PRESS RELEASE

Pantarhei Oncology reports breakthrough in prostate cancer treatment

Zeist, 11 May 2021 – The leading scientific journal European Urology Open Science (EUROS) has reported the results of a new treatment of advanced prostate cancer developed by Pantarhei Oncology, a biotech company located in Zeist, the Netherlands. Pantarhei Oncology has demonstrated, that by combining the standard of care androgen deprivation therapy (ADT) with the natural estrogen Estetrol (E4), side effects of ADT are significantly reduced and additional long term anti-tumor effects are expected[1].

Pantarhei Oncology has developed a new concept for the endocrine treatment of locally infiltrating and/or metastatic prostate cancer in collaboration with two renowned Dutch urologists, Prof. Frans Debruyne, formerly at the Radboud UMC, Nijmegen and Prof. Jeroen van Moorselaar, Free University, Amsterdam. This collaboration has resulted in the performance of the prospective, randomized, double-blind, placebo-controlled PCombi study in four Dutch urology centers by Dr. Erik Roos (Sneek), Dr. Rik Somford (Nijmegen), Dr. Ton Roeleveld (Alkmaar) and Dr. Tjard de Haan (Zwolle) in men with advanced prostate cancer, who started luteinizing hormone-releasing hormone (LHRH) agonist ADT treatment to suppress testosterone levels. Major side effects of ADT are loss of libido and sexual function, but since the loss of testosterone also implies the loss of testosterone derived estrogens, especially estradiol (E2), most side effects of ADT are related to estrogen deficiency. These side effects are the same as the symptoms of estrogen deficiency occurring in postmenopausal women and include hot flushes and sweatings, joint pain (arthralgia), sleep disturbances, mood changes and depression, fatigue, loss of energy, muscle weakness (sarcopenia), cognition problems, bone loss and an increased fracture risk with, especially in aging males, a higher risk of mortality.

Estetrol causes significant improvements of prostate cancer treatment

The ADT treated patients in the PCombi study were co-treated for 24-weeks with the natural estrogen Estetrol (E4). In this phase II study 62 patients participated; 41 patients were co-treated with 40 mg E4 and 21 patients received an identical appearing placebo tablet. Several significant estrogen replacement and biochemical anti-tumor effects were found. With E4, 6% of the patients reported hot flushes compared to 55% of patients treated with placebo. Based on bone marker data, serious bone loss occurred in the placebo group, which was completely prevented by E4 co-treatment. Follicle-stimulating hormone (FSH) levels, related to tumor growth and cardiovascular risk, were 98% suppressed with HDE4 compared to 57% in the ADT only group. Suppression of free testosterone and prostate-specific antigen (PSA) was significantly more rapid and more profound compared to placebo, suggesting potentially enhanced disease control by the E4 co-treatment. No safety problems, especially no increased E4 related cardiovascular side effects were observed.

Further development of E4 for prostate and breast cancer

Further phase III studies have to confirm the promising results of this PCombi study. With the international PCombi Advisory Board of Pantarhei Oncology, chaired by Prof. Frans Debruyne with top experts from Europe, the USA, Canada and Japan, preparations are made for final phase III development. Earlier, Pantarhei Oncology, founded in 2014, has already obtained favorable effects of E4 in women with advanced breast cancer in a study in Germany, supervised and published by Prof. Marcus Schmidt at the University Medical Center Mainz (Nov 2020, Journal Cancer Research and Clinical Oncology). Further phase II breast cancer studies are in preparation. In collaboration with merchant bank Kempen & Co in Amsterdam, Pantarhei Oncology has started the search for a strategic partner for the further development of these promising treatments for two of the most frequent and lethal human cancers.

Comments by Pantarhei Oncology

Prof. Herjan Coelingh Bennink (HCB), founder and President of the Pantarhei companies, is very pleased about these important results: “This clinical PCombi study has demonstrated that this new estrogen Estetrol can prevent many estrogen deficiency related side effects of ADT for advanced prostate cancer and will most likely also have additional anti-tumor effects”. Prof. HCB further stresses that: “Earlier this year, Health Canada, the CHMP of the European Medicines Agency (EMA) and the Food & Drug Administration (FDA) in the USA have approved a new hormonal oral contraceptive containing E4. This contraceptive pill has been developed by Pantarhei Bioscience from 2001 until 2015, when E4 was sold to the Belgian company Mithra Pharmaceuticals for Women’s Health applications, who completed the phase III oral contraceptive development. Since the pill is used by young healthy women, the safety requirements set by authorities are extremely high. These approvals in Europe, the USA and Canada represent independent and critical confirmations of the safety of E4”, according to HCB.

About Estetrol

Estetrol is a natural fetal estrogen, produced by the human fetal liver during pregnancy only and identified by Egon Diczfalusy at the Karolinska Institute in Stockholm in 1965. E4 was discovered as a potentially safer estrogen for human use by Herjan Coelingh Bennink at Pantarhei Bioscience in the Netherlands in 2001, based on the assumption that an estrogen present in high concentrations during human pregnancy, might be a safe drug for human use. Thanks to its favorable pharmacodynamics and pharmacokinetic profile, its tolerability and safety margins, and the lower interaction with liver function compared with other estrogens, E4 potentially represents a major breakthrough as a new hormonal treatment for contraception, menopause, osteoporosis and hormone-dependent cancers, such as prostate and breast cancer.

About Pantarhei Oncology

Pantarhei Oncology (PRO), part of Pantarhei Bioscience, is a Dutch biopharmaceutical company, specialized in the development of new hormonal treatments of cancer in the field of “Reproductive Endocrine Oncology (REO)”. PRO develops patent protected new treatment concepts until “proof-of-concept” (PoC) phase II in humans.

At present PRO is focusing on the further oncological development of high dose E4 (HDE4) for the treatment of advanced breast and prostate cancer after having proven PoC for both applications. In addition, PRO is developing a new immunotherapy based on the natural ovarian antigen Zona Pellucida 3 (ZP3) for the treatment of tumors expressing ZP3 such as ovarian and non-small cell lung cancer (NSCLC). This project is in the final stage of preclinical development.

https://www.pantarheibio.com/
https://www.pantarheioncology.nl/

1) Coelingh Bennink HJT, van Moorselaar JA, Crawford ED et.al. Estetrol Cotreatment of Androgen Deprivation Therapy in Infiltrating or Metastatic, Castration-sensitive Prostate Cancer: A Randomized, Double-blind, Phase II Trial (PCombi). EUROS 2021;28:52-61

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Note for response, not for publication

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