

Quantitative digital pathology defines immune activation following aglatimagene besadenovec immunotherapy in localized prostate cancer

F. Barone¹, J. Dwyer¹, A. Manzanera¹, J. Buie¹, A. Cruz¹, M. Lee², J. Leech², M. Chung², M. Alderdice², M. Garzotto³, G. Gejerman⁴, J. Sylvester⁵, R. Tutrone⁶, S. Finkelstein⁷, W.G. Nichols¹, P.P. Tak¹

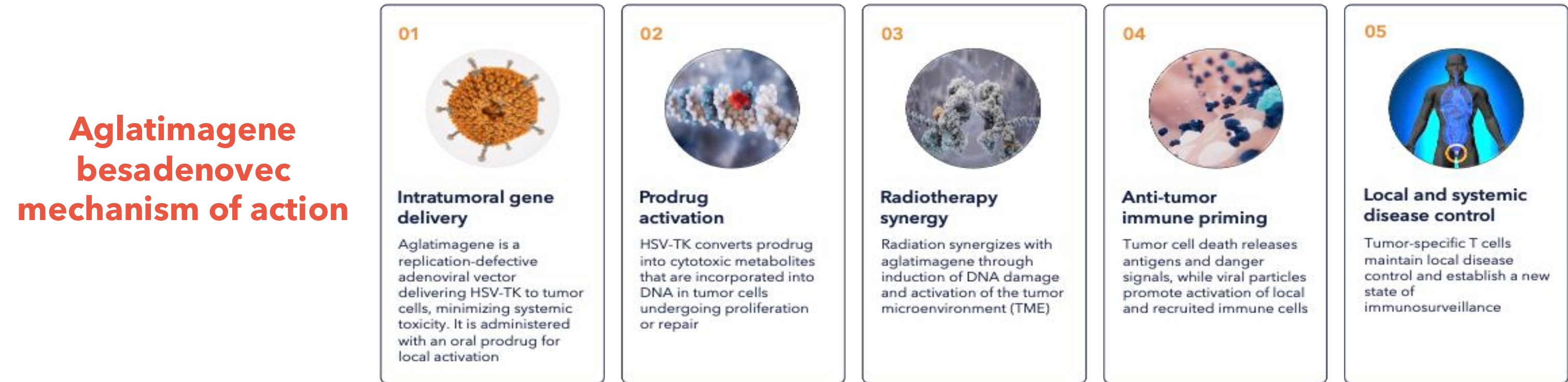
¹ Candel Therapeutics, Needham, MA, USA; ² Sonrai Analytics, Belfast, Northern Ireland; ³ VA Portland Health Care System/OHSU, Portland, OR, USA; ⁴ New Jersey Urology, Summit Health, Saddlebrook, NJ, USA; ⁵ Atlantic Urology Clinics, Myrtle Beach, NC, USA; ⁶ Chesapeake Urology Research Associates, Towson, MD, USA; ⁷ Associated Medical Professionals of NY, US Urology Partners, Syracuse, NY, USA



Contact: info@candeltx.com
ASTRO Annual Meeting 2026

Background

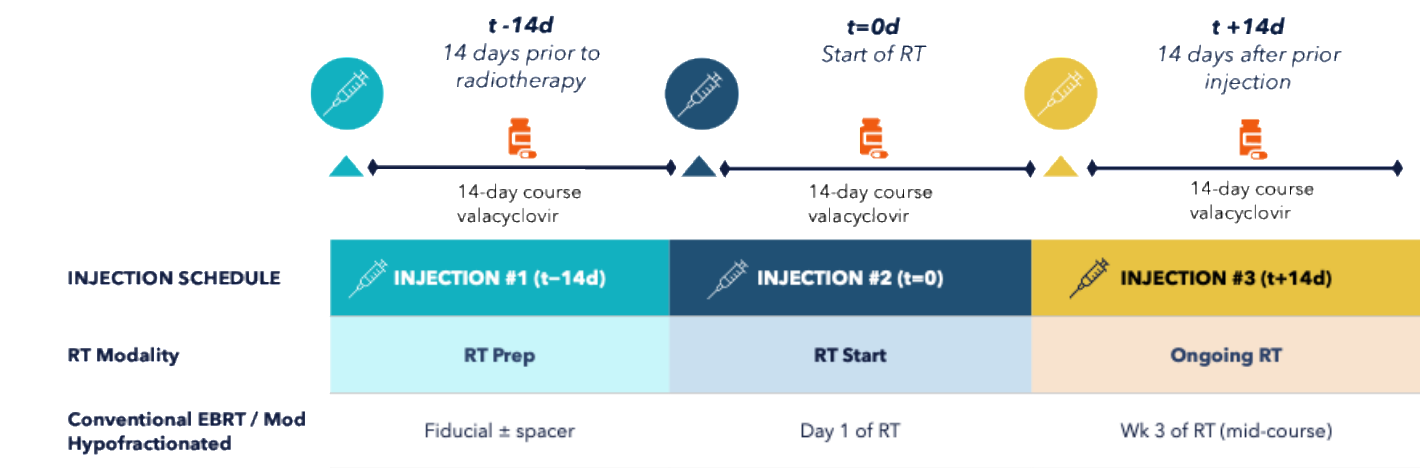
Aglatimagene besadenovec (aglatimagene) is a replication-defective adenoviral vector encoding the herpes simplex virus thymidine kinase (HSV-tk) gene. Preclinical and clinical data show that aglatimagene, combined with valacyclovir, induces local and systemic antitumoral activity that is synergistic with radiation therapy.



Despite treatment with curative-intent external beam radiation therapy (EBRT), approximately 30% of patients with localized, intermediate- to high-risk prostate cancer (PCa) experience recurrence.

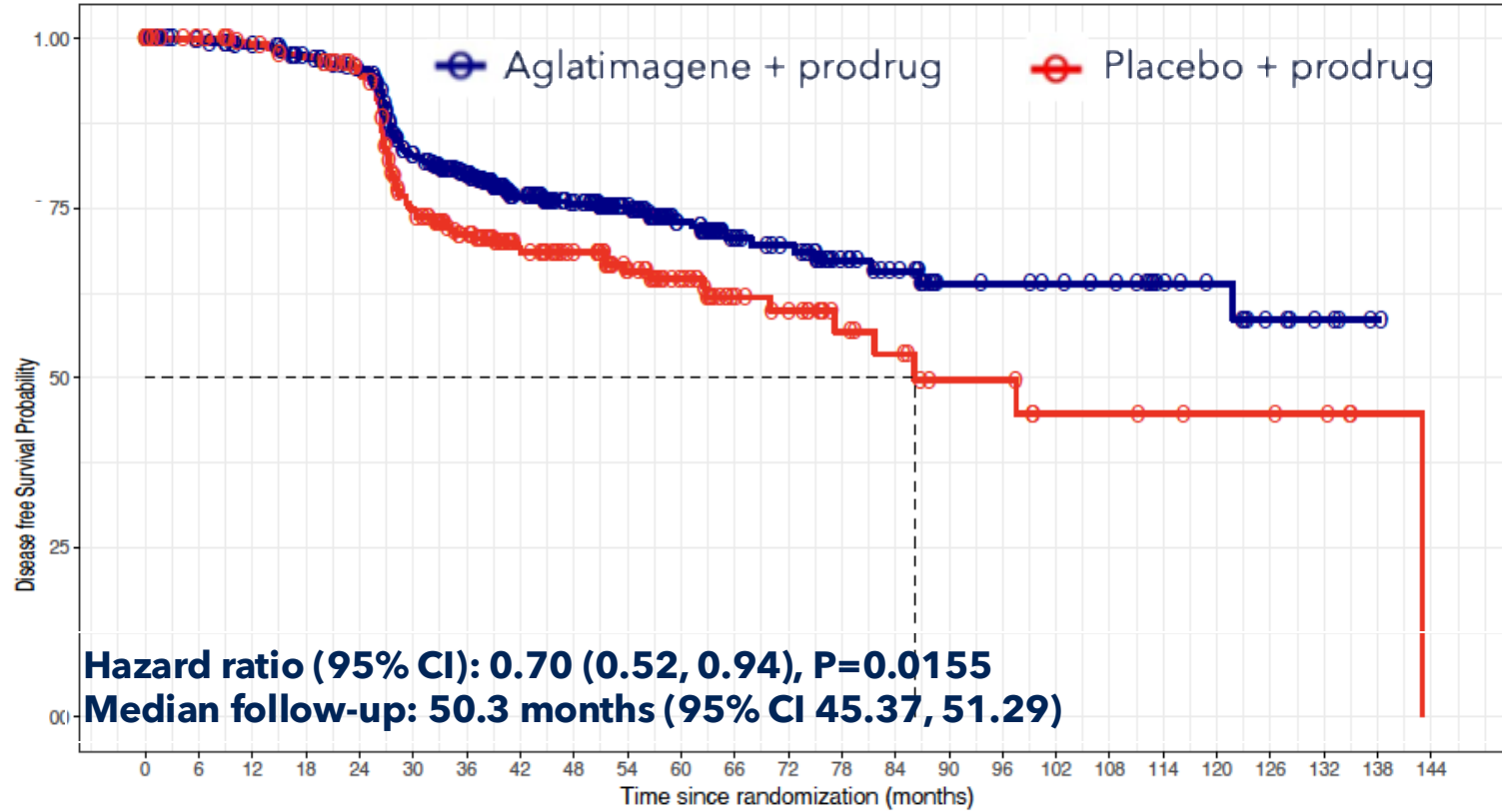
A pivotal placebo-controlled phase 3 trial of aglatimagene + valacyclovir with EBRT in 745 patients with intermediate- to high-risk, localized PCa demonstrated significant improvement (~30%) in disease-free survival (DFS) compared to standard of care radiotherapy +/- short term androgen deprivation therapy, independent of radiotherapy regimen and short-term androgen deprivation therapy use.

NCT01436968 (PrTK03) clinical trial



Clinical trial results

Aglatimagene significantly improved DFS, PrCa specific DFS and PSA nadir compared to SoC EBRT+/- ADT



Extended follow up:

After an additional ~20 months of follow up, treatment with aglatimagene was associated with:

- Improved time to biochemical failure with aglatimagene (HR=0.72; 95% CI 0.39 - 1.31)
- Improved time to salvage anticancer therapy with aglatimagene (HR=0.72; 95% CI 0.40 - 1.31)
- Lower incidence of, and improved time to, metastasis in the aglatimagene arm after extended follow-up (ITT, N=745; HR=0.58; 95% CI 0.21 - 1.59) with incidence of new metastatic disease in 8/496 (1.6%) patients treated with aglatimagene + SoC vs 7/249 (2.8%) patients treated with placebo +SoC EBRT+/-ADT

*EBRT= External beam radiation, ADT= Androgen deprivation therapy, ITT= Intent-to-Treat

Aglatimagene administration

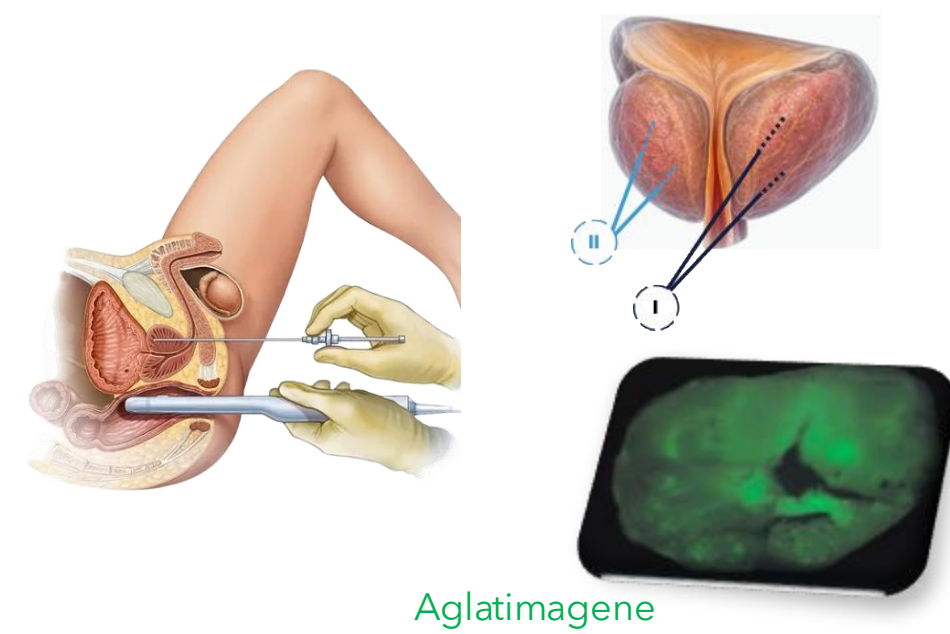


Figure 1. Aglatimagene is administered directly into the 4 quadrants of the prostate via transrectal or transperineal administration. 2 mL total volume (0.5 mL per quadrant) is delivered under transrectal ultrasound guidance. Oral valacyclovir prodrug therapy is initiated 1-3 days after each injection and continued for 14 days

Pathological complete response and biopsy evaluable population

Aglatimagene + EBRT significantly improved the negative biopsy rate in 2-year biopsies compared with the placebo + EBRT control arm

- 451 post-treatment biopsies centrally reviewed by at least 2 blinded independent readers
- 313 post-treatment biopsies available for review for the 2-year (22-26 mos after EBRT) histologic analysis
- *11 biopsies (6 of which in the 2-year window) were defined indeterminate and excluded from the pathological complete response analysis

Significant difference between arms, χ^2 test; $p=0.0018$

Methods

- AI models trained on balanced pre- and post-radiation datasets annotated by expert pathologists

- Post-treatment biopsy analysis on imaging evaluable paired samples was limited to slides with pathologist-confirmed tumor presence

- Yellow cells indicate lymphocytes; red cells indicate tumor cells. Magnification guide in bottom left corner indicates 50µM distance.

- Representative H&E images are shown below.

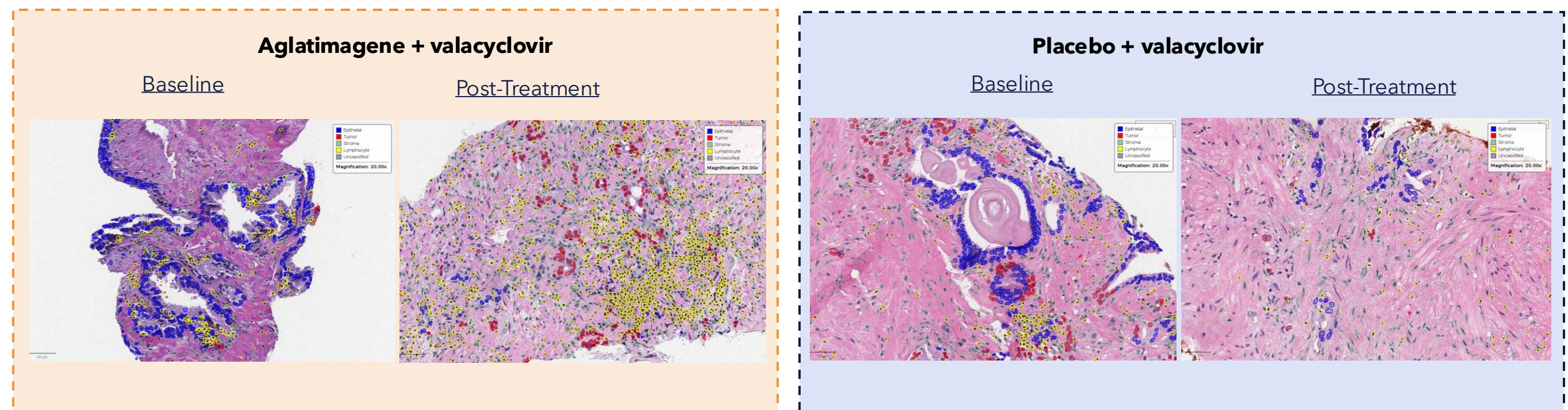


Figure 2. Spatial tumor-immune quantification from AI analyzed H&E images. Representative whole-slide images of baseline and post-treatment biopsies from each treatment arm, with AI-predicted cell classes overlaid: yellow indicates lymphocytes and red indicates tumor cells. Magnification guide in the lower left corner indicates 50 µm.

Aglatimagene enhanced post-treatment increases in lymphocytic fraction

Across all collected biopsies, overall lymphocytic fraction increased in post-treatment samples in both arms (A, $p<0.001$), with a significantly greater increase in the aglatimagene arm versus EBRT alone (B, $p=0.048$).

Figure 3.

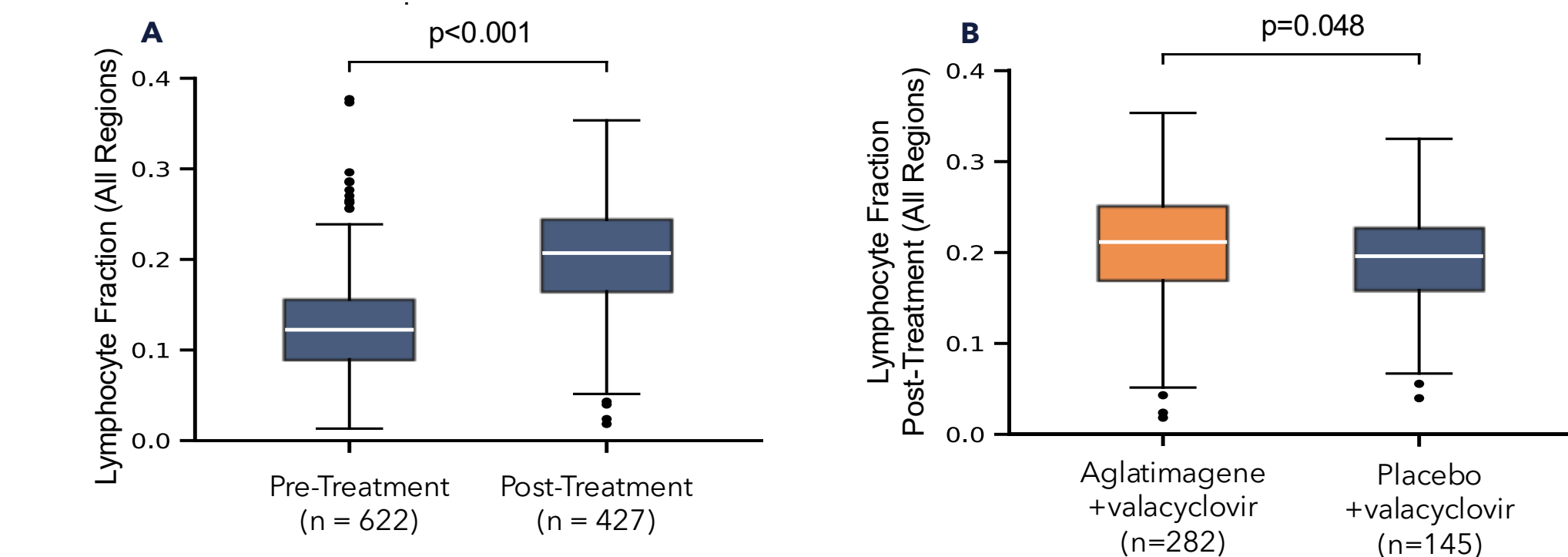


Figure 3. Lymphocyte fraction across all tissue regions in evaluable biopsies. (A) Pre- versus post-treatment samples (n = 622 and n = 427; $p < 0.001$). (B) Post-treatment values by arm: aglatimagene + valacyclovir (n = 282) versus placebo + valacyclovir (n = 145); $p = 0.048$.

Aglatimagene plus EBRT increased lymphocyte fraction and improved changes in lymphocyte/tumor interaction relative to placebo plus EBRT (paired biopsies only analysis)

Among patients with detectable disease in post-treatment biopsies, aglatimagene significantly increased lymphocyte/tumor enrichment score, intratumoral lymphocyte fraction, and lymphocyte-tumor mixing score (**Figure 4**). Aglatimagene + valacyclovir (vcv) n=62 and placebo + valacyclovir n=46.

Figure 4.

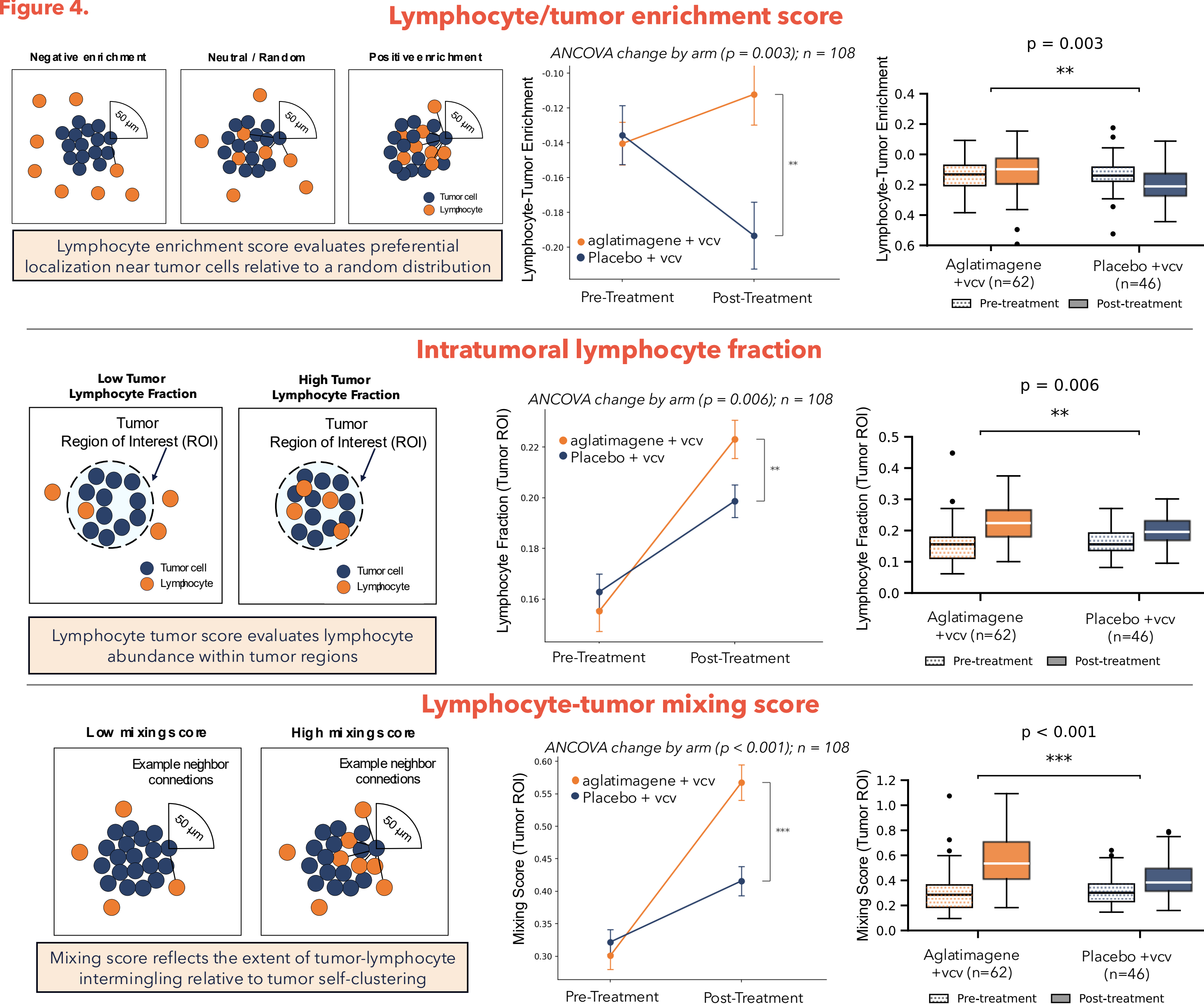


Figure 4. AI-based spatial analysis of paired pre- and post-treatment biopsies (n = 108) quantifying metrics listed above within tumor regions of interest. Plots show pre- versus post-treatment values for aglatimagene + valacyclovir (aglatimagene + vcv; n = 62) and placebo + valacyclovir (placebo + vcv; n = 46). Line plots depict mean and standard error. Boxplots represent medians and interquartile range. All three metrics increased significantly with aglatimagene versus placebo (ANCOVA change by arm: $p = 0.003$, $p = 0.006$, and $p < 0.001$, respectively). P-values are nominal and not adjusted for multiple comparisons.

Conclusions

- Addition of aglatimagene to standard-of-care EBRT increased intratumoral lymphocyte infiltration and remodeled the tumor microenvironment beyond EBRT alone.
- This immune signature is still detectable in biopsies collected at more than 2 years after treatment, indicating durable rather than transient immune remodeling.
- Its presence even in tumor-positive biopsies supports sustained immune surveillance and continued lymphocyte engagement with tumor cells as a mechanism for the improved disease-free survival observed with aglatimagene in PrTK03.

References and Acknowledgements

References: 1. DeWeese TL, et al. Aglatimagene besadenovec (CAN-2409) with radiotherapy for patients with localised prostate cancer: a phase 3, multicentre, randomised, double-blind, placebo-controlled trial. *Lancet Oncology*. 2026;27:673-685.

Acknowledgements: We gratefully acknowledge the patients, investigators, and study site personnel who contributed to the PrTK03 study. This study was sponsored by Candel Therapeutics.

Garzotto M. AUA Oral presentation 2026