Bölüm 17

BİRİNCİ BASAMAK TEDAVİYE DİRENÇLİ KRONİK MYELOİD LÖSEMİDE GÜNCEL TEDAVİ

Aysun GÖNDEREN[1]

GİRİŞ

Kronik miyeloid lösemi(KML), Philadelphia kromozomu t(9;22) (q34;q11) ile ilişkili, BCR-ABL1 füzyon geniyle sonuçlanan myeloproliferatif bir neoplazmdır. Bu genetik anormallik sonucu oluşan gen ürünü olan peptid, tirozinkinaz aktivitesine sahiptir. Oluşan bu aktif tirozin kinaz sayesinde hematopoetik öncüllerde proliferasyon ve antiapoptotik etki ortaya çıkar. KML klinik seyrinde üç evre bulunmaktadır. Tanı anında hastaların çoğunluğunu oluşturan kronik evre (KE), tedavisiz kalan veya tedaviye yanıt alınamayan vakalarda gözlenebilen akselere=hızlanmış evre(AE) ve blastikevre(BE) olarak sınıflanabilir.

Dünya Sağlık Örgütü (WHO) tanımına göre AE (Cortes& ark. 2006) ve BE (Faderl& ark. 1999) aşağıdaki kriterlerden birini veya birkaçını gösteren KML'li hastalar olarak tanımlanır:

AKSELERE EVRE KML:

- Periferik kan veya kemik iliğinde blast oranı %10-19
- Periferik kan bazofilleri ≥%20
- Tedavi ile ilişkisiz <100,000 / microLtrombositler
- Tedaviye cevap vermeyen >1,000,000 / microLtrombositler
- Tedaviye cevap vermeyen artan beyaz hücre sayısı (>10.000/mm3)
- Tedaviye yanıtsız giderek artan splenomegali
- Sitogenetik evrim (Philadelphia kromozomuna ek olarak kromozomal anormalliklerin gelişimi olarak tanımlanır)

BLASTİK EVRE KML:

- Periferik kan veya kemik iliğinde %≥20 blast
- Kemik iliği biyopsisinde blast kümeleri

[1] Doktor Öğretim Üyesi, Kütahya Sağlık Bilimleri Üniversitesi Tıp Fakültesi, dr.aysunbaz@gmail.com

Transplantasyonu takiben en az her üç ila altı ayda bir BCR-ABL1 transkriptlerinin kantitatif polimeraz zincir reaksiyonu (Q-PCR) ile takibi önerilmektedir.

KAYNAKÇA

Baccarani M, Deininger MW, Rosti G, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. Blood 2013; 122:872.

Biggs JC, Szer J, Crilley P, et al. Treatment of chronic myeloid leukemia with allogeneic bone marrow transplantation after preparation with BuCy2. Blood 1992; 80:1352.

Chalandon Y, Passweg JR, Guglielmi C, et al. Early administration of donor lymphocyte infusions upon molecular relapse after allogeneic hematopoietic stem cell transplantation for chronic myeloid leukemia: a study by the Chronic Malignancies Working Party of the EBMT. Haematologica 2014; 99:1492.

Clift RA, Buckner CD, Thomas ED, et al. Marrow transplantation for patients in accelerated phase of chronic myeloid leukemia. Blood 1994; 84:4368.

Cortes J, Digumarti R, Parikh PM, et al. Phase 2 study of subcutaneous omacetaxinemepesuccinate for chronic-phase chronic myeloid leukemia patients resistant to or intolerant of tyrosine kinase inhibitors. Am J Hematol 2013; 88:350.

Cortes JE, Hochhaus A, le Coutre PD, et al. Minimal cross-intolerance with nilotinib in patients with chronic myeloid leukemia in chronic or accelerated phase who are intolerant to imatinib. Blood 2011; 117:5600.

Cortes JE, Kantarjian HM, Rea D, et al. Final analysis of the efficacy and safety of omacetaxinemepesuccinate in patients with chronic- or accelerated-phase chronic myeloid leukemia: Results with 24 months of follow-up. Cancer 2015; 121:1637.

Cortes JE, Kim DW, Pinilla-Ibarz J, et al. A phase 2 trial of ponatinib in Philadelphia chromosome-positive leukemias. N Engl J Med 2013; 369:1.

Cortes J, Kim DW, Raffoux E, Martinelli G, Ritchie E, Roy L, Coutre S, Corm S, Hamerschlak N, Tang JL, Hochhaus A, Khoury HJ, Brummendorf TH, Michallet M, Rege-Cambrin G, Gambacorti-Passerini C, Radich JP, Ernst T, Zhu C, Van Tornout JM, Talpaz M. Efficacy and safety of dasatinib in imatinib-resistant or -intolerant patients with chronic myeloid leukemia in blast phase. Leukemia 2008;22:2176-2183.).

Cortes J, Lipton JH, Rea D, et al. Phase 2 study of subcutaneous omacetaxinemepesuccinate after TKI failure in patients with chronic-phase CML with T315I mutation. Blood 2012; 120:2573.

Cortes JE, Talpaz M, O'Brien S, et al. Staging of chronic myeloid leukemia in the imatinib era: an evaluation of the World Health Organization proposal. Cancer 2006; 106:1306.

Druker BJ, Sawyers CL, Kantarjian H, et al. Activity of a specific inhibitor of the BCR-ABL tyrosine kinase in the blast crisis of chronic myeloid leukemia and acute lymphoblastic leukemia with the Philadelphia chromosome. N Engl J Med 2001; 344:1038.

Faderl S, Talpaz M, Estrov Z, et al. The biology of chronic myeloid leukemia. N Engl J Med 1999; 341:164.

Goldman JM, Apperley JF, Jones L, et al. Bone marrow transplantation for patients with chronic myeloid leukemia. N Engl J Med 1986; 314:202.

Gratwohl A, Hermans J, Goldman JM, et al. Risk assessment for patients with chronic myeloid leukaemia before allogeneic blood or marrow transplantation. Chronic Leukemia Working Party of the European Group for Blood and Marrow Transplantation. Lancet 1998; 352:1087.

Kantarjian H, Cortes J, Kim DW, et al. Phase 3 study of dasatinib 140 mg once daily versus 70 mg twice daily in patients with chronic myeloid leukemia in accelerated phase resistant or intolerant to imatinib: 15-month median follow-up. Blood 2009; 113:6322.

Kantarjian HM, Cortes JE, Kim DW, et al. Bosutinib safety and management of toxicity in leukemia patients with resistance or intolerance to imatinib and other tyrosine kinase inhibitors. Blood 2014; 123:1309.

Kantarjian HM, Giles F, Gattermann N, Bhalla K, Alimena G, Palandri F, Ossenkoppele GJ, Nicolini FE, O'Brien SG, Litzow M, Bhatia R, Cervantes F, Haque A, Shou Y, Resta DJ, Weitzman A, Hochhaus A, le Coutre P. Nilotinib (formerly AMN107), a highly selective BCR-ABL tyrosine kinase inhibitor, is effective in patients with Philadelphia chromosome-positive chronic myelogenous leukemia in chronic phase following imatinib resistance and intolerance. Blood 2007;110:3540-3546.

Kantarjian H, Pasquini R, Hamerschlak N, et al. Dasatinib or high-dose imatinib for chronic-phase chronic myeloid leukemia after failure of first-line imatinib: a randomized phase 2 trial. Blood 2007; 109:5143.

Kantarjian H, Pasquini R, Lévy V, et al. Dasatinib or high-dose imatinib for chronic-phase chronic myeloid leukemia resistant to imatinib at a dose of 400 to 600 milligrams daily: two-year follow-up of a randomized phase 2 study (START-R). Cancer 2009; 115:4136.

Kantarjian H, Shah NP, Hochhaus A, Cortes J, Shah S, Ayala M, Moiraghi B, Shen Z, Mayer J, Pasquini R, Nakamae H, Huguet F, Boque C, Chuah C, Bleickardt E, Bradley-Garelik MB, Zhu C, Szatrowski T, Shapiro D, Baccarani M. Dasatinib versus imatinib in newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med 2010;362:2260-2270.

Lipton JH, Chuah C, Guerci-Bresler A, et al. Ponatinib versus imatinib for newly diagnosed chronic myeloid leukaemia: an international, randomised, open-label, phase 3 trial. Lancet Oncol 2016; 17:612.

Milojkovic D, Apperley JF, Gerrard G, et al. Responses to second-line tyrosine kinase inhibitors are durable: an intention-to-treat analysis in chronic myeloid leukemia patients. Blood 2012; 119:1838

Neil P. Shah, Philippe Rousselot, Charles Schiffer, Delphine Rea, Jorge E. Cortes, Jorge Milone, Hesham Mohamed, Diane Healey, HagopKantarjian, Andreas Hochhaus, and Giuseppe Saglio American Journal of Hematology, Vol. 91, No. 9, September 2016-doi:10.1002/ajh.24423

Nicolini FE, Basak GW, Kim DW, et al. Overall survival with ponatinib versus allogeneic stem cell transplantation in Philadelphia chromosome-positive leukemias with the T315I mutation. Cancer 2017; 123:2875

O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med 2003; 348:994.

O'Dwyer ME, Mauro MJ, Blasdel C, et al. Clonal evolution and lack of cytogenetic response are adverse prognostic factors for hematologic relapse of chronic phase CML patients treated with imatinibmesylate. Blood 2004; 103:451.

Ohanian M, Kantarjian HM, Quintas-Cardama A, et al. Tyrosine kinase inhibitors as initial therapy for patients with chronic myeloid leukemia in accelerated phase. Clin Lymphoma Myeloma Leuk 2014;

O'Hare T, Eide CA, Deininger MW. Bcr-Abl kinase domain mutations, drug resistance,

and the road to a cure for chronic myeloid leukemia. Blood 2007; 110:2242

Olavarria E, Siddique S, Griffiths MJ, et al. Posttransplantationimatinib as a strategy to postpone the requirement for immunotherapy in patients undergoing reduced-intensity allografts for chronic myeloid leukemia. Blood 2007; 110:4614.

Porkka K, Koskenvesa P, Lundán T, et al. Dasatinib crosses the blood-brain barrier and is an efficient therapy for central nervous system Philadelphia chromosome-positive leukemia. Blood 2008; 112:1005.

Puttini M, Coluccia AM, Boschelli F, et al. In vitro and in vivo activity of SKI-606, a novel Src-Abl inhibitor, against imatinib-resistant Bcr-Abl+ neoplastic cells. Cancer Res 2006; 66:11314.

Saglio G, Kim DW, Issaragrisil S, le Coutre P, Etienne G, Lobo C, Pasquini R, Clark RE, Hochhaus A, Hughes TP, Gallagher N, Hoenekopp A, Dong M, Haque A, Larson RA, Kantarjian HM, Investigators EN. Nilotinib versus imatinib for newly diagnosed chronic myeloid leukemia. N Engl J Med 2010;362:2251-2259.)

Saussele S, Lauseker M, Gratwohl A, et al. Allogeneic hematopoietic stem cell transplantation (allo SCT) for chronic myeloid leukemia in the imatinib era: evaluation of its impact within a subgroup of the randomized German CML Study IV. Blood 2010; 115:1880.

Shah NP, Kim DW, Kantarjian H, et al. Potent, transient inhibition of BCR-ABL with dasatinib 100 mg daily achieves rapid and durable cytogenetic responses and high transformation-free survival rates in chronic phase chronic myeloid leukemia patients with resistance, suboptimal response or intolerance to imatinib. Haematologica 2010; 95:232.

Silver RT, Talpaz M, Sawyers CL, et al. Four years of follow-up of 1027 patients with late chronic phase, accelerated phase, or blast crisis chronic myeloid leukemia treated with imatinib in three large phase II trials (abstract). Blood 2004; 104:abstract 23.

Soverini S, Hochhaus A, Nicolini FE, et al. BCR-ABL kinase domain mutation analysis in chronic myeloid leukemia patients treated with tyrosine kinase inhibitors: recommendations from an expert panel on behalf of European LeukemiaNet. Blood 2011; 118:1208.

Soverini S, Martinelli G, Rosti G, et al. ABL mutations in late chronic phase chronic myeloid leukemia patients with up-front cytogenetic resistance to imatinib are associated with a greater likelihood of progression to blast crisis and shorter survival: a study by the GIMEMA Working Party on Chronic Myeloid Leukemia. J ClinOncol 2005; 23:4100.

Talpaz M, Silver RT, Druker BJ, et al. Imatinib induces durable hematologic and cytogenetic responses in patients with accelerated phase chronic myeloid leukemia: results of a phase 2 study. Blood 2002; 99:1928.

Tomasz Sacha & Giuseppe Saglio, Nilotinib in the treatment of chronic myeloid Leukemia,10.2217/fon-2018-0468,future oncology ISSN 1479-6694

http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/203585lbl.pdf?et_cid=30334780&et_rid=463648356&linkid=http%3a%2f%2fwww.accessdata.fda.gov%2fdrugsatfda_docs%2flabel%2f2012%2f203585lbl.pdf (Accessed on October 26, 2012).

http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm370971.htm (Accessed on October 15, 2013)

http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/203469s007s008lbl.pdf (Accessed on January 22, 2014).

Wallen H, Gooley TA, Deeg HJ, et al. Ablative allogeneic hematopoietic cell transplantation in adults 60 years of age and older. J ClinOncol 2005; 23:3439.

WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, revised 4th edition, Swerdlow SH, Campo E, Harris NL, et al (Eds), International Agency for Research on Cancer (IARC), Lyon 2017.