RWD70

Barriers to Genetic Risk Factor Molecular Testing in CLL: An Analysis of Real-World Practice and Alignment with 2023 Guidelines in Germany

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OBJECTIVES

Despite the 2023 German chronic lymphocytic leukemia (CLL) guidelines highlighting the importance of TP53 and IGHV testing for treatment decisions, many patients remain untested. This study aims to evaluate current molecular testing practices in Germany and explore barriers to implementation. The objectives are to assess adherence to TP53 and IGHV testing guidelines[1], identify physician-reported barriers such as perceived relevance, logistical issues, and systemic constraints, and examine how factors like patient's age, treatment choice, and resource availability affect testing rates. Findings from this study may help inform efforts to better align real-world practice with clinical guidelines and enhance molecular testing in CLL care.

METHODS

- **Study Design:** Retrospective, single-group observational study
- **Data Source:** Anonymized data from active healthcare institutions; 58 between HY2 2021 and HY2 2023
- **Data Collection:** eCRF from July 1, 2021 – December 31, 2023, for incident and prevalent CLL pts receiving causal treatment
- **Cohort:** 28 centers with low molecular testing rate (July 1, 2021 – December 31, 2023,), including UH, NUH, and OBP
- **Patient Data** (December 2023):
  - Total cohort: 673 first line (1L) patients
  - Molecular profiling: 554 1L patients
  - Untested: 116 1L pts
- **Testing Rates:** Identified centers with low testing rates
- **Clinician Feedback:** Thematically analyzed qualitative feedback
- **Investigated Barriers:** Patient factors, clinical workflow challenges, and systemic issues

Figure 1. Institutional Distribution

The 58 centers that retrospectively reported data from July 1, 2021, to December 31, 2023, were drawn from a cohort of 321 highly relevant treatment centers identified in a 2022 German HSCA analysis.

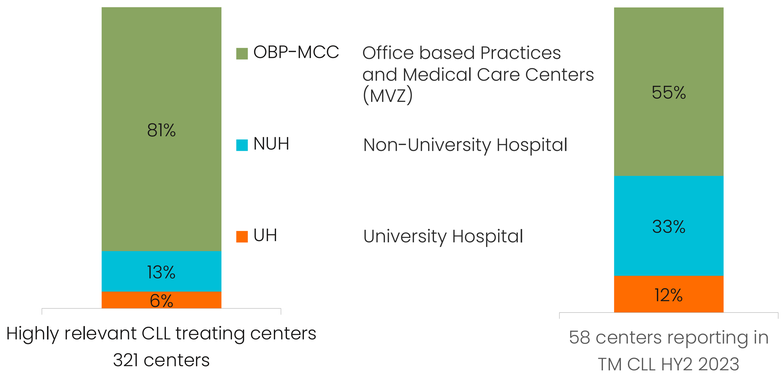


Figure 2. Molecular Testing Adherence

In a cohort of 673 1L prevalent patients, approx. 80% underwent molecular testing, despite 2023 CLL guideline recommendations emphasizing its role in guiding treatment decisions.

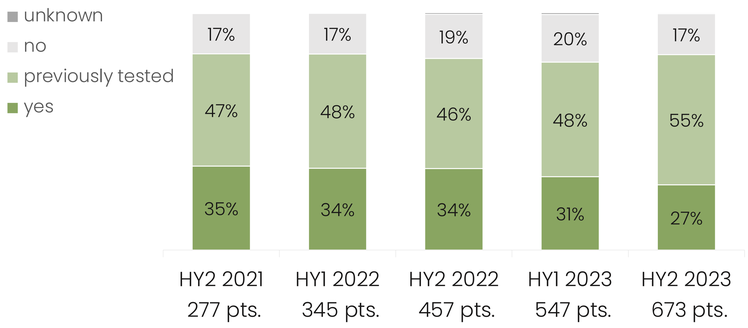


Figure 3. Genetic Risk Factor Distribution

Among the tested population (554 out of 673 1L patients), IGHV-unmutated status was the most frequently observed molecular risk factor, identified in approximately 50% of cases, followed by TP53 abnormalities, present in around 17% of patients.

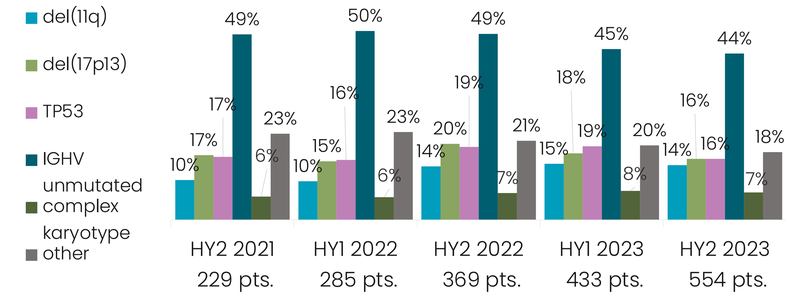
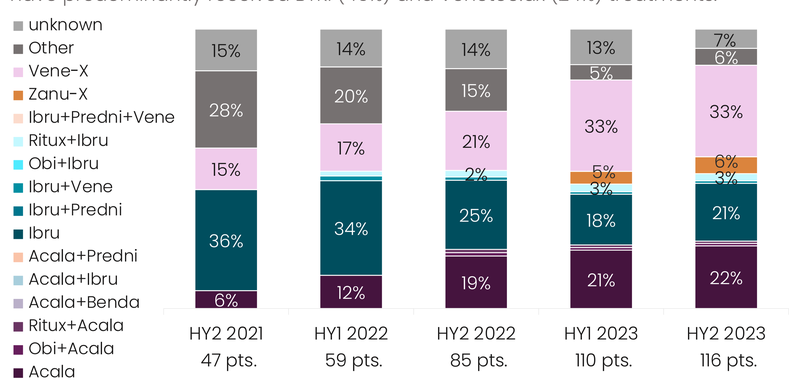


Figure 4. Treatment Decisions in Patients Without Molecular Genetic Risk Factor Testing

116 1L patients who have not undergone testing for molecular genetic risk factors have predominantly received BTKi (46%) and Venetoclax (24%) treatments.



RESULTS

Despite the 2023 German CLL guidelines emphasizing molecular testing for treatment decisions, observed real-world adherence remains around 80%, below the optimum near 100%. IGHV unmutated status is found in about 50% of tested patients, and TP53 abnormalities are detected in approximately 17%. Among untested patients, 46% received BTK inhibitors (BTKi), and 24% received Venetoclax. A cohort of 28 centers with low molecular testing rate was identified and 15 centers (54%) provided reasons for non-adherence.

Table 1. Clinician-Reported Barriers to Molecular Testing Adherence

Key barriers to molecular testing adherence, categorized thematically, with corresponding rationale and the proportion of clinicians reporting each barrier.

Barrier Category	Rationale	Proportion of Respondents (n; %)
Perceived Relevance	Testing was considered unnecessary for older patients on long-term therapies or with pre-determined treatment plans.	9; 60%
Practice Patterns	Testing was viewed as prognostic rather than predictive, especially for BTKi treatments in older patients.	3; 20%
Cost & Resource Constraints	High costs and insufficient sample availability discouraged testing, with additional testing deemed unnecessary.	2; 13%
Historical Practices	Inconsistent testing for older patients or those with pre-planned BTKi regimens led to gaps in molecular data in later lines.	4; 27%
Referral Issues	Patients from private practices or with outdated diagnostics lacked molecular data due to insufficient testing at initial diagnosis.	5; 33%

CONCLUSIONS

These findings expose gaps in molecular testing, driven by perceptions of limited clinical relevance, logistical barriers, and systemic issues. Addressing these challenges through education, streamlined workflows, and strategies to mitigate cost together with material constraints is crucial for aligning real-world practice with treatment guidelines.

[1] Deutsche Gesellschaft für Hämatologie und Medizinische Onkologie e.V. (DGHO). Chronische Lymphatische Leukämie (CLL)—Leitlinie 2023.

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