

The Women's Health Research Program

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Investigating the Prevention of Endometrial CAncer with Metformin (PECAM Study)

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Over 75 per cent of women diagnosed with breast cancer in Australia have hormone sensitive disease. Of these, at least 1/3 will be treated with a drug called tamoxifen, which blocks oestrogen action.

A recent large study has shown that 10 years of tamoxifen therapy is more effective than 5 years in prolonging the survival of women with hormone sensitive breast cancer.

However, there are established downsides to tamoxifen therapy:

- The development of uterine abnormalities occur in the first year of treatment;
- a 75 per cent increase in the risk of uterine (endometrial) cancer;
- Weight gain;
- Fatty liver; and
- Development of insulin resistance.



Presently there is no treatment to prevent endometrial cancer in women treated with tamoxifen, or for that matter for women in general.

- Endometrial cancer, the most common gynaecologic cancer, affects approximately 1 in 73 Australian women by the age of 75 years and 1 in 52 by the age of 85 years.

Metformin, a medication in widespread use to treat diabetes, might prevent all of these adverse tamoxifen effects:

- In animal models metformin prevents tamoxifen-induced uterine changes;
- Metformin is effective in the treatment of nonalcoholic fatty liver disease and we have recently shown metformin reduces insulin resistance and weight in non-diabetic women; and
- Metformin is being evaluated in other studies to treat breast cancer.

The aim of this study is to evaluate a novel approach to prevent the development of endometrial cancer ▶



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in women taking tamoxifen therapy. We will investigate whether metformin blocks cellular pathways by which tamoxifen (and oestrogen) stimulates uterine cell growth, and thus evaluate the possibility that metformin might be useful in preventing uterine cancer.

In summary this study will help us determine:

- If metformin *prevents* tamoxifen-induced weight gain and insulin resistance;

- How common abnormalities of the uterine lining are in women who are to start tamoxifen (reported to be as high as 21 per cent); and
- How common uterine abnormalities are after 12 months of tamoxifen treatment
- Whether all women who are to start tamoxifen should have screening of their uterus by ultrasound before starting.

This study will commence in 2014. We will be recruiting women who are post-

menopausal, have hormone sensitive breast cancer and have been recommended to start tamoxifen and are less than 75 years old.

We will provide more information about this study in the new year.

Does anti-androgen therapy affect the way women with polycystic ovarian syndrome think?

There is evidence that testosterone is important for normal brain function in women. If this is the case then blocking testosterone action might impair normal brain function. Women with a condition called polycystic ovarian syndrome (PCOS) tend to have elevated testosterone levels. PCOS is the most common hormonal disorder in women, affecting around 15% of women of reproductive age. Affected women commonly experience excessive facial and body hair and acne. The standard treatment for this is “anti-androgen” therapy (spironolactone) which blocks testosterone production and action.

We are going to undertake a study to determine whether anti-androgen (spironolactone) treatment of women with PCOS results in any change in brain function assessed by sensitive tests of verbal and spatial learning and memory. The findings will not only inform us about the safety of this treatment in women with PCOS but also add to our understanding of the role of testosterone in brain function in women.

We wish to recruit women with PCOS who are presently taking spironolactone and women with PCOS who are to commence spironolactone.

We will assess learning and memory using a highly sensitive computer based testing system called CogState that was developed in Australia to assess the cognitive function of healthy people. We have used this in several published studies.

Women who have PCOS who are aged 18-35 years and are either presently taking spironolactone or planning to commence this treatment are invited to contact us about participating in this study.

This study has been approved by the Cabrini Human Research Ethics Committee and Monash University Human Research Ethics Committee.

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