Real-world first line chronic lymphocytic leukemia treatment in Germany in the era of targeted agents

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INTRODUCTION

- The approval of novel drugs targeting BTK (ibrutinib, acalabrutinib, zanubrutinib) and BCL2 (venetoclax) lead to a profound change in the German chronic lymphocytic leukemia (CLL) treatment guidelines.[1-5]
- While age, comorbidities and physical status were essential for the decision to initiate chemoimmunotherapy (CIT), patients (pts) are now mainly classified according to the genetic risk profile of the disease.[1]
- However, only limited real-world observational data regarding the implementation of the updated recommendations is available.

AIM

To investigate factors that influenced first line (1L) treatment-decisions (BTKi-based, VEN-based, CIT) in the real-world setting

METHOD

- A retrospective, observational investigation conducted in 53 national institutions with a representative sample of university hospitals, smaller hospitals, Medical Care Centers, and practices was initiated.
- Between 1st July 2021 and 30th July 2023 481 pts that initiated first-line CLL treatment were included
- Data was collected in an eCRF by the treating physician and verified via central monitoring of pseudonymized patient documents
- Bivariate analysis identified predictive variables for treatment decisions with p-value below 0.05 regarded as statistically significant.

RESULTS

Table 1: Patient characteristics

Characteristics	Total, N = 481	BTKi, N = 262	VEN, N = 122	CIT, N = 46	χ^2	p-value
Sex - male	280	154	72	36	0.218	0.897
Age > 70	342	199	66	43	19.449	5.981E-05
Genetic risk factor tested	377	214	86	46	6.169	0.046
Del(11q)	67	42	8	13	9.750	0.008
Del(17p13)	61	43	12	1	10.482	0.005
TP53 aberration	97	63	25	3	10.712	0.005
IGHV unmutated	168	98	45	20	22.551	1.268E-05
Staging Binet C	208	135	43	24	7.215	0.027
Hypertension	235	145	49	27	7.990	0.018
Cardiac arrythmia	54	21	20	11	8.963	0.011
Diabetes	98	69	16	9	10.008	0.007
Anemia/thrombocytopenia	267	171	57	35	11.901	0.003

Fig. 1: Institutional Distribution

Distribution of the 53 centers that included patients in the retrospective investigation.

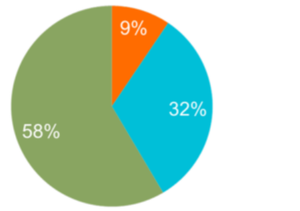

Fig. 2: Binet Staging

BTKi-treated pts were more frequently staged Binet C and VEN-treated pts more frequently staged Binet A and B.

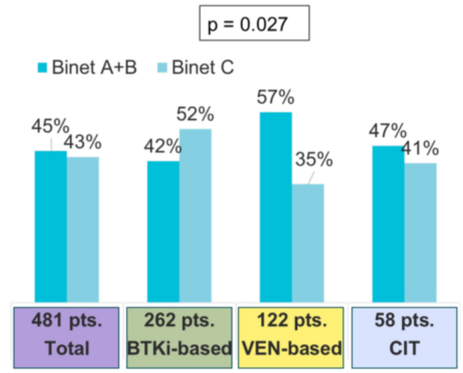

Fig. 3: Reasons to initiate treatment

Anemia or thrombocytopenia was the leading reason to initiate treatment among BTKi and CIT treated pts.

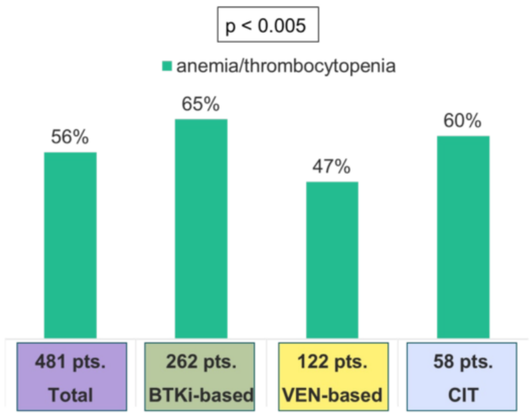

Fig. 4: Genetic risk factors

TP53 aberrant was more frequent among BTKi and VEN treated in comparison to CIT treated pts.

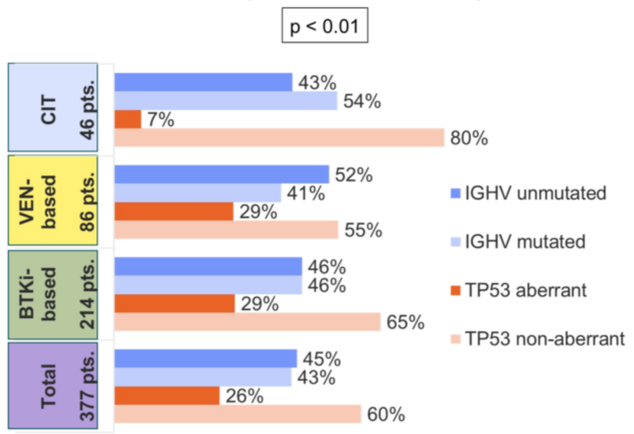

Fig 5: Comorbidities

Pts with cardiac arrythmia were less likely to receive BTKi-based treatment. Hypertension was more frequently diagnosed among BTKi treated pts.

CONCLUSIONS

- The essential genetic factors for risk-stratification and choice of treatment were available for most, but not for all pts of our real-world cohort.
- Though CIT was avoided in pts with a known TP53 alteration, IGHV mutational status and TP53 alterations were not associated with a specific targeted treatment. Advanced disease stage Binet C was associated with BTKi-based treatment.
- In summary, our observational investigation suggests that multiple factors influence the selection of treatment in the real-world setting and treatment decisions were not necessarily based on recommendations regarding the genetic risk stratification.

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