MONASH University

MONASH INNOVATION

ECTOPIC PREGNANCY TREATMENT

A combination therapeutic approach to resolve ectopic pregnancies that are stable, with no clinical suspicion of rupture (90-95%). This medication could replace surgery for most cases of ectopic pregnancy and revolutionise contemporary gynaecological care.

- **Ectopic pregnancy is cured through a single injection of methotrexate with a short course of tablets (gefitinib)**
- **Late clinical stage**
- **Safer – reduces the need for invasive surgery**
- **Faster – reduces time to resolution compared to current standard of care**
- **Preserves fertility, as the fallopian tube is not removed**
- **Cheaper (medications replace surgery)**

THE CHALLENGE

Ectopic pregnancies are conceptions implanting outside the uterus, mainly in the fallopian tube. They are life-threatening since they may rupture, causing catastrophic and fatal bleeding. They are a leading cause of maternal morbidity and mortality in the first trimester. About 2% of all pregnancies that present are ectopic, which equates to 5,000 per year in Australia and 100,000 in the USA.

Most ectopic pregnancies are treated surgically. While laparoscopy is safe, important surgical risks remain. The operation usually results in removal of the entire fallopian tube, compromising the woman's fertility.

While very small ectopic pregnancies can be treated medically (intramuscular methotrexate, MTX), only a minority of cases are suitable (~25%) and the mainstay of treatment is surgery.

THE TECHNOLOGY

This technology offers a new medical treatment regimen for ectopic pregnancies, comprising a single MTX injection with a short course of oral gefitinib, an inhibitor of Epidermal Growth Factor Receptor (EGFR).

The placenta has the highest expression of EGFR of all non-malignant tissues in the body and is critically dependent on the EGFR to survive. Blocking EGFR is a novel strategy that selectively targets the placenta. Monash researchers (Prof. Stephen Tong and Prof. Terence Johns) have undertaken extensive pre-clinical work, robustly demonstrating that co-administering getfitinb (EGFR inhibitor) and MTX is supra-additive in potently killing placental tissue.[1]
A regimen combining MTX with oral gefitinib has now been successfully tested in three clinical trials. A single arm phase I trial (ACTRN12610000684022) in 12 women supported high efficacy.[2] A Phase II Open-Label Single-Arm Study in 28 women with tubal ectopic pregnancies demonstrated even better efficacy.[3] A further trial conducted in eight women with large non-tubal ectopic pregnancies had 100% efficacy in this difficult-to-treat condition[4]. **These early stage trials support a prompt and potent cure of ectopic pregnancies, with no serious toxicities observed to date.**

Currently, this asset has progressed to Phase 3, with GEM III, a double blind placebo-controlled trial testing 328 women comparing MTX/getfitinib to MTX alone. This trial, currently recruiting, is being conducted in the UK and led by the University of Edinburgh (Prof. Andrew Horne) with co-principal investigator, Prof. Stephen Tong (EudraCT No: 2015-005013-76).

Potential products and applications

Most ectopic pregnancies that present for medical attention will be suitable for this treatment (we estimate 95%). Only where it is suspected that the ectopic has already ruptured will the treatment not be suitable (5% or less). Notably, the treatment will also be applicable to non-tubal ectopic pregnancy, which is currently difficult to manage. Thus, those patients who would normally have surgery could be treated with this drug combination instead. This regimen provides a safer, easy to administer, cheaper treatment that may reduce the risk of compromising fertility. It offers the advantage of being more effective and a faster cure than MTX alone.

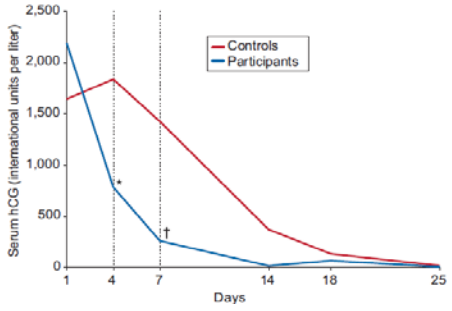

Figure 1: Serum human chorionic gonadotropin (hCG) levels in trial participants treated with gefitinib and methotrexate compared with historic controls given methotrexate alone. Subanalysis of six participants and 71 historic controls in which pretreatment serum hCG levels were between 1,000 and 3,000 international units per liter in both groups. Comparisons of hCG levels were made between the groups at days 1, 4, and 7. At day 1, serum hCG levels between both cohorts were not significantly different..hCG is a marker of ectopic pregnancy size. Serum hCG is used clinically to track response, where a drop to zero signifies a cure[2]. *P,.05.†P,.01

Intellectual property: Granted patents: United States 8,858,939 and Australia 2010212513; Canadian application 2713610.

Key Publications

1. Nilsson U *et al* (2013) *Obstet Gynecol;* 122:737-44
2. Skubisz M. *et* al (2013) *Obstet Gynecol*; 122:745-51; ACTRN12610000684022
3. Horne A *et al* (2014) *Human Reproduction* 29(7) 1375-79.

THE OPPORTUNITY

Monash is seeking a licensee for this technology.

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