# A switch to dactinomycin: What is the cutoff value for hCG?. (Mini-commentary on BJOG-19-1677.R1)

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May 5, 2020

Mini-commentary on BJOG-19-1677.R1: Risk-factors for second-line dactinomycin failure after methotrexate treatment for low-risk gestational trophoblastic neoplasia: a retrospective study

**A switch to dactinomycin: What is the cutoff value for hCG?**

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A third of patients with gestational trophoblastic disease (GTD) scored as low risk (FIGO score 0-6) failed the initial methotrexate (MTX) treatment. These patients require second-line treatment, either with single-agent (dactinomycin) or with combination chemotherapy (EMA/CO). The successful treatment rates for second-line dactinomycin is approximately 85%. Compared with dactinomycin, EMA/CO had higher rates of hCG normalisation and lower relapse rates after treatment completion. But treatments with combination chemotherapy are associated with an increased risk of secondary malignancies and hasten the onset of menopause (Rustin et al. J Clin Oncol 1996;14:2769–73).

Choices of treatment regimens after resistance to MTX have been dependent on varied serum hCG values. Those with hCG levels greater than 100 or 300 IU/l commenced on combination chemotherapy although higher hCG did not preclude dactinomycin use (McNeish et al. J Clin Oncol 2002; 20: 1838–1844 and Sita-Lumsden et al. Br J Cancer. 2012 Nov 20; 107(11): 1810-1814). The present study examined the question of whether there is an hCG level beyond which second-line dactinomycin may fail in women who still scored in the low-risk category (BJOG 2020 xxxx). The cure rate (66.7%) after second-line dactinomycin therapy was lower than reported probably because patients who withdrew from MTX due to intolerance and toxicity were excluded for this analysis.

Although not statistically significant, discrepancies exist with regard to the histopathologic diagnosis between groups as more post-molar GTN were treated in the dactinomycin-success group. Two patients had choriocarcinoma in the dactinomycin-failure group which were clinical relevant to increased resistance to chemotherapy (Strohl et al. Gynecol Oncol. 2016 May;141(2):276-280).

Roles of second curettage or hysterectomy for resistant or relapsed disease are still under clinical debate and the presence of lung metastases in low-risk GTD is associated with MTX resistance (Frijstein et al. BJOG. 2020 Feb;127(3):389-395). Despite being limited by its retrospective design and small sample size, the authors included these variables in their analysis. Only the hCG level pre-dactinomcycin treatment remained predictive of treatment failure on multivariate analysis with odds ratio 2.93 (95% CI 1.02-8.40,

p=0.045). Without selection based on pre-treatment hCG levels, the authors demonstrated the reducing efficacy of second-line dactinomycin with increasing hCG levels and suggested treatment with EMA/CO directly at hCG level above 40 ng/mL. However, the cut-off concentration of hCG should not be applied using other assays as performed in the present study.

The disease site and FIGO score for the 45 MTX-failure patients were not analysed in this study therefore whether the dactinomycin failure group represented a less favourable subgroup predisposing to treatment failures is unanswered. I agree with the authors that high hCG level pre-dactinomcycin treatment is a significant adverse factor. Nevertheless, cure rates with the established therapies for GTD are extremely high; therefore increased treatment duration (in this study, a maximum of 3.5 month) led by resistance to second-line dactinomycin should be balanced against the toxicity profiles of combination chemotherapy.

**Disclosure of interests:** None declared. A completed disclosure of interest form is available to view online as supporting information.