Persistence with oral therapy as reflection of actual compliance for chronic lymphocytic leukemia (CLL) – a national prescribed drug and patient register study from Sweden

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Background

Real-world data has demonstrated discrepancies between clinical trial outcomes and clinical practice and the impact of comorbidities on drug-related discontinuation (Aarup et al., 2020; Rotbain et al., 2021). Sweden has comprehensive national patient and prescription registers which make them a unique base for real-world data on oral drug use. By utilizing such data, it could be possible to study the use and persistence of oral chronic lymphocytic leukemia (CLL) drugs, also in relation to comorbidities.

Aims

Aims of the study were to gather real-world insights by describing oral drug persistence in CLL patients and to quantify the prevalence and incidence of patients treated with such drugs in Sweden.

Methods

Pseudonymized data from the National Prescribed Drugs Register and National Patient Register in Sweden was used. All patients with a new prescription of an oral CLL drug for continuous use (ibrutinib, idelalisib, and acalabrutinib) during the period 1 January 2017 – 31 December 2021 were selected. Patients with CLL (ICD-10 C91.1) or SLL (C83-0) diagnosis were further assessed in 3 disease groups (infections, autoimmune diseases, and cardiovascular diseases) to analyze how common comorbidities affect the persistence. Persistence was defined as the duration between starting and discontinuing an oral drug, i.e., the proportion of patients that are continuing to pick-up and refill their prescription of each drug. Persistence outcome was described using the Kaplan-Meier method and comparisons made through log-rank with a Z test. A grace period of 90 days was utilized to not exclude patients with short treatment breaks and a “lookback period” of 9 months was included to identify patients that were new to treatment. We had no data on previous intravenous treatment.

Results

Prescription data from 2479 patients were collected, of these, 1425 had CLL and 115 SLL. The majority (87%) of the CLL patients were prescribed ibrutinib. The lead of ibrutinib prescriptions (n=1234) was followed by acalabrutinib (n=117) and idelalisib (n=80). For CLL patients, the drug persistence at 36 months for ibrutinib was 50%, less than 10% for idelalisib (where a 50% persistence was reached at about 10 months), while acalabrutinib patients, having a very short follow-up, had a 9-month persistence of 92 % (Figure 1). For patients with CLL or SLL, 62% had a comorbidity diagnosis at the time or after their first prescription and the most common was a type of cardiovascular disease. CLL patients treated with ibrutinib that either contracted an

infectious disease (p<0.05, n=111) or developed a cardiovascular comorbidity (p<0.05, n=168) were more likely to discontinue their treatment compared to the overall CLL patient population.

Summary/Conclusion

Persistence with oral therapy is a well-recognized factor for an effective treatment. We found that half of the CLL patients treated with ibrutinib were still picking up their prescriptions after 36 months. Even though we have no information on previous intravenous treatment, most of the patients presumably have a relapsed/refractory (R/R) disease. In comparison, published real-world studies of R/R patients report a median progression-free survival (PFS) varying from 30 to 41 months for ibrutinib and about 16 months for idelalisib. Hence, it appears that drug persistence could reflect the actual compliance for CLL patients treated with an oral drug for continuous use and possibly function as a potential proxy for PFS. Furthermore, this study underlines that comorbidity is an important factor for lower drug persistence.

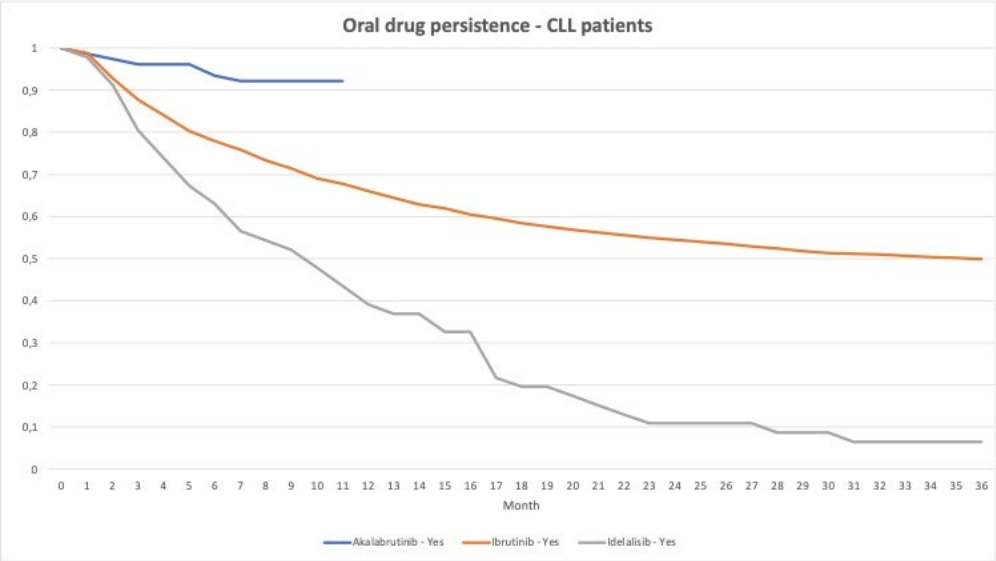

Figure 1

References

Aarup K, Rotbain E.C, Enggaard L, et al. Eur J Haematol 2020 Nov;105(5):646-654.
Rotbain E.C, Rostgaard K, Andersen M.A, et al. Clin Epidemiol. 2021 Dec 30;13:1155-1165.