

## Bölüm 27

# GESTASYONEL TROFOBLASTİK TÜMÖRLERİN SİSTEMİK TEDAVİSİ VE TAKİBİ

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### GİRİŞ

Gestasyonel trofoblastik tümörler (diğer adıyla gestasyonel trofoblastik neoplaziler) trofoblastik dokunun anormal proliferasyonu sonucu oluşan bir grup malign neoplazmi ifade eder. Gestasyonel trofoblastik neoplaziler (GTN) invaziv mol, koryokarsinom, plasental site trofoblastik tümör (PSTT) ve epitelioid trofoblastik tümör (ETT) olmak üzere 4 histolojik alt tipten oluşmaktadır <sup>(1)</sup>. Günümüzde bir hayli etkin kemoterapi ajanları mevcut olup doğru tedavi stratejisi ile hastaların büyük çoğunluğunda kür elde edilebilmekte ve üreme potansiyelleri korunabilmektedir <sup>(2)</sup>. İnsan koryonik gonadotropin (hCG) hormonu tanıda, tedavi etkinliğini değerlendirmede ve relapsın saptanmasında önemli bir tümör marker olup tüm trofoblastik neoplaziler tarafından üretilmektedir <sup>(3)</sup>.

### TEDAVİ ÖNCESİ DEĞERLENDİRME

GTN tanısı konulan tüm hastalar tedavi öncesi ayrıntılı değerlendirilerek hastalığın yaygınlığı ve hastanın kemoterapiye uygunluğu belirlenmelidir.

1. Ayrıntılı öykü ve fizik muayene. Ayrıntılı pelvik muayene yapılarak spekulum ile vajinal metastaz açısından dikkatli değerlendirme yapılmalıdır. Vajinal metastazların bir hayli vasküler olması ve kanama riskinin yüksek olması nedeniyle biyopsi alınmamalıdır. Özellikle akciğer, karaciğer ve santral sinir sistemi metastazları göz önünde bulundurularak sistemik muayene yapılmalıdır.
2. Tedavi öncesi serum hCG seviyesi ölçülmelidir.
3. Tedavi öncesi tam kan sayımı, karaciğer, böbrek ve tiroid fonksiyon testleri yapılmalıdır.

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## Tedavi sonrası izlem

Komplet remisyon elde edilen hastalarda serum hCG düzeyi ayda bir kez ölçülmelidir. Bir yıl boyunca normal serum hCG düzeyi elde edildiği gösterilerek ayda bir kez ölçüm devam edilmelidir <sup>(12,54)</sup>. Nükslerin yaklaşık %85-95' i ilk 18 ay içinde gerçekleşmekte olup genellikle artmış serum hCG düzeyi ile saptanmaktadır <sup>(55)</sup>.

## Sonuç

GTN kürabilitesi yüksek bir hastalık olup prognozu mükemmeldir. Prognostik risk skoruna göre hastanın risk grubunun belirlenmesi tedavi yaklaşımını belirleyen en önemli noktadır. Düşük riskli hastalıkta %100' e varan oranda sağ kalım oranları elde edilebilmekte iken yüksek riskli hastalıkta bu oran % 80-90'lara ulaşabilmektedir <sup>(34,56)</sup>. Nadir görülen bir hastalık olması nedeniyle tedavinin deneyimli merkezlerde multidisipliner ekip tarafından yapılması önemlidir.

**Anahtar Kelimeler:** Gestasyonel trofoblastik neoplaziler, Gestasyonel trofoblastik tümörler, Metotreksat

## KAYNAKÇA

1. Sebire NJ, Lindsay I (2010) Current issues in the histopathology of gestational trophoblastic tumors. *Fetal Pediatr Pathol* 29 (1):30-44. doi:10.3109/15513810903266120
2. Goldstein DP, Berkowitz RS (2012) Current management of gestational trophoblastic neoplasia. *Hematology/oncology clinics of North America* 26 (1):111-131. doi:10.1016/j.hoc.2011.10.007
3. Goldstein DP, BR The diagnosis and management of molar pregnancy. In: EA F (ed) *Gestational Trophoblastic Neoplasms: Clinical Principles of Diagnosis and Management*. WB Saunders, Philadelphia, pp 143-175
4. Gamer EI, Garrett A, Goldstein DP, et al (2004) Significance of chest computed tomography findings in the evaluation and treatment of persistent gestational trophoblastic neoplasia. *The Journal of reproductive medicine* 49 (6):411-414
5. Ngan HY, Chan FL, Au VW, et al (1998) Clinical outcome of micrometastasis in the lung in stage IA persistent gestational trophoblastic disease. *Gynecologic oncology* 70 (2):192-194. doi:10.1006/gyno.1998.5088
6. Berkowitz RS, Birnholz J, Goldstein DP, Bernstein MR et al (1983) Pelvic ultrasonography and the management of gestational trophoblastic disease. *Gynecologic oncology* 15 (3):403-412
7. Bakri Y, Berkowitz RS, Goldstein DP, et al (1994) Brain metastases of gestational trophoblastic tumor. *The Journal of reproductive medicine* 39 (3):179-184
8. Athanassiou A, Begent RH, Newlands ES, Parker D, Rustin GJ, Bagshawe KDet et al. (1983) Central nervous system metastases of choriocarcinoma. 23 years' experience at Charing Cross Hospital. *Cancer* 52 (9):1728-1735. doi:10.1002/1097-0142(19831101)52:9<1728::aid-cnrcr2820520929>3.0.co;2-u
9. Horowitz NS, Goldstein DP, Berkowitz RS (2017) Placental site trophoblastic tumors and epithelioid trophoblastic tumors: Biology, natural history, and treatment modalities. *Gynecologic oncology* 144 (1):208-214. doi:10.1016/j.ygyno.2016.10.024
10. FIGO staging for gestational trophoblastic neoplasia 2000. FIGO Oncology Committee (2002). *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics* 77 (3):285-287

11. Kohorn EI (2002) Negotiating a staging and risk factor scoring system for gestational trophoblastic neoplasia. A progress report. *The Journal of reproductive medicine* 47 (6):445-450
12. ACOG Practice Bulletin #53. Diagnosis and treatment of gestational trophoblastic disease (2004). *Obstetrics and gynecology* 103 (6):1365-1377
13. Mortakis AE, Braga CA (1990) "Poor prognosis" metastatic gestational trophoblastic disease: the prognostic significance of the scoring system in predicting chemotherapy failures. *Obstetrics and gynecology* 76 (2):272-277
14. Dubuc-Lissoir J, Zweizig S, Schlaerth JB, Morrow CP et al (1992) Metastatic gestational trophoblastic disease: a comparison of prognostic classification systems. *Gynecologic oncology* 45 (1):40-45
15. DuBeshter B, Berkowitz RS, Goldstein DP, Cramer DW, Bernstein MR et al (1987) Metastatic gestational trophoblastic disease: experience at the New England Trophoblastic Disease Center, 1965 to 1985. *Obstetrics and gynecology* 69 (3 Pt 1):390-395
16. Lurain JR, Schink JC (2012) Importance of salvage therapy in the management of high-risk gestational trophoblastic neoplasia. *The Journal of reproductive medicine* 57 (5-6):219-224
17. Lurain JR (2002) Treatment of gestational trophoblastic tumors. *Curr Treat Options Oncol* 3 (2):113-124
18. Ngan HYS, Seckl MJ, Berkowitz RS, et al (2018) Update on the diagnosis and management of gestational trophoblastic disease. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics* 143 Suppl 2:79-85. doi:10.1002/ijgo.12615
19. Sita-Lumsden A, Short D, Lindsay I, et al (2012) Treatment outcomes for 618 women with gestational trophoblastic tumours following a molar pregnancy at the Charing Cross Hospital, 2000-2009. *British journal of cancer* 107 (11):1810-1814. doi:10.1038/bjc.2012.462
20. McNeish IA, Strickland S, Holden L, et al (2002) Low-risk persistent gestational trophoblastic disease: outcome after initial treatment with low-dose methotrexate and folinic acid from 1992 to 2000. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 20 (7):1838-1844. doi:10.1200/jco.2002.07.166
21. Lurain JR (2003) Pharmacotherapy of gestational trophoblastic disease. *Expert Opin Pharmacother* 4 (11):2005-2017. doi:10.1517/14656566.4.11.2005
22. Alazzam M, Tidy J, Hancock BW, et al. R, (2012) First-line chemotherapy in low-risk gestational trophoblastic neoplasia. *The Cochrane database of systematic reviews* (7):Cd007102. doi:10.1002/14651858.CD007102.pub3
23. Berkowitz RS, Goldstein DP, Bernstein MR (1990) Methotrexate infusion and folinic acid in the primary therapy of nonmetastatic gestational trophoblastic tumors. *Gynecologic oncology* 36 (1):56-59
24. Garrett AP, Garner EO, Goldstein DP, et al (2002) Methotrexate infusion and folinic acid as primary therapy for nonmetastatic and low-risk metastatic gestational trophoblastic tumors. 15 years of experience. *The Journal of reproductive medicine* 47 (5):355-362
25. Wong LC, Choo YC, Ma HK (1985) Methotrexate with citrovorum factor rescue in gestational trophoblastic disease. *American journal of obstetrics and gynecology* 152 (1):59-62. doi:10.1016/s0002-9378(85)80178-2
26. Shah NT, Barroilhet L, Berkowitz RS, et al (2012) A cost analysis of first-line chemotherapy for low-risk gestational trophoblastic neoplasia. *The Journal of reproductive medicine* 57 (5-6):211-218
27. Aghajanian C (2011) Treatment of low-risk gestational trophoblastic neoplasia. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 29 (7):786-788. doi:10.1200/jco.2010.31.0151
28. Growdon WB, Wolfberg AJ, Goldstein DP, et al. (2009) Evaluating methotrexate treatment in patients with low-risk postmolar gestational trophoblastic neoplasia. *Gynecologic oncology* 112 (2):353-357. doi:10.1016/j.ygyno.2008.11.003

29. Berkowitz RS, Goldstein DP, Bernstein MR (1986) Ten year's experience with methotrexate and folinic acid as primary therapy for gestational trophoblastic disease. *Gynecologic oncology* 23 (1):111-118
30. Maesta I, Nitecki R, Horowitz NS, et al (2018) Effectiveness and toxicity of first-line methotrexate chemotherapy in low-risk postmolar gestational trophoblastic neoplasia: The New England Trophoblastic Disease Center experience. *Gynecologic oncology* 148 (1):161-167. doi:10.1016/j.ygyno.2017.10.028
31. Ross GT, Goldstein DP, Hertz R, et al. (1965) Sequential use of methotrexate and actinomycin D in the treatment of metastatic choriocarcinoma and related trophoblastic diseases in women. *American journal of obstetrics and gynecology* 93:223-229. doi:10.1016/0002-9378(65)90661-7
32. Ross GT, Stolbach LL, Hertz R (1962) Actinomycin D in the treatment of methotrexate-resistant trophoblastic disease in women. *Cancer research* 22:1015-1017
33. Osathanondh R, Goldstein DP, Pastorfide GB (1975) Actinomycin D as the primary agent for gestational trophoblastic disease. *Cancer* 36 (3):863-866. doi:10.1002/1097-0142(197509)36:3<863::aid-cncr2820360306>3.0.co;2-g
34. Lawrie TA, Alazzam M, Tidy J, et al (2016) First-line chemotherapy in low-risk gestational trophoblastic neoplasia. *The Cochrane database of systematic reviews* (6):Cd007102. doi:10.1002/14651858.CD007102.pub4
35. Lurain JR, Chapman-Davis E, Hoekstra AV, et al (2012) Actinomycin D for methotrexate-failed low-risk gestational trophoblastic neoplasia. *The Journal of reproductive medicine* 57 (7-8):283-287
36. Deng L, Zhang J, Wu T, et al (2013) Combination chemotherapy for primary treatment of high-risk gestational trophoblastic tumour. *The Cochrane database of systematic reviews* (1):Cd005196. doi:10.1002/14651858.CD005196.pub4
37. Kim SJ, Bae SN, Kim JH, et al (1998) Effects of multiagent chemotherapy and independent risk factors in the treatment of high-risk GTN--25 years experiences of KRI-TRD. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics* 60 Suppl 1:S85-96
38. Alifrangis C, Agarwal R, Short D, et al. (2013) EMA/CO for high-risk gestational trophoblastic neoplasia: good outcomes with induction low-dose etoposide-cisplatin and genetic analysis. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 31 (2):280-286. doi:10.1200/jco.2012.43.1817
39. Bower M, Newlands ES, Holden L, et al. (1997) EMA/CO for high-risk gestational trophoblastic tumors: results from a cohort of 272 patients. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 15 (7):2636-2643. doi:10.1200/jco.1997.15.7.2636
40. Turan T, Karacay O, Tulunay G, et al (2006) Results with EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) chemotherapy in gestational trophoblastic neoplasia. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society* 16 (3):1432-1438. doi:10.1111/j.1525-1438.2006.00606.x
41. Xiang Y, Sun Z, Wan X, et al (2004) EMA/EP chemotherapy for chemorefractory gestational trophoblastic tumor. *The Journal of reproductive medicine* 49 (6):443-446
42. Kong Y, Yang J, Jiang F, et al (2017) Clinical characteristics and prognosis of ultra high-risk gestational trophoblastic neoplasia patients: A retrospective cohort study. *Gynecologic oncology* 146 (1):81-86. doi:10.1016/j.ygyno.2017.04.010
43. Wang J, Short D, Sebire NJ, et al. (2008) Salvage chemotherapy of relapsed or high-risk gestational trophoblastic neoplasia (GTN) with paclitaxel/cisplatin alternating with paclitaxel/etoposide (TP/TE). *Annals of oncology : official journal of the European Society for Medical Oncology* 19 (9):1578-1583. doi:10.1093/annonc/mdn181
44. Matsui H, Suzuka K, Iitsuka Y, et al. (2002) Salvage combination chemotherapy with 5-fluorouracil and actinomycin D for patients with refractory, high-risk gestational trophoblastic tumors. *Cancer* 95 (5):1051-1054. doi:10.1002/cncr.10790

45. Rathod PS, Kundargi R, Pallavi VR, et al. (2015) Refractory Gestational Trophoblastic Neoplasia: A Novel Drug Combination With Paclitaxel and Carboplatin Produces Durable Complete Remission. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society* 25 (9):1737-1741. doi:10.1097/igc.0000000000000552
46. Popadiuk C, Power P (2016) Pegylated Liposomal Doxorubicin Is an Active Agent for Chemotherapy-Resistant Choriocarcinoma: A Report of Two Cases. *The Journal of reproductive medicine* 61 (5-6):215-218
47. Newlands ES, Mulholland PJ, Holden L, et al. (2000) Etoposide and cisplatin/etoposide, methotrexate, and actinomycin D (EMA) chemotherapy for patients with high-risk gestational trophoblastic tumors refractory to EMA/cyclophosphamide and vincristine chemotherapy and patients presenting with metastatic placental site trophoblastic tumors. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 18 (4):854-859. doi:10.1200/jco.2000.18.4.854
48. Newlands ES, Bower M, Fisher RA, et al. (1998) Management of placental site trophoblastic tumors. *The Journal of reproductive medicine* 43 (1):53-59
49. Hyman DM, Bakios L, Gualtiere G, et al. (2013) Placental site trophoblastic tumor: analysis of presentation, treatment, and outcome. *Gynecologic oncology* 129 (1):58-62. doi:10.1016/j.ygyno.2012.12.029
50. Papadopoulos AJ, Foskett M, Seckl MJ, et al (2002) Twenty-five years' clinical experience with placental site trophoblastic tumors. *The Journal of reproductive medicine* 47 (6):460-464
51. Kingdon SJ, Coleman RE, Ellis L, et al. (2012) Deaths from gestational trophoblastic neoplasia: any lessons to be learned? *The Journal of reproductive medicine* 57 (7-8):293-296
52. Lybol C, Sweep FC, Harvey R, et al. (2012) Relapse rates after two versus three consolidation courses of methotrexate in the treatment of low-risk gestational trophoblastic neoplasia. *Gynecologic oncology* 125 (3):576-579. doi:10.1016/j.ygyno.2012.03.003
53. Golfier F, Labrousse C, Frappart L, et al. (2007) [Evaluation of treatment relating to gestational trophoblastic tumor registered to the French Trophoblastic Disease Reference Center (TDRC) in Lyon from 1999 to 2005]. *Gynecologie, obstetrique & fertilité* 35 (3):205-215. doi:10.1016/j.gyobfe.2006.12.023
54. Society of Gynecologic Oncologists Clinical Practice Guidelines. Practice guidelines: gestational trophoblastic disease (1998). *Oncology (Williston Park, NY)* 12 (3):455-458, 461
55. Mutch DG, Soper JT, Babcock CJ, et al. (1990) Recurrent gestational trophoblastic disease. Experience of the Southeastern Regional Trophoblastic Disease Center. *Cancer* 66 (5):978-982.
56. Lurain JR, Elfstrand EP (1995) Single-agent methotrexate chemotherapy for the treatment of nonmetastatic gestational trophoblastic tumors. *American journal of obstetrics and gynecology* 172 (2 Pt 1):574-579. doi:10.1016/0002-9378(95)90575-8