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Cardiovascular safety in users of different combined oral contraceptives – Final results from the INAS-SCORE study

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Background: A new combined oral contraceptive (COC) with a 26-day regimen containing estradiol valerate (EV) and dienogest (DNG), known as Qlaira (and Natazia in the US), was launched in 2009. It was unknown whether this new regimen and combination has an impact on the cardiovascular risk associated with the use of COCs. The INAS-SCORE study was conducted to investigate the cardiovascular long- and short-term safety of the EV/DNG containing COC compared to established COCs.

Design/methods: The ‘International Active Surveillance Study – Safety of Contraceptives: Role of Estrogens’ (INAS-SCORE) was requested by the Medicines Evaluation Board as a post-authorisation safety study. It was a large, prospective, controlled, non-interventional, long-term cohort study with active surveillance of the study participants. It was conducted in the US as well as in Austria, France, Germany, Italy, UK, Poland and Sweden. Women prescribed a new COC (either first-time user or switcher) were recruited by a network of prescribing physicians. Recruitment started in 2009 and was finished in 2012. Every 6 months during the first two years and yearly thereafter, the woman was contacted and specifically asked about hormonal contraceptive use and family history of VTE lead to HRs of 0.4 (95% CI: 0.2–1.1), respectively. ATE incidences were very low with 0.7 ATE/10,000 WY for Qlaira and 3.5 ATE/10,000 WY for Other COCs. With regard to ATE, no results from the standard model were available because the minimum number of events per cohort was not reached. As requested by the FDA, a modified COX model was used with only duration of use and exposure as time-dependent covariates. The adjusted hazard ratio (HRadj) for EV/DNG vs. COCcontrol and vs. LNG sub-cohort were 0.1 (95% CI 0.0–0.6) and 0.1 (95% CI 0.0–1.2), respectively.

Conclusions: The results do not suggest a higher VTE or ATE risk of Qlaira users compared to users of Other COCs in a study population that is representative of actual users.

Disclosure statement

This was a post-authorisation safety study (PASS), which was requested by the European Medicines Agency (EMA). It was supervised by an Independent Safety Monitoring and Advisory Board. The study was supported by an unconditional grant from Bayer AG.
of barriers, including the federal requirements for observed dosing, practitioner training, practitioner registration, physician-only prescribing and dispensing. Pharmacist dispensing directly to women, and nurse-practitioner prescribing are now allowed in Canada.

**Conclusions:** This study identified and mitigated health policy, system and service barriers to mifepristone abortion access, accelerating its implementation across Canada. The rapid uptake of our study findings into practice and policy demonstrate the impact of iKT on implementation/dissemination of new practices, and may facilitate increased access to equitable, safe, confidential abortion care closer to home.

**Methodologies:**

**Design and methods:** In this prospective cohort study, we evaluate the risk of unintended pregnancy among women of different contraceptive status. All women in the city of Vantaa, Southern Finland, have been entitled to their first LARC method free-of-charge at public family planning clinics since 2013. The cohort consisted of all non-sterilised, non-pregnant women aged 15–44 living in Vantaa during 2013–2014, and the outcome was unintended pregnancy during 2013–2016. As information on unintended pregnancy is scarce, we measured induced abortions and the proportion of pregnancies ending in abortion as proxies for unintended pregnancy. We compared the following contraceptive statuses: (i) women entitled to a free-of-charge LARC method, but not visiting a family planning clinic, (ii) women entitled to a free-of-charge LARC method, visiting a family planning clinic but chose a short-acting method, (iii) women who obtained a LARC method at no-cost at a public family planning clinic.

**Results:** During 2013–2014, there were 41,525 women entitled to a LARC method that did not visit a public family planning clinic. Of them, 8721 became pregnant (21.0%) and 1718 women had an abortion (19.6% of the pregnancies, 4.1% of all women, incidence rate 11.9/1000 person years). Of the 8347 women who visited a public family planning clinic, 985 women chose a LARC method free-of-charge and among these there were 91 pregnancies (9.2%) and 11 abortions (12.1% of all pregnancies, 1.1% of all women, incidence rate 3.63/1000 person years). The corresponding numbers among the 7362 women not choosing a LARC method were 1098 pregnancies (14.9%) and 235 abortions (21.4% of all pregnancies, 3.2% of all women). In our preliminary, unadjusted Poisson regression analysis of abortions among LARC-users vs. non-LARC-users, we found that the relative risk for an induced abortion was 0.43 (95% CI = 0.21, 0.79, p < 0.005).

**Conclusions:** The abortion rate among FPC visitors was twice as high as in the general population. Initiation of a LARC method was effective in reducing the pregnancy and abortion rate among women choosing it. Women seeking counseling on contraception are sexually active and at great risk of unintended pregnancy. Providing the most effective reversible contraception is an efficient means to meet the need of family planning.