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Title: Extended follow-up shows accumulating benefit for patients treated with aglatimagene besadenovec (CAN-2409) +prodrug in combination with standard of care external beam radiation (EBRT) in men with localized prostate cancer: update from a randomized placebo-controlled phase 3 clinical trial.

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Introduction

Current standard of care (SoC) for localized prostate cancer (PCa) treated with curative intent includes surgery or EBRT ± ADT. Still, ~ 30% of men experience disease recurrence, leading to salvage therapies associated with reduced quality of life. Aglatimagene, a replication-defective adenovirus encoding HSV-tk, combined with valacyclovir (prodrug), induces immunogenic cell death. Topline results from the phase 3 NCT01436968 randomized, double-blind, placebo (PBO)- controlled trial in intermediate- (IR) and high-risk PCa patients (pts) demonstrated that aglatimagene added to SoC EBRT+/- ADT (≤6 mos) improved disease-free survival (DFS) by 30% compared to PBO (p=0.0155, HR 0.70, 95% CI 0.52, 0.94; data as of Aug 30,2024), supported by secondary endpoints (median follow-up 50.3 months, CI 45.4, 51.3) (All CI represents 95% CI). Here we report PCa-specific outcomes after extended follow-up.

Methods

745 pts were randomized 2:1 (496 to aglatimagene and 249 to PBO) and stratified by NCCN risk group and ADT use; 635 had IR PCa (422 into aglatimagene arm and 213 in to PBO arm). Three intraprostatic injections of aglatimagene CAN-2409 (5x10 ^{11}vp/2mL) or PBO were administered, each followed by 14 days of prodrug. We evaluated PCa-specific DFS (time from randomization to PCa recurrence or PCa death) in the total intent-to-treat population (ITT) and in the IR subset as of March 15, 2026. Secondary and exploratory endpoints included time to biochemical failure (TTBF), time to metastasis (TTM), and time to new therapy (TTNT). PCa-specific DFS median follow-up was 58.0 mos, CI 56.6, 60.2.

Results

The aglatimagene arm exhibited 39% improvement in PCa-specific DFS vs PBO (HR= 0.61; CI: 0.44, 0.85; p=0.0031). There were only 2 PCa-specific deaths, one in each arm. Trends

consistently favor aglatimagene vs PBO for TTBF (HR 0.72, CI 0.40, 1.31), rate of metastasis (1.6% (8/496) vs PBO 2.8% (7/249)), TTM (HR 0.58, CI 0.21, 1.59), and TTNT (HR 0.72, CI 0.39, 1.31); curves are still immature. Within the IR subgroup, aglatimagene shows an even greater effect: 41% improvement in PCa-specific DFS vs PBO (HR 0.59, CI 0.41, 0.84; p=0.0034). We observed improvement in TTBF (HR 0.48, CI 0.22, 1.03), rate of metastasis (0.24% (1/422) vs 2.35% (5/213)), TTM (HR 0.1, CI 0.01, 0.85), and TTNT (HR 0.51, CI 0.24, 1.1), comparing the aglatimagene arm vs PBO.

Conclusions

Aglatimagene significantly improved PCa-specific DFS when added to SoC EBRT± ADT. Further exploratory analyses after extended follow-up show accumulating benefit for PCa-specific clinical outcomes. If approved, aglatimagene could represent a new therapy for pts treated with EBRT with curative intent for localized PCa.

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