

# 8. Bölüm

## İTERSTİSYEL AKCİĞER HASTALIKLARINDA TEDAVİ

Şilan IŞIK<sup>1</sup>

### GİRİŞ

Diffüz parankimal akciğer hastalıkları benzer klinik, radyografik, fizyolojik veya patolojik bulgular nedeniyle birlikte sınıflandırılan ve genellikle interstisyel akciğer hastalıkları olarak adlandırılan heterojen bir hastalık grubudur (1). İnterstisyel akciğer hastalıkları klinik, etyolojik ve histopatolojik özelliklerine göre birbirinden ayrılan yaklaşık 200 kadar farklı hastalığı içeren bir hastalık grubudur (2). Tedavi seçenekleri ve prognoz interstisyel akciğer hastalıkları tipleri arasında farklılık göstermektedir, bu nedenle doğru tanı bu hastalık grubunda önem taşımaktadır.

### GENEL ÖNLEMLER

#### a.Multidisipliner Yaklaşım

Hastaların interstisyel akciğer hastalıkları üzerine spesifikleşmiş bir merkezde göğüs hastalıkları, kardiyoji, radyoloji, romatoloji, göğüs cerrahi ve patoloji uzmanları ile oluşan multidisipliner bir ekip tarafından tanıdan tedaviye kadar olan süreçte izlenmesi gerekmektedir (3).

<sup>1</sup> Uzm. Dr., S.B.Ü.Van Bölge Eğitim ve Araştırma Hastanesi, Göğüs Hastalıkları Klğini, dr.silan.ankara@gmail.com

## SONUÇ

İAH yaşam kalitesini ileri derece düşürdüğünden uygun hasta yönetimi önemlidir. Bu hastalık multi- disiplinler bir yaklaşımı gerekmektedir. Tedavi ve prognoz İAH'nın türüne göre değişir. Bu hastalık gruplarında en sık kullanılan tedaviler kortikosteroidler, immünsüpresifler, antifibrotik ve antioksidan ajanlardır. Tedavi başlanmış olgularda ilaç yan etkileri açısından dikkatli izlem gereklidir. Gereken olgularda oksijen desteği başlanmalıdır. Son dönem fibrozis gelişen olgularda akciğer nakli açısından değerlendirme yapılmalıdır.

## KAYNAKÇA

1. Schwartz M, King Jr TE. (2011) *Interstitial Lung disease*. Shelton : People's Medical Clearing House,.
2. Demedts M, Wells AU, Antó JM, et al. Interstitial lung diseases: an epidemiological overview. 32: 2-16., *Eur Respir J Suppl*, 2001.
3. Wells AU, Hirani N and BTS interstitial lung diseases guideline group: İnterstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. *Thorax* 2008: 6.
4. Tabak L, Özdemir Kumbasar Ö, editörler.(2013). Diffüz parankimal akciğer hastalıkları. İstanbul : *Türk Toraks Derneği Toraks Kitapları*,.
5. Collard HR, Tino G, Noble PW, etc.( 2017), Patient experiences with pulmonary fibrosis.: *Respir Med., Cilt ;101(6):1350*.
6. Ferreira A, Garvey C, Connors GL, et al .Pulmonary rehabilitation in interstitial lung disease: benefits and predictors of response. *Chest. 2009;135(2):442*. Epub 2008 Oct 10. .
7. Vainshelboim B, Oliveira J, Yehoshua L, et al.Exercise training-based pulmonary rehabilitation program is clinically beneficial for idiopathic pulmonary fibrosis. . *Respiration, 2014, Cilt 88(5):378*. Epub 2014 Oct 23. .
8. Bradley B, Branley HM, Egan JJ, et al. (2008).İnterstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. *Thorax*.;63(suppl\_5):1-58.
9. Lee JS, McLaughlin S, Collard HR. Comprehensive care of the patient with idiopathic pulmonary fibrosis. *Curr Opin Pulm Med. 2011 Sep;17(5):348-54*. .
10. King TE Jr. Idiopathic interstitial pneumonias. [kitap yaz.] King TE Jr (eds). *Schwarz MI. Interstitial Lung Disease*. Londra : BC Decker Inc, Hamilton, 2003: 701-86.
11. Kim R, Meyer KC. Therapies for interstitial lung disease: past,present and future. *Therapeutic Advances in Respiratory Disease 2008; 2: 319-38*.
12. Westall GP, Stirling RG, Cullinan P, et al. Sarcoidosis. [kitap yaz.] King TE Jr (eds). *Schwarz MI. Interstitial Lung Disease*. Londra : yazarı bilinmiyor, 2003.
13. Alberts C, Van der Mark TW, Jansen HM. Inhaled budesonide in pulmonary sarcoiidosis.a double-blind, placebo-controlled study. *Eur Respir J* 1995; 8: 682-8.
14. TS/ERS. Idiopathic pulmonary fibrosis: diagnosis and treatment (international consensus statement).(2000). *Am J Respir Crit Care Med ve 646-64., 161*:.
15. Raghu G, Anstrom KJ, King TE Jr, et al.Idiopathic Pulmonary Fibrosis Clinical Research Network,. Prednisone, azathioprine, and N-acetylcysteine for pulmonary fibrosis. *N Engl J Med. 2012;366(21):1968*. Epub 2012 May 20. .

16. Haslam PL, Turton CW, Lukoszek A, et al. Bronchoalveolar lavage fluid cell counts in cryptogenic fibrosing alveolitis and their relation to therapy. *Thorax* 1980;38:328-39, 35.
17. Kolb M, Kirschner J, Riedel W, et al. Cyclophosphamide pulse therapy in idiopathic pulmonary fibrosis. *Eur Respir J*. 1998;12(6):1409.
18. Johnson MA, Kwan S, Snell NJ, et al. Randomised controlled trial comparing prednisolone alone with cyclophosphamide and low dose prednisolone in combination in cryptogenic fibrosing alveolitis. *Thorax*. 1989;44(4):280.
19. Collard HR, Ryu JH, Douglas WW, et al. Combined corticosteroid and cyclophosphamide therapy does not alter survival in idiopathic pulmonary fibrosis. *Chest*. 2004;125(6):2169.
20. King TE Jr, King TE. Idiopathic interstitial pneumonias. . [kitap yaz.] King TE Jr (eds). *Schwarz MI. Interstitial Lung Disease*. 3 ed. London: BC Decker Inc, Hamilton, 2003: 701-86.
21. Swigris JJ, Olson AL, Fisher A, et al. Mycophenolate mofetil is safe, well tolerated and preserves lung function in patients with connective tissue disease-related interstitial lung disease. *Chest* 2006; 130: 30-6.
22. Alton EW, Johnson M, Turner-Warwick M. Advanced cryptogenic fibrosing alveolitis: preliminary report on treatment with cyclosporin A. *Respir Med*. 1989;83(4):277.
23. Lower, EE, Baughman, RP, Winget, D. The long term use of methotrexate in patients with chronic symptomatic sarcoidosis. *Sarcoidosis*. 1992; 9:465S.
24. Baughman RP, Winget DB, Lower EE. Methotrexate is steroid sparing in acute Sarcoidosis: results of a double blind, randomized trial. 12. basım .*Sarcoidosis Vasc Diffuse Lung Dis* 2000; 17: 60-6.
25. Behr J, Degenkolb B, Krombach F, Vogelmeier C. Intracellular glutathione and bronchoalveolar cells in fibrosing alveolitis: effects of N-acetylcysteine. *Eur Respir J*. 2002;19(5):906.
26. Demedts M, Behr J, Buhl R, Costabel U, et al. High-dose acetylcysteine in idiopathic pulmonary fibrosis. *N Engl J Med*. 2005;353(21):2229.
27. Martinez FJ, de Andrade JA, Anstrom KJ, .Randomized trial of acetylcysteine in idiopathic pulmonary fibrosis. . Idiopathic Pulmonary Fibrosis Clinical Research Network, *N Engl J Med*. 2014;370(22):2093. Epub 2014 May 18.
28. Raghu G, DeAndrade J, Anstrom KJ, et al. A double blind, placebo-controlled, randomized trial of N-acetylcysteine in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med*. 2014;189:A6601.
29. Scotton CJ, Chambers RC. Molecular targets in pulmonary fibrosis: the myofibroblast in focus. *Chest*. 2007;132(4):1311.
30. Nathan SD, Albera C, Bradford WZ, et al. Effect of pirfenidone on mortality: pooled analyses and meta-analyses of clinical trials in idiopathic pulmonary fibrosis. *Lancet Respir Med*. 2017 Jan;5(1):33-41.
31. US Food and Drug Administration (FDA) approved product information. US National Library of Medicine. Pirfenidone. <http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=0ab861c2-d5ca-4f92-854c-6477971a1b38> (Accessed on October 30, 2014).
32. Wollin L, Wex E, Pautsch A, et al. Mode of action of nintedanib in the treatment of idiopathic pulmonary fibrosis. *Eur Respir J* 2015; 45: 1434-45.
33. Laursen S, Sidhu R, Goodall M, Adler AI, NICE guidance on nintedanib for treating idiopathic pulmonary fibrosis. *Lancet Respir Med*. 2016;4(3):176. Epub 2016 Jan 27.
34. Richeldi L, du Bois RM, Raghu G, et al. Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. *N Engl J Med* 2014; 370: 2071-82.
35. Wuyts WA, Kolb M, Stowasser S, et al. First data on efficacy and safety of nintedanib in patients with idiopathic pulmonary fibrosis and forced vital capacity of  $\leq 50$  % of predicted value. *Lung* 2016; 194: 739-43.
36. Douglas WW, Ryu JH, Schroeder DR. Idiopathic pulmonary fibrosis: Impact of oxygen and colchicine, prednisone, or no therapy on survival. *Am J Respir Crit Care Med*. 2000;161(4 Pt 1):1172.

37. Raghu G, Brown KK, Bradford WZ, et al. A placebo controlled trial of interferon gamma- 1b in patients with idiopathic pulmonary fibrosis. *New Engl J Med* 2004; 350: 125-33.
38. Gagermeier J, Dauber J, Yousem S, et al .Abnormal vascular phenotypes in patients with idiopathic pulmonary fibrosis and secondary pulmonary hypertension. *Chest* 2005; 128: 601.
39. Kubo H, Nakayama K, Yanai M, et al.Anticoagulant therapy for idiopathic pulmonary fibrosis. *Chest*. 2005;128(3):1475. .
40. Raghu G, Rochweg B, Zhang Y, et al. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis. An Update of the 2011 Clinical Practice Guideline. ...American Thoracic Society.; *Am J Respir Crit Care Med*. 2015;192(2):e3. .
41. Raghu G, King TE Jr, Behr J, et al .Quality of life and dyspnoea in patients treated with bosentan for idiopathic pulmonary fibrosis (BUILD-1) *Eur Respir J* 2010; 35: 118.
42. Raghu G, Million-Rousseau R, Morganti A, , MUSIC Study Group. Macitentan for the treatment of idiopathic pulmonary fibrosis: the randomised controlled MUSIC trial. *Respir J*. 2013 Dec;42(6):1622-32. *Epub* 2013 May 16. .
43. Raghu G, Behr J, Brown KK, et al., ARTEMIS-ITreatment of idiopathic pulmonary fibrosis with ambrisentan: a parallel, randomized trial. *Ann Intern Med*. 2013;158(9):641. .
44. Raghu G, Collard HR, Egan JJ,et al.An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med*. 2011;183(6):788. .
45. Behr J, Kolb M, Song JW,et al. Nintedanib and Sildenafil in Patients with Idiopathic Pulmonary Fibrosis and Right Heart Dysfunction. A Prespecified Subgroup Analysis of a Double-Blind Randomized Clinical Trial (INSTAGE). *Am J Respir Crit Care Med*. 2019;200(12):1505. .
46. Murray LA, Chen Q, Kramer MS, et al.TGF-beta driven lung fibrosis is macrophage dependent and blocked by Serum amyloid P. . *Int J Biochem Cell Biol*. 2011;43(1):154. *Epub* 2010 Oct 29. .
47. Raghu G, van den Blink B, Hamblin MJ,et al. Effect of Recombinant Human Pentraxin 2 vs Placebo on Change in Forced Vital Capacity in Patients With Idiopathic Pulmonary Fibrosis: A Randomized Clinical Trial. *JAMA*. 2018;319(22):2299. .
48. Maher TM, van der Aar EM, Van de Steen O, et al. Safety, tolerability, pharmacokinetics, and pharmacodynamics of GLPG1690, a novel autotaxin inhibitor, to treat idiopathic pulmonary fibrosis (FLORA): a phase 2a randomised placebo-controlled trial. *Lancet Respir Med*. 2018;6(8):627. *Epub* 2018 May 20. .
49. Group, Toronto Lung Transplant. Unilateral lung transplantation for pulmonary fibrosis.: *N Engl J Med*. 1986;314(18):1140. .
50. International Society for Heart and Lung Transplantation Registry. Adult Lung Transplantation Statistics: Kaplan-Meier Survival by Major Diagnosis. <https://ishltregistries.org/registries/slides.asp> (Accessed on July 21, 2020).
51. Weill D, Benden C, Corris PA, et al.Transplantation., A consensus document for the selection of lung transplant candidates: 2014--an update from the Pulmonary Transplantation Council of the International Society for Heart and Lung. *J Heart Lung Transplant*. 2015;34(1):1. .
52. Bradley B, Branley HM, Egan JJ, et al. Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. . 63(suppl\_5):1-58., *Thorax*, 2008.
53. Holland AE, Hill CJ, Conron M,et al. Short term improvement in exercise capacity and symptoms following exercise training in interstitial lung disease. *Thorax*, 2008, *Cilt* ;63(6):549.
54. Ferreira A, Garvey C, Connors GL,et al. Pulmonary rehabilitation in interstitial lung disease: benefits and predictors of response. *Chest*, 2009, *Cilt* 135(2):442. *Epub* 2008 Oct 10.
55. Vainshelboim B, Oliveira J, Yehoshua L, et al. Exercise training-based pulmonary rehabilitation program is clinically beneficial for idiopathic pulmonary fibrosis. *Respiration*, 2014, *Cilt* 88(5):378. *Epub* 2014 Oct 23. .