Effect of Efavirenz on the Pharmacokinetics of Ethynyl Estradiol and Norgestimate in Healthy Female Subjects

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Introduction
A double-blind, 4-arm, open-label, randomized, 3-period, 4-treatment study was conducted in order to provide a better understanding of the pharmacokinetics (PK) of ethinyl estradiol (EE) and norgestimate (NGMN), active metabolites of oral contraceptives (OCs), when coadministered with efavirenz (EFV). The study was conducted in healthy, non-smoking, non-pregnant female subjects aged 18 to 42 years with a mean age of 28 years (range: 18 - 42 years). The study was conducted in order to determine the effect of coadministration of EFV on the pharmacokinetics of EE and NGMN, an active metabolite of the progestin norgestimate when coadministered with OCs.

Methods
\textbf{Study Design}:
- Open-label, 3-period, 4-treatment single sequence study in healthy female subjects who had been receiving a stable regimen of OCs for at least 2 months.

\textbf{Methods}:
- \textbf{Safety}:
- To determine the effect of coadministration of EFV on the pharmacokinetics (PK) of EE and NGMN, an active metabolite of the progestin norgestimate when coadministered with OCs.
- To assess the safety of EFV coadministered with Ortho Cyclen.
- To assess the safety of EFV coadministered with Ortho Tri-Cyclen.
- To assess the safety of EFV coadministered with Ortho Tri-Cyclen LO.

- \textbf{Pharmacokinetics}:
- To determine the effect of coadministration of EFV on the pharmacokinetics of EE and NGMN, an active metabolite of the progestin norgestimate when coadministered with OCs.
- To determine the effect of coadministration of EFV on the pharmacokinetics of EE and NGMN, an active metabolite of the progestin norgestimate when coadministered with Ortho Cyclen.

- \textbf{Pharmacodynamics}:
- To assess the safety of EFV coadministered with Ortho Cyclen.
- To assess the safety of EFV coadministered with Ortho Tri-Cyclen.
- To assess the safety of EFV coadministered with Ortho Tri-Cyclen LO.

Results

\textbf{Safety}:
- No serious adverse events were reported during the study. The most common adverse event reported was headache, which was observed in 22% of subjects.

\textbf{Pharmacokinetics}:
- The geometric mean ratio (GMR) for EE following coadministration of EFV 600 mg with Ortho Cyclen was 0.99 (90% CI: 0.73, 1.37).
- The geometric mean ratio (GMR) for NGMN following coadministration of EFV 600 mg with Ortho Cyclen was 0.52 (90% CI: 0.37, 0.74).

\textbf{Pharmacodynamics}:
- Metrorrhagia was the most frequent adverse event reported, occurring in 14% of subjects.

Discussion
- EFV significantly reduces exposure to NGMN and LNG when coadministered with Ortho Cyclen.

Conclusions
- EFV significantly reduces exposure to NGMN and LNG when coadministered with Ortho Cyclen.

References