Time Trends in Frontline Systemic Therapy Utilization for Chronic Lymphocytic Leukemia in the United States

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BACKGROUND

- Immunochemotherapy has been the treatment mainstay for patients with a diagnosis of chronic lymphocytic leukemia (CLL) requiring therapeutic intervention.
- The introduction of next-generation targeted therapies, such as ibrutinib, a first-in-class Bruton's tyrosine kinase inhibitor, for treatment of CLL is expected to redefine the therapeutic landscape.
- Several clinical studies are currently underway to evaluate targeted therapies in combination with immunochemotherapy for potential benefits in response rate and survival.[1]
- However, limited data exist in the current literature about patterns in treatment selection and temporal trends in treatment utilization among patients with a diagnosis of CLL.

OBJECTIVE

- To describe recent trends in utilization of frontline systemic therapies for CLL in the United States (US)

METHODS

Data Source

- Data for this retrospective cohort study were taken from the Truven databases, which include information on more than 60 million unique individuals enrolled in employer-sponsored private health insurance plans across the US.
- These databases provide longitudinal data on medical and pharmacy service utilization, and associated payments, collected from nearly 350 employers and payers in the US.

Patient Selection

- Patients with a diagnosis of CLL during the patient selection window (from July 1, 2012, through June 30, 2015) were identified using the following diagnosis codes:
  - ICD-9-CM: 204.1x (CLL)
  - ICD-10-CM: C91.1x (CLL) or C83.0x (for small cell B-cell lymphoma [small lymphocytic lymphoma], which denotes nonleukemic cases with the tissue morphology and immunophenotype of CLL)
- Patients were required to (1) have at least 2 medical claims on separate dates with a diagnosis code for CLL, (2) be ≥ 18 years of age at CLL diagnosis, and (3) have had ≥ 12 months of continuous enrollment in medical and drug plans before the first recorded CLL diagnosis.
- Patients must have initiated a systemic therapy, after the diagnosis of CLL, during the period from July 2012 through June 2016.
- Patients were followed through the earlier of disenrollment from the medical and/or drug plan or end of the study period (June 30, 2016).

Study Measures and Analysis

- Baseline patient characteristics, including demographics and comorbid conditions, were assessed at CLL diagnosis or during the 12-month period before CLL diagnosis.
- CLL-directed treatments were identified using relevant National Drug Codes, brand and generic product names, Healthcare Common Procedure Coding System codes, and ICD-9 and ICD-10 procedure/diagnosis codes as applicable.
- A treatment regimen was defined as the combination of all agents observed on or within 35 days after the first claim for a systemic therapy drug—based on previously published literature.[2,3]
- The following treatment regimens or regimen groups were assessed:
  - Ibrutinib (monotherapy or combination)
  - Rituximab monotherapy (R-monotherapy)
  - Bendamustine/rituximab (BR)
  - Fludarabine/cyclophosphamide/rituximab (FCR)
  - Other rituximab combinations (except with ibrutinib)
  - Other regimens
- The percentages of patients treated with various first-line regimens were assessed by calendar year and stratified by age group (< 65 years and ≥ 65 years).
- All analyses were descriptive and were performed using SAS version 9.4.

RESULTS

- A total of 1,379 patients met the selection criteria.
- Almost equal proportions of patients were aged <65 years (49.9%) and ≥ 65 years (50.1%); a majority (64%) were male.
- The numbers of patients with any systemic therapy by calendar year were 143 (2012 [Jul-Dec]), 360 (2013), 470 (2014), 309 (2015), and 97 (2016 [Jan-Jun]).
- Utilization of BR as the frontline therapy increased from 23.1% in 2012 to 31.4% in 2015 but declined sharply to 13.4% in early 2016, with a corresponding increase in the use of ibrutinib from 11.7% in 2015 to 25.8% in early 2016 (Figure 1).
- The use of FCR and other rituximab-based immunochemotherapy regimens declined during the study period; the use of R-monotherapy remained approximately stable, with slightly increased use in 2014 and 2016 (Figure 1).
- For patients aged < 65 years, BR and R-monotherapy were also the preferred treatments in the early study years, but again BR use decreased in 2016, with increasing use of ibrutinib during the last 3 years of the study (from 10% to 24%) in this age group (Figure 2A).
- For patients aged ≥ 65 years, BR and R-monotherapy were the preferred treatments in the early years of the study, but the use of BR decreased considerably by 2016, with increasing use of ibrutinib from 13% to 28% of patients during the last 3 years of the study in this age group (Figure 2B).
- FCR was predominantly used in patients aged < 65 years, but its use decreased in both age groups during the study period (Figure 2).

Figure 1. Trend in the Utilization of CLL-Directed Treatment Regimens, Total Sample

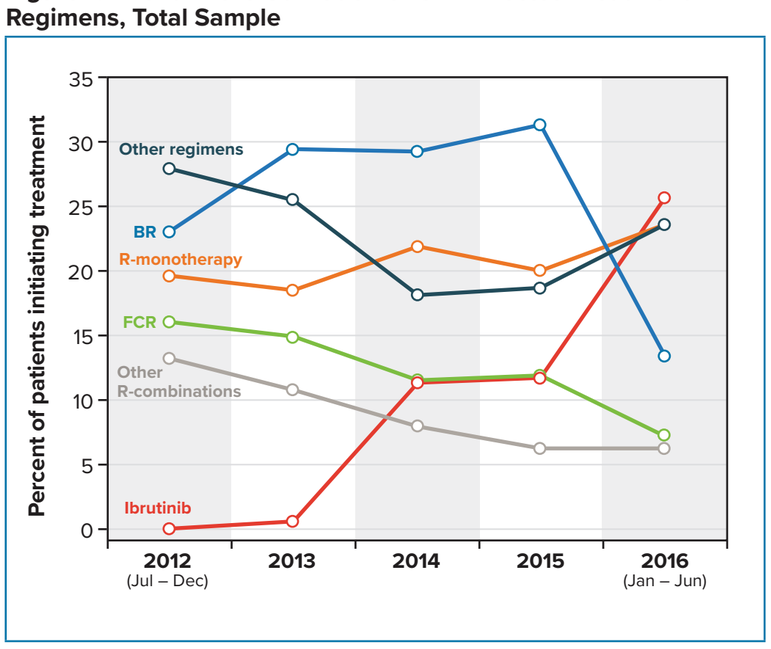
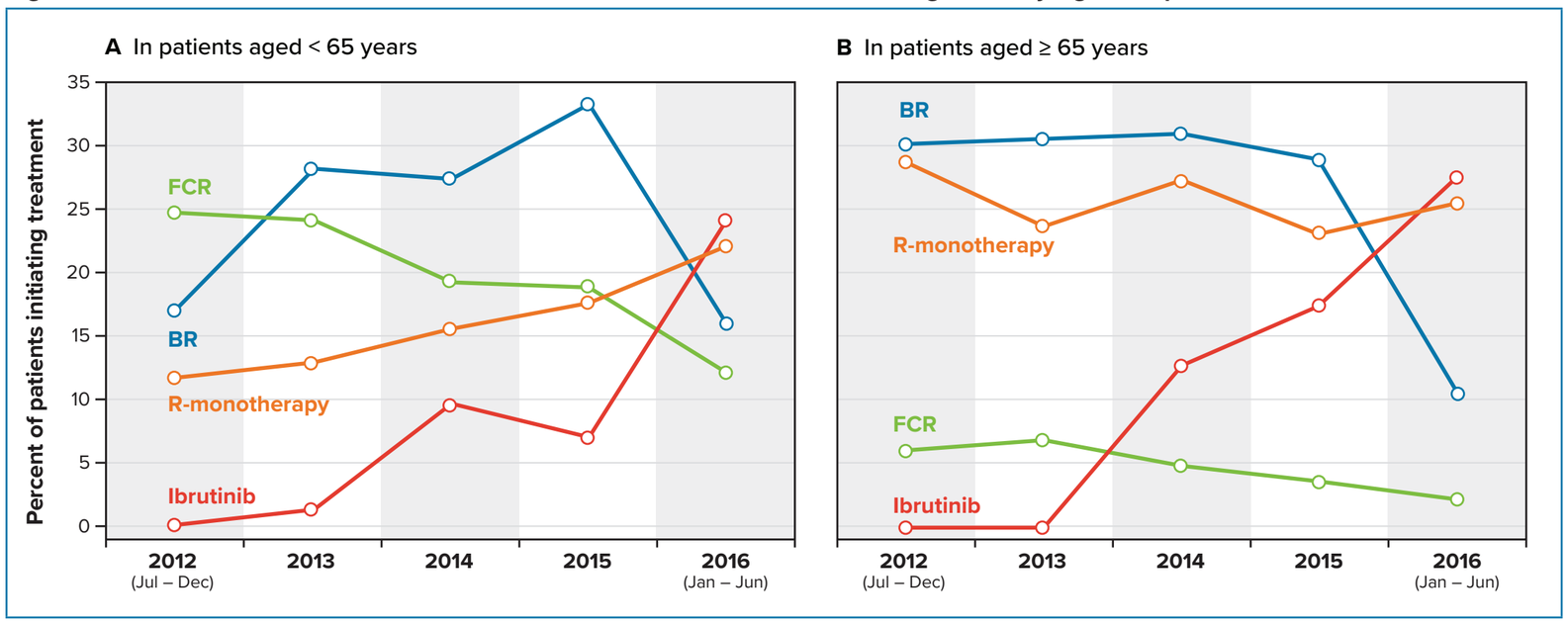


Figure 2. Trends in Utilization of the 4 Most Common CLL-Directed Treatment Regimens, by Age Group



DISCUSSION AND LIMITATIONS

- To the best of our knowledge, this is the first analysis reporting population-based time trends in utilization of CLL-directed treatments during recent years.
- The decline in the use of immunochemotherapy regimens, FCR and BR, in recent years corresponds to an increase in the uptake of ibrutinib, a novel targeted therapy that was approved by the US Food and Drug Administration in March 2016 as a first-line therapy for all patients with CLL. (Its previous US Food and Drug Administration–approved indication, granted in July 2014, was limited to patients with CLL with del 17p.)
- These findings are subject to limitations commonly associated with analyses based on insurance claims databases, and as such, the methods to identify CLL-directed treatments relied on claims-based algorithms and the accuracy of coding; therefore, some misclassification may be present.
- Additionally, the analyses are based on a commercially enrolled population of patients in the US, and therefore, our study findings may not be generalizable to the general population.

CONCLUSIONS

- This study demonstrates a decline in the utilization of rituximab-based immunochemotherapy regimens and a substantial increase in the uptake of ibrutinib as the frontline therapy for CLL in the US during study period (July 2012 through June 2016). The uptake of ibrutinib was slightly more prominent in patients aged ≥ 65 years than in younger patients.
- The trends observed in this study signal a shift in physician preference for selection of frontline treatment with the availability of novel targeted therapy alternatives.
- As more novel targeted agents are approved or included in the treatment guidelines for CLL (e.g., venetoclax, acalabrutinib), further research should evaluate subsequent utilization trends overall and stratified by age and by line of therapy.

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