Use of Ibrutinib for Chronic Lymphocytic Leukemia in Routine Clinical Practice: Results From the Belgian Ibrutinib Real-World Data (BiRD) Study

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OBJECTIVE

This interim analysis of the BiRD study aims to understand characteristics and treatment patterns of patients with chronic lymphocytic leukemia (CLL) in Belgium who are being treated with ibrutinib, including demographics, prior treatments, genetic status, medical history, and comorbidities.

METHODS

Study Design

BiRD is an ambispective, noninterventional, multicenter, observational study. Patients were aged ≥ 18 years, had a confirmed diagnosis of CLL, and were eligible for reimbursed ibrutinib treatment according to International Workshop on Chronic Lymphocytic Leukemia criteria¹ at the time of treatment start. Patients with relapsed/refractory (R/R) CLL or patients with 17p deletion (del17p) or *TP53* mutation initiated reimbursed ibrutinib therapy (according to the National Institute for Health and Disability Insurance²) on or after its commercial availability (August 1, 2015), or had participated in the Medical Need Program (MNP) for CLL and switched to reimbursed ibrutinib.

Interim Analysis

Patients received ≥ 1 dose of ibrutinib with ≥ 3 months of therapy. The planned study duration is expected to be ~ 4 years.

RESULTS

140 patients were included in this interim analysis; 126 (90.0%) of these patients had received prior lines of therapy (R/R). Median age at treatment initiation was 71 years, 62.1% were male, and 13.3% (13/98 patients; data missing: $n = 42$) had an Eastern Cooperative Oncology Group performance status ≥ 2 . Median time between diagnosis and ibrutinib initiation was 6.3 years. 41 patients (29.3%) had received second-line treatment, 49 (35.0%) third-line, and 36 (25.7%) ≥ 3 prior lines.

Patient Demographics by Prior Line of Therapy

Treatment-free periods preceding ibrutinib initiation ranged from 10.5 months (≥ 3 prior lines) to 25.8 months (1 prior line). Most frequently used treatments prior to ibrutinib are shown in **Figure 1**. Overall, combination therapy was most frequently used in all lines prior to ibrutinib.

Figure 1. Most Frequently Used Treatment in Most Recent Line Immediately Prior to Ibrutinib (N = 126)

BR, bendamustine + rituximab; FCR, fludarabine + cyclophosphamide + rituximab.

REFERENCES

1. Hallek M, et al. *Blood*. 2008;111:5446-5456.
2. <http://ondpanon.riziv.fgov.be/SSPWebApplicationPublic/nl/Public/ProductSearch> (Accessed January 26, 2018.)
3. <http://www.riziv.fgov.be/SiteCollectionDocuments/infospot-2016-01-nl.pdf> (Accessed January 26, 2018.)

Patient Demographics by Genetic Status

Genetic status of patients is shown in **Figure 2**. All patients receiving first-line ibrutinib had a del17p and/or *TP53* mutation (33.3% [6/18 patients; data missing: $n = 18$] for patients with ≥ 3 prior lines). Patients with del17p and/or *TP53* mutation ($n = 49$) were younger (median 70.0 vs 75.0 years), more likely to have fewer prior lines, and had a shorter time from diagnosis to ibrutinib initiation (4.3 vs 8.9 years) than patients without del17p and/or *TP53* mutation ($n = 33$).

The number of patients tested for del17p and/or *TP53* mutation status decreased with increasing lines (no missing values in treatment-naïve [TN] patients; 14/41 missing for second-line; 26/49 missing for third-line, 18/36 missing for ≥ 3 prior lines). The most frequently used prior treatment was FCR (with del17p and/or *TP53* mutation: $n = 15$; 30.6%; without del17p and/or *TP53* mutation: $n = 20$; 60.6%).

Figure 2. Genetic Status at Ibrutinib Initiation (N = 140)

Medical History and Comorbidities at Ibrutinib Initiation

22/134 (16.4%) patients had a history of cardiovascular disease. Creatinine clearance was < 30 mL/min in 3/130 (2.3%) patients, and ≥ 30 to < 70 mL/min in 41/130 (31.5%) patients. 16.4% of patients were using ≥ 1 antithrombotic agent when starting on ibrutinib.

Prescribed Dose of Ibrutinib at Initiation

Ibrutinib dose was lower (140-280 mg) than recommended (420 mg) in 19/157 (12.1%) patients. Reasons for the lower starting dose were mainly physician's preference ($n = 13$; 68.4%) and concomitant medication/comorbidities ($n = 4$; 21.1%).

CONCLUSIONS

- As expected from the reimbursement situation, CLL patients in BiRD receiving ibrutinib were mainly R/R; all TN patients had del17p and/or *TP53* mutation.
- FCR and BR were the most frequent treatment choice in all prior lines of therapy.
- At treatment initiation, del17p/*TP53* mutation status is not always known, though guidelines recommend testing this prognostic factor. *IGHV* mutation status was only tested in 37.1% ($n = 52$) of patients, of which 71.2% ($n = 37$) were unmutated.
- Platelet aggregation-inhibitor and anticoagulant use was low; higher percentages could be expected in this age group.³
- The ibrutinib starting dose was lower than recommended in the Summary of Product Characteristics in 12.1% of patients.

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