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**O-010 The ULTRA trial: transvaginal ULTRASound-guided ovarian ablation using the novel May Health device in women with PCOS-related infertility: first-in-human feasibility clinical trial**

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**Study question:** Is transvaginal ULTRASound (TVUS)-guided ovarian ablation using May Health device feasible, safe, and effective in inducing ovulation in Clomiphene citrate and/or Letrozole (CC/LTZ)-resistant PCOS women?

**Summary answer:** TVUS-guided ovarian ablation using the May Health device seems feasible, safe and effective in inducing ovulation in PCOS-related anovulatory infertility, with additional, larger studies needed.

**What is known already:** Laparoscopic ovarian drilling (LOD) is widely accepted and recommended as an effective second line treatment in PCOS-related infertility. However, it is an invasive procedure that requires general anaesthesia and carries significant risks. Furthermore, the off-the-shelf devices used for LOD are not specifically designed to precisely deliver the desired and effective amount of ablation. In contrast, the May Health device has been designed to induce a precisely calculated amount of ovarian ablation via a much less invasive route without general anaesthesia. May Health therefore transforms an invasive surgical procedure to an office-based technique similar in access to the well-established oocyte retrieval.

**Study design, size, duration:** This study included two phase-I feasibility, single-arm clinical trials running in parallel in the US and EU assessing the May Health Device in performing TVUS-guided ovarian ablation in anovulatory PCOS women resistant to first-line ovulation induction drugs. Sample size was 35 participants with post-procedure follow-up (FU) of 24 months in EU and 12 months in US. Endpoints included procedure feasibility (successful ablation of at least one ovary), safety, and effectiveness (ovulation and pregnancy rates).

**Participants/materials, setting, methods:** Seven fertility centres (UK, France, Belgium, US) participated in the trials. Participants were CC/LTZ-resistant PCOS women aged 18-40 years. PCOS was diagnosed according to Rotterdam criteria. Participants underwent TVUS-guided ovarian ablation using May Health device. The initial five participants underwent laparoscopy concurrent with TVUS-ablation. Post-procedure, serum progesterone was measured weekly until confirmation of ovulation or up to 12 weeks. Women were evaluated at 3 and 6 months, then telephoned at 9, 12 and 24 months.

**Main results and the role of chance:** Twenty-three participants (mean  $\pm$  sd age,  $31.8 \pm 3.1$  years; BMI,  $29.8 \pm 5.0$  kg/m<sup>2</sup>) underwent May Health TVUS-guided ovarian ablation and completed at least three-months FU. Of those, 10 (43.5%) ovulated spontaneously during the first three months. Six more women ovulated between three- and nine-months FU, some with CC/LTZ, giving a total ovulation rate of 69.6% (16/23). Of the 11 participants who completed nine-months FU, five conceived. Two more participants conceived before 9-months giving a total pregnancy rate of 53.8% (7/13).

In 19 cases (82.6%), ablation was achieved successfully in both ovaries, while in four cases (17.4%) one of the ovaries was not ablated either because it was too small (as per protocol) (n = 3) or inaccessible (n = 1).

Overall, 14 participants experienced 29 adverse events (AEs), of which 25 were mild, two moderate and two severe. Nine mild/moderate AEs were deemed related to the device/ablation procedure. Examples of mild/moderate AEs included mild self-limiting vaginal bleeding (n = 5), pain (n = 5) and headache (n = 2). None of the severe AEs were deemed related to the device/ablation procedure. One participant in phase Ia who underwent laparoscopy concurrent with the ablation, sustained a bowel injury involving the ilium near the ileocecal junction. Independent expert investigation concluded that the injury was likely caused by laparoscopic veress needle.

**Limitations, reasons for caution:** One possible limitation of this study is the lack of a comparator treatment / placebo arm. However, this was not necessary for this feasibility phase I trial. Furthermore, given the nature of TVUS-ovarian ablation, it would be difficult to compare it with other ovulation induction drugs or to a placebo.

**Wider implications of the findings:** These preliminary data suggest that the novel May Health device offers a promising office-based second line ovulation inducing procedure for CC/Letrozole-resistant anovulatory PCOS women.

**Trial registration number:** NCT03760926