VIE21-0467 . 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 has demonstrated efficacy over placebo in clinical trials, but the lack of direct comparisons, particularly with regard to safety, difficults the selection and positioning of these drugs in this new scenario.

Aim and objectives

The aim of this study is to compare relative safety of darolutamide versus apalutamide and enzalutamide using clinical trial data in order to approach the positioning and objectify 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 trial for each drug (ARAMIS, PROSPER AND SPARTAN trials). The three studies had a **similar design** and included **population with similar characteristics**. We calculated **risk differences and Number needed to harm (NNH) for each relevant outcome** and selected those with statiscally significant difference.

Results

The results obtained are shown in the following tables:

Adverse event (AE)	Risk differences Darolutamida vs Placebo (CI 95%)	Risk differences Enzalutamida vs Placebo (CI 95%)
AE	6,3% (2,1% to 10,6%)	9,5% (5,1% to 13,8%)
AE Grade 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%)

Adverse event	Risks differences Darolutamida vs Placebo (CI 95%)	Risk differences Apalutamida vs Placebo (CI 95%)
AE	6,3% (2,1% a 10,6%)	3,3% (0,5% a 6,1%)
AE Grade 3-4	5,2% (1,0% a 9.5%)	10,9% (5,1% a 16,7%)
Serious AE	4,8% (0,5% a 9,1%)	1,7% (-3,4% a 6,8%)
AE leading to discontinuation	0,2% (-2,7% a 3,2%)	3,6% (0,3% a 6,8%)

No statiscally difference was found using Bucher´s method for any outcome so NNH was not calculated.

Conclusion and relevance

Apparently there are no differences in safety profiles in the drugs evaluated, although the number of patients for some variables is small. According to preclinical studies darolutamide do not crosses the blood-brain barrier. This could explain the similar incidence of AE in darolutamide and placebo groups in ARAMIS trial. Data including larger patient samples are needed to find differences.