



SPANISH REAL-LIFE PRACTICE CONFIRMS ZANUBRUTINIB AS A SAFE AND EFFECTIVE TREATMENT FOR RELAPSED OR REFRACTORY MARGINAL ZONE LYMPHOMA: RESULTS OF A COHORT OF 118 PATIENTS ON BEHALF OF GELTAMO.



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INTRODUCTION

- There is no established standard of care for relapsed or refractory (R/R) marginal zone lymphoma (MZL).
- Zanubrutinib, a second generation covalent BTK inhibitor, was approved for R/R MZL based on the results of the phase 2 MAGNOLIA trial, which included 68 patients.

AIM

- To evaluate the characteristics and outcomes of 118 patients with R/R MZL treated with zanubrutinib in routine clinical practice across Spain.

METHODS

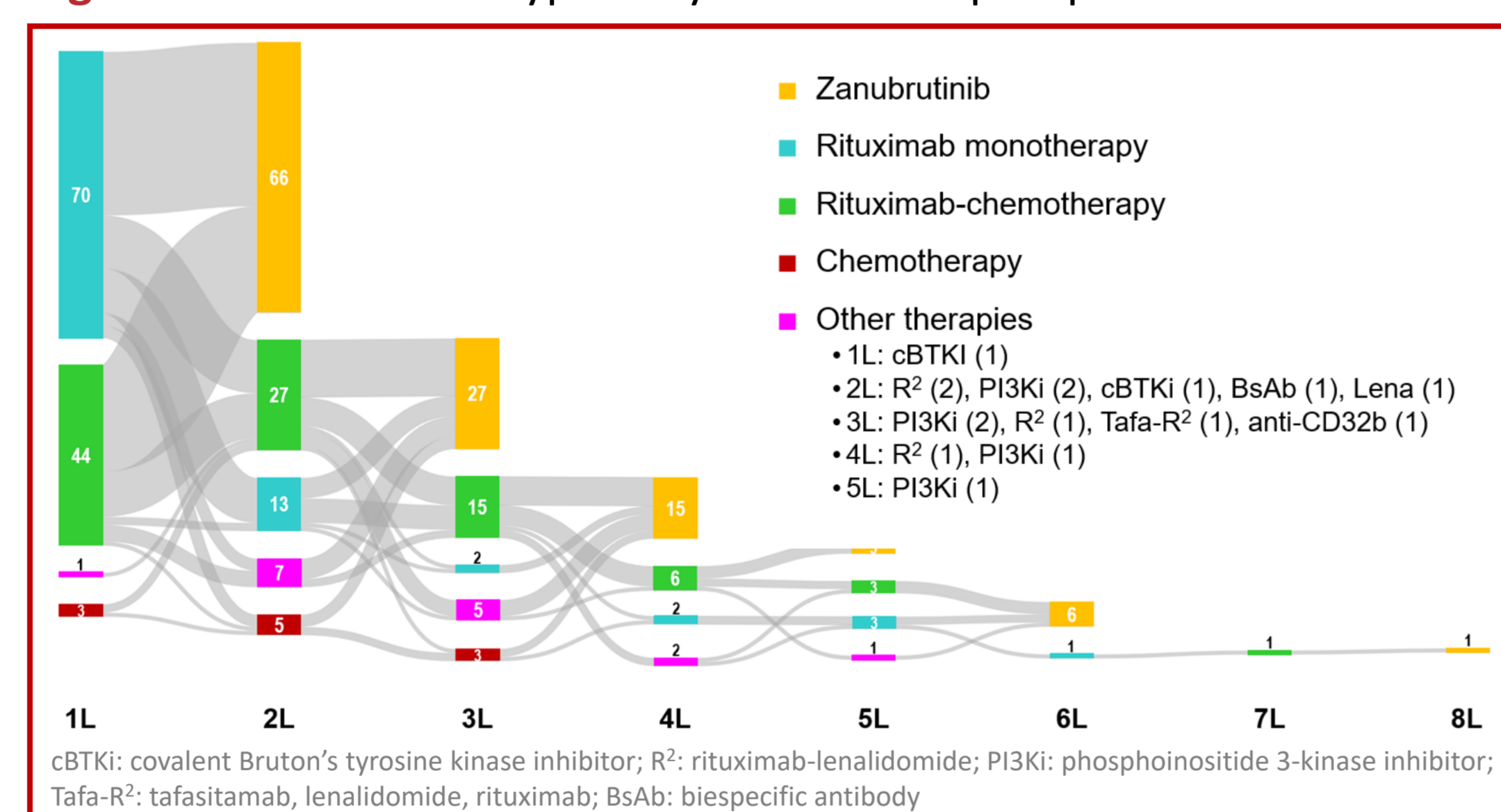
- This retrospective study included adult patients with R/R MZL previously treated with at least one anti-CD20-based regimen and requiring further therapy.
- Patients received zanubrutinib at 39 Spanish centers (GELTAMO).
- All MZL subtypes were included: mucosa-associated lymphoid tissue (MALT), splenic (SMZL), and nodal (NMZL).
- Baseline characteristics, prior lines of treatment (LoT), response rates, survival, adverse events (AEs), and reasons for discontinuation were analyzed.

RESULTS

Table 1. Main clinical characteristics at zanubrutinib initiation.

Characteristic at Zanubrutinib initiation		Comorbidities	
Median age, years (range)	75 (36 - 93)	Any cardiovascular comorbidity	80/118 (68%)
ECOG		Patients with > 1 comorbidity	51/118 (43%)
0	37/116 (32%)	Diabetes mellitus	33/117 (28%)
1	62/116 (53%)	Hypertension on therapy	56/117 (48%)
2	13/116 (11%)	Cardiopathy	25/117 (21%)
3	4/116 (4%)	Atrial fibrillation / flutter	10/25
Ann Arbor		Ischemic cardiopathy	6/25
I	12/116 (10%)	Heart failure	5/25
II	6/116 (6%)	Valvular dysfunction	3/25
III	13/116 (11%)	Ventricular dysfunction	2/25
IV	85/116 (73%)	Other arrhythmia disorder	2/25
Monoclonal serum paraprotein	39/115 (34%)	Dyslipidemia	19/118 (16%)
B symptoms	37/117 (32%)	Smoking	8/118 (7%)
MYD88 L265P mutation	7/35 (20%)	Obesity	7/118 (6%)
HPLS/ABC score for SMZL (n=64)		Chronic obstructive pulmonary disease	2/118 (1.7%)
A	2/63 (3%)	Peripheral arteriopathy	1/118 (0.8%)
B	50/63 (79%)	Serious bleeding	4/118 (3%)
C	11/63 (18%)	Antithrombotic therapy	33/117 (29%)
MALT-IPI score for MALT (n=22)		Only anticoagulant	17/33
Low	4/21 (19%)	Only antiagregant	14/33
Intermediate	13/21 (62%)	Both therapies	2/33
High	4/21 (19%)		
POD24	69/116 (59%)	MAGNOLIA exclusion criteria	31/118 (26%)
Refractoriness to immediately previous line	30/116 (26%)	Zanubrutinib initial dosing	
Median number of prior lines (range)	1.5 (1-7)	Standard	111 (94%)
Median time from diagnosis to zanubrutinib, months		160mg BID	84/111
SMZL	56.7 (IQR 25.2-93)	320mg QD	27/111
NMZL	62.7 (IQR 29.3-111.3)	Reduced	7 (6%)
MALT	37.8 (IQR 20.7-79.8)	80mg BID	5/7
		240mg QD	2/7

Figure 1. Number and type of systemic therapies prior to zanubrutinib.

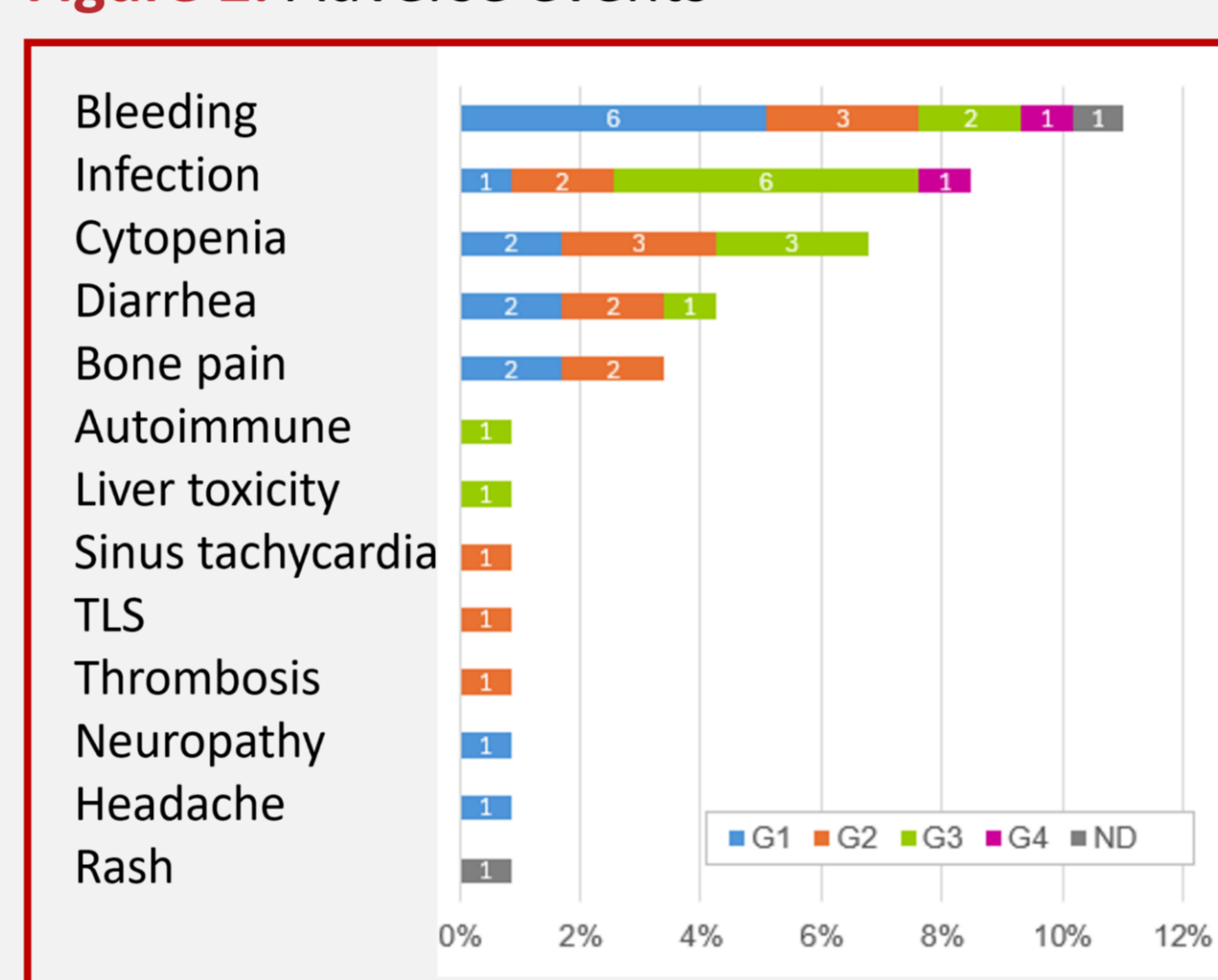


- At lymphoma diagnosis median age was 69 years, 56% were female and 93% had good performance status (ECOG 0-1).
- According to MZL subtype: 55% were SMZL, 20% NMZL, 19% MALT, and 6% no-classifiable.

SAFETY

49 AEs were documented in 40 patients (34.1%), of which 17 (34.6%) were grade ≥ 3 .

Figure 2. Adverse events



- Bleeding was higher among those patients on anticoagulants ($p=0.039$).
- No cases of hypertension, atrial fibrillation or grade 5 AEs occurred.
- MAGNOLIA ineligible patients had higher AEs incidence ($p=0.017$) and discontinuation rates ($p=0.009$).
- Overall, 32 patients (27%) discontinued Zanubrutinib:
 - 9 (28%) due to toxicity or intolerance
 - 19 (59%) due to progressive disease
 - 4 (13%) due to other reasons
- Median time to discontinuation was: 5.4 months (IQR 2.6-11.1).
- AEs leading to treatment discontinuation related to zanubrutinib toxicity or intolerance included: bleeding (n=3), infection (n=3), diarrhea (n=1), rash (n=1) and 1 unknown.

CONCLUSIONS

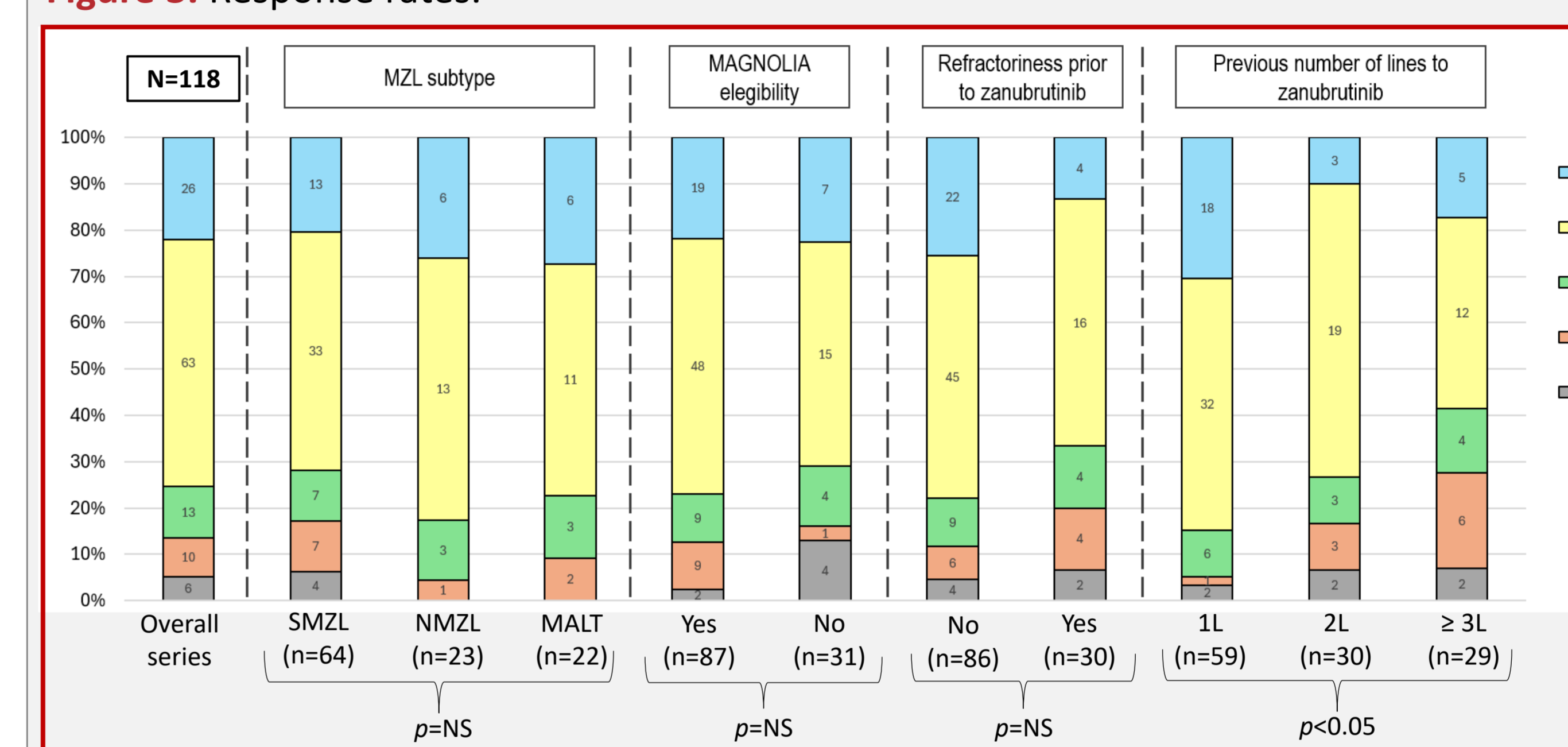
- To our knowledge, this is the **largest real-world series of zanubrutinib in R/R MZL** to date.
- Zanubrutinib demonstrated **favorable efficacy and safety across all MZL subtypes**, independently of MAGNOLIA trial eligibility.
- Outcomes were significantly better in patients treated earlier in their disease course, **supporting the use of zanubrutinib as a second-line option in R/R MZL**.

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EFFICACY

Figure 3. Response rates.

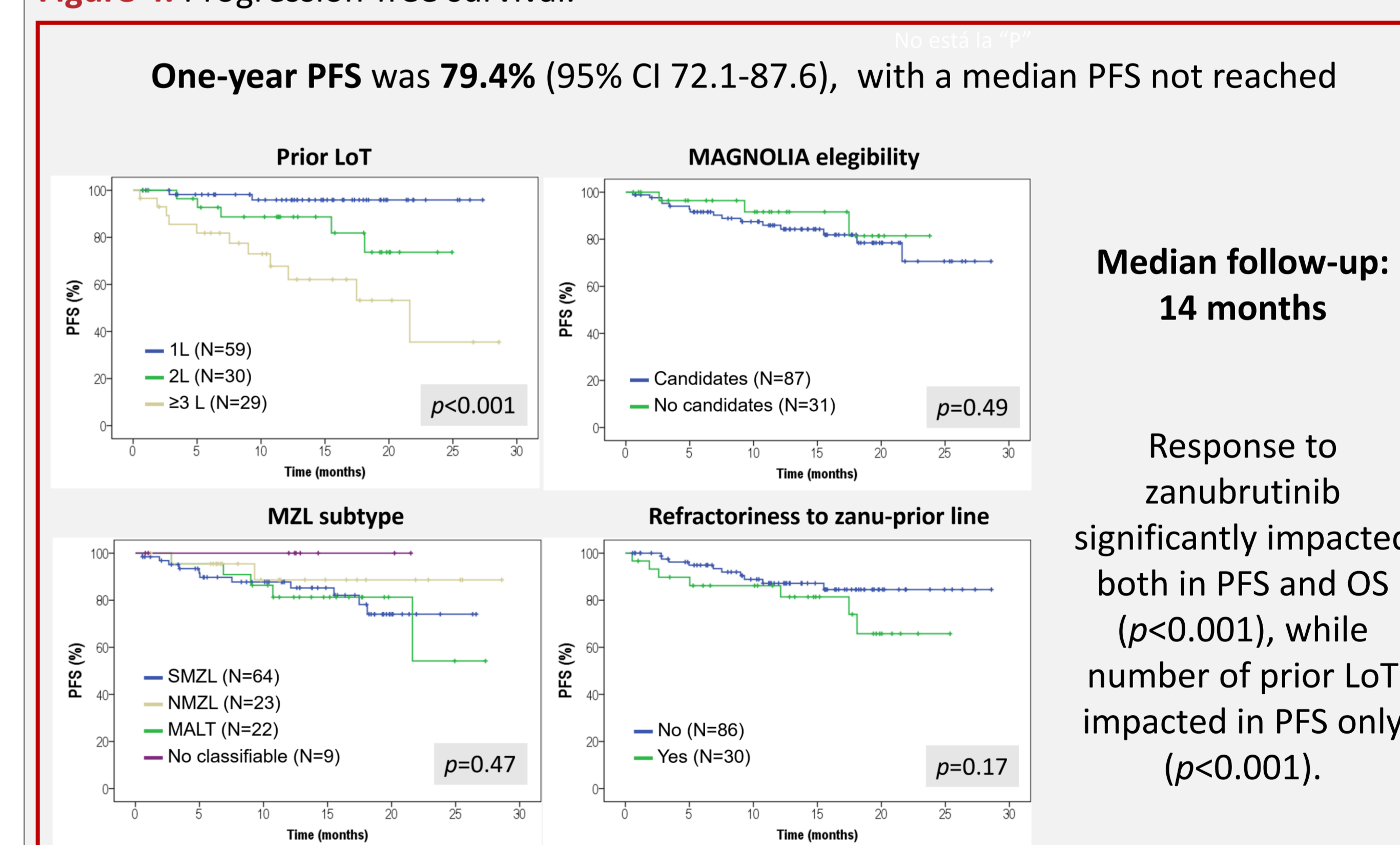


Median DoR: 6.8 months (IQR 4.5 -9.6)

Median time to best response: 5.8 months (IQR 3.7-9.9)

No statistically significant differences in ORR or CR were found according to Ann Arbor stage, MYD88, POD24, or age (\geq or $<$ 60 years).

Figure 4. Progression-free survival.



One-year OS was 86.8% (95% CI 80.5-93.5).

No significant differences in OS were seen by MZL subtype, POD24, or MAGNOLIA eligibility.

Sixteen patients had died, 50% due to lymphoma (n=8)

At last follow-up, 86 patients (72.8%) remained on treatment

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