

## Bölüm 14

# NÜKS/METASTATİK BAŞ BOYUN KANSERLERİNDE GÜNCEL SİSTEMİK TEDAVİLER

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### GİRİŞ

Baş-boyun kanserleri; oral kavite, orofarenks, nazofarenks, hipofarenks, larinks, nazal kavite, paranazal sinüsler ve tükrük bezlerinden kaynaklanan heterojen bir hastalık grubudur. %95'ten fazlası skuamoz hücreli karsinom histolojisine sahiptir. Tüm dünyada yıllık 550000 yeni vaka ve 380000 ölümlle en sık altıncı insidansa sahip tümör grubudur (Fitzmaurice & ark. 2016). Kemoterapi ve radyoterapi yanında yeni nesil tedavi seçenekleri olan hedefe yönelik tedaviler ve immunoterapilerdeki tüm gelişmelere rağmen ileri evre baş ve boyun kanserinde prognoz kötüdür ve 5 yıllık sağkalımlar %20'nin altındadır.

Sağkalım üzerinde etkili olduğu bilinen bazı faktörler tanımlanmıştır. ECOG performans skoru 0-1 olanlar, kötü diferansiye histolojiye sahip olanlar, birinci seri kemoterapiye iyi yanıt verenler ve human papilloma virus (HPV) ilişkili orofarengeal kanserler daha iyi prognoza sahiptir. Tanı sırasında kilo kaybı olması, ECOG performans skoru 2 ve üzerinde olması, daha önce radyoterapi (RT) öyküsü olması, aktif sigara kullanıcısı olması ve komorbid hastalıkların olması kötü prognozla ilişkilidir (Recondo & ark. 1991).

Metastatik baş ve boyun kanserlerinde cerrahi veya kemoradyoterapi gibi kuratif tedavi seçenekleri ile kür elde etmek mümkün olmadığı için öncelikle sistemik tedaviler gündeme gelmektedir. Hastanın ECOG performans skoru, primer tümör lokalizasyonu, hastalık yükü, histolojik alt tipi, hastanın daha önce aldığı tedaviler, komorbid hastalıklar ve semptom varlığı tedavi seçiminde göz önünde bulundurulması gereken faktörlerdir. Temel tedavi seçenekleri; en iyi destek tedavisi ile birlikte tek ajan kemoterapi rejimleri, kombinasyon kemoterapileri, kemoterapi ve hedefe yönelik tedavi kombinasyonları, immunoterapiler ve palyatif RT olarak sıralanabilir.

leri ve %25 oranında uzun dönem sağkalımlar bildirilmektedir. Tümör biyolojisi ve immünolojisi anlaşıldıkça ve yeni nesil immunoterapi ajanları ile birlikte daha uzun süreli sağkalımların elde edilebileceği öngörülmektedir.

## **KAYNAKLAR**

1. Argiris A, Ghebremichael M, Gilbert J, Lee JW, Sachidanandam K, Kolesar JM, et al. Phase III randomized, placebo-controlled trial of docetaxel with or without gefitinib in recurrent or metastatic head and neck cancer: an Eastern Cooperative Oncology Group trial. *J Clin Oncol* 2013;31(11):1405–14.
2. Bauml J, Seiwert TY, Pfister DG, et al. Pembrolizumab for Platinum- and Cetuximab-Refractory Head and Neck Cancer: Results From a Single-Arm, Phase II Study. *J Clin Oncol* 2017; 35:1542.
3. Burtneß B, Goldwasser MA, Flood W, Mattar B, Forastiere AA. Eastern Cooperative Oncology Group. Phase III randomized trial of cisplatin plus placebo compared with cisplatin plus cetuximab in metastatic/recurrent head and neck cancer: an Eastern Cooperative Oncology Group study. *J Clin Oncol*. 2005;23(34):8646–54.
4. Burtneß B, Harrington KJ, Greil R, et al. KEYNOTE-048: Phase 3 study of first-line pembrolizumab for recurrent/metastatic head and neck squamous cell carcinoma (abstract). *ESMO* 2018; LBA8\_PR
5. Carter SK, Slavik M. Current investigational drugs of interest in the chemotherapy program of the National Cancer Institute. *Natl Cancer Inst Monogr*. 1977;45:101–21.
6. Cohen EE, Davis DW, Karrison TG, Seiwert TY, Wong SJ, Nattam S, et al. Erlotinib and bevacizumab in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck: a phase I–II study. *Lancet Oncol*. 2009;10(3):247–57.
7. Cohen EEW, Soulières D, Le Tourneau C, et al. Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. *Lancet* 2019; 393:156.
8. Colevas AD, Posner MR. Docetaxel in head and neck cancer: a review. *Am J Clin Oncol* 1998; 21:482.
9. Ferris RL, Blumenschein G Jr, Fayette J, et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. *N Engl J Med* 2016; 375:1856.
10. Fitzmaurice C, Allen C, et al. Global Burden of Disease Cancer Collaboration, Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. *JAMA Oncol*. 2016.
11. Forastiere AA, Metch B, Schuller DE, et al. Randomized comparison of cisplatin plus fluorouracil and carboplatin plus fluorouracil versus methotrexate in advanced squamous-cell carcinoma of the head and neck: a Southwest Oncology Group study. *J Clin Oncol* 1992; 10:1245.
12. Forastiere AA, Shank D, Neuberg D, et al. Final report of a phase II evaluation of paclitaxel in patients with advanced squamous cell carcinoma of the head and neck: an Eastern Cooperative Oncology Group trial (PA390). *Cancer* 1998; 82:2270.
13. Gibson MK, Li Y, Murphy B, et al. Randomized phase III evaluation of cisplatin plus fluorouracil versus cisplatin plus paclitaxel in advanced head and neck cancer (E1395): an intergroup trial of the Eastern Cooperative Oncology Group. *J Clin Oncol* 2005; 23:3562.
14. Glisson BS, Murphy BA, Frenette G, et al. Phase II Trial of docetaxel and cisplatin combination chemotherapy in patients with squamous cell carcinoma of the head and neck. *J Clin Oncol* 2002; 20:1593.
15. Harrington KJ, Ferris RL, Blumenschein G Jr, et al. Nivolumab versus standard, single-agent therapy of investigator's choice in recurrent or metastatic squamous cell carcinoma of the head and neck (CheckMate 141): health-related quality-of-life results from a randomised, phase 3 trial. *Lancet Oncol* 2017; 18:1104.

16. Jacobs C, Lyman G, Velez-García E, et al. A phase III randomized study comparing cisplatin and fluorouracil as single agents and in combination for advanced squamous cell carcinoma of the head and neck. *J Clin Oncol* 1992; 10:257.
17. Machiels JP, Haddad RI, Fayette J, Licitra LE, Tahara M, Vermorken JB, et al. Afatinib versus methotrexate as second-line treatment in patients with recurrent or metastatic squamous cell carcinoma of the head and neck progressing on or after platinum-based therapy (LUX Head and Neck 1): an open-label, randomized phase III trial. *Lancet Oncol.* 2015;16(5):583–94.
18. Malhotra B, Moon J, Kucuk O, et al. Phase II trial of biweekly gemcitabine and paclitaxel with recurrent or metastatic squamous cell carcinoma of the head and neck: Southwest Oncology Group study S0329. *Head Neck* 2014; 36:1712.
19. Nakano K, Marshall S, Taira S, et al. A comparison of weekly paclitaxel and cetuximab with the EXTREME regimen in the treatment of recurrent/metastatic squamous cell head and neck carcinoma. *Oral Oncol.* 2017;73:21–6.
20. Peeters M, Cohn A, Kohne CH, Douillard JY. Panitumumab in combination with cytotoxic chemotherapy for the treatment of metastatic colorectal carcinoma. *Clin Colorectal Cancer.* 2012;11:14–23.
21. Recondo G, Armand JP, Tellez-Bernal E, et al. Recurrent and/or metastatic head and neck squamous cell carcinoma: a clinical, univariate and multivariate analysis of response and survival with cisplatin-based chemotherapy. *Laryngoscope* 1991; 101:494.
22. Schöffski P, Catimel G, Planting AS, et al. Docetaxel and cisplatin: an active regimen in patients with locally advanced, recurrent or metastatic squamous cell carcinoma of the head and neck. Results of a phase II study of the EORTC Early Clinical Studies Group. *Ann Oncol* 1999; 10:119.
23. Soulieres D, Senzer NN, Vokes EE, Hidalgo M, Agarwala SS, Siu LL. Multicenter phase II study of erlotinib, an oral epidermal growth factor receptor tyrosine kinase inhibitor, in patients with recurrent or metastatic squamous-cell cancer of the head and neck. *J Clin Oncol.* 2004;22(1):77–85.
24. Stewart JS, Cohen EE, Licitra L, Van Herpen CM, Khorprasert C, Soulieres D, et al. Phase III study of gefitinib compared with intravenous methotrexate for recurrent squamous-cell carcinoma of the head and neck [corrected]. *J Clin Oncol.* 2009;27(11):1864–71.
25. Taylor RJ, Chan SL, Wood A. FcγRIII polymorphism and cetuximab induced cytotoxicity in squamous-cell carcinoma of the head and neck. *Cancer Immunol Immunother.* 2009;58:997–1006.
26. Vermorken JB, Mesia R, Rivera F, et al. Platinum-based chemotherapy plus cetuximab in head and neck cancer. *N Engl J Med* 2008; 359:1116.
27. Vermorken JB, Stohlmacher-Williams J, Davidenko I, Licitra L, Winquist E, Villanueva C, et al. Cisplatin and fluorouracil with or without panitumumab in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck (SPECTRUM): an open-label phase III randomized trial. *Lancet Oncol.* 2013;14(8):697–710.
28. Vermorken JB, Trigo J, Hitt R, Koralewski P, Diaz-Rubio E, Rolland F, et al. Open-label, uncontrolled, multicenter phase II study to evaluate the efficacy and toxicity of cetuximab as single agent in patients with recurrent and/or metastatic squamous-cell carcinoma of the head and neck who failed to respond to platinum-based therapy. *J Clin Oncol.* 2007;25(16):2171–7.
29. Wirth LJ, Dakhil S, Kornek G, Axelrod R, Adkins D, Pant S, et al. PARTNER: an open-label, phase II study of docetaxel/cisplatin with or without Panitumumab as first-line treatment for recurrent or metastatic squamous cell carcinoma of the head and neck. *Oral Oncol.* 2016;61:31–40.
30. Wittes RE. Chemotherapy of head and neck cancer. *Otolaryngol Clin North Am.* 1980;13:515–20.
31. Wittes RE, Cvitkovic E, Shah J, Gerold FP, Strong EW. CIS-Dichlorodiammineplatinum(II) in the treatment of epidermoid carcinoma of head and neck. *Cancer Treat Rep.* 1977;61(3):359–66.
32. Wittes R, Heller K, Randolph V, Howard J, Vallejo A, Farr H, et al. Cis-Dichlorodiammineplatinum(II)-based chemotherapy as initial treatment of advanced head and neck cancer. *Cancer Treat Rep.* 1979;63(9–10):1533–8.