

GOG-0275: A PHASE III RANDOMIZED TRIAL OF PULSE ACTINOMYCIN-D VERSUS MULTI-DAY METHOTREXATE FOR THE TREATMENT OF LOW-RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA

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KEY ELIGIBILITY CRITERIA

Target Accrual: 384 Patients

- WHO (2002) risk score 0-6
- FIGO stage I, II, or III
- Post Molar GTN
 - Patients must have undergone evacuation of a complete or partial hydatidiform mole and meet the criteria for GTN defined as:
 - A < 10% decrease in the hCG level using as a reference the first value in the series of 4 values taken over a 3-week period (>50 mIU/ml minimum).
 - OR
 - A > 20% sustained rise in the hCG taking as a reference the first value in the series of 3 values taken over a 2-week period (>50 mIU/ml minimum).
 - OR
 - A persistently elevated hCG level more than 6 months following the initial curettage (>50 mIU/ml minimum).
- Choriocarcinoma
 - Histologically proven non-metastatic choriocarcinoma.
 - OR
 - Histologically proven metastatic choriocarcinoma if the metastatic site(s) is one (or more) of the following: vagina, parametrium or lung.

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Study Chair: Julian Schink, MD



Eligible patients:
Low-risk persistent GTN
FIGO Stage I, II, III
WHO Score 0-6

R
A
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Arm Regimen 1: Patients will receive IV pulse actinomycin-D (1.25mg/m²) every 14 days. (2mg max dose)

Arm Regimen 2: Patients will receive their institutional preference of either:

- IV methotrexate (0.4 mg/kg) daily for 5 days every 14 days. (25mg max daily dose)

OR

- IM methotrexate(50mg) on Days 1, 3, 5, 7 (4 doses per cycle) with Leucovorin (15mg) on Days 2, 4, 6, 8. Repeat every 14 days.

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QUALITY OF LIFE ASSESSMENT

Prior to cycles 1,3,5,7 & at 26 weeks after starting treatment

Overall Measures

- Physical symptoms
- Functional Assessment
- Social well-being
- Emotional well-being

FACIT Supplemental Items

- Potential toxicities
- Side-effects & other treatment issues

Exploratory Items

- Likert scale evaluation – degree of life disruption from chemo
- Rank item addressing factors associated with chemo

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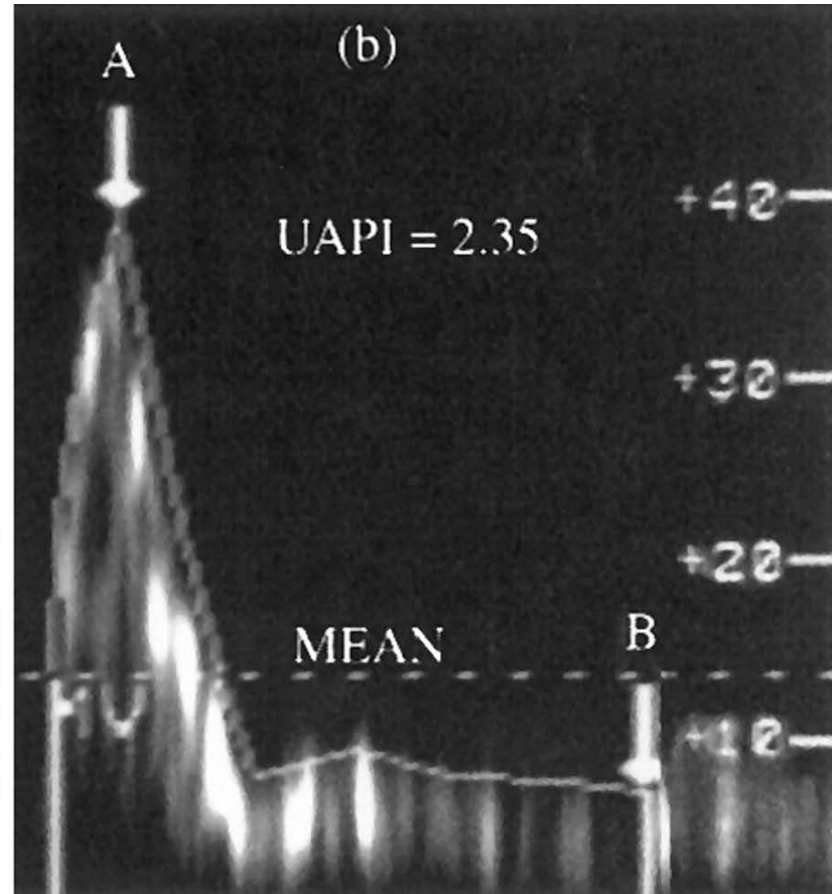
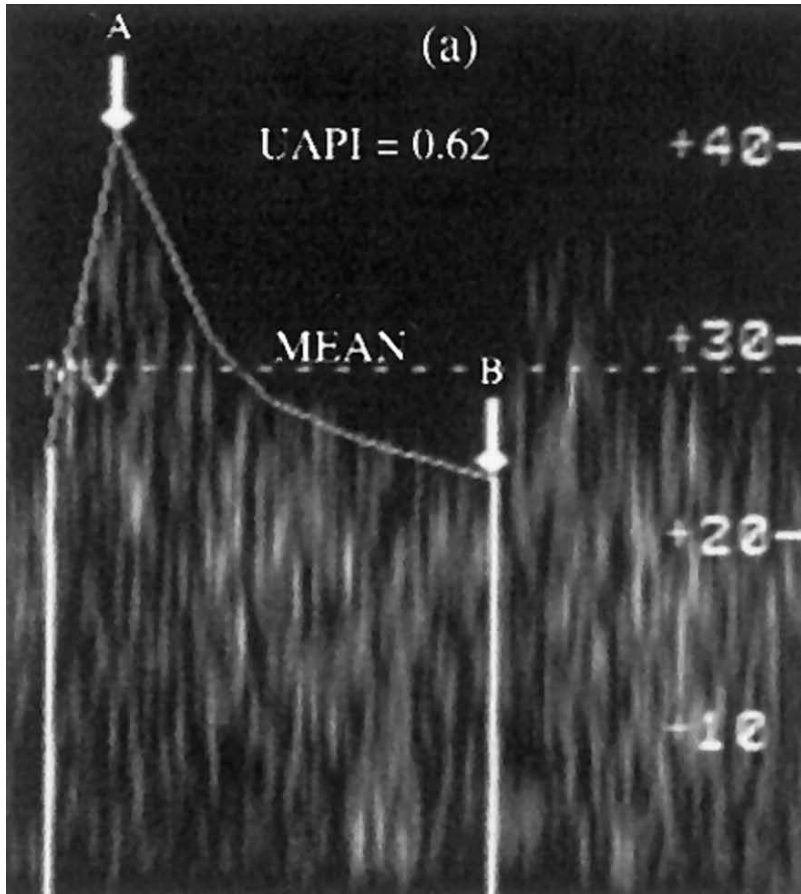
OPTIONAL UAPI STUDY

Charing Cross reported patients with persistent GTN, FIGO score 0-6, treated with MTX and UAPI ≤ 1 had increased risk of treatment resistance regardless of FIGO score



Uterine artery pulsatility index (UAPI) measurement at time of the pelvic ultrasound will confirm or refute prognostic significance

Doppler traces of the uterine artery in patients with GTT. a, a patient with a UAPI of 0.62 who developed MTX-R. b, a patient with a UAPI of 2.35 who did not develop MTX-R.



Agarwal R et al. Clin Cancer Res 2002;8:1142-1147

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STUDY DURATION

Patients treated for 3 cycles after hCG $<5\text{mIU/ml}$ or until evidence of biologic or disease progression or unacceptable toxicity

Upon normalization of hCG ($<5\text{mIU/ml}$), hCG monitored every 4 weeks for 1 year beginning 1st day of the last chemotherapy cycle

QOL will be assessed for all patients at 26 weeks from the start of treatment, regardless of treatment status

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STATISTICAL CONSIDERATIONS

- Study is designed as a two arm randomized phase III non-inferiority trial
 - Control arm: ACT-D
 - Experimental arm: multi-day MTX regimen (institution preference)
- In the event the null hypothesis of inferiority is rejected, a test of the superiority of the MTX regimen will be carried out and reported.

Statistical test characteristics: probabilities of accepting each regimen under different settings

Methotrexate response P_m	ACT-D response P_d	$P_d - P_m$	$P(\text{accept MTX} p_m, p_d)$	$P(\text{accept ACT-D} p_m, p_d)$
0.80	0.70	-0.10	0.95	0.05
0.70	0.70	0.00	0.27	0.73
0.65	0.70	0.05	0.05	0.95

PROPOSED CONCEPT

A Randomized Phase II Trial Comparing the Toxicity of Paclitaxel & Etoposide (TE) Alternating Two Weekly with Paclitaxel & Cisplatin (TP) with Etoposide & Cisplatin (EP) Alternating Weekly with Etoposide, Methotrexate & Dactinomycin (EMA) in GTN Patients Failing Non-Platinum Based Combination Agent Therapies

Study Chair: Michael Seckl, MD, PhD

Eligible Patients

GTN progression or relapse following EMA/CO other non-platinum non-taxane containing first and/or second/third line therapies.
PS \leq 2 and suitable for chemotherapy

Randomize

TE/TP Arm 1

Paclitaxel 135mg/m² and Etoposide 150mg/m²
Alternating two weekly with Paclitaxel 135mg/m² and Cisplatin 60mg/m²

EP/EMA Arm 2

Etoposide 150mg/m² and Cisplatin 75mg/m²
Alternating weekly with Etoposide 100mg/m², Methotrexate 300mg/m², and Dactinomycin 0.5mg