

- 3 **Prediktivní testování plicních nádorů – pohled onkologa**
prof. MUDr. Luboš Petruželka, CSc. Onkologická klinika 1. LF UK a VFN a ÚVN, ÚRO, IPVZ, Praha
MUDr. Jiří Votruba, Ph.D. I. klinika tuberkulózy a respiračních onemocnění, 1. LF UK a VFN, Praha
MUDr. Ludmila Křížová Onkologická klinika 1. LF UK a VFN, Praha
MUDr. Jan Špaček, Ph.D. Onkologická klinika 1. LF UK a VFN a ÚVN, Ústav radiační onkologie FN Bulovka, Katedra klinické onkologie IPVZ, Praha
doc. MUDr. Milada Zemanová, Ph.D. Onkologická klinika 1. LF UK a VFN, Praha
MUDr. Petra Zemanová I. klinika tuberkulózy a respiračních onemocnění, 1. LF UK a VFN, Praha
- 3 **Imunoterapie u malobuněčného plicního karcinomu**
MUDr. Martin Svatoň, Ph.D. Klinika pneumologie a fteologie, FN Plzeň a LF v Plzni, UK
- 3 **Karcinom plic na virtuálním ASCO 2021**
MUDr. Leona Koubková Pneumologická klinika 2. LF UK a FN v Motole, Praha
- 4 **Entrectinib v léčbě pacientů s pokročilými nebo metastatickými nádory s fúzní mutací *NTRK***
doc. MUDr. Milan Vošmik, Ph.D. Klinika onkologie a radioterapie, LF UK a FN Hradec Králové
- 4 **Současné možnosti a výhledy léčby pacientek s karcinomem prsu**
MUDr. Martina Zimovjanová, Ph.D. Onkologická klinika VFN a 1. LF UK, Praha
- 5 **Nemetastatický kastročně rezistentní prostatický karcinom**
prof. MUDr. Jindřich Fínek, Ph.D., MHA Onkologická a radioterapeutická klinika FN a LF UK, Plzeň
- 5 **Role multikinázových inhibitorů v léčbě diseminovaných nádorů ledvin v první linii léčby**
doc. MUDr. Alexandr Poprach, Ph.D. | MUDr. Radek Lakomý, Ph.D. Klinika komplexní onkologické péče a LF MU, Brno
- 5 **Systémová léčba kožních nádorů kromě melanomu**
doc. MUDr. Alexandr Poprach, Ph.D. | MUDr. Radek Lakomý, Ph.D. Klinika komplexní onkologické péče a LF MU, Brno
- 5 **Adjuvantní terapie melanomu v přehledu**
MUDr. Ivana Krajsová, MBA Dermatovenerologická klinika 1. LF UK a VFN, Praha
- 5 **Systémová léčba pokročilých uroteliálních nádorů**
doc. MUDr. Tomáš Büchler, Ph.D. Onkologická klinika 1. LF UK a Thomayerovy nemocnice, Praha
- 6 **Nové klinické poznatky o využití biosimilárního bevacizumabu v onkologii**
doc. MUDr. Jiří Slíva, Ph.D. Ústav farmakologie, 3. LF UK, Praha
- 6 **Současné možnosti léčby karcinomu vaječníků**
prof. MUDr. Michal Zikán, Ph.D. Gynekologicko-porodnická klinika 1. LF UK a Fakultní nemocnice Bulovka, Praha
- 6 **Léčba ovariálních nádorů PARP inhibitory**
MUDr. Tomáš Svoboda, Ph.D. Onkologická a radioterapeutická klinika, KOC FN Plzeň
- 7 **Změna managementu léčby LSIL**
prof. MUDr. Michal Zikán, Ph.D. Gynekologicko-porodnická klinika 1. LF UK a Fakultní nemocnice Bulovka, Praha
- 7 **Dlouhodobá odpověď na lenvatinib u pacienta s hepatocelulárním karcinomem – kazuistika**
MUDr. Marián Liberko | doc. MUDr. Renata Soumarová, Ph.D., MBA Radioterapeutická a onkologická klinika FN KV a 3. LF UK, Praha
- 7 **Oyavas 25 mg/ml koncentrát pro infuzní roztok – lékový profil**
doc. MUDr. Jiří Slíva, Ph.D. Ústav farmakologie, 3. LF UK, Praha
- 7 **Antitrombotická profylaxe jako součást komplexního přístupu k onkologicky nemocnému**
prof. MUDr. Jindřich Fínek, Ph.D., MHA Onkologická a radioterapeutická klinika FN a LF UK v Plzni
- 7 **Malnutrice onkologického pacienta**
Mgr. et MUDr. Petra Holečková, Ph.D., MBA Ústav radiační onkologie, FNB a 1. LF UK, Praha

- 8 [Měnící se pohled na iniciační léčbu chronické lymfocytární leukemie](#)
prof. MUDr. Tomáš Papajík, CSc. | prof. MUDr. Zuzana Kubová, CSc. | MUDr. Peter Turcsányi, Ph.D. | MUDr. Renata Urbanová, Ph.D. Hemato-onkologická klinika FN a LF UP v Olomouci
- 8 [Novinky v léčbě chronické lymfocytární leukemie](#)
MUDr. Martin Brejcha, Ph.D. Nemocnice AGEL Nový Jičín, a. s.
- 9 [Výhled léčby pacientů s difúzním B-velkobuněčným lymfomem](#)
doc. MUDr. David Belada, Ph.D. IV. interní hematologická klinika, FN a LF UK v Hradci Králové
- 9 [Protinádorový synergismus mezi venetoklaxem a azacytidinem](#)
prof. MUDr. Pavel Klener, Ph.D. I. interní klinika – hematologie, VFN a 1. LF UK, Praha
- 9 [Současná doporučení pro léčbu mnohočetného myelomu](#)
MUDr. Hana Plonková | MUDr. Tomáš Jelínek, Ph.D. | MUDr. Tereza Popková | prof. MUDr. Roman Hájek, CSc.
Klinika hematooonkologie FN Ostrava, LF Ostravské univerzity, Ostrava
- 10 [Pacient s mnohočetným myelomem léčený přípravkem Ninlaro ve vyšších liniích léčby – kazuistika](#)
MUDr. Viera Sandecká, Ph.D. Interní hematologická a onkologická klinika, FN Brno
- 10 [Vývoj léčby chronické myeloidní leukemie](#)
MUDr. Hana Klamová, CSc. Ústav hematologie a krevní transfuze, Praha
- 11 [Praktické příklady použití gemtuzumab ozogamicinu v léčbě nově diagnostikované akutní myeloidní leukemie](#)
doc. MUDr. Tomáš Szotkowski, Ph.D. | MUDr. Martin Čerňan | Mgr. Jana Navrátilová | MUDr. Jaromír Hubáček, Ph.D. | prof. MUDr. Tomáš Papajík, CSc. Hemato-onkologická klinika FN Olomouc a LF UP v Olomouci
- 11 [Idiopatická multicentrická Castlemanova choroba: diagnostika a léčba v roce 2021](#)
MUDr. Marta Šimůnková, Praha
- 11 [Idiopatická multicentrická Castlemanova choroba: diagnostika a léčba v roce 2021 – komentář k článku](#)
prof. MUDr. Zdeněk Adam, CSc. | prof. MUDr. Luděk Pour, Ph.D. Interní hematologická a onkologická klinika LF MU a FN Brno
- 12 [Význam eltrombopagu v léčbě závažné a velmi závažné aplastické anemie](#)
prof. MUDr. Pavel Žák, Ph.D. IV. interní hematologická klinika, LF UK a FN Hradec Králové

Prediktivní testování plicních nádorů – pohled onkologa

prof. MUDr. Luboš Petruželka, CSc. Onkologická klinika 1. LF UK a VFN a ÚVN, ÚRO, IPVZ, Praha

MUDr. Jiří Votruba, Ph.D. I. klinika tuberkulózy a respiračních onemocnění, 1. LF UK a VFN, Praha

MUDr. Ludmila Křížová Onkologická klinika 1. LF UK a VFN, Praha

MUDr. Jan Špaček, Ph.D. Onkologická klinika 1. LF UK a VFN a ÚVN, Ústav radiační onkologie FN Bulovka, Katedra klinické onkologie IPVZ, Praha

doc. MUDr. Milada Zemanová, Ph.D. Onkologická klinika 1. LF UK a VFN, Praha

MUDr. Petra Zemanová I. klinika tuberkulózy a respiračních onemocnění, 1. LF UK a VFN, Praha

- Hodson, R.: Precision oncology. *Nature*, 2020, 585, s. 51–51.
- Stricker, T. – Catenacci, D. – Seiwert, T.: Molecular profiling of cancer—the future of personalized cancer medicine: a primer on cancer biology and the tools necessary to bring molecular testing to the clinic. *Semin Oncol*, 2011, 38, s. 173–185.
- Křížová, L. – Petruželka, L.: Sekvenování nové generace (NGS) a molekulární onkologický multidisciplinární tým (Molecular Tumor Board, MTB) z pohledu onkologa. *Čs Patol*, 2021, v tisku.
- Dundr, P. – Matěj, R. – Němejcova, K., et al.: *Klin Onkol*, 2020, 33, suppl. 1, s. S1–S6.
- Petruželka L. – Špaček, J. – Křížová, L.: Budoucnost léčby karcinomu plic. *Klin Onkol*, 2021, 34, suppl. 1, s. S71–S81.
- Skoulidis, F. – Heymach, J. V.: Co-occurring genomic alterations in non-small-cell lung cancer biology and therapy. *Nat Rev Cancer*, 2019, 19, s. 495–509.
- Pao, W. – Girard, N.: New driver mutations in non-small-cell lung cancer. *Lancet Oncol*, 2011, 12, s. 175–180.
- Van der Velden, D. L. – Van Herpen, C. M. L. – Van Laarhoven, H. W. M., et al.: Molecular Tumor Boards: current practice and future needs. *Ann Oncol*, 2017, 28, s. 3070–3075.
- Limaye, S. – Patil, D. – Akolkar, D. B., et al.: Multi-analyte liquid biopsies based treatment in advanced refractory cancers. *J Clin Oncol*, 2020, 38, s. e15623.
- Dalton, W. B. – Forde, P. M. – Kang, H., et al.: Personalized medicine in the oncology clinic: personalized medicine in the oncology clinic: implementation and outcomes of the Johns Hopkins Molecular Tumor Board. *JCO Precis Oncol*, 2017, 2017:PO.16.00046.
- Lantuejoul, S. – Sound-Tsao, M. – Cooper, W. A., et al.: PD-L1 testing for lung cancer in 2019: perspective from the IASLC pathology committee. *J Thorac Oncol*, 2020, 15, s. 499–519.
- Patel, S. P. – Kurzrock, R.: PD-L1 Expression as a predictive biomarker in cancer immunotherapy. *Mol Cancer Ther*, 2015, 14, s. 847–856.
- de Ruiter, E. J. – Mulder, F. J. – Koomen, B. M., et al.: Comparison of three PD-L1 immunohistochemical assays in head and neck squamous cell carcinoma (HNSCC). *Mod Pathol*, 2021, 34, s. 1125–1132.
- De Marchi, P. – Leal, L. F. – Duval da Silva, V., et al.: PD-L1 expression by tumor proportion score (TPS) and combined positive score (CPS) are similar in non-small cell lung cancer (NSCLC). *J Clin Pathol*, 2021, jclinpath-2020-206832.
- Qin, A. – Coffey, D. G. – Warren, E. H., et al.: Mechanisms of immune evasion and current status of checkpoint inhibitors in non-small cell lung cancer. *Cancer Med*, 2016, 5, s. 2567–2578.
- Mu, C. Y. – Huang, J. A. – Chen, Y., et al.: High expression of PD-L1 in lung cancer may contribute to poor prognosis and tumor cells immune escape through suppressing tumor infiltrating dendritic cells maturation. *Med Oncol*, 2011, 28, s. 682–688.
- Steuer, C. E. – Ramalingam, S. S.: Tumor mutation burden: Leading immunotherapy to the era of precision medicine? *J Clin Oncol*, 2017, 76, s. 8770.
- Fancelli, L. – Gandini, S. – Pelicci, P. G., et al.: Tumor mutational burden quantification from targeted gene panels: Major advancements and challenges. *J Immunother Cancer*, 2019, 7, s. 183.
- Merino, D. M. – McShane, L. M. – Fabrizio, D., et al.: Establishing guidelines to harmonize tumor mutational burden (TMB): in silico assessment of variation in TMB quantification across diagnostic platforms: phase I of the Friends of Cancer Research TMB Harmonization Project. *J Immunother Cancer*, 2020, 8, s. e000147.
- Zitvogel, L. – Ma, Y. – Raouf, D., et al.: The microbiome in cancer immunotherapy: Diagnostic tools and therapeutic strategies. *Science*, 2018, 359, s. 1366–1370.
- Jiang, T. – Qiao, M., et al.: Pretreatment neutrophil-to-lymphocyte ratio is associated with outcome of advanced-stage cancer patients treated with immunotherapy: a meta-analysis. *Cancer Immunol Immunother*, 2018, 67, s. 713–727.
- Huang, Y. – Shen, A.: The prediction potential of neutrophil-to-lymphocyte ratio for the therapeutic outcomes of programmed death receptor-1/programmed death ligand 1 inhibitors in non-small cell lung cancer patients. *Medicine*, 2020, 99, s. 34.
- Fundytus, A. – Booth, C. M. – Tannock, I. F.: How low can you go? PD-L1 expression as a biomarker in trials of cancer immunotherapy. *Ann Oncol*, 2001, 32, s. 7.
- Socinski, M. A. – Jotte, R. M. – Cappuzzo, F., et al.: Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC. *N Engl J Med*, 2018, 378, s. 2288–2301.
- Aguilar, E. J. – Ricciuti, B. – Gainor, J. F., et al.: Outcomes to first-line pembrolizumab in patients with non-small-cell lung cancer and very high PD-L1 expression. *Ann Oncol*, 2019, 30, s. 1653–1659.
- Reck, M. – Ciuleanu, T. E. – Cobo Dols, M., et al.: Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx) for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA. *J Clin Oncol*, 2020, 38, suppl. 15, s. 9501–9501.
- Duchemann, B. – Remon, J. – Naigeon, M., et al.: Current and future biomarkers for outcomes with immunotherapy in non-small cell lung cancer. *Transl Lung Cancer Res*, 2021, 10, s. 2937–2954.
- De Groot, A. S.: Immunomics: discovering new targets for vaccines and therapeutics. *Drug Discov Today*, 2006, 11, s. 203–209.

Imunoterapie u malobuněčného plicního karcinomu

MUDr. Martin Svatoň, Ph.D. Klinika pneumologie a fizeologie, FN Plzeň a LF v Plzni, UK

- Dingemans, A. M. C. – Früh, M. – Ardizzone, A., et al.: Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *An Oncol*, 2021.
- Ready, N. – Farago, A. F. – de Braud, F., et al.: Third-line nivolumab monotherapy in recurrent SCLC: CheckMate 032. *J Thorac Oncol*, 2019, 14, s. 237–244.
- Ott, P. A. – Elez, E. – Hiret, S., et al.: Pembrolizumab in patients with extensive-stage small-cell lung cancer: results from the phase Ib KEYNOTE-028 study. *J Clin Oncol*, 2017, 35, s. 3823–3829.
- Marabelle, A. – Fakih, M. – Lopez, J., et al.: Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab: prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. *Lancet Oncol*, 2020, 21, s. 1353–1365.
- Merck. Merck provides update on KEYTRUDA® (pembrolizumab) indication in metastatic small cell lung cancer in the US. Dostupné z: <https://www.merck.com/news/merck-provides-update-on-keytruda-pembrolizumab-indication-in-metastatic-small-cell-lung-cancer-in-the-us/>, vyhledáno 20. 5. 2021.
- BMS. Bristol Myers Squibb statement on Opdivo (nivolumab) small cell lung cancer U.S. indication. Dostupné z: <https://news.bms.com/news/details/2020/Bristol-Myers-Squibb-Statement-on-Opdivo-nivolumab-Small-Cell-Lung-Cancer-US-Indication/default.aspx>, vyhledáno 20. 5. 2021.
- Spigel, D. R. – Vicente, D. – Ciuleanu, T. E., et al.: Second-line nivolumab in relapsed small-cell lung cancer: CheckMate 331. *An Oncol*, 2021, 32, s. 631–641.
- Pujol, J. L. – Greillier, L. – Audigier-Valette, C., et al.: A randomized non-comparative phase II study of anti-programmed cell death-ligand 1 atezolizumab or chemotherapy as second-line therapy in patients with small cell lung cancer: results from the IFCT-1603 trial. *J Thorac Oncol*, 2019, 14, s. 903–913.
- Antonia, S. J. – López-Martín, J. A. – Bendell, J., et al.: Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): a multicentre, open-label, phase 1/2 trial. *Lancet Oncol*, 2016, 17, s. 883–895.
- Hellmann, M. D. – Callahan, M. K. – Awad, M. M., et al.: Tumor mutational burden and efficacy of nivolumab monotherapy and in combination with ipilimumab in small-cell lung cancer. *Cancer Cell*, 2019, 35, s. 329.
- Pujol, J. L. – Greillier, L. – Audigier Valette, C., et al.: A randomized non-comparative phase II study of anti-PD-L1 ATEZOLIZUMAB or chemotherapy as second-line therapy in patients with small cell lung cancer: Results from the IFCT-1603 trial. *An Oncol*, 2018, 29, s. viii596.
- Reck, M. – Luft, A. – Szczesna, A., et al.: Phase III randomized trial of ipilimumab plus etoposide and platinum versus placebo plus etoposide and platinum in extensive-stage small-cell lung cancer. *J Clin Oncol*, 2016, 34, s. 3740–3748.
- Horn, L. – Mansfield, A. S. – Szczesna, A., et al.: First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *N Engl J Med*, 2018, 379, s. 2220–2229.
- Paz-Ares, L. – Dvorkin, M. – Chen, Y., et al.: Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. *Lancet*, 2019, 394, s. 1929–1939.
- Liu, S. V. – Reck, M. – Mansfield, A. S., et al.: Updated overall survival and PD-L1 subgroup analysis of patients with extensive-stage small-cell lung cancer treated with atezolizumab, carboplatin, and etoposide (IMpower133). *J Clin Oncol*, 2021, 39, s. 619–630.
- Goldman, J. W. – Dvorkin, M. – Chen, Y., et al.: Durvalumab, with or without tremelimumab, plus platinum-etoposide versus platinum-etoposide alone in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): updated results from a randomised, controlled, open-label, phase 3 trial. *Lancet Oncol*, 2021, 22, s. 51–65.
- Goldman, J. W. – Garassino, M. C. – Chen, Y., et al.: Patient-reported outcomes with first-line durvalumab plus platinum-etoposide versus platinum-etoposide in extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase III study. *Lung Cancer*, 2020, 149, s. 46–52.
- Rudin, C. M. – Awad, M. M. – Navarro, A., et al.: Pembrolizumab or placebo plus etoposide and platinum as first-line therapy for extensive-stage small-cell lung cancer: randomized, double-blind, phase III KEYNOTE-604 study. *J Clin Oncol*, 2020, 38, s. 2369–2379.
- Owonikoko, T. K. – Kim, H. R. – Govindan, R., et al.: Nivolumab (nivo) plus ipilimumab (ipi), nivo, or placebo (pbo) as maintenance therapy in patients (pts) with extensive disease small cell lung cancer (ED-SCLC) after first-line (1L) platinum-based chemotherapy (chemo): Results from the double-blind, rando. *An Oncol*, 2019, 30, s. ii77.

Karcinom plic na virtuálním ASCO 2021

MUDr. Leona Koubková Pneumologická klinika 2. LF UK a FN v Motole, Praha

- Wakelee, H. A. – Altorki, N. K. – Zhou, C., et al.: IMpower010: Primary results of a phase III global study of atezolizumab versus best supportive care after adjuvant chemotherapy in resected stage II-IIA non-small cell lung cancer (NSCLC). *J Clin Oncol*, 2021, 39, suppl. s. 8500–8500.
- Spicer, J. – Wang, C. – Tanaka, F., et al.: Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer (NSCLC). *J Clin Oncol*, 2021, 39, suppl. 15, s. 8503–8503.
- Spigel, D. – Faires-Finn, C. – Gray, J. E., et al.: Five-year survival outcomes with durvalumab after chemoradiotherapy in unresectable stage III NSCLC: An update from the PACIFIC trial. *J Clin Oncol*, 2021, 39, suppl. 15, s. 8511–8511.
- Akinboro, O. – Vallejo, J. J. – Mishra-Kalyani, P. S., et al.: Outcomes

of anti-PD(L1) therapy in combination with chemotherapy versus immunotherapy (IO) alone for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 score 1-49%: FDA pooled analysis. *J Clin Oncol*, 2021, 39, suppl. 15, s. 9001-9001.

- Paz-Ares, L. G. – Ciuleanu, T. E. – Lee, J. S., et al.: Nivolumab (NIVO) plus ipilimumab (IPI) versus chemotherapy (chemo) as first-line (1L) treatment for advanced non-small cell lung cancer (NSCLC): 4-year update from CheckMate 227. *J Clin Oncol*, 2021, 39, suppl. 15, s. 9016, doi:10.1200/JCO.2021.39.15_suppl.9016.
- Reck, M. – Ciuleanu, T. E. – Cobo, M., et al.: First-line nivolumab (NIVO)

plus ipilimumab (IPI) plus two cycles of chemotherapy (chemo) versus chemo alone (4 cycles) in patients with advanced non-small cell lung cancer (NSCLC): two-year update from CheckMate 9LA. *J Clin Oncol*, 2021, 39, suppl. 15, s. 9000-9000.

- Curigliano, G. – Gaior, J. F. – Griesinger, F., et al.: Safety and efficacy of pralsetinib in patients with advanced RET fusion-positive non-small cell lung cancer: Update from the ARROW trial. *J Clin Oncol*, 2021, 39, suppl. 15, s. 9089-9089.
- Wolf, J. – Garon, E. B. – Groen, H. J. M., et al.: Capmatinib in MET exon 14-mutated, advanced NSCLC: Updated results from the GEOMETRY

mono-1 study. *J Clin Oncol*, 2021, 39, suppl. 15, s. 9020-9020.

- Pasi, A. J., et al.: Efficacy and safety of patritumab deruxtecan (HER3-DXd) in EGFR inhibitor-resistant, EGFR-mutated (EGFRm) non-small cell lung cancer (NSCLC). *J Clin Oncol*, 2021, 39, suppl. 15, s. 9007-9007.
- Skoulidis, F. – Li, B. T. – Govindan, R., et al.: Overall survival and exploratory subgroup analyses from the phase 2 CodeBreak 100 trial evaluating sotrasorib in pretreated KRAS p.G12C mutated non-small cell lung cancer. *J Clin Oncol*, 2021, 39, suppl. 15, s. 9003-9003.

Entrectinib v léčbě pacientů s pokročilými nebo metastatickými nádory s fúzní mutací NTRK

doc. MUDr. Milan Vošmik, Ph.D. Klinika onkologie a radioterapie, LF UK a FN Hradec Králové

- Gambardella, V. – Tarazona, N. – Cejalvo, J. M., et al.: Personalized medicine: recent progress in cancer therapy. *Cancers*, 2020, 12, s. 1009.
- Yan, L. – Zhang, W.: Precision medicine becomes reality-tumor type-agnostic therapy. *Cancer Commun*, 2018, 38, s. 6.
- Calella, A. M. – Nerlov, C. – Lopez, R. G., et al.: Neurotrophin/Trk receptor signaling mediates C/EBPalpha, -beta and Neuro Drecruitment to immediate-early gene promoters in neuronal cells and requires C/EBPs to induce mediate-early gene transcription. *Neural Dev*, 2007, 2, s. 4.
- Amatu, A. – Sartore-Bianchi, A. – Bencardino, K., et al.: Tropomyosin receptor kinase (TRK) biology and the role of NTRK gene fusions in cancer. *Ann Oncol*, 2019, 30, suppl. 8, s. viii5-viii15.
- Martin-Zanca, D. – Hughes, S. H. – Barbacid, M.: A human oncogene formed by the fusion of truncated tropomyosin and protein tyrosine kinase sequences. *Nature*, 1986, 319, s. 743-748.
- Chen, Y. – Chi, P.: Basket trial of TRK inhibitors demonstrates efficacy in TRK fusion-positive cancers. *J Hematol Oncol*, 2018, 11, s. 78.
- Sartore-Bianchi, A. – Ardini, E. – Bosotti, R., et al.: Sensitivity to entrectinib associated with a novel LMNA-NTRK1 gene fusion in metastatic colorectal cancer. *J Natl Cancer Inst*, 2015, 108, s. djv306.
- Drilon, A. – Siena, S. – Ou, S. I., et al.: Safety and antitumor activity of the multitargeted pan-TRK, ROS1, and ALK inhibitor entrectinib: combined results from two phase I trials (ALKA-372-001 and STARTRK-1). *Cancer Discov*, 2017, 7, s. 400-409.
- Doebbele, R. C. – Drilon, A. – Paz-Ares, L., et al.; trial investigators: Entrectinib in patients with advanced or metastatic NTRK fusion-positive solid tumours: integrated analysis of three phase 1-2 trials. *Lancet Oncol*, 2020, 21, s. 271-282.
- Robinson, G. – Desai, A. – Basu, E., et al.: Entrectinib in recurrent or refractory solid tumours, including primary CNS tumors: Updated data in children and adolescents. *Neuro Oncol*, 2020, 22, suppl. 3, s. iii344.
- Delgado, J. – Pean, E. – Melchiorri, D., et al.: The European Medicines Agency review of entrectinib for the treatment of adult or paediatric patients with solid tumours who have a neurotrophic tyrosine receptor kinase gene fusions and adult patients with non-small-cell lung cancer harbouring ROS1 rearrangements. *ESMO Open*, 2021, 6, s. 100087.
- Rozlytrek. Souhrn údajů o přípravku (SPC). Dostupné z: https://www.ema.europa.eu/en/documents/product-information/rozlytrek-epar-product-information_cs.pdf, vyhledáno 14. 9. 2021.
- Marchiò, C. – Scaltitri, M. – Ladanyi, M., et al.: ESMO recommendations on the standard methods to detect NTRK fusions in daily practice and clinical research. *Ann Oncol*, 2019, 30, s. 1417-1427.
- Büchler, T. – Dundr, P. – Finek, J., et al.: Praktický návod pro testování a cílenou léčbu dospělých pacientů se solidními nádory s NTRK genovou fúzí v běžné klinické praxi. *Klin Onkol*, 2020, 33, s. 414-419.

Současné možnosti a výhledy léčby pacientek s karcinomem prsu

MUDr. Martina Zimovjanová, Ph.D. Onkologická klinika VFN a 1. LF UK, Praha

- Sharma, P. – López-Tarruella, S. – García-Saenz, J. A., et al.: Pathological response and survival in triple-negative breast cancer following neoadjuvant carboplatin plus docetaxel. *Clin Cancer Res*, 2018, 24, s. 5820-5829.
- Schmid, P. – Cortes, J. – Pusztai, L., et al.: Pembrolizumab for early triple-negative breast cancer. *N Engl J Med*, 2020, 382, s. 810-821.
- von Minckwitz, G. – Schneeweiss, A. – Loibl, S., et al.: Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): A randomised phase 2 trial. *Lancet Oncol*, 2014, 15, s. 747-756.
- Sikov, W. M. – Berry, D. A. – Perou, C. M., et al.: Impact of the addition of carboplatin and/or bevacizumab to neoadjuvant once-per-week paclitaxel followed by dose-dense doxorubicin and cyclophosphamide on pathologic complete response rates in stage II to III triple-negative breast cancer: CALGB 40603 (Alliance). *J Clin Oncol*, 2015, 33, s. 13-21.
- Liedtke, C. – Mazouni, C. – Hess, K. R., et al.: Response to neoadjuvant therapy and long-term survival in patients with triple-negative breast cancer. *J Clin Oncol*, 2008, 26, s. 1275-1281.
- American Cancer Society: Breast cancer facts and figures 2019-2020. Dostupné z: <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2019-2020.pdf>, vyhledáno 16. 7. 2021.
- Robson, M. – Im, S. A. – Senkus, E., et al.: Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. *N Engl J Med*, 2017, 377, s. 523-533.
- Litton, J. K. – Rugo, H. S. – Ettl, J., et al.: Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. *N Engl J Med*, 2018, 379, s. 753-763.
- Tutt, A. – Garber, J. E. – Kaufman, B., et al.: OlympiA: A phase III, multicentre, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer. *J Clin Oncol*, 2021, 39, suppl., DOI: 10.1200/JCO.2021.39.15_suppl.LBA1.
- Tutt, A. N. J. – Garber, J. E. – Kaufman, B., et al.: Adjuvant olaparib for patients with BRCA1- or BRCA2-mutated breast cancer. *N Engl J Med*, 2021, 384, s. 2394-2405.
- Greenup, R. – Buchanan, A. – Lorizio, W., et al.: Prevalence of BRCA mutations among women with triple-negative breast cancer (TNBC) in a genetic counseling cohort. *Ann Surg Oncol*, 2013, 20, s. 3254-3258.
- Schmid, P. – Adams, S. – Rugo, H. S., et al.: Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. *N Engl J Med*, 2018, 379, s. 2108-2121.
- Schmid, P. – Rugo, H. S. – Adams, S., et al.: Atezolizumab plus nab-paclitaxel as first-line treatment for unresectable, locally advanced or metastatic triple-negative breast cancer (IMpassion130). *Lancet Oncol*, 2020, 21, s. 44-59.
- Miles, D. – Gligorov, J. – André, F., et al.: Primary results from IMpassion131, a double-blind, placebo-controlled, randomised phase III trial of first-line paclitaxel with or without atezolizumab for unresectable locally advanced/metastatic triple-negative breast cancer. *Ann Oncol*, 2021, 32, s. 994-1004.
- Roche provides update on Tecentriq US indication for PD-L1-positive, metastatic triple-negative breast cancer. Roche Media and Investor Release, Basilej, 27. 8. 2021.
- Cortes, J. – Cescon, D. W. – Rugo, H. S., et al.: Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): A randomised, placebo-controlled, double-blind, phase 3 clinical trial. *Lancet*, 2020, 396, s. 1817-1828.
- Schmid, P. – Cortes, J. – Dent, R., et al.: KEYNOTE-522: Phase 3 study of neoadjuvant pembrolizumab plus chemotherapy versus placebo plus chemotherapy, followed by adjuvant pembrolizumab versus placebo for early-stage triple-negative breast cancer. ESMO Virtual Plenary. Abstract VP7-2021. Dostupné z: [https://www.annalsofoncology.org/article/S0923-7534\(19\)60363-7/pdf](https://www.annalsofoncology.org/article/S0923-7534(19)60363-7/pdf), vyhledáno 1. 9. 2021.
- Bardia, A. – Hurvitz, S. A. – Tolane, S. M., et al.: Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med*, 2021, 384, s. 1529-1541.
- Swain, S. M. – Baselga, J. – Kim, S. B., et al.: Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. *N Engl J Med*, 2015, 372, s. 724-734.
- Verma, S. – Miles, D. – Gianni, L., et al.: Trastuzumab emtansine for HER2-positive advanced breast cancer. *N Engl J Med*, 2012, 367, s. 1783-1791.
- Modi, S. – Saura, C. – Yamashita, T., et al.: Trastuzumab deruxtecan in previously treated HER2-positive breast cancer. *N Engl J Med*, 2020, 382, s. 610-621.
- Murthy, R. K. – Loi, S. – Okines, A., et al.: Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. *N Engl J Med*, 2020, 382, s. 597-609.
- Rugo, H. S. – Im, S. A. – Cardoso, F., et al.: Efficacy of margetuximab vs trastuzumab in patients with pretreated ERBB2-positive advanced breast cancer: A phase 3 randomized clinical trial. *JAMA Oncol*, 2021, 7, s. 573-584.
- Ibrance: SPC souhrn údajů o přípravku, ceny a úhrady 2021. Dostupné z: <https://www.sukl.cz/modules/medication/detail.php?code=0219109&tab=texts>, vyhledáno 1. 9. 2021.
- Kisqali: SPC souhrn údajů o přípravku, ceny a úhrady 2020. Dostupné z: <https://www.sukl.cz/modules/procedures/detail.php?spz=SUJLS116543%2F2020>, vyhledáno 1. 9. 2021.
- Verzenio: SPC souhrn údajů o přípravku, ceny a úhrady 2021. Dostupné z: <https://www.sukl.cz/modules/medication/detail.php?code=0238311&tab=texts>, vyhledáno 1. 9. 2021.
- Johnston, S. R. D. – Harbeck, N. – Hegg, R., et al.: Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2-, node-positive, high-risk, early breast cancer (monarchE). *J Clin Oncol*, 2020, 38, s. 3987-3998.
- André, F. – Ciruelos, E. M. – Juric, D., et al.: Alpelisib plus fulvestrant for PIK3CA-mutated, hormone receptor-positive, human epidermal growth factor receptor-2-negative advanced breast cancer: final overall survival results from SOLAR-1. *Ann Oncol*, 2021, 32, s. 208-217.
- Bardia, A. – Hurvitz, S. A. – DeMichele, A., et al.: Phase I/II trial of exemestane, ribociclib, and everolimus in women with HR+/HER2- advanced breast cancer after progression on CDK4/6 inhibitors (TRINITY-1). *Clin Cancer Res*, 2021, 27, s. 4177-4185.
- Rugo, H. S. – Lerebours, F. – Ciruelos, E., et al.: Alpelisib plus fulvestrant in PIK3CA-mutated, hormone receptor-positive advanced breast cancer after a CDK4/6 inhibitor (BYLieve): one cohort of a phase 2, multicentre, open-label, non-comparative study. *Lancet Oncol*, 2021, 22, s. 489-498.
- Tung, N. M. – Robson, M. E. – Ventz, S., et al.: TBCRC 048: phase II study of olaparib for metastatic breast cancer and mutations in homologous recombination-related genes. *J Clin Oncol*, 2020, 38, s. 4274-4282.
- Baselga, J. – Camponne, M. – Piccart, M., et al.: Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. *N Engl J Med*, 2012, 366, s. 520-529.
- Cook, M. M. – Al Rabadi, L. – Kaempf, A. J., et al.: Everolimus plus exemestane treatment in patients with metastatic hormone receptor-positive breast cancer previously treated with CDK4/6 inhibitor therapy. *Oncologist*, 2021, 26, s. 101-106.
- Jones, R. H. – Casbard, A. – Carucci, M., et al.: Fulvestrant plus capivasertib versus placebo after relapse or progression on an aromatase inhibitor in metastatic, oestrogen receptor-positive breast cancer (FAKTION): a multicentre, randomised, controlled, phase 2 trial. *Lancet Oncol*, 2020, 21, s. 345-357.

Nemetastatický kastročně rezistentní prostatický karcinom

prof. MUDr. Jindřich Fínek, Ph.D., MHA Onkologická a radioterapeutická klinika FN a LF UK, Plzeň

- 1 Smith, M. R. – Saad, F. – Chowdhury, S., et al.: Apalutamide treatment and metastasis-free survival in prostate cancer. *N Engl J Med*, 2018, 378, s. 1408–1418.
- 2 Sternberg, C. N. – Fizazi, K. – Saad, F., et al.: Enzalutamide and survival in nonmetastatic, castration-resistant prostate cancer. *N Engl J Med*, 2020, 382, s. 2197–2206.
- 3 Fizazi, K. – Shore, N. – Tammela, T. L., et al.: Nonmetastatic, castration-resistant prostate cancer and survival with darolutamide. *N Engl J Med*, 2020, 383, s. 1040–1049.

Role multikinázových inhibitorů v léčbě diseminovaných nádorů ledvin v první linii léčby

doc. MUDr. Alexandr Poprach, Ph.D. | MUDr. Radek Lakomý, Ph.D. Klinika komplexní onkologické péče a LF MU, Brno

- 1 Powles, T. – Plimack, E. R. – Soulières, D., et al.: Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial. *Lancet Oncol*, 2020, 21, s. 1563–1573.
- 2 Choueiri, T. K. – Motzer, R. J. – Rini, B. I., et al.: Updated efficacy results from the JAVELIN Renal 101 trial: first-line avelumab plus axitinib versus sunitinib in patients with advanced renal cell carcinoma. *Ann Oncol*, 2020, 31, s. 1030–1039.
- 3 Choueiri, T. K. – Powles, T. – Burotto, M., et al.: CheckMate 9ER Investigators: Nivolumab plus cabozantinib versus sunitinib for advanced renal-cell carcinoma. *N Engl J Med*, 2021, 384, s. 829–841.
- 4 Motzer, R. – Alekseev, B. – Rha, S. Y., et al.: CLEAR Trial Investigators: Lenvatinib plus pembrolizumab or everolimus for advanced renal cell carcinoma. *N Engl J Med*, 2021, 384, s. 1289–1300.
- 5 Escudier, B. – Motzer, R. J. – Tannir, N. M., et al.: Efficacy of nivolumab plus ipilimumab according to number of IMDC risk factors in CheckMate 214. *Eur Urol*, 2020, 77, s. 449–453.

Systémová léčba kožních nádorů kromě melanomu

doc. MUDr. Alexandr Poprach, Ph.D. | MUDr. Radek Lakomý, Ph.D. Klinika komplexní onkologické péče a LF MU, Brno

- 1 Dušek, L. – Mužík, J. – Kubásek, M., et al.: Epidemiologie zhoubných nádorů v České republice. Masarykova univerzita, online. Dostupné z: <http://www.svod.cz>, vyhledáno 8. 6. 2021.
- 2 LoRusso, P. M. – Rudin, C. M. – Reddy, J. C., et al.: Phase I trial of hedgehog pathway inhibitor vismodegib (GDC-0449) in patients with refractory, locally advanced or metastatic solid tumors. *Clin Cancer Res*, 2011, 17, s. 2502–2511.
- 3 Sekulic, A. – Migden, M. R. – Basset-Seguín, N., et al.: ERIVANCE BCC Investigators: Long-term safety and efficacy of vismodegib in patients with advanced basal cell carcinoma: final update of the pivotal ERIVANCE BCC study. *BMC Cancer*, 2017, 17, s. 332.
- 4 Migden, M. R. – Khushalani, N. I. – Chang, A. L. S., et al.: Cemiplimab in locally advanced cutaneous squamous cell carcinoma: results from an open-label, phase 2, single-arm trial. *Lancet Oncol*, 2020, 21, s. 294–305.
- 5 Keeping, S. – Xu, Y. – Chen, C. I., et al.: Comparative efficacy of cemiplimab versus other systemic treatments for advanced cutaneous squamous cell carcinoma. *Future Oncol*, 2021, 17, s. 611–627.
- 6 Romero, D.: Cemiplimab is a new option in BCC. *Nat Rev Clin Oncol*, 2021, dostupné z: <https://doi.org/10.1038/s41571-021-00528-7>, vyhledáno 16. 6. 2021.
- 7 D'Angelo, S. P. – Russell, J. – Lebbé, C., et al.: Efficacy and safety of first-line avelumab treatment in patients with stage IV metastatic Merkel cell carcinoma: A preplanned interim analysis of a clinical trial. *JAMA Oncol*, 2018, 4, e180077.
- 8 Epstein, E. H.: Basal cell carcinomas: attack of the hedgehog. *Nat Rev Cancer*, 2008, 8, s. 743–754.
- 9 Sekulic, A. – Migden, M. R. – Basset-Seguín, N., et al.: Long-term safety and efficacy of vismodegib in patients with advanced basal cell carcinoma: final update of the pivotal ERIVANCE BCC study. *BMC Cancer*, 2017, 17, s. 332.
- 10 Basset-Seguín, N. – Hauschild, A. – Kunstfeld, R., et al.: Vismodegib in patients with advanced basal cell carcinoma: Primary analysis of STEVE, an international, open-label trial. *Eur J Cancer*, 2017, 86, s. 334–348.
- 11 Bertrand, N. – Guerreschi, P. – Basset-Seguín, N., et al.: Vismodegib in neoadjuvant treatment of locally advanced basal cell carcinoma: First results of a multicenter, open-label, phase 2 trial (VISMONEO study): Neoadjuvant vismodegib in locally advanced basal cell carcinoma. *E Clinical Medicine*, 2021, 35, 100844.
- 12 Montaudí, H. – Viotti, J. – Combemale, P., et al.: Cetuximab is efficient and safe in patients with advanced cutaneous squamous cell carcinoma: a retrospective, multicenter study. *Oncotarget*, 2020, 11, s. 378–385.
- 13 Lazar, A. D. – Dinescu, S. – Costache, M.: Deciphering the molecular landscape of cutaneous squamous cell carcinoma for better diagnosis and treatment. *J Clin Med*, 2020, 9, s. 2228.
- 14 Migden, M. R. – Khushalani, N. I. – Chang, A. L. S., et al.: Cemiplimab in locally advanced cutaneous squamous cell carcinoma: results from an open-label, phase 2, single-arm trial. *Lancet Oncol*, 2020, 21, s. 294–305.
- 15 Rischin, D. – Khushalani, N. I. – Schmults, C. D., et al.: Phase II study of cemiplimab in patients (pts) with advanced cutaneous squamous cell carcinoma (CSCC): Langer follow-up. *J Clin Oncol*, 2020, 38, suppl. 15, s. 10018.
- 16 Keeping, S. – Xu, Y. – Chen, C. I., et al.: Comparative efficacy of cemiplimab versus other systemic treatments for advanced cutaneous squamous cell carcinoma. *Future Oncol*, 2021, 17, s. 611–627.
- 17 Stratigos, A. J. – Sekulic, A. – Peris, K., et al.: Cemiplimab in locally advanced basal cell carcinoma after hedgehog inhibitor therapy: an open-label, multi-centre, single-arm, phase 2 trial. *Lancet Oncol*, 2021, 22, s. 848–857.
- 18 D'Angelo, S. – Lebbé, C. – Mortier, L., et al.: First-line avelumab treatment in patients with metastatic Merkel cell carcinoma: primary analysis after ≥15 months of follow-up from JAVELIN Merkel 200, a registration phase 2 trial. *J Immunother Cancer*, 2019, 7, s. 282.
- 19 D'Angelo, S. P. – Bhatia, S. – Brohl, A. S., et al.: Avelumab in patients with previously treated metastatic Merkel cell carcinoma: long-term data and biomarker analyses from the single-arm phase 2 JAVELIN Merkel 200 trial. *J Immunother Cancer*, 2020, 8, e000674.
- 20 Walker, J. W. – Lebbé, C. – Grignani, G., et al.: Efficacy and safety of avelumab treatment in patients with metastatic Merkel cell carcinoma: experience from a global expanded access program. *J Immunother Cancer*, 2020, 8, e000313.

Adjuvantní terapie melanomu v přehledu

MUDr. Ivana Krajsová, MBA Dermatovenerologická klinika 1. LF UK a VFN, Praha

- 1 Testori, A. A. E. – Chiellino, S. – van Akkooi, A. C. J.: Adjuvant therapy for melanoma: past, current, and future developments. *Cancers*, 2020, 12, s. 1994.
- 2 Dummer, R. – Hauschild, A. – Santinami, M., et al.: Five-year analysis of adjuvant dabrafenib plus trametinib in stage III melanoma. *N Engl J Med*, 2020, 383, s. 1139–1148.
- 3 Atkinson, V. – Robert, C. – Grob, J. J., et al.: Improved pyrexia-related outcomes associated with an adapted pyrexia-adverse event (AE) management algorithm in patients (pts) treated with adjuvant dabrafenib + trametinib (dab + tram): primary results of COMBI-APLS. *J Clin Oncol*, 2021, 39, suppl. 15, abstrakt 9525.
- 4 Ascierto, P. A. – DelVecchio, M. – Mandalá, M., et al.: Adjuvant nivolumab versus ipilimumab in resected stage IIIb–C and stage IV melanoma (CheckMate 238): 4-year results from a multicenter, double-blind, randomised, controlled, phase 3 trial. *Lancet Oncol*, 2020, 21, s. 1465–1477.
- 5 Eggermont, A. M. M. – Blank, C. U. – Mandalá, M., et al.: Longer follow-up confirms recurrence-free survival benefit of adjuvant pembrolizumab in high-risk stage III melanoma: updated results from the EORTC 1325-MG/KEYNOTE-054 trial. *J Clin Oncol*, 2020, 38, s. 3925–3936.
- 6 Toor, K. – Middleton, M. R. – Chan, K., et al.: Comparative efficacy and safety of adjuvant nivolumab versus other treatments in adults with resected melanoma: a systematic literature review and network meta-analysis. *BMC Cancer*, 2021, 21, 3, doi:10.1186/s12885-020-07538-1.
- 7 Bello, D. M. – Faries, M. B.: The landmark series: MSLT-1, MSLT-2 and DeCOG (Management of Lymph Nodes). *Ann Surg Oncol*, 2020, 27, s. 15–21.
- 8 Seth, R. – Messersmith, H. – Kaur, V., et al.: Systemic therapy for melanoma: ASCO Guideline. *J Clin Oncol*, 2020, 38, s. 3947–3970.
- 9 Krishnan, T. – Menzies, A. M. – Roberts-Thomson, R.: Applying adjuvant therapy for melanoma into clinical practice. *Expert Rev Anticancer Ther*, 2021, 21, s. 129–133.

Systémová léčba pokročilých uroteliálních nádorů

doc. MUDr. Tomáš Büchler, Ph.D. Onkologická klinika 1. LF UK a Thomayerovy nemocnice, Praha

- 1 Dušek, L. – Mužík, J. – Kubásek, M., et al.: Epidemiologie zhoubných nádorů v České republice. Masarykova univerzita, 2005, cit. 3. 3. 2019, dostupné z: <http://www.svod.cz>.
- 2 Stadler, W. M. – Kuzel, T. – Roth, B., et al.: Phase II study of single-agent gemcitabine in previously untreated patients with metastatic urothelial cancer. *J Clin Oncol Off J Am Soc Clin Oncol*, 1997, 15, s. 3394–3398.
- 3 De Santis, M. – Bellmunt, J. – Mead, G., et al.: Randomized phase II/III trial assessing gemcitabine/carboplatin and methotrexate/carboplatin/vinblastine in patients with advanced urothelial cancer who are unfit for cisplatin-based chemotherapy: EORTC study 30986. *J Clin Oncol Off J Am Soc Clin Oncol*, 2012, 30, s. 191–199.
- 4 von der Maase, H. – Sengelov, L. – Roberts, J. T., et al.: Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer. *J Clin Oncol Off J Am Soc Clin Oncol*, 2005, 23, s. 4602–4608.
- 5 Sternberg, C. N. – de Mulder, P. – Schornagel, J. H., et al.: Seven year update of an EORTC phase III trial of high-dose intensity M-VAC chemotherapy and G-CSF versus classic M-VAC in advanced urothelial tract tumours. *Eur J Cancer*, 2006, 42, s. 50–54.
- 6 Bellmunt, J. – Théodore, C. – Demkov, T., et al.: Phase III trial of vinflunine plus best supportive care compared with best supportive care alone after a platinum-containing regimen in patients with advanced transitional cell carcinoma of the urothelial tract. *J Clin Oncol Off J Am Soc Clin Oncol*, 2009, 27, s. 4454–4461.
- 7 Powles, T. – Park, S. H. – Voog, E., et al.: Avelumab maintenance

- therapy for advanced or metastatic urothelial carcinoma. *N Engl J Med*, 2020, 383, s. 1218–1230.
- 8 Balar, A. V. – Galsky, M. D. – Rosenberg, J. E., et al.: Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: a single-arm, multicentre, phase 2 trial. *Lancet*, 2017, 389, s. 67–76.
 - 9 Powles, T. – Duran, I. – van der Heijden, M. S., et al.: Atezolizumab versus chemotherapy in patients with platinum-treated locally advanced or metastatic urothelial carcinoma (IMvigor211): a multicentre, open-label, phase 3 randomised controlled trial. *Lancet*, 2018, 391, s. 748–757.
 - 10 Sharma, P. – Retz, M. – Siefker-Radtke, A., et al.: Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial. *Lancet Oncol*, 2017, 18, s. 312–322.
 - 11 Vuky, J. – Balar, A. V. – Castellano, D. E., et al.: Updated efficacy and safety of KEYNOTE-052: A single-arm phase 2 study investigating first-line pembrolizumab (pembro) in cisplatin-ineligible advanced urothelial cancer (UC). *J Clin Oncol*, 2018, 36, s. 4524–4524.
 - 12 Bellmunt, J. – de Wit, R. – Vaughn, D. J., et al.: Pembrolizumab as second-line therapy for advanced urothelial carcinoma. *N Engl J Med*, 2017, 376, s. 1015–1026.
 - 13 Vlachostergios, P. J. – Jakubowski, C. D. – Niaz, M. J., et al.: Antibody-drug conjugates in bladder cancer. *Bl cancer*, 2018, 4, s. 247–259.
 - 14 Grivas, P. – Drakaki, A. – Friedlander, T. W., et al.: Conceptual framework for therapeutic development beyond anti-PD-1/PD-L1 in urothelial cancer. *Am Soc Clin Oncol Educ book Am Soc Clin Oncol Annu Meet*, 2019, 39, s. 284–300.
 - 15 Powles, T. – Rosenberg, J. E. – Sonpavde, G., et al.: Primary results of EV-301: A phase III trial of enfortumab vedotin versus chemotherapy in patients with previously treated locally advanced or metastatic urothelial carcinoma. *J Clin Oncol*, 2021, 39, s. 393–393.
 - 16 McGreggor, B. A. – Balar, A. V. – Rosenberg, J. E., et al.: Enfortumab vedotin in cisplatin-ineligible patients with locally advanced or metastatic urothelial cancer who received prior PD-1/PD-L1 inhibitors: An updated analysis of EV-201 Cohort 2. *J Clin Oncol*, 2021, 39, s. 4524–4524.
 - 17 Loriot, Y. – Necchi, A. – Park, S. H., et al.: Erdafitinib in locally advanced or metastatic urothelial carcinoma. *N Engl J Med*, 2019, 381, s. 338–348.
 - 18 Siefker-Radtke, A. O. – Necchi, A. – Park, S. H., et al.: Erdafitinib in locally advanced or metastatic urothelial carcinoma (mUC): Long-term outcomes in BLC2001. *J Clin Oncol*, 2020, 38, s. 5015–5015.
 - 19 Tagawa, S. T. – Balar, A. V. – Petrylak, D. P., et al.: TROPHY-U-01: A phase II open-label study of sacituzumab govitecan in patients with metastatic urothelial carcinoma progressing after platinum-based chemotherapy and checkpoint inhibitors. *J Clin Oncol*, 2021, JCO2003489, doi: 10.1200/JCO.20.03489.
 - 20 Flaig, T. W. – Spiess, P. E. – Agarwal, N., et al.: Bladder Cancer, Version 3.2020, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*, 2020, 18, s. 329–354.
 - 21 Witjes, J. A. – Babjuk, M. – Bellmunt, J., et al.: EAU-ESMO Consensus Statements on the Management of Advanced and Variant Bladder Cancer-An International Collaborative Multistakeholder Effort: Under the Auspices of the EAU-ESMO Guidelines Committees. *Eur Urol*, 2020, 77, s. 223–250.

Nové klinické poznatky o využití biosimilárního bevacizumabu v onkologii

doc. MUDr. Jiří Slíva, Ph.D. Ústav farmakologie, 3. LF UK, Praha

- 1 Tobelem, G.: VEGF: a key therapeutic target for the treatment of cancer-insights into its role and pharmacological inhibition. *Target Oncol*, 2007, 2, s. 153–614.
- 2 EMA. Biosimilars in the EU. Information guide for healthcare professionals. Prepared jointly by the European Medicines Agency and the European Commission, 2017. Dostupné z: https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf, vyhledáno 19. 8. 2021.
- 3 Sacristán, D. – Beydon, M. E. – Ruppen, I., et al.: Analytical similarity assessment of bevacizumab biosimilar candidate MB02 using multiple state-of-the-art assays. *DIA Europe*, 2021.
- 4 Trukhin, D. – Poddubskaya, E. – Andric, Z., et al.: Efficacy, safety and immunogenicity of MB02 (bevacizumab biosimilar) versus reference bevacizumab in advanced non-small cell lung cancer: a randomized, double-blind, phase III study (STELLA). *Bio Drugs*, 2021, 35, s. 429–444.
- 5 Romera, A. – Peredpaya, S. – Shparyk, Y., et al.: Bevacizumab biosimilar BEVZ92 versus reference bevacizumab in combination with FOLFOX or FOLFIRI as first-line treatment for metastatic colorectal cancer: a multicentre, open-label, randomised controlled trial. *Lancet Gastroenterol Hepatol*, 2018, 3, s. 845–855.

Současné možnosti léčby karcinomu vaječníků

prof. MUDr. Michal Zikán, Ph.D. Gynekologicko-porodnická klinika 1. LF UK a Fakultní nemocnice Bulovka, Praha

- 1 Oza, A. M. – Cook, A. D. – Pfisterer, J., et al.: ICON7 trial investigators: Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. *Lancet Oncol*, 2015, 16, s. 928–936.
- 2 Aghajanian, C. – Goff, B. – Nycum, L. R., et al.: Final overall survival and safety analysis of OCEANS, a phase 3 trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent ovarian cancer. *Gynecol Oncol*, 2015, 139, s. 10–16.
- 3 Poveda, A. M. – Selle, F. – Hilpert, F., et al.: Bevacizumab combined with weekly paclitaxel, pegylated liposomal doxorubicin or topotecan in platinum-resistant recurrent ovarian cancer: analysis by chemotherapy cohort of the randomized phase III AURELIA trial. *J Clin Oncol*, 2015, 33, s. 3836–3838.
- 4 Pfisterer, J. – Plante, M. – Vergote, I., et al.: Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. *J Clin Oncol*, 2006, 24, s. 4699–4707.
- 5 Burger, R. A. – Sill, M. W. – Monk, B. J., et al.: Phase II trial of bevacizumab in persistent or recurrent epithelial ovarian cancer or primary peritoneal cancer: A Gynecologic Oncology Group study. *J Clin Oncol*, 2007, 28, s. 5156–5171.
- 6 Cannistra, S. A. – Matulonis, U. A. – Penson, R. T., et al.: Phase II study of bevacizumab in patients with platinum-resistant ovarian cancer or peritoneal serous cancer. *J Clin Oncol*, 2007, 25, s. 5180–5186.
- 7 Aghajanian, C. – Blank, S. V. – Goff, B. A., et al.: OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. *J Clin Oncol*, 2017, 30, s. 2039–2045.
- 8 Ledermann, J. – Harter, P. – Gourley, C., et al.: Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: a preplanned retrospective analysis of outcomes by BRCA status in a randomised phase 2 trial. *Lancet Oncol*, 2014, 15, s. 852–861.
- 9 Ledermann, J. – Harter, P. – Gourley, C., et al.: Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer. *N Engl J Med*, 2012, 366, s. 1382–1392.
- 10 Dušek, L. – Mužík, J. – Kubásek, M., et al.: Epidemiologie zhoubných nádorů v České republice [online]. Masarykova univerzita, 2005. Dostupné z: <http://www.svod.cz>, verze 7.0, vyhledáno 20. 6. 2019.
- 11 Moore, K. – Colombo, N. – Scambia, G., et al.: Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med*, 2018, 379, s. 2495–2505.
- 12 Pujade-Lauraine, E. – Ledermann, J. A. – Selle, F., et al.: Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/EN-GOT-Ov21): a double blind, randomised, placebo-controlled, phase 3 trial. *Lancet Oncol*, 2017, 18, s. 1274–1284.
- 13 Mirza, M. R. – Monk, B. J. – Herrstedt, J., et al.: Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. *N Engl J Med*, 2016, 375, s. 2154–2164.
- 14 Berek, J. S. – Matulonis, U. A. – Peen, U., et al.: Safety and dose modification for patients receiving niraparib. *Ann Oncol*, 2018, 29, s. 1784–1792.
- 15 Wang, J. – Zhang, Z.-Y. – Mirza, M. R., et al.: The exposure-response relationship of niraparib in patients with BRCA mut and non gBRCA mut: results from the ENGOT-OV16/NOVA trial. *Ann Oncol*, 2017, 28.
- 16 Gonzalez, A. – Mirza, M. R. – Vergote, I., et al.: A prospective evaluation of tolerability of niraparib dosing based upon baseline body weight (wt) and platelet (blpl) count: blinded pooled interim safety data from the PRIMA study. *Ann Oncol*, 2018, 29, suppl. 8.
- 17 Kristeleit, R. – Shapiro, G. I. – Burris, H. A., et al.: A phase I-II study of the oral PARP inhibitor rucaparib in patients with germline BRCA1/2-mutated ovarian carcinoma or other solid tumors. *Clin Cancer Res*, 2017, 23, s. 4095–4106.
- 18 Swisher, E. M. – Lin, K. K. – Oza, A. M., et al.: Rucaparib in relapsed, platinum-sensitive high-grade ovarian carcinoma (ARIEL2 Part 1): an international, multicentre, open-label, phase 2 trial. *Lancet Oncol*, 2017, 18, s. 75–87.
- 19 Oza, A. M. – Tinker, A. V. – Oaknin, A., et al.: Antitumor activity and safety of the PARP inhibitor rucaparib in patients with high grade ovarian carcinoma and a germline or somatic BRCA1 or BRCA2 mutation: integrated analysis of data from Study 10 and ARIEL2. *Gynecol Oncol*, 2017, 147, s. 267–275.
- 20 Coleman, R. L. – Oza, A. M. – Lorusso, D., et al.: Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*, 2017, 390, s. 1949–1961.
- 21 González-Martín, A. – Pothuri, B. – Vergote, I., et al.: PRIMA/ENGOT-OV26/GOG-3012 Investigators: Niraparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med*, 2019, 381, s. 2391–2402.

Léčba ovariálních nádorů PARP inhibitory

MUDr. Tomáš Svoboda, Ph.D. Onkologická a radioterapeutická klinika, KOC FN Plzeň

- 1 Farmer, H. – McCabe, N. – Lord, C. J., et al.: Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy. *Nature*, 2005, 434, s. 917–921.
- 2 Konstantinopoulos, P. A. – Ceccaldi, R. – Shapiro, G. I., et al.: Homologous recombination deficiency: exploiting the fundamental vulnerability of ovarian cancer. *Cancer Discov*, 5, s. 1137–1154.
- 3 Berek, J. S. – Matulonis, U. A. – Peen, U., et al.: Safety and dose modification for patients receiving niraparib. *Ann Oncol*, 2018, 29, s. 1784–1792.
- 4 Moore, K. – Colombo, N. – Scambia, G., et al.: Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med*, 2018, 379, s. 2495–2505.
- 5 González-Martín, A. – Pothuri, B. – Vergote, I., et al.: Niraparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med*, 2019, 381, s. 2391–2402.
- 6 Ray-Coquard, I. L. – Pautier, P. – Pignata, S., et al.: 3955 – Phase III PAOLA-1/ENGOT-ov25 trial: Olaparib plus bevacizumab (bev) as maintenance therapy in patients (pts) with newly diagnosed, advanced ovarian cancer (OC) treated with platinum-based chemotherapy (PCh) plus bev. *ESMO 2019. Ann Oncol*, 2019, 30, suppl. 5, s. v851–v934.
- 7 Tew, W. P. – Lachcetti, Ch. – Ellis, A., et al.: PARP inhibitors in the management of ovarian cancer: ASCO Guideline. *J Clin Oncol*, 2020, 38, s. 3468–3493.
- 8 Pilié, P. G. – Tang, Ch. – Mills, G. B., et al.: State-of-the-art strategies for targeting the DNA damage response in cancer. *Nat Rev Clin Oncol*, 2019, 16, s. 81–104.
- 9 Coleman, R. L. – Fleming, G. F. – Brady, M. F., et al.: 2772 – VELIA/GOG-3005: Integration of veliparib (V) with front-line chemotherapy and maintenance in women with high-grade serous carcinoma of ovarian, fallopian tube, or primary peritoneal origin (HGSC). *Ann Oncol*, 2019, 30, suppl. 5, s. v851–v934.
- 10 ClinicalTrials.gov, dostupné z: <https://clinicaltrials.gov/ct2/home>.
- 11 Westin, S. N. – Coleman, R. L. – Fellman, B. M., et al.: EFFORT: Efficacy of adavosertib in parp Resistance: A randomized two-arm non-comparative phase II study of adavosertib with or without olaparib in women with PARP-resistant ovarian cancer. *J Clin Oncol*, 2021, 39, s. 5505–5505.
- 12 Mirza, M. R. – Coleman, R. L. – González-Martín, A. – Moore, K. N., et al.: The forefront of ovarian cancer therapy: update on PARP inhibitors. *Ann Oncol*, 2020, 31, s. 1148–1159.
- 13 Moore, K. N. – Pothuri, B. – Monk, B., et al.: PARP Inhibition in recurrent ovarian cancer. *Clin Adv Hematol Oncol*, 2020, 18, s. 647–655.
- 14 Marmé, F.: Comparison of pharmacologic properties of approved PARP inhibitors. Dostupné z: <https://www.clinicaloptions.com/oncology/programs/parpi-in-ovarian-ca/slidesets/slides-2>, vyhledáno 20. 8. 2021.
- 15 Dostupné z: <https://www.clinicaloptions.com/oncology/slides?q&sortBy&sortOrder=asc&page=1>, vyhledáno 20. 8. 2021.

Změna managementu léčby LSIL

prof. MUDr. Michal Zikán, Ph.D. Gynekologicko-porodnická klinika 1. LF UK a Fakultní nemocnice Bulovka, Praha

- 1 Levine, D. A. – Gaillard, S. L. – Lin, L. L., et al.: *Principles and practice of gynecologic oncology*. Wolters Kluwer, Philadelphia, 2021.
- 2 Serrano, L. – López, A. C. – González, S. P.: Efficacy of a coriolus versicolor-based vaginal gel in women with human papillomavirus-dependent cervical lesions: the PALOMA study. *J Low Genit Tract Dis*, 2021, 25, s. 130–136.
- 3 Criscuolo, A. A. – Sesti, F. – Piccione, E., et al.: Therapeutic efficacy of a coriolus versicolor-based vaginal gel in women with cervical Uterine high-risk HPV infection: a retrospective observational study. *Adv Ther*, 2021, 38, s. 1202–1211.

DLouhodobá odpověď na lenvatinib u pacienta s hepatocelulárním karcinomem – kazuistika

MUDr. Marián Liberko | doc. MUDr. Renata Soumarová, Ph.D., MBA Radioterapeutická a onkologická klinika FN KV a 3. LF UK, Praha

- 1 Kudo, M. – Finn, R. S. – Qin, S., et al.: Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. *Lancet*, 2018, 391, s. 1163–1173.

Oyavas 25 mg/ml koncentrát pro infuzní roztok – lékový profil

doc. MUDr. Jiří Slíva, Ph.D. Ústav farmakologie, 3. LF UK, Praha

- 1 Homsí, J. – Daud, A. I.: Spectrum of activity and mechanism of action of VEGF/PDGF inhibitors. *Cancer Control*, 2007, 14, s. 285–294.
- 2 Borgstrom, P. – Gold, D. P. – Hillan, K. J. – Ferrara, N.: Importance of VEGF for breast cancer angiogenesis in vivo: implications from intravital microscopy of combination treatments with an anti-VEGF neutralizing monoclonal antibody and doxorubicin. *Anticancer Res*, 1999, 19, s. 4203–4214.
- 3 Fernando, N. H. – Hurwitz, H. I.: Inhibition of vascular endothelial growth factor in the treatment of colorectal cancer. *Semin Oncol*, 2003, 30, s. 39–50.
- 4 Ignoffo, R. J.: Overview of bevacizumab: a new cancer therapeutic strategy targeting vascular endothelial growth factor. *Am J Health Syst Pharm*, 2004, 61, s. S21–S26.
- 5 Gordon, M. S. – Margolin, K. – Talpaz, M., et al.: Phase I safety and pharmacokinetic study of recombinant human anti-vascular endothelial growth factor in patients with advanced cancer. *J Clin Oncol*, 2001, 19, s. 843–850.
- 6 Lu, J. F. – Bruno, R. – Eppler, S., et al.: Clinical pharmacokinetics of bevacizumab in patients with solid tumors. *Cancer Chemother Pharmacol*, 2008, 62, s. 779–786.
- 7 Garnier-Viougat, N. – Rixe, O. – Pintaudo, G., et al.: Pharmacokinetics of bevacizumab in haemodialysis. *Nephrol Dial Transplant*, 2007, 22, s. 975.
- 8 Horimatsu, T. – Miyamoto, S. – Morita, S., et al.: Pharmacokinetics of oxaliplatin in a hemodialytic patient treated with modified FOLFOX-6 plus bevacizumab therapy. *Cancer Chemother Pharmacol*, 2011, 68, s. 263–266.
- 9 Garcia, J. – Hurwitz, H. I. – Sandler, A. B., et al.: Bevacizumab (Avastin(R)) in cancer treatment: A review of 15 years of clinical experience and future outlook. *Cancer Treat Rev*, 2020, 86, s. 102017.
- 10 Li, M. – Kroetz, D. L.: Bevacizumab-induced hypertension: Clinical presentation and molecular understanding. *Pharmacol Ther*, 2018, 182, s. 152–160.
- 11 Bevacizumab + sunitinib: microangiopathic haemolytic anaemia. A serious drug interaction between 2 cancer drugs. *Prescrire Int*, 2009, 18, s. 165.
- 12 Kitagawa, Y. – Osumi, H. – Shinozaki, E., et al.: Clinical utility of polyethylene glycol conjugated granulocyte colony-stimulating factor (PEG-G-CSF) for preventing severe neutropenia in metastatic colorectal cancer patients treated with FOLFOXIRI plus bevacizumab: a single-center retrospective study. *BMC Cancer*, 2020, 20, s. 358.
- 13 Nose, Y. – Kagawa, Y. – Hata, T., et al.: Neutropenia is an indicator of outcomes in metastatic colorectal cancer patients treated with FTD/TPI plus bevacizumab: a retrospective study. *Cancer Chemother Pharmacol*, 2020, 86, s. 427–433.

Antitrombotická profylaxe jako součást komplexního přístupu k onkologicky nemocnému

prof. MUDr. Jindřich Fínek, Ph.D., MHA Onkologická a radioterapeutická klinika FN a LF UK v Plzni

- 1 Streiff, J. B. – Abutalib, S. A. – Farge, D., et al.: Update on guidelines for the management of cancer-associated thrombosis. *Oncologist*, 2021, 26, s. e24–e40.
- 2 *Modrá kniha české onkologické společnosti*. 2021, Brno, www.links.cz.
- 3 Streiff, M. B., et al.: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines. Cancer-Associated Venous Thromboembolic Disease. NCCN Guidelines Version 1.2020. Dostupné z: <http://medi-guide.medtool.com/ytmtpdf/9E219C23-6627-2971-9CC9-2BB-8D86873AA.pdf>, vyhledáno 13. 9. 2021.
- 4 Carrier, M. – Khorana, A. A. – Moretto, P., et al.: Lack of evidence to support thromboprophylaxis in hospitalized medical patients with cancer. *Am J Med*, 2014, 127, s. 82–86.e1.
- 5 Kroger, K. – Weiland, D. – Ose, C., et al.: Risk factors for venous thromboembolic events in cancer patients. *Ann Oncol*, 2006, 17, s. 297–303.
- 6 Key, N. S. – Khorana, A. A. – Kuderer, N. M., et al.: Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO clinical practice guideline update. *J Clin Oncol*, 2020, 38, s. 496–520.
- 7 Wang, T. F. – Zwicker, J. L. – Ay, C., et al.: The use of direct oral anticoagulants for primary thromboprophylaxis in ambulatory cancer patients: Guidance from the SSC of the ISTH. *J Thromb Haemost*, 2019, 17, s. 1772–1778.
- 8 Agnelli, G. – Gussone, G. – Bianchini, C., et al.: Nadroparin for the prevention of thromboembolic events in ambulatory patients with metastatic or locally advanced solid cancer receiving chemotherapy: A randomised, placebo-controlled, double-blind study. *Lancet Oncol*, 2009, 10, s. 943–949.
- 9 Agnelli, G. – George, D. J. – Kakkar, A. K., et al.: Semuloparin for thromboprophylaxis in patients receiving chemotherapy for cancer. *N Engl J Med*, 2012, 366, s. 601–609.
- 10 Khorana, A. A. – Kuderer, N. M. – Culakova, E., et al.: Development and validation of a predictive model for chemotherapy-associated thrombosis. *Blood*, 2008, 111, s. 4902–4907.
- 11 ENOXACAN Study Group: Efficacy and safety of enoxaparin versus unfractionated heparin for prevention of deepvein thrombosis in elective cancer surgery: A double-blind randomized multicentre trial with venography assessment. *Br J Surg*, 1997, 84, s. 1099–1103.
- 12 Bergqvist, D. – Agnelli, G. – Cohen, A. T., et al.: Duration of prophylaxis against venous thromboembolism with enoxaparin after surgery for cancer. *N Engl J Med*, 2002, 346, s. 975–980.
- 13 Rasmussen, M. S. – Jorgensen, L. N. – Wille-Jorgensen, P., et al.: Prolonged prophylaxis with dalteparin to prevent late thromboembolic complications in patients undergoing major abdominal surgery: A multicenter randomized open-label study. *J Thromb Haemost*, 2006, 4, s. 2384–2390.

Malnutrice onkologického pacienta

Mgr. et MUDr. Petra Holečková, Ph.D., MBA Ústav radiační onkologie, FNB a 1. LF UK, Praha

- 1 Martin, L. – Senese, P. – Gioulbasanis, I., et al.: Diagnostic criteria for the classification of cancer-associated weight loss. *J Clin Oncol*, 2015, 33, s. 90–99.
- 2 Baracos, V. – Kazemi-Bajestani, S. M.: Clinical outcomes related to muscle mass in humans with cancer and catabolic illnesses. *Int J Biochem Cell Biol*, 2013, 45, s. 2302–2308.
- 3 Mošňová, V. – Šachlová, M. – Benešová, V. – Holečková, P. – Maňásek, V., et al.: Nutriaction – nutriční screening v onkologických ambulancích. 2011 XXXV. Brněnské onkologické dny. Poster. Abstrakt 212p.
- 4 Holečková, P.: Výživa onkologických pacientů. *Acta medicae*, 2015, 8, s. 24–26.
- 5 Kondrup, J. – Allison, S. P. – Elia, M., et al.: ESPEN Guidelines for Nutrition Screening 2002. *Guideline Clin Nutr*, 2003, 22, s. 415–421.
- 6 Dotazník hodnocení nutričního rizika. 2010, 1–2. Dotupné z: www.links.cz/files/60XX_Dotaznik%20nutricniho%20rizika%20A4_K5.pdf, vyhledáno 14. 9. 2021.
- 7 Mourtzakis, M. – Prado, C. M. – Lieffers, J. R., et al.: A practical and precise approach to quantification of body composition in cancer patients using computer tomography images acquired during routine care. *Appl Physiol Nutr Metab*, 2008, 33, s. 997–1006.
- 8 Martin, L. – Birdsell, L. – Macdonald, N., et al.: Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *J Clin Oncol*, 2013, 31, s. 1539–1547.
- 9 Prado, C. M. M. – Antoun, S. – Sawyer, M. B., et al.: Two faces of drug therapy in cancer: drug-related lean tissue loss and its adverse consequences to survival and toxicity. *Curr Opin Clin Nutr Metab Care*, 2011, 14, s. 250–254.
- 10 Antoun, S. – Baracos, V. E. – Birdsell, L., et al.: Low body mass index and sarcopenia associated with dose-limiting toxicity of sorafenib in patients with renal cell carcinoma. *Ann Oncol*, 2010, 21, s. 1594–1598.
- 11 Pekař, M. – Pekařová, A. – Chovancová, T., et al.: Sarkopenická obezita – aktuální přehled problematiky. *Vnitř Lek*, 2020, 66, s. 39–43.
- 12 Barret, M. – Malka, D. – Aparicio, T., et al.: Nutritional status affects treatment tolerability and survival in metastatic colorectal cancer patients: results of an AGE0 prospective multicenter study. *Oncology*, 2011, 81, s. 395–402.
- 13 Lee, J. S. – Kim, Y. S. – Kim, E. Y. – Jin, W.: Prognostic significance of CT-determined sarcopenia in patients with advanced gastric cancer. *PLoS One*, 2018, 13, s. e0202700.
- 14 Baracos, V. E. – Arribas, L.: Sarcopenic obesity: hidden muscle wasting and its impact for survival and complications of cancer therapy. *Ann Oncol*, 2018, 29, suppl. 2, s. ii 1–ii 9.
- 15 Norman, K. – Pichard, C. – Lochs, H. – Pirlich, M.: Prognostic impact of disease-related malnutrition. *Clin Nutr*, 2008, 27, s. 5–15.
- 16 Arends, J. – Bachmann, P. – Baracos, V., et al.: ESPEN guidelines on nutrition in cancer patients. *Clin Nutr*, 2017, 36, s. 11–48.

Měnící se pohled na iniciační léčbu chronické lymfocytární leukemie

prof. MUDr. Tomáš Papajík, CSc. | prof. MUDr. Zuzana Kubová, CSc. | MUDr. Peter Turcsányi, Ph.D. | MUDr. Renata Urbanová, Ph.D.

Hemato-onkologická klinika FN a LF UP v Olomouci

- Dostupné z: <https://seer.cancer.gov/statfacts/html/cllyl.html>, vyhledáno 1. 7. 2021.
- Dostupné z: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/leukaemia-cll/incidence#heading=Two>, vyhledáno 1. 7. 2021.
- Dostupné z: <http://www.uzis.cz/registry-nzis/nor>, vyhledáno 1. 7. 2021.
- Hallek, M.: Chronic lymphocytic leukemia: 2020 update on diagnosis, risk stratification and treatment. *Am J Hematol*, 2019, 94, s. 1266–1287.
- Eichhorst, B. – Robak, T. – Montserrat, E., et al.: Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*, 2021, 32, s. 23–33.
- Burger, J. A. – O'Brien, S.: Evolution of CLL treatment – from chemoimmunotherapy to targeted and individualized therapy. *Nat Rev Clin Oncol*, 2018, 15, s. 510–527.
- Zoellner, A. K. – Höhler, T. – Fries, S., et al.: Altered treatment of chronic lymphocytic leukemia in Germany during the last decade. *Ann Hematol*, 2016, 95, s. 853–861.
- Pulte, D. – Redaniel, M. T. – Bird, J., et al.: Survival for patients with chronic leukemias in the US and Britain: age-related disparities and changes in the early 21st century. *Eur J Haematol*, 2015, 94, s. 540–545.
- Dostupné z: <https://www.cancerresearchuk.org/about-cancer/chronic-lymphocytic-leukaemia-cll>, vyhledáno 12. 7. 2021.
- Ghamlouch, H. – Nguyen-Khac, F. – Bernard, O. A.: Chronic lymphocytic leukaemia genomics and the precision medicine era. *Br J Haematol*, 2017, 178, s. 852–870.
- Gaidano, G. – Rossi, D.: The mutational landscape of chronic lymphocytic leukemia and its impact on prognosis and treatment. *Hematology Am Soc Hematol Educ Program*, 2017, 2017, s. 329–337.
- Hampel, P. J. – Parikh, S. A. – Call, T. G.: Incorporating molecular biomarkers into the continuum of care in chronic lymphocytic leukemia. *Leuk Lymphoma*, 2021, 62, s. 1289–1301.
- Woyach, J. A.: Treatment-naive CLL: lessons from phase 2 and phase 3 clinical trials. *Hematology Am Soc Hematol Educ Program*, 2019, 2019, s. 476–481.
- Rhodes, J. M. – Barrientos, J. C.: Chemotherapy-free frontline therapy for CLL: is it worth it? *Hematology Am Soc Hematol Educ Program*, 2020, 2020, s. 24–32.
- Schiattone, L. – Ghia, P. – Scarfó, L.: The evolving treatment landscape of chronic lymphocytic leukemia. *Curr Opin Oncol*, 2019, 31, s. 568–573.
- CLL Trialists' Collaborative Group: Chemotherapeutic options in chronic lymphocytic leukemia: a meta-analysis of the randomized trials. *J Natl Cancer Inst*, 1999, 91, s. 861–868.
- Hoechstetter, M. A. – Busch, R. – Eichhorst, B., et al.: Early, risk-adapted treatment with fludarabine in Binet stage A chronic lymphocytic leukemia patients: results of the CLL1 trial of the German CLL study group. *Leukemia*, 2017, 31, s. 2833–2837.
- Hering, C. D. – Cymbalista, F. – Groß-Ophoff-Müller, C., et al.: Early treatment with FCR versus watch and wait in patients with stage Binet A high-risk chronic lymphocytic leukemia (CLL): a randomized phase 3 trial. *Leukemia*, 2020, 34, s. 2038–2050.
- Langerbeins, P. – Bahlo, J. – Rhein, C., et al.: Ibrutinib versus placebo in patients with asymptomatic, treatment-naïve early stage chronic lymphocytic leukemia (CLL): primary endpoint results of the phase 3 double-blind randomized CLL12 trial. Prezentováno na 2019 EHA Congress, 13.–16. 6. 2019, Amsterdam, Nizozemsko, abstrakt LB2602.
- Hallek, M. – Cheson, B. D. – Catovsky, D., et al.: iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. *Blood*, 2018, 131, s. 2745–2760.
- Fischer, K. – Bahlo, J. – Fink, A. M., et al.: Long-term remissions after FCR chemoimmunotherapy in previously untreated patients with CLL: updated results of the CLL8 trial. *Blood*, 2016, 127, s. 208–215.
- Eichhorst, B. – Fink, A. M. – Bahlo, J., et al.: First-line chemoimmunotherapy with bendamustine and rituximab versus fludarabine, cyclophosphamide, and rituximab in patients with advanced chronic lymphocytic leukaemia (CLL10): an international, open-label, randomised, phase 3, non-inferiority trial. *Lancet Oncol*, 2016, 17, s. 928–942.
- Goede, V. – Fischer, K. – Dyer, M. J. S., et al.: Overall survival benefit of obinutuzumab over rituximab when combined with chlorambucil in patients with chronic lymphocytic leukemia and comorbidities: Final survival analysis of the CLL11 study. *EHA Library*, 2018, 215923, s. S151.
- Byrd, J. C. – Brown, J. R. – O'Brien, S., et al.: RESONATE Investigators: Ibrutinib versus ofatumumab in previously treated chronic lymphoid leukemia. *N Engl J Med*, 2014, 371, s. 213–223.
- Burger, J. A. – Barr, P. M. – Robak, T., et al.: Long-term efficacy and safety of frontline ibrutinib treatment for patients with CLL/SLL: 5 years of follow-up from the phase 3 RESONATE-2 study. *Leukemia*, 2020, 34, s. 787–798.
- Woyach, J. A. – Ruppert, A. S. – Heerema, N. A., et al.: Ibrutinib regimens versus chemoimmunotherapy in older patients with untreated CLL. *N Engl J Med*, 2018, 379, s. 2517–2528.
- Moreno, C. – Greil, R. – Demirkan, F., et al.: Ibrutinib plus obinutuzumab versus chlorambucil plus obinutuzumab in first-line treatment of chronic lymphocytic leukaemia (ILLUMINATE): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol*, 2019, 20, s. 43–56.
- Shanafelt, T. D. – Wang, X. V. – Kay, N. E., et al.: Ibrutinib-rituximab or chemoimmunotherapy for chronic lymphocytic leukemia. *N Engl J Med*, 2019, 381, s. 432–443.
- Shanafelt, T. D. – Wang, V. – Kay, N. E., et al.: Ibrutinib and rituximab provides superior clinical outcome compared to FCR in younger patients with chronic lymphocytic leukemia (CLL): extended follow-up from the E1912 Trial. *Blood*, 2019, 134, suppl. 1, s. 33.
- Allan, J. N. – Shanafelt, T. – Wiestner, A., et al.: Long-term efficacy of first-line ibrutinib treatment for chronic lymphocytic leukemia (CLL) with 4 years of follow-up in patients with TP53 aberrations (del(17p) or TP53 mutation): A pooled analysis from 4 clinical trials. *Blood*, 2020, 136, suppl. 1, s. 23–24.
- Byrd, J. C. – Woyach, J. A. – Furman, R. R., et al.: Acalabrutinib in treatment-naïve chronic lymphocytic leukemia. *Blood*, 2021, 137, s. 3327–3338.
- Sharman, J. P. – Egyed, M. – Jurczak, W., et al.: Acalabrutinib with or without obinutuzumab versus chlorambucil and obinutuzumab for treatment-naïve chronic lymphocytic leukaemia (ELEVATE TN): a randomised, controlled, phase 3 trial. *Lancet*, 2020, 395, s. 1278–1291.
- Roberts, A. W. – Davids, M. S. – Pagel, J. M., et al.: Targeting BCL2 with venetoclax in relapsed chronic lymphocytic leukemia. *N Engl J Med*, 2016, 374, s. 311–322.
- Scott, L. J.: Venetoclax: a review in relapsed/refractory chronic lymphocytic leukemia. *Target Oncol*, 2019, 14, s. 493–504.
- Seymour, J. F. – Kipps, T. J. – Eichhorst, B., et al.: Venetoclax-rituximab in relapsed or refractory chronic lymphocytic leukemia. *N Engl J Med*, 2018, 378, s. 1107–1120.
- Fischer, K. – Al-Sawaf, O. – Bahlo, J., et al.: Venetoclax and obinutuzumab in patients with CLL and coexisting conditions. *N Engl J Med*, 2019, 380, s. 2225–2236.
- Al-Sawaf, O. – Zhang, C. – Tandon, M., et al.: Venetoclax plus obinutuzumab versus chlorambucil plus obinutuzumab for previously untreated chronic lymphocytic leukaemia (CLL14): follow-up results from a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol*, 2020, 21, s. 1188–1200.

Novinky v léčbě chronické lymfocytární leukemie

MUDr. Martin Břejcha, Ph.D. Nemocnice AGEL Nový Jičín, a. s.

- International CLL-IPi working group. An international prognostic index for patients with chronic lymphocytic leukaemia (CLL-IPi): a meta-analysis of individual patient data. *Lancet Oncol*, 2016, 17, s. 779–790.
- Binet, J. L. – Auquier, A. – Dighiero, G., et al.: A new prognostic classification of chronic lymphocytic leukemia derived from a multivariate survival analysis. *Cancer*, 1981, 48, s. 198–206.
- Rai, K. R.: A critical analysis of staging in CLL. In: Gale, R. P. – Rai, K. R. (eds.). *Chronic lymphocytic leukemia: recent progress and future directions*. New York, Alan R. Liss, 1987, s. 253–264.
- Hallek, M.: Chronic lymphocytic leukemia: 2017 update on diagnosis, risk stratification, and treatment. *Am J Hematol*, 2017, 92, s. 946–965.
- Hallek, M. – Cheson, B. D. – Catovsky, D., et al.: iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. *Blood*, 2018, 131, s. 2745–2760.
- Hallek, M.: Chronic lymphocytic leukemia: 2020 update on diagnosis, risk stratification and treatment. *Am J Hematol*, 2019, 94, s. 1266–1287.
- Eichhorst, B. – Robak, T. – Montserrat, E., et al.: Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up (dagger). *Ann Oncol*, 2020, 42469-X, S0923–7534.
- Farooqui, M. Z. – Valdez, J. – Martyr, S., et al.: Ibrutinib for previously untreated and relapsed or refractory chronic lymphocytic leukaemia with TP53 aberrations: a phase 2, single-arm trial. *Lancet Oncol*, 2015, 16, s. 169–176.
- Hallek, M. – Fischer, K. – Fingerle-Rowson, G., et al.: International Group of Investigators: German Chronic Lymphocytic Leukaemia Study Group Addition of rituximab to fludarabine and cyclophosphamide in patients with chronic lymphocytic leukaemia: a randomised, open-label, phase 3 trial. *Lancet*, 2010, 376, s. 1164–1174.
- Fischer, K. – Al-Sawaf, O. – Bahlo, J., et al.: Venetoclax and obinutuzumab in patients with CLL and coexisting conditions. *N Engl J Med*, 2019, 380, s. 2225–2236.
- Doubek, M. – Špaček, M. – Pospíšilová, Š., et al.: Doporučení pro diagnostiku a léčbu chronické lymfocytární leukemie (CLL) – 2018. *Transfuzie Hematol Dnes*, 2018, 24, s. 208–220.
- Pospíšilová, S. – Gonzalez, D. – Malcikova, J., et al.: ERIC recommendations for identification in chronic lymphocytic leukemia. *Leukemia*, 2012, 26, s. 1458–1461.
- Břejcha, M. – Stoklasova, M. – Brychtova, Y., et al.: Clonal evolution in chronic lymphocytic leukemia detected by fluorescence in situ hybridization and conventional cytogenetics after stimulation with Cp Golligo nucleotides and interleukin-2: a prospective analysis. *Leuk Res*, 2014, 38, s. 170–175.
- Malcikova, J. – Tausch, E. – Rossi, D., et al.: ERIC recommendations for TP53 mutation analysis in chronic lymphocytic leukemia-update on methodological approaches and results interpretation. *Leukemia*, 2018, 32, s. 1070–1080.
- Eichhorst, B. – Robak, T. – Montserrat, E., et al.: Chronic lymphocytic leukaemia: ESMO clinical practice guidelines for diagnosis, treatment and follow-up (dagger). *Ann Oncol*, 2020, 42469-X, S0923–7534.
- Burger, J. A. – Barr, P. M. – Robak, T., et al.: Long-term efficacy and safety of first-line ibrutinib treatment for patients with CLL/SLL: 5 years of follow-up from the phase 3 RESONATE-2 study. *Leukemia*, 2020, 34, s. 787–798.
- Fischer, K. – Al-Sawaf, O. – Bahlo, J., et al.: Venetoclax and obinutuzumab in patients with CLL and coexisting conditions. *N Engl J Med*, 2019, 380, s. 2225–2236.
- Brown, J. R. – Byrd, J. C. – Coutre, S. E., et al.: Idelalisib, an inhibitor of phosphatidylinositol 3-kinase p110 δ , for relapsed/refractory chronic lymphocytic leukemia. *Blood*, 2014, 123, s. 3390–3397.
- Mato, A. R. – Hill, B. T. – Lamanna, N., et al.: Optimal sequencing of ibrutinib, idelalisib, and venetoclax in chronic lymphocytic leukemia: results from a multicenter study of 683 patients. *Ann Oncol*, 2017, 28, s. 1050–1056.
- Dreger, P. – Corradini, P. – Kimby, E., et al.: Indications for allogeneic stem cell transplantation in chronic lymphocytic leukemia: the EBMT transplant consensus. *Leukemia*, 2007, 21, s. 12–17.
- Ghia, P. – Pluta, A. – Wach, M., et al.: ASCEND: Phase III, randomized trial of acalabrutinib versus idelalisib plus rituximab or bendamustine plus rituximab in relapsed or refractory chronic lymphocytic leukemia. *J Clin Oncol*, 2020, 38, s. 2849–2861.
- Byrd, J. C. – Hillmen, P. – Ghia, P., et al.: Acalabrutinib versus ibrutinib in previously treated chronic lymphocytic leukemia: results of the first randomized phase III trial. *J Clin Oncol*, 2021, JCO2101210.
- Tam, C. S. – Trotman, J. – Opat, S., et al.: Phase 1 study of the selective BTK inhibitor zanubrutinib in B-cell malignancies and safety and efficacy evaluation in CLL. *Blood*, 2019, 134, s. 851–859.
- Flinn, I. W. – Hillmen, P. – Montillo, M., et al.: The phase 3 DUO trial: duvelisib vs ofatumumab in relapsed and refractory CLL/SLL. *Blood*, 2018, 132, s. 2446–2455.
- Rogers, K. A. – Huang, Y. – Ruppert, A. S., et al.: Phase II study of combination obinutuzumab, ibrutinib, and venetoclax in treatment-naïve and relapsed or refractory chronic lymphocytic leukemia. *J Clin Oncol*, 2020, 38, s. 3626–3637.
- Kater, A. – Owen, C. – Moreno, C., et al.: Fixed-duration ibrutinib and venetoclax versus chlorambucil plus obinutuzumab for first-line chronic lymphocytic leukemia: Primary analysis of the phase 3 GLOW study. *EHA Library*, 2021, 330172, LB1902 (EHA LB1902).
- Frey, N. V. – Gill, S. – Hexner, E. O., et al.: Long-term outcomes from a randomized dose optimization study of chimeric antigen receptor modified T cells in relapsed chronic lymphocytic leukemia. *J Clin Oncol*, 2020, 38, s. 2862–2871.

Výhled léčby pacientů s difúzním B-velkobuněčným lymfomem

doc. MUDr. David Belada, Ph.D. IV. interní hematologická klinika, FN a LF UK v Hradci Králové

- 1 Coiffier, B. – Lepage, E. – Briere, J., et al.: CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. *N Engl J Med*, 2002, 346, s. 235–242.
- 2 Kühn, A. – Cunningham, D. – Counsell, N., et al.: Outcome of elderly patients with diffuse large B-cell lymphoma treated with R-CHOP: results from the UK NCRI R-CHOP14v21 trial with combined analysis of molecular characteristics with the DSHNHL RICOVER-60 trial. *Ann Oncol*, 2017, 28, s. 1540–1546.
- 3 Younes, A. – Sehn, L. H. – Johnson, P., et al.: Randomized phase III trial of ibrutinib and rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone in non-germinal center B-cell diffuse large B-cell lymphoma. *J Clin Oncol*, 2019, 37, s. 1285–1295.
- 4 Nowakowski, G. S. – Chiappella, A. – Witzig, T. E., et al.: ROBUST: lenalidomide-R-CHOP versus placebo-R-CHOP in previously untreated ABC-type diffuse large B-cell lymphoma. *Future Oncol*, 2016, 12, s. 1553–1563.
- 5 Davies, A. – Cummin, T. E. – Barrans, S., et al.: Gene-expression profiling of bortezomib added to standard chemioimmunotherapy for diffuse large B-cell lymphoma (REMOB-LB): an open-label, randomised, phase 3 trial. *Lancet Oncol*, 2019, 20, s. 649–662.
- 6 Barlett, N. – Wilson, W., et al.: Dose-adjusted EPOCH-R compared with R-CHOP as frontline therapy for diffuse large B-cell lymphoma: clinical outcomes of the phase III Intergroup Trial Alliance/CALGB 50303. *J Clin Oncol*, 2019, 37, s. 1790–1799.
- 7 Belada, D. – Kopeckova, K., et al.: First-in-class: a phase IB, open-label, a randomized study to assess safety of tafasitamab or tafasitamab+lenalidomide in addition to R-CHOP in patients with newly diagnosed DLBCL. *Hematological Oncology*, 2021, 39, suppl. 2, abstrakt 237.
- 8 Zhang, M., et al.: Genetic subtype guided rituximab-based immunotherapy improves outcome in newly diagnosed diffuse large B-CELL lymphoma: First report of a randomized phase 2 study. *Hematological Oncology*, 2021, 39, suppl. 2, abstrakt 026.
- 9 Crump, M. – Neelapu, S. S. – Farooq, U., et al.: Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study. *Blood*, 2017, 130, s. 1800–1808.
- 10 Sehn, L. – Herrera, A., et al.: Polatumumab vedotin in relapsed or refractory diffuse large B-cell lymphoma. *J Clin Oncol*, 2020, 38, s. 155–165.
- 11 Schuster, S. J. – Bishop, M. R. – Tam, C. S., et al.: Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma. *N Engl J Med*, 2019, 380, s. 45–56.
- 12 Neelapu, S. S. – Jacobson, C. A. – Oluwole, O. O., et al.: Outcomes of older patients in ZUMA-1, a pivotal study of axicabtagene ciloleucel in refractory large B-cell lymphoma. *Blood*, 2020, 135, s. 2106–2109.
- 13 Schuster, S. J.: Bispecific antibodies for the treatment of lymphomas: Promises and challenges. *Hematol Oncol*, 2021, 39, suppl. 1, s. 113–116.

Protinádorový synergismus mezi venetoklaxem a azacytidinem

prof. MUDr. Pavel Klener, Ph.D. I. interní klinika – hematologie, VFN a 1. LF UK, Praha

- 1 Hanahan, D. – Weinberg, R. A.: Hallmarks of cancer: the next generation. *Cell*, 2011, 144, s. 646–674.
- 2 Robertson, K. D.: DNA methylation and human disease. *Nature Reviews Genetics*, 2005, 6, s. 597–610.
- 3 Lauria, F. – Raspadori, D. – Rondelli, D., et al.: High bcl-2 expression in acute myeloid leukemia cells correlates with CD34 positivity and complete remission rate. *Leukemia*, 1997, 11, s. 2075–2078.
- 4 Campos, L. – Rouault, J. P. – Sabido, O., et al.: High expression of bcl-2 protein in acute myeloid leukemia cells is associated with poor response to chemotherapy. *Blood*, 1993, 81, s. 3091–3096.
- 5 Sorm, F. – Piskala, A. – Cihák, A., et al.: 5-Azacytidine, a new, highly effective cancerostatic. *Experientia*, 1964, 20, s. 202–203.
- 6 de Vos, D. – van Overveld, W.: Decitabine: a historical review of the development of an epigenetic drug. *Ann Hematol*, 2005, 84, suppl. 1, s. 3–8.
- 7 Krečmerová, M. – Otmar, M.: 5-azacytosine compounds in medicinal chemistry: current stage and future perspectives. *Future Med Chem*, 2012, 4, s. 991–1005.
- 8 Stomper, J. – Rotonondo, J. C. – Greve, G., et al.: Hypomethylating agents (HMA) for the treatment of acute myeloid leukemia and myelodysplastic syndromes: mechanisms of resistance and novel HMA-based therapies. *Leukemia*, 2021, 35, s. 1873–1889.
- 9 Diesch, J. – Zwick, A. – Garz, A. K., et al.: A clinical-molecular update on azanucleoside-based therapy for the treatment of hematologic cancers. *Clin Epigenetics*, 2016, 8, s. 71.
- 10 Kantarjian, H. – Issa, J. P. – Rosenfeld, C. S., et al.: Decitabine improves patient outcomes in myelodysplastic syndromes: results of a phase III randomized study. *Cancer*, 2006, 106, s. 1794–1803.
- 11 Kaminskis, E. – Farrell, A. – Abraham, S., et al.: Approval summary: azacitidine for treatment of myelodysplastic syndrome subtypes. *Clinical cancer research. J Am Assoc Cancer Research*, 2005, 11, s. 3604–3608.
- 12 Welch, J. S. – Pettit, A. A. – Miller, C. A., et al.: TP53 and decitabine in acute myeloid leukemia and myelodysplastic syndromes. *New Eng J Med*, 2016, 375, s. 2023–2036.
- 13 Craddock, C. – Quek, L. – Goardon, N., et al.: Azacitidine fails to eradicate leukemic stem/progenitor cell populations in patients with acute myeloid leukemia and myelodysplasia. *Leukemia*, 2013, 27, s. 1028–1036.
- 14 Figueroa, M. E. – Lugthart, S. – Li, Y., et al.: DNA methylation signatures identify biologically distinct subtypes in acute myeloid leukemia. *Cancer Cell*, 2010, 17, s. 13–27.
- 15 Souers, A. J. – Leverson, J. D. – Boghaert, E. R., et al.: ABT-199, a potent and selective BCL-2 inhibitor, achieves antitumor activity while sparing platelets. *Nature Medicine*, 2013, 19, s. 202–208.
- 16 Konopleva, M. – Pollyea, D. A. – Potluri, J., et al.: Efficacy and biological correlates of response in a phase II study of venetoklax monotherapy in patients with acute myelogenous leukemia. *Cancer Discovery*, 2016, 6, s. 1106–1117.
- 17 Chan, S. M. – Thomas, D. – Corces-Zimmerman, M. R., et al.: Isocitrate dehydrogenase 1 and 2 mutations induce BCL-2 dependence in acute myeloid leukemia. *Nature Medicine*, 2015, 21, s. 178–184.
- 18 Lagadinou, E. D. – Sach, A. – Callahan, K., et al.: BCL-2 inhibition targets oxidative phosphorylation and selectively eradicates quiescent human leukemia stem cells. *Cell Stem Cell*, 2013, 12, s. 329–341.
- 19 Bogenberger, J. M. – Kornblau, S. M. – Pierce, W. E., et al.: BCL-2 family proteins as 5-azacytidine-sensitizing targets and determinants of response in myeloid malignancies. *Leukemia*, 2014, 28, s. 1657–1665.
- 20 Bogenberger, J. M. – Delman, D. – Hansen, N., et al.: Ex vivo activity of BCL-2 family inhibitors ABT-199 and ABT-737 combined with 5-azacytidine in myeloid malignancies. *Leukemia & Lymphoma*, 2015, 56, s. 226–229.
- 21 DiNardo, C. D. – Pratz, K. W. – Letai, A., et al.: Safety and preliminary efficacy of venetoklax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukaemia: a non-randomised, open-label, phase 1b study. *Lancet Oncol*, 2018, 19, s. 216–228.
- 22 DiNardo, C. D. – Pratz, K. – Pullarkat, V., et al.: Venetoklax combined with decitabine or azacitidine in treatment-naive, elderly patients with acute myeloid leukemia. *Blood*, 2019, 133, s. 7–17.
- 23 DiNardo, C. D. – Jonas, B. A. – Pullarkat, V., et al.: Azacitidine and venetoklax in previously untreated acute myeloid leukemia. *New Eng J Med*, 2020, 383, s. 617–629.
- 24 Tsao, T. – Shi, Y. – Kornblau, S., et al.: Concomitant inhibition of DNA methyltransferase and BCL-2 protein function synergistically induce mitochondrial apoptosis in acute myelogenous leukemia cells. *Ann Hematol*, 2012, 91, s. 1861–1870.
- 25 Jin, S. – Cojocari, D. – Purkal, J. J., et al.: 5-Azacytidine induces NOXA to prime AML cells for venetoklax-mediated apoptosis. *Clinical cancer research. J Am Assoc Cancer Research*, 2020, 26, s. 3371–3383.
- 26 Nguyen, L. X. T. – Troadec, E. – Kalvala, A., et al.: The BCL-2 inhibitor venetoklax inhibits Nrf2 antioxidant pathway activation induced by hypomethylating agents in AML. *J Cell Physiol*, 2019, 234, s. 14040–14049.
- 27 Pollyea, D. A. – Stevens, B. M. – Jones, C. L., et al.: Venetoklax with azacitidine disrupts energy metabolism and targets leukemia stem cells in patients with acute myeloid leukemia. *Nature Med*, 2018, 24, s. 1859–1866.
- 28 Lin, K. H. – Xie, A. – Rutter, J. C., et al.: Systematic dissection of the metabolic-apoptotic interface in AML reveals heme biosynthesis to be a regulator of drug sensitivity. *Cell Metabolism*, 2019, 29, s. 1217–1231.e7.
- 29 Chen, X. – Glytsou, C. – Zhou, H., et al.: Targeting mitochondrial structure sensitizes acute myeloid leukemia to venetoklax treatment. *Cancer Discovery*, 2019, 9, s. 890–909.
- 30 Lee, J. B. – Khan, D. H. – Hurren, R., et al.: Venetoklax enhances T cell-mediated antileukemic activity by increasing ROS production. *Blood*, 2021, 138, s. 234–245.
- 31 Inguva, A. – Pollyea, D. A.: SOHO State of the Art Updates and Next Questions: The Past, Present and Future of Venetoclax-Based Therapies in AML. *Clin Lymph Myelom Leuk*, 2021, S2152–2650(21)00283–00284.
- 32 Contieri, B. – Duarte, B. K. L. – Lazarini, M.: Updates on DNA methylation modifiers in acute myeloid leukemia. *Ann Hematol*, 2020, 99, s. 693–701.

Současná doporučení pro léčbu mnohočetného myelomu

MUDr. Hana Plonková | MUDr. Tomáš Jelínek, Ph.D. | MUDr. Tereza Popková | prof. MUDr. Roman Hájek, CSc.

Klinika hematookologie FN Ostrava, LF Ostravské univerzity, Ostrava

- 1 Moreau, P. – San Miguel, J. – Sonneveld, P., et al.: ESMO Guidelines Committee. Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*, 2017, 28, suppl. 4, s. iv52–iv61.
- 2 Moreau, P. – Kumar, S. K. – San Miguel, J., et al.: Treatment of relapsed and refractory multiple myeloma: recommendations from the International Myeloma Working Group. *Lancet Oncol*, 2021, 22, s. e105–e118.
- 3 Dimopoulos, M. A. – Moreau, P. – Terpos, E., et al.: Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*, 2021, 32, s. 309–322.
- 4 Dimopoulos, M. A. – Moreau, P. – Terpos, E., et al.: Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Hemasphere*, 2021, 5, s. e528.
- 5 Moreau, P. – Attal, M. – Facon, T.: Frontline therapy of multiple myeloma. *Blood*, 2015, 125, s. 3076–3084.
- 6 Roussel, M. – Lauwers-Cances, V. – Robillard, N., et al.: Front-line transplantation program with lenalidomide, bortezomib, and dexamethasone combination as induction and consolidation followed by lenalidomide maintenance in patients with multiple myeloma: a phase II study by the Intergroupe Francophone du Myélome. *J Clin Oncol*, 2014, 32, s. 2712–2717.
- 7 Rosinol, L. – Oriol, A. – Rios, R., et al.: Bortezomib, lenalidomide, and dexamethasone as induction therapy prior to autologous transplant in multiple myeloma. *Blood*, 2019, 134, s. 1337–1345.
- 8 Moreau, P. – Attal, M. – Hulin, C., et al.: Bortezomib, thalidomide, and dexamethasone as induction therapy prior to autologous transplant in multiple myeloma. *Blood*, 2019, 134, s. 1337–1345.
- 9 Voorhees, P. M. – Kaufman, J. L. – Laubach, J. P., et al.: Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial. *Blood*, 2020, 136, s. 936–945.
- 10 Attal, M. – Lauwers-Cances, V. – Hulin, C., et al.: Study IFM. Lenalidomide, bortezomib, and dexamethasone with transplantation for myeloma. *N Engl J Med*, 2017, 376, s. 1311–1320.
- 11 Cavo, M. – Gay, F. – Beksac, M., et al.: Autologous haematopoietic stem-cell transplantation versus bortezomib-melphalan-prednisone, with or without bortezomib-lenalidomide-dexamethasone consolidation therapy, and lenalidomide maintenance for newly diagnosed multiple myeloma (EMN02/HO95): a multicentre, randomised, open-label, phase 3 study. *Lancet Haematol*, 2020, 7, s. e456–e468.
- 12 Cavo, M. – Petrucci, M. T. – Di Raimondo, F., et al.: Up front single versus double autologous stem cell transplantation for newly diagnosed multiple myeloma: An intergroup, multicenter, phase III study of the European Myeloma Network (EMN02/HO95 MM Trial). *Blood*, 2016, 128, s. 991.
- 13 Hájek, R. – Maisnar, V. – Krejčí, M., et al.: Diagnostika a léčba mnohočetného myelomu. *Transf Hematol Dnes*, 2018, suppl. 1, s. 1–155.
- 14 McCarthy, P. L. – Holstein, S. A. – Petrucci, M. T., et al.: Lenalidomide

- maintenance after autologous stem-cell transplantation in newly diagnosed multiple myeloma: A meta-analysis. *J Clin Oncol*, 2017, 35, s. 3279–3289.
- 15 Durie, B. G. M. – Hoering, A. – Abidi, M. H., et al.: Bortezomib with lenalidomide and dexamethasone versus lenalidomide and dexamethasone alone in patients with newly diagnosed myeloma without intent for immediate autologous stem-cell transplant (SWOG S0777): a randomised, open-label, phase 3 trial. *Lancet*, 2017, 389, s. 519–527.
 - 16 Facon, T. – Dimopoulos, M. A. – Dispenzieri, A., et al.: Final analysis of survival outcomes in the phase 3 FIRST trial of up-front treatment for multiple myeloma. *Blood*, 2018, 131, s. 301–310.
 - 17 Mateos, M. V. – Cavo, M. – Blade, J., et al.: Overall survival with daratumumab, bortezomib, melphalan, and prednisone in newly diagnosed multiple myeloma (ALCYONE): a randomised, open-label, phase 3 trial. *Lancet*, 2020, 395, s. 132–141.
 - 18 Facon, T. – Kumar, S. – Plesner, T., et al.: Daratumumab plus lenalidomide and dexamethasone for untreated myeloma. *N Engl J Med*, 2019, 380, s. 2104–2115.
 - 19 San Miguel, J. – Weisel, K. – Moreau, P., et al.: Pomalidomide plus low-dose dexamethasone versus high-dose dexamethasone alone for patients with relapsed and refractory multiple myeloma (MM-003): a randomised, open-label, phase 3 trial. *Lancet Oncol*, 2013, 14, s. 1055–1066.
 - 20 Richardson, P. G. – Oriol, A. – Beksac, M., et al.: Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISM): a randomised, open-label, phase 3 trial. *Lancet Oncol*, 2019, 20, s. 781–794.
 - 21 Attal, M. – Richardson, P. G. – Rajkumar, S. V., et al.: Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study. *Lancet*, 2019, 394, s. 2096–2107.
 - 22 Dimopoulos, M. A. – Terpos, E. – Boccadoro, M., et al.: APOLLO Trial Investigators: Daratumumab plus pomalidomide and dexamethasone versus pomalidomide and dexamethasone alone in previously treated multiple myeloma (APOLLO): an open-label, randomised, phase 3 trial. *Lancet Oncol*, 2021, 22, s. 801–812.
 - 23 Dimopoulos, M. A. – Dytfield, D. – Grosicki, S., et al.: ELOTUZUMAB plus pomalidomide and dexamethasone for multiple myeloma. *N Engl J Med*, 2018, 379, s. 1811–1822.
 - 24 Sonneveld, P. – Zweegman, S. – Cavo, M., et al.: Carfilzomib, pomalidomide and dexamethasone (KPd) in patients with multiple myeloma refractory to bortezomib and lenalidomide. the EMN011 trial. *Blood*, 2018, s. 801–801.
 - 25 Krishnan, A. – Kapoor, P. – Palmer, J. M., et al.: Phase I/II trial of the oral regimen ixazomib, pomalidomide, and dexamethasone in relapsed/refractory multiple myeloma. *Leukemia*, 2018, 32, s. 1567–1574.
 - 26 Dimopoulos, M. – Quach, H. – Mateos, M.-V., et al.: Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): results from a randomised, multicentre, open-label, phase 3 study. *Lancet*, 2020, 396, s. 186–197.
 - 27 Dimopoulos, M. – Quach, H. – Mateos, M.-V., et al.: Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone in relapsed or refractory multiple myeloma: updated efficacy and safety results of the phase 3 Candor study. ASH Annual Meeting and Exposition, 2020, abstrakt 2325.
 - 28 Moreau, P. – Dimopoulos, M. – Mikhael, J., et al.: Isatuximab plus carfilzomib and dexamethasone vs carfilzomib and dexamethasone in relapsed/refractory multiple myeloma (IKEMA): a multicentre, open-label, randomised phase 3 trial. *Lancet*, 2021, 397, s. 2361–2371.
 - 29 Mateos, M.-V. – Sonneveld, P. – Hungria, V., et al.: Daratumumab, bortezomib, and dexamethasone versus bortezomib and dexamethasone in patients with previously treated multiple myeloma: three-year follow-up of CASTOR. *Clin Lymphom Myel Leuk*, 2020, 20, s. 509–518.
 - 30 Dimopoulos, M. A. – Moreau, P. – Palumbo, A., et al.: Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open label, multicentre study. *Lancet Oncol*, 2016, 17, s. 27–38.
 - 31 Harrison, S. – Cavo, M. – De La Rubia, J., et al.: T(11;14) and high BCL2 expression are predictive biomarkers of response to venetoclax in combination with bortezomib and dexamethasone in patients with relapsed/refractory multiple myeloma: Biomarker analyses from the phase 3 Bellini study. *Blood*, 2019, 134, s. 14.
 - 32 Dimopoulos, M. – Weisel, K. – Moreau, P., et al.: Pomalidomide, bortezomib, and dexamethasone for multiple myeloma previously treated with lenalidomide (OPTIMISM): outcomes by prior treatment at first relapse. *Leukemia*, 2021, 35, s. 1722–1731.
 - 33 Dimopoulos, M. A. – Oriol, A. – Nahi, H., et al.: Daratumumab, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*, 2016, 375, s. 1319–1331.
 - 34 Stewart, A. K. – Rajkumar, S. V. – Dimopoulos, M. A., et al.: Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. *N Engl J Med*, 2015, 372, s. 142–152.
 - 35 Siegel, D. S. – Dimopoulos, M. A. – Ludwig, H., et al.: Improvement in overall survival with carfilzomib, lenalidomide, and dexamethasone in patients with relapsed or refractory multiple myeloma. *J Clin Oncol*, 2018, 36, s. 728–734.
 - 36 Moreau, P. – Masszi, T. – Grzasko, N., et al.: Oral ixazomib, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*, 2016, 374, s. 1621–1634.
 - 37 Lonial, S. – Dimopoulos, M. – Palumbo, A., et al.: ELOTUZUMAB therapy for relapsed or refractory multiple myeloma. *N Engl J Med*, 2015, 373, s. 621–631.
 - 38 Bahlis, N. J. – Dimopoulos, M. A. – White, D. J., et al.: Daratumumab plus lenalidomide and dexamethasone in relapsed/refractory multiple myeloma: extended follow-up of POLLUX, a randomized, open-label, phase 3 study. *Leukemia*, 2020, 34, s. 1875–1884.
 - 39 Gandhi, U. H. – Cornell, R. F. – Lakshman, A., et al.: Outcomes of patients with multiple myeloma refractory to CD38-targeted monoclonal antibody therapy. *Leukemia*, 2019, 33, s. 2266–2275.
 - 40 San-Miguel, J. F. – Hungria, V. T. M. – Yoon, S.-S., et al.: Panobinostat plus bortezomib and dexamethasone versus placebo plus bortezomib and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma: a multicentre, randomised, double-blind phase 3 trial. *Lancet Oncol*, 2014, 15, s. 1195–1206.
 - 41 Chari, A. – Vogl, D. T. – Gavriatopoulou, M., et al.: Oral selinexor-dexamethasone for triple-class refractory multiple myeloma. *N Engl J Med*, 2019, 381, s. 727–738.
 - 42 Dimopoulos, M. – Delimpasi, S. – Simonova, M., et al.: Weekly selinexor, bortezomib, and dexamethasone (Svd) versus twice weekly bortezomib and dexamethasone (Vd) in patients with multiple myeloma (MM) after one to three prior therapies: initial results of the phase III BOSTON study. *J Clin Oncol*, 2020, 38, suppl. 15, s. 8501–8501.
 - 43 Lonial, S. – Lee, H. C. – Badros, A., et al.: Belantamab mafodotin for relapsed or refractory multiple myeloma (DREAMM-2): a two-arm, randomised, open-label, phase 2 study. *Lancet Oncol*, 2020, 21, s. 207–221.
 - 44 Richardson, P. G. – Brinchen, S. – Voorhees, P., et al.: Melflufen plus dexamethasone in relapsed and refractory multiple myeloma (O-12-M1): a multicentre, international, open-label, phase 1-2 study. *Lancet Haematol*, 2020, 7, s. e395–e407.
 - 45 Raje, N. – Berdeja, J. – Lin, Y., et al.: Anti-BCMA CAR T-cell therapy bb2121 in relapsed or refractory multiple myeloma. *N Engl J Med*, 2019, 380, s. 1726–1737.

Pacient s mnohočetným myelomem léčený přípravkem Ninlaro ve vyšších liniích léčby – kazuistika

MUDr. Viera Sandecká, Ph.D. Interní hematologická a onkologická klinika, FN Brno

- 1 Radocha, J. – Pour, L. – Spicka, I., et al.: Registry of monoclonal gammopathies (RMG) in the Czech Republic. *Blood*, 2015, 123, s. 4514.
- 2 Kumar, S. K. – Rajkumar, S. V. – Dispenzieri, A., et al.: Improved survival in multiple myeloma and the impact of novel therapies. *Blood*, 2008, 111, s. 2516–2520.
- 3 Sherbenou, D. W. – Mark, T. M. – Forsberg, P.: Monoclonal antibodies in multiple myeloma: a new wave of the future. *Clin Lymphoma Myeloma Leuk*, 2017, 17, s. 545–554.
- 4 Moreau, P. – Masszi, T. – Grzasko, N., et al.: Oral ixazomib, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*, 2016, 374, s. 1621–1634.
- 5 Richardson, P. G. – Baz, R. – Wang, M., et al.: Phase 1 study of twice-weekly ixazomib, an oral proteasome inhibitor, in relapsed/refractory multiple myeloma patients. *Blood*, 2014, 124, s. 1038–1046.
- 6 Kumar, S. K. – Bensing, W. I. – Zimmermann, T. M., et al.: Phase 1 study of weekly dosing with the investigational oral proteasome inhibitor ixazomib in relapsed/refractory multiple myeloma. *Blood*, 2014, 124, s. 1047–1055.
- 7 Kumar, S. K. – Moreau, P. – Hari, P., et al.: Management of adverse events associated with ixazomib plus lenalidomide/dexamethasone in relapsed/refractory multiple myeloma. *Br J Haematol*, 2017, doi:10.1111/bjh.14733.
- 8 Durie, B. G. – Salmon, S. E.: A clinical staging system for multiple myeloma. Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. *Cancer*, 1975, 36, s. 842–854.
- 9 Greipp, P. R. – San Miguel, J. – Durie, B. G., et al.: International staging system for multiple myeloma. *J Clin Oncol*, 2005, 23, s. 3412–3420.
- 10 Palumbo, A. – Avet-Loiseau, H. – Oliva, S., et al.: Revised international staging system for multiple myeloma: a report from International Myeloma Working Group. *J Clin Oncol*, 2015, 33, s. 2863–2869.
- 11 Mateos, M. V. – Nahi, H. – Legiec, W., et al.: Subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma (COLLUMBA): a multicentre, open-label, non-inferiority, randomised, phase 3 trial. *Lancet Haematol*, 2020, 7, s. e370–e380.
- 12 ClinicalTrials.gov Identifier: NCT03194867: Isatuximab in combination with cemiplimab in relapsed/refractory multiple myeloma (RRMM) patients. Dostupné z: <https://clinicaltrials.gov/ct2/show/NCT03194867>, vyhledáno 20. 9. 2021.

Vývoj léčby chronické myeloidní leukemie

MUDr. Hana Klamová, CSc. Ústav hematologie a krevní transfuze, Praha

- 1 Vardiman, J. W. – Melo, J. V. – Baccarani, M., et al.: Chronic myeloid leukaemia, BCR-ABL1-positive. In: Swerdlow, S. H. – Campo, E. – Lee Harris, N., et al.: *WHO classification of tumours of haematopoietic and lymphoid tissue*. Lyon, International Agency for Research on Cancer. 2017, s. 30–36.
- 2 Faderl, S. – Talpaz, M. – Estrov, Z., et al.: The biology of chronic myeloid leukemia. *New Engl J Med*, 1999, 34, s. 164–172.
- 3 Hoffman, V. – Baccarani, M. – Hasford, J., et al.: The EUTOS population-based registry: incidence and clinical characteristics of 2904 CML patients in 20 countries. *Leukemia*, 2015, 29, s. 1136–1143.
- 4 Kantarjian, H. M. – O'Brien, S. – Cortes, J. E., et al.: Complete cytogenetic and molecular responses to IFN-alfa based therapy for chronic myelogenous leukemia are associated with excellent long-term prognosis. *Cancer*, 2003, 97, s. 1033–1041.
- 5 Hehlmann, R. – Berger, U. – Pfirman, M.: Drug treatment is superior to allografting as first-line therapy in chronic myeloid leukemia. *Blood*, 2007, 109, s. 4786–4692.
- 6 Drucker, B. J. – Guilhot, F. – O'Brien, S. G., et al.: Five-year follow-up patients receiving imatinib for chronic myeloid leukemia. *N Engl J Med*, 2000, 355, s. 2408–2417.
- 7 Hochhaus, A. – O'Brien, S. G. – Guilhot, F., et al.: Six-year follow-up of patients receiving imatinib for the first-line treatment of chronic myeloid leukemia. *Leukemia*, 2009, 23, s. 1054–1061.
- 8 Hehlmann, R. – Hochhaus, A. – Baccarani, M., et al.: On behalf of the European Leukemia Net. Chronic myeloid leukemia. *Lancet*, 2007, 370, s. 342–350.
- 9 Databáze léků Státního ústavu pro kontrolu léčiv: www.sukl.cz
- 10 Baccarani, M. – Deininger, M. W. – Rosti, G., et al.: European Leukemia Net recommendations for the management of chronic myeloid leukemia. *Blood*, 2013, 122, s. 872–884.
- 11 Mayer, J. (ed.): *Léčebné postupy v hematologii: doporučení České hematologické společnosti ČLS JEP*. Česká hematologická společnost ČLS JEP, Praha, 2016.
- 12 Rousselot, P. – Huguet, F. – Rea, D., et al.: Imatinib mesylate discontinuation on patients with chronic myeloid leukemia in complete molecular remission for more than 2 years. *Blood*, 2007, 109, s. 68–70.
- 13 Etienne, G. – Rea, D. – Guilhot, J., et al.: Long-term follow-up of the French Stop Imatinib Study in patients with chronic myeloid leukemia. *J Clin Oncol*, 2017, 35, s. 298–305.
- 14 Rea, D. – Nicolini, F. E. – Tulliez, M., et al.: Discontinuation of dasatinib or nilotinib in chronic myeloid leukemia: interim analysis of the STOP 2G-TKI study. *Blood*, 2017, 129, s. 846–854.
- 15 Saussele, S. – Richter, J. – Hochhaus, A., et al.: The concept of treatment-free remission in chronic myeloid leukemia. *Leukemia*, 2016, 30, s. 1638–1647.
- 16 Saussele, S. – Richter, J. – Guilhot, 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, s. 747–757.
- 17 National Comprehensive Cancer Network (NCCN) Clinical Practice

Praktické příklady použití gemtuzumab ozogamicinu v léčbě nově diagnostikované akutní myeloidní leukemie

doc. MUDr. Tomáš Szotkowski, Ph.D. | MUDr. Martin Čerňan | Mgr. Jana Navrátilová | MUDr. Jaromír Hubáček, Ph.D. | prof. MUDr. Tomáš Papajík, CSc. Hemato-onkologická klinika FN Olomouc a LF UP v Olomouci

- 1 Ricart, A. D.: Antibody-drug conjugates of calicheamicin derivative: gemtuzumab ozogamicin and inotuzumab ozogamicin. *Clin Cancer Res*, 2011, 17, s. 6417–6427.
- 2 Bross, P. F. – Beitz, J. – Chen, G., et al.: Approval summary: Gemtuzumab ozogamicin in relapsed acute myeloid leukemia. *Clin Cancer Res*, 2001, 7, s. 1490–1496.
- 3 Petersdorf, S. H. – Kopecky, K. J. – Slovak, M., et al.: A phase 3 study of gemtuzumab ozogamicin during induction and postconsolidation therapy in younger patients with acute myeloid leukemia. *Blood*, 2013, 121, s. 4854–4860.
- 4 Hills, R. K. – Castaigne, S. – Appelbaum, F. R., et al.: The addition of gemtuzumab ozogamicin to induction chemotherapy in acute myeloid leukaemia: an individual patient data meta-analysis of randomised trials in adults. *Lancet Oncol*, 2014, 15, s. 986–996.
- 5 Dostupné z: <https://www.ema.europa.eu/en/medicines/human/EPAR/mylotarg-0>, vyhledáno 31. 8. 2021.
- 6 Lambert, J. – Pautas, C. – Terré, C., et al.: Gemtuzumab ozogamicin for de novo acute myeloid leukemia: final efficacy and safety updates from the open-label, phase III ALFA-0701 trial. *Haematologica*, 2019, 104, s. 113–119.
- 7 Dostupné z: <https://www.sukl.cz/modules/medication/detail.php?code=0222910&tab=prices>, vyhledáno 31. 8. 2021.

Idiopatická multicentrická Castlemanova choroba: diagnostika a léčba v roce 2021

MUDr. Marta Šimůnková, Praha

- 1 Ostrowska, B. – Romejko-Jarosířská, J. – Domańska-Czyż, K., et al.: Idiopathic multicentric Castleman disease: pathogenesis, clinical presentation and recommendations for treatment based on the Castleman Disease Collaborative Network (CDCN). *Acta Haematol Pol*, 2021, 52, s. 29–37.
- 2 Van Rhee, F., et al.: International, evidence-based consensus treatment guidelines for idiopathic multicentric Castleman disease. *Blood*, 2018, 132, s. 2115–2124.
- 3 Fajgenbaum, D. C., et al.: International, evidence-based consensus diagnostic for HHV-8-negative/idiopathic multicentric Castleman disease. *Blood*, 2017, 129, s. 1646–1657.
- 4 Szturz, P. – Adam, Z. – Doubek, M.: www.vzacne-diagnozy.cz.
- 5 Van Rhee, F. – Wong, R. S. – Munshi, N., et al.: Siltuximab for multicentric Castleman's disease: a randomised, double-blind, placebo-controlled trial. *Lancet Oncol*, 2014, 15, s. 966–974.
- 6 Morra, D. E. – Pierson, S. – Shilling, D., et al.: Predictors of response to anti-IL-6 monoclonal antibody therapy (siltuximab) in idiopathic multicentric Castleman disease: secondary analyses of phase II clinical trial data. *Br J Haematol*, 2018, 184, s. 232–241.
- 7 Sylvant, SPC, EMA, 2014.
- 8 Nishimoto, N. – Honda, O. – Sumikawa, H., et al.: A long-term (5-year) sustained efficacy of tocilizumab for multicentric Castleman's disease and the effect on pulmonary complications. *Blood*, 2007, 110, s. 646–646.
- 9 Zhang, L. – Zhao, A. L. – Duan, M.-H., et al.: Phase 2 study using oral thalidomide-cyclophosphamide-prednisone for idiopathic multicentric Castleman disease. *Blood*, 2019, 133, s. 1720–1728.
- 10 Fajgenbaum, D. C. – Langan, R. A. – Japp, A. S., et al.: Identifying and targeting pathogenic PI3K/AKT/mTOR signaling in IL-6-blockade-refractory idiopathic multicentric Castleman disease. *J Clin Invest*, 2019, 129, s. 4451–4463.
- 11 Masaki, Y. – Kawabata, H. – Takai, K., et al.: Proposed diagnostic criteria, disease severity classification and treatment strategy for TAFRO syndrome, 2015 version. *Int J Hematol*, 2016, 103, s. 686–692.
- 12 Cheson, B. D. – Horning, S. J. – Coiffier, B., et al.: Report of an international work-shop to standardize response criteria for non-Hodgkin's lymphomas. NCI Sponsored International Working Group. *J Clin Oncol*, 1999, 17, s. 1244.

Další literatura podrobně na: https://journals.viamedica.pl/acta_haematologica_polonica/article/view/74863.

Idiopatická multicentrická Castlemanova choroba: diagnostika a léčba v roce 2021 – komentář k článku

prof. MUDr. Zdeněk Adam, CSc. | prof. MUDr. Luděk Pour, Ph.D. Interní hematologická a onkologická klinika LF MU a FN Brno

- 1 van Rhee, F. – Voorhees, P. – Dispenzieri, A., et al.: International, evidence-based consensus treatment guidelines for idiopathic multicentric Castleman disease. *Blood*, 2018, 132, s. 2115–2124.
- 2 van Rhee, F. – Oksenhendler, E. – Srkalovic, G., et al.: International evidence-based consensus diagnostic and treatment guidelines for unicentric Castleman disease. *Blood Adv*, 2020, 4, s. 6039–6050.
- 3 Tóthová, E. – Fričová, M. – Sokol, L.: Castlemanova choroba. *Hematológia & transfuziologie*, 1993, 3, s. 19–26.
- 4 Fichtle, J. – Treška, V. – Šulc, R., et al.: Castlemanova choroba – neobvyklý nález při operaci tumoru retroperitonea u mladého nemocného. *Rozhledy v chirurgii*, 2016, 95, s. 91–94.
- 5 Škach, J. – Vytiska, J. – Gaalová, R., et al.: Castlemanova choroba imitující tumor perikardu. *Kazuistiky v alergologii, pneumologii a ORL*, 2014, 11, s. 3–7.
- 6 Zavalová, Š. – Jiráček, P. – Sýrůček, M., et al.: Castlemanova choroba – Mimicking a malignant lymphoma. *Otorinolaryngologie a foniatrie*, 2014, 63, s. 246–250.
- 7 Szturz, P. – Plank, L. – Křístek, J., et al.: Castlemanova choroba v obrazech. *Postgraduální medicína*, 2014, 16, s. 81–88.
- 8 Rovenský, J. – Lee, B. – Kozák, I.: Castlemanova choroba – multicentrická angiofolikulární lymfoidní hyperplazie. In: *Oftalmorevmatologie*. Praha, Galén, 2017, s. 221–226.
- 9 Penka, I. – Kala, Z. – Zetelová, A., et al.: Castleman's disease – surgical treatment, case reports. *Rozhledy v chirurgii*, 2016, 95, s. 457–461.
- 10 Jakubec, P. – Kolek, V. – Jakubcová, T., et al.: Castlemanova nemoc – asymptomatický tumor mediastina. *Studia pneumologica et phthisiologica*, 2005, 65, s. 166–171.
- 11 Smolár, M. – Šutiak, L. – Mikolajčík, A., et al.: Lymfóm žalúdka ako príčina masívneho krvácania u pacienta s Castlemanovou chorobou. *Rozhledy v chirurgii*, 2010, 89, s. 320–324.
- 12 Chang, K. C. – Wang, Y. C. – Hung, L. Y., et al.: Monoclonality and cytogenetic abnormalities in hyaline vascular Castleman disease. *Mod Pathol*, 2014, 27, s. 823–831.
- 13 Král, Z. – Adam, Z. – Krejčí, M., et al.: Léčba multicentrické a uniceentrické formy Castlemanovy nemoci. *Transfúze a hematologie dnes*, 2020, 26, s. 186–195.
- 14 Mohan, M. – Meek, J. C. – Meek, M. E., et al.: Combinatorial treatment for resectable unicentric Castleman disease. *Eur J Haematol*, 2021, doi: 10.1111/ejh.13685.
- 15 Bandera, B. – Ainsworth, C. – Shikle, J., et al.: Treatment of unicentric Castleman disease with neoadjuvant rituximab. *Chest*, 2010, 138, s. 1239–1241.
- 16 Baek, H. J. – Kook, H. – Han, D. K., et al.: Unicentric Castleman disease relapsed after rituximab-CHOP chemotherapy or radiation therapy in an adolescent. *J Pediatr Hematol Oncol*, 2012, 34, s. e206–e208.
- 17 Jakubiková, M. – Pitha, J. – Latta, J., et al.: Myasthenia gravis, Castleman disease, pemphigus, and anti-phospholipid syndrome. *Muscle and nerve*, 2013, 47, s. 447–451.
- 18 Král, Z. – Adam, Z. – Volfová, P., et al.: Castlemanova nemoc, jedna z příčin chronické systémové zánětlivé reakce, někdy i retence tekutin, vaskulitida a poruch imunity – Mezinárodní diagnostická kritéria z roku 2017. *Transfúze a hematologie dnes*, 2020, 26, s. 92–100.
- 19 Cibířková, L. – Soukup, T. – Bradna, P., et al.: Asociace revmatoidní artritidy a Castlemanovy choroby. *Česká revmatologie*, 2005, 13, s. 106–109.
- 20 Sun, D. P. – Chen, W. M. – Wang, L., et al.: Clinical characteristics and immunological abnormalities of Castleman disease complicated with autoimmune diseases. *J Cancer Res Clin Oncol*, 2021, 147, s. 2107–2115.
- 21 Petersdorf, R. G. – Beeson, P. B.: Fever of unexplained origin: report on 100 cases. *Medicine*, 1961, 40, s. 1–30.
- 22 Knockaert, D. C. – Vanderschueren, S. – Blockmans, D.: Fever of unknown origin in adults: 40 years on. *J Intern Med*, 2003, 253, s. 263–275.
- 23 Kaaba, H.: Clinical features and treatment of multicentric Castleman disease. *J Clin Exper Hematol*, 2013, 53, s. 66–77.
- 24 Koujzer, I. J. E. – Mulders-Manders, C. M., et al.: Fever of unknown origin: the value of FDG-PET/CT. *Semin Nucl Med*, 2018, 48, s. 100–107.
- 25 Schönau, V. – Vogel, K. – Englbrecht, M., et al.: The value of ¹⁸F-FDG-PET/CT in identifying the cause of fever of unknown origin (FUO) and inflammation of unknown origin (IUO): data from a prospective study. *Ann Rheum Dis*, 2018, 77, s. 70–77.
- 26 Doležal, J. – Slanina, M. – Kriegl, T., et al.: Neobvyklá detekce izolované sarkoidózy tracheobronchiálního kmene u pacientky s teplotami nejasného původu pomocí 18F-FDG PET/CT. *Česká radiologie*, 2015, 69, s. 266–269.
- 27 Ferda, J. – Ferdová, E. – Záhlava, J., et al.: Fever of unknown origin: a value of (18)F-FDG-PET/CT with integrated full diagnostic isotropic CT imaging. *Eur J Radiol*, 2010, 73, s. 518–525.
- 28 Ferdová, E. – Záhlava, J. – Ferda, J.: Horečky nejasného původu, význam hybridního zobrazení 18F-FDG-PET/CT: původní práce. *Česká radiologie*, 2008, 62, s. 23–33.
- 29 Kotík, L.: Teploty nejasného původu. *Interní medicína pro praxi*, 2006, 8, s. 493–495.
- 30 Křivanová, A. – Adam, Z. – Mayer, J., et al.: Teplota nejasné etiologie: příčiny a diagnostický postup. *Vnitřní lékařství*, 2007, 53, s. 169–178.
- 31 Vargová, V.: Horúčka neznámého původu. *Pediatrica*, 2006, 1, s. 65–68.
- 32 Eun, Ji Han: FDG PET/CT Findings of Castleman Disease Assessed by Histologic Subtypes and Compared with Laboratory Findings. *Diagnostics*, 2020, 10, s. 998.
- 33 Koa, B., et al.: Emerging role of 18F-FDG PET/CT in Castleman disease: a review. *Insights Imaging*, 2021, 12, s. 35.
- 34 Oksenhendler, E.: The full spectrum of Castleman disease: 273 patients studied over 20 years. *Br J Haematol*, 2018, 180, s. 206–216.
- 35 Koukalová, R. – Selingerová, I. – Řehák, Z.: FDG-PET/CT v diagnostice a hodnocení léčebné odpovědi Castlemanovy choroby – retrospektivní studie 29 případů z jednoho centra. *Klinická onkologie*, 2021, 34, s. 120–127.
- 36 Adam, Z. – Pour, L. – Krejčí, M.: Rituximab je základem léčby Castlemanovy nemoci multicentrického typu. *Postgraduální medicína*, 2017, 19, s. 548–549.
- 37 Adam, Z. – Szturz, P. – Koukalová, R., et al.: PET-CT dokumentovaná remise multicentrické formy Castlemanovy choroby po léčbě rituximabem. Popis případu a přehled literatury. *Vnitřní lékařství*, 2015, 61,

- s. 251–258.
- 38 Adam, Z. – Szturz, P. – Krejčí, M., et al.: Léčba 14 případů Castlemanovy nemoci: zkušenosti jednoho centra a přehled literatury. *Vnitřní lékařství*, 2016, 62, s. 287–298.
- 39 Abramson, J. S.: Diagnosis and management of Castleman disease. *J Natl Compr Canc Netw*, 2019, 17, s. 1417–1419.
- 40 Kaegi, C. – Wuest, B. – Schreiner, J., et al.: Systematic review of safety and efficacy of rituximab in treating immune-mediated disorders. *Front Immunol*, 2019, 10, s. 1990, doi:10.3389/fimmu.2019.01990.
- 41 Dong, Y. – Zhang, L. – Nong, L., et al.: Effectiveness of rituximab-containing treatment regimens in idiopathic multicentric Castleman disease. *Ann Hematol*, 2018, 97, s. 1641–1647.
- 42 Marchetti, M. – Feyles, E. – Zinzani, P.: Frontline siltuximab and rituximab in TAFRO syndrome: A case report. *Eur J Haematol*, 2020, 105, s. 505–507.
- 43 Adam, Z. – Pour, L. – Krejčí, M.: Účinnost lenalidomidu u vzácných krevních chorob: u histiocytózy z Langerhansových buněk, multicentrické Castlemanovy choroby, POEMS syndromu, Erdheimovy-Chesterovy choroby a angiomatózy. Popis případů a přehled literatury. *Vnitřní lékařství*, 2012, 58, s. 856–866.
- 44 Szturz, P. – Adam, Z. – Rehák, Z., et al.: Salvage lenalidomide in four rare oncological diseases. *Tumori*, 2013, 99, s. e251–e256.
- 45 Cai, S. – Zhong, Z. – Li, X., et al.: Treatment of multicentric Castleman disease through combination of tocilizumab, lenalidomide and glucocorticoids: Case report. *Medicine*, 2019, 98, s. e17681.
- 46 Zhou, X. – Wei, J. – Lou, Y., et al.: Salvage therapy with lenalidomide containing regimen for relapsed/refractory Castleman disease: a report of three cases. *Front Med*, 2017, 11, s. 287–292.
- 47 Szturz, P. – Adam, Z. – Chovancová, J., et al.: Lenalidomide: a new treatment option for Castleman disease. *Leuk Lymphoma*, 2012, 53, s. 2089–2091.
- 48 Adam, Z. – Szturz, P. – Křen, L.: PET-CT dokumentovaný rychlý nástup léčebné odpovědi cyklofosfamidu, thalidomidu a dexametazonu u multicentrické formy Castlemanovy nemoci. Popis případů a přehled informací o léčbě. *Vnitřní lékařství*, 2013, 59, s. 301–312.
- 49 Zhang, L. – Zhao, A. L. – Duan, M. H., et al.: Phase 2 study using oral thalidomide-cyclophosphamide-prednisone for idiopathic multicentric Castleman disease. *Blood*, 2019, 133, s. 1720–1728.
- 50 Ramasamy, K. – Gandhi, S. – Tenant-Flowers, M., et al.: Rituximab and thalidomide combination therapy for Castleman disease. *Br J Haematol*, 2012, 158, s. 421–423.
- 51 Wang, X. – Ye, S. – Xiong, C., et al.: Successful treatment with bortezomib and thalidomide for POEMS syndrome associated with multicentric mixed-type Castleman's disease. *Jpn J Clin Oncol*, 2011, 41, s. 1221–1224.
- 52 Lin, Q. – Fang, B. – Huang, H., et al.: Efficacy of bortezomib and thalidomide in the recrudescence form of multicentric mixed-type Castleman's disease. *Blood Cancer J*, 2015, 5, s. e298.
- 53 Stary, G. – Kohrgruber, N. – HERNETH, A. M., et al.: Complete regression of HIV-associated multicentric Castleman disease treated with rituximab and thalidomide. *AIDS*, 2008, 22, s. 1232–1234.
- 54 Menegato, M. A. – Canelles, M. F. – Tonutti, E., et al.: Remission of nephrotic syndrome after thalidomide therapy in a patient with Castleman's disease. *Clin Nephrol*, 2004, 61, s. 352–356.
- 55 van Rhee, F. – Wong, R. S. – Munshi, N., et al.: Siltuximab for multicentric Castleman's disease: a randomised, double-blind, placebo-controlled trial. *Lancet Oncol*, 2014, 15, s. 966–974.
- 56 van Rhee, F. – Casper, C. – Voorhees, P. M., et al.: A phase 2, open-label, multicenter study of the long-term safety of siltuximab (an anti-interleukin-6 monoclonal antibody) in patients with multicentric Castleman disease. *Oncotarget*, 2015, 6, s. 30408–30419.
- 57 van Rhee, F. – Casper, C. – Voorhees, P. M., et al.: Long-term safety of siltuximab in patients with idiopathic multicentric Castleman disease: a prespecified, open-label, extension analysis of two trials. *Lancet Haematol*, 2020, 7, s. e209–e217.
- 58 van Rhee, F. – Rossi, J. F. – Simpson, D., et al.: Newly diagnosed and previously treated multicentric Castleman disease respond equally to siltuximab. *Br J Haematol*, 2021, 192, s. e28–e31.
- 59 Tonialini, L. – Bonfichi, M. – Ferrero, S., et al.: Siltuximab in relapsed/refractory multicentric Castleman disease: Experience of the Italian NPP program. *Hematol Oncol*, 2018, 36, s. 689–692.
- 60 Ostrowska, B. – Szymczyk, A. – Olszewska-Szopa, M., et al.: Efficacy of siltuximab in the treatment of idiopathic multicentric Castleman disease, the first Polish, real-world experience with long-term observation. *Leuk Lymphoma*, 2021, doi: 10.1080/10428194.2021.1941926.
- 61 Ebisawa, K. – Shimura, A. – Honda, A., et al.: Hemoglobin and C-reactive protein levels as predictive factors for long-term successful glucocorticoid treatment for multicentric Castleman's disease. *Leuk Lymphoma*, 2021, 62, s. 614–619.
- 62 Morra, D. E. – Pierson, S. K. – Shilling, D., et al.: Predictors of response to anti-IL6 monoclonal antibody therapy (siltuximab) in idiopathic multicentric Castleman disease: secondary analyses of phase II clinical trial data. *Br J Haematol*, 2019, 184, s. 232–241.
- 63 Pierson, S. K. – Shenoy, S. – Oromendia, A. B., et al.: Discovery and validation of a novel subgroup and therapeutic target in idiopathic multicentric Castleman disease. *Blood Adv*, 2021, doi:10.1182/bloodadvances.2020004016.
- 64 Sun, Y. – Wang, D. – Salvadore, G.: The effects of interleukin-6 neutralizing antibodies on symptoms of depressed mood and anhedonia in patients with rheumatoid arthritis and multicentric Castleman's disease. *Brain Behav Immun*, 2017, 66, s. 156–164.
- 65 Yu, L. – Shi, M. – Cai, Q., et al.: A novel predictive model for idiopathic multicentric Castleman disease: The International Castleman Disease Consortium Study. *Oncologist*, 2020, 25, s. 963–973.
- 66 Liu, A. Y. – Nabel, C. S. – Finkelman, B. S., et al.: Idiopathic multicentric Castleman's disease: a systematic literature review. *Lancet Haematol*, 2016, 3, s. e163–e175.

Význam eltrombopagu v léčbě závažné a velmi závažné aplastické anemie

prof. MUDr. Pavel Žák, Ph.D. IV. interní hematologická klinika, LF UK a FN Hradec Králové

- 1 Young, N. S.: Aplastic anemia. *N Engl J Med*, 2018, 379, s. 1643–1656.
- 2 Young, N. S. – Calado, R. T. – Scheinberg, P. A.: Current concepts in the pathophysiology and treatment of aplastic anemia. *Blood*, 2006, 108, s. 2509–2519.
- 3 Ku, H. – Yonemura, Y. – Kaushansky, K., et al.: Thrombopoietin, the ligand for the Mpl receptor, synergizes with steel factor and other early acting cytokines in supporting proliferation of primitive hematopoietic progenitors of mice. *Blood*, 1996, 87, s. 4544–4551.
- 4 Garnock-Jones, K. P. – Keam, S. J.: Eltrombopag. *Drugs*, 2009, 69, s. 567–576.
- 5 Olmes, M. J. – Scheinberg, P. – Calvo, K. R., et al.: Eltrombopag and improved hematopoiesis in refractory aplastic anemia. *N Engl J Med*, 2012, 367, s. 11–19.
- 6 Townsley, D. M. – Scheinberg, P. – Winkler, T., et al.: Eltrombopag added to standard immunosuppression for aplastic anemia. *N Engl J Med*, 2017, 376, s. 1540–1550.
- 7 Assi, R. – Garcia-Manero, G. – Ravandi, F., et al.: Addition of eltrombopag to immunosuppressive therapy in patients with newly diagnosed aplastic anemia. *Cancer*, 2018, 124, s. 4192–4201.
- 8 Peffault de Latour, R. – Marsh, J. – Iacobelli, S., et al.: Results of the EBMT saawp phase III prospective randomized multicenter race study of horse ATG and ciclosporine with or without eltrombopag in naive SAA patients. Prezentováno na 46. výročním setkání EBMT, 22.–25. 3. 2020, Madrid, Španělsko. Dostupné z: <https://www.professionallababstracts.com/ebmt2020/iplanner/#/presentation/776>, vyhledáno 17. 9. 2021.
- 9 European Medicines Agency. Refusal of a change to the marketing authorisation for Revolade (eltrombopag). Dostupné z: https://www.ema.europa.eu/en/documents/smop/questions-answers-refusalchange-marketing-authorisation-revoladeeltrombopag_en.pdf (2019), vyhledáno 22. 2. 2021.
- 10 Zhao, Z. – Sun, Q. – Sokoll, L. J., et al.: Eltrombopag mobilizes iron in patients with aplastic anemia. *Blood*, 2018, 131, s. 2399–2402.
- 11 Ogawa, S.: Clonal hematopoiesis in acquired aplastic anemia. *Blood*, 2016, 128, s. 337–347.
- 12 Winkler, T. – Fan, X. – Cooper, J., et al.: Treatment optimization and genomic outcomes in refractory severe aplastic anemia treated with eltrombopag. *Blood*, 2019, 133, s. 2575–2585.
- 13 Kalota, A. – Selak, M. A. – Garcia-Cid, L. A., et al.: Eltrombopag modulates reactive oxygen species and decreases acute myeloid leukemia cell survival. *PLoS One*, 2015, 10, e0126691, doi.org/10.1371/journal.pone.0126691.
- 14 Marsh, J. C. – Ball, S. E. – Cavenagh, J., et al.: Guidelines for the diagnosis and management of aplastic anaemia. *Br J Haematol*, 2009, 147, s. 43–70.
- 15 Killick, S. B. – Bown, N. – Cavenagh, J., et al.: Guidelines for the diagnosis and management of adult aplastic anaemia. *Br J Haematol*, 2016, 172, s. 187–207.