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Real World Outcome of Ibrutinib in Patients With Chronic Lymphocytic Leukemia From the German REALITY Study

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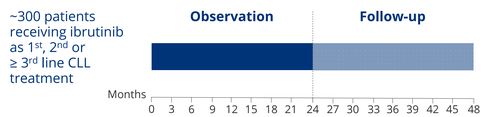
BACKGROUND

- Chronic lymphocytic leukemia (CLL) is characterized by abnormal survival and proliferation of mature B cells.
- Ibrutinib is a first-in-class once-daily Bruton's tyrosine kinase inhibitor, which demonstrated beneficial progression-free survival (PFS) and overall survival (OS) in multiple phase 3 trials for CLL patients[1,2,3].
- Ibrutinib is approved as treatment for patients with previously untreated (first-line=1L) or relapsed/refractory CLL.

Study Design

- REALITY was a prospective, multicenter, non-interventional study (NIS) to evaluate the effectiveness and safety of single-agent ibrutinib as 1st, 2nd, or ≥3rd line CLL treatment in routine clinical practice in Germany.

FIGURE 1: Study design



- Planned: 75 sites; 300 patients, 3 cohorts (C1 = 1L, C2 = 2L and C3 ≥ 3L)
- Observation: until end of ibrutinib therapy, maximum until end of 2-year observation period
- Follow-up: from the end of observation until start of new non-ibrutinib therapy, maximum until end of study

METHODS

- Patients:
  - ≥18 years old
  - Confirmed diagnosis of CLL and requiring treatment (iwCLL criteria and at discretion of treating physician)
  - Selected to be treated with ibrutinib according to approved indications prior to inclusion and independent of this study
- Key study endpoints:
  - Retention rate (ratio of patients on ibrutinib to the number of patients at risk)
  - PFS and OS
  - Time to next therapy
  - Safety
- Analysis: exploratory, no formal hypotheses
- Study duration: 20 January 2017 – 21 July 2021
- Participating study centers: 57 sites

B-CELL MALIGNANCIES

RESULTS

Patient Disposition and Baseline Characteristics

FIGURE 2: Patient disposition

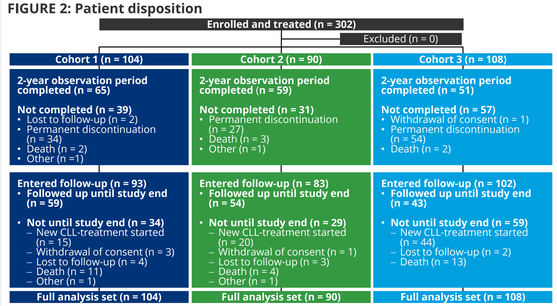


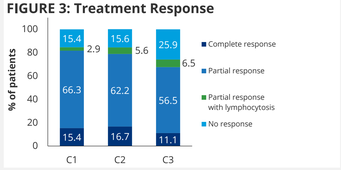
TABLE 1: Baseline characteristics

		Cohort 1, N=104	Cohort 2, N=90	Cohort 3, N=108
Male, n (%)		59 (56.7)	63 (70.0)	76 (70.4)
Age [years] at initial diagnosis, median (range)		70.0 (37 to 89)	65.5 (44 to 87)	62.0 (42 to 83)
Age [years] at ibrutinib initiation, median (range)		74.0 (44 to 91)	72.5 (49 to 90)	73.0 (48 to 90)
Binet stage, n (%)	A	19 (18.3)	19 (21.1)	19 (17.6)
	B	46 (44.2)	24 (26.7)	34 (31.5)
	C	34 (32.7)	34 (37.8)	47 (43.5)
Cytogenetics, n (%)	Chromosome deletion 17p	34 (32.7)	11 (12.2)	13 (12.0)
	TP53 mutation	31 (29.8)	14 (15.6)	21 (19.4)
	Chromosome deletion 11q	23 (22.1)	27 (30.0)	28 (25.9)
	IgHV unmutated	41 (39.4)	34 (37.8)	37 (34.3)
ECOG performance status, n (%)	0	49 (47.1)	33 (36.7)	30 (27.8)
	1	31 (29.8)	35 (38.9)	57 (52.8)
	2	8 (7.7)	5 (5.6)	10 (9.3)
	3	2 (1.9)	1 (1.1)	2 (1.9)
Relapsed disease, n (%)		-	73 (81.1)	83 (76.9)
Median follow-up in this study, months		30.6	31.5	30.9

ECOG=Eastern Cooperative Oncology Group; N=total number of patients; n=number of patients; IgHV= immunoglobulin heavy chain gene

Overall Treatment Response and Time to Best Response (TTBR)

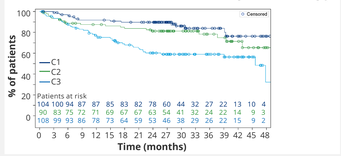
FIGURE 3: Treatment Response



- Complete or partial response was documented for most patients, but less often for C3 patients.
- Median TTBR was
  - C1: 181 days
  - C2: 202 days
  - C3: 173 days.

Time to Next Therapy

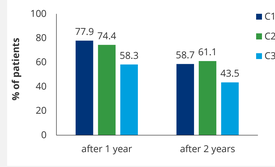
FIGURE 4: Patients without Subsequent Therapy



- During the 2 years, 9.6% of C1 patients, 17.8% of C2 patients and 37.0% of C3 patients started a new therapy.
- Median TTNT was only reached by C3 patients (45.7 months). The log-rank test indicated a difference of the survival curves between C2 and C3 and between C1 and C3 (p=0.0065; p<0.0001)

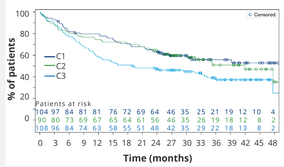
Retention Rates and Time to Treatment Discontinuation (TTD)

FIGURE 5: Retention rates



- Primary endpoint: the retention rate after 1 year was highest in 1L patients (C1).

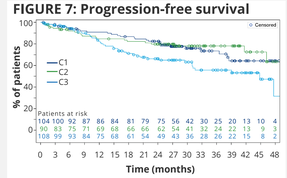
FIGURE 6: Patients on treatment



- Median TTD was not reached by C1 patients, 42.0 months for C2 patients and 19.0 months for C3 patients.
- TTD was comparable between C1 and C2. After 2 years, almost 60% of C1 patients were still on therapy.

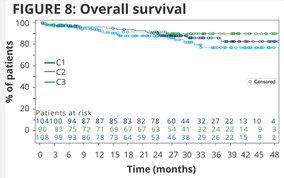
PFS and OS

FIGURE 7: Progression-free survival



- Median PFS was not reached. The log-rank test indicated a difference of the PFS curves between C1 and C3 and between C2 and C3 (p=0.0214; p=0.0152).
- After 2 years, 82.7% of 1L patients, 81.1% of C2 patients and 70.4% of C3 patients had no progression or death documented.

FIGURE 8: Overall survival



- Median OS was not reached. Comparison of the OS curves by the log-rank test did not indicate any difference between the cohorts.
- After 2 years, 90.4% of C1 patients, 92.2% of C2 patients and 89.8% of C3 patients were still alive.

Safety

TABLE 2: Overview of adverse events of CTCAE-Grade 3 or more and SAEs

	Cohort 1, N=104	Cohort 2, N=90	Cohort 3, N=108
Patients with at least 1 AE; n(%)	74 (71.2)	66 (73.3)	81 (75.0)
Related to study medication*	40 (38.5)	28 (31.1)	51 (47.2)
Leading to permanent treatment discontinuation	26 (25.0)	24 (26.7)	36 (33.3)
Most common AEs (SOC); n(%)**			
Blood & lymphatic system disorders	27 (26.0)	22 (24.4)	27 (25.0)
Infections & infestations	21 (20.2)	19 (21.1)	32 (29.6)
Cardiac disorders	13 (12.5)	14 (15.6)	18 (16.7)
Neoplasms benign, malignant and unspecified	8 (7.7)	10 (11.1)	16 (14.8)
General disorders and administration site conditions	6 (5.8)	8 (8.9)	13 (12.0)
Vascular disorders	9 (8.7)	9 (10.0)	6 (5.6)
Gastrointestinal disorders	6 (5.8)	8 (8.9)	9 (8.3)
Nervous system disorders	5 (4.8)	15 (16.7)	3 (2.8)
Musculoskeletal and connective tissue disorders	6 (5.8)	7 (7.8)	6 (5.6)
Renal and urinary disorders	4 (3.8)	8 (8.9)	5 (4.6)
Respiratory, thoracic and mediastinal disorders	3 (2.9)	5 (5.6)	9 (8.3)
Patients with at least 1 SAE; n(%)	49 (47.1)	49 (54.4)	57 (52.8)
Related to study medication*	13 (12.5)	14 (15.6)	27 (25.0)
Leading to permanent treatment discontinuation	18 (17.3)	19 (21.1)	27 (25.0)
Leading to death	7 (6.7)	6 (6.7)	10 (9.3)

*possible, probable or very likely **multiple responses possible
AE = adverse event; n = number of patients; SAE = serious adverse event; SOC = system organ class

KEY TAKEAWAY

- Ibrutinib is a highly effective treatment option for CLL patients, especially as first-line treatment.
- Effectiveness and safety profile in this real-world dataset were consistent with clinical trials.

CONCLUSIONS

- REALITY provides first-time real-world evidence for the use of ibrutinib in a large cohort of CLL patients in German clinical practice.
- Long-term benefit of ibrutinib therapy: 90.4% of 1L-patients did not start a subsequent CLL-treatment during the 2-year observation period.
- No new safety signals were observed.

ACKNOWLEDGMENTS

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