RUBIN
Registry platform
Hematologic Malignancies

15-YEAR RESULTS FROM THE PROSPECTIVE RUBIN REGISTRY

CHANGE IN THE STANDARD OF CARE OF SECOND-LINE TREATMENT FOR MANTLE CELL LYMPHOMA IN ROUTINE CARE IN GERMANY

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INTRODUCTION

Mantle cell lymphoma (MCL), a rare subtype of non-Hodgkin's lymphoma with a heterogenous course of disease, is currently considered incurable. Approval of the Bruton's tyrosine kinase (BTK) inhibitor ibrutinib in 2014 has improved therapeutic options for the second-line (2L) treatment of relapsed/refractory (r/r) MCL.

RUBIN, the continuation and extension of the Tumor Registry Lymphatic Neoplasms (TLN), provides prospective long-term observation and offers valuable insights into the real world treatment of patients with MCL in Germany.

CONCLUSION

Real-world data on patients in routine care outside of clinical trials have become increasingly important for a variety of research questions. These data show how quickly new treatments are implemented into patient care, how patients differ in their characteristics from those included in clinical trials and what impact these differences might have on their prognosis.

For second-line treatment of patients with MCL, data from RUBIN indicate a rapid change in the standard of care since the approval of BTK inhibitors in 2014. Currently, patients with MCL are predominantly treated with the BTK inhibitor ibrutinib.

Future analyses will focus on the implementation of newly approved BTK inhibitors in front-line treatment of MCL and their impact on the outcome of patients in Germany.

PATIENTS AND METHODS

The TLN and RUBIN (NCT06043011, approved by ethic committees) prospectively follow patients with non-Hodgkin's lymphoma and CLL in approximately 200 sites in Germany since 2009. Details on the methodology have been published previously (Knauf et al., 2015, 2021).

Here we focussed on second-line treatment reality of patients with MCL (both, r/rMCL and MCL after first line had to be discontinued due to toxicity) who were not scheduled for stem cell transplantation or treatment with CAR-T cells (hereinafter called 2L). Patients were assigned to the group "prior to" (G1) or "after" (G2) approval of ibrutinib (24-JUL-2014).

Data cut: 31-DEC-2024.

RESULTS

At data cut, data of 316 patients with MCL from 66 sites were evaluable for analysis **(Figure 1).**

Patient characteristics at start of second-line treatment

Of these patients, 120 patients were identified as 2L, with 29 % (35/120, G1) having started 2L prior to and 71 % (85/120, G2) after the approval of ibrutinib for the treatment of patients with r/rMCL **(Figure 1/Table 1).**

Median age at start of 2L was 77 and 78 years, respectively; 57 % and 67 % of patients were male. Further characteristics are shown in **Table 2.**

Systemic treatment prior to / after approval of ibrutinib in 2014

Overall, the use of R-bendamustine decreased from 71 % (25/35, G1) to 18 % (15/85, G2), the use of ibrutinib increased from 0 % to 64 % (54/85, G2). For 2L treatment having started in 2024 (n=13), the proportions were 0 % (0/13) for R-bendamustine and 69 % (9/13) for ibrutinib **(Figure 3).**

Among the 85 patients of G2, prior 1L treatment comprised eight patients with autologous SCT. The most frequent regimens in 1L were R-bendamustine (59 %, 50/85) and R-CHOP (18 %, 15/85).

Outcome

Of all patients with at least two years of follow-up (n = 91), 57 patients were alive and 26 were alive and without progression after 2L treatment at the time of data cut. Further analyses on outcome are planned.

Figure 1: Patient FlowChart

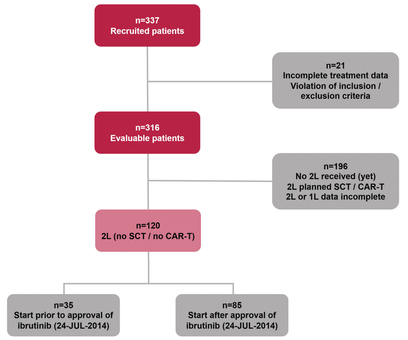
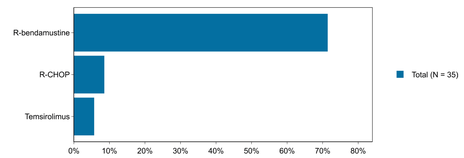


Figure 2: 2L treatment (no SCT / no CAR-T): Most frequent regimens with start prior to approval of ibrutinib (24-JUL-2014)



R: rituximab | R-CHOP: rituximab + cyclophosphamide + doxorubicin + vincristine + prednisolo(n)

Figure 3: 2L treatment (no SCT / no CAR-T): Most frequent regimens with start after approval of ibrutinib, total and by year

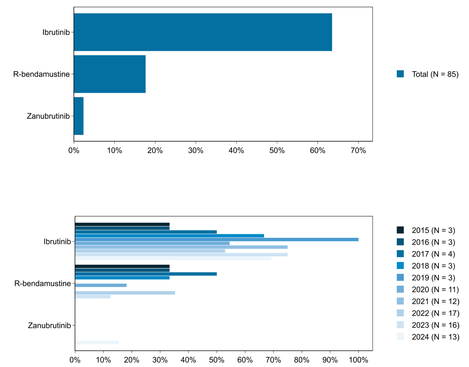


Table 1: Treatment strategy per line of treatment

	First line	Second line	Third line
Patients (N)	**253**	**126**	**47**
Treatment group			
No planned SCT / no planned CAR-T	212 (83.8 %)	120 (95.2 %)	41 (87.2 %)
Planned SCT	37 (14.6 %)	2 (1.6 %)	3 (6.4 %)
Planned CAR-T	0 (0.0 %)	1 (0.8 %)	1 (2.1 %)
Missing	4 (1.6 %)	3 (2.4 %)	2 (4.3 %)

CAR-T: Chimeric antigen receptor T cell | SCT: Stem cell transplantation.

Table 2: 2L treatment (no SCT / no CAR-T): Patient characteristics

	Second line with start prior to approval of ibrutinib (24-JUL-2014)	Second line with start after approval of ibrutinib (24-JUL-2014)
Patients (N)	**35**	**85**
Sex		
Female	15 (42.9 %)	28 (32.9 %)
Male	20 (57.1 %)	57 (67.1 %)
Age at start of second-line treatment (years)		
Median	77.1	77.7
25 %/75 % quantiles	73.4 / 82.2	73.2 / 82.4
<65	4 (11.4 %)	4 (4.7 %)
≥65	31 (88.6 %)	81 (95.3 %)
ECOG at start of second-line treatment		
0	7 (20.0 %)	21 (24.7 %)
1	11 (31.4 %)	21 (24.7 %)
≥2	0 (0.0 %)	15 (17.6 %)
Unknown to site	5 (14.3 %)	8 (9.4 %)
Missing	12 (34.3 %)	20 (23.5 %)
Comorbidities at start of second-line treatment		
Yes	23 (65.7 %)	72 (84.7 %)
No	4 (11.4 %)	6 (7.1 %)
Unknown to site	0 (0.0 %)	0 (0.0 %)
Missing	8 (22.9 %)	7 (8.2 %)
Charlson comorbidity index (CCI) at start of second-line treatment [0 – 24]		
0	23 (65.7 %)	38 (44.7 %)
1	4 (11.4 %)	10 (11.8 %)
≥2	0 (0.0 %)	30 (35.3 %)
Missing	8 (22.9 %)	7 (8.2 %)

CCI: Comorbidities according to Charlson et al. 1987, current weighting according to Quan et al. 2011. Range 0 – 24.
ECOG: Eastern Cooperative Oncology Group (Oken et al. 1982).

Abbreviations:

BTK(i): Bruton tyrosine kinase (inhibitor) | CAR-T: Chimeric antigen receptor T cell | CCI: Charlson comorbidity index | CLL: Chronic lymphocytic leukemia | ECOG: Eastern Cooperative Oncology Group | MCL: Mantle cell lymphoma | r/rMCL: Relapsed or refractory MCL | SCT: Stem cell transplantation | TLN: Tumor Registry Lymphatic Neoplasms R-bendamustine: rituximab + bendamustine | R-CHOP: rituximab + cyclophosphamide + doxorubicin + vincristine + prednisolo(n)n

Literature:

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