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CONSEJERÍA DE SALUD



DAROLUTAMIDE, ENZALUTAMIDE AND APALUTAMIDE: PLACE IN THERAPEUTICS OF CASTRATION RESISTANT NON METASTATIC PROSTATE CANCER VIE21-0442

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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 lack of direct comparisons difficults the selection and positioning of these drugs in this new scenario. Taking into account the social and economic importance it is essential to develop studies that provide answers to this lack of information.

AIM AND OBJECTIVES

The aim of this study is to compare relative efficacy of darolutamide versus apalutamide and enzalutamide using clinical trial data in order to approach the positioning of new antiandrogenic drugs in the treatment of nmCRPC.

MATERIAL AND METHODS - Similar design ARAMIS trial (darolutamide) - Population with simila PROSPER trial (enzalutamide) SPARTAN trial (apalutamide) characteristics Main clinical trial for each drug The variable used for darolutamide The outcome used was **metastasis** free in the darolutamide vs enzalutamide survival (MFS), which was the main IC was progression free survival outcome. (**PFS**), due to PROSPER design. MFS and PFS were compared with MFS demonstrated to be an adequate placebo in the three studies. surrogate variable of overall survival¹. Indirect comparisons (IC): Bucher's method **RESULTS**

The three evaluated drugs demonstrated it superiority over placebo in the analysed endpoints. 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 favored enzalutamide and its result was 0,76 (IC 0.59-0.98; p=0.037). In the IC. darolutamide (MFS=40.4m vs 18.4m) versus apalutamide (MFS= 40.5m vs 14.7m) HR favored apalutamide: 1,41 (IC1,07-1,87; p=0.015). Both IC yielded a stastiscally significant result.

CONCLUSION AND RELEVANCE

While indirect comparisons has limitations, this analysis shows slight superiority in HR in delaying appearance of metastasis 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 result. Real world data is needed in order to deepen knowledge of castration resistant non metastatic prostate cancer treatment.

¹ Xie W, Regan MM, Buyse M, Halabi S, Kantoff P, Sartor O, et al. Metastasis-free survival is astrong Surrogate of overall survival in localized prostate cancer. J Clin Oncol. 2017 Sep20;35(27):3097–104.