**THE ADENOSINE AXIS**

The tumor microenvironment contains high levels of immunosuppressive adenosine, which leads to a decreased activity of the α7AR and A2aR antagonists (AB) with a small molecule in a phase 2b/3 clinical trial for the treatment of α7AR antagonist activity. In certain tumor types, other enzymes, such as adenosine deaminase (N1) in prostate cancer, may also be involved in immunosuppression.

AB928 is a dual antagonist of adenosine receptor α7AR and A2aR that is designed to inhibit specific subtypes of immunity. It has shown a good safety profile in clinical trials with α7AR and A2aR antagonist activity and has been associated with a decrease in tumor volume and improved survival in murine models.

**BIOLGY IN PROSTATE CANCER**

Prostatic cancer is characterized by an increased expression of A2aR in the tumor microenvironment. Recent clinical data have shown that inhibition of tumor growth after treatment with AB680, a combination of α7AR and A2aR antagonists, can result in significant reductions in tumor volume and improved survival.

**RATIONAL FOR mCRPC COMBINATIONS**

Adenose Inhibition Enhances PD-1 Activity in Tumor Models

Treatment with AB928 and AB680 (small molecule CD73 inhibitors) in combination with anti-PD-1 has demonstrated increased tumor growth in multiple preclinical models. In preclinical models, AB928 and AB680 plus anti-PD-1 leads to an increase in intratumoral CD8+ T cells and a decrease in A2aR expression. This combination has shown a significant increase in anti-tumor activity compared to single-agent therapy.

**ANDRENogenous DEPRESSION THERAPY INHIBITS PROSTATE CANCER CELLS TO CELL KILLING**

Arondt et al. (2014) showed an increased sensitivity of prostate cancer cells treated with a combination of AB680 and AB928 to inhibition of tumor growth after treatment with AB680. This combination has shown a significant increase in anti-tumor activity compared to single-agent therapy.

**EARLY EVALUATION OF AB928 IN mCRPC**

**CONCLUSIONS**

This phase 1b/2 study is the first to target the adenosine axis using a dual α7AR/A2aR (AB928) combination. In preclinical models, AB928 in combination with anti-PD-1 is highly immunosuppressive, demonstrating a significant increase in anti-tumor activity compared to single-agent therapy. The study is ongoing in the United States; results will be shared in upcoming scientific conferences.

**ACKNOWLEDGEMENTS**

We thank the Principal Investigators, site staff, and study participants for their efforts on behalf of this study. Contact: Melissa Peacock, mpeacock@arcbiosc.com

**REFERENCES**


---

**THE ADENOSINE AXIS**

*The adenosine axis plays a critical role in immunosuppression and tumor growth.*

**PROSTATIC PHOSPHATASE (PAP) CREATES AN ADENOSINE- RICH TUMOR MICROENVIRONMENT IN PROSTATE CANCER**

Recent clinical data demonstrated early activity of adenosine pathway inhibitors in metastatic castration-resistant prostate cancer (mCRPC) supporting further development in this indication (Bendell et al., 2014). α7AR expression correlates with unfavorable survival in prostate cancer. The current understanding of adenosine receptor expression in prostate cancer is critical to developing novel therapeutic approaches.

**MATERIALS AND METHODS**

This phase 1b/2, open-label, platform study evaluated the efficacy and safety of AB928-based treatment combinations in participants with metastatic castrate-resistant prostate cancer (ARC-6).

**RESULTS**

An increased sensitivity of prostate cancer cells treated with a combination of AB680 and AB928 to inhibition of tumor growth after treatment with AB680. This combination has shown a significant increase in anti-tumor activity compared to single-agent therapy.

**CONCLUSIONS**

This phase 1b/2 study is the first to target the adenosine axis using a dual α7AR/A2aR (AB928) combination. In preclinical models, AB928 in combination with anti-PD-1 is highly immunosuppressive, demonstrating a significant increase in anti-tumor activity compared to single-agent therapy. The study is ongoing in the United States; results will be shared in upcoming scientific conferences.