Aim and objectives The aim of this study was to compare the relative efficacy of darolutamide versus apalutamide and enzalutamide using clinical trial data to determine the positioning of new antiandrogenic drugs in the treatment of nmCRPC.
Material and methods We performed adjusted indirect comparisons using Bucher´s method. We selected the main clinical trial for each drug (ARAMIS, PROSPER and SPARTAN trials). The three studies had a similar design and included populations with similar characteristics. The main outcome used was metastasis free survival (MFS). MFS was demonstrated to be an adequate surrogate variable for overall survival.[1] The variable used for darolutamide in the darolutamide versus enzalutamide IC was progression free survival (PFS) due to the PROSPER design. MFS and PFS were compared with placebo in the three studies.
Results The three drugs were superior to placebo for the endpoints analysed. In the comparison between enzalutamide (MFS=36.6 months (m) vs 14.7 m) versus darolutamide (PFS=36.8 m vs 14.8 m), HR calculated using Bucher's method favoured enzalutamide (0.76 (IC 0.59–0.98); p=0.037). In the IC darolutamide (MFS=40.4 m vs 18.4 m) versus apalutamide (MFS= 40.5 m vs 14.7 m) HR favoured apalutamide (1.41 (IC 1.07–1.87); p=0.015). Both IC yielded a statistically significant result.
Conclusion and relevance While indirect comparisons had limitations, this analysis showed the slight superiority in HR in delaying the appearance of metastases for enzalutamide and apalutamide. Despite the data obtained, the inferiority of darolutamide cannot be assured. The biases involved in the comparison may have influenced the results. Real world data are needed to expand our knowledge of castration resistant non-metastatic prostate cancer treatment.

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Conflict of interest No conflict of interest

4CPS-307 SAFETY EVALUATION OF NEW ANTIANDROGENIC DRUGS IN CASTRATION RESISTANT NON-METASTATIC PROSTATE CANCER

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Background and importance Apalutamide, enzalutamide and darolutamide have recently been approved for treating castration resistant non-metastatic prostate cancer (nmCRPC). The three drugs demonstrated efficacy over placebo in clinical trials, but the lack of direct comparisons, particularly with regard to safety, makes the selection and positioning of these drugs in this new scenario difficult.
Aim and objectives The aim of this study was to compare the relative safety of darolutamide versus apalutamide and enzalutamide using clinical trial data to determine the positioning and objective differences in security profiles of new antiandrogenic drugs in the treatment of nmCRPC.
Material and methods We performed adjusted indirect comparisons using Bucher´s method. We used security data from the main clinical trials for each drug (ARAMIS, PROSPER and SPARTAN trials). The three studies had a similar design and included populations with similar characteristics. We calculated risk differences and number needed to harm (NNH) for each relevant outcome and selected those with statistically significant difference.
Results The results are shown in tables 1 and 2.

Abstract 4CPS-307 Table 1

Adverse event (AE)	Risk differences darolutamide vs placebo (95% CI)	Risk differences enzalutamide vs placebo (95% CI)
AE	6.3% (2.1% to 10.6%)	9.5% (5.1% to 13.8%)
AE grades 3–4	5.2% (1.0% to 9.5%)	8% (3.1% to 12.8%)
Serious AE	4.8% (0.5% to 9.1%)	6% (1.6% to 10.5%)
AE leading to discontinuation	0.2% (−2.7% to 3.2%)	3.3% (0.5% to 6.2%)

Abstract 4CPS-307 Table 2

Adverse event	Risks differences darolutamide vs placebo (95% CI)	Risk differences apalutamide vs placebo (95% CI)
AE	6.3% (2.1% to 10.6%)	3.3% (0.5% to 6.1%)
AE grades 3–4	5.2% (1.0% to 9.5%)	10.9% (5.1% to 16.7%)
Serious AE	4.8% (0.5% to 9.1%)	1.7% (−3.4% to 6.8%)
AE leading to discontinuation	0.2% (−2.7% to 3.2%)	3.6% (0.3% to 6.8%)

No statistically significant difference was found using Bucher´s method for any outcome so the NNH was not calculated.
Conclusion and relevance There were no differences in the safety profiles of the drugs evaluated, although the number of patients for some variables was small. According to preclinical studies, darolutamide does not cross the blood–brain barrier. This could explain the similar incidence of AE in the darolutamide and placebo groups in the ARAMIS trial. Data on larger patient samples are needed to determine differences.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest No conflict of interest

4CPS-308 EXPERIENCE WITH TERIFLUNOMIDE TREATMENT FOR MULTIPLE SCLEROSIS IN A UNIVERSITY HOSPITAL

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Background and importance Teriflunomide (TRF) is a once daily oral immunomodulatory drug approved in over 80 countries for multiple sclerosis (MS). It is indicated in young adults and contraindicated in pregnant women or women of reproductive age because of the potential for fetal harm. TRF

became available as a unique option for oral MS treatment in our hospital in 2017.

Aim and objectives To describe our experience with the use of TRF and assess its safety profile, as disease modifying therapies (DMTs) work differently and have different adverse reactions (AR).

Material and methods An observational retrospective study was conducted from January 2017 to January 2020. Collected variables from medical records were: age, sex, expanded disability status scale score (EDSS), previous DMTs, safety profile (AR, suspension of TRF treatment) and results of blood tests. Sustained disability progression was defined as at least a 1 point increase from the baseline EDSS score ≤5.5 (or at least a 0.5 point increase for those with a baseline EDSS score >5.5) sustained for at least 12 weeks.[1]

Results 45 patients were analysed, 10 men and 35 women (mean age 35.7 years). TRF was the firstline drug for 10 patients, the rest had switched to TRF from parenteral therapies: 7 subcutaneous glatiramer acetate, 20 intramuscular or subcutaneous interferon beta and 2 intravenous natalizumab. The main reasons for change were: convenience of oral administration, poor tolerance and AR at the site of injection. The average duration for TRF was 2.5 years with no suspension recorded. In this period, for 30 patients EDSS score remained stable. The mean change in EDSS from baseline was 0.7; no increase in disability progression. 30 patients showed no AR and 15 patients presented gastrointestinal disorders (9), temporary alopecia (4) or headache (2). 9 patients experienced moderate elevation of liver enzymes.

Conclusion and relevance TRF seemed to have a manageable safety profile, was well tolerated, and no new or unexpected AR were reported and there were no suspensions of treatment. Because our experience reflects only 3 years, increased monitoring is necessary to assess the long term safety.

REFERENCES AND/OR ACKNOWLEDGEMENTS

1. AUBAGIO (package insert). Cambridge, MA: Genzyme Corporation

Conflict of interest No conflict of interest

4CPS-309 BARRIERS TO ADHERENCE WITH PRESCRIBED TREATMENTS IN MULTIPLE SCLEROSIS PATIENTS

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Background and importance Multiple sclerosis (MS) is a chronic progressive disease, one of the main causes of invalidity among young adults. Adherence may be difficult because treatment benefits are not immediately apparent, and most disease modifying therapies (DMTs) have tolerability and safety issues.

Aim and objectives In our hospital, where almost 800 MS patients are treated monthly, no study has assessed adherence, so the purpose of this study was to evaluate adherence and identify patient reported barriers regarding adherence.

Material and methods An observational retrospective study was conducted (January 2017 to January 2019). We evaluated adherence using missed dose ratio (MDR), and identified and quantified barriers to adherence using the MS treatment adherence questionnaire (MSTAQ). This tool has 30 items in three subscales: DMT barriers to adherence, DMT side effects (SE) and DMT coping strategies. We also collected demographic (age, sex) and treatment information (current DMT, DMT history, reason for switch therapy and exposure to treatment).

Abstract 4CPS-309 Table 1

MS-TAQ subscale	No of items	Score		
		Mean	Range	Observations
DMT barriers	13	2.18[1]	0-39	63% of patients reported no barriers (score 0)
DMT side effects	10	9.30[2]	0-40	Only 11.6% reported no SE (score 0)
DMT coping strategies	7	1.22[3]	0-7	36.6% do not use coping strategies

[1]Most common barriers, for 22 patients, were forgetting to administer DMT (58%), not "in the mood" to take DMT (22%) and feeling tired of taking DMT (16%).
[2]88.4% of patients reported SE such as injection phobia, injection site reaction and tolerability concerns.
[3]15 patients reported SE but no coping strategies in place, maybe because they were not aware of them.

Results 60 patients (44 women), average age 40.47 years had a mean treatment exposure of 6.38 years. Adherence was high because only 11 had missed one or more doses in the last month (MDR >0). When asked about missed dose in general, 22 patients reported barriers to taking medication. DMT scores are described in table 1.

Conclusion and relevance Overall, adherence was high even though there were some barriers to adherence. SE and long duration of treatment could affect adherence, which is why it is important to detect and overcome barriers using such questionaries, to identify in time non-adherent patients and counsel them appropriately on how to use more coping strategies.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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4CPS-310 TOFACITINIB EFFECTIVENESS AND SAFETY RESULTS: REAL WORLD DATA

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Background and importance Tofacitinib is an oral JAK inhibitor indicated for the treatment of rheumatoid arthritis, psoriasis arthritis and ulcerative colitis. The efficacy and safety of tofacitinib have been shown in several randomised clinical trials.

Aim and objectives To evaluate the effectiveness and safety of tofacitinib in all indications used in a real world cohort of patients in a third level hospital.

Material and methods This was a retrospective observational study of patients who received tofacitinib from 2017 to March 2020. Demographic, clinical characteristics at baseline and outcomes analysed were: age, sex, diagnosis, number of days treated with tofacitinib, previous lines of treatment, objective response and adverse effects.