Real-World Experience with Zanubrutinib in Chronic Lymphocytic Leukaemia – Patient Profile, Treatment Patterns, and Safety: Preliminary Analysis of French ROZALY Study

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Background
Zanubrutinib, a next-generation Bruton tyrosine kinase (BTK) inhibitor, has shown high efficacy and favourable safety in chronic lymphocytic leukaemia (CLL) in the phase 3 SEQUOIA and ALPINE trials, and is approved in Europe for treatment-naïve (TN) and relapsed/refractory (R/R) disease. ROZALY was designed to generate real-world data on its use in France in a rapidly evolving treatment landscape.

Aims
To describe patient and disease characteristics and treatment use in patients initiated with zanubrutinib for CLL in both TN and R/R real-world settings.

Methods
ROZALY is a prospective, longitudinal, non-interventional, multicentre study conducted in 55 sites in France. Patients were prospectively enrolled at treatment start (M0) and followed up to 5 years. This preliminary analysis was performed with 121 patients recruited in the first inclusion year (Dec 2024–Dec 2025) and depicts demographic and clinical characteristics and preliminary data.

Results
Of the 121 patients treated with zanubrutinib, 59 were TN (48.8%) and 62 were R/R (51.2%). The median age was 76 years (range, 50.6-93.4), with 27 patients aged ≥80 years. Sixty-two percent of patients were male. *TP53* mutation (mut) or del(17p) was present in 45.8% of TN and 35.5% of R/R patients (**Table**). Complex karyotype (>3) was observed in 22.3% of overall patients. IGHV was unmutated in 52.5% of TN and 45.2% of R/R patients. Among 72 patients without *TP53* mut and del(17p), IGHV was unmutated in 51.4% (TN: 65.6%; R/R: 40.0%).

Among patients with prior treatment (n=56), 33.9% had received FCR, 35.7% venetoclax, and 41.1% a BTK inhibitor (ibrutinib, 32.1%; acalabrutinib, 10.7%). A direct change from a prior BTK inhibitor to zanubrutinib occurred in 14 patients, mostly due to adverse event (AE; 35.7%) or physician decision (28.6%). Zanubrutinib was started at the labeled dose in 84.3% of patients; the remaining 15.7%, with a median age of 82.6 years, received reduced doses. At the time of analysis (median treatment exposure, 2.1 months), 3 patients discontinued zanubrutinib (2 AEs and 1 patient inconvenience).

Most patients (74.4%) had comorbidities, including 22.3 % with cardiovascular (CV) disorders (6.6% with atrial fibrillation) and 37.2% with hypertension. Of 80 patients with follow-up, treatment-related (TR) AEs were reported in 23 patients (28.8%), Grade ≥3 treatment-related AEs (TRAEs) occurred in 12.5% of patients, and TRAEs leading to discontinuation in 3.8%. Most frequent TRAEs were haemorrhagic events (10%), diarrhoea (5.0%), and neutropenia (3.8%). CV

TRAEs occurred in 3 patients (3.8%); 2 patients had grade ≥3 cardiac failures and 1 had grade 2 hypertension.

Conclusion

ROZALY is the first prospective real-world European study of zanubrutinib in CLL, describing patient characteristics and treatment use in routine practice. The cohort reflects an older population with more comorbidities than phase 3 trials. Nearly half of first-line patients had high-risk disease (*TP53* mut/del(17p)), consistent with French guideline recommendations and clinical trial evidence supporting continuous BTK inhibitor therapy. Longer follow-up is needed to assess real-world effectiveness and tolerability.

Table. Patient and Disease Characteristics at M0

Characteristic	**TN CLL (n=59)**	**R/R CLL (n=62)**	**Overall (N=121)**
Age, median (range), year	76.3 (50.6-90.7)	75.9 (50.8-93.4)	76 (50.6-93.4)
Sex			
Male, n (%)	39 (66.1)	36 (58.1)	75 (62.0)
Female, n (%)	20 (33.9)	26 (41.9)	46 (38.0)
ECOG performance status, n (%)			
0	20 (33.9)	24 (38.7)	44 (36.4)
1	23 (39.0)	19 (30.6)	42 (34.7)
2	2 (3.4)	5 (8.1)	7 (5.8)
3	1 (1.7)	4 (6.5)	5 (4.1)
Missing	13 (22.0)	10 (16.1)	23 (19.0)
TP53 mutation or del(17p) status, n (%)			
TP53 mutation or del(17p)	27 (45.8)	22 (35.5)	49 (40.5)
Del(17p)	19 (42.2)[a]	6 (14.3)[a]	25 (28.7)[a]
TP53 mutation	23 (41.8)[a]	22 (43.1)[a]	45 (42.5)[a]
Del(11q) status, n (%)			
Del(11q)	6 (10.2)	12 (19.4)	18 (14.9)
Not tested	16 (27.1)	22 (35.5)	38 (31.4)
IGHV mutation status, n (%)			
Mutated	12 (20.3)	13 (21.0)	25 (20.7)
Unmutated	31 (52.5)	28 (45.2)	59 (48.8)
Not tested	16 (27.1)	21 (33.9)	37 (30.6)
Unmutated IGHV without *TP53* mutation and del(17p)	21 (35.6%)	16 (25.8%)	37 (30.6%)
Complex karyotype, n (%)			
>3 abnormalities	14 (23.7)	13 (21.0)	27 (22.3)
Not tested	17 (28.8)	22 (35.5)	39 (32.2)
Bulky disease, n (%)			
Yes	3 (5.1)	6 (9.7)	9 (7.4)
No	52 (88.1)	51 (82.3)	103 (85.1)
Unknown	4 (6.8)	5 (8.1)	9 (7.4)

[a]Percentage of patients with deletion or mutation divided by number patients tested.