SOCIETY OF ENDOMETRIOSIS AND UTERINE DISORDERS - FRANKFURT, GERMANY

Prolactin Receptor Blockade With ABS-201 Relieves Pain and Inflammation in a Homologous Transplant Mouse Model of Endometriosis

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INTRODUCTION

Endometriosis affects an estimated 10% of reproductive-age women worldwide. Under estrogen and progesterone control, endometriotic lesions produce local prolactin that promotes lesion growth, inflammation, and chronic pelvic pain. Current standard of care is primarily palliative hormonal treatments that lack disease-modifying capability and are associated with risks such as osteoporosis and impaired fertility. The aim of this study was to test ABS-201, an AI-designed, highly selective prolactin receptor–blocking (PRLR) antibody, as a non-sex hormonal and potentially disease modifying therapeutic for endometriosis.

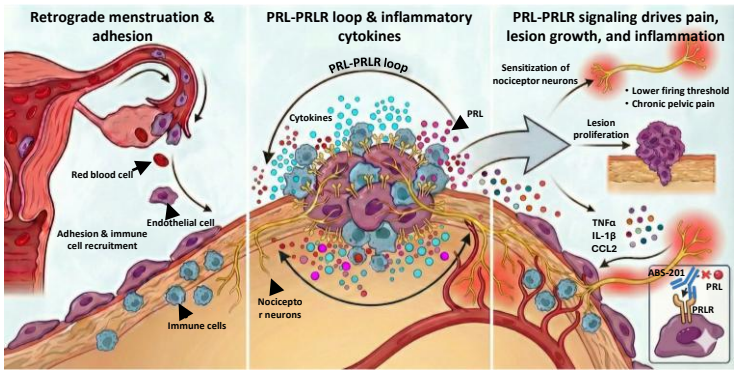

Figure 1. Events representing the central role of PRL-PRLR signaling in the pathogenesis of endometriosis

MATERIALS AND METHODS

Endometriosis was established in immunocompetent mice by homologous transplantation of syngeneic pseudodecidualized endometrial-like tissue into the peritoneal cavity, with RFID transponder chip implantation enabling longitudinal home-cage analysis. Two-weeks post lesion establishment, mice received ABS-201 or control IgG1 twice weekly for 4 weeks, or leuprolide (GnRh modulator) with the placebo weekly. Functional assessment of non-evoked pain was performed by measuring distance traveled and expressing values as percent distance normalized to each animal's baseline. Evoked mechanical pain was assessed using Von Frey filament testing to determine paw withdrawal thresholds, with data presented as percent recovery. Peritoneal fluid samples were analyzed for cytokines by ELISA. One-way ANOVA was used for statistical comparisons.

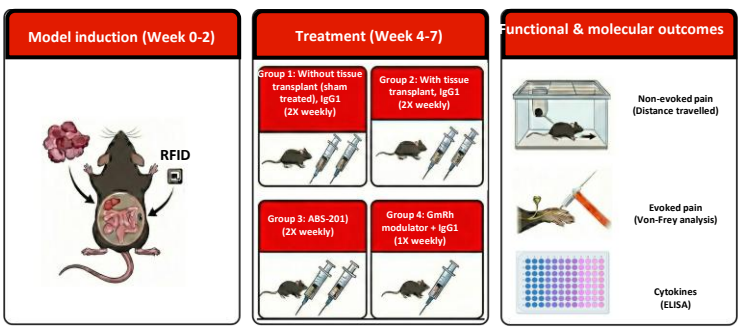

Figure 2. Study design. RFID, Radio frequency identification; GnRh, Gonadotropin releasing hormone.

RESULTS

ABS-201 RELIEVES NON-EVOKED AND EVOKED PAIN RESPONSE IN A HOMOLOGUS TRANSPLANT MOUSE MODEL OF ENDOMETRIOSIS

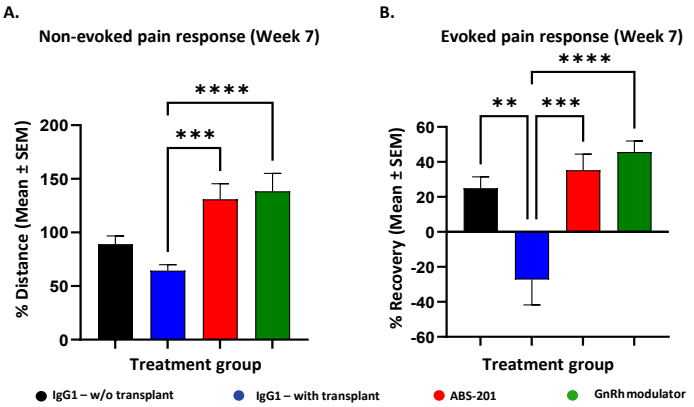

Figure 3. (A) Distance traveled by mice treated with the indicated agents was used as a surrogate measure of non-evoked pain behavior and is expressed as percent distance traveled normalized to each animal's baseline measurement. Statistical analysis using one-way ANOVA. N = 8-12/ arm/experiment. Combined results of three independent experiments. ***p=0.001, ****p< 0.0001. (B) Von Frey analysis was used to measure mechanical withdrawal thresholds (evoked mechanical pain), with data presented as % recovery relative to baseline. Statistical analysis using one-way ANOVA. N=8-12/ arm/experiment. Combined results of three independent experiments. **p=0.0035, ***p= 0.0003. ****p<0.0001

ABS-201 SUPPRESSES INFLAMMATORY CYTOKINES IN A HOMOLOGUS TRANSPLANT MOUSE MODEL OF ENDOMETRIOSIS

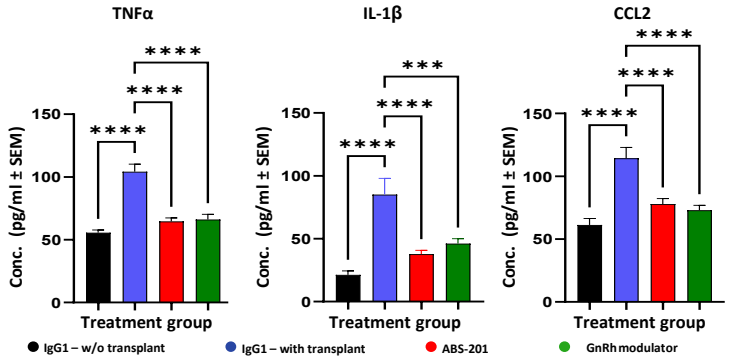

Figure 4. ABS-201 and GnRh treatment significantly reduce the inflammatory cytokines TNFα, IL-1β and CCl2 in the peritoneal fluid, assessed by ELISA. Statistical analysis using one-way ANOVA. N=8-12/arm/experiment. Combined results of three independent experiments. ***p= 0.0004. ****p< 0.0001.

CONCLUSION

- **ABS-201 treatment significantly reduced spontaneous and evoked pain versus IgG1 control in a murine endometriosis model, as evidenced by increased locomotion and higher mechanical thresholds.**
- **ABS-201 significantly reduced the inflammatory cytokines in the peritoneal fluid-which have been shown to be elevated in endometriosis patients.**
- **A phase 2 study to evaluate the efficacy and safety of ABS-201 in women with endometriosis is anticipated to be initiated in Q4 2026.**

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