Real-World Outcomes of Idelalisib in Relapsed/Refractory CLL (2016–2025)

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INTRODUCTION

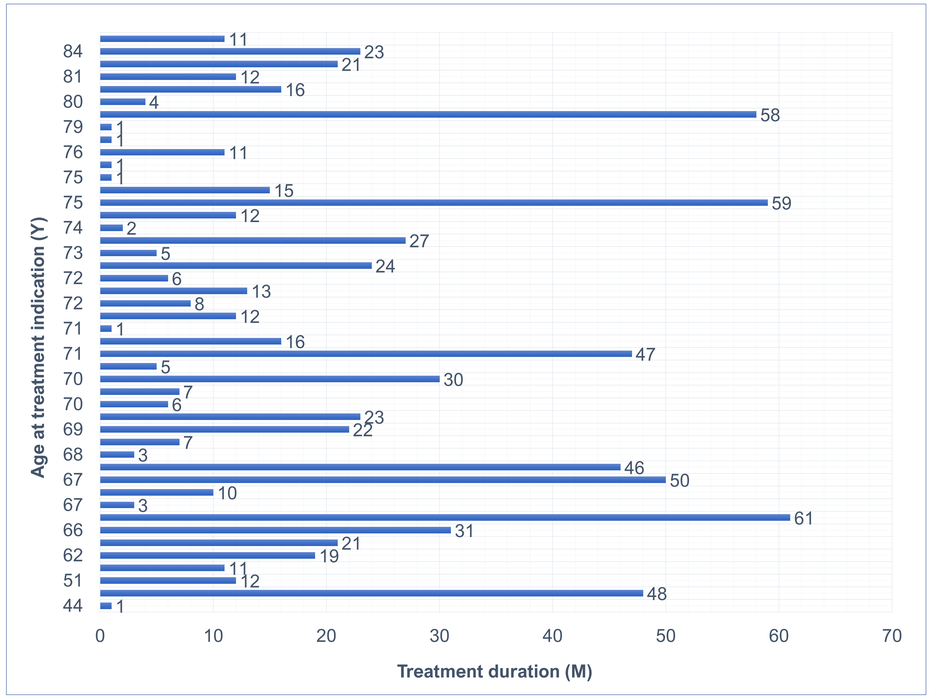
Despite major advances, therapeutic options after BTK and/or BCL2 inhibitor failure in CLL are limited, especially for TP53-aberrant disease. Idelalisib (PI3Kδ) remains a salvage option, but real-world durability is challenged by toxicity. **We report a single-center experience (2016–2025) and quantify time on idelalisib and reasons for discontinuation, including results in TP53-aberrant and previously BTKi/BCL2-treated patients.**

PATIENTS AND CASES DESCRIPTION

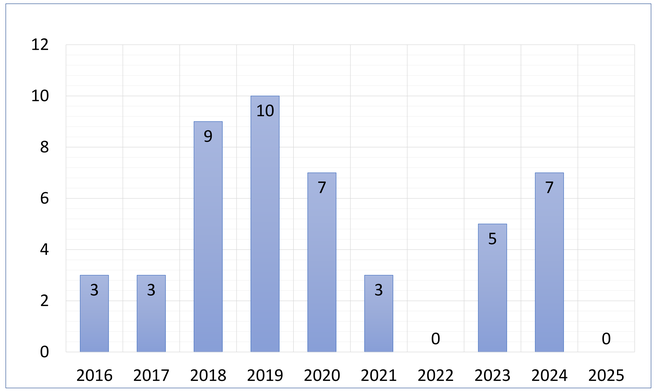
- We retrospectively reviewed **46 patients with R/R CLL** treated with idelalisib (± rituximab) between 2016 and 2025 at the Hemato-Oncology Clinic, University Hospital Olomouc.
- Median age was 71 years, range: 44–84.
- IGHV mutation status was unmutated in 83% (33 of 40 tested).
- TP53 mutation and/or del(17p) was detected in 37% (17/46).
- Most patients were heavily pretreated, with a median of 3 prior therapy lines.

RESULTS

Treatment duration corelated with age of initiation



Frequency of patients treated at the center over time



Parameter	Findings
Median treatment duration (all)	17.9 months (0.5-61)
del17p/p53 subgroup	20.1 months (1-58)
Treatment discontinued (42 pts)	20 PD (4RT), median 19.6 months (1-50) 14AE, median 8 months (1-24) 1 second malignancy
Ongoing treatment	4 pts, median 40.2 months
Adverse events (46%)	Colitis 26% (12) Infections 9% (5) Hepatopathy 6% (3) Pneumonitis 2% (1) Fatal: 1 COVID, 1 hepatitis/MODS
Therapy after idelalisib failure	Venetoclax (15 pts), ORR 60% Ibrutinib (2pts), PD
Idelalisib after bcl2/BTKi failure	10 pts (7 double refractory), ORR 50%, median 8.1 months (1-21)

CONCLUSION

- Idelalisib demonstrated clinical activity in relapsed/refractory CLL, including patients with high-risk features (del17p/p53).
- Treatment was limited by adverse events, most commonly colitis and infections, leading to discontinuation in a substantial proportion of patients.
- A subset of patients achieved durable benefit, with some continuing treatment beyond 40 months.
- Subsequent therapies after idelalisib failure (venetoclax, BTKi) showed meaningful efficacy.
  Idelalisib also retained activity in heavily pretreated patients after bcl2/BTKi failure, with a 50% response rate.