A cost-consequence analysis of ponatinib versus imatinib in patients with newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) in the United States

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Background

- Hematopoietic stem cell transplantation (HSCT) plays a critical role in the management of ALL; however, the associated costs and risks of HSCT complications are burdensome to patients and payers[1,2]
- The addition of tyrosine kinase inhibitors (TKIs) to chemotherapy regimens has improved outcomes in patients with ALL and may delay or avoid the need for HSCT[3]
- The PhALLCON trial (NCT03589326) is the first randomized study comparing ponatinib and imatinib (both in combination with chemotherapy) in patients with newly diagnosed (ND) Ph+ ALL. At the time of the final analysis for the primary endpoint (data cutoff date: August 12, 2022), ponatinib was shown to be superior to imatinib,[4] and the exploratory efficacy endpoint time-to-HSCT showed that ponatinib may offer benefits over imatinib by delaying HSCT
- Ponatinib in combination with chemotherapy for the treatment of adult patients with ND Ph+ ALL was approved on March 19, 2024, under accelerated approval by the US Food and Drug Administration[5]

Objective

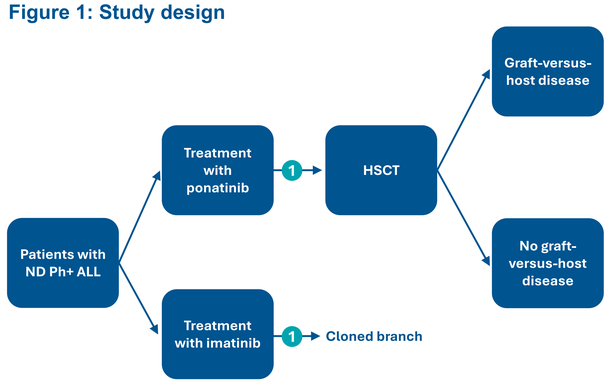
- To assess the clinical economic impacts of delayed or avoided HSCT in the treatment of patients with ND Ph+ ALL receiving first-line ponatinib versus imatinib over a 3-year time horizon from a US commercial health plan perspective

Methods

Study design

- A cost-consequence model (CCM) was developed using individual patient data on time-to-HSCT from the PhALLCON trial over a 3-year time horizon from a US commercial health plan perspective **(Figure 1)**

Figure 1: Study design



Executive Summary/Abstract

- **HSCT is an important treatment for patients with ND Ph+ ALL; however, it is a resource-intensive and costly procedure associated with complications and morbidity**
- **Patients with ND Ph+ ALL may be able to avoid or delay HSCT through treatment with TKIs**
- **The PhALLCON trial shows that ponatinib may offer benefits over imatinib by delaying HSCT**
- **This analysis demonstrates that for patients with ND Ph+ ALL, ponatinib may offer more efficient care by delaying or avoiding HSCT and complications thereof at a modest cost versus treatment with imatinib**

- The CCM considers Ph+ ALL epidemiology and costs associated with drug acquisition, HSCT, and graft-versus-host disease in a cohort of 1 million commercially insured individuals
  - Drug costs are assumed to be continuously accrued until HSCT
  - Imatinib drug costs are generic
- Model inputs (epidemiology, clinical, and costs) are informed by clinical trial results, published literature, and public databases **(Table 1)**

Table 1: Model inputs

	Parameter	Value
Epidemiology	Incidence of ALL (%)	0.002[6]
	Ph+ ALL (% of ALL)	25[7]
	HSCT distribution	
	Autologous (%)	36.4[8]
	Allogeneic (%)	63.6[8]
	Graft-versus-host disease incidence (%)	36.4[9]
Costs (USD)	HSCT procedure	307,914[10]
	Annual cost	
	Ponatinib	245,034[11]
	Imatinib (generic)	30,325[11]
	Pretransplant	
	Autologous harvest	643[12]
	Allogeneic harvest	823[12]
	Median HSCT hospitalization costs	98,866[3]
	Post-HSCT monthly cost	2,527[13]
	Graft-versus-host disease	89,061[9]

USD, US dollar.

Figure 2: Model equations

1 $$RMST_x = \sum_{t=0}^{x} KM\ estimate_t$$

2 $$NNT_{RMST} = \frac{1}{\frac{RMST_{ponatinib}}{RMST_{imatinib}} - 1}$$

KM, Kaplan-Meier; NNT, number needed to treat; RMST, restricted mean survival time

- KM estimates of the time-to-HSCT by treatment arm from the PhALLCON trial are used to estimate RMST, defined as the number of HSCT-free months, for ponatinib and imatinib **(Figures 2 and 3)**
  - For this analysis, RMST represents the mean time until a patient receives HSCT (cumulative HSCT-free months)
  - RMST is measured or calculated as the area under the KM curve from time 0 to a selected time point
- The NNT to avert 1 HSCT was calculated using the relative difference in RMST between ponatinib and imatinib at Years 1, 2, and 3 **(Figure 2)**
- Cumulative total costs are calculated for Years 1, 2, and 3
- Total costs are reported as follows:
  - Per month of delayed HSCT with ponatinib compared with imatinib
  - Per patient per month (PMPM)

Results

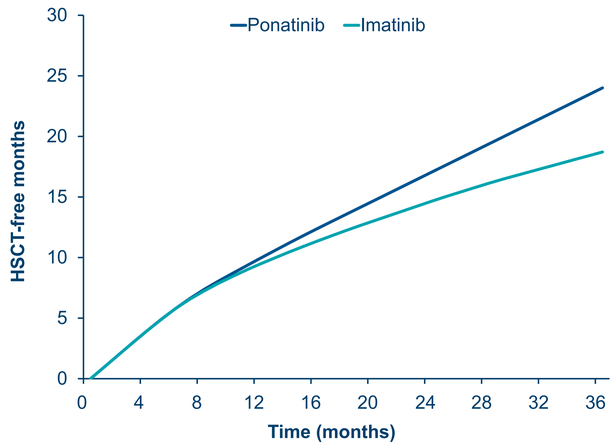
Model outcomes

- In a 1-million-member commercial health plan, an estimated 4.6 patients will develop Ph+ ALL each year
- Following these 4.6 patients over a 3-year time horizon, treatment with ponatinib results in 1.2 averted HSCTs on average versus imatinib
- By Year 3, the NNT to avert 1 HSCT with ponatinib is estimated to be 3.5, and patients treated with ponatinib experience on average up to 5.3 additional HSCT-free months versus imatinib **(Figure 3)**
- The incremental cost per month of delayed HSCT was $22,802 in Year 1 and declined to $1,712 by Year 3 with ponatinib **(Table 2)**
- Total incremental PMPM costs were $0.05 and $0.04 in Year 1 and Year 3, respectively

Table 2: CCM outcomes

Outcomes	Year 1	Year 2	Year 3
Total averted HSCTs	0.57	0.82	1.18
NNT (based on RMST)	19.94	6.10	3.54
HSCT-free months (based on RMST)			
Ponatinib	9.98	17.06	24.00
Imatinib	9.50	14.65	18.71
Delayed-HSCT months	0.48	2.40	5.29
Cumulative total costs per patient (USD)			
Ponatinib	376,097	546,234	688,109
Imatinib	254,898	319,645	367,053
Cost/HSCT-free month (USD)			
Ponatinib	37,691	32,027	28,667
Imatinib	26,826	21,812	19,614
Cost/month of delayed HSCT with ponatinib (USD)	22,802	4254	1712
Total costs PMPM (USD)			
Ponatinib	0.14	0.10	0.09
Imatinib	0.10	0.06	0.05
Cost difference	0.05	0.04	0.04

Figure 3: Cumulative HSCT-free months in patients treated with ponatinib and imatinib



Conclusion

- This analysis demonstrates that treatment of ND Ph+ ALL patients with ponatinib may offer more efficient care by delaying or avoiding HSCT and complications thereof at a modest cost versus treatment with imatinib

References

1. Khera N, et al. Blood 2012;120:1545–51.
2. Godara A, et al. JCO Oncol Pract 2021;17:e355–68.
3. Vetterranta K, et al. Front Pediatr 2021;9:807002.
4. Aldoss I, et al. Blood 2023;142(Supp 1):2871.
5. ICLUSIG® (ponatinib) [package insert]. Takeda Pharmaceuticals U.S.A. Inc. Accessed April 9, 2024.
6. National Cancer Institute, Cancer Stat Facts. Available at: https://seer.cancer.gov/statfacts/html/alyl.html. Accessed April 18, 2004.
7. Leukemia & Lymphoma Society. PH-Positive ALL Therapy. Available at: https://www.lls.org/leukemia/acute-lymphoblastic-leukemia/treatment/ph-positive-all-therapy. Accessed April 18, 2004.
8. Bonafede M, et al. J Med Econ 2017;20:1244–51.
9. Farhadfar N, et al. Transplant Cell Ther. 2021 Dec;27:1007.e1-1007.e8.
10. Agency for Healthcare Research and Quality. Healthcare cost & utilization project user support. Available at: www.hcup-us.ahrq.gov/toolssoftware/ccsr/dxccsr.jsp. Accessed April 18, 2024.
11. ProspectoRx. Elsevier. 2021. Accessed December 7, 2023. https://prospectorx.com.
12. Practice Management Information Corporation (PMIC). Usual, customary and reasonable fees. ISBN: 978-1-57066-725-1.
13. Brown PA, et al. J Natl Compr Canc Netw 2021;19:1079–1109.

Acknowledgments

This study was funded by Takeda Pharmaceuticals, Inc.

Disclosures

LH, **CL**, and **LER:** employment and stock ownership (Takeda)
SD and **IJ:** employment (PRECISIONheor)

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