

BÖLÜM

11

MİKOZİS FUNGOİDESTE SİSTEMİK TEDAVİ

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GİRİŞ

Mikozis fungoides (MF) derinin birincil lenfoması olarak tanımlanmaktadır. Ancak ileri evre hastalarda, lenf nodu, iç organlar vb. tutulum yapabilen T hücre aracılı Non-Hodgkin lenfoma sınıfında yer almaktadır. Sezary Sendromu (SS) ise periferik kanda malign Sezary hücrelerinin gözlendiği daha agresif bir varyantıdır.

MF için standart evreleme sistemi deri (T), lenf düğümleri (N), iç organ tutulumu (M) ve kanın (B) değerlendirilmesine dayanır (Duate ve ark., 2008). MF tedavisinde topikal ve sistemik kullanılabilen birçok tedavi yöntemi mevcuttur. Sistemik tedaviler daha çok, ileri evre MF tedavilerinde tercih edilir. Bu bölümde MF tedavisinde kullanılabilen sistemik tedavilerden bahsedilecektir.

MF ülkemizde dermatologlar, hematologlar ve onkologlar tarafından multi-disipliner bir ekip tarafından takip edilir. Özellikle erken evre MF hastaları daha sık dermatologlar tarafından, ileri evre ise hematolog veya onkologlar tarafından takip edilir. İleri MF genellikle kronik ve tekrarlayıcı bir kliniğe sahip olabilir. Tedavi amaçları semptomların gerilemesi, uzun süreli hastalık kontrolü veya hastalığın kontrol altına alınması sayılabilir (Olsen ve ark., 2011).

Topikal tedaviler ile yeterince yanıt alınamayan hastalarda sistemik tedavi ajanları seçilebilir. Sistemik tedavi yöntemleri tek veya kombine halde kullanılabilir. Unutulmaması gereken hastalığın nüks etme olasılığının yüksek olmasıdır.

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KAYNAKLAR

- Duarte, R. F., Schmitz, N., Servitje, O., & Sureda, A. (2008). Haematopoietic stem cell transplantation for patients with primary cutaneous T-cell lymphoma. *Bone marrow transplantation*, 41(7), 597-604.
- Olsen, E. A., Rook, A. H., Zic, J., Kim, Y., Porcu, P., Querfeld, C., ... & Duvic, M. (2011). Sezary syndrome: immunopathogenesis, literature review of therapeutic options, and recommendations for therapy by the United States Cutaneous Lymphoma Consortium (USCLC). *Journal of the American Academy of Dermatology*, 64(2), 352-404.
- Zackheim, H. S., Kashani-Sabet, M., & Hwang, S. T. (1996). Low-dose methotrexate to treat erythrodermic cutaneous T-cell lymphoma: results in twenty-nine patients. *Journal of the American Academy of Dermatology*, 34(4), 626-631.
- Wilson, L. D., Licata, A. L., Braverman, I. M., Edelson, R. L., Heald, P. W., Feldman, A. M., & Kacinski, B. M. (1995). Systemic chemotherapy and extracorporeal photochemotherapy for T3 and T4 cutaneous T-cell lymphoma patients who have achieved a complete response to total skin electron beam therapy. *International journal of radiation oncology, biology, physics*, 32(4), 987-995.
- Scarlsbrick, J. J., Morris, S., Azurdia, R., Illidge, T., Parry, E., Graham-Brown, R., ... & Wain, E. M. (2013). UK consensus statement on safe clinical prescribing of bexarotene for patients with cutaneous T-cell lymphoma. *British Journal of Dermatology*, 168(1), 192-200.
- Duvic, M., Hymes, K., Heald, P., Breneman, D., Martin, A. G., Myskowski, P., ... & Yocum, R. C. (2001). Bexarotene is effective and safe for treatment of refractory advanced-stage cutaneous T-cell lymphoma: multinational phase II-III trial results. *Journal of clinical oncology*, 19(9), 2456-2471.
- Abel, E. A., Sendagorta, E., Hoppe, R. T., & Hu, C. H. (1987). PUVA treatment of erythrodermic and plaque-type mycosis fungoides: ten-year follow-up study. *Archives of dermatology*, 123(7), 897-901.
- Hönigsmann, H., Brenner, W., Rauschmeier, W., Konrad, K., & Wolff, K. (1984). Photochemotherapy for cutaneous T cell lymphoma: a follow-up study. *Journal of the American Academy of Dermatology*, 10(2), 238-245.
- Kuzel, T. M., Roenigk Jr, H. H., Samuelson, E., Herrmann, J. J., Hurria, A., Rademaker, A. W., & Rosen, S. T. (1995). Effectiveness of interferon alfa-2a combined with phototherapy for mycosis fungoides and the Sézary syndrome. *Journal of clinical oncology*, 13(1), 257-263.
- Olsen, E. A., Rosen, S. T., Vollmer, R. T., Variakojis, D., Roenigk Jr, H. H., Diab, N., & Zeffren, J. (1989). Interferon alfa-2a in the treatment of cutaneous T cell lymphoma. *Journal of the American Academy of Dermatology*, 20(3), 395-407.
- Kuzel, T. M., Roenigk Jr, H. H., Samuelson, E., & Rosen, S. T. (1992). Suppression of Anti-Interferon α -2a Antibody Formation in Patients With Mycosis Fungoides by Exposure to Long-Wave UV Radiation in the A Range and Methoxsalen Inges-

- tion. *JNCI: Journal of the National Cancer Institute*, 84(2), 119-121.
- Piekarz, R. L., Frye, R., Turner, M., Wright, J. J., Allen, S. L., Kirschbaum, M. H., ... & Bates, S. E. (2009). Phase II multi-institutional trial of the histone deacetylase inhibitor romidepsin as monotherapy for patients with cutaneous T-cell lymphoma. *Journal of clinical oncology*, 27(32), 5410.
- Whittaker, S. J., Demierre, M. F., Kim, E. J., Rook, A. H., Lerner, A., Duvic, M., ... & Kim, Y. H. (2010). Final results from a multicenter, international, pivotal study of romidepsin in refractory cutaneous T-cell lymphoma. *J Clin Oncol*, 28(29), 4485-4491.
- Mann, B. S., Johnson, J. R., He, K., Sridhara, R., Abraham, S., Booth, B. P., ... & Pazdur, R. (2007). Vorinostat for treatment of cutaneous manifestations of advanced primary cutaneous T-cell lymphoma. *Clinical Cancer Research*, 13(8), 2318-2322.
- Olsen, E. A., Kim, Y. H., Kuzel, T. M., Pacheco, T. R., Foss, F. M., Parker, S., ... & Duvic, M. (2007). Phase IIb multicenter trial of vorinostat in patients with persistent, progressive, or treatment refractory cutaneous T-cell lymphoma. *Journal of clinical oncology*, 25(21), 3109-3115.
- Kim, Y. H., Tavallaee, M., Sundram, U., Salva, K. A., Wood, G. S., Li, S., ... & Horwitz, S. M. (2015). Phase II investigator-initiated study of brentuximab vedotin in mycosis fungoides and Sézary syndrome with variable CD30 expression level: a multi-institution collaborative project. *Journal of Clinical Oncology*, 33(32), 3750.
- Fuji, S., Inoue, Y., Utsunomiya, A., Moriuchi, Y., Uchimar, K., Choi, I., ... & Fukuda, T. (2016). Pretransplantation anti-CCR4 antibody mogamulizumab against adult T-cell leukemia/lymphoma is associated with significantly increased risks of severe and corticosteroid-refractory graft-versus-host disease, nonrelapse mortality, and overall mortality. *Journal of Clinical Oncology*, 34(28), 3426-3433.
- Lundin, J., Hagberg, H., Repp, R., Cavallin-Ståhl, E., Fredén, S., Juliusson, G., ... & Osterborg, A. (2003). Phase 2 study of alemtuzumab (anti-CD52 monoclonal antibody) in patients with advanced mycosis fungoides/Sézary syndrome. *Blood*, 101(11), 4267-4272.
- Lenihan, D. J., Alencar, A. J., Yang, D., Kurzrock, R., Keating, M. J., & Duvic, M. (2004). Cardiac toxicity of alemtuzumab in patients with mycosis fungoides/Sézary syndrome. *Blood*, 104(3), 655-658.
- Bernengo, M. G., Quaglino, P., Comessatti, A., Ortoncelli, M., Novelli, M., Lisa, F., & Fierro, M. T. (2007). Low-dose intermittent alemtuzumab in the treatment of Sézary syndrome: clinical and immunologic findings in 14 patients. *Haematologica*, 92(6), 784-794.
- Gottlieb, S. L., Wolfe, J. T., Fox, F. E., DeNardo, B. J., Macey, W. H., Bromley, P. G., ... & Rook, A. H. (1996). Treatment of cutaneous T-cell lymphoma with extracorporeal photopheresis monotherapy and in combination with recombinant interferon alfa: a 10-year experience at a single institution. *Journal of the American Academy of Dermatology*, 35(6), 946-957.

- Richardson, S. K., Lin, J. H., Vittorio, C. C., Kim, E. J., Yoon, J. S., Junkins-Hopkins, J., & Rook, A. H. (2006). High clinical response rate with multimodality immunomodulatory therapy for Sezary syndrome. *Clinical Lymphoma and Myeloma*, 7(3), 226-232.
- Cheeley, J., Sahn, R. E., DeLong, L. K., & Parker, S. R. (2013). Acitretin for the treatment of cutaneous T-cell lymphoma. *Journal of the American Academy of Dermatology*, 68(2), 247-254.
- Bunn, P. A., Hoffman, S. J., Norris, D., Golitz, L. E., & Aeling, J. L. (1994). Systemic therapy of cutaneous T-cell lymphomas (mycosis fungoides and the Sezary syndrome). *Annals of internal medicine*, 121(8), 592-602.
- Rosen, S. T., & Foss, F. M. (1995). Chemotherapy for mycosis fungoides and the Sezary syndrome. *Hematology/oncology clinics of North America*, 9(5), 1109-1116.