



The Contraception Journal Publishes a Scientific Paper on the Haemostatic Effects of Estetrol; Results Are Encouraging for the Estelle® Product Candidate

- Mithra Pharmaceuticals announces today the publication of a scientific paper highlighting the reduced haemostatic effects of the Estetrol (E4)/Drospirenone (DRSP) combination, namely the Estelle® product candidate developed by Mithra, in a comparative study with another combined oral contraceptive.
- The published results are particularly interesting for the scientific community, as they suggest a low procoagulant effect of the E4/DRSP combination that should be clinically verified for low antithrombotic consequences.
- The Contraception Journal is an international journal on reproductive health ranked among the best publications in the fields of obstetrics and gynaecology. The Contraception Journal is well-known among worldwide specialists and serves as a reference in the medical sphere.

Liège, Belgium, 8 September 2016 – Mithra Pharmaceuticals announces today the publication of a paper in the peer-reviewed Contraception Journal.

The scientific paper entitled “*Reduced haemostatic effects with drospirenone-based oral contraceptives containing estetrol versus ethinylestradiol*” demonstrates haemostatic effects of an estrogen+progestin combination based on Estetrol (E4) and Drospirenone (DRSP), compared to the reference combination based on ethinylestradiol (EE) and Drospirenone (DRSP).

The oral estrogens such as EE are known for significant effects on estrogenic and haemostatic variables. These markers are used to evaluate the potential venous thromboembolic (VTE) risks.

The paper demonstrates that the effects of oral Estetrol (E4) combined with DRSP are significantly less for these variables compared to the reference combination used in this study. These data suggest a low procoagulant effect of E4/DRSP that should be clinically verified for low antithrombotic consequences.

The results showed in this paper are rather positive in the development of the Estelle® product candidate in the field of Combined Oral Contraceptives (COC)¹.

¹ Estelle® is indeed composed of 15mg Estetrol (E4) and 3mg Drospirenone (DRSP).

About the paper entitled *“Reduced haemostatic effects with drospirenone-based oral contraceptives containing estetrol versus ethinylestradiol”*

Objective:

The effects of estetrol (E4), a natural foetal estrogen, combined with drospirenone (DRSP) were evaluated on plasma levels of Sex Hormone Binding Globulin (SHBG), angiotensinogen and 12 haemostasis markers.

Study design:

Combinations of 3 mg DRSP with 5 or 10 mg E4 were compared with the YAZ[®] pill (a combined pill composed of 20 µg ethinyl estradiol (EE) and 3 mg DRSP) in parallel groups of 15–18 years old young women.

Main outcome was the relative change of these haemostatic markers from the cycle before treatment (pre-treatment) to the end (day 24±1) of the third treatment cycle.

Results:

All E4 combinations showed low estrogen impact compared to EE/DRSP. Effects on SHBG and angiotensinogen of 10 mg E4 combined with 3 mg DRSP on plasma levels and angiotensinogen were 15–20% lower than of EE/DRSP.

Both E4/DRSP combinations reduced D-dimer plasma levels and the 5 mg E4/DRSP combination also decreased plasma levels of F1+2.

Conclusions:

The reduction in coagulation markers suggests an anticoagulant effect from DRSP.

The indications of a low thrombosis risk for E4 preparations should be validated in larger studies implying more subjects.

Implication statement:

The oral estrogens such as 17-β-estradiol and ethinyl estradiol (EE) are known for significant effects on estrogenic and haemostatic variables.

Effects of oral estetrol (E4) combined with DRSP are significantly less for these variables.

These data suggest a low procoagulant effect of E4/DRSP that should be clinically verified for low antithrombotic consequences.

This article published in the Contraception Journal is available on the Journal website: www.contraceptionjournal.org

Pictures

For pictures of François Fornieri, please click here on the following link:

<http://www.mithra.com/en/logo/>

For more information, please contact:

Press

Julie Dessart

Chief Communication Officer

+32 4 349 28 22

+32 475 86 41 75

press@mithra.com

Investor Relations

François Fornieri, CEO

+32 4 349 28 22

investorrelations@mithra.com

Steven Peters, CFO,

+32 4 349 28 22

investorrelations@mithra.com

About Mithra

Mithra Pharmaceuticals SA, founded in 1999 as a spin-off of the University of Liège by Mr. François Fornieri and Prof. dr. Jean-Michel Foidart, is a pharmaceutical company focused on Women's Health. Mithra's mission is to support and assist women at every stage of their life, thereby improving their overall quality of life. As such the Company aims to become a worldwide leader in women's health by developing, manufacturing and commercialising proprietary, innovative and differentiated drugs and complex therapeutical entities in four therapeutic fields of women's health, fertility and contraception, menopause and osteoporosis, vaginal infections and cancers.

Mithra has a total headcount of approximately 85 staff members and is headquartered in Liège, Belgium. Further information can be found at: www.mithra.com

Important information

The contents of this announcement include statements that are, or may be deemed to be, "forward-looking statements". These forward-looking statements can be identified by the use of forward-looking terminology, including the words "believes", "estimates," "anticipates", "expects", "intends", "may", "will", "plans", "continue", "ongoing", "potential", "predict", "project", "target", "seek" or "should", and include statements the Company makes concerning the intended results of its strategy. By their nature, forward-looking statements involve risks and uncertainties and readers are cautioned that any such forward-looking statements are not guarantees of future performance. The Company's actual results may differ materially from those predicted by the forward-looking statements. The Company undertakes no obligation to publicly update or revise forward-looking statements, except as may be required by law.

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