. **JMR** has served as a consultant or advisor for Incyte, Pfizer, BMS, Novartis, and Takeda; and received research funding from Amgen. **JM** has received personal fees from BMS, Takeda, Blueprint Medicine, PharmaEssentia, CTI, GSK, Incyte, Amgen, and Jazz Pharmaceuticals. **JXW** has served as advisor to Abbvie. **SG** has no disclosures

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**Presented at the Society of Hematologic Oncology SOHO 2024 Annual Meeting, Houston, TX, USA, 4-7 September, 2024**