



## *Candida Vaccine PEV7*

Vulvovaginal *Candida* infection is a significant health problem in developed countries with no sufficient treatment options and no long-term protection available. Pevion Biotech is developing a state-of-the-art subunit vaccine based on a prime target antigen, a key virulence factor of *Candida* which is formulated with Pevion Biotech's market-approved virosomes. The vaccine candidate PEV7 achieved excellent results in preclinical studies and has entered clinical testing.

### MEDICAL NEED

Vulvovaginal candidiasis (VVC) is the second most common cause of vaginitis. It affects 50-75% of healthy women at least once during their reproductive life. Symptoms are continuous vaginal discharges, itching, soreness and irritation. Predisposing factors to VVC include pregnancy, diabetes mellitus, use of broad-spectrum antibiotics and AIDS. Pregnancy, diabetes mellitus and AIDS are all associated with decrease in host immune defenses, whereas antibiotics can damage the vaginal flora allowing an overgrowth of *Candida*. However, VVC can also occur in the absence of these factors.

About 5-8% of the infected women suffer from recurrent VVC, which is difficult to control and remains never completely cured until menopause. Usually, patients with recurrent VVC complain of at least four acute attacks per year, strongly impacting quality of life. *Candida albicans* is the predominant species causing 70-90% of cases.

Currently, there is no prophylactic treatment available and therapeutic treatments are associated with significant disadvantages. Long-term protection does not exist. Therapy of acute infections is based on anti-fungal drugs. Guidelines recommend an induction therapy with 10-14 days of a topical or oral azole followed by a suppressive regimen for at least 6 months (usually oral fluconazole once weekly). However, anti-fungal drugs have many adverse effects including local irritation and pain, hepatotoxicity, interactions with some contraceptives and oral hypoglycemic agents, and supposed teratogenicity of some therapies (limitation of use during pregnancy). The number of azole-resistant *Candida* infections has significantly increased in the past years, presumably due to the frequent and partially inappropriate use of both prescribed and OTC medications. Therefore, alternative, more sustainable treatment options are urgently needed.

### RATIONALE FOR VACCINE DESIGN

At present, there is no vaccine available for prevention of candidiasis. Pevion Biotech exclusively in-licensed a recombinant protein antigen, which has been identified as a main virulence factor and represents a prime vaccine target. The use of a protein antigen requires a suitable carrier and adjuvant system, and Pevion Biotech's virosome technology is the ideal choice for this purpose. Women suffering from recurrent VVC are the primary target group for the *Candida* vaccine.

Very little is known about the immunological mechanism functioning at the vaginal mucosa, and much of what is known comes from animal rather than human data. *Candida*-specific cell-mediated immunity has for a long time been considered the major host defense mechanism against mucosal *Candida* infections. However, recent studies have demonstrated the important role of

### Key advantages of Pevion Biotech's *Candida* vaccine

- Identification of main virulence factor as prime target antigen (recombinant protein, exclusive rights)
- Demonstrated efficacy of carrier & adjuvant system for high-quality antibody responses to subunit antigens
- Market-approved safety and local tolerability of carrier & adjuvant system
- Established GMP manufacturing on a commercial scale

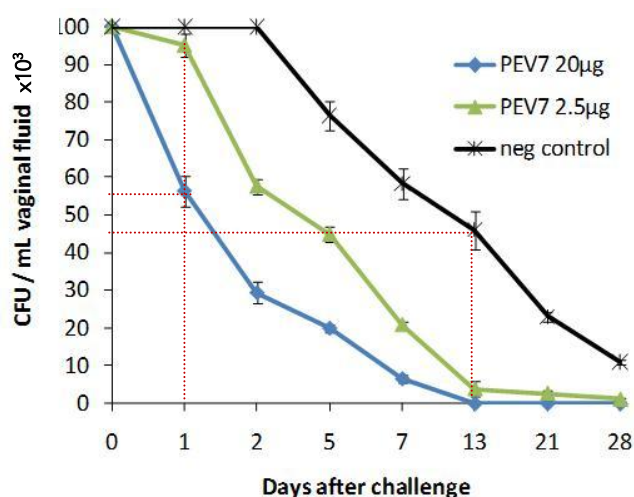
humoral immunity in protection against mucosal candidiasis. According to clinical observations, anti-Candida IgA and IgG antibodies bind to Candida species, thereby reducing their ability to adhere to epithelial cells and thus preventing the tissue penetration phase. Based on this concept, the goal of Pevion Biotech's Candida vaccine is to elicit a strong protective antibody response that prevents recurrence.

#### VACCINE PROFILE

Pevion Biotech is developing a state-of-the-art vaccine PEV7 against recurrent vulvovaginal candidiasis (VVC) caused by the pathogenic form of Candida albicans especially in pre-menopausal women of childbearing age with a history of recurrent VVC. In a later stage of development, application of the vaccine may be extended to oropharyngeal candidiasis. The vaccine candidate uses a recombinant protein antigen, one of the main Candida albicans virulence factors, formulated with Pevion Biotech's virosomes. In addition to the standard intramuscular application form, Pevion Biotech has developed a formulation for intravaginal mucosal application in order to evaluate a potential superiority of a locally induced immune response. Presentation of the vaccine in capsule form would also be more convenient for the patient.

#### EXCELLENT PRECLINICAL RESULTS

Pevion Biotech has clearly demonstrated in preclinical studies that intravaginal administration of its vaccine candidate PEV7 generates a good and long-lasting immune response to the native antigen target in the vagina and at the same time confers protection against Candida infections. Both antibody isotypes, IgA and IgG, which are essential for mucosal immunity, were present in vaginal fluid of immunized animals. Furthermore, it has been proven that the virosome-based component enhances both immunogenicity and the protective effect of the antigen. Moreover, the vaginal mucosal application route represents a novelty for virosome-based vaccines and may pave the way for further developments.



**Figure: Challenge study in rats.** Rats were immunized with the Candida vaccine PEV7 and then challenged with pathogenic Candida albicans. In immunized rats the pathogen was rapidly cleared from vaginal fluid (>40% reduction of CFU after 1 day versus 5% in unvaccinated animals (neg control); complete clearance after 13 days versus 55% reduction in unvaccinated animals).

In summary, key findings from rat and mouse challenge models are as follows:

- Immunization with the vaccine candidate elicited robust antibody levels in vaginal fluid, both IgA and IgG, specific for the native target protein
- Immunization conferred protection against pathogenic *Candida albicans* challenge as shown by rapid pathogen clearance from the vagina (see figure)
- Intranasal, sublingual, and vaginal routes of administration resulted in comparable protection

Toxicity studies in rats, rabbits, and minipigs showed no abnormalities and merely very mild local irritation

#### DEVELOPMENT STATUS

Recently, the vaccine candidate has entered a clinical Phase I study, which is designed to evaluate the safety and tolerability of the vaccine, administered by two different routes (intramuscular and intravaginal) as primary endpoint. Immunogenicity will be evaluated as secondary endpoint. Enrollment began in February 2010.

#### IP SITUATION

Pevion Biotech has a complete patent portfolio regarding virosomes covering all aspects and applications of the virosome technology platform. In addition, Pevion Biotech holds exclusive license rights to a prime target *Candida* antigen and its use in vaccine formulations. Pevion Biotech has full freedom to operate for its *Candida* vaccine.

#### SELECTED REFERENCES

Anticandidal immunity and vaginitis: novel opportunities for immune intervention. Cassone A, De Bernardis F, Santoni G. *Infect Immun*. 2007 Oct;75(10):4675-86. Epub 2007 Jun 11. Review

Vulvovaginal candidosis. Sobel JD. *Lancet*. 2007 Jun 9;369(9577):1961-71.

Recurrent *Candida* infection. Hurley, R. 1981.. *Clin. Obstet. Gynaecol*. 8:209-214.

Evidence that members of the secretory aspartyl proteinase gene family, in particular SAP2, are virulence factors for *Candida* vaginitis. De Bernardis, F., S. Arancia, L. Morelli, B. Hube, D. Sanglard, W. Schafer, and A. Cassone. 1999.. *J Infect. Dis*. 179:201-208.

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