Abstract 3081

Predictors of Ponatinib Therapy Duration Among Real-world Chronic-Phase Chronic Myeloid Leukemia (CP-CML) Patients in the US

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INTRODUCTION

- Ponatinib is a potent oral tyrosine kinase inhibitor (TKI) active against native and mutant forms of BCR-ABL, including the T315I mutation, which renders other TKIs ineffective[1]
- Ponatinib is approved for the treatment of adult patients with chronic myeloid leukemia (CML) or Philadelphia chromosome–positive acute lymphoblastic leukemia (Ph+ ALL) for whom no other TKI therapy is indicated or for those with the T315I mutation[2,3]
- The US prescribing information recommends a ponatinib starting dose of 45 mg/d,[2] with consideration of lower starting doses in patients with selected comorbidities
- In the US, ponatinib is available exclusively through a specialty pharmacy (Biologics, Inc., Cary, NC, USA) that maintains prescribing data for all US ponatinib-treated patients
- Analyses of dispensed ponatinib prescriptions for chronic-phase CML (CP-CML) patients show that median therapy duration exceeds 1.5 years but is variable across groups

OBJECTIVE

- To examine demographic, clinical, and physician characteristics from real-world US pharmacy data for ponatinib to determine predictors of ponatinib therapy duration in patients with CP-CML

METHODS

Study design	• Retrospective analysis of patients starting treatment with ponatinib over the 2.5-year period from January 1, 2014 to June 30, 2016
Patients	• N=475, US patients with CP-CML (“real-world”)
Data source	• Referring physicians, patient intake forms, and pharmacy dispensing records from Biologics
Analyses	• Kaplan-Meier techniques and log-rank tests were used to compare duration of therapy by patient and prescribing physician characteristics • Multivariate proportional hazard regression (PH-REG) was used to generate adjusted hazard ratios and identify primary drivers of ponatinib therapy duration • PH-REG results are reported adjusting for all available variables as well as using stepwise selection, in which only those variables with a relationship to duration at *P*>0.1 at model entry are included

Potential Predictors of Ponatinib Therapy Duration

- Gender (male/female)
- Age (</≥65 years)
- Reported T315I status (yes/no)
- Line of therapy (second–fifth)
- Most recent prior TKI (imatinib, nilotinib, dasatinib, or bosutinib)
- Starting dose (15, 30, or 45 mg/d)
- Prescribing physician practice type (academic/community)
- Number of ponatinib patients treated by physician (1, 2, 3, or more)

RESULTS

Duration of Therapy by Patient and Prescribing Physician Characteristics

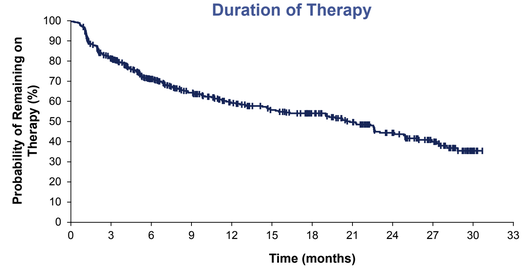
Characteristics	Total N=475	Median, mo	*P* Value
Gender,[a] n (%)			
Male	247 (52%)	22.4	0.049
Female	225 (48%)	15.5	
Age, n (%)			
<65 years	338 (71%)	20.7	0.816
≥65 years	137 (29%)	20.7	
Reported T315I, n (%)			
Yes	48 (10%)	27.9	0.067
No	427 (90%)	19.2	
Line of therapy,[b] n (%)			
Second-line	56 (15%)	22.2	0.516
Third-line	109 (29%)	21.9	
Fourth-line	140 (37%)	22.6	
Fifth-line	69 (18%)	12.3	
Most recent line prior TKI,[c] n (%)			
Imatinib	42 (11%)	26.1	0.274
Nilotinib	90 (24%)	20.1	
Dasatinib	146 (39%)	19.2	
Bosutinib	95 (25%)	24.4	
Starting dose of ponatinib, n (%)			
45 mg/d	223 (47%)	19.3	0.246
30 mg/d	140 (29%)	15.9	
15 mg/d	112 (24%)	22.5	
Physician practice type,[d] n (%)			
Community	125 (41%)	22.3	0.314
Academic	182 (59%)	20.1	
Ponatinib patients per physician, n (%)			
1	361 (76%)	18.9	0.121
2	48 (10%)	11.9	
≥3	66 (14%)	26.1	

[a] 3 missing values; [b] 101 missing values; [c] 102 missing values; [d] 168 missing values

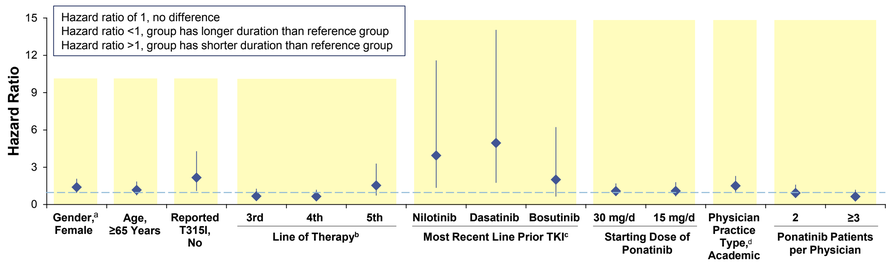
- About one-half of patients were male
- Most patients were <65 years of age
- Only 10% of patients were reported to have the T315I mutation
- Most patients were in their third- or fourth-line of therapy, and had most commonly switched from dasatinib
- Nearly one-half of patients had a ponatinib starting dose of 45 mg/d
- Slightly more than one-half of prescribing physicians were in academic settings, and more than three-quarters had only 1 ponatinib patient

- Median time on ponatinib therapy was 20.7 months by Kaplan-Meier estimate
- Unadjusted Kaplan-Meier analysis showed:
  - Gender was the only significant predictor of time on therapy when assessing each predictor individually
    - Women had significantly shorter duration of treatment than men
  - There was a trend for patients with the T315I mutation to have longer duration of treatment than patients without the T315I mutation

Duration of Therapy



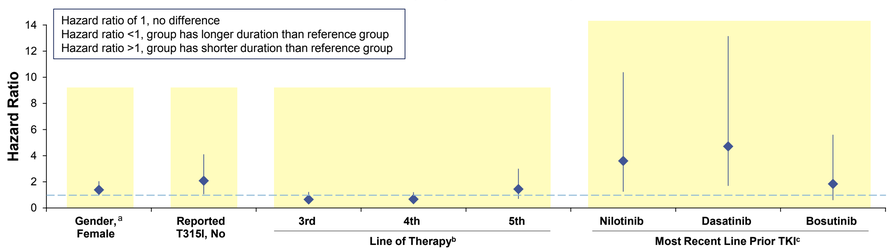
Duration of Therapy: Hazard Ratios (PH-REG) Adjusted for All Available Variables



Reference Group	Gender, Male	Age, <65 Years	Reported T315I, Yes	Line of Therapy, 2nd			Most Recent Line Prior TKI, Imatinib			Starting Dose of Ponatinib, 45 mg/d		Physician Practice Type, Community	Ponatinib Patients per Physician, 1	
P value	0.099	0.507	0.028	0.033[a]	0.033[a]	0.033[a]	0.002[e]	0.002[e]	0.002[e]	0.927[e]	0.927[e]	0.056	0.364[e]	0.364[e]
HR (CI)	1.40 (0.94–2.07)	1.17 (0.74–1.85)	2.16 (1.09–4.29)	0.68 (0.36–1.27)	0.65 (0.36–1.19)	1.54 (0.72–3.29)	3.94 (1.34–11.59)	4.95 (1.75–14.05)	2.01 (0.65–6.23)	1.08 (0.68–1.70)	1.09 (0.66–1.80)	1.51 (0.99–2.30)	0.92 (0.53–1.60)	0.64 (0.34–1.19)

[a] 3 missing values; [b] 101 missing values; [c] 102 missing values; [d] 168 missing values; [e] Overall *P* value for characteristic
CI, confidence interval; HR, hazard ratio

Duration of Therapy: Hazard Ratios (PH-REG) Adjusted for Variables With a Relationship to Duration at *P*>0.1 at Entry (Stepwise Selection)



Reference Group	Gender, Male	Reported T315I, Yes	Line of Therapy, 2nd			Most Recent Line Prior TKI, Imatinib		
P value	0.085	0.033	0.054[d]	0.054[d]	0.054[d]	0.001[d]	0.001[d]	0.001[d]
HR (CI)	1.40 (0.95–2.05)	2.09 (1.06–4.11)	0.67 (0.36–1.24)	0.68 (0.38–1.22)	1.45 (0.70–3.01)	3.61 (1.25–10.39)	4.72 (1.69–13.15)	1.85 (0.61–5.61)

[a] 3 missing values; [b] 101 missing values; [c] 102 missing values; [d] Overall *P* value for characteristic
CI, confidence interval; HR, hazard ratio

- In analyses adjusted for other covariates:
  - Significantly shorter durations of ponatinib therapy were observed for:
    - Non-T315I patients
    - Patients whose most recent TKI was not imatinib
  - Borderline significantly shorter duration of ponatinib therapy was observed in women versus men, and in academic versus community physician practice type
  - Versus second-line, patients in third- and fourth-line had longer duration, while fifth-line had shorter duration
  - No significant differences in therapy duration were observed in the analyses by age (<65, vs ≥65 years), starting dose (45, vs 30 and 15 mg/d), and physician experience with ponatinib (as measured by number of ponatinib patients per physician)

Study Strengths

- Complete dispensing data are available for all US ponatinib patients from a single-source specialty pharmacy
- Up to 2.5 years of patient follow-up have accrued after initial ponatinib prescription

Study Limitations

- Exclusion of patients with missing CML phase may have excluded an unknown number of CP-CML patients from this analysis
- Assessment of drivers of treatment duration was limited to available patient and physician data
- Missing data for a number of characteristics limited power to examine these characteristics and may have biased results

SUMMARY & CONCLUSIONS

- Real-world US data for CP-CML patients receiving ponatinib show that a number of subgroups have median duration on ponatinib exceeding 2 years
- Differences between adjusted and unadjusted results suggest complex interaction between presence of T315I mutation, line of therapy, and most recent prior TKI in predicting therapy duration:
  - Controlling for presence of T315I, therapy duration in second-line is shorter than third- and fourth-line, likely owing to the availability of treatment alternatives in earlier lines
  - Controlling for T315I and therapy line, patients receiving ponatinib after imatinib have significantly longer therapy duration than those receiving ponatinib after a second-generation TKI
- Both unadjusted and adjusted analyses suggest female gender may be associated with shorter duration
- Treatment in an academic setting may be associated with shorter therapy duration after adjustment for T315I, line of therapy, and most recent prior TKI (*P*=0.056)
  - Difference may reflect greater use of transplant and clinical trial enrollment in academic settings
- Age, ponatinib starting dose (45, vs 30 and 15 mg/d), and physician experience with ponatinib were not significant predictors of therapy duration
- Drivers of ponatinib therapy duration may be complex, including disease-, patient-, and physician-related factors

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DISCLOSURES

This study was sponsored by ARIAD Pharmaceuticals, Inc.
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