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Faculty of Medicine– Final Degree Project
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USE OF OCRELIZUMAB IN PATIENTS WITH PRIMARY PROGRESSIVE MULTIPLE SCLEROSIS

UTILIZACIÓN DE OCRELIZUMAB EN PACIENTES CON ESCLEROSIS MÚLTIPLE PRIMARIA PROGRESIVA

UTILITZACIÓ D'OCRELIZUMAB EN PACIENTS AMB ESCLEROSI MÚLTIPLE PRIMÀRIA PROGRESSIVA

SUMMARY:

Background: This study focuses on the treatment of Primary Progressive Multiple Sclerosis (PPMS), a subtype of MS characterized by a continuous deterioration of symptoms, affecting approximately 10-15% of MS patients. Ocrelizumab (Ocrevus®) is the only drug that has shown positive results in patients with PPMS despite therapeutic efforts. However, its prescription is limited to certain criteria according to the AEMPS. As an alternative, rituximab is widely used in the treatment of PPMS in those who do not meet the criteria to receive ocrelizumab.

Objective: The therapeutic indications presented by this drug led us to believe that due to the pathology it covers, the indications are strict and inconsistent with the demographic characteristics of PPMS patients, which leads to a limited use of ocrelizumab among these patients. The main objective of this study is to analyze the use of ocrelizumab in patients with PPMS.

Results: Patients with shorter disease duration and with inflammatory activity at the time of diagnosis received treatment with anti CD20. Subsequently, age was a determining factor for the indication of ocrelizumab, as opposed to rituximab, since 80% of these patients were under 55 years of age.

Conclusions: The decision to initiate anti CD20 therapy is determined by two factors: shorter disease duration and the presence of MRI activity at diagnosis, both criteria according to the AEMPS. The choice between ocrelizumab or rituximab is based on patient age. The limitations inherent in the prescription of this drug make it difficult for the treatment to reach older patients.

RESUMEN:

Contexto: Este estudio, se centra en el tratamiento de la Esclerosis Múltiple Progresiva Primaria (EMPP), un subtipo de EM que se caracteriza por un deterioro continuo de los síntomas y afecta aproximadamente al 10-15% de los pacientes con EM. Ocrelizumab (Ocrevus®) es el único fármaco que ha mostrado resultados positivos en pacientes con EMPP a pesar de los esfuerzos terapéuticos realizados. Sin embargo, su prescripción está limitada a ciertos criterios según la AEMPS. Como alternativa, rituximab, se utiliza ampliamente en el tratamiento de EMPP de los que no cumplen con los criterios para recibir ocrelizumab.

Objetivo: Las indicaciones terapéuticas que presenta dicho fármaco nos llevaron a pensar que debido a la patología que abarca, las indicaciones son estrictas e inconsistentes con las características demográficas de los pacientes con EMPP, lo que conlleva una limitada utilización de ocrelizumab entre estos pacientes. El objetivo principal de este estudio es analizar la utilización de ocrelizumab en pacientes afectos de EMPP.

Resultados: Los pacientes con menor duración de la enfermedad y con actividad inflamatoria en el momento del diagnóstico recibieron tratamiento con anti CD20. Posteriormente, la edad fue un factor determinante para la indicación de ocrelizumab, frente a rituximab, ya que el 80% de estos pacientes tenían menos de 55 años.

Conclusiones: La decisión de iniciar una terapia anti CD20 está determinada por dos factores: la menor duración de la enfermedad y la presencia de actividad en la RM en el momento del diagnóstico, ambos criterios según la AEMPS. La elección entre ocrelizumab o rituximab se basa en la edad del paciente. Las limitaciones inherentes a la prescripción de este fármaco dificultan que el tratamiento llegue a aquellos de mayor edad.

RESUM:

Context: Aquest estudi es centra en el tractament de l'Esclerosi Múltiple Progressiva Primària (EMPP), un subtipus d'EM que es caracteritza per un deteriorament continu dels símptomes i afecta aproximadament al 10-15% dels pacients amb EM. L'ocrelizumab (Ocrevus®) és l'únic fàrmac que ha mostrat resultats positius en pacients amb EMPP malgrat els esforços terapèutics realitzats. No obstant això, la seva prescripció està limitada a certes indicacions segons l'AEMPS. Com a alternativa, el rituximab s'utilitza àmpliament en el tractament de l'EMPP en aquells que no compleixen els criteris per rebre ocrelizumab.

Objectiu: Les indicacions terapèutiques que presenta aquest fàrmac ens van portar a pensar que, a causa de la patologia que abasta, les indicacions són estrictes i inconsistents amb les característiques demogràfiques dels pacients amb EMPP, el que comporta una utilització limitada d'ocrelizumab entre aquests pacients. L'objectiu principal d'aquest estudi és analitzar la utilització d'ocrelizumab en pacients afectats d'EMPP.

Resultats: Els pacients amb menor durada de la malaltia i amb activitat inflamatòria en el moment del diagnòstic van rebre tractament amb anti CD20. Posteriorment, l'edat va ser un factor determinant per a la indicació d'ocrelizumab, enfront de rituximab, ja que el 80% d'aquests pacients tenien menys de 55 anys.

Conclusions: La decisió d'iniciar una teràpia anti CD20 està determinada per dos factors: la menor durada de la malaltia i la presència d'activitat en la RM en el moment del diagnòstic, ambdós criteris segons l'AEMPS. La elecció entre ocrelizumab o rituximab es basa en l'edat del pacient. Les limitacions inherents a la prescripció d'aquest fàrmac dificulten que el tractament arribi als de major edat.

INTRODUCTION:

Inflammatory demyelinating diseases, including Multiple Sclerosis (MS), are heterogeneous disorders characterized by acute or chronic inflammatory processes in the central nervous system (CNS) (1)

Most studies consider the etiology of this entity to be a genetic and epigenetic interaction, but it remains partially idiopathic. The pathogenesis is also complex and not completely known, however, there is consensus that the pillars of the disease are inflammation and neurodegeneration.(2)

MS is the most common demyelinating disease of the CNS and is the leading cause of non-traumatic neurological disability in young adults. The global prevalence of MS is estimated at 36 per 100,000 people, which means that there are 2.8 million adults living with MS worldwide. It has its onset around the age of 25-30 years and most often affects females.(3)

Regarding clinical semiology and neuroimaging findings, it is considered a multifocal and heterogeneous disease, since symptoms will vary depending on the areas of the CNS affected.

Accurate descriptions of the clinical course of MS are important for patient communication and disease prognosis, as well as for clinical trial design and recruitment and treatment decision making.(4) Differences in disease course between patients give rise to the phenotype classification of MS as relapsing-remitting (RRMS), secondary progressive (SPMS) or primary progressive (PPMS).

Most of the patients (80-85%) will present with RRMS, characterized by an acute exacerbation followed by partial or complete recovery, whereas PPMS is associated with a continuous worsening of symptoms that is only observed in about 10-15% of patients. Furthermore, there are substantial differences in epidemiology between the two phenotypes, with PPMS appearing at later ages and the incidence being equal for both sexes.(5–7).

Disability in MS predominantly accumulates in the progressive forms of the disease, creating a substantial health care burden at the individual, family, and community levels.(8)

The complexity of the pathology slows down the investigation and information of affected patients, mainly PPMS patients. It also makes it impossible to offer this population group a prognosis of their disease, which also hinders their development at the therapeutic and evolutionary level.(9)

Therapeutically, the treatment of RRMS has a greater therapeutic arsenal than PPMS. As a result, most anti-inflammatory drugs that have regulatory approval for the treatment of RRMS have little or no efficacy in PPMS.

The development of therapies that prevent or reverse the progression of PPMS has been slower due, in part, to the lack of knowledge of the pathophysiology of PPMS. Currently, thanks to several scientific

studies, it is suggested that depletion of CD20-expressing B cells may be useful for treatment. B cells contribute to the pathogenesis of PPMS through antigen presentation and antibody production. In addition, B cells are present in the meningeal inflammation that is characteristic of chronic inflammation.(10)

Ocrelizumab, whose trade name is Ocrevus®, is a recombinant humanized monoclonal antibody that selectively reduces CD20-expressing B lymphocytes. The exact mechanisms of this drug have not been fully elucidated, but it is believed to be involved in immunomodulation through the reduction of the number and function of CD20-expressing B lymphocytes.(11)

This drug has been shown to reduce the risk of confirmed disability progression by 24% compared to placebo in PPMS patients, reducing the rates of clinical progression and MRI involvement. (10) Thus, ocrelizumab becomes the first agent to demonstrate positive results in both phenotypes of MS (RRMS and PPMS).(8)

Even so, this drug is limited to certain patients with specific clinical characteristics and, therefore, it cannot be administered to all affected patients. The therapeutic indications according to the Spanish Association of Medicines and Health Products ("AEMPS") are those adult patients with early PPMS, in reference to the duration of the disease and the level of disability, and who present inflammatory activity in imaging tests.

According to the articles studied and according to the AEMPS, the profile of patients with PPMS who meet the approval characteristics for resorting to this therapeutic measure is very specific. It includes younger patients (age between 18 and 55 years), with shorter disease duration (<10 years) and with appearance of new lesions and/or gadolinium enhancement demonstrated in a control MRI scan. (10) Therefore, a low percentage of affected patients with PPMS benefit from ocrelizumab.

The use of ocrelizumab is restricted to "early" PPMS in relation to the degree of disability and duration of disease, as well as imaging features indicating inflammatory activity. However, the prescription of this drug is even more limited in local institutions due to its high cost and that is why there is an alternative which is rituximab.(12,13)

Rituximab is another chimeric anti CD20 antibody which has been widely used to treat patients with PPMS, prior to the approval of ocrelizumab and as an alternative to ocrelizumab. (13)

Due to the pathology involved and considering the demographic characteristics of PPMS patients, the indications are strict, leading to a limited use of ocrelizumab among these patients.

The main objective of the present scientific study is the confirmation or ratification of the supposed hypothesis, investigating the main characteristics of the patients both at the time of diagnosis and before starting treatment.

The characteristics of the patients selected to receive anti CD20 treatment will be analyzed in order to establish a detailed profile of the patients at the time of diagnosis. Subsequently, a comparison will be made between those patients treated with ocrelizumab and those treated with rituximab, with the aim of defining the particularities and differences between both groups at the time of diagnosis and before the start of treatment.

The aim of this research is to obtain a deeper understanding of the therapeutic indications followed at a practical level for the prescription of ocrelizumab.

The results obtained will contribute to the advancement of knowledge in the field of MS and may serve as a basis for future research and improvements in the care and treatment of patients affected by the PPMS phenotype.

METHODS:

Type of study:

The present study used a retrospective cohort design with data from 89 patients whose first visit was made at the Multiple Sclerosis Center of Catalonia (Cemcat) in the last 5 years and who were finally diagnosed with PPMS. Therefore, the sample spans from 1st of January 2018 to 1st of January 2023. We will study those patients treated with anti CD20 therapy (ocrelizumab or rituximab) and those who have not been treated with anti CD20 therapy (ocrelizumab or rituximab).

Inclusion criteria:

- Patients over 18 years of age.
- Patients diagnosed with PPMS using the diagnostic criteria of Thompson et al.(14)
- Patients whose first visit was performed at Cemcat in the last 5 years, between 2018 and 2023.
- Patients who have given informed consent.

Exclusion criteria:

- Patients who have refused to enter the study by not signing the informed consent form.
- Patients whose diagnostic orientation has changed during the follow-up of the disease.
- Patients whose follow-up has been done through another center for which we do not have access to the clinical history.

Data collection and analysis:

The research has been approved by the ethics committee of the corresponding center, ensuring compliance with the ethical principles established in the Declaration of Helsinki.

The information was collected during the period between March 13 and April 10, 2023, by reviewing the electronic medical records of the cohort of patients. The anonymity of the patients has been always preserved by means of codes and with the supervision of a medical professional from the Neurology Service - Cemcat of the Vall d'Hebron University Hospital to enter the database.

Several variables of interest were evaluated, which can be divided into the characteristics of the patients at the time of diagnosis and those before the start of treatment. The collection and creation of the database was carried out using Excel and statistically analyzed using SPSS software version 29.0.

The results were obtained using frequencies for qualitative variables. For quantitative variables, the mean and standard deviation were used for those with a normal distribution, and for those with a non-

normal distribution, the median and the interquartile range or the maximum minimum, as in the case of the EDSS, were used.

To evaluate the significance of the comparisons of results, different statistical tests were applied according to the nature of the variables. For normally distributed quantitative variables, the student's t-test for independent samples was used. In the case of non-normal distribution, nonparametric tests were performed using the Mann-Whitney U test. Qualitative variables were analyzed using Chi-square.

RESULTS:

At the beginning of the study the sample size was 89 patients with PPMS, but 7 of them were not included in the statistical analysis because they lost follow-up with the center during the evolution of the disease. For this reason, the final statistical analysis was made with 82 patients of whom only 52 (63.4%) ended up receiving treatment due to their characteristics at the time of diagnosis. Of those patients who received treatment 94% received treatment with anti CD20; 29 patients with ocrelizumab and 20 patients with rituximab. The remaining 3 patients received a different treatment. (Figure 1)

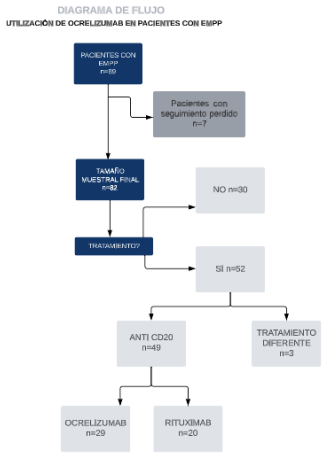

Figure.1: *Flowchart of the patients included in the study.*

Descriptive characteristics at diagnosis are detailed in Table 1, showing a typical cohort of PPMS patients. (Table 1).

It is worth noting that the median duration of the disease at the time of the first visit, considering the date of the first symptom as the onset of the disease, was approximately 4 years (2.2-8.1).

Table 1. Baseline descriptive characteristics of the cohort of PPMS patients:

		n=82[a]
Age at onset (years) (mean; SD)		48.1 (10.6)
Sex (female)		40 (48.8%)
Debut symptom		
	Pyramidal	60 (73.2%)
	Cerebellar	6 (7.3%)
	Other	16 (19.5%)
Baseline EDSS (median, IQR)		4.5 (3.0-6.0)
Positive oligoclonal bands [b]		36 / 50 (72.0%)
Number of patients with gadolinium enhancement in MRI [c]		15 / 64 (23.4%)
Disease duration at 1st visit (median, IQR)		4.4 (2.2-8.1)

All values are expressed as n (%) unless specified. a: 7 no follow-up: not performed; c: 13 not administered/5 lost. Abbreviations: EDSS: expanded disability status scale; IQR: interquartile range; MRI: magnetic resonance imaging; SD: standard deviation.

Comparative statistical analysis was performed between the groups of patients according to whether they received anti CD20 treatment at the time of diagnosis or not to compare the characteristics of the two groups. (Table 2)

Firstly, it is observed that a higher percentage of patients who received anti CD2O treatment had lesions enhancing with Gadolinium at the time of diagnosis compared to those who did not receive treatment (32.5% vs. 8.5%, p=0.034). We can also see this more visually in Figure 2 graph A.

Secondly, a shorter disease duration is observed in patients who received anti CD20 treatment compared to those who did not receive treatment (3.6 vs. 7.4 p=0.008). We can also see this in Figure 2 graph B.

Table 2: Comparative table of characteristics at the first visit between patients treated with Anti CD20 and those without treatment.

	Treatment Anti CD20 n=49	No Treatment n=33[a]	p-value
Age at onset (years) (mean; SD)	46.23 (9.82)	50.9 (11.43)	*0.051*
Sex (female)	23 (46.9%)	17 (51.5%)	0.684
Pyramidal debut symptom	33 (67.3%)	27 (81.8%)	0.147
Baseline EDSS (median, min-max)	4.00 (1.5-7.5)	4.5 (2.0-8.0)	0.372
Positive oligoclonal bands[b]	24/34 (70.6%)	12/14 (75%)	0.465
Number of patients with gadolinium enhancement [c]	13/40 (32.5%)	2/24 (8.3%)	**0.034**
Disease duration at 1st visit (Median, IQR)	3.67 (1.89-6.42)	7.40 [3.95-9.92]	**0.008**

All values are expressed as n (%) unless specified. a: 30 without treatment and 3 with a different treatment. b: 34 not performed; c: 18 not administered. Abbreviations: EDSS: Expanded Disability Status Scale; IQR: interquartile range; SD: standard deviation.

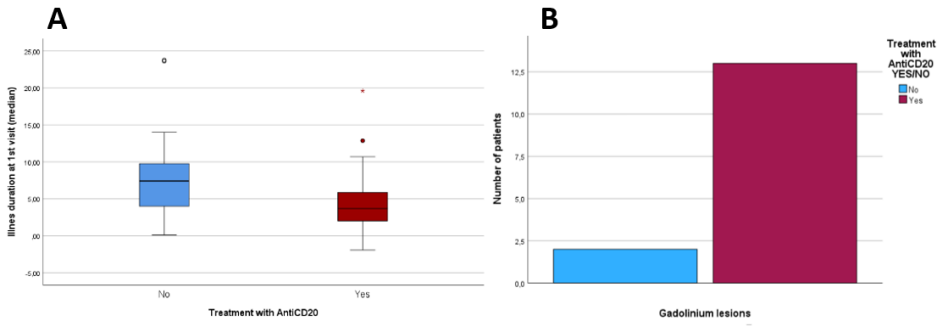

***Figure.2: A** Bar chart of the differences in the percentage of patients with lesions enhancing with Gadolinium with or without anti CD20 treatment.**B:** Differences in the duration of disease at diagnosis of both groups.*

Finally, the comparative statistical analysis was performed according to the type of anti-CD20 prescribed. The comparative table is divided in this case into; a first part of the characteristics of the patients at the time of diagnosis (Table 3) and a second part in which the characteristics of the same patients at the time of initiating treatment are specified according to the indicated treatment: ocrelizumab or rituximab (Table 4).

A significant p-value (p=0.004) was observed in the age of disease onset since patients who received ocrelizumab had a lower age of disease onset than those who received rituximab (42.5 vs. 51 years on average), as shown in Figure 3.

In addition, when analyzing gender, a significant discrepancy was found. In the sample of patients treated with ocrelizumab, a lower proportion of women was observed, representing only 28% of the cases, compared to the sample of patients treated with rituximab where women constituted 75% of the cases. As there was no plausible explanation for the gender differences, we decided to analyze whether there was any relationship between these differences and age. We found that, of the 23 total women treated, 13 of them were older than 55 years. This information further highlights the importance of considering gender as a confounding factor in the results.

In the comparative Table 4 we can see that, at the time of initiating treatment, ocrelizumab was prescribed to a younger sample of patients with a mean age of 48 years, compared to patients who initiated rituximab who were observed to have a mean age of 51 years, with a p-value of 0.005. We can see this result in a dichotomous way since 80% of the patients who initiated ocrelizumab were under 55 years of age (Figure 4).

Table 3.1: Comparative table of patients treated with Anti CD20 at diagnosis:

	Ocrelizumab n=29	**Rituximab n=20**	**p-value**
Age at onset (years) (mean; IQR)	42.59 (37.62-48.70)	51.07 (46.99-55.93)	0.004
Sex (female)	8 (27.6%)	15 (75%)	0.001
Pyramidal debut symptom	21 (72.4%)	12 (60%)	0.362
Baseline EDSS (median, min-max)	4.00 (1.5-7.5)	4.5 (2.0-6.5)	0.455
Positive oligoclonal bands[a]	16/21 (76.2%)	8/13(61.5%)	0.451
Number of patients with gadolinium enhancement in MRI [b]	8/24 (33.3%)	5/16 (31.2%)	0.890
Disease duration at 1st visit (Median, IQR)	3.67(1.89-7.11)	3.74(1.83-4.93)	0.943

Table.3*: All values are expressed as n (%) unless specified. a: 15 not performed; b: 9 not administered/missed. Abbreviations: EDSS: Expanded Disability Status Scale; IQR: interquartile range; SD: standard deviation.*

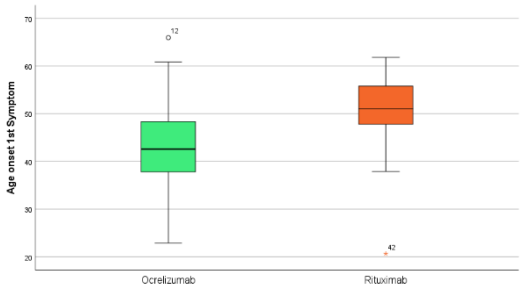

Figure.3: *Differences in age at disease onset according to anti CD20 type.*

Table 4: Comparative table of patients treated with Anti CD20 at the time before starting treatment:

	Ocrelizumab n=29	**Rituximab n=20**	**p-value**
Age at start treatment (mean;SD)	48.07 (9.39)	55.77(8,25)	0.005
Age at start treatment >55 years old	6/29 (20.7%)	13/20 (65%)	0.002
EDSS pre Anti CD20 (median, IQR)	4.00 (3.50-4.50)	4.5 (3.00-6.00)	0.432
Disease duration at treatment onset (median,IQR)	3.8 (2.46-5.65)	4.27 (2.44-6.20)	0.640
Disease duration at treatment onset < 10 years	27/29 (96.4%)	3/20 (15%)	0.162
MRI new activity before treatment	10/23 (43.5%)	4/19 (21.1%)	0.125

All values are expressed as n (%) unless specified. Abbreviations: EDSS: Expanded Disability Status Scale; IQR: interquartile range; MRI: magnetic resonance imaging; SD: standard deviation.

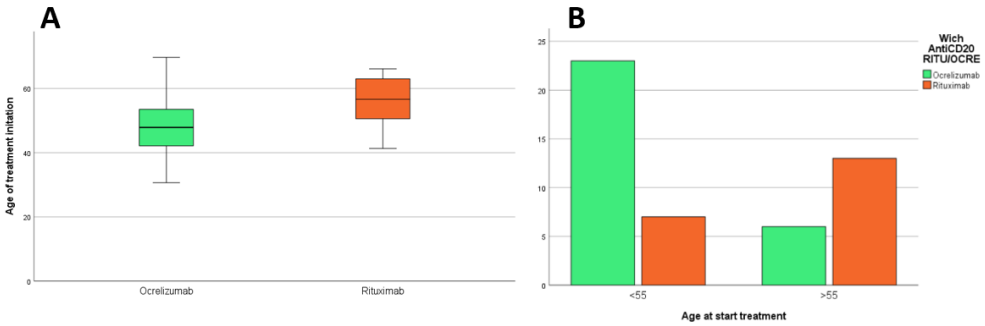

***Figure 4**: **A:** Representation of the mean of the variable. **B**: dichotomous variable according to whether they are older or younger than 55 years of*

DISCUSSION:

In recent years the use of anti CD20 therapies, has proven to be effective in the treatment of PPMS representing an important therapeutic advance for these patients. However, the choice of treatment for affected patients is a challenge for physicians since they must consider several factors.(15)

The results obtained in this study demonstrate that the clinical-radiological characteristics at the time of the first visit determine the indication for anti CD20 therapy in patients with PPMS. Thus, it is more likely that this therapy will be offered to patients with inflammatory and/or disease activity since it seems that in this group of patients the treatment could be more effective. These patients are candidates for treatment possibly to control inflammatory activity and reduce disease progression as anti CD20 therapies exert strong anti-inflammatory activity, and their neuroprotective effects could be mainly secondary to the prevention of further inflammatory disease activity.(16)

In addition, this study has also shown that the presence of Gadolinium-enhancing lesions is not the only determining factor for initiating anti CD20 treatment but is also determined by the time of disease progression at the first visit. The shorter the time elapsed, the greater the chance of initiating anti CD20 treatment. Several studies suggest that those patients who were younger (<40 years) and with baseline disease activity (≥1 Gadolinium-enhanced lesions) had a greater benefit from anti CD20 treatment.(17)

Subsequently, among patients who initiate treatment with anti-CD20 therapy, the use of ocrelizumab has been specifically investigated. In this study it was observed that the main indication for deciding the type of anti CD20 drug, whether it is rituximab or ocrelizumab, is age, with a younger age being more favorable for starting treatment with ocrelizumab in both cases. In reference to this finding, a confusing result was obtained with gender, since we found a lower percentage of women who were treated with ocrelizumab, but this was because they were diagnosed later.

A study on the diagnosis of PPMS in women would be interesting. It could reveal differences in the initial presentation of symptoms and possible reasons for later consultation. These factors could influence access to ocrelizumab treatment, especially considering that, according to the data reported in our study, they are often diagnosed at a later age. Gaining more knowledge about these aspects would allow for a more personalized therapeutic approach for these women.

An observational multicenter study of patients with PPMS similar to ours in the Valencian Community has recently been published. In this study, patients were studied for 1 year according to whether they were treated with ocrelizumab or rituximab according to clinical practice and data were collected prospectively and retrospectively. This study, unlike ours, showed that patients treated with rituximab had significantly higher initial EDSS, time to initiation of treatment and previous treatment with anti

CD20 compared to those treated with ocrelizumab.(13) In our case the only significant difference between the cohort of patients who received treatment with ocrelizumab with respect to rituximab was a lower age at disease onset and a lower age at treatment initiation.

Possibly this is due to disease screening, such as the difference in disease duration at diagnosis and Gadolinium-enhancing lesions that have previously marked the decision on whether to receive anti CD20 therapy or not.

Ocrelizumab is associated with lower rates of clinical and MRI progression than placebo, yet we would need more long-term studies to compare efficacy with rituximab.(10,13)

Considering the results obtained and the therapeutic recommendations established in the technical data sheet of ocrelizumab, it can be concluded that once the need to initiate anti CD20 therapy is determined, which is marked by the duration of the disease and its baseline activity, the variable of age plays a significant role in the decision to opt or not for this pharmacological treatment.

One possible limitation of our study is the relatively low number of patients included, nevertheless, PPMS represents 10% of patients with MS. Another possible limitation is being a referral center, patients seek a second opinion at more advanced stages of their disease, looking for therapeutic alternatives and/or the possibility of participating in clinical trials, so it is possible that the sample of patients who do not meet treatment criteria is overrepresented. Finally, indications for treatment with anti CD20 therapies often occur shortly after the first visit to the unit, so that the same brain MRI used for diagnosis constitutes the brain MRI prior to the start of treatment, without being able to assess the presence of new lesions in a control MRI that could have increased the number of patients who would present radiological activity before starting treatment and therefore be candidates for anti CD20 treatment and even for ocrelizumab.

The therapeutic indications presented by this drug lead us to think that, due to the pathology it encompasses, the indications are strict and inconsistent with the demographic characteristics of these patients, resulting in limited utilization of ocrelizumab among them.

It is also worth noting that, in many studies, the sample of patients studied constitutes a highly selected group and is not necessarily representative of the PPMS patient population, characterized by young patients with poorly progressive disease without advanced disability as indicated by the drug protocol. (18)

It would be interesting to carry out a collaborative study with other centers within the Catalan and Spanish territory, to confirm that the differences in our study on the clinical-radiological characteristics

that lead to the indication of an anti CD2O therapy and subsequently ocrelizumab, are maintained in other hospitals that share the same therapeutic indications.

In addition, it would be interesting to study those patients older than 55 years who receive treatment with ocrelizumab, since their efficacy is not expected to differ. However, it is possible that the safety profile may be less favorable in this older population compared to the study population.(18)

CONCLUSIONS:

In view of the results obtained, we can conclude that the decision to indicate anti CD20 therapy is determined by the shorter duration of the disease and the presence of inflammatory activity in the brain MRI at the time of the first visit, both criteria for therapeutic indication according to the AEMPS.

Subsequently, the decision on whether to initiate ocrelizumab or rituximab is determined by the patient's age, so that those patients under 55 years of age (as indicated by the AEMPS) will receive ocrelizumab.

According to the results obtained, slightly more than half of the patients with PPMS receive treatment with anti CD20 therapy. However, only one third of patients with PPMS will receive ocrelizumab. The limitations inherent to the prescription of this drug in this group of patients make it difficult for the treatment to reach an older group of patients, since the disease usually debuts at a later age, between 35 and 45 years, and due to its semiology, there is sometimes a diagnostic delay.

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