# Treatment-Emergent Adverse Events Associated With Patient-Reported Treatment Burden in Patients With Ph+ ALL: Results From the Phase 3 PhALLCON Study

ALL-514

Ling Shi,[1] Christopher Dieyi,[2] Ajibade Ashaye,[2] Shien Guo[1]

[1] PPD Evidera Patient-Centered Research, Thermo Fisher Scientific, Waltham, MA, USA; [2] Takeda Development Center Americas, Inc., Cambridge, MA, USA



## Background

- PhALLCON, a phase 3 randomized trial, compared ponatinib versus imatinib, each combined with reduced-intensity chemotherapy, in patients with newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL).[1]
- FACT-GP5 ("I am bothered by side effects of treatment") is a validated single-item measure of overall treatment-related side-effect burden.[2]
- Greater FACT-GP5 burden has previously been shown to be associated with clinically meaningful deterioration in health-related quality of life (HRQoL).[3,4]
- Linking clinician-reported adverse events (AEs) with patient-reported burden may identify toxicities most relevant to the patient experience and inform symptom-management strategies.

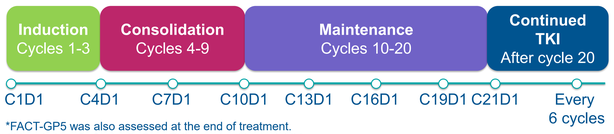
## Objectives

- To identify treatment-emergent adverse events and symptom patterns associated with patient-reported treatment burden in patients with newly diagnosed Ph+ ALL enrolled in PhALLCON.

## Methods

- Data source: Phase 3 PhALLCON, a randomized, open-label trial in adults with newly diagnosed Ph+ ALL
- Analysis population: all patients receiving ≥1 dose of study treatment (N=244; ponatinib n=163; imatinib n=81)
- FACT-GP5: "I am bothered by side effects of treatment" (7-day recall), defined as a binary outcome in two ways:
  - High bother = "Quite a bit" or "Very much"
  - Moderate-to-high bother = "Somewhat" to "Very much"

**Treatment phases and FACT-GP5 assessment schedule***




*FACT-GP5 was also assessed at the end of treatment.
Abbreviation: C, Cycle; D, Day; TKI, tyrosine kinase inhibitor

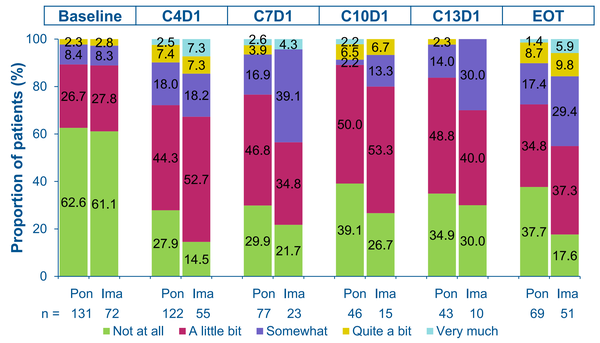
- AE-PRO alignment: ≤7-day window (matched FACT-GP5 recall period)
- Selected symptomatic and clinically relevant treatment-emergent AEs were identified a priori based on frequency (≥10%), burden potential, and known treatment associations.
- Longitudinal mixed-effects logistic regression assessed associations between time-varying AEs and repeated FACT-GP5 assessments (for both "high" and "moderate-to-high" bother definitions), adjusting for treatment arm, time since first dose, and baseline FACT-GP5.
  - Each selected AE was evaluated as the following time-varying covariates:
    - Presence (yes/no)
    - Severity (grade 1 and grade ≥2 vs no corresponding AE)
    - Cumulative concurrent AE burden (number of ongoing AEs within 7-day window)

## Results

### Patient-reported bother over time

- FACT-GP5 assessments were available for 203 patients (83.2%) at Baseline (C1D1), 177 (72.5%) at C4D1, 100 (41.0%) at C7D1, 61 (25.0%) at C10D1, 53 (21.7%) at C13D1, and 120 (49.2%) at EOT.
- Most FACT-GP5 responses were in the lower-bother categories. However, the ponatinib arm generally showed a higher proportion of responses in the lower-bother categories (**Figure 1**).

**Figure 1: FACT-GP5 response distribution by visit and treatment arm**

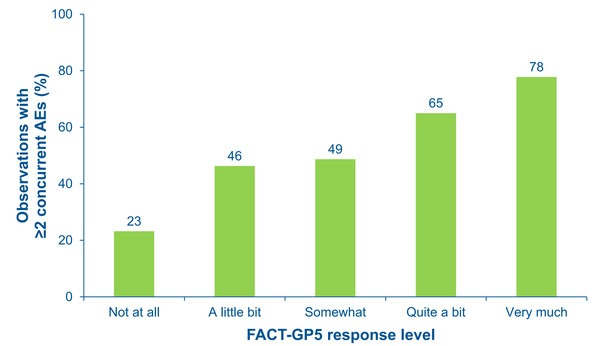



Abbreviation: C, cycle; D, day; EOT, end of treatment; FACT-GP5, Functional Assessment of Cancer Therapy – General Population Item 5 ("I am bothered by side effects of treatment"); Ima, imatinib; Pon, ponatinib

### Cumulative concurrent AE and patient-reported bother

- Cumulative concurrent AE burden demonstrated one of the strongest and most consistent associations with patient-reported bother.
  - Patients reporting greater treatment burden were substantially more likely to experience multiple concurrent AEs (**Figure 2**).
- Each additional concurrent AE increased the odds of
  - High bother by 29% (OR 1.29, [95% CI, 1.09–1.51])
  - Moderate-to-high bother by 17% (OR 1.17, [95% CI, 1.03–1.33])

**Figure 2: Proportion of observations with ≥2 concurrent AEs by FACT-GP5 response level**




Abbreviation: AE, adverse event.

### AE presence and patient-reported bother

- Among the predefined symptomatic AEs evaluated, vomiting (OR=5.13), constipation (OR=2.62), nausea (OR=2.48), and hypertension (OR=2.61) showed the strongest associations with increased odds of high bother (**Figure 3A**).
- Vomiting (OR=4.12), constipation (OR=2.16), and nausea (OR=1.98) also showed the strongest associations with increased odds of moderate-to-high bother (**Figure 3B**).
- Grade ≥2 diarrhea, headache, vomiting, fluid retention/edema, and hypertension were associated with substantially higher odds of high patient-reported bother (odds ratio [OR] 2.93–6.84).

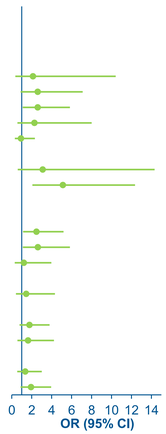
**Figure 3: Forest plot of ORs for the association of AE presence with (A) high bother and (B) moderate-to-high bother**

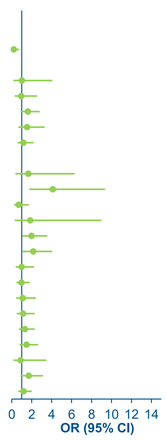
**A.**

| | OR (95% CI; AE: yes vs no) | Nominal p-value |
|---|---|---|
| Dyspnea | NE (NE, NE) | NE |
| Cough | NE (NE, NE) | NE |
| Cardiac arrhythmias | NE (NE, NE) | NE |
| Febrile neutropenia | NE (NE, NE) | NE |
| Venous thromboembolic events | 2.13 (0.44, 10.34) | 0.348 |
| Hemorrhage | 2.61 (0.97, 7.03) | 0.057 |
| **Hypertension*** | 2.61 (1.18, 5.75) | 0.018 |
| Fluid retention and edema | 2.28 (0.65, 7.93) | 0.197 |
| Fatigue or asthenia | 0.93 (0.39, 2.24) | 0.871 |
| Pyrexia | NE (NE, NE) | NE |
| Diarrhea | 3.11 (0.68, 14.24) | 0.143 |
| **Vomiting*** | 5.13 (2.15, 12.28) | <0.001 |
| Pancreatitis/lipase elevation | NE (NE, NE) | NE |
| Oral mucositis | NE (NE, NE) | NE |
| **Nausea*** | 2.48 (1.21, 5.11) | 0.013 |
| **Constipation*** | 2.62 (1.19, 5.75) | 0.017 |
| Abdominal pain | 1.22 (0.38, 3.89) | 0.740 |
| Rash and related conditions | NE (NE, NE) | NE |
| Peripheral sensory neuropathy | 1.45 (0.50, 4.25) | 0.495 |
| Paresthesia | NE (NE, NE) | NE |
| Peripheral neuropathy | 1.78 (0.86, 3.71) | 0.121 |
| Headache | 1.64 (0.65, 4.15) | 0.293 |
| Myalgia | NE (NE, NE) | NE |
| Arthralgia | 1.36 (0.63, 2.93) | 0.435 |
| Hepatotoxicity | 1.94 (0.97, 3.87) | 0.061 |

**B.**

| | OR (95% CI; AE: yes vs no) | Nominal p-value |
|---|---|---|
| Dyspnea | NE (NE, NE) | NE |
| Cough | NE (NE, NE) | NE |
| **Cardiac arrhythmias*** | 0.21 (0.07, 0.65) | 0.007 |
| Febrile neutropenia | NE (NE, NE) | NE |
| Venous thromboembolic events | 1.02 (0.26, 3.98) | 0.977 |
| Hemorrhage | 0.95 (0.37, 2.45) | 0.919 |
| Hypertension | 1.62 (0.97, 2.72) | 0.066 |
| Fluid retention and edema | 1.54 (0.74, 3.22) | 0.253 |
| Fatigue or asthenia | 1.17 (0.65, 2.10) | 0.593 |
| Pyrexia | NE (NE, NE) | NE |
| Diarrhea | 1.66 (0.44, 6.21) | 0.450 |
| **Vomiting*** | 4.12 (1.83, 9.26) | 0.001 |
| Pancreatitis/lipase elevation | 0.71 (0.31, 1.63) | 0.426 |
| Oral mucositis | 1.86 (0.39, 8.89) | 0.438 |
| **Nausea*** | 1.98 (1.13, 3.48) | 0.018 |
| **Constipation*** | 2.16 (1.17, 3.97) | 0.013 |
| Abdominal pain | 1.00 (0.47, 2.15) | 0.998 |
| Rash and related conditions | 0.98 (0.55, 1.72) | 0.931 |
| Peripheral sensory neuropathy | 1.11 (0.53, 2.33) | 0.779 |
| Paresthesia | 1.14 (0.58, 2.23) | 0.710 |
| Peripheral neuropathy | 1.32 (0.79, 2.23) | 0.289 |
| Headache | 1.48 (0.86, 2.55) | 0.156 |
| Myalgia | 0.90 (0.24, 3.40) | 0.878 |
| Arthralgia | 1.71 (0.96, 3.05) | 0.070 |
| Hepatotoxicity | 1.19 (0.74, 1.92) | 0.463 |




High bother: FACT-GP5 "Quite a bit" or "Very much" vs lower categories. Moderate-to-high bother: FACT-GP5 "Somewhat" to "Very much" vs lower categories. OR >1 indicates higher odds of bother. *AEs showing a statistically significant association with high or moderate-to-high bother. Abbreviation: AE, adverse event; CI, confidence interval; NE, not estimable due to event size; OR, odds ratio.

### Burden-associated AE profiles by treatment arm

- Gastrointestinal (GI)-related AEs and fluid retention/edema were more prominent with imatinib, whereas constipation and hypertension were more prominent with ponatinib (**Table 1**).
- Incidence of AEs was mostly higher during induction phase and lower during later treatment phases.

**Table 1: Incidence and duration of key bothersome AEs by treatment arm**

| AE | Arm | % patients with event | Events/ patient-year | Median duration (days) |
|---|---|---|---|---|
| Constipation | **Ponatinib** | **38.0%** | **0.56** | **35.0** |
| | Imatinib | 21.0% | 0.45 | 19.0 |
| Nausea | Ponatinib | 35.0% | 0.78 | 16.0 |
| | **Imatinib** | **50.6%** | **1.58** | **30.0** |
| Vomiting | Ponatinib | 22.1% | 0.35 | 2.0 |
| | **Imatinib** | **38.3%** | **0.92** | **11.0** |
| Diarrhea | Ponatinib | 17.2% | 0.30 | 5.5 |
| | **Imatinib** | **33.3%** | **0.83** | **24.0** |
| Headache | Ponatinib | 44.2% | 0.91 | 16.0 |
| | Imatinib | 43.2% | 0.83 | 9.0 |
| Hypertension | **Ponatinib** | **31.9%** | **0.55** | **73.0** |
| | Imatinib | 13.6% | 0.29 | 109.0 |
| Fluid retention and edema | Ponatinib | 23.3% | 0.42 | 23.0 |
| | **Imatinib** | **48.2%** | **1.43** | **26.0** |

Incidence reflects the percentage of patients experiencing the AE during the entire treatment period. Events per patient-year were calculated over the entire treatment period. Median duration of an event was calculated among patients experiencing the AE.
Abbreviation: AE, adverse event

## Key limitations

- Not all clinician-reported AEs were considered in the analysis.
- Grade ≥ 3 AEs and some selected AEs had sparse data; thus, the model may not converge to provide estimates.
- FACT-GP5 data from the later single-agent phase, during which patients received ponatinib or imatinib after Cycle 20, were insufficient to support the analysis.

## Conclusions

- Among the individual AEs evaluated, constipation, nausea, vomiting, and hypertension showed the most consistent associations with patient-reported bother.
- Concurrent AE burden also showed a strong and consistent relationship with patient-reported bother.
- GI-related AEs and edema were more prominent with imatinib; constipation and hypertension were more prominent with ponatinib.
- These findings suggest that integrating FACT-GP5 with clinician-reported safety data may support proactive, patient-centered, treatment-specific symptom management by helping identify AEs that may be most relevant to patients' experience.

### References

1. Jabbour E, et al. *JAMA*. 2024;331:1814-1823.
2. Pearman TP, et al. *Cancer*. 2018;124:991-997.
3. Ashaye A, et al. *Leukemia*. 2025;39:1342-1350.
4. Ashaye A, et al. *Ann Hematol*. 2025;104:4669-4678.

### Acknowledgments

Medical writing assistance was provided by Hui Zhang, PhD (PPD clinical research business of Thermo Fisher Scientific) in accordance with Good Publication Practice guidelines and was funded by Takeda. We thank the investigators, the clinical study teams, and the patients and their families who made this study possible.

### Disclosures

LS and SG are employees of PPD Evidera Patient-Centered Research, Thermo Fisher Scientific. CD and AA are employees of Takeda Development Center Americas, Inc.

**Presented at the Society of Hematologic Oncology Annual Meeting (SOHO 2026), Houston, TX, USA, September 9–12, 2026. For questions or comments, please contact Christopher Dieyi: Christopher.Dieyi@takeda.com**