

## Záver

Ešte pred vyše 3 desaťročiami bola CML fatálnym ochorením s mediánom prežívania 4–6 rokov, s progresiou do blastovej fázy, ktorej prognóza je krajne nepriaznivá. Vývoj liečebných možností od alogénnych transplantácií krvotvorných buniek v 90. rokoch 20. storočia smerom k cielenej terapii TKI po roku 2000 spôsobil prevrat v liečebnej stratégii, keďže zásadne došlo k predĺženiu celkového prežívania ako aj k zlepšeniu prognózy pacientov. V súčasnej modernej ére liečby CML dochádza len zriedka k progresii ochorenia do blastovej krízy, väčšina pacientov veľmi dobre reaguje na TKI, no problémom môže byť vznik nežiaducich účinkov dlhodobo podávanej terapie, ktoré môžu v niektorých prípadoch limitovať adekvátne dávkovanie liekov.

## LITERATÚRA

- O'Brien S, Berman E, Moore JO et al. NCCN Task Force report: tyrosine kinase inhibitor therapy selection in the management of patients with chronic myelogenous leukemia. *J Natl Compr Cancer Netw* 2011; 9: (Suppl. 2): S1–S25.
- Hehlmann R, Hochhaus A, Baccarani M European Leukemia Net. Chronic myeloid leukaemia. *Lancet* 2007; 370: 342–350.
- Bower H, Björkholm M, Dickman PW et al. Life expectancy of patients with chronic myeloid leukemia approaches the life expectancy of the general population. *J Clin Oncol* 2016; 34: 2851–2857.
- Sokal JE, Cox EB, Baccarani M et al. Prognostic discrimination in „good-risk“ chronic granulocytic leukemia. *Blood* 1984; 63: 789–799.
- Žáčková D Tyrozinkinázové inhibitory v léčbě starších pacientů s chronickou myeloidní leukémií - editorial. *Vnitř Lék* 2015; 61: 760–761.
- Hochhaus A, Larson RA, Guilhot MD et al. Long-Term Outcomes of Imatinib Treatment for Chronic Myeloid Leukemia. *N Engl J Med* 2017; 376: 917–927.
- Kantarjian H, Shah NP, Hochhaus A et al. Dasatinib versus imatinib in newly diagnosed chronic-phase chronic myeloid leukaemia. *N Engl J Med* 2010; 362: 2260–2270.
- Hehlmann R, Laussek M, Sauße S et al. Assessment of imatinib as first-line treatment of chronic myeloid leukemia: 10-year survival results of the randomized CML study IV and impact of non-CML determinants. *Leukemia* 2017; 31: 2398–2406.
- Kantarjian HM, Giles F, Bhatta K et al. Nilotinib is effective in patients with chronic myeloid leukemia in chronic phase after imatinib resistance or intolerance: 24-month follow-up results. *Blood* 2011; 117: 1141–1144.
- Klamová H, Žížková H, Burda P et al. Současné trendy v léčbě a diagnostice chronické myeloidní leukémie. *Transfuzie Hematol dnes* 2017; 23: (Suppl. 1): S34–S46.
- Etienne G, Guilhot J, Rea D et al. Long-Term Follow-Up of the French Stop Imatinib (STIM1) Study in Patients With Chronic Myeloid Leukemia. *J Clin Oncol* 2017; 35: 298–305.
- Saussele S, Richter J, Gilhot J et al. Discontinuation of tyrosine kinase inhibitor therapy in chronic myeloid leukaemia (EURO-SKI): a prespecified interim analysis of a prospective, multicentre, non-randomised, trial. *Lancet Oncol* 2018; 19: 747–757.
- Rea D, Nicolini FE, Tulliez M et al. Discontinuation of dasatinib or nilotinib in chronic myeloid leukemia: interim analysis of the STOP 2G-TKI study. *Blood* 2017; 129: 846–854.
- Baccarani M, Deininger MW, Rosti G et al. European LeukemiaNet Recommendations for the management of chronic myeloid leukemia 2013. *Blood* 2013; 122: 872–884.
- Alhurajji A, Kantarjian H, Boddou P et al. Prognostic significance of additional chromosomal abnormalities at the time of diagnosis in patients with chronic myeloid leukemia treated with frontline tyrosine kinase inhibitors. *Am J Hematol*. 2018; 93: 84–90.
- Radich JP, Deininger M, Abboud CN et al. Chronic Myeloid Leukemia, Version 1.2019, NCCN Clinical Practice Guidelines in Oncology. *J Natl Vanc Netw* 2018; 16: 1108–1135.
- Cohen MH, Williams G, Johnson G et al. Approval summary for imatinib mesylate capsules in the treatment of chronic myelogenous leukemia. *Clin Cancer Res* 2002; 8: 935–942.
- Guilhot J, Baccarani M, Clark RE et al. Definitions, methodological and statistical issues for phase 3 clinical trials in chronic myeloid leukemia: a proposal by the European Leukemia Net. *Blood* 2012; 119: 5963–5971.
- Hehlmann R, Berger U, Pfirrmann M et al. Drug treatment is superior to allografting as first-line therapy in chronic myeloid leukemia. *Blood* 2007; 109: 4686–4692.
- Gratwohl A, Pfirrmann M, Zander A et al. Long-term outcome of patients with newly diagnosed chronic myeloid leukemia: a randomized comparison of stem cell transplantation with drug treatment. *Leukemia* 2016; 30: 562–569.
- Westin JR, Kurzrock R It's about time: lessons for solid tumors from chronic myelogenous leukemia therapy. *Mol Cancer Ther* 2012; 11: 2549–2555.
- Mayer J, Klamová H, Žáčková D et al. Imatinib v první linii léčby nemocných s nově diagnostikovanou chronickou myeloidní leukémií v chronické fázi. *Transfuzie Hematol dnes* 2008; 14: 150–158.

Na základe odporúčaní odborných spoločností ELN z roku 2013, ESMO z roku 2017 a NCCN pre rok 2019 máme možnosť v 1. línii liečby zväziť u novodiagnostikovaného pacienta imatinib, dasatinib, nilotinib alebo bosutinib (14, 16, 55). Výber TKI závisí od stratifikácie rizika CML u individuálneho pacienta, jeho veku, komorbidít ako aj profilu nežiaducich účinkov zvažovaného TKI. Imatinib je lacnejší než druhogeneračné TKI a k dispozícii sú už generiká imatinibu, ktoré môžu znížiť ekonomické náklady na inak finančne náročnú dlhodobú terapiu v mnohých krajinách.

Výzvou do budúcnosti je veľmi aktuálna problematika možnosti tzv. TFR, ktorá je nádejou aj pre mnohých pacientov s CML na možné vyliečenie ochorenia bez užívania TKI.

- Hughes T, White D Which TKI? An embarrassment of riches for chronic myeloid leukemia patients. *Hematology* 2013; 2013: 168–175.
- 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: 994–1004.
- Breccia M, Cannella L, Frustraci A et al. Pleural-pericardial effusion as uncommon complication in CML patients treated with Imatinib. *Eur J Haematol* 2005; 74: 89–90.
- Hochhaus A, Baccarani M, Deininger M et al. Dasatinib induces durable cytogenetic responses in patients with chronic myelogenous leukemia in chronic phase with resistance or intolerance to imatinib. *Leukemia* 2008; 22: 1200–1206.
- 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: 232–240.
- Cortes JE, Saglio G, Kantarjian HM et al. Final 5-year study results of DASISION: The dasatinib versus imatinib study in treatment-naïve chronic myeloid patients trial. *J Clin Oncol* 2016; 34: 2333–2340.
- Breccia M, Stagno F, Luciano L et al. Dasatinib first-line: Multicentric Italian experience outside clinical trials. *Leuk Res* 2016; 40: 24–29.
- Shah NP, Rousset P, Schiffer Ch et al. Dasatinib in imatinib-resistant or intolerant chronic-phase, chronic myeloid leukemia patients: 7-year follow-up of study CA180-034. *Am J Hematol* 2016; 91: 869–874.
- Saglio G, Kim DW, Issaragrisil S et al. Nilotinib versus imatinib for newly diagnosed chronic myeloid leukemia. *N Engl J Med* 2010; 362: 2251–2259.
- Saglio G, Hochhaus A, Hughes TP et al. ENESTnd Update: nilotinib (NIL) vs imatinib (IM) in patients (PTS) with newly diagnosed chronic myeloid leukemia in chronic phase (CML-CP) and the impact of early molecular response (EMR) and Sokal risk at diagnosis on long-term outcomes. *Blood* 2013; 122: abstract 92.
- Hughes TP, Saglio G, Kantarjian HM et al. Early molecular response predicts outcomes in patients with chronic myeloid leukemia in chronic phase treated with frontline nilotinib or imatinib. *Blood* 2014; 123: 1353–1360.
- Hochhaus A, Saglio G, Larson RA et al. Nilotinib is associated with a reduced incidence of BCR-ABL mutations vs imatinib in patients with newly diagnosed chronic myeloid leukemia in chronic phase. *Blood* 2013; 121: 3703–3708.
- Castagnetti F, Breccia M, Gugliotta G et al. Nilotinib 300 mg twice daily: an academic single-arm study of newly diagnosed chronic phase chronic myeloid leukemia patients. *Haematologica* 2016; 101: 1200–1207.
- Cortes JE, Kantarjian HM, Brümmendorf TH et al. Safety and efficacy of bosutinib (SKI-606) in chronic phase Philadelphia chromosome-positive chronic myeloid leukemia patients with resistance or intolerance to imatinib. *Blood* 2011; 118: 4567–4576.
- Cortes JE, Gambacorti-Passerini C, Deininger MW et al. Bosutinib versus imatinib for newly diagnosed chronic myeloid leukemia: results from the randomized BFORE trial. *J Clin Oncol* 2018; 36: 231–237.
- Cortes JE, Khoudry HJ, Kantarjian HM et al. Long-term bosutinib for chronic phase chronic myeloid leukemia after failure of imatinib plus dasatinib and/or nilotinib. *Am J Hematol* 2016; 91: 1206–1214.
- O'Hare T, Shakespeare WC, Zhu X et al. AP24534, a pan-BCR/ABL inhibitor for chronic myeloid leukemia, potently inhibits the T315I mutant and overcomes mutation-based resistance. *Cancer Cell* 2009; 16: 401–412.

Ďalší literatúra u autorky  
a na [www.casopisvnitrnilekarstvi.cz](http://www.casopisvnitrnilekarstvi.cz)