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 end-points 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.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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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