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A Review of TITAN Trial for Prostate Cancer

Daniel García Flores[1], José Armando Pérez Espinoza[2]

[1]Universidad Autónoma de Guadalajara

[2]Instituto Mexicano del Seguro Social

ABSTRACT

The TITAN trial, a phase III, randomized, double-blind, placebo-controlled study, evaluated the efficacy and safety of apalutamide in combination with androgen deprivation therapy (ADT) for patients with metastatic castration-sensitive prostate cancer (mCSPC). The trial included 1,052 patients randomized to receive apalutamide or placebo plus ADT, with primary endpoints of overall survival (OS) and radiographic progression-free survival (rPFS). Results demonstrated that apalutamide significantly improved OS and rPFS, with a 35% reduction in the risk of death (HR, 0.65; 95% CI, 0.53–0.79; P<0.001) at a median follow-up of 44 months. Health-related quality of life (HRQOL) was maintained during treatment. Adverse events more common in the apalutamide group included rash (27.1%), hypothyroidism, and ischemic heart disease, but these were manageable.

The TITAN trial established apalutamide plus ADT as an effective and well-tolerated treatment option for mCSPC, offering significant survival benefits while preserving quality of life.

KEYWORDS: TITAN trial, Apalutamide, Androgen deprivation therapy (ADT)

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INTRODUCTION

The TITAN trial is a pivotal phase III, randomized, double-blind, placebo-controlled study that evaluated the efficacy and safety of apalutamide in combination with androgen deprivation therapy (ADT) in patients with metastatic castration-sensitive prostate cancer (mCSPC). The trial included 1,052 patients who were randomized to receive either apalutamide (240 mg daily) plus ADT or placebo plus ADT. The primary endpoints of the study were overall survival (OS) and radiographic progression-free survival (rPFS).[1-2]

The results of the TITAN trial demonstrated that the addition of apalutamide to ADT significantly improved both OS and rPFS compared to ADT alone. At a median follow-up of 22.7 months, the study reported a hazard ratio (HR) for radiographic progression or death of 0.48 (95% CI, 0.39–0.60; P<.001) and an HR for death of 0.67 (95% CI, 0.51–0.89; P=.005).[1] The final analysis, with a median follow-up of 44 months, confirmed these benefits, showing a 35% reduction in the risk of death (HR, 0.65; 95% CI, 0.53–0.79; P<.001).[2]

The trial also assessed health-related quality of life (HRQOL) and found that it was maintained during treatment with apalutamide.[3] Adverse events more common with apalutamide included rash, hypothyroidism, and ischemic heart disease.[1] The study's findings have led to the approval of apalutamide as a treatment option for patients with mCSPC, highlighting its role in improving survival outcomes while maintaining quality of life.[1-2]

Outcomes

The TITAN trial, a phase III, randomized, double-blind study, evaluated the efficacy of apalutamide in combination with androgen deprivation therapy (ADT) in patients with metastatic castration-sensitive prostate cancer (mCSPC). The primary outcomes measured in this trial were overall survival (OS) and radiographic progression-free survival (rPFS).

In the initial analysis, with a median follow-up of 22.7 months, the trial demonstrated that the addition of apalutamide to ADT significantly improved both primary endpoints. The 24-month radiographic progression-free survival rate was 68.2% in the apalutamide group compared to 47.5% in the placebo group, with a hazard ratio (HR) for radiographic progression or death of 0.48 (95% CI, 0.39 to 0.60; P<0.001).[1-2] Similarly, the 24-month overall survival rate was 82.4% in the apalutamide group versus 73.5% in the

placebo group, with a hazard ratio for death of 0.67 (95% CI, 0.51 to 0.89; P=0.005).[1-2]

The final analysis, conducted after a median follow-up of 44 months, confirmed these findings. The median overall survival was not reached in the apalutamide group, compared to 52.2 months in the placebo group, with a hazard ratio for death of 0.65 (95% CI, 0.53 to 0.79; P<0.0001).[3-5] These results underscore the significant survival benefit of adding apalutamide to ADT in this patient population.

Potential side effects

In the TITAN trial, the addition of apalutamide to androgen deprivation therapy (ADT) in patients with metastatic castration-sensitive prostate cancer was associated with several adverse events. Notably, the trial reported a higher incidence of rash, hypothyroidism, and ischemic heart disease in the apalutamide group compared to the placebo group.[1-3] Rash was particularly common, occurring in 27.1% of patients receiving apalutamide versus 8.5% in the placebo group.[2] Hypothyroidism was also more frequent in the apalutamide group, although these events were generally mild (grade 1 or 2) and manageable with medical therapy.[4] Additionally, ischemic heart disease was noted as a more common adverse event in the apalutamide group.[1] These findings highlight the importance of monitoring for these specific adverse events during treatment with apalutamide.

CONCLUSION

The TITAN trial has established apalutamide in combination with androgen deprivation therapy (ADT) as a highly effective treatment for metastatic castration-sensitive prostate cancer (mCSPC). The trial demonstrated significant improvements in overall survival (OS) and radiographic progression-free survival (rPFS) with apalutamide compared to placebo, with a 35% reduction in the risk of death confirmed at the final analysis. Additionally, health-related quality of life (HRQOL) was maintained during treatment, reinforcing the clinical benefit of this therapy.

While the addition of apalutamide was associated with specific adverse events, including rash, hypothyroidism, and ischemic heart disease, these were generally manageable with appropriate medical intervention. The findings of the TITAN trial support the integration of apalutamide into standard treatment protocols for mCSPC, offering substantial survival benefits while maintaining quality of life. Continued monitoring for adverse events remains crucial to optimize patient outcomes and safety.

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