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[Intervention Review]

# Chemotherapy for resistant or recurrent gestational trophoblastic neoplasia

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## ABSTRACT

### Background

Gestational trophoblastic neoplasia (GTN) is a highly curable group of pregnancy-related tumours; however, approximately 25% of GTN tumours will be resistant to, or will relapse after, initial chemotherapy. These resistant and relapsed lesions will require salvage chemotherapy with or without surgery. Various salvage regimens are used worldwide. It is unclear which regimens are the most effective and the least toxic.

### Objectives

To determine which chemotherapy regimen/s for the treatment of resistant or relapsed GTN is/are the most effective and the least toxic.

### Search methods

We searched the Cochrane Gynaecological Cancer Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL, Issue 4), MEDLINE and EMBASE up to October 2011. In addition, we handsearched the relevant society conference proceedings and study reference lists.

### Selection criteria

Only randomised controlled trials (RCTs) were included.

### Data collection and analysis

We designed a data extraction form and planned to use random-effects methods in Review Manager 5.1 for meta-analyses.

### Main results

The search identified no RCTs; therefore we were unable to perform any meta-analyses.

### Authors' conclusions

RCTs in GTN are scarce owing to the low prevalence of this disease and its highly chemosensitive nature. As chemotherapeutic agents may be associated with substantial side effects, the ideal treatment should achieve maximum efficacy with minimal side effects. For

methotrexate-resistant or recurrent low-risk GTN, a common practice is to use sequential five-day dactinomycin, followed by MAC (methotrexate, dactinomycin, cyclophosphamide) or EMA/CO (etoposide, methotrexate, dactinomycin, cyclophosphamide, vinblastine) if further salvage therapy is required. However, five-day dactinomycin is associated with more side effects than pulsed dactinomycin, therefore an RCT comparing the relative efficacy and safety of these two regimens in the context of failed primary methotrexate treatment is desirable.

For high-risk GTN, EMA/CO is the most commonly used first-line therapy, with platinum-etoposide combinations, particularly EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin), being favoured as salvage therapy. Alternatives, including TP/TE (paclitaxel, cisplatin/ paclitaxel, etoposide), BEP (bleomycin, etoposide, cisplatin), FAEV (floxuridine, dactinomycin, etoposide, vincristine) and FA (5-fluorouracil (5-FU), dactinomycin), may be as effective as EMA/EP and associated with fewer side effects; however, this is not clear from the available evidence and needs testing in well-designed RCTs. In the UK, an RCT comparing interventions for resistant/recurrent GTN will be very challenging owing to the small numbers of patients with this scenario. International multicentre collaboration is therefore needed to provide the high-quality evidence required to determine which salvage regimen/s have the best effectiveness-to-toxicity ratio in low- and high-risk disease. Future research should include economic evaluations and long-term surveillance for secondary neoplasms.

## PLAIN LANGUAGE SUMMARY

### Anti-cancer drug treatment for gestational trophoblastic neoplasia (GTN) that does not respond to first-line treatment or that re-occurs

This review concerns anti-cancer drug treatment for women with GTN that does not respond to first-line treatment or that re-occurs. GTN is the name given to a type of cancer that arises from placental tissue following pregnancy, most frequently a molar pregnancy. Molar pregnancies are benign abnormal growths of placental tissue inside the womb. Most are cured by evacuation (D&C) of the womb, however, in up to 20% of cases they become malignant. GTN is usually very responsive to anti-cancer drugs (chemotherapy), however, these drugs can be toxic, therefore the aim of treatment is to achieve a cure with the least side effects. To help doctors select the most appropriate treatment for women with GTN, the disease is classified as low- or high-risk according to specific risk factors.

Chemotherapy treatment for low-risk GTN usually only requires a single drug, whereas high-risk tumours are treated with a combination of drugs. The most common combination consisting of five drugs is abbreviated as EMA/CO. Doctors assess the response to treatment by checking the levels of the pregnancy hormone (hCG) in the blood. If the chemotherapy is deemed not to be working an alternative (or salvage) treatment must be started. This is necessary in about 25% of cases and a variety of drug combinations are in use.

We undertook this review because it was unclear which of the various salvage combinations, if any, was the most effect and the least toxic. We searched the literature up to November 2011 to find all relevant studies. Unfortunately, we were unable to find any good quality studies that compared the different types of salvage treatments. This is partly because the disease has a high cure rate with several combination chemotherapy options, but is also owing to the rarity of the disease that makes recruiting for large studies difficult. Hence we were unable to draw conclusions about how these drug combinations compare with regard to their effectiveness and side effects, and we urge researchers in this field to collaborate to provide this important evidence.