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 criteria 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 Insurance) 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, 36 (25.7%) third-line, and 35 (25.0%) patients had received prior lines of therapy (R/R). The number of patients tested for del17p and/or TP53 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%).

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)

<table>
<thead>
<tr>
<th>Prior Lines</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FCR</td>
</tr>
<tr>
<td>2</td>
<td>BR, Chlorambucil</td>
</tr>
<tr>
<td>≥ 3</td>
<td>Bendamustine + rituximab</td>
</tr>
</tbody>
</table>

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

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%).

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.
• The ibrutinib starting dose was lower than recommended in the Summary of Product Characteristics in 12.1% of patients.

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REFERENCES

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