

## **The POET Prevention of Endometrial Tumours Study**

POET (Prevention of Endometrial Tumours) is an interventional, open, randomised control trial looking at the efficacy of the Mirena Intrauterine System (IUS) with surveillance, versus surveillance alone, in reducing the development of Atypical Endometrial Hyperplasia (AEH) and carcinoma in women aged 35-65y with Hereditary Non-Polyposis Colorectal Cancer (HNPCC) or Lynch Syndrome

This cohort of women has been selected based on age (35-65 years old) for inclusion into the study because the risk of Endometrial Cancer (EC) in women with Lynch syndrome rises from 35y age. This is when surveillance is recommended to start, according to current guidelines [30]. The risk of EC continues to rise post-menopausally so the prophylactic effects of the Mirena IUS could be more significant in this age group.

The primary aim of this study is to determine if treatment with intrauterine progestogen reduces the incidence of AEH and EC in women with Lynch syndrome. Secondary aims are to address the following questions:

- 1) What is the age-related incidence of AEH and EC in women with Lynch syndrome?
- 2) What is the sensitivity and specificity of surveillance with TransVaginal Sonography (TVS) and Endometrium Biopsy (EB) to detect AEH and carcinoma in women with Lynch syndrome?
- 3) What is the premalignant pathway to carcinoma in women with Lynch syndrome?
- 4) Does the Mirena IUS reduce the rate of therapeutic hysterectomy for AEH or cancer in women with Lynch syndrome?
- 5) Are there psychological benefits or adverse effects from the use of the Mirena IUS?
- 6) What is the satisfaction and compliance with screening?
- 7) What is the extent of adverse effects of surveillance and use of the Mirena IUS? (subsequent investigation of abnormalities detected on surveillance or side-effects of the Mirena)
- 8) In the longer term, with separate funding, we will determine the molecular changes associated with pre-malignant changes in the endometrium in women with Lynch syndrome, and possibly the utility of tests on cervical mucus samples to diagnose endometrial neoplasia.

The rationale is that women with Lynch syndrome are at a substantial risk of developing EC [3,4,5,6,7] (up to 65% lifetime risk, average 1-2% annual risk in 35-65 age group), particularly premenopausally, when symptom detection is more difficult. The efficacy of surveillance by the recommended annual TVS with EB from 35y age is not established, and some women opt for prophylactic hysterectomy. A trial of intrauterine progestogens for reduction of AEH and EC in Lynch syndrome has not been performed to date.

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