Mithra Announces Topline Results for COVID-19 Phase II Study

- **Estetrol (E4) did not differ from placebo on the primary study endpoint, but no firm conclusion can be made due to confounding factors**
- **E4 was well-tolerated with no apparent safety signals in hospitalized men or post-menopausal women suffering from moderate COVID-19**
- **No adverse effect observed on clotting markers or COVID-19 related embolic events**
- **These first data in comorbid patients, both male and female, further support the unique safety profile of estetrol**

Liege, Belgium, 24 September 2021 – 7:45 CEST – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health today announces topline results of the Coronesta Phase II study, which aimed to assess the safety and efficacy of estetrol (E4) for the treatment of patients who were hospitalized with moderate COVID-19. E4 is a native occurring estrogen produced by the human fetus during pregnancy.

Phase II Design

The Phase II Study[1] was an international, multi-center study that evaluated the safety and efficacy of estetrol (E4) 15 mg tablet, relative to placebo, in 175 patients (male/female) hospitalized with moderate COVID-19 (i.e., not on high flow oxygen or mechanical ventilation). Patients were randomly assigned to receive either E4 or identical placebo for 21 days. All patients received anticoagulant therapy as part of standard-of-care for COVID-19 for 21 days. The clinical program included centers in Belgium, Russia, and Poland.

The primary assessment of the study was the ability of E4 to increase the percentage of patients hospitalized with moderate COVID-19 that recover within 28 days compared with placebo. The secondary assessments included evaluation of safety (including markers of potential blood clotting), and measurements of disease worsening, time to recovery and viral load. Exploratory biochemical markers of inflammation and other measures of disease progress were also collected.

This is the first prospective clinical trial of an estrogen to report results in COVID-19.

Results

Out of 175 patients who entered the study, 171 patients were evaluated for efficacy and all patients were evaluated for safety.

There were no safety or tolerability concerns reported with E4 in patients hospitalized with moderate COVID-19. All deaths reported during the study were considered to be related to progression of COVID-19 (ten patients) or underlying illness (one patient). Patients, all of whom received standard-of-care heparin, had similar rates of COVID-19 related clotting events in the E4 and placebo treatment groups.

[1] More information about the Study (ClinicalTrials.gov Identifier: NCT04801836) available here

Overall, blood clots were infrequent and were seen less often than typically reported in the literature for patients with COVID-19 [1, 2].

The primary assessment did not show an improvement in recovery at Day 28 for E4 compared with placebo in either males or females, nor was there an improvement in admission to ICU or all-cause mortality. In the patients studied, there were a number of confounding factors, including an imbalance between the two groups in disease severity at entry, multiple COVID-19 risk factors, and varying doses of corticosteroids. Similar studies of 'Standard of Care' antivirals and anti-inflammatory agents have shown conflicting and inconclusive results, and therefore no firm conclusion from this study can be made.

Strengthening of E4-asset safety

Mithra is continuing to explore the complexity of the data, especially the possible impact on the study outcome of the patients' multiple other medical conditions and treatments, as well as further analysing laboratory markers including viral load. At this stage, Mithra does not envisage to conduct further clinical developments in this field.

The encouraging safety results, in particular those relating to clotting, strengthen the argument that patients can continue on E4 in the event of moderate hospitalized COVID-19 infection. These first data in comorbid patients, both male and female, further support the unique safety profile of estetrol.

Graham Dixon, CSO Mithra Women's Health, commented: "*New therapies against COVID-19 and its variants remain a priority in the evolving global pandemic and it has yet to be seen whether estrogens might play a role. It is extremely reassuring that E4 was well-tolerated even in such comorbid patients, male and female.*"

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About Mithra

Mithra (Euronext: MITRA) is a Belgian biotech company dedicated to transforming Women's Health by offering new choices through innovation, with a particular focus on contraception and menopause. Mithra's goal is to develop products offering better efficacy, safety and convenience, meeting women's needs throughout their life span. Mithra explores the potential of the unique native estrogen Estetrol in a wide range of applications in women health and beyond. Mithra also develops and manufactures complex therapeutics in the areas of contraception, menopause and hormone-dependent cancers. It offers partners a complete spectrum of research, development and specialist manufacturing at its technological platform Mithra CDMO. Active in more than 100 countries around the world, Mithra has an approximate headcount of 300 staff members and is headquartered in Liège, Belgium. www.mithra.com

Important information

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