INTRODUCTION

Background
- In January 2014, the tyrosine kinase inhibitor (TKI) ponatinib was reintroduced to the US market after an 11-week withdrawal to revise data on vascular occlusive events, review US prescribing information (USPI), and implement a risk evaluation and mitigation strategy (REMS).
- The USPI was revised to narrow the indicated population, include new and updated warnings, relax the starting dose of 45 mg, and add consideration of dose reduction in responding patients and discontinuation in non-responders, as follows.

Revised ponatinib label, 12/2013

INDICATIONS AND USAGE
Iclusig (ponatinib) is a kinase inhibitor indicated for the:
- Treatment of adult patients with T315I-positive chronic myeloid leukemia (CML) (chronic phase [CP], accelerated phase [AP], or blast phase [BP]) or T315I-positive Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL).
- Treatment of adult patients with CP-, AP-, or BP-CML or Ph+ ALL, for whom no other TKI therapy is indicated.

These indications are based upon response rate in diseases related to tyrosine kinase inhibition.

RECOMMENDED DOING

The optimal dose of Iclusig has not been identified. In clinical trials, the starting dose of Iclusig was 45 mg administered orally once daily; however, 98% of the patients required dose reductions to 30 mg or 15 mg once daily during the course of therapy.

Start dosing with 45 mg once daily. Consider reducing the dose of Iclusig for BP-CML, CP-CML, and AP-CML patients who have achieved a major cytogenetic response.

Consider discontinuing Iclusig if response has not occurred by 30 days (90 days).

METHODS

We performed a retrospective analysis of data for patients starting treatment with ponatinib between January 1, 2014 and September 30, 2015.

Data were obtained from referring physicians, patient intake forms, and the specialty pharmacy dispensing records.

Patient and prescriber characteristics, and dosing and dose modifications were quantified.

Clinical, demographic, and physician characteristics were examined as predictors of initial dose and dose modification using logistic regression.

Therapy duration was assessed using Kaplan–Meier methods and proportional hazards regression.

RESULTS

Characteristics of patients receiving ponatinib

- A total of 944 patients initiated treatment with ponatinib (ie, were new starts) in the US during the 21-month analysis period.
- Data were obtained from referring physicians, patient intake forms, and the specialty pharmacy dispensing records.
- Patients initiating ponatinib ranged in age from 3 to 94 years, with a median of 65 years; 44% were female.
- More than 97% of patients had CML and nearly a quarter had Ph+ ALL; the remainder had other hematologic cancers or solid tumors (Figure 1).

Ponatinib prescribing patterns and outcomes in US patients

- Of the 543 prescribers with available practice-location information, 55.2% and 44.8% of the patients with CML and Ph+ ALL, respectively, had at least one ponatinib patient.
- More than 80% of ponatinib prescribers wrote scripts for just a single ponatinib patient.
- Among patients with information on line of ponatinib therapy, a lower proportion of those with CML vs Ph+ ALL received ponatinib in second line or higher (Figure 2).
- Among patients with information on most recent prior TKI, the most common TKI therapy received prior to initiation of ponatinib was dasatinib, followed by nilotinib (Figure 3).

Ponatinib dosing

- Despite current dosing recommendations, only approximately one-half of the CML and Ph+ ALL patients initiated ponatinib at the standard 45-mg dose (Figure 4); the percentage of patients starting ponatinib at 15 mg was nearly twice as high in patients with CML as in those with Ph+ ALL.
- Across all patients, males were more likely to be prescribed ponatinib at a 45-mg starting dose than females (multivariate OR=1.48, 95% CI 1.02–2.11, P=0.042).
- Across all patients, 31% of patients had at least one dose adjustment, including 22% with dose reductions.
- Among the 73 CP-CML patients initially prescribed ponatinib 45 mg who had at least 6 months of therapy, 37.5% reduced their ponatinib dose 41% to 30% and 10% to 15 mg (percentages refer to first switch; some patients switched dose more than once).

Ponatinib prescriber characteristics

- More than 80% of prescribers wrote scripts for just a single ponatinib patient during the analysis period (Table 1).
- Of the 543 prescribers with available practice-location information, 55.2% and 44.8% practiced in academic and community settings, respectively (Table 1).

CONCLUSIONS

- These real-world US data demonstrate that ponatinib is generally prescribed according to the approved label indications, with approximately 95% of treated patients having the indicated Ph+ leukemias (CML and Ph+ ALL).
- Ponatinib is prescribed across lines of therapy and disease phases.
- Physicians are using lower-than-recommended starting doses for approximately one-half of patients; dose reduction is also common.
- Most prescribers have only one ponatinib patient, but those with three or more are more likely to utilize lower starting doses.
- CP-CML patients initiated on ponatinib at 15 mg appear to have similar or better treatment duration compared with those started at higher doses.

References


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Disclosures:

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Abbreviations: Ph+ ALL: Philadelphia chromosome-positive acute lymphoblastic leukemia; CML: chronic myeloid leukemia; Dasatinib: a tyrosine kinase inhibitor; nilotinib: a tyrosine kinase inhibitor; nilotinib: a tyrosine kinase inhibitor; AP: accelerated phase; BP: blast phase; CML: chronic myeloid leukemia; CP: chronic phase; Ph+ ALL: Philadelphia chromosome-positive acute lymphoblastic leukemia; CP-CML: chronic phase chronic myeloid leukemia; AP-CML: accelerated phase chronic myeloid leukemia; BP-CML: blast phase chronic myeloid leukemia; Ph+ ALL: Philadelphia chromosome-positive acute lymphoblastic leukemia; TKI: tyrosine kinase inhibitor; AML: acute myeloid leukemia; HCL: hairy cell leukemia; DLBCL: diffuse large B-cell lymphoma; Ph: Philadelphia chromosome; BCR-ABL: break point cluster region-Abelson tyrosine kinase; CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease; OS: overall survival; PFS: progression-free survival; TKI: tyrosine kinase inhibitor; EMI: expected median interval; CI: confidence interval; HR: hazard ratio; OR: odds ratio; CI: confidence interval; "n" represents number of patients; "%" represents percentage of patients; "N" represents number of patients who received ponatinib; "%" represents percentage of patients who received ponatinib.

Figure 1. Distribution of new ponatinib patients by diagnosis

- Among patients with information on line of ponatinib therapy, a lower proportion of those with CML vs Ph+ ALL received ponatinib in second line or higher (Figure 2).
- Among patients with information on most recent prior TKI, the most common TKI therapy received prior to initiation of ponatinib was dasatinib, followed by nilotinib (Figure 3).

Figure 2. Distribution of new ponatinib patients with Ph+ ALL or CML by line of therapy

- Among patients with information on most recent prior TKI, the most common TKI therapy received prior to initiation of ponatinib was dasatinib, followed by nilotinib (Figure 3).

Figure 3. Distribution of new ponatinib patients with Ph+ ALL or CML by most recent prior TKI

- Among patients with information on most recent prior TKI, the most common TKI therapy received prior to initiation of ponatinib was dasatinib, followed by nilotinib (Figure 3).

Figure 4. Kaplan–Meier curves for estimated time on ponatinib treatment for new ponatinib patients with Ph+ ALL or CML by diagnosis/indication phase

- Among patients with information on most recent prior TKI, the most common TKI therapy received prior to initiation of ponatinib was dasatinib, followed by nilotinib (Figure 3).

Figure 5. Kaplan–Meier curves for estimated time on ponatinib treatment for new ponatinib patients with Ph+ ALL or CML by diagnosis/indication phase

- Among patients with information on most recent prior TKI, the most common TKI therapy received prior to initiation of ponatinib was dasatinib, followed by nilotinib (Figure 3).

Figure 6. Kaplan–Meier curves for estimated time on ponatinib therapy for new ponatinib patients with CP-CML by initial ponatinib dose

- Among patients with information on most recent prior TKI, the most common TKI therapy received prior to initiation of ponatinib was dasatinib, followed by nilotinib (Figure 3).