Patient characteristics and treatment patterns in patients with Mantle Cell Lymphoma in Spain: a real-world, cross-sectional study

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Background

Mantle Cell Lymphoma (MCL) is a rare, incurable, hematologic malignancy characterized by the proliferation of malignant B-cells within the lymph nodes and other lymphoid tissues[1].

This non-Hodgkin lymphoma subtype accounts for around 5-6% of all lymphomas diagnosed in Spain[2].

Given its rarity and the lack of standard treatment regimens[3], understanding Spanish patient characteristics and the treatment patterns used is of paramount importance.

Objective

To describe the profile and management of patients with mantle cell lymphoma (MCL) in a real world setting in Spain.

Study Design/Methods

Real-world data were drawn from the Adelphi MCL Disease-Specific Programme™ (DSP), a cross-sectional survey conducted between March-October 2022 among hematologists and hem-oncologists across Spain. Physicians extracted medical records for MCL patients´ demographics, clinical profiles and treatment patterns.

Patients were included if they had a physician confirmed diagnosis of MCL, were 18 years or older and were actively treated with systemic treatment.

Patients who had received stem cell transplantation for reasons other than MCL or were participating in clinical trials at the time of data collection were excluded.

Thirty physicians completed medical record forms for four consecutive patients with a 1:3 ratio of first-line: relapsed/refractory patients. Descriptive analyses were reported.

Results

Demographics and clinical characteristics

- Data from 119 patients were collected, with 71% male, median age 70 years (range 38-90), and median time since diagnosis of 34 months (range 1-181) at data collection.
- At the time of initial diagnosis, 55% of patients presented stage IV and 38% as ECOG 1, with median of 4 (0-25) nodal locations.
- The most frequent MCL histologic subtype was classic (82%), followed by blastoid/pleomorphic (10%).
- Bulky disease (diameter >5cm) was present in 11%.
- In their most recent Ki-67 test, 74 patients (96%) had high expression according to clinician´s criteria (n=77). Among the 77 patients who underwent Ki67 testing, 44% were tested at the time of diagnosis, 4% during disease progression, and 52% at both stages.
- Of the 61 patients that underwent TP53 mutation testing, 16 (26%) tested positive. Among these 61 patients, 46% were tested at the time of diagnosis, 8% during disease progression, and 46% at both stages. (Table 1).

Table 1. Patient demographics and clinical characteristics

		n= 119
At diagnosis		
Median age, years (range)		70.0 (38.0-90.0)
Gender	Male	84 (71%)
	Female	35 (29%)
Classification	Classic	98 (82%)
	Pleomorphic/ Blastoid	12 (10%)
	Indolent	7 (6%)
	Unknown	2 (2%)
Stage[a]	I	3 (3%)
	II	20 (17%)
	III	30 (25%)
	IV	65 (55%)
ECOG[b] **score at diagnosis**	0	32 (27%)
	1	45 (38%)
	2	33 (28%)
	3	6 (5%)
	4	1 (1%)
Median number of nodes at diagnosis[c] (range)		4.0 (0-25.0)
Co-morbidities at diagnosis (>10%)	Hypertension	60 (50%)
	Anemia	36 (30%)
	Dyslipidemia	35 (29%)
	Diabetes	28 (23%)
	Hyperlipidaemia	23 (19%)
	Atrial fibrillation	13 (11%)
	Anxiety	13 (11%)
	None	25 (21%)
At data collection		
Median months since diagnosis[d] (range)		34.0 (1.0-181.0)
Bulky disease[e]	Yes	13 (11%)
	No	106 (89%)
Ki-67 status[f]	High expression	74 (62%)
	Low expression	2 (2%)
	Unknown	1 (1%)
	Not tested	42 (35%)
TP53 mutation[f]	Positive	16 (13%)
	Negative	43 (36%)
	Unknown	2 (2%)
	Not tested	58 (49%)

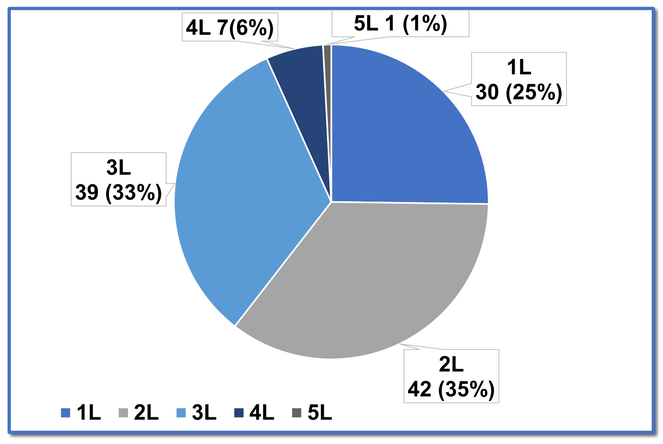
SD standard deviation *IQR* interquartile range [a](Ann Arbor classification) [b]Eastern Cooperative Oncology Group [c](n = 95) [d](n = 111) [e](extranodal maximum tumour diameter >5cm) [f]most recent

Results

Treatments

- At data capture, 25% of patients were in first line (1L) of treatment, 35% in the second (2L) and 39% in the third or successive lines (Figure 1). Moreover, 42 patients (35%) were considered eligible for stem cell transplantation (SCT).

Figure 1. Lines of treatment patient had received in total at data collection



- The most frequent drug treatments were R-CHOP in 1L (30%), ibrutinib in 2L (64%) and bendamustine with rituximab in 3L (21%) (Table 4).
- In 1L, 15 patients (13%) received maintenance, all of whom received rituximab. Also, 18 patients (15%) received autologous SCT at 1L, with no patients receiving allogeneic SCT.
- The observed median treatment duration was numerically shorter in 1L and 2L compared to later lines. In contrast, the observed time intervals between treatment lines were numerically longest between 1L and 2L (Table 2).
- Overall response rates were 79%, 57% and 47% in 1L, 2L and 3L respectively. (Figure 2).

Table 2. Duration of treatment lines and time intervals between treatments lines

	Median time[a] (months (range))
Time between initial diagnosis and initiation of drug treatment[b]	0.4 (0 – 71.2)
Duration of 1L (primary therapy) [c]	5.0 (1.0 - 33.9)
Duration between the end of 1L to start of 2L[d]	12.0 (0 – 75.5)
Duration of 2L (primary therapy) [e]	8.7 (1.3 – 106.5)
Duration between the end of 2L to start of 3L[f]	1.0 (0 – 71.2)
Duration of 3L (primary therapy) [g]	11.0 (3.3 – 50.4)
Duration between the end of 3L to start of 4L[h]	1.0 (0.2 – 23.1)

[a]Only for patients who had a known date for each category [b](n = 108) [c](n = 82) [d](n = 73) [e](n = 47) [f](n = 43) [g](n = 10) [h](n = 8)

- The most frequently reported reason for therapy discontinuation at 1L was 'entered remission/disease-free' (38%), however at 2L and 3L this was 'disease progression/relapse' (44% and 40% respectively). Other frequently reported reasons were 'regimen completed - complete response' at 1L (35%) and 2L (26%) and 'regimen completed - maximum response achieved' at 3L (30%) (Table 3).
- At the time of data collection, 61 patients (51%) had experienced a side effect from their current treatment.

Table 3. Reason for treatment cessation (induction treatment or drug treatment alone)[a]

	1L (n = 96)	2L (n = 50)	3L (n= 10)	4L (n = 2)
Entered remission / disease free	36 (38%)	12 (24%)	3 (30%)	
Regimen completed – maximum response achieved	22 (23%)	10 (20%)	3 (30%)	
Regimen completed – complete response	34 (35%)	13 (26%)	2 (20%)	
Regimen completed – partial response	8 (8%)	5 (10%)	2 (20%)	
Regimen completed – stable disease	1 (1%)	4 (8%)		
Disease progression/relapse	6 (6%)	22 (44%)	4 (40%)	1 (50%)
Patient refractory to treatment	6 (6%)	6 (12%)	1 (10%)	
Unacceptable tolerability e.g. side-effects / adverse events	8 (8%)	4 (8%)		
Unacceptable impact on patient's quality of life		2 (4%)		
Frequency of administration	1 (1%)			
Mode of administration		1 (2%)		
For palliative care	1 (1%)			
Poor compliance to therapy		1 (2%)		
Don't know /Other reason	2 (2%)	1 (2%)		
No response	3 (3%)	5 (10%)	1 (10%)	1 (50%)

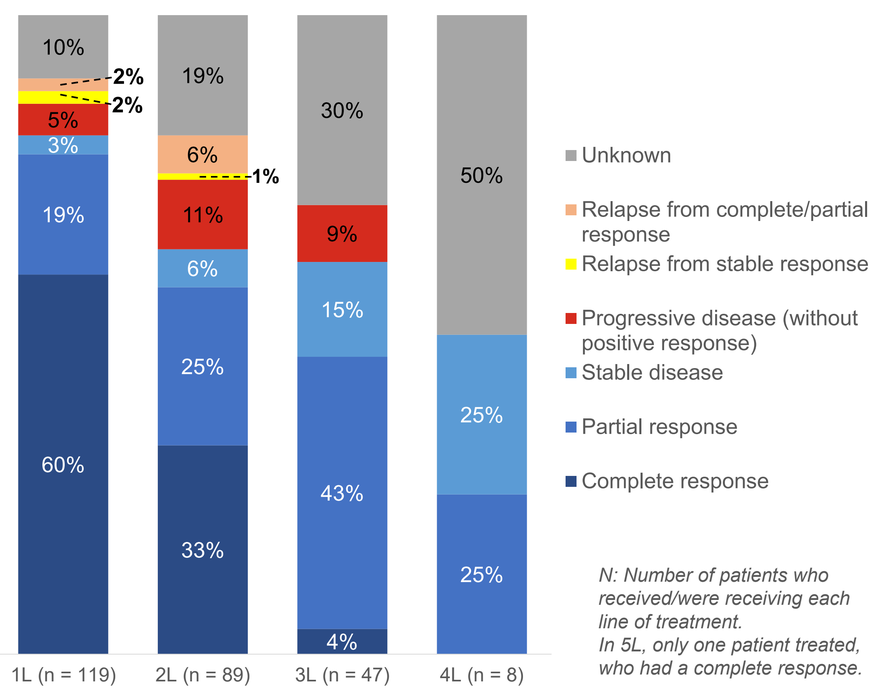
N: Number of patients who received therapy in each respective line, including those on that line who received induction treatment and maintenance therapy.

Table 4. Details of drug treatment history

	1L (n = 119)	2L (n = 89)	3L (n = 47)	4L (n = 8)	5L (n = 1)
R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone)	36 (30%)	5 (6%)	1 (2%)		
Bruton's Tyrosine Kinase Inhibitors	18 (15%)	59 (66%)	10 (21%)	1 (13%)	
Ibrutinib	18 (15%)	57 (64%)	7 (15%)	1 (13%)	
Acalabrutinib		2 (2%)	3 (6%)		
Other drug therapy/regimen	17 (14%)	7 (8%)	3 (6%)	3 (38%)	
VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin and prednisone)	14 (12%)	1 (1%)	6 (13%)	1 (13%)	
BR (bendamustine and rituximab)	12 (10%)	9 (10%)	10 (21%)	1 (13%)	
R-hyper-CVAD (rituximab and hyper-CVAD)	11 (9%)				
Hyper-CVAD (hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone with high-dose Arc-C and methotrexate)	4 (3%)				
NORDIC regimen	3 (3%)		1 (2%)		
R-CVP (rituximab, cyclophosphamide, vincristine, prednisolone)	3 (3%)	1 (1%)	1 (2%)		
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone)	1 (1%)				
Lenalidomide	1 (1%)	1 (1%)	4 (9%)	2 (25%)	
Rituximab	1 (1%)	2 (2%)	2 (4%)	2 (25%)	
Venetoclax		2 (2%)	3 (6%)		
Temsirolimus		1 (1%)	1 (2%)		
Chimeric Antigen Receptor T-cell therapy (CAR-T)			1 (2%)		1 (100%)
R-DHAP (rituximab, doxorubicin, cisplatin, dexamethasone)	1 (1%)		1 (2%)		
R-BAC (rituximab, bleomycin, doxorubicin, cyclophosphamide)	1 (1%)		3 (6%)		
R-ICE (rituximab, ifosfamide, carboplatin, etoposide)		1 (1%)			
FCMR (fludarabine, cyclophosphamide, mitoxantrone, rituximab)		1 (1%)			
R-chlorambucil (rituximab, chlorambucil)		1 (1%)	2 (4%)		

N: Number of patients who received/were receiving each line of treatment

Figure 2. Treatment response



N: Number of patients who received/were receiving each line of treatment.
In 5L, only one patient treated, who had a complete response.

Conclusions

- **A notable number of patients presented advanced disease stages and high Ki-67 expression.**
- **The treatment patterns predominantly follow the recommendations of clinical practice guidelines in Spain[3].**
- **The emergence of disease progression as the predominant reason for discontinuation from the second line onward, coupled with the progressive reduction in response as treatment lines advance, underscores the necessity for future research to identify novel therapeutic targets within the relapsed or refractory setting.**

Limitations

- The DSP is not based on a true random sample of physicians or patients. While minimal inclusion criteria governed the selection of the participating physicians, participation is influenced by willingness to complete the survey. Participating patients may not reflect the general MCL population as patients who consult their physicians more frequently had a greater chance of selection.
- The inclusion criterion of requiring treatment at the time of data collection may lead to underrepresentation of current 'watch and wait' patients.
- The extended times since diagnosis of some patients, combined with the inclusion of patients who may have undergone previous treatments in clinical trials, could result in the treatments represented here not being an accurate reflection of current real-world clinical practice.

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Disclosures
LEB, RV, AM, SDC and AK are employees and shareholders of Eli Lilly. NM is employee of Adelphi Real World. All authors contributed to analysis and interpretation of data and reviewed and approved this poster.

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