

RESULTS FROM THE INTERIM ANALYSIS 1 (IA1) OF THE ARIADNE STUDY

FIRST REAL-WORLD INSIGHTS INTO MEDICAL RESOURCE UTILIZATION IN PATIENTS WITH WALDENSTRÖM'S MACROGLOBULINEMIA (WM) TREATED WITH ZANUBRUTINIB

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BACKGROUND

Treatment with Bruton's tyrosine kinase inhibitors (BTKi) in Waldenström's macroglobulinemia (WM) is recommended for treatment-naïve and relapsed/refractory patients. Zanubrutinib is a 2nd-generation BTKi, which was approved for WM in 11/2021. Real-world insights into patient population, medical resource utilization, and effectiveness are important and complementary to clinical trial data.

METHODS

The prospective, non-interventional ARIADNE study aims to enroll up to 400 patients from 70 sites across Germany and Austria to gain insights into effectiveness, tolerability, and Patient-Reported outcomes (PROs) of zanubrutinib in WM, CLL, MZL and FL (Figure 1). Here, we present the IA1 results for WM, including patient- and disease characteristics and medical resource utilization, which compiles any hospitalizations and emergency unit visits during zanubrutinib treatment regardless of disease association.

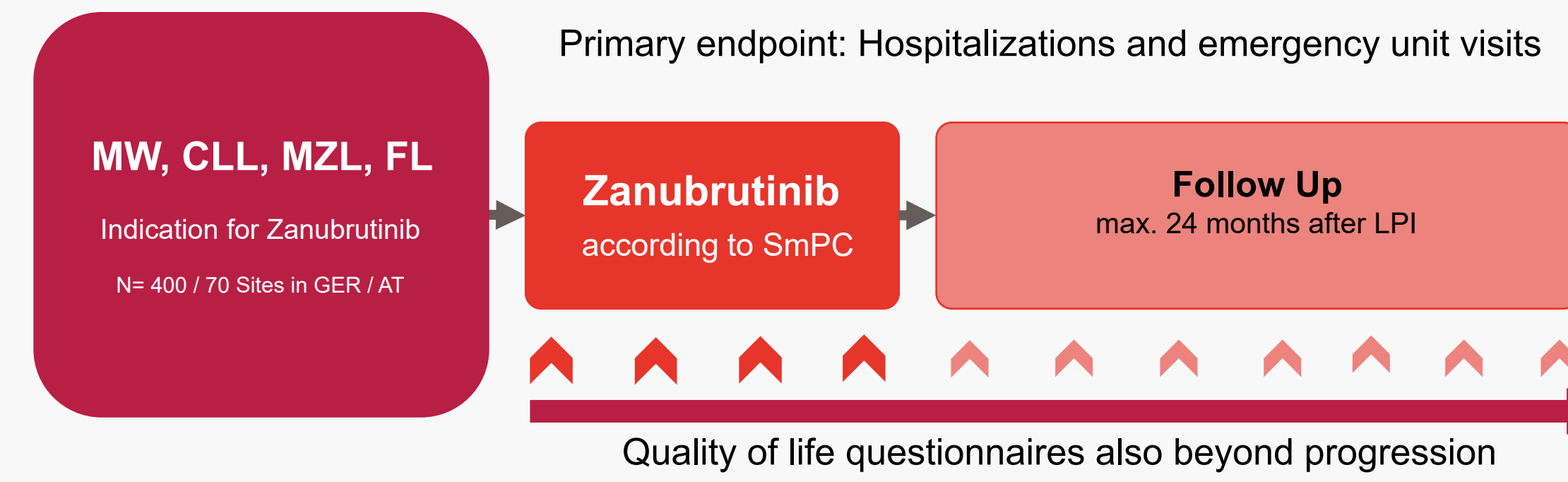


Figure 1: Study design ARIADNE
MW=Waldenström's macroglobulinemia; CLL=Chronic lymphocytic leukemia; MZL=Marginal zone lymphoma; FL=Follicular lymphoma; GER=Germany; AT=Austria; SmPC=Summary of Product Characteristics; LPI= Last patient in

RESULTS

Between 04/2022 and 11/2023, 195 patients were enrolled. 100 were observed for >6 months and 95 patients including 49 WM, 41 CLL and 5 MZL patients were evaluable for analyses. Of the 49 WM patients, 32.7% were included for first-line and 67.3% for later-line treatment. At database cut on the 30-Nov-2023, 73.5% patients were still on treatment. Median age was 75.8 years (range 50-94), 55.1% were male and 32.7% had ECOG ≥2 at inclusion (Table 1). Median bone marrow WM infiltration was 45.0% measured in 10 patients. 51.0% had a watch&wait phase before start of first-line, which was in median 17.58 months (Table 2). All later-line patients received a first-line containing either bendamustine or ritux-

imab. No patient received a prior stem cell transplantation and only 4.1% received prior plasmapheresis (Table 3). Regarding medical resource utilization, 69.4% of the patients did not require hospitalization. 28.6% had a hospital stay and 6.1% had an emergency room visit (Table 4). The ORR (i.e., CR, VGPR, PR) was 55.1%. ORR was comparable in first- vs later-line (56.2% vs 54.5%). As best response, 4.1% achieved CR, 10.2% VGPR, 40.8% PR, 4.1% MR, 16.3% SD and 1 patient (2.0%) had PD. For 11 patients, no assessment was documented. Response was comparable in first- vs later-line: CR 0 vs 6.1%, VGPR 6.2 vs 12.1%, PR 50.0 vs 36.4%, MR 0 vs 6.1%, SD 12.5 vs 18.2% and PD 6.2 vs 0.0% (Table 5).

CONCLUSION

The ARIADNE IA1, 19 months after FPI, shows a real-world WM patient population, that is older and more frail compared to the pivotal trial. About one third of patients received zanubrutinib as first-line. Furthermore, more than two-thirds of pts did not require hospitalization. The ORR was 55.1% and both ORR and best response was comparable in first- vs later-line. Response might deepen over time.

Table 2: Disease characteristics at inclusion (n=49).

	n (%)
Patients with pre-malignant plasma cell disorder	
Yes	17 (34.7)
No	29 (59.2)
Unknown to site	3 (6.1)
Patients with watch&wait prior to 1L	
Yes	25 (51.0)
No	24 (49.0)
Duration of watch&wait (months)	
Median (Q1-Q3)	17.6 (8.4-108.1)
Missing	1
ISSWM	
Low	5 (10.2)
Intermediate	13 (26.5)
High	8 (16.3)
Unknown to site	23 (46.9)
WM cell infiltration (%)	
Median (Q1-Q3)	50.5 (40.0-71.3)
Missing	39
Cryoglobulinemia	
Yes	3 (6.1)
No	28 (57.1)
Unknown to site	7 (14.3)
Any organs involved	
Yes	14 (28.6)
No	28 (57.1)
Unknown to site	7 (14.3)
Involved organs*	
Lymph nodes (lymphadenopathy)	7 (14.3)
Spleen (splenomegaly)	6 (12.2)
Liver (hepatomegaly)	1 (2.0)
Others	2 (4.1)
Missing	2 (4.1)

*Multiple answers possible.

Table 3: Prior treatment (n=49).

	n (%)
Prior treatment	
Yes	33 (67.3)
No (i.e., inclusion at 1 st line)	16 (32.7)
Prior treatment lines	
1	33 (67.3)
2	11 (22.4)
3	3 (6.1)
4	3 (6.1)
5	2 (4.1)
6	2 (4.1)
7	1 (2.0)
Bendamustine and/or Rituximab containing regimens in respective line	
1	33 (67.3)
2	6 (12.2)
3	2 (4.1)
4	2 (4.1)
5	1 (2.0)
6	1 (2.0)
7	0 (0.0)
BTK inhibitor containing regimens in respective line	
1	0 (0.0)
2	5 (10.2)
3	1 (2.0)
4	1 (2.0)
5	1 (2.0)
6	0 (0.0)
7	1 (2.0)
Prior stem cell transplantation	
Yes	0 (0.0)
No	33 (67.3)
Unknown to site	0 (0.0)
NA (i.e., inclusion at 1 st line)	16 (32.7)
Prior plasmapheresis	
Yes	2 (4.1)
No	28 (57.1)
Unknown to site	3 (6.1)
NA (i.e., inclusion at 1 st line)	16 (32.7)

Table 4: Medical resource utilization (n=49).

	n (%)
Number of hospitalizations	
Median (Q1-Q3)	0.0 (0.0 - 1.0)
Missing	0
Hospitalizations*	
Yes	15 (30.6)
No	34 (69.4)
Missing	0 (0.0)
Hospital stays	
Yes	14 (28.6)
No	35 (71.4)
Missing	0 (0.0)
Emergency Unit visits	
Yes	3 (6.1)
No	46 (93.9)
Missing	0 (0.0)

*Hospitalization includes hospital stays and/or emergency unit visits

Table 5: Best overall response and response rates (n=49).

	1st line (N = 16) n (%)	Later-line (N = 33) n (%)	Total (N = 49) n (%)
Best response of systemic treatment			
Complete response (CR)	0 (0.0%)	2 (6.1%)	2 (4.1%)
Very good partial response (VGPR)	1 (6.2%)	4 (12.1%)	5 (10.2%)
Partial response (PR)	8 (50.0%)	12 (36.4%)	20 (40.8%)
Minor response (MR)	0 (0.0%)	2 (6.1%)	2 (4.1%)
Stable disease (SD)	2 (12.5%)	6 (18.2%)	8 (16.3%)
Progressive disease (PD)	1 (6.2%)	0 (0.0%)	1 (2.0%)
Assessment not done	4 (25.0%)	7 (21.2%)	11 (22.4%)
ORR [95% CI]	56.2% [29.9, 80.2] (n=9)	54.5% [36.4, 71.9] (n=18)	55.1% [40.2, 69.3] (n=27)

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Abbreviations:
AT: Austria | BTKi: Bruton's tyrosine kinase inhibitors | CLL: Chronic lymphocytic leukemia | CR: Complete remission | FL: Follicular Lymphoma | GER: Germany | IA: Interim Analysis | LPI: Last patient in | MR: Minor Remission | MZL: Marginal Zone Lymphoma | ORR: Overall response rate | PD: Progressive disease | PR: Partial Remission | PRO: Patient-reported outcomes | SD: Stable disease | SmPC: Summary of Product Characteristics | VGPR: Very Good Partial Remission | WM: Waldenström's macroglobulinemia
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