GYNAECOLOGICAL CANCERS

31MO Comparing efficacy of avelumab + methotrexate vs. methotrexate alone in low-risk gestational trophoblastic neoplasia: A national registry-based external control comparison

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Background: Low-risk gestational trophoblastic neoplasia (GTN) affects young women. The standard "8-day methotrexate" (MTX) regimen achieves a 70—80% cure rate as first-line treatment, but resistance may require second-line chemotherapy, delaying fertility and causing toxicity. The TROPHAMET single-arm phase I/II trial showed that combining avelumab (AVE) with MTX achieved a 96.2% success rate.

Methods: To compare these first-line strategies before a potential phase III trial, we designed an external control comparison in the target trial framework using data from GTN patients with a FIGO (International Federation of Gynecology and Obstetrics) score $\leq$6 treated between 2020 and 2025 and prospectively registered to the French Reference Center for Trophoblastic Diseases (FRCTD). The main outcome was serum human chorionic gonadotropin (hCG) normalization allowing treatment discontinuation. G-computation was performed to compare results between MTX + AVE and MTX alone, using the FIGO score as the main confounding factor. The 95% confidence intervals (CI) for risk ratio and risk difference estimates were constructed using a percentile-based bootstrap CI with 10,000 bootstrap samples. Several sensitivity analyses were performed.

Results: Among the 276 eligible patients in the FRCTD database (mean age, 35 years, 268 post molar GTN [97%], 44 FIGO score 5-6 [16%], 104 FIGO stage III [38%]), 29 received the experimental treatment MTX + AVE (i.e., the single-arm group) and 247 received the control treatment MTX (i.e., the external control group). In the patients treated with MTX + AVE, the observed probability of hCG normalization was 96.6%. Risk ratio was 1.21 (95%CI, 1.06 to 1.39) and risk difference was 0.17 (95%CI, 0.05 to 0.28). Sensitivity analyses showed consistent results.

Conclusions: This study shows that, for low-risk GTN patients, a first-line treatment of MTX+AVE leads to a higher rate of hCG normalization than MTX alone. These findings reinforce the suggestions of the TROPHAMET clinical trial and encourage the conduct of a phase III trial.

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32MO Long-term follow-up shows improved outcomes for stage IC-IV MOGCTs in a multicentre international analysis

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Background: Malignant ovarian germ cell tumors (MOGCTs) are rare, aggressive malignancies predominantly affecting young women. The literature mainly consists of small studies suggesting advanced stage as an adverse prognostic factor. Few long-term follow-up data are available, showing 65% overall survival in stage IV disease. Here, we examine a large international series to define long-term prognosis.

Methods: We analysed data from 254 FIGO stage IC/M-IV MOGCT patients, requiring surgery and chemotherapy between 1971 and 2018 at Charing Cross Hospital and Mount Vernon Cancer Center (UK) and the Multicentre Italian Trials in Ovarian Cancer (MITO) centres.

Results: Most patients (87.8%, n=223) received surgery as initial treatment (50.4%, n=128 fertility-sparing, 37.4%, n=95 non-sparing). Chemotherapy mainly consisted of BEP (48%, n=122) and POMB/ACE (42.5%, n=108). First-line treatment resulted in a complete response in 84.6% (n=215), partial response or stable disease in 7.9% (n=20), while 4.7% (n=12) progressed. Overall, 37 patients (14.6%) died of disease, with the last death recorded 8 years after initial diagnosis. 5-, 10-, and 20-year estimated cancer-specific survival (CSS) rates were 85.9% (95%CI, 80.6-89.8), 83.2% (95%CI, 77.3-87.7), and 83.2% (95%CI, 77.3-87.7), respectively. According to FIGO-stage, 10-year estimated CSS rates were 92.3% (95%CI, 82.1-96.8) for stage IC/M, 79.5% (95%CI, 56.2-91.3) for stage II, 79.4%, (95%CI, 69.5-86.4) for stage III and 79.4% (95%CI, 61.5-89.7) for stage IV. The 10-year estimated CSS for dysgerminoma and Grade 2/3 immature teratoma was 94.7% (95%CI, 84.4-98.3) and 97.5% (95%CI, 83.4-99.6), respectively. For other histologies, CSS was significantly lower: 77.8% (95%CI, 61.4-87.9) for mixed MOGCTs; 71.7% (95%CI, 58.4-81.4) for yolk sac tumors (YST); 50.0% (95%CI, 5.9-84.5) for choriocarcinoma; and 33.3% (95%CI, 1.0-77.4) for embryonal carcinoma, $p<0.001$.

Conclusions: Our analysis shows (1) improved outcomes of patients with stage IC-IV MOGCTs, compared to previously published data with 80% long-term survival in stage IV disease and (2) a need for long term follow up, as late relapses can occur.

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