1212: Targeted agents in chronic lymphocytic leukemia (CLL): Data on outcomes and subsequent therapies of patients observed within the German CLL Study Group (GCLLSG) registry

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INTRODUCTION

BCL2-inhibitors (BCL2i) and BTK-inhibitors (BTKi) have profoundly improved the outcome of patients (pts) with chronic lymphocytic leukemia (CLL) and are considered standard treatment. However, the translation from novel treatments evaluated within clinical trials into routine clinical practice can be complex. The German CLL Study Group (GCLLSG) Registry provides real world data of pts with CLL on therapy choices outside of clinical trials in Germany. We here present data on efficacy and subsequent therapies of a large cohort of pts treated with either BCL2i (Venetoclax) or BTKi.

METHODS

- Patients with confirmed diagnosis of CLL and with at least one documented first-line CLL treatment between July 1st 2014 and January 30th 2023 were included in this analysis.
- Treatments were categorized according to the backbone of therapy and pts were allocated to either the venetoclax or the BTKi cohort depending on their first treatment with targeted agents
- Treatment sequences were visualized with a sankey-diagram. Time to next treatment (TTNT), event-free survival (EFS) and overall survival (OS) were analyzed using Kaplan-Meier methods.

RESULTS

- A total of 274 pts were allocated to the Venetoclax cohort while 915 pts were allocated to the BTKi cohort as first therapy using targeted agents
- Median observation time from the first documented treatment in the Venetoclax cohort was 26 months (range 0 – 296) and 78 months (range 0-266) for BTKi treatment.

Patient characteristics by cohort	Venetoclax (N = 274)		BTKi (N = 915)	
Age (years)	**274**		**915**	
Median (Range)	71 (32-87)		72 (32-92)	
≤ 65 (%)	93	(33.9)	282	(30.8)
Gender, N (%)	**274**		**915**	
Male	172	(62.8)	628	(68.6)
CIRS total score	**165**		**491**	
Median (Range)	2 (0-13)		3 (0-17)	
> 6 (%)	27	(16.4)	81	(16.5)
CIRS organ system heart, N (%)	**164**		**481**	
> 0	53	(32.3)	118	(24.5)
CIRS organ system blood pressure, N (%)	**165**		**487**	
> 0	78	(47.3)	254	(52.2)
ECOG performance status, N (%)	**160**		**476**	
= 0	80	(50.0)	204	(42.9)
= 1	68	(42.5)	227	(47.7)
= 2	11	(6.9)	42	(8.8)
= 3	1	(0.6)	3	(0.6)
Binet stage, N (%)	**137**		**487**	
A	29	(21.2)	92	(18.9)
B	56	(40.9)	194	(39.8)
C	52	(38.0)	201	(41.3)
Cytogenetic subgroup, N (%)	**57**		**175**	
Deletion 17p	7	(12.3)	42	(24.0)
Deletion 11q	7	(12.3)	22	(12.6)
Trisomy 12	4	(7.0)	19	(10.9)
No abnormalities	20	(35.1)	52	(27.7)
Deletion 13q	19	(33.3)	40	(22.9)
IGHV mutation status, N (%)	**57**		**162**	
Unmutated	32	(56.1)	108	(66.7)
TP53 mutation status, N (%)	**74**		**182**	
Mutated	9	(12.2)	67	(36.8)
TP53 status, N (%)	**51**		**130**	
Deletion and/or mutation	9	(17.6)	59	(45.4)
CLL-IPI score, N (%)	**58**		**145**	
Low	4	(6.9)	4	(2.8)
Intermediate	12	(20.7)	24	(16.6)
High	31	(53.4)	71	(49.0)
Very high	11	(19.0)	46	(31.7)

Table 1) Patient characteristics

RESULTS

Number of administered prior treatments before first Venetoclax/BTKi regimen	Venetoclax		BTKi	
Number of administered prior treatments	**274**		**915**	
Median (Range)	0 (0-9)		1 (0-12)	
Number of prior treatments, N (%)	**274**		**915**	
= 0 (Venetoclax/BTKi as first-line regimen)	152	(55.5)	352	(38.5)
= 1	69	(25.2)	273	(29.8)
= 2	32	(11.7)	157	(17.2)
= 3	7	(2.6)	68	(7.4)
= 4	6	(2.2)	37	(4.0)
= 5	4	(1.5)	14	(1.5)
= 6	2	(0.7)	5	(0.5)
= 7	1	(0.4)	5	(0.5)
= 8	0	(0.0)	1	(0.1)
= 9	1	(0.4)	0	(0.0)
= 10	0	(0.0)	2	(0.2)
= 11	0	(0.0)	0	(0.0)
= 12	0	(0.0)	1	(0.1)

Last administered prior treatments before first Venetoclax/BTKi regimen	Venetoclax		BTKi	
All last administered prior treatments	**122**		**563**	
Chemotherapy	8	(6.6)	45	(8.0)
Chemoimmunotherapy	87	(71.3)	426	(75.7)
PI3K-based	14	(11.5)	29	(5.2)
Other	13	(10.7)	63	(11.2)
Alemtuzumab	2	(1.6)	7	(1.2)
Alemtuzumab/Dexamethasone	1	(0.8)	0	(0.0)
CC-115	0	(0.0)	1	(0.2)
Lenalidomide	2	(1.6)	0	(0.0)
Obinutuzumab	2	(1.6)	11	(2.0)
Ofatumumab	3	(2.5)	8	(1.4)
Radiation	0	(0.0)	2	(0.4)
Rituximab	3	(2.5)	29	(5.2)
Allogeneic stem cell transplantation	0	(0.0)	5	(0.9)

All first administered subsequent treatments after first Venetoclax/BTKi regimen	Venetoclax		BTKi	
All last administered prior treatments	**26**		**264**	
Venetoclax-based	**6**	**(23.1)**	**68**	**(25.8)**
Venetoclax	6	(23.1)	67	(25.4)
Venetoclax/Vincristine	0	(0.0)	1	(0.4)
Anti-CD20+Venetoclax-based	**2**	**(7.7)**	**41**	**(15.2)**
Bendamustine/Obinutuzumab/Venetoclax	0	(0.0)	1	(0.4)
Cyclophosphamide/Doxorubicin/Prednisone/Rituximab/ Vincristine/Venetoclax	0	(0.0)	1	(0.4)
Obinutuzumab/Venetoclax	0	(0.0)	8	(3.0)
Rituximab/Venetoclax	2	(7.7)	31	(11.7)
BTKi-based	**10**	**(38.5)**	**65**	**(24.6)**
Acalabrutinib	5	(19.2)	19	(7.2)
Ibrutinib	5	(19.2)	46	(17.4)
Anti-CD20+BTKi-based	**1**	**(3.8)**	**5**	**(1.9)**
Ibrutinib/Obinutuzumab	1	(3.8)	2	(0.8)
Ibrutinib/Ofatumumab	0	(0.0)	2	(0.8)
Idelalisib/Obinutuzumab/Tirabrutinib	0	(0.0)	1	(0.4)
Anti-CD20+BTKi+Venetoclax-based	**1**	**(3.8)**	**1**	**(0.4)**
Acalabrutinib/Obinutuzumab/Venetoclax	1	(3.8)	0	(0.0)
Ibrutinib/Rituximab/Venetoclax	0	(0.0)	1	(0.4)
Chemotherapy	**2**	**(7.7)**	**13**	**(4.9)**
Chemoimmunotherapy	**2**	**(7.7)**	**34**	**(12.9)**
PI3K-based	**0**	**(0.0)**	**11**	**(4.2)**
Other	**2**	**(7.7)**	**26**	**(9.8)**
Bortezomib	1	(3.8)	0	(0.0)
Dexamethasone/Lenalidomide	0	(0.0)	1	(0.4)
Obinutuzumab	0	(0.0)	9	(3.4)
Ofatumumab	0	(0.0)	2	(0.8)
Rituximab	0	(0.0)	7	(2.7)
Allogeneic stem cell transplantation	1	(3.8)	7	(2.7)

Table 2) administered treatment by cohort

Survival from first Venetoclax containing regimen				Rate (%) at month			
Survival	N	Events, N (%)	Median (months)	24	36	48	60
OS	274	23 (8.4)	96.5	89.5	82.7	82.7	77.5
TTNT	274	26 (9.5)	63.7	90.8	83.6	62.3	55.4
EFS	274	47 (17.2)	31.8	66.6	36.6	18.3	12.2

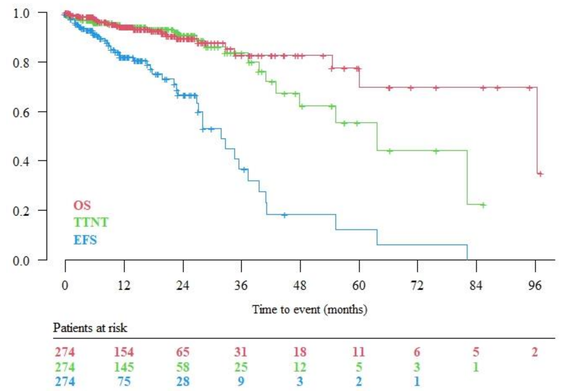


Figure 1) Survival from start of first Venetoclax containing regimen

Survival from first BTKi containing regimen				Rate (%) at month			
Survival	N	Events, N (%)	Median (months)	24	36	48	60
OS	915	204 (22.3)	85.9	84.9	79.0	71.9	64.4
TTNT	915	264 (28.9)	68.4	75.6	67.4	58.2	54.3
EFS	915	395 (43.2)	23.2	48.6	32.3	20.2	12.7

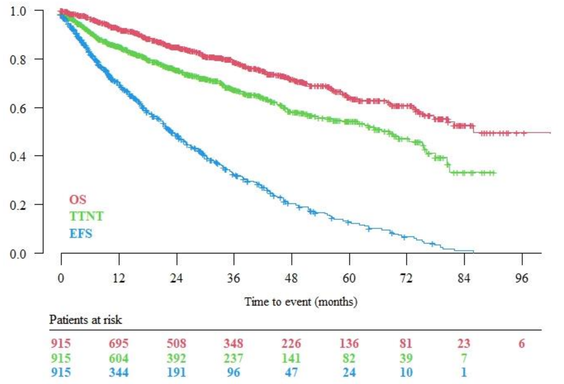
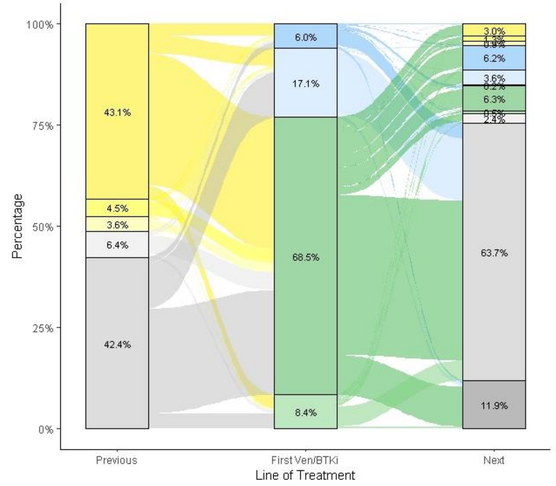


Figure 2) Survival from start of first BTKi containing regimen



The last column shows (from top to bottom):

- Chemoimmunotherapy (3.0%)
- Chemotherapy (1.3%)
- PI3K-based (0.9%)
- Venetoclax-based (6.2%)
- Anti-CD20+Venetoclax-based (3.6%)
- Anti-CD20+BTKi+Venetoclax-based (0.2%)
- BTKi-based (6.3)
- Anti-CD20+BTKi-based (0.5%)
- Other (2.4%)
- None (63.7)
- Patients Died (11.9%).

Figure 3) Sankey plot of last previous treatments (before) first Venetoclax/BTKi regimen and first subsequent treatments (after) first Venetoclax/BTKi regimen

CONCLUSION

In our dataset of patients being treated within the GCLLSG registry between 2014 and 2023

targeted therapies with **Venetoclax** were administered as firstline treatment in 152 of 274 pts (55.5%)

while 352 of 915 pts (38.5%) were treated with a **BTKi** as firstline treatment.

If prior treatments were given, the majority of pts still received chemo(immuno)therapy.

EFS, TTNT and OS were comparable between the Venetoclax and BTKi-based treatment cohort.

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