Literatura ACTA MEDICINAE 3/2021 Biologická a cílená léčba

Inhibitory JAK u Ph-negativních myeloproliferativních onemocnění

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1 **Kontzias, A. – Kotlyar, A. – Laurence, A., et al.**: Jakinibs: a new class of kinase inhibitors in cancer and autoimmune disease. *Curr Opin Pharmacol*, 2012, 12, s. 464–470.

2 **Furumoto, Y. – Gadina, M.**: The arrival of JAK inhibitors: advancing the treatment of immune and hematologic disorders. *Bio Drugs*, 2013, 27, s. 431–438.

3 **James, C. – Ugo, V. – Le Couedic, J. P., et al.**: A unique clonal JAK2 mutation leading to constitutive signalling causes polycythaemia vera. *Nature*, 2005, 434, s. 1144–1148.

4 **Baxter, E. J. – Scott, L. M. – Campbell, P. J., et al.**: Acquired mutation of the tyrosine kinase JAK2 in human myeloproliferative disorders. *Lancet*, 2005, 365, s. 1054–1061.

5 **Levine, R. L. – Wadleigh, M. – Cools, J., et al.**: Activating mutation in the tyrosine kinase JAK2 in polycythemia vera, essential thrombocythemia, and myeloid metaplasia with myelofibrosis. *Cancer Cell*, 2005, 7, s. 387–397.

6 **Kralovics, R. – Passamonti, F. – Buser, A. S., et al.**: A gain-of-function mutation of JAK2 in myeloproliferative disorders. *N Engl J Med*, 2005, 352, s. 1779–1790.

7 **Pardanani, A. – Vannucchi, A. M. – Passamonti, F., et al.**: JAK inhibitor therapy for myelofibrosis: critical assessment of value and limitations. *Leukemia*, 2011, 25, s. 218–225.

8 **Kyttaris, V. C.**: Kinase inhibitors: a new class of antirheumatic drugs. *Drug Des Devel Ther*, 2012, 6, s. 245–250.

9 **Keohane, C. – Mesa, R. – Harrison, C.**: The Role of JAK1/2 inhibitors in the treatment of chronic myeloproliferative neoplasms. *Am Soc Clin Oncol Educ Book*, 2013, 33, s. 301–305.

10 **Červinek, L. – Doubek, M. – Penka, M., et al.**: JAK2 inhibitory v léčbě primární myelofibrózy. *Vnitř Lék*, 2014, 60, s. 158–163.

11 **Verstovsek, S. – Mesa, R. A. – Gotlib, J., et al.**: A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. *N Engl J Med*, 2012, 366, s. 799–807.

12 **Harrison, C. – Kiladjian, J. J. – Al-Ali, H. K., et al.**: JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. *N Engl J Med*, 2012, 366, s. 787–798.

13 **Verstovsek, S. – Mesa, R. A. – Gotlib, J., et al.**: Efficacy, safety and survival with ruxolitinib treatment in patients with myelofibrosis: results of a median 2-year follow-up of COMFORT-I. *Haematologica*, 2013, 98, s. 1865–1867.

14 **Cervantes, F. – Vannucchi, A. M. – Kiladjian, J. J., et al.**: Three-year efficacy, safety, and survival findings from COMFORT-II, a phase 3 study comparing ruxolitinib with best available therapy for myelofibrosis. *Blood*, 2013, 122, s. 4047–4053.

15 **Cervantes, F. Mesa, R. – Harrison, C.**: JAK inhibitors: beyond spleen and symptoms? *Haematologica*, 2013, 98, s. 160–162.

16 **Li, B. – Rampal, R. K. – Xiao, Z.**: Targeted therapie for myeloproloferative neoplasms. *Biomarkes Research*, 2019, 7, s. 15.

17 **Verstovsek, S. – Kantarjian, H. – Mesa, R. A., et al.**: Safety and efficacy of INCB018424, a JAK1 and JAK2 inhibitor, in myelofibrosis. *N Engl J Med*, 2010, 363, s. 1117–1127.

18 **Cervantes, F. – Dupriez, B. – Pereira, A., et al.**: New prognostic scoring system for primary myelofibrosis based on a study of the International Working Group for Myelofibrosis Research and Treatment. *Blood*, 2009, 113, s. 2895–2901.

19 **Tefferi, A. – Thiele, J. – Orazi, A., et al.**: Proposals and rationale for revision of the World Health Organization diagnostic criteria for polycythemia vera, essential thrombocythemia, and primary myelofibrosis: recommendations from an ad hoc international expert panel. *Blood*, 2007, 110, s. 1092–1097.

20 **Al-Ali, H. K. – Griesshammer, M. – le Coutre, P., et al.**: Safety and efficacy of ruxolitinib in an open-label, multicenter, single-arm phase 3b expanded-access study in patients with myelofibrosis: a snapshot of 1144 patients in the JUMP trial. *Haematologica*, 2016, 101, s. 1065–1073.

21 **Wilkins, B. S. – Radia, D. – Woodley, C., et al.**: Resolution of bone marrow fibrosis in a patient receiving JAK1/JAK2 inhibitor treatment with ruxolitinib. *Haematologica*, 2013, 98, s. 1872–1876.

22 **Tefferi, A. – Pardanani, A.**: Serious adverse events during ruxolitinib treatment discontinuation in patients with myelofibrosis. *Mayo Clin Proc*, 2011, 86, s. 1188–1191.

23 **Passamonti, F. – Saydam, G. – Lim, L., et al.**: RESPONSE 2: a phase 3b study evaluating the efficacy and safety of ruxolitinib in patients with hydroxyurea-resistant/intolerant polycytheinia vera versus best available therapy. *J Clin Oncol*, 2014, 32, s. 15.

24 **Mascarenhas, J.**: The role of JAK2 inhibition in polycythemia vera. *J Target Ther Cancer*, 2018, Doi: https://www.targetedonc.com/view/the-role-of-jak2-inhibition-in-polycythemia-vera.

25 **Hatalova, A. – Schwarz, J. – Gotic, M., et al.**: Recommendations for the diagnosis and treatment of patients with polycythaemia vera. *Eur J Haematol*, 2018, 101, s. 654–664.

26 **Tefferi, A. – Cortes, J. E. – Hochhaus, A., et al.**: A randomized phase II, open-label trial of orally administered SAR302503 in patients with polycythemia vera (PV) or essential thrombocythemia (ET) who are resistant or intolerant to hydroxyurea. Prezentováno na 2012 ASCO Annual Meeting, 4. 6. 2012. *J Clin Oncol*, 2012, 30, suppl., abstr TPS6641.

27 **Mesa, R. A. – Kiladjian, J. J. – Catalano, J. V., et al.**: SIMPLIFY-1: a phase III randomized trial of momelotinib versus ruxolitinib in Janus kinase inhibitor-naïve patients with myelofibrosis. *J Clin Oncol*, 2017, 35, s. 3844–3850.

28 **Harrison, C. N. – Vannucchi, A. M. – Platzbecker, U., et al.**: Momelotinib versus best available therapy in patients with myelofibrosis previously treated with ruxolitinib (SIMPLIFY 2): a randomised, open-label, phase 3 trial. *Lancet Haematol*, 2018, 5, s. e73–e81.

29 **Mascarenhas, J. – Hoffman, R. – Talpaz, M., et al.**: Pacritinib vs best available therapy, including ruxolitinib, in patients with myelofibrosis: a randomized clinical trial. *JAMA Oncol*, 2018, 4, s. 652–659.

30 **Mesa, R. A. – Vannucchi, A. M. – Mead, A., et al.**: Pacritinib versus best available therapy for the treatment of myelofibrosis irrespective of baseline cytopenias (PERSIST-1): an international, randomised, phase 3 trial. *Lancet Haematol*, 2017, 4, s. 225–236.

31 **Harrison, C. N. – Schaap, N. – Vannucchi, A. M., et al.**: Janus kinase-2 inhibitor fedratinib in patients with myelofibrosis previously treated with ruxolitinib (JAKARTA-2): a single-arm, open-label, non-randomised, phase 2, multicentre study. *Lancet Haematol*, 2017, 4, s. 317–324.

32 **Jamieson, C. – Hasserjian, R. – Gotlib, J., et al.**: Effect of treatment with a JAK2-selective inhibitor, fedratinib, on bone marrow fibrosis in patients with myelofibrosis. *J Transl Med*, 2015, 13, s. 294.

33 **Pardanani, A. – Harrison, C. – Cortes, J. E., et al.**: Safety and efficacy of fedratinib in patients with primary or secondary myelofibrosis: a randomized clinical trial. *JAMA Oncol*, 2015, 1, s. 643–651.

34 **Verstovsek, S. – Talpaz, M. – Ritchie, E., et al.**: A phase I, open-label, dose escalation, multicenter study of the JAK2 inhibitor NS-018 in patients with myelofibrosis. *Leukemia*, 2017, 31, s. 393–402.

35 **Zerbini, C. A. – Lomonte, A. B.**: Tofacitinib for the treatment of rheumatoid arthritis. *Exp Rev Clin Immunol*, 2012, 8, s. 319–331.

36 **Kuriya, B. – Cohen, M. D. – Keystone, E.**: Baricitinib in rheumatoid arthritis: evidence-to-date and clinical potential. *Ther Adv Musculoskelet Dis*, 2017, 9, s. 37–44.

37 **Combe, B. – Kivitz, A. – Tanaka, Y., et al.**: Efficacy and safety of filgotinib for patients with rheumatoid arthritis with inadequate response to methotrexate: FINCH1 primary outcome results [abstract]. *Arthritis Rheumatol*, 2019, 71, suppl. 10, dostupné z: https://acrabstracts.org/abstract/efficacy-and-safety-of-filgotinib-for-patients-with-rheumatoid-arthritis-with-inadequate-response-to-methotrexate-finch1-primary-outcome-results/, vyhledáno 1. 3. 2021.

38 **Labetoulle, R. – Paul, S. – Roblin, X.**: Filgotinib for the treatment of Crohn's disease. *Expert Opin Investig Drugs*, 2018, 27, s. 295–300.

39 **Simpson, E. L. –Sinclair, R. – Forman, S., et al.**: Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomized, placebo-controlled, phase 3 trial. *Lancet*, 2020, 396, s. 255–266.

40 **Liu, D. – Mamorska-Dyga, A.**: Syk inhibitors in clinical development for hematological malignancies. *J Hematol Oncol*, 2017, 10, s. 145.

41 **Berdeja, J. – Palandri, F. – Baer, M. R., et al.**: Phase 2 study of gandotinib (LY2784544) in patients with myeloproliferative neoplasms. *Leuk Res*, 2018, 71, s. 82–88.

42 **Kadia, T. M. – Ravandi, F. – Cortes, J., et al.**: New drugs in acute myeloid leukemia. *Ann Oncol*, 2016, 27, s. 770–778.

43 **Monaghan, K. A., et al.**: The novel JAK inhibitor CYT387 suppresses multiple signalling pathways, prevents proliferation and induces apoptosis in phenotypically diverse myeloma cells. *Leukemia*, 2011, 25, s. 1891–1899.

44 **Ng, K. – Hendifar, A. – Starodub, A., et al.**: Phase 1 dose-escalation study of momelotinib, a Janus kinase 1/2 inhibitor, combined with gemcitabine and nab-paclitaxel in patients with previously untreated metastatic pancreatic ductal adenocarcinoma. *Invest New Drugs*, 2019, 37, s. 159–165.

45 **Hatzimichael, E. – Tsolas, E. – Briasoulis, E.**: Profile of pacritinib and its potential in the treatment of hematologic disorders. *J Blood Med*, 2014, 5, s. 143–152.

Alzheimerova choroba: biologická léčba na obzoru?

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1 **Aftab, A. – Lam, J. A. – Liu, F., et al.**: Recent developments in geriatric psychopharmacology. *Expert Rev Clin Pharmacol*, 5. 2. 2021, s. 1–15.

2 **Fillit, H. – Green A.**: Aducanumab and the FDA – where are we now? *Nat Rev Neurol*, 2021, 1–2, doi: https://www.nature.com/search?q=fillit.

3 **Godyn, J. – Jonczyk, J. – Panek, D., et al.**: Therapeutic strategies for Alzheimer's disease in clinical trials. *Pharmacol Rep*, 2016, 68, s. 127–138.

4 **Chen, Y. – Wei, G. – Zhao, J., et al.**: Computational investigation of gantenerumab and crenezumab recognition of Aβ fibrils in Alzheimer's disease brain tissue. *ACS Chem Neurosci*, 2020, 11, s. 3233–3244.

5 **Klein, G. – Delmar, P. – Kerchner, G. A., et al.**: Thirty-six-month amyloid positron emission tomography results show continued reduction in amyloid burden with subcutaneous gantenerumab. *J Prevent Alzheim Dis*, 2021, 8, s. 3–6.

6 **Lacosta, A. M. – Pascual-Lucas, M. – Pesini, P., et al.**: Safety, tolerability and immunogenicity of an active anti-Aβ(40) vaccine (ABvac40) in patients with Alzheimer's disease: a randomised, double-blind, placebo-controlled, phase I trial. *Alzheimers Res Ther*, 2019, doi:10.1186/s13195-018-0340-8.

7 **Novak, P. – Zilka, N. – Zilkova, M., et al.**: AADvac1, an active immunotherapy for Alzheimer's disease and non Alzheimer tauopathies: an overview of preclinical and clinical development. *J Prev Alzheimers Dis*, 2019, 6, s. 63–69.

8 **Panza, F. – Logroscino, G. – Imbimbo, B. P., et al.**: Is there still any hope for amyloid-based immunotherapy for Alzheimer's disease? *Curr Opin Psychiatry*, 2014, 27, s. 128–137.

9 **Sevigny, J. – Chiao, P. – Bussière, T., et al.**: The antibody aducanumab reduces Abeta plaques in Alzheimer's disease. *Nature*, 2016, 537, s. 50–56.

10 **Schneider, L.**: A resurrection of aducanumab for Alzheimer's disease. *Lancet Neurol*, 2020, 19, s. 111–112.

11 **Vaz, M. – Silvestre, S.**: Alzheimer's disease: Recent treatment strategies. *Eur J Pharmacol*, 2020, 887, s. 173554.

12 **Wang, C. Y. – Wang, P.-N. – Chiu, M.-J., et al.**: UB-311, a novel UBITh(®) amyloid β peptide vaccine for mild Alzheimer's disease. *Alzheimers Dement*, 2017, 3, s. 262–272.

13 **Weninger, S. – Sperling, B. – Alexander, R., et al.**: Active immunotherapy and alternative therapeutic modalities for Alzheimer's disease. *Alzheimers Dement*, 2020, 6, s. e12090.

14 **Zhou, Z. D. – Chan, C. H. – Ma, Q. H., et al.**: The roles of amyloid precursor protein (APP) in neurogenesis: Implications to pathogenesis and therapy of Alzheimer disease. *Cell Adh Migr*, 2011, 5, s. 280–292.

Inhibitory SGLT2 jsou renoprotektivní i u nediabetických onemocnění ledvin

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1 **Gerstein, H. C. – Colhoun, H. M. – Dagenais, G. R., et al.**: Dulaglutide and renal outcomes in type 2 diabetes: an exploratory analysis of the REWIND randomised, placebo-controlled trial. *Lancet*, 2019, 394, s. 131–138.

2 The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia): Randomised placebo-controlled trial of effect of ramipril on

decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy. *Lancet*, 1997, 349, s. 1857–1863.
3 **Heerspink, H. J. L. – Kosiborod, M. – Inzucchi, S. E., et al.**: Renoprotective effects of sodium-glucose cotransporter-2 inhibitors. *Kidney Int*, 2018, 94, s. 26–39.
4 **Heerspink, H. J. L. – Stefansson, B. V. – Chertow, G. M., et al.**: Rationale and protocol of the dapagliflozin and prevention of adverse outcomes in chronic kidney disease (DAPA-CKD) randomized controlled trial. *Nephrol Dial Transplant*, 2020, 35, s. 274–282.
5 **Heerspink, H. J. L. – Stefánsson, B. V. – Corre-Roter, R., et al.**: Dapagliflozin in patients with chronic kidney disease. *N Engl J Med*, 2020, 383, s. 1436–1446.
6 **Hung, A. M. – Roumie, C. L. – Greevy, R. A., et al.**: Comparative effectiveness of incident oral antidiabetic drugs on kidney function. *Kidney Int*, 2012, 81, s. 698–706.
7 KDIGO Diabetes Work Group: KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int*, 2020, 98, s. S1–S115.
8 **Maschio, G. – Alberti, D. – Janin, G., et al.**: Effect of the angiotensin-converting-enzyme inhibitor benazepril on the progression of chronic renal insufficiency. The Angiotensin-Converting-Enzyme Inhibition in Progressive Renal Insufficiency Study Group. *N Engl J Med*, 1996, 334, s. 939–945.
9 **McMurray, J. V. – Solomon, S. D. – Inzucchi, S. E., et al.**: Dapagliflozin in patients with heart failure and reduced ejection fratcion. *N Engl J Med*, 2019, 381, s. 1995–2008.
10 **Mosenzon, O. – Wiviott, S. D. – Cahn, A., et al.**: Effects of dapagliflozin on development and progresion of kidney disease in patients with type 2 diabetes: an analysis from DECLARE-TIMI 58 randomised trial. *Lancet Diabetes Endocrinol*, 2019, 7, s. 606–617.
11 **Neal, B. – Perkovic, V. – Mahaffey, K. W., et al.**: Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med*, 2017, 377, s. 644–657.
12 **Neuen, B. L. – Jardine, M. J. – Perkovic, V.**: Sodium-glucose cotransporter 2 inhibition: which patients with chronic kidney disease should be treated in the future? *Nephrol Dial Transplant*, 2020, 35, suppl. 1, s. i48–i55.
13 **Packer, M. – Anker, S. D. – Butler, J., et al.**: Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med*, 2020, 383, s. 1413–1424.
14 **Perkovic, V. – De Zeeuw, D. – Mahaffey, K. W., et al.**: Canagliflozin and renal outcomes in type 2 diabetes: results form the CANVAS program randomised clinical trials. *Lancet Diabetes Endocrinol*, 2018, 6, s. 691–704.
15 **Perkovic, V. – Jardine, M. J. – Neal, B., et al.**: Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med*, 2019, 380, s. 2295–2306.
16 **Rosenstock, J. – Perkovic, V. – Johansen, O. E., et al.**: Effect of linagliptin vs placebo on major cardiovascular events in adults with type 2 diabetes and high cardiovascular and renal risk: The CARMELINA randomized clinical trial. *JAMA*, 2019, 321, s. 69–79.
17 **Ruggenenti, P. – Perna, A. – Gherardi, G., et al.**: Renal function and requirement for dialysis in chronic nephropathy patients on long-term ramipril: REIN follow-up trial. Gruppo Italiano di Studi Epidemiologici in Nefrologia (GISEN). Ramipril Efficacy in Nephropathy. *Lancet*, 1998, 352, s. 1252–1256.
18 **Torres, V. E. – Chapman, A. B. – Devuyst, O., et al.**: Tolvaptan in patients with autosomal dominant polycystic kidney disease. *N Engl J Med*, 2012, 367, s. 2407–2418.
19 **Torres, V. E. – Chapman, A. B. – Devuyst, O., et al.**: Tolvaptan in later-stage autosomal dominant polycystic kidney disease. *N Engl J Med*, 2017, 377, s. 1930–1942.
20 **Tuttle, R. K. – Lakshamanan, M. C. – Rayner, B., et al.**: Dulaglutide versus insulin glargine in patients with type 2 diabetes and moderate-to-severe chronic kidney disease (AWARD-7): a multicentre, open-label, randomised trial. *Lancet Diabetes Endocrinol*, 2018, 6, s. 605–617.
21 **Wanner, C. – Inzucchi, S. E. – Lachin, J. M. et al.**: Empagliflozin and progression of kidney disease in type 2 diabetes. *N Engl J Med*, 2016, 375, s. 323–334.
22 **Wheeler, D. C. – Stefansson, B. V. – Batiushin, M., et al.**: The dapagliflozin and prevention of adverse outcomes in chronic kidney disease (DAPA-CKD) trial: baseline characteristics. *Nephrol Dial Transplant*, 2020, 35, s. 1700–1711.
23 **Wiviott, S. D. – Raz, I. – Bonaca, M. P., et al.**: Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med*, 2019, 380, s. 347–357.
24 **Zannad, F. – Ferreira, J. P. – Pocock, S. J., et al.**: SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials. *Lancet*, 2020, 396, s. 819–829.
25 **Zelniker, T. A. – Wiviott, S. D. – Raz, I., et al.**: SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. *Lancet*, 2019, 393, s. 31–39.
26 **Zinman, B. – Wanner, C. – Lachin, J. M., et al.**: Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*, 2015, 373, s. 2117–2128.

Ustekinumab v léčbě idiopatických střevních zánětů

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1 **Krejsek, J.**: Modulace signálních drah IL-12/IL-23 ustekinumabem tlumí poškozující zánět u pacientů s Crohnovou nemocí. *Gastroent Hepatol*, 2018, 72, s. 334–339.
2 **Lukáš, M.**: Ustekinumab, nová biologická léčba pro nemocné s Crohnovou chorobou. *Gastroent Hepatol*, 2017, 71, s. 178–180.
3 **Sandborn, W. J. – Gasink, C. – Gao, L. L., et al.**: Ustekinumab induction and maintenance therapy in refractory Crohn's disease. *N Engl J Med*, 2012, 367, s. 1519–1528.
4 **Feagan, B. G. – Sandborn, W. J. – Gasink, C., et al.**: Ustekinumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*, 2016, 375, s. 1946–1960.
5 Redakce kongresového zpravodajství: *Gastro Hepatol*, 2020, 74, 6: Terapie v gastroenterologii UEG, Week Virtual 2020.
6 **Khorrami, S. – Ginard, D. – Marin Jimenez, I., et al.**: Ustekinumab for the treatment of recractory Crohn's disease: The Spanish experience in a large multicenter open-label cohort. *Inflamm Bowel Dis*, 2016, 22, s. 1662–1669.
7 **Sandborn, W. – Sands, B. E. – Panaccione, R., et al.**: Efficacy and safety of ustekinumab as manintenance therapy in ulcerative colitis: week 44 results from UNIFI. *J Crohn's Colitis,* 2019, 13, s. S025–S026.
8 **Friedman, K. – Marano, C. – Zhang, H., et al.**: Effects of ustekinumab induction therapy on endoscopic and histological healing in the UNIFI phase 3 study in ulcerative colitis. *J Crohn's Colitis*, 2019, 13, s. S073.
9 **Adedokun, O. J. – Xu, Z. – Marano, C., et al.**: Pharmacokinetics and exposure-response relationships of intravenously administered ustekinumab during induction treatment patients with ulcerative colitis: results from the UNIFI induction study. DDW 2019, San Diego Tu1749.
10 **Honap, S. – Cunningham, G. – Tamilarasan, A. G., et al.**: Positioning biologics and new therapies in the management of inflammatory bowel disease. *Curr Opin Gastroenterol*, 2019, 35, s. 296–301.

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1 **Gladman, D. D. – Antoni, C. – Mease, P., et al.**: Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis*, 2005, 64, suppl. 2, s. ii14–ii17.
2 **Taylor, W. – Gladman, D. – Helliwell, P., et al.**: Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum*, 2006, 54, s. 2665–2673.
3 **Kavanaugh, A. – Helliwell, P. – Ritchlin, C. T.**: Psoriatic arthritis and burden of disease: patient perspectives from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP) survey. *Rheumatol Ther*, 2016, 3, s. 91–102.
4 **McHugh, N. J. – Balachrishnan, C. – Jones, S. M.**: Progression of peripheral joint disease in psoriatic arthritis: a 5-yr prospective study. *Rheumatology*, 2003, 42, s. 778–783.
5 **Kane, D. – Stafford, L. – Bresnihan, B., et al.**: A prospective, clinical and radiological study of early psoriatic arthritis: an early synovitis clinic experience. *Rheumatology*, 2003, 42, s. 1460–1468.
6 **Gottlieb, A. – Korman, N. J. – Gordon, K. B., et al.**: Guidelines of care for the management of psoriasis and psoriatic arthritis: section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. *J Am Acad Dermatol*, 2008, 58, s. 85164.
7 **Mease, P. – McInnes, I. B.**: Secukinumab: a new treatment option for psoriatic arthritis. *Rheumatol Ther*, 2016, 3, s. 529.
8 **Menon, B. – Gullick, N. J. – Walter, G. J., et al.**: Interleukin-17+CD8+ T cells are enriched in the joints of patients with psoriatic arthritis and correlate with disease activity and joint damage progression. *Arthritis Rheumatol*, 2014, 66, s. 127281.
9 **Rossini, M. – Viapiana, O. – Adami, S., et al.**: Focal bone involvement in inflammatory arthritis: the role of IL17. *Rheumatol Int*, 2016, 36, s. 46982.
10 **Gossec, L. – Smolen, J. S. – Ramiro, S., et al.**: European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis*, 2016, 75, s. 499–510.
11 **Coates, L. C. – Kavanaugh, A. – Mease, P. J., et al.**: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 Treatment Recommendations for Psoriatic Arthritis. *Arthritis Rheumatol*, 2016, 68, s. 1060–1071.
12 **Ogdie, A. – Weiss, P.**: The epidemiology of psoriatic arthritis. *Rheum Dis Clin North Am*, 2015, 41, s. 545–568.
13 **Villani, A. P. – Rouzaud, M. – Sevrain, M., et al.**: Prevalence of undiagnosed psoriatic arthritis among psoriasis patients: Systematic review and meta-analysis. *J Am Acad Dermatol*, 2015, 73, s. 242–248.
14 **Scher, J. U. – Ogdie, A. – Merola, J. F., et al.**: Preventing psoriatic arthritis: focusing on patients with psoriasis at increased risk of transitiv. *Nat Rev Rheumatol*, 2019, 15, s. 153–166.
15 **Lloyd, P. – Ryan, C. – Menter, A.**: Psoriatic arthritis: an update. *Arthritis*, 2012, 2012, s. 176298
16 **Crowley, J.**: Scalp psoriasis: an overview of the disease and available therapies. *J Drugs Dermatol*, 2010, 9, s. 912–918.
17 **Helliwell, P. S. – Favier, G. – Gladman, D. D., et al.**: Best-practice indicators in psoriatic disease care. *J Rheumatol*, 2019, 95, suppl., s. 38–45.
18 **McGonagle, D. G. – McInnes, I. B. – Kirkham, B. W., et al.**: The role of IL-17A in axial spondyloarthritis and psoriatic arthritis: recent advances and controversies. *Ann Rheum Dis*, 2019, 78, s. 1167–1178.
19 **Tan, A. L. – Benjamin, M. – Toumi, H., et al.**: The relationship between the extensor tendon enthesis and the nail in distal interphalangeal joint disease in psoriatic arthritis—a high-resolution MRI and histological study. *Rheumatol*, 2007, 46, s. 253–256.
20 **Smith, J. A. – Colbert, R. A.**: The IL-23/IL-17 Axis in Spondyloarthritis Pathogenesis: Th17 and Beyond. *Arthritis Rheumatol*, 2014, 66, s. 231–241.

Upadacitinib v monoterapii v léčbě aktivní revmatoidní artritidy

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1 **Smolen, J. S. – Landewe, R. – Bijlsma, J., et al.**: EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic d-rugs: 2016 update. *Ann Rheum Dis*, 2017, 76, s. 960–977.
2 **Emery, P. – Breedveld, F. C. – Hall, S., et al.**: Comparison of methotrexate monotherapy with a combination of methotrexate and etanercept in active, early, moderate to severe rheumatoid arthritis (COMET): a randomised, couble-blind, parallel treatment trial. *Lancet*, 2008, 372, s. 375–382.
3 **Bello, A. E. – Perkins, E. L. – Jay, R., et al.**: Recommendations for optimizing methotrexate treatment for patients with rheumatoid arthritis (review). *Open Access Rheumatol*, 2017, 9, s. 67–79.
4 **Emery, P. – Sebba, A. – Huizinga, T. W.**: Biologic and oral disease-modifying antirheumatic drug monotherapy in rheumatoid arthritis. *Ann Rheum Dis*, 2013, 72, s. 1897–1904.

5 **Walker, J. G. – Smith, M. D.**: The Jak-STAT pathway in rheumatoid arthritis. *J Rheumatol,* 2005, 32, s. 1650–1653.
6 **Van der Heijde, D. – Tanaka, Y. – Fleischman, R., et al.**: Tofacitinib in patients with rheumatoid arthritis receiving methotrexate. Twelve months data from a twenty-four months phase III. randomized radiographic study. *Arthritis Rheum*, 2013, 65, s. 559–570.
7 **Fleischmann, R. – Schiff, M. – van der Heijde, D., et al.**: Baricitinib, methotrexate, or combination in patients with rheumatoid arthritis and no or limited prior disease-modifying antirheumatic drug treatment. *Arthritis Rheum*, 2017, 69, s. 506–517.
8 **Fleischmann, R. – Pangan, A. L. – Song, I. H., et al.**: Upadacitinib versus placebo or adalimumab in patients with rheumatoid arthritis and an inadequate response to methotrexate: results of a phase III, double-blind, randomized controlled trial. *Arthritis Rheumatol*, 2019, 71, s. 1788–1800.
9 **Westhovens, R. – Taylor, O. P. C. – Alten, R., et al.**: Filgotinib, an oral JAK selective inhibitor is effective in combination with methotrexate on patients with active rheumatoid arthritis and insufficient response to MTX. Results from a randomised, dose-finding study (DARWIN 1). *Ann Rheum Dis*, 2017, 76, s. 859–1008.
10 **Kivitz, A. J. – Giutierez-Ureña, S. R. – Polley, J., et al.**: Peficitinib, a JAK inhibitor in the treatment moderate to severe rheumatoid arthritis in patients with inadequate response to MTX. *Arthritis Rheumatol*, 2017, 69, s. 709–719.
11 **van Vollenhoven, R. – Takeuchi, T. – Pangan, A. L., et al.**: Efficacy and safety of upadacitinib monotherapy in methotrexate naive patients with moderately to severely active rheumatoid arthritis (SELECT-EARLY): A multicenter, multi-country, randomized, double-blind, active comparator – controlled trial. *Arthritis Rheumatol*, 2020, 72, s. 1607–1620.
12 **Smolen, J. S. – Pangan, A. L. – Emery, P., et al.**: Upadacitinib as monotherapy in patients with active rheumatoid arthritis and inadequate response to methotrexate (SELECT-MONOTHERAPY): a randomised, placebo-controlled, double-blind phase 3 study. *Lancet*, 2019, 393, s. 2303–2311.
13 **Genovese, M. C. – Fleischmann, R. – Combe, B., et al.**: Safety and efficacy of upadacitinib in patients with active rheumatoid arthritis refractory to biologic disease-modifying antirheumatic drugs (SELECT-BEYOND): a double-blind, randomised controlled phase 3 trial. *Lancet*, 2018, 391, s. 2513–2524.
14 **Burmester, G. R. – Kremer, J. M. – van den Bosch, F., et al.**: Safety and efficacy of upadacitinib in patients with rheumatoid arthritis and inadequate response to conventional synthetic disease-modifying antirheumatic drugs (SELECT-NEXT): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*, 2018, 391, s. 2503–2512.
15 **Strand, V. – Tundia, N. – Wells, A., et al.**: Upadacitinib monotherapy improves patient – reported outcomes in rheumatoid arthritis: results from SELECT-EARLY and SELECT-MONOTHERAPY. *Rheumatology*, 2020, 00, s. 1–13.
16 **Nash, P. – Kerschbaumer, A. – Dörner, T., et al.**: Points to consider for the treatment of immune-mediated inflammatory diseases with Janus kinase inhibitors: a consensus statement. *Ann Rheum Dis*, 2021, 80, s. 71–87.
17 **Wollenhaupt, J. – Lee, E.-B. – Curtis, J. R., et al.**: Safety and efficacy of tofacitinib for up to 9,5 years in the treatment of rheumatoid arthritis: final results of a global, open-label, long-term extension study. *Arthritis Res Ther*, 2019, 21, s. 89.
18 **European Medicines Agency (EMA)**: Xeljanz to be used with caution for all patients at high risk of blood clots, 2019. EMA/584781/2019. Dostupné z: https://www. ema. europa. eu/en/documents/referral/xeljanz-article-20-procedure-xeljanz-be-used-caution-all-patients-high-risk-blood-clots_en. pdf, vyhledáno 6. 2. 2021.
19 **Van Vollenhoven, R. – Takeuchi, T. – Pangan, A. L., et al.**: A phase 3, randomized, controlled trial comparing upadacitinib monotherapy to MTX monotherapy in MTX-naïve patients with active rheumatoid arthritis. ACR 2018, abstrakt 891.
20 **Van Vollenhoven, R., et al.**: A study to compare upadacitinib (ABT-494) monotherapy to methotrexate (MTX) monotherapy in adults with rheumatoid arthritis (RA) who have not previously taken methotrexate (SELECT-EARLY). EULAR 2019, poster THU0197; ClinicalTrials.gov (NCT02706873).
21 **Van Vollenhoven, R., et al.**: Monotherapy with upadacitinib in MTX-naïve patients with rheumatoid arthritis: results at 48 weeks. THU0197. *Ann Rheum Dis*, 2019, 78, s. 376–377.
22 **Strand, V., et al.**: THU0192 Upadacitinib montherapy improves patients-reported outcomes in methotrexate-naïve patients with moderately to severely active rheumatoid arthitis: results from SELECT-EARLY. EULARD 2019. *Ann Rheum Dis*, 2019, 78, s. 372–373.
23 **Van Vollenhoven, R., et al.**: THU0197 Monotehrapy with upadacitinib in MTX-native patients with rheumatoid arthritis? Results at 48 weeks from select-early study. *Ann Rheum Dis*, 2019, 78, s. 376–377.
24 **Smolen, J. S., et al.**: Upadacitinib as monotherapy in patients with active rheumatoid arthritis and inadequate response to methotrexate (SELECT-MONOTHERAPY): a randomised, placebo-controlled, double-blind phase 3 study. *Lancet*, 2019, 393, s. 2303–2311.

Etanercept nebo metotrexát u pacientů s revmatoidní artritidou v trvalé remisi

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1 **Edwards, C. J. – Galeazzi, M. – Bellinvia, S., et al.**: Can we wean patients with inflammatory arthritis from biological therapies? *Autoimmun Rev*, 2019, 18, 102399.
2 **Singh, J. A. – Saag, K. G. – Bridges, S. L. Jr., et al.**: 2015 American College of Rheumatology Guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*, 2016, 68, s. 1–26.
3 **Smolen, J. S. – Landewe, R. B. M. – Bijlsma, J. W. J., et al.**: EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis*, 2020, 79, s. 685–699.
4 **Treharne, G. J. – Douglas, K. M. – Iwaszko, J., et al.**: Polypharmacy among people with rheumatoid arthritis: the role of age, disease duration and comorbidity. *Musculoskeletal Care*, 2007, 5, s. 175–190.
5 **Curtis, J. R. – Emery, P. – Karis, E., et al.**: Etanercept or methotrexate withdrawal in rheumatoid arthritis patients in sustained remission on combination therapy: a randomized, double-blind trial. *Arthritis Rheumatol*, 18. 11. 2020, doi: 10.1002/art.41589.

Dlouhodobá bezpečnost tofacitinibu: integrovaná analýza klinických zkušeností

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1 **Cross, M. – Smith, E. – Hoy, D., et al.**: The global burden of rheumatoid arthritis: estimates from the global burden of disease 2010 study. *Ann Rheum Dis*, 2014, 73, s. 1316–1322.
2 **Smolen, J. S. – Landewé, R. – Bijlsma, J., et al.**: EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*, 2017, 76, s. 960–977.
3 **Wang, F. – Sun, L. – Wang, S., et al.**: Efficacy and safety of tofacitinib, baricitinib, and upadacitinib for rheumatoid arthritis: a systematic review and meta-analysis. *Mayo Clin Proc*, 2020, 95, s. 1404–1419.
4 **Kerschbaumer, A. – Sepriano, A. – Smolen, J. S., et al.**: Efficacy of pharmacological treatment in rheumatoid arthritis: a systematic literature research informing the 2019 update of the EULAR recommendations for management of rheumatoid arthritis. *Ann Rheum Dis*, 2020, 79, s. 744–759.
5 US Food and Drug Administration. Safety trial finds risk of blood clots in the lungs and death with higher dose of tofacitinib (Xeljanz, Xeljanz XR) in rheumatoid arthritis patients; FDA to investigate. 2019. Dostupné z: https://www.fda.gov/media/120485/download, vyhledáno 12. 3. 2021.
6 **Cohen, S. B. – Tanaka, Y. – Mariette, X., et al.**: Long-term safety of tofacitinib for the treatment of rheumatoid arthritis up to 8.5 years: integrated analysis of data from the global clinical trials. *Ann Rheum Dis*, 2017, 76, s. 1253–1262.
7 **Cohen, S. B. – Tanaka, Y. – Mariette, X., et al.**: Long-term safety of tofacitinib up to 9.5 years: a comprehensive integrated analysis of the rheumatoid arthritis clinical development programme. *RMD Open*, 2020, 6, e001395.

Dlouhodobá účinnost tofacitinibu u revmatoidní artritidy

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

1 **van der Heijde, D.**: How to read radiographs according to the Sharp/van der Heijde method. *J Rheumatol*, 2000, 27, s. 261–263.
2 **Smolen, J. S. – Landewé, R. – Bijlsma, J., et al.**: EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*, 2017, 76, s. 960–977.
3 **van der Heijde, D. – Landewé, R. B. M. – Wollenhaupt, J., et al.**: Assessment of radiographic progression in patients with rheumatoid arthritis treated with tofacitinib in long-term studies. *Rheumatology*, 15. 10. 2020, keaa476, doi: 10.1093/rheumatology/keaa476, Epub před tiskem.

Axiální spondyloartritidy u žen a možnosti léčby

prof. MUDr. Karel Pavelka, DrSc. Revmatologický ústav, Praha

1 **Dougados, M. – Baeten, D.**: Spondyloarthritis. *Lancet*, 2011, 377, s. 2127–2137.
2 **van der Linden, S. – Valkenburg, H. A. – Cats, A.**: Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum*, 1984, 27, s. 361–368.
3 **Rudwaleit, M. – van der Heide, D. – Landewé, R.**: The development of assessment of spondyloarthritis international society classification criteria for axial spondyloarthritis. *Ann Rheum Dis*, 2009, 68, s. 777–783.
4 **Poddubnyy, D. – Rudwaleit, M. – Jaibel, H., et al.**: Rates and predictors of radiographic sacroiliitis progression over 2 years in patients with axial spondyloarthritis. *Ann Rheum Dis*, 2011, 70, s. 1369–1374.
5 **Bennet, A. N., et al.**: Severity of baseline magnetic resonance imaging evident sacroiliitis and HLA B27 status in early inflammatory back pain predict evident ankylosing spondylitis in eight years. *Arthritis Rheum*, 2008, 58, s. 3413–3418.
6 **Rudwaleit, M. – Sieper, J.**: Referral strategies for early diagnosis of axial spondyloarthritis. *Nat Rev Rheumatol*, 2012, 7, s. 262–268.
7 **Malaviya, A. N. – Kalyani, A. – Rawat, R., et al.**: Comparison of patients with AS and non-radiographic axial spondyloarthritis (nr-axSpA) from a single rheumatology clinic in New Delhi. *Int J Rheumatol*, 2015, 18, s. 736–741.
8 **López-Medina C. – Ramiro, S. – van der Heijde, D., et al.**: Characteristics and burden of disease in patients with radiographic and non-radiographic axial spondyloarthritis: a comparison by systematic literature review and meta-analysis. *RMD Open*, 2019, 5, e001108, doi:10.1136/rmdopen-2019-001108.
9 **Haroon, N. N. – Peterson, J. M. – Li, P.**: Increasing proportion of female patients with ankylosing spondylitis: a population based study of trends in the incidence of AS. *BMJ Open*, 2014, 4, e006634, doi: 10.1136/bmjopen-2014-006634.

10 **Jakobsen, G. L. – Stephanson, O. – Askling, J., et al.**: Pregnancy outcomes in patients with ankylosing spondylitis: a nationwide register study. *Ann Rheum Dis*, 2015, 0, s. 1–5.
11 **van der Heijde, D. – Ramiro, S. – Landewé, R., et al.**: 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis*, 2017, 76, s. 978–991.
12 **Inman, R. D. – Davies, J. C. – van der Heijde, D., et al.**: Efficacy and safety of golimumab in patients with ankylosing spondylitis: results of a randomised, double blind, placebo-controlled, phase III trial. *Arthritis Rheum*, 2008, 58, s. 3402–3412.
13 **Baeten, D. – Sieper, J. – Braun, J., et al.**: Secukinunab an interleukin 17 inhibitor in ankylosing spondylitis. *N Engl J Med*, 2015, 373, s. 2534–2548.
14 **van der Heijde, D. – Cheng-Chung Wei, J. – Dougados, M., et al.**; COAST-V study group: Ixekizumab, an interleukin-17A antagonist in the treatment of ankylosing spondylitis or radiographic axial spondyloarthritis in patients previously untreated with biological disease-modifying anti-rheumatic drugs (COAST-V): 16 week results of a phase 3 randomised, double-blind, active-controlled and placebo-controlled trial. *Lancet*, 2018, 392, s. 2441–2451.
15 **Noureldin, B. – Barkham, N.**: The current standard of care and the unmet needs for axial spondyloarthritis. *Rheumatology*, 2018, 57, s. vi10–vi17.
16 **Sieper, J. – van der Heijde, D. – Dougados, M.**: Efficacy and safety an adalimumab in patients with non-radiographic axial spondyloarthritis results of a randomized, placebo controlled trial (ABILITY). *Ann Rheum Dis*, 2013, 72, s. 815–822.
17 **Landewé, R. – Braun, J. – Deodhar, A., et al.**: Efficacy of certolizumab pegol on signs and symptoms of axial spondyloarthritis including ankylosing spondylitis: 24-week results of a double blind randomised placebo-controlled phase 3 study. *Ann Rheum Dis*, 2014, 73, s. 39–47.
18 **Landewé, R. B. M. – van der Heijde, D. – Dougados, M., et al.**: Maintenance of clinical remission in early axial spondyloarthritis following certolizumab pegol dose reduction. *Ann Rheum Dis*, 2020, 79, s. 920–928.
19 **Deodhar, A. – Gensler, L. S. – Kay, J., et al.**: A fifty-two-week, randomized, placebo-controlled trial of certolizumab pegol in nonradiographic axial spondyloarthritis. *Arthritis Rheum*, 2019, 71, s. 1101–1111.
20 **van der Horst-Bruinsma, I. – van Bentum, R. – Verbraak, F. D., et al.**: The impact of certolizumab pegol treatment on the incidence of anterior uveitis flares in patients with axial spondyloarthritis: 48-week interim results from C-VIEW. *RMD Open*, 2020, 6, e001161.
21 **Götestam Skorpen, C., et al.**: The EULAR point to consider for use of antirheumatic drugs before pregnancy and during pregnancy and lactation. *Ann Rheum Dis*, 2016, 0, s. 1–16.
22 **Mariette, X. – Förger, F. – Abraham, B., et al.**: Lack of placental transfer of certolizumab pegol during pregnancy: results from CRIB, a prospective, postmarketing, pharmacokinetic study. *Ann Rheum Dis*, 2018, 77, s. 228–233.
23 **Clowse, M. E. B. – Förger, F. – Hwang, C., et al.**: Minimal to no transfer of certolizumab pegol into breast milk: results from CRADLE, a prospective, postmarketing, multicentre, pharmacokinetic study. *Ann Rheum Dis*, 2017, 76, s. 1890–1896.

Galkanezumab v preventivní léčbě migrény

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1 **Martin, V. – Samaas, K. H. – Sheena, A., et al.**: Efficacy and safety of galcanezumab for the preventive treatment of migraine: a narrative review. *Adv Therapy*, 2020, 37, s. 2034–2049.
2 **Kotas, R., et al.**: *Migréna, patofyziologie a léčba*. Praha, Maxdorf, 2001.
3 **Nežádal, T.**: Migréna – současné možnosti terapie. *Bolest*, 2020, 23, s. 12–20.
4 **Detke, H. C. – Goadsby, P. J. – Wang, S., et al.**: Galcanezumab in chronic migraine: the randomized, double-blind, placebo-controlled REGAIN study. *Neurology*, 2018, 91, s. e2211–e2221.
5 **Camporeale, A., et al.**: A phase 3, long-term, open-label safety study of galcanezumab in patients with migraine. *BMC Neurol*, 2018, 18, s. 188.

Biologická léčba migrény – zkušenosti z praxe

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1 **Raffaelli, B. – Reuter, U.**: The biology of monoclonal antibodies: focus on calcitonin gene-related peptide for prophylactic migraine therapy. *Neurotherapeutics*, 2018, 15, s. 324–335.
2 Aimovig, INN-erenumab (europa.eu). Dostupné z: https://www.ema.europa.eu/en/documents/product-information/aimovig-epar-product-information_cs.pdf, vyhledáno 20. 1. 2021.
3 **Bártková, A.**: Akutní a profylaktická terapie migrény. *Prakt lékáren*, 2019, 15, s. 208–212.
4 AJOVY, INN-fremanezumab (europa.eu). Dostupné z: https://www.ema.europa.eu/en/documents/product-information/ajovy-epar-product-information_cs.pdf, vyhledáno 20. 1. 2021.
5 Emgality, INN-galcanezumab (europa.eu). Dostupné z: https://www.ema.europa.eu/en/medicines/human/EPAR/emgality, vyhledáno 20. 1. 2021.
6 **Raffaelli, B. – Neeb, L. – Reuter, U.**: Monoclonal antibodies for the prevention of migraine. *Expert Opin Biol Ther*, 2019, 19, s. 1307–1317.

Kam se posunula biologická léčba astmatu v průběhu roku 2020

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1 2006 GINA Report. Global Strategy for Asthma Management and Prevention. Dostupné z: www.ginasthma.org/archived-reports, vyhledáno 27. 1. 2021.
2 **Tan, R. – Liew, M. F. – Lim, H. F., et al.**: Promises and challenges of biologics for severe asthma. *Biochem Pharmacol*, 2020, 179, s. 114012.
3 **Menzies-Gow, A. – Colice, G. – Griffiths, J. M., et al.**: NAVIGATOR: a phase 3 multicentre, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the efficacy and safety of tezepelumab in adults and adolescents with severe, uncontrolled asthma. *Respir Res*, 2020, 21, s. 266.
4 **Harrison, T. – Canonica, G. W. – Chupp, G., et al.**: Real-world mepolizumab in the prospective severe asthma REALITI-A study: initial analysis. *Eur Respir J*, 2020, 56, s. 2000151.
5 **Pitlick, M. M. – Joshi, A. Y.**: Considerations for asthma management and viral transmission in the era of COVID-19. *Allergy Asthma Proc*, 2021, 42, s. 93–96.
6 **Assaf, S. M. – Tarasevych, S. P. – Diamant, Z., et al.**: Asthma and severe acute respiratory syndrome coronavirus 2019: current evidence and knowledge gaps. *Curr Opin Pulm Med*, 2021, 27, s. 45–53.

Avelumab s axitinibem a algoritmus léčby první linie metastatického renálního karcinomu

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1 **Zarrabi, K. – Fang, C. – Wu, S.**: New treatment options for metastatic renal cell carcinoma with prior anti-angiogenesis therapy. *J Hematol Oncol*, 2017, 10, s. 38.
2 **Vaishampayan, U. – Schoffski, P. – Ravaud, A., et al.**: Avelumab monotherapy as first-line or second-line treatment in patients with metastatic renal cell carcinoma: phase I bresults from the JAVELIN Solid Tumor trial. *J Immunother Cancer*, 2019, 7, s. 275.
3 **Motzer, R. J. – Penkov, K. – Haanen, J., et al.**: Avelumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. *N Engl J Med*, 2019, 380, s. 1103–1115.
4 **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.
5 National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: kidney cancer. Dostupné z: https://www.nccn.org/professionals/physician_gls/PDF/kidney.pdf. 1/2021, vyhledáno 14. 3. 2021.
6 ESOU 2021: EUO Lecture: Systemic Treatment of Metastatic Renal Cell Carcinoma.

Léčba pacienta s metastatickým renálním karcinomem, dlouhotrvající parciální regrese onemocnění při léčbě pazopanibem – kazuistika

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1 **Motzer, R. J. – Bacik, J. – Murphy, B. A., et al.**: Interferon-alfa as a komparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. *J Clin Oncol*, 2002, 20, s. 289–296.
2 **Sternberg, C. N. – Hawkins, R. E. – Wagstaff, J., et al.**: A randomised, double-blind phase III study of pazopanib in patients with advanced and/or metastatic renal cell carcinoma: final overall survival results and safety update. *Eur J Cancer*, 2013, 49, s. 1287–1296.
3 **Motzer, R. J. – Hutson, T. E. – Cella, D., et al.**: Pazopanib versus sunitinib in metastatic renal-cell carcinoma. *N Engl J Med*, 2013, 369, s. 722–731.
4 **Sánchez-Heras, A. B. – Castillejo, A. – García-Díaz, J. D., et al.**: Hereditary leiomyomatosis and renal cell cancer syndrome in Spain: *Clinical and Genetic Characterization Cancers* , 2020, 12, s. 3277.

Eskalace a deeskalace léčby u časného karcinomu prsu s HER2 pozitivitou

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1 **Siegel, R. L. – Miller, K. – Jemal, A.**: Cancer statistics 2020. *Ca Cancer J Clin*, 2020, 7, s. 7–30.
2 **Romond, E. H. – Perez, E. A. – Bryant, J., et al.**: Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *N Engl J Med*, 2005, 353, s. 1673–1684.
3 **Cameron, D. – Piccart-Gebhart, M. J. – Gelber, R. D., et al.**: 11 years' follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive early breast cancer: final analysis of the HERceptin Adjuvant (HERA) trial. *Lancet*, 2017, 389, s. 1195–1205.
4 **Piccart-Gebhart, M. J. – Procter, M. – Leyland-Jones, B., et al.**: Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. *N Engl J Med*, 2005, 353, s. 1659–1672.
5 **Pernas, S. – Barroso-Sousa, R. – Tolaney, S. M.**: Optimal treatment of early stage HER2-positive breast cancer. *Cancer*, 2018, 124, s. 4455–4466.
6 **Kreutzfeldt, J. – Rozeboom, B. – Dey, N – De, P.**: The trastuzumab era: current and upcoming targeted HER2+ breast cancer therapies. *Am J Cancer Res*, 2020, 10, s. 1045–1067.
7 **Joensuu, H. – Bono, P. – Kataja, V., et al.**: Fluorouracil, epirubicin, and cyclophosphamide with either docetaxel or vinorelbine, with or without trastuzumab, as adjuvant treatments of breast cancer: final results of the FinHer Trial. *J Clin Oncol*, 2009, 27, s. 5685–5692.
8 **Earl, H. M. – Hiller, L. – Vallier, A. L., et al.**: Six versus 12 months of adjuvant trastuzumab for HER2-positive early breast cancer (PERSEPHONE): 4-year disease-free survival results of a randomised phase 3 non-inferiority trial. *Lancet*, 2019, 393, s. 2599–2612.
9 **Pivot, X. – Romieu, G. – Debled, M., et al.**: Six months versus 12 months of adjuvant trastuzumab for patients with HER2-positive early breast cancer (PHARE): a randomised phase 3 trial. *Lancet Oncol*, 2013, 14, s. 741–748.
10 **Conte, P. – Frassoldati, A. – Bisagni, G., et al.**: Nine weeks versus 1 year adjuvant trastuzumab in combination with chemotherapy: final results of the phase III randomized Short-HER study. *Ann Oncol*, 2018, 29, s. 2328–2333.
11 **Dieci, M. V. – Bisagni, G. – Brandes, A. A., et al.**: Validation of the AJCC prognostic stage for HER2-positive breast cancer in the ShortHER trial. *BMC Med*, 2019, 17, s. 207.
12 **Dieci, M. V. – Conte, P. – Bisagni, G., et al.**: Association of tumor-infiltrating lymphocytes with distant disease-free survival in the ShortHER randomized adjuvant trial for patients with early HER2+ breast cancer. *Ann Oncol*, 2019, 30, s. 418–423.
13 **Slamon, D. – Eiermann, W. – Robert, N., et al.**; Breast Cancer International Research Group: Adjuvant trastuzumab in HER2-positive breast cancer. *N Engl J Med*, 2011, 365, s. 1273–1283.
14 **Goel, A. K. – Zamre, V. – Chaudhary, P., et al.**: APT Trial: would it really help in de-escalation of therapy? *J Clin Oncol*, 2019, 37, s. 2953–2954.
15 **Gianni, L. – Pienkowski, T. – Im, Y. H., et al.**: Five-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial. *Lancet Oncol*, 2016, 17, s. 791–800.
16 **Nitz, U. A. – Gluz, O. – Christgen, M., et al.**: De-escalation strategies in HER2-positive early breast cancer (EBC): final analysis of the WSG-ADAPT HER2+/HR– phase II trial: efficacy, safety, and predictive markers for 12 weeks of neoadjuvant dual blockade with trastuzumab and pertuzumab ± weekly paclitaxel. *Ann Oncol*, 2017, 28, s. 2768–2772.
17 **Gianni, L. – Bisagni, G. – Colleoni, M., et al.**: Neoadjuvant treatment with trastuzumab and pertuzumab plus palbociclib and fulvestrant in HER2-positive, ER-positive breast cancer (NA-PHER2): an exploratory, open-label, phase 2 study. *Lancet Oncol*, 2018, 19, s. 249–256.
18 **Llombart-Cussac, A. – Cortés, J. – Paré, L., et al.**: HER2-enriched subtype as a predictor of pathological complete response following trastuzumab and lapatinib without chemotherapy in early-stage HER2-positive breast cancer (PAMELA): an open-label, single-group, multicentre, phase 2 trial. *Lancet Oncol*, 2017, 18, s. 545–554.
19 **Prat, A. – Pascual, T. – De Angelis, C., et al.**: HER2-enriched subtype and ERBB2 expression in HER2-positive breast cancer treated with dual HER2 blockade. *J Natl Cancer Inst*, 2020, 112, s. 46–54.
20 **Chan, A. – Moy, B. – Mansi, J., et al.**; ExteNET Study Group: Final efficacy results of neratinib in HER2-positive hormone receptor-positive early-stage breast cancer from the phase III ExteNET Trial. *Clin Breast Cancer*, 2021, 21, s. 80–91.e7.
21 **Xu, Z. Q. – Zhang, Y. – Li, N., et al.**: Efficacy and safety of lapatinib and trastuzumab for HER2-positive breast cancer: a systematic review and meta-analysis of randomised controlled trials. *BMJ Open*, 2017, 7, s. e013053.
22 **McCullough, A. E. – Dell'orto, P. – Reinholz, M. M., et al.**: Central pathology laboratory review of HER2 and ER in early breast cancer: an ALTTO trial [BIG 2-06/NCCTG N063D (Alliance)] ring study. *Breast Cancer Res Treat*, 2014, 143, s. 485–492.
23 **Lambertini, M. – Agbor-Tarh, D. – Metzger-Filho, O., et al.**: Prognostic role of distant disease-free interval from completion of adjuvant trastuzumab in HER2-positive early breast cancer: analysis from the ALTTO (BIG 2-06) trial. *ESMO Open*, 2020, 5, s. e000979.
24 **Schneeweiss, A. – Chia, S. – Hickish, T., et al.**: Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). *Ann Oncol*, 2013, 24, s. 2278–2284.
25 **Swain, S. M. – Ewer, M. S. – Viale, G., et al.**: Pertuzumab, trastuzumab, and standard anthracycline- and taxane-based chemotherapy for the neoadjuvant treatment of patients with HER2-positive localized breast cancer (BERENICE): a phase II, open-label, multicenter, multinational cardiac safety study. *Ann Oncol*, 2018, 29, s. 646–653.
26 **von Minckwitz, G. – Procter, M. – de Azambuja, E., et al.**; APHINITY Steering Committee and Investigators: Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. *N Engl J Med*, 2017, 377, s. 122-131. Erratum in: *N Engl J Med*, 2017, 377, s. 702.
27 **Martínez, M. T. – Pérez-Fidalgo, J. A. – Martín-Martorell, P., et al.**: Treatment of HER2 positive advanced breast cancer with T-DM1: A review of the literature. *Crit Rev Oncol Hematol*, 2016, 97, s. 96–106.
28 **von Minckwitz, G. – Huang, C. S. – Mano, M. S., et al.**; KATHERINE Investigators: Trastuzumab emtansine for residual invasive HER2-positive breast cancer. *N Engl J Med*, 2019, 380, s. 617–628.
29 **Dieci, M. V. – Vernaci, G. – Guarneri, V.**: Escalation and de-escalation in HER2 positive early breast cancer. *Cur Opin Oncol*, 2019, 31, s. 35–42.
30 **Piccart, M. – Procter, M. – Fumagalli, D., et al.**: Updated APHINITY trial data show addition of pertuzumab to trastuzumab plus chemotherapy continues to yield clinical benefit in patients with operable HER2-positive early breast cancer. Dostupné z: https://www.sabcs.org/sabcs/2019/pressreleases/1_xa6Fcb46Gtsr_Updated%20APHINITY%20Trial%20Data.pdf, vyhledáno 22. 3. 2021.
31 **Martin, M. – Holmes, F. A. – Ejlersten, B., et al.**: Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*, 2017, 18, s. 1688–1700.
32 **Gianni, L. – Pienkowski, T. – Im, Y.-H., et al.**: Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. *Lancet Oncol*, 2012, 13, s. 25–32.
33 **Basho, R. K. – McArthur, H. L.**: Optimizing (neo)adjuvant treatment of HER2-positive breast cancer. *Ther Adv Med Oncol*, 2018, 10, 1758835918775697.

Talazoparib v léčbě karcinomu prsu

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1 National Cancer Institute. BRCA mutations: cancer risk and genetic testing. Dostupné z: https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet#q1, vyhledáno 13. 12. 2018.
2 **Levin, B. – Lech, D. – Friedenson, B.**: Evidence that BRCA1- or BRCA2-associated cancers are not inevitable. *Molecular Medicine*, 2012, 18, s. 1327 –1337.
3 What is a gene mutation and how do mutations occur? U.S. National Library of Medicine. Dostupné z: https://ghr.nlm.nih.gov/primer/mutationsanddisorders/genemutation, vyhledáno 13. 12. 2018.
4 National Cancer Institute. Dostupné z: https://seer.cancer.gov/statfacts/html/breast-subtypes.html, vyhledáno 16. 3. 2021.
5 **Tung, N. – Lin, N. U. – Kidd, J., et al.**: Frequency of germline mutations in 25 cancer susceptibility genes in a sequential series of patients with breast cancer. *J Clin Oncol*, 2016, 34, s. 1460–1468.
6 **Howlader, N. – Altekruse, S. F. – Li, Ch. I., et al.**: US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status. *J Natl Cancer Inst*, 2014, 106, dju055, doi:10.1093/jnci/dju055.
7 **Robertson, L., et al.**: BRCA1 testing should be offered to individuals with triple-negative breast cancer diagnosed below 50 years. *Br J Cancer*, 2012, 106, s. 1234–1238.
8 **Atchley, D. P., et al.**: Clinical and pathologic characteristics of patients with BRCA-positive and BRCA-negative breast cancer. *J Clin Oncol*, 2008, 26, s. 4282–4288.
9 BRCA1 and BRCA2: cancer risk and genetic testing. National Cancer Institute at the National Institutes of Health. Dostupné z: https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet, vyhledáno 16. 3. 2021.
10 **Kim, R. – Peterson, A. – Isherwood, A., et al.**: Incidence of germline BRCA1- and BRCA2-mutated breast cancer in the US. SABCS 2016, poster P5-08-28. .
11 **Godet, I. – Gilkes, D. M.**: BRCA1 and BRCA2 mutations and treatment strategies for breast cancer. *Integr Cancer Sci Ther*, 2017, 4, 10.15761/ICST.1000228.
12 **Lord, C. J. – Ashworth, A., et al.**: PARP inhibitors: synthetic lethality in the clinic. *Science*, 2017, 355, s. 1152–1158.
13 **Polyak, K. – Garber, J., et al.**: Targeting the missing links for cancer therapy. *Nat Med*, 2011, 17, s. 283–284.
14 **Murain, J., et al.**: Stereospecific PARP trapping by BMN 673 and comparison with olaparib and rucaparib. *Mol Cancer Ther*, 2014, 13, s. 433–443.
15 **de Bono, J., et al.**: Phase I, dose-escalation, two-part trial of the PARP inhibitor talazoparib in patients with advanced germline BRCA1/2 mutations and selected sporady cancers. *Cancer Discov*, 2017, 7, s. 620–629.
16 **Turner, N. C., et al.**: Final results of a phase 2 study of talazoparib (TALA) following platinum or multiple cytotoxic regimens in advanced breast cancer patients (pts) with germline BRCA1/2 mutations (ABRAZO). Prezentováno na American Society of Clinical Oncology 2017 Annual Meeting, Chicago, 2.–6. 6. 2017, abstrakt.
17 **Jeniffer, K., et al.**: Talazoparib in patients with advanced breast cancer and germline BRCA mutation. *N Engl J Med*, 2018, 379, s. 753–763.
18 **Litton, J. K., et al.**: Talazoparib versus chemotherapy in patients with germline BRCA1/2-mutated HER-negative advanced breast cancer: final overal survival resultes from the EMBRACA trial. *Ann Oncol*, 2020, 31, s. 1526–1535.
19 **Hurvitz, S. A., et al.**: Talazoparib in patients with a germline BRCA-mutated advanced breast cancer: detailed safety analyses from the phase III EMBRACA trial. *Oncologist*, 2020, 25, s. e439–e450.

Imunoterapie karcinomu plic a základní principy fungování imunitního systému

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1 Společnost českých patologů ČLS JEP. Nová pravidla pro testování prediktivních markerů (aktualizace z 8.6.2018), dostupné z: http://www.patologie.info/standardy/35, vyhledáno 10. 3. 2020.
2 **Brahmer, J. R. – Rodriguez-Abreu, D. – Robinson, A. G., et al.**: Health-related quality-of-life results for pembrolizumab versus chemotherapy in advanced, PD-L1-positive NSCLC (KEYNOTE-024): a multicentre, international, randomised, open-label phase 3 trial. *Lancet Oncol*, 2017, 18, s. 1600–1609.
3 **Brahmer, J. R. – Rodriguez-Abreu, D. – Robinson, A., et al.**: OA 17.06 updated analysis of KEYNOTE-024: pembrolizumab vs platinum-based chemotherapy for advanced NSCLC with PD-L1 TPS 50%. *J Thorac Oncol*, 2017, 12, s. S1793–S1794.
4 **Gandhi, L. – Rodriguez-Abreu, D. – Gadgeel, S., et al.**: Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. *N Engl J Med*, 2018, 378, s. 2078–2092.
5 **Gadgeel, S. M. – Garassino, M. C. – Esteban, E., et al.**: KEYNOTE-189: Updated OS and progression after the next line of therapy (PFS2) with pembrolizumab (pembro) plus chemo with pemetrexed and

platinum vs placebo plus chemo for metastatic nonsquamous NSCLC. *J Clin Oncol*, 2019, 39, suppl., abstrakt 9013.
6 **Paz-Ares, L. G. – Luft, A. – Vicente, D., et al.**: Pembrolizumab plus chemotherapy for squamous non-small-cell lung cancer. *N Engl J Med*, 2018, 379, s. 2040–2051.
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.
8 **Reck, M. – Mok, T. S. K. – Nishio, M., et al.**: Atezolizumab plus bevacizumab and chemotherapy in non-small-cell lung cancer (IMpower150): key subgroup analyses of patients with EGFR mutations or baseline liver metastases in a randomised, open-label phase 3 trial. *Lancet Respir Med*, 2019, 7, s. 387–401.

Pacient s diseminovaným NSCLC s fúzí ROS1 s téměř kompletní remisí na biologické léčbě – kazuistika

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1 **Skřičková, J. – Kolek, V. – Pešek, M., et al.**: Mapování epidemiologické situace nemalobuněčného karcinomu plic a obraz léčebné péče v ČR s důrazem na léčbu neresekovatelného a metastatického stadia v letech 2007–2013. ICOP edu – Edukační a informační platforma onkologických center pro podporu a modernizaci vzdělávání v lékařských a příbuzných medicínských oborech. Dostupné z: https://www.icop.cz/res/file/odborne-zpravy/nsclc-epidemiologie-lecba-20160401.pdf, vyhledáno 25. 3. 2021.
2 **Zemanova, M.**: Léčba pokročilého nemalobuněčného plicního karcinomu. *Klin Farmakol Farm*, 2015, 29, s. 16–21.
3 **Petruželka, L. – Špaček, J. – Křížová, L.**: Budoucnost léčby karcinomu plic. *Klinic Onkol*, 2021, suppl., v tisku.
4 **Wang, K. – Chen, R. – Feng, Z., et al.**: Identification of differentially expressed genes in non-small cell lung cancer. *Aging*, 2019, 11, s. 11170–11185.
5 **Davies, K. D. – Le, A. T. – Theodoro, M. F., et al.**: Identifying and targeting ROS1 gene fusions in NSLCL. *Clin Cancer Res*, 2013, 18, s. 4570–4579.
6 **Aisner, D. L. – Nguyen, T. T. – Paskulin, D. D., et al.**: ROS1 and ALK fusions in colorectal cancer, with evidence of intratumoral heterogeneity for molecular drivers. *Molecular Cancer Research*, 2013, 12, s. 111–118.
7 **Lassen, U.**: Entrectinib for ROS1 fusion-positive NSCLC and NTRK fusion-positive solid tumours. *Lancet Oncol*, 2020, 21, s. 193–194.
8 SÚKL. Příloha i souhrn údajů o přípravku Rozlytrek. Publikováno online, 2018, s. 1–33.
9 **Doebele, R. C. – Drilon, A. – Paz-Ares, L., et al.**: 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.
10 **Drilon, A. – Siena, S. – Dziadziuszko, R., et al.**: Entrectinib in ROS1 fusion-positive non-small-cell lung cancer: integrated analysis of three phase 1–2 trials. *Lancet Oncol*, 2020, 21, s. 261–270.
11 **Facchinetti, F. – Friboulet, L.**: Profile of entrectinib and its potential in the treatment of ROS1-positive NSCLC: Evidence to date. *Lung Cancer Targets Ther*, 2019, 10, s. 87–94.

Léčba osimertinibem u nemalobuněčného karcinomu plic – kazuistika

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1 **Yu, H. A. – Arcila, M. E. – Rekhtman, N., et al.**: Analysis of tumor specimens at the time of acquired resistance to EGFR-TKI therapy in 155 patients with EGFR-mutant lung cancers. *Clin Cancer Res*, 2013, 19, s. 2240–2247.
2 **Mok, T. S. – Wu, Y. L. – Ahn, M. J., et al.**: Osimertinib or platinum–pemetrexed in EGFR T790M–positive lung cancer. *N Engl J Med*, 2017, 376, s. 629–640.
3 Souhrn údajů o přípravku osimertinib, www.sukl.cz.

Brigatinib

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1 **Elsayed, M. – Christopoulos, P.**: Therapeutic sequencing in ALK+ NSCLC. *Pharmaceuticals*, 2021, 14, s. 80, https://doi.org/10.3390/ph14020080.
2 **Hoy, S. M.**: Brigatinib: a review in ALK-inhibitor naïve advanced ALK-positive NSCLC. *Drugs*, 2. 2. 2021, doi: 10.1007/s40265-020-01449-y.
3 **Camidge D. R. – Kim, H. R. – Ahn, M. J., et al.**: Brigatinib versus crizotinib in advanced ALK inhibitor-naive ALK-positive non-small cell lung cancer: second interim analysis of the phase III ALTA-1L trial. *J Clin Oncol*, 2020, 38, s. 3592–3603.
4 ALUNBRIG (brigatinib) Extended Progression-Free Survival (PFS) Two-fold vs crizotinib (ITT Population). Dostupné z: https://www.alunbrig.com/hcp/efficacy/systemic-efficacy/, vyhledáno 2. 3. 2021.
5 Souhrn údajů o přípravku Alunbrig 2020. Dostupné z: https://www.ema.europa.eu/en/documents/product-information/alunbrig-epar-product-information_en.pdf, vyhledáno 9. 3. 2021.
6 **Zhang, S. – Anjum, R. – Squillace, R., et al.**: The potent ALK inhibitor brigatinib (AP26113) overcomes mechanisms of resistance to first- and second-generation ALK inhibitors in preclinical models. *Clin Cancer Res*, 2016, 22, s. 5527–5538.
7 **Camidge, D. R. – Doebele, R. C.**: Treating ALK-positive lung cancer: early successes and future challenges. *Nat Rev Clin Oncol*, 2012, 9, s. 268–277.
8 **Gainor, J. F. – Dardaei, L. – Yoda, S., et al.**: Molecular mechanisms of resistance to first- and second-generation ALK inhibitors in ALK-rearranged lung cancer. *Cancer Discovery*, 2016, 6, s. 1118–1133.

Novinky v léčbě melanomu

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

1 **Robert, C. – Grob, J. J. – Stroyakovskiy, D., et al.**: Five-year outcomes with dabrafenib plus trametinib in metastatic melanoma. *N Engl J Med*, 2019, 381, s. 626–636.
2 **Ascierto, P. A. – McArthur, G. A. – Dréno, B., et al.**: Cobimetinib combined with vemurafenib in advanced BRAF(V600)-mutant melanoma (coBRIM): updated efficacy results from a randomised, double-blind, phase 3 trial. *Lancet Oncol*, 2016, 17, s. 1248–1260.
3 **Dummer, R. – Ascierto, P. A. – Gogas, H. J., et al.**: Encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with BRAF-mutant melanoma (COLUMBUS): a multicentre, open-label, randomised phase 3 trial. *Lancet Oncol*, 2018, 19, s. 603–615.
4 **Ascierto, P. A. – Dummer, R. – Gogas, H. J., et al.**: Update on tolerability and overall survival in COLUMBUS: landmark analysis of a randomised phase 3 trial of encorafenib plus binimetinib vs vemurafenib or encorafenib in patients with BRAF V600-mutant melanoma. *Eur J Cancer*, 2020, 126, s. 33–44.
5 **Ascierto, P. A. – Del Vecchio, M. – Robert, C., et al.**: Ipilimumab 10 mg/kg versus ipilimumab 3 mg/kg in patients with unresectable or metastatic melanoma: a randomised, double-blind, multicentre, phase 3 trial. *Lancet Oncol*, 2017, 18, s. 611–622.
6 **Carreau, N. A. – Pavlick, A. C.**: Nivolumab and ipilimumab: immunotherapy for treatment of malignant melanoma. *Future Oncol*, 2019, 15, s. 349–358.
7 **Schachter, J. – Ribas, A. – Long, G. V., et al.**: Pembrolizumab versus ipilimumab for advanced melanoma: final overall survival results of a multicentre, randomised, open-label phase 3 study (KEYNOTE-006). *Lancet*, 2017, 390, s. 1853–1862.
8 **Wolchok, J. D. – Chiarion-Sileni, V. – Gonzalez, R., et al.**: Overall survival with combined nivolumab and ipilimumab in advanced melanoma. *N Engl J Med*, 2017, 377, s. 1345–1356.
9 **Larkin, J. – Chiarion-Sileni, V. – Gonzalez, R., et al.**: Five-year survival with combined nivolumab and ipilimumab in advanced melanoma. *N Engl J Med*, 2019, 381, s. 1535–1546.
10 **Eggermont, A. M. – Chiarion-Sileni, V. – Grob, J. J., et al.**: Prolonged survival in stage III melanoma with ipilimumab adjuvant therapy. *N Engl J Med*, 2016, 375, s. 1845–1855.
11 **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.
12 **Ascierto, P. A. – Del Vecchio, 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 multicentre, double-blind, randomised, controlled, phase 3 trial. *Lancet Oncol*, 2020, 21, s. 1465–1477.
13 **Eggermont, A. M. M. – Blank, C. U. – Mandala, 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.

Kompletní remise generalizovaného karcinomu gastroezofageální junkce při léčbě kombinací paklitaxelu a ramucirumabu – kazuistika

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1 **Al-Batran, S. E. – Homann, N. – Pauligk, C., et al.**: Effect of neoadjuvant chemotherapy followed by surgical resection on survival in patients with limited metastatic gastricor gastroesophageal junction cancer: the AIO-FLOT3 trial. *JAMA Oncol*, 2017, 3, s. 1237–1244.
2 **Wilke, H. – Muro, K. – Van Cutsem, E., et al.**: RAINBOW Study Group: Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. *Lancet Oncol*, 2014, 15, s. 1224–1235.

Imunoterapie v léčbě dMMR/MSI-H nádorových onemocnění – přehledový článek

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1 **Robert, C.**: A decade of immune-checkpoint inhibitors in cancer therapy. *Nat Commun*, 2020, 11, 3801, https://doi.org/10.1038/s41467-020-17670-y.
2 **Li, G. M.**: Mechanisms and functions of DNA mismatch repair. *Cell Res*, 2008, 18, s. 85–98.
3 **Toor, S. M. – Sasidharan Nair, V. – Murshed, K., et al.**: Tumor-infiltrating lymphoid cells in colorectal cancer patients with varying disease stages and microsatellite instability-high/stable tumors. *Vaccines*, 2021, 9, s. 64.
4 **Bonneville, R. – Krook, M. A. – Kautto, E. A., et al.**: Landscape of microsatellite instability across 39 cancer types. *JCO Precis Oncol*, 2017, 2017:PO.17.00073, doi: 10.1200/PO.17.00073.
5 **Overman, M. J. – Morse, M.**: Tissue-agnostic cancer therapy: DNA mismatch repair deficiency, tumor mutational burden, and response to immune checkpoint blockade in solid tumors. Dostupné z: https://www.uptodate.com/contents/tissue-agnostic-cancer-therapy-dna-mismatch-repair-deficiency-tumor-mutational-burden-and-response-to-immune-checkpoint-blockade-in-solid-tumors?search=MSI&source=search_result&selectedTitle=2~58&usage_type=default&display_rank=2#H3859445625, vyhledáno 16. 3. 2021.
6 **André, T. – Shiu, K. K. – Kim, T. W., et al.**; KEYNOTE-177 Investigators: Pembrolizumab in microsatellite-instability-high advanced colorectal cancer. *N Engl J Med*, 2020, 383, s. 2207–2218.
7 **Le, D. T. – Uram, J. N. – Wang, H., et al.**: PD-1 blockade in tumors with mismatch-repair deficiency. *N Engl J Med*, 2015, 372, s. 2509–2520.
8 **Overman, M. J. – Lonardi, S. – Wong, K. Y. M., et al.**: Nivolumab (NIVO) + low-dose ipilimumab (IPI) in previously treated patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Long-term follow-up. *J Clin Oncol*, 2019, 37, 4, suppl., s. 635–635.
9 **Overman, M. J. – McDermott, R. – Leach, J. L., et al.**: Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): an open-label, multicentre, phase 2 study. *Lancet Oncol*, 2017, 18, s. 1182–1191.
10 **O'Malley, D. – Marabelle, A. – De Jesus-Acosta, A., et al.**: Pembrolizumab in patients with MSI-H advanced endometrial cancer from the KEYNOTE-158 study. *Ann Oncol*, 2019, 30, suppl. 5, abstrakt 1044P, s. V425–V426.
11 **Marabelle, A. – Le, D. T. – Ascierto, P. A., et al.**: Efficacy of pembrolizumab in patients with noncolorectal high microsatellite instability/mismatch repair-deficient cancer: results from the phase II KEYNOTE-158 study. *J Clin Oncol*, 2020, 38, s. 1–10.

Aktuality v léčbě hepatocelulárního karcinomu

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1 **Farazi, P. A. – DePinho, R. A.**: Hepatocellular carcinoma pathogenesis: from genes to environment. *Nat Rev Cancer*, 2006, 6, s. 674–687.
2 **Villanueva, A. – Newel, P. – Chiang, D. Y., et al.**: Genomics and signaling pathways in hepatocellular carcinoma. *Semin Liver Dis*, 2007, 27, s. 55–76.
3 **Gherardi, E. – Birchmeier, W. – Birchmeier, C., et al.**: Targeting MET in cancer: rationale and progress. *Nat Rev Cancer*, 2012, 12, s. 89–103.
4 **Goyal, L. – Muzumdar, M. D. – Zhu, A. X.**: Targeting the HGF/c-MET pathway in hepatocellular carcinoma. *Clin Cancer Res*, 2013, 19, s. 2310–2318.
5 **Lee, H. J. – Jeng, Y. M. – Chen, Y. L., et al.**: Gas6/Axl pathway promotes tumor invasio through the transcriptional activation of Slug in hepatocellular carcinoma. *Carcinogenesis*, 2014, 35, s. 769–775.
6 **Zhou, L. – Liu, X. D. – Sun, M., et al.**: Targeting MET and AXL over comes resistence to sunitinib therapy in renal cell carcinoma. *Oncogene*, 2016, 35, s. 2687–2697.
7 **Carmeliet, P. – Jain, R. K.**: Molecular mechanisms and clinical application so angiogenesis. *Nature*, 2011, 473, s. 298–307.
8 **Schoenleber, S. J. – Kurtz, D. M. – Talwalkar, J. A., et al.**: Prognostic role of vascular endothelial growth factor in hepatocellular carcinoma: systematic review and meta-analysis. *Br J Cancer*, 2009, 100, s. 1385–1392
9 **Chen, D. S. – Irving, B. A. – Hodi, F. S.**: Molecular pathways: next-generation immunotherapy – inhibiting programmed death-ligand 1 and programmed death-1. *Clin Cancer Res*, 2012,18, 6580.
10 **Ott, P. A. – Hodi, F. S. – Buchbinder, E. I.**: Inhibition of immune checkpoints and vascular endothelial growth factor as combination therapy for metastatic melanoma: an overview of rationale, preclinical evidence, and initial clinical data. *Front Oncol*, 2015, 5, s. 202.
11 **Manegold, C. –Dingemans, A.-M. C. – Gray, J. E., et al.**: The potential of combined immunotherapy and antiangiogenesis for the synergistic treatment of advanced NSCLC. *J Thorac Oncol*, 2017, 12, s. 194–207.
12 **Finn, R. S. – Qin, S. – Ikeda, M., et al.**: Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. *N Engl J Med*, 2020, 382, s. 1894–1905.
13 **Finn, R. S. – Qin, S. – Ikeda, M., et al.**: IMbrave150: Updated overall survival (OS) data from a global, randomized, open-label phase III study of atezolizumab (atezo) + bevacizumab (bev) versus sorafenib (sor) in patients (pts) with un resectable hepatocellular carcinoma (HCC). *J Clin Oncol*, 2021, 39, s. 267–267.
14 **Cheng, A.-L. – Qin, S. – Ikeda, M., et al.**: IMbrave150: efficacy and safety results from a ph III study evaluatin gatezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) as first treatment (tx) for patients (pts) with unresectable hepatocellular carcinoma (HCC). *Ann Oncol*, 2019, 30, suppl. 9, https://doi.org/10.1093/annonc/mdz446.002.
15 **Galle, P. R. – Finn, R. S. – Qin, S., et al.**: Patient-reported outcomes (PROs) from the phase III IMbrave150 trial of atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) as first-line treatment (tx) for patients (pts) with unresectable hepatocellular carcinoma (HCC). *J Clin Oncol*, 2020, 38, suppl. 4, abstrakt 476.
16 **Yau, T. – Zagonel, V. – Santoro, A.**: Nivolumab (NIVO) + ipilimumab (IPI) + cabozantinib (CABO) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from Check Mate 040. *J Clin Oncol*, 2020, 38, suppl. 4, abstrakt 478.
17 **El-Khoueiry, A. B. – Kim, R. D. – Harris, W. P., et al.**: Phase Ib study of regorafenib (REG) plus pembrolizumab (PEMBRO) for first-line treatment of advanced hepatocellular carcinoma (HCC). *J Clin Oncol*, 2020, 38, suppl. 4, abstrakt 564.
18 **Ikeda, M. – Sung, M. W. – Kudo, M., et al.**: A phase 1b trial of lenvatinib (LEN) plus pembrolizumab (PEM) in patients (pts) with unresectable hepatocellular carcinoma (uHCC). *J Clin Oncol*, 2018, 36, suppl., abstrakt 4076.
19 **Kudo, M.**: Combination cancer immunotherapy in hepatocellular carcinoma. *Liver Cancer*, 2018, 7, s. 20–27.
20 **El-Khoueiry, A. B. – Yau, T. – Kang, Y. K., et al.**: Nivolumab (NIVO) plus ipilimumab (IPI) combination therapy in patients (Pts) with advanced hepatocellular carcinoma (aHCC): Long-term results from Check Mate 040. *Clin Oncol*, 2021, 39, suppl. 3, abstrakt 269.

Nové trendy v biologické léčbě mnohočetného myelomu – rok 2020

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1 **Nandakumar, B. – Kapoor, P. – Binder, M., et al.**: Continued improvement in survival of patients with newly diagnosed multiple myeloma (MM). ASH 2020, abstrakt 2280.
2 **Tai, Y. T. – Anderson, K. C.**: Targeting B-cell maturation antigen in multiple myeloma. *Immunotherapy*, 2015, 7, s. 1187–1199.
3 **Alley, S. C. – Okeley, N. M. – Senter, P. D.**: Antibody-drug conjugates: targeted drug delivery for cancer. *Curr Opin Chem Biol*, 2010, 14, s. 529–537.
4 **Trudel, S. – Lendvai, N. – Popat, R., et al.**: Targeting B-cell maturation antigen with GSK2857916 antibody-drug conjugate in relapsed or refractory multiple myeloma (BMA117159): a dose escalation and expansit phase 1 trial. *Lancet Oncol*, 2018, 19, s. 1641–1653.
5 **Tai, Y. T. – Mayes, P. A. – Acharya, C., et al.**: Novel anti-B-cell maturation antigen antibody-drug conjugate (GSK2857916) selectively induce skilling of multiple myeloma. *Blood*, 2014, 123, s. 3128–3138.
6 **Trudel, S. – Lendvai, N. – Popat, R., et al.**: Targeting B-cell maturation antigen with GSK2857916 antibody-drug conjugate in relapsed or refractory multiple myeloma (BMA117159): a dose escalation and expansionphase 1 trial. *Lancet Oncol*, 2018, 19, s. 1641–1653.
7 **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.
8 **Nooka, A. – Stockerl-Goldstein, K. – Quach, H., et al.**: DREAMM-6: Safety and tolerability of belantamab mafodotin in combination with bortezomib/dexamethasone in relapsed/refractory multiple myeloma (RRMM). *J Clin Oncol*, 2020, 38, abstrakt 8502.
9 **Shah, N. N. – Krishnan, A. Y. – Shah, N. D., et al.**: Preliminary results of a phase 1 dose escalation study of the first-in-class anti-CD74 antibody drug conjugate (ADC), STRO-001, in patients with advanced B-cell malignancies. *Blood*, 2019, 134, abstrakt 5329.
10 **Lee, H. C. – Raje, N. S. – Landgren, O., et al.**: Phase 1 study of the anti-BCMA antibody-drug conjugate AMG 224 in patients with relapsed/refractory multiple myeloma. *Leukemia*, 2021, 35, s. 255–258.
11 **Jagannath, S. – Heffner, L. T. Jr. – Ailawadhi, S., et al.**: Indatuximab ravtansine (BT062) monotherapy in patients with relapsed and/or refractory multiple myeloma. *Clin Lymphoma Myeloma Leuk*, 2019, 19, s. 372–380.
12 **Ellerman, D.**: Bispecific T-cell engagers: toward sunder standing variables influencing the in vitro potency and tumor selectivity and their modulation to enhance thein efficacy and safety. *Methods*, 2019, 154, s. 102–117.
13 **Saxena, A. – Wu, D.**: Advances in therapeutic engineering – modulation of IgG-associated effect or functions and serum half-life. *Front Immunol*, 2016, 7, s. 580.
14 **Topp, M. S. – Duell, J. – Zugmaier, G., et al.**: Anti-B-cell maturation antigen BiTEmolecule AMG 420 induces responses in multiple myeloma. *J Clin Oncol*, 2020, 38, s. 775–783.
15 **Cho, S.-F. – Lin, L. – Xing, L., et al.**: AMG 701 potently induces anti-multiple myeloma (MM) functions of T cells and IMiDs further enhance its efficacy to prevent MM relapse in vivo. *Blood*, 2019, 134,

suppl. 1.
16 **Usmani, S. – Mateos, M.-V. – Nahi, H., et al.**: Phase I study of teclistamab, a humanized B-cell maturation antigen (BCMA) x CD3 bispecific antibody, in relapsed/refractory multiple myeloma (R/R MM). J Clin Oncol, 2020, 38, s. 100–100.
17 **Costa, L. J. – Wong, S. W. – Bermúdez, A., et al.**: First clinical study of the B-cell maturation antigen (BCMA) 2+1 T cell engager (TCE) CC-93269 in patients (pts) with relapsed/refractory multiple myeloma (RRMM): interim results of a phase 1 multicenter trial. *Blood*, 2019, 134, s. 143.
18 **Madduri, D. – Berdeja, J. G. – Usmani, S. Z.**: 177 CARTITUDE-1: Phase 1b/2 study of ciltacabtagene autoleucel, a B-cell maturation antigen–directed chimeric antigen receptor T cell therapy, in relapsed/refractory multiple myeloma. ASH 2020, dostupné z: https://ash.confex.com/ash/2020/webprogram/Paper136307.html, vyhledáno 29. 1. 2021.
19 **Wu, L. – Seung, E. – Xu, L., et al.**: Trispecific antibodies enhance the therapeutic efficacy of tumor-directed T cells through T cell receptor co-stimulation. *Nat Can*, 2020, 1, s. 86–98.
20 **Hammill, J. A. – Van Seggelen, H. – Helsen, C. W., et al.**: Designed ankyrin repeat proteins are effective targeting elements for chimeric antigen receptors. *J Immunother Cancer*, 2015, 3, s. 55.
21 **Binz, H. K. – Bakker, T. R. – Phillips, D. J., et al.**: Design and characterization of MP0250, a tri-specific anti-HGF/anti-VEGF DARPin drug candidate. *MAbs*, 2017, 9, s. 1262–1269.
22 **Kim, C., et al.**, online přednáška na 62nd ASH Annual Meeting and Exposition, 5. 12. 2020, abstrakt 2566.

Polatuzumab vedotin v léčbě difuzního velkobuněčného B lymfomu

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1 National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) B-cell lymphomas, version 7.2017 (2017). Dostupné z: www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf, vyhledáno 15. 3. 2021.
2 **Avivi, I. – Canals, C. – Vernant, J. P., et al.**: Matched unrelated donor allogeneic transplantation provides comparable long-term outcome to HLA-identical sibling transplantation in relapsed diffuse large B-cell lymphoma. *Bone Marrow Transplant*, 2014, 49, s. 671–678.
3 **Avivi, I. – Boumendil, A. – Finnel, H., et al.**: Autologous stem cell transplantation for primary mediastinal B-cell lymphoma in the rituximab era: a retrospective study by the EBMT Lymphoma Working Party. American Society of Hematology (ASH) 56th Annual Meeting and Exposition. San Francisco, CA, USA, 6.–9. 12. 2014, abstrakt 1195.
4 **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.
5 **Janikova, A. – Michalka, J. – Bortlicek, Z., et al.**: The interval between progression and therapy initiationis the key prognostic parameter in relapsing diffuse large B-cell lymphoma. Analysis from the Czech Lymphoma Study Group Database (NIHIL). *Ann Hematol*, 2020, 99, s. 1583–1594.
6 **Dornan, D. – Bennett, F. – Chen, Y., et al.**: Therapeutic potential of an anti-CD79b antibody-drug conjugate, anti-CD79b-vc-MMAE, for the treatment of Non-Hodgkin lymphoma. *Blood*, 2009, 114, s. 2721–2729.
7 **Palanca-Wessels, M. C. A. – Czuczman, M. – Salles, G., et al.**: Safety and activity of the anti-CD79B antibody-drug conjugate polatuzumab vedotin in relapsed or refractory B-cell non-Hodgkin lymphoma and chronic lymphocytic leukemia. A phase 1 study. *Lancet Oncol*, 2015, 16, s. 704–715.
8 **Morschhauser, F. – Flinn, I. W. – Advani, R., et al.**: Polatuzumab vedotin or pinatuzumab vedotin plus rituximab in patients with relapsed or refraktory non-Hodgkin lymphoma: final results from a phase 2 randomised study (ROMULUS). *Lancet Haematol*, 2019, 6, s. e254–e265.
9 **Gritti, G. – Marlton, P. – Phillips, T. J., et al.**: Polatuzumab vedotin plus venetoclax with rituximab in relapsed/refractory diffuse large B-cell lymphoma: primary efficacy analysis of a phase Ib/II study. 62-nd ASH Annual Meeting, 2020, abstrakt 599.
10 **Sehn, L. H. – Herrera, A. F. – Flowers, C. R., et al.**: Polatuzumab vedotin in relapsed or refractory diffuse large B-cell lymphoma. *J Clin Oncol*, 2020, 38, s. 155–165.
11 **Sehn, L. H. – Hertzberg, M. – Opat, S., et al.**: Polatuzumab vedotin plus bendamustin and rituximab in relapsed/refractory diffuse large B-cell lymphoma: updated results of a phase Ib/II randomized study and preliminary results of a single-arm extension. 62-nd ASH Annual meeting, 2020, abstrakt 3020.
12 **Tilly, H. – Morschhauser, F. – Bartlett, N. L., et al.**: Polatuzumab vedotin in combination with immunochemotherapy in patients with previously untreated diffuse large B-cell lymphoma: an open-label, non-randomised, phase 1b-2 study. *Lancet Oncol*, 2019, 20, s. 998–1010.
13 **Segman, Y. – Ribakovsky, E. – Avigdor, A., et al.**: Outcome of relapsed/refractory diffuse large B-cell lymphoma patients treated with polatuzumab vedotin-based therapy: real-life experience. *Leuk Lymphoma*, 2020, DOI: 10.1080/10428194.2020.1824069.

Hereditární hemoragická teleangiektazie neboli Oslerův-Renduův-Weberův syndrom – klinický obraz a léčba

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1 **Faughnan, M. E. – Palda, V. A. – Garcia-Tsao, G., et al.** for HHT Foundation International – Guidelines Working Group: International guidelines for the diagnosis and management of hereditary haemorrhagic telangiectasia. *J Med Genet*, 2011, 48, s. 73–87.
2 **Faughnan, M. E. – Mager, J. J. – Hetts, S. W., et al.**: Second international guidelines for the diagnosis and management of hereditary hemorrhagic telangiectasia. *Ann Intern Med*, 2020, 173, s. 989–1001.
3 **Kritharis, A. – Al-Samkari, H. – Kuter, D. J.**: Hereditary hemorrhagic telangiectasia: diagnosis and management from the hematologist's perspective. *Haematologica*, 2018, 103, s. 1433–1443.
4 **Ferry, A. M. – Wright, A. E. – Baillargeon, G., et al.**: Epidemiology and trends of hereditary hemorrhagic telangiectasia in the United States. *Am J Rhinol Allergy*, 2020, 34, s. 230–237.
5 **Ernest, J. – Poláčková, V. K. – Charvát, F.**: Oční komplikace po embolizaci v povodí arteria karotis interna. Popis případu. *Cesk Slov Oftalmol*, 2008, 64, s. 202–206.
6 **Takác, M. – Koval, S. – Klimcík, J.**: Hereditární hemoragická teleangiektasie a vznik artriovenózní fistuly po 24 letech. *Vnitř Lék*,1997, 43, s. 599–601.
7 **Krahulec, B. – Jergus, P. – Bátovský, M., et al.**: Telangiektazie v žaludku u pacienta s Oslerovou chorobou. *Bratisl Lek Listy*, 1988, 89, s. 11–13.
8 **Šťastný, B. – Kroslák, M.**: Chirurgická léčba epistaxe u pacienta s morbus Osler-Rendu-Weber. *Česk Otolaryngol*, 1981, 30, s. 53–56.
9 **Izák, M.**: Sturge-Weber-Krabbe syndrom. *Česk Oftalmol*, 1971, 27, s. 267–272.
10 **Chvojka, J.**: Zástava epistaxe u pacienta s morbus Osler-Rendu-Weber. *Česk Otolaryngol*, 1967, 16, s. 211–214.
11 **Orizaga-Y-Quiroga, T. L. – Villarreal-Martínez, A., et al.**: Osler-Weber-Rendu syndrome in relation to dermatology. *Actas Dermosifiliogr*, 2019, 110, s. 526–532.
12 **Hashimoto, Y. – Yokoyama, K. – Kumagai, H., et al.**: Juvenile polyposis syndrome-hereditary hemorrhagic telangiectasia associated with a SMAD4 mutation in a girl. *Clin J Gastroenterol*, 2020, 13, s. 1096–1101.
13 **Snellings, D. A. – Gallione, C. J. – Clark, D. S., et al.**: Somatic mutations in vascular malformations of hereditary hemorrhagic telangiectasia result in bi-allelic loss of ENG or ACVRL1. *Am J Hum Genet*, 2019, 105, s. 894–906.
14 **Shovlin, C. L. – Guttmacher, A. E. – Buscarini, E., et al.**: Diagnostic criteria for hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). *Am J Med Genet*, 2000, 91, s. 66–67.
15 **Brinjikji, W. – Iyer, V. N. – Yamaki, V., et al.**: Neurovascular manifestations of hereditary hemorrhagic telangiectasia: a consecutive series of 376 patients during 15 years. *Am J Neuroradiol*, 2016, 37, s. 1479–1486.
16 **Chowdhury, F. N. – Chandrarathne, G. S. – Masilamani, K. D., et al.**: Between strokes and hereditary hemorrhagic telangiectasia: a population-based study. *Can J Neurol Sci*, 2019, 46, s. 44–50.
17 **Dupuis-Girod, S. – Cottin, V. – Shovlin, C. L.**: The lung in hereditary hemorrhagic telangiectasia. *Respiration*, 2017, 94, s. 315–330.
18 **Yokokawa, T. – Sugimoto, K. – Kimishima, Y., e al.**: Pulmonary hypertension and hereditary hemorrhagic telangiectasia related to an ACVRL1 mutation. *Intern Med*, 2020, 59, s. 221–227.
19 **Tellapuri, S. – Park, H. S. – Kalva, S. P.**: Pulmonary arteriovenous malformations. *Int J Cardiovasc Imaging*, 2019, 35, s. 1421–1428.
20 **Krynytska, I. – Marushchak, M. – Mikolenko, A., et al.**: Differential diagnosis of hepatopulmonary syndrome (HPS): Portopulmonary hypertension (PPH) and hereditary hemorrhagic telangiectasia (HHT). *Bosn J Basic Med Sci*, 2017, 17, s. 276–285.
21 **Harder, E. M. – Fares, W. H.**: Hospitalizations with hereditary hemorrhagic telangiectasia and pulmonary hypertension in the United States from 2000 to 2014. *Respir Med*, 2019, 147, s. 26–30.
22 **Olsen, L. B. – Kjeldsen, A. D. – Poulsen, M. K., et al.**: High output cardiac failure in 3 patients with hereditary hemorrhagic telangiectasia and hepatic vascular malformations, evaluation of treatment. *Orphanet J Rare Dis*, 2020, 15, s. 334.
23 **Wu, P. R. – Horwith, A. – Mai, S., et al.**: High-output cardiac failure due to hereditary hemorrhagic telangiectasia: a case of an extra-cardiac left to right shunt. *Int J Angiol*, 2017, 26, s. 125–129.
24 **Jackson, S. B. – Villano, N. P. – Benhammou, J. N., et al.**: Gastrointestinal manifestations of hereditary hemorrhagic telangiectasia (HHT): a systematic review of the literature. *Dig Dis Sci*, 2017, 62, s. 2623–2630.
25 **Tortora, A. – Riccioni, M. E. – Gaetani, E., et al.**: Rendu-Osler-Weber disease: a gastroenterologist's perspective. *Orphanet J Rare Dis*, 2019, 14, s. 130.
26 **Kim, Y. H. – Kim, M. J. – Choe, S. W., et al.**: Selective effects of oral antiangiogenic tyrosine kinase inhibitors on an animal model of hereditary hemorrhagic telangiectasia. *J Thromb Haemost*, 2017, 15, s. 1095–1102.
27 **Singh, K. – Zubair, A. – Prindle, A., et al.**: Diagnostic yield of capsule endoscopy for small bowel arteriovenous malformations in patients with hereditary hemorrhagic telangiectasia: a systematic review and meta-analysis. *Endosc Int Open*, 2019, 7, s. E282–E289.
28 **Welle, C. L. – Welch, B. T. – Brinjikji, W., et al.**: Abdominal manifestations of hereditary hemorrhagic telangiectasia: a series of 333 patients over 15 years. *Abdom Radiol*, 2019, 44, s. 2384–2391.
29 **Harwin, J. – Sugi, M. D. – Hetts, S. W., et al.**: The role of liver imaging in hereditary hemorrhagic telangiectasia. *J Clin Med*, 2020, 9, s. 3750.
30 **Song, X. – Chen, H. Q. – Chen, Y. X., et al.**: Individualized management of hepatic diseases in hereditary hemorrhagic telangiectasia. *Am Surg*, 2011, 77, s. 281–285.
31 **Sabbà, C. – Pompili, M.**: Review article: the hepatic manifestations of hereditary haemorrhagic telangiectasia. *Aliment Pharmacol Ther*, 2008, 28, s. 523–533.
32 **Garcia-Tsao, G.**: Liver involvement in hereditary hemorrhagic telangiectasia. *J Hepatol*, 2007, 46, s. 499–507.
33 **Felli, E. – Addeo, P. – Faitot, F., et al.**: Liver transplantation for hereditary hemorrhagic telangiectasia: a systematic review. *HPB*, 2017, 19, s. 567–572.
34 **Iyer, V. N. – Saberi, B. – Heimbach, J. K., et al.**: Liver transplantation trends and outcomes for hereditary hemorrhagic telangiectasia in the United States. *Transplantation*, 2019, 103, s. 1418–1424.
35 **Dumortier, J. – Dupuis-Girod, S. – Valette, P. J., et al.**: Recurrence of hereditary hemorrhagic telangiectasia after liver transplantation: clinical implications and physiopathological insights. *Hepatology*, 2019, 69, s. 2232–2240.
36 **Ejiri, K. – Akagi, S. – Nakamura, K., et al.**: Liver transplantation in a patient with hereditary haemorrhagic telangiectasia and pulmonary hypertension. *Pulm Circ*, 2019, 9, 2045894019896677.

37 **Scelzo, C. – Greco, S. – Bonanni, L., et al.**: The role of liver transplantation in the treatment of hereditary hemorrhagic telangiectasia: a short literature review. *Transplant Proc*, 2007, 39, s. 2045–2047.

38 **Lee, M. – Sze, D. Y. – Bonham, C. A., et al.**: Hepatic arteriovenous malformations from hereditary hemorrhagic telangiectasia: treatment with liver transplantation. *Dig Dis Sci*, 2010, 55, s. 3059–3062.

39 **Lerut, J. – Orlando, G. – Adam, R., et al.**: Liver transplantation for hereditary hemorrhagic telangiectasia: report of the European liver transplant registry. *Ann Surg*, 2006, 244, s. 854–864.

40 **Geisthoff, U. W. – Seyfert, U. T. – Kubler, M., et al.**: Treatment of epistaxis in HHT with tranexamic acid – double blind placebo controlled cross over phase IIIB study. *Thromb Res*, 2014, 134, s. 565–571.

41 **Tunkel, D. E. – Anne, S. – Payne, S. C., et al.**: Clinical Practice Guideline: Nosebleed (Epistaxis). *Otolaryngol Head Neck Surg*, 2020, 162, s. S1–S38.

42 **Robard, L. – Michel, J. – Prulière Escabasse, V., et al.**: Guidelines of the French Society of Otorhinolaryngology (SFORL) (short version). Specific treatment of epistaxis in Rendu-Osler-Weber disease. *Eur Ann Otorhinolaryngol Head Neck Dis*, 2017, 134, s. 37–41.

43 **Lupa, M. D. – Wise, S. K.**: Comprehensive management of hereditary hemorrhagic telangiectasia. *Curr Opin Otolaryngol Head Neck Surg*, 2017, 25, s. 64–68.

44 **Kühnel, T. – Wirsching, K. – Wohlgemuth, W., et al.**: Hereditary hemorrhagic telangiectasia. *Otolaryngol Clin North Am*, 2018, 51, s. 237–254.

45 **Whitehead, K. J. – Sautter, N. B. – McWilliams, J. P., et al.**: Effect of topical intranasal therapy on epistaxis frequency in patients with hereditary hemorrhagic telangiectasia: a randomized clinical trial. *JAMA*, 2016, 316, s. 943–951.

46 **Khoueir, N. – Borsik, M. – Camous, D., et al.**: Injection of bevacizumab and cyanoacrylate glue for hereditary hemorrhagic telangiectasia. *Laryngoscope*, 2019, 129, s. 2210–2215.

47 **Halderman, A. A. – Ryan, M. W. – Clark, C., et al.**: Medical treatment of epistaxis in hereditary hemorrhagic telangiectasia: an evidence-based review. *Int Forum Allergy Rhinol*, 2018, 8, s. 713–728.

48 **Fang, J. – Chen, X. – Zhu, B., et al.**: Thalidomide for epistaxis in patients with hereditary hemorrhagic telangiectasia: a preliminary study. *Otolaryngol Head Neck Surg*, 2017, 157, s. 217–221.

49 **Houghton, K. D. – Umar, B. – Schairer, J.**: Successful treatment of hereditary hemorrhagic telangiectasia with octreotide. *ACG Case Rep J*, 2019, 6, s. e00088.

50 **Kroon, S. – Snijder, R. J. – Mager, J. J., et al.**: Octreotide for gastrointestinal bleeding in hereditary hemorrhagic telangiectasia: A prospective case series. *Am J Hematol*, 2019, 94, s. E247–E249.

51 **Becq, A. – Rahmi, G. – Perrod, G., et al.**: Hemorrhagic angiodysplasia of the digestive tract: pathogenesis, diagnosis, and management. *Gastrointest Endosc*, 2017, 86, s. 792–806.

52 **Lee, B. L. – Turner, J. – Hurley, J., et al.**: Two for the price of one: a dual treatment benefit of long-acting octreotide in occult bleeding and diuretic intractable ascites. *Frontline Gastroenterol*, 2011, 2, s. 226–229.

53 **Jeanneret, S. – Regazzoni, L. – Favrat, B.**: Rendu-Osler disease: treatment with oestrogen/progestagen versus octreotide. *BMJ Case Rep*, 2011, bcr1120103534.

54 **Woodall, M. N. – Nakaji, P. – Spetzler, R. F.**: Benefits of treating arteriovenous malformations in hereditary hemorrhagic telangiectasia: a retrospective analysis of 14 patients. *World Neurosurg X*, 2019, 3, 100029.

55 **Ratnani, R. – Sutphin, P. D. – Koshti, V., et al.**: Retrospective comparison of pulmonary arteriovenous malformation embolization with the polytetrafluoroethylene-covered nitinol microvascular plug, AMPLATZER plug, and coils in patients with hereditary hemorrhagic telangiectasia. *J Vasc Interv Radiol*, 2019, 30, s. 1089–1097.

56 **Lacout, A. – Marcy, P. Y. – El Hajjam, M., et al.**: Tranexamic acid and bevacizumab in hereditary hemorrhagic telangiectasia patients presenting with epistaxis. *Cutis*, 2013, 91, s. 173–174.

57 **Albiñana, V. – Bernabeu-Herrero, M. E., et al.**: Estrogen therapy for hereditary haemorrhagic telangiectasia (HHT): Effects of raloxifene, on endoglin and ALK1 expression in endothelial cells. *Thromb Haemost*, 2010, 103, s. 525–534.

58 **Yaniv, E. – Preis, M. – Hadar, T., et al.**: Antiestrogen therapy for hereditary hemorrhagic telangiectasia: a double-blind placebo-controlled clinical trial. *Laryngoscope*, 2009, 119, s. 284–288.

59 **Yaniv, E. – Preis, M. – Shevro, J. – Nageris, B., et al.**: Anti-estrogen therapy for hereditary hemorrhagic telangiectasia – a long-term clinical trial. *Rhinology*, 2011, 49, s. 214–216.

60 **Zheng, J. W. – Zhou, Q. – Yang, X. J., et al.**: Anti-estrogenic agents might be more favorable option for treatment of hereditary hemorrhagic telangiectasia. *Med Hypotheses*, 2009, 72, s. 230–231.

61 **Hsu, Y. P. – Hsu, C. W. – Bai, C. H., et al.**: Medical treatment for epistaxis in hereditary hemorrhagic telangiectasia: a meta-analysis. *Otolaryngol Head Neck Surg*, 2019, 160, s. 22–35.

62 **Therapontos, C. – Erskine, L. – Gardner, E. R., et al.**: Thalidomide induces limb defects by preventing angiogenic outgrowth during early limb formation. *Proc Natl Acad Sci*, 2009, 106, s. 8573–8578.

63 **D'Amato, R. J. – Loughnan, M. S. – Flynn, E., et al.**: Thalidomide is an inhibitor of angiogenesis. *Proc Natl Acad Sci*, 1994, 91, s. 4082–4085.

64 **Buscarini, E. – Botella, L. M. – Geisthoff, U., et al.**: Safety of thalidomide and bevacizumab in patients with hereditary hemorrhagic telangiectasia. *Orphanet J Rare Dis*, 2019, 14, s. 28.

65 **Halderman, A. A. – Ryan, M. W. – Clark, C., et al.**: Medical treatment of epistaxis in hereditary hemorrhagic telangiectasia: an evidence-based review. *Int Forum Allergy Rhinol*, 2018, 8, s. 713–728.

66 **Harrison, L. – Kundra, A. – Jervis, P.**: The use of thalidomide therapy for refractory epistaxis in hereditary haemorrhagic telangiectasia: systematic review. *J Laryngol Otol*, 2018, 132, s. 866–871.

67 **Nakamura, T. – Ogo, T. – Tahara, N., et al.**: Thalidomide for hereditary hemorrhagic telangiectasia with pulmonary arterial hypertension. *Circ J*, 2018, 82, s. 1205–1207.

68 **Franchini, M. – Lippi, G.**: Thalidomide for hereditary haemorrhagic telangiectasia. *Lancet Haematol*, 2015, 2, s. e457–e458.

69 **Hosman, A. – Westermann, C. J. – Snijder, R., et al.**: Follow-up of thalidomide treatment in patients with hereditary haemorrhagic telangiectasia. *Rhinology*, 2015, 53, s. 340–344.

70 **Invernizzi, R. – Quaglia, F. – Klersy, C., et al.**: Efficacy and safety of thalidomide for the treatment of severe recurrent epistaxis in hereditary haemorrhagic telangiectasia: results of a non-randomised, single-centre, phase 2 study. *Lancet Haematol*, 2015, 2, s. e465–e473.

71 **Colombo, G. – Bortolotti, F. – Chiapponi, V., et al.**: Nasal powders of thalidomide for local treatment of nose bleeding in persons affected by hereditary hemorrhagic telangiectasia. *Int J Pharm*, 2016, 514, s. 229–237.

72 **Franchini, M. – Frattini, F. – Crestani, S., et al.**: Novel treatments for epistaxis in hereditary hemorrhagic telangiectasia: a systematic review of the clinical experience with thalidomide. *J Thromb Thrombolysis*, 2013, 36, s. 355–357.

73 **Bauditz, J.**: Effective treatment of gastrointestinal bleeding with thalidomide – chances and limitations. *World J Gastroenterol*, 2016, 22, s. 3158–3164.

74 **Chen, C. H. – Hsu, H. H. – Hu, R. H., et al.**: Long-term therapy with thalidomide in hereditary hemorrhagic telangiectasia: case report and literature review. *J Clin Pharmacol*, 2012, 52, s. 1436–1440.

75 **Wang, X. Y. – Chen, Y. – Du, Q.**: Successful treatment of thalidomide for recurrent bleeding due to gastric angiodysplasia in hereditary hemorrhagic telangiectasia. *Eur Rev Med Pharmacol Sci*, 2013, 17, s. 1114–1116.

76 **Lacout, A. – Marcy, P. Y. – El Hajjam, M., et al.**: Pulmonary arteriovenous malformations etiologies in HHT patients and potential utility of thalidomide. *Med Hypotheses*, 2013, 80, s. 587–588.

77 **Frei-Jones, M. – McKinstry, R. C. – Perry, A., et al.**: Use of thalidomide to diminish growth velocity in a life-threatening congenital intracranial hemangioma. *J Neurosurg Pediatr*, 2008, 2, s. 125–129.

78 **Piribauer, M. – Czech, T. – Dieckmann, K., et al.**: Stabilization of a progressive hemangioblastoma under treatment with thalidomide. *J Neurooncol*, 2004, 66, s. 295–299.

79 **Jarvi, K. – Roebuck, D. J. – Sebire, N. J., et al.**: Successful treatment of extensive infantile hemangiomatosis of the small bowel in a-month-old with thalidomide and somatostatin analog. *J Pediatr Gastroenterol Nutr*, 2008, 46, s. 593–597.

80 **Bölke, E. – Gripp, S. – Peiper, M., et al.**: Multifocal epithelioid hemangioendothelioma: case report of a clinical chamaeleon. *Eur J Med Res*, 2006, 11, s. 462–466.

81 **Mascarenhas, R. C. – Sanghvi, A. N. – Friedlander, L., et al.**: Thalidomide inhibits the growth and progression of hepatic epithelioid hemangioendothelioma. *Oncology*, 2004, 67, s. 471–475.

82 **Adam, Z. – Pour, L. – Krejčí, M., et al.**: Úspěšná léčba angiomatózy thalidomidem a interferonem alfa. Popis 5 případů a přehled léčby angiomatózy a proliferujících hemangiomů. *Vnitř Lék*, 2010, 56, s. 810–823.

83 **Lebrin, F. – Srun, S. – Raymond, K.**: Thalidomide stimulates vessel maturation and reduces epistaxis in individual with hereditary hemorrhagic teleangiectasia. *Nat Med*, 2010, 16, s. 420–428.

84 **Khatri, N. V. – Patel, B. – Kohli, D. R., et al.**: Lenalidomide as a novel therapy for gastrointestinal angiodysplasia in von Willebrand disease. *Haemophilia*, 2018, 24, s. 278–282.

85 **Pallotti, M. C. – Nannini, M. – Agostinelli, C., et al.**: Long-term durable response to lenalidomide in a patient with hepatic epithelioid hemangioendothelioma. *World J Gastroenterol*, 2014, 20, s. 7049–7054.

86 **Bowcock, S. J. – Patrick, H. E.**: Lenalidomide to control gastrointestinal bleeding in hereditary haemorrhagic telangiectasia: potential implications for angiodysplasias? *Br J Haematol*, 2009, 146, s. 220–222.

87 **Epperla, N. – Hocking, W.**: Blessing for the bleeder: bevacizumab in hereditary hemorrhagic telangiectasia. *Clin Med Res*, 2015, 13, s. 32–35.

88 **Albitar, H. A. H. – Almodallal, Y. – Gallo De Moraes, A., et al.**: Intravenous bevacizumab in hereditary hemorrhagic telangiectasia-related bleeding and high-output cardiac failure: significant inter-individual variability in the need for maintenance therapy. *Mayo Clin Proc*, 2020, 95, s. 1604–1612.

89 **Al-Samkari, H. – Albitar, H. A. – Olitsky, S. E., et al.**: An international survey to evaluate systemic bevacizumab for chronic bleeding in hereditary haemorrhagic telangiectasia. *Haemophilia*, 2020, 26, s. 1038–1045.

90 **Al-Samkari, H. – Albitar, H. A. – Olitsky, S. E., et al.**: Systemic bevacizumab for high-output cardiac failure in hereditary hemorrhagic telangiectasia: an international survey of HHT centers. *Orphanet J Rare Dis*, 2019, 14, s. 256.

91 **Al-Samkari, H. – Kasthuri, R. S. – Parambil, J. G., et al.**: An international, multicenter study of intravenous bevacizumab for bleeding in hereditary hemorrhagic telangiectasia: the InHIBIT-Bleed study. *Haematologica*, 16. 7. 2020, doi: 10.3324/haematol.2020.261859.

92 **Al-Samkari, H.**: Systemic bevacizumab for hereditary hemorrhagic telangiectasia: considerations from observational studies. *Otolaryngol Head Neck Surg*, 2019, 160, s. 368.

93 **Arizmendez, N. P. – Rudmik, L. – Poetker, D. M.**: Intravenous bevacizumab for complications of hereditary hemorrhagic telangiectasia: a review of the literature. *Int Forum Allergy Rhinol*, 2015, 5, s. 1042–1047.

94 **Bernardes, C. – Santos, S. – Loureiro, R., et al.**: Bevacizumab for Refractory gastrointestinal bleeding in Rendu-Osler-Weber disease. *GE Port J Gastroenterol*, 2018, 25, s. 91–95.

95 **Brinkerhoff, B. T. – Poetker, D. M. – Choong, N. W.**: Long-term therapy with bevacizumab in hereditary hemorrhagic telangiectasia. *N Engl J Med*, 2011, 364, s. 688–689.

96 **Dupuis-Girod, S. – Ginon, I. – Saurin, J. C., et al.**: Bevacizumab in patients with hereditary hemorrhagic telangiectasia and severe hepatic vascular malformations and high cardiac output. *JAMA*, 2012, 307, s. 948–955.

97 **Dupuis-Girod, S.**: Intravenous bevacizumab in hereditary hemorrhagic telangiectasia: a role that is still to be defined. *Mayo Clin Proc*, 2020, 95, s. 1565–1566.

98 **Epperla, N. – Kleman, A. – Karafin, M., et al.**: Re-treatment versus extended treatment strategy of systemic bevacizumab in hereditary hemorrhagic telangiectasia: which is better? *Ann Hematol*, 2018, 97, s. 1727–1729.

99 **Gossage, J. R.**: The current role of bevacizumab in the treatment of hereditary hemorrhagic telangiectasia-related bleeding. *Mayo Clin Proc*, 2018, 93, s. 130–132.

100 **Guilhem, A. – Fargeton, A. E. – Simon, A. C., et al.**: Intra-venous bevacizumab in hereditary hemorrhagic telangiectasia (HHT): A retrospective study of 46 patients. *PLoS One*, 2017, 12, s. e0188943.

101 **Halderman, A. A. – Ryan, M. W. – Marple, B. F., et al.**: Bevacizumab for epistaxis in hereditary hemorrhagic telangiectasia: an evidence-based review. *Am J Rhinol Allergy*, 2018, 32, s. 258–268.

102 **Hsu, Y. P. – Hsu, C. W. – Chen, C.**: Response to "Systemic Bevacizumab for Hereditary Hemorrhagic Telangiectasia: Considerations from Observational Studies". *Otolaryngol Head Neck Surg*, 2019, 160, s. 369–370.

103 **Huemer, F. – Dejaco, M. – Grabmer, C., et al.**: Intermittent low-dose bevacizumab in hereditary hemorrhagic telangiectasia: A case report. *Wien Klin Wochenschr*, 2017, 129, s. 141–144.

104 **Iyer, V. N. – Apala, D. R. – Pannu, B. S., et al.**: Intravenous Bevacizumab for refractory hereditary hemorrhagic telangiectasia-related epistaxis and gastrointestinal bleeding. *Mayo Clin Proc*, 2018, 93, s. 155–166.

105 **Kini, S. D. – Yiu, D. W. – Weisberg, R. A., et al.**: Bevacizumab as treatment for epistaxis in hereditary hemorrhagic telangiectasia: a literature review. *Ann Otol Rhinol Laryngol*, 2019, 128, s. 467–471.

106 **Ou, G. – Galorport, C. – Enns, R.**: Bevacizumab and gastrointestinal bleeding in hereditary hemorrhagic telangiectasia. *World J Gastrointest Surg*, 2016, 8, s. 792–795.

107 **Samkari, H. – Kritharis, A. – Rodriguez-Lopez, J. M., et al.**: Systemic bevacizumab for the treatment of chronic bleeding in hereditary haemorrhagic telangiectasia. *J Intern Med*, 2019, 285, s. 223–231.

108 **Santos, S. – Bernardes, C. – Borges, V., et al.**: Gastric antral vascular ectasia (GAVE) and hereditary hemorrhagic telangiectasia (HHT): two different conditions, one treatment. *Ann Hematol*, 2020, 99, s. 367–369.

109 **Vázquez, C. – Gonzalez, M. L. – Ferraris, A., et al.**: Bevacizumab for treating hereditary hemorrhagic telangiectasia patients with severe hepatic involvement or refractory anemia. *PLoS One*, 2020, 15, s. e0228486.

110 **Wee, J. W. – Jeon, Y. W. – Eun, J. Y., et al.**: Hereditary hemorrhagic telangiectasia treated with low dose intravenous bevacizumab. *Blood Res*, 2014, 49, s. 192–195.

111 **Ospina, F. E. – Echeverri, A. – Posso-Osorio, I., et al.**: Bevacizumab as a treatment for hereditary hemorrhagic telangiectasia in children: a case report. *Colomb Med (Cali)*, 2017, 48, s. 88–93.

112 **Amedee, R. G.**: Efficacy of intranasal bevacizumab (avastin) treatment in patients with hereditary hemorrhagic telangiectasia-associated epistaxis. *Am J Rhinol Allergy*, 2011, 25, s. 368.

113 **Brinkerhoff, B. T. – Choong, N. W. – Treisman, J. S., et al.**: Intravenous and topical intranasal bevacizumab (Avastin) in hereditary hemorrhagic telangiectasia. *Am J Otolaryngol*, 2012, 33, s. 349–351.

114 **Dupuis-Girod, S. – Ambrun, A. – Decullier, E., et al.**: Effect of bevacizumab nasal spray on epistaxis duration in hereditary hemorrhagic telangectasia: a randomized clinical trial. *JAMA*, 2016, 316, s. 934–942.

115 **Chen, S. 4th – Karnezis, T. – Davidson, T. M.**: Safety of intranasal bevacizumab (Avastin) treatment in patients with hereditary hemorrhagic telangiectasia associated epistaxis. *Laryngoscope*, 2011, 121, s. 644–646.

116 **Chin, C. J.**: Is bevacizumab effective for reducing epistaxis in hereditary hemorrhagic telangiectasia? *Laryngoscope*, 2017, 127, s. 289–290.

117 **Karnezis, T. T. – Davidson, T. M.**: Treatment of hereditary hemorrhagic telangiectasia with submucosal and topical bevacizumab therapy. *Laryngoscope*, 2012, 122, s. 495–497.

118 **Riss, D. – Burian, M. – Wolf, A., et al.**: Intranasal submucosal bevacizumab for epistaxis in hereditary hemorrhagic telangiectasia: a double-blind, randomized, placebo-controlled trial. *Head Neck*, 2015, 37, s. 783–787.

119 **Steineger, J. – Geirdal, A. Ø. – Osnes, T., et al.**: Intranasal bevacizumab injections improve quality of life in HHT patients. *Laryngoscope*, 2020, 130, s. E284–E288.

120 **Steineger, J. – Osnes, T. – Heimdal, K., et al.**: Long-term experience with intranasal bevacizumab therapy. *Laryngoscope*, 2018, 128, s. 2237–2244.

121 **Stokes, P. – Rimmer, J.**: Intranasal bevacizumab in the treatment of HHT-related epistaxis: a systematic review. *Rhinology*, 2018, 56, s. 3–10.

122 **Whitehead, K. J. – Sautter, N. B. – McWilliams, J. P., e al.**: Effect of topical intranasal therapy on epistaxis frequency in patients with hereditary hemorrhagic telangiectasia: a randomized clinical trial. *JAMA*, 2016, 316, s. 943–951.

123 **Lindner, D. J.**: Interferons as antiangiogenic agents. *Curr Oncol Rep*, 2002, 4, s. 510–514.

124 **Wheatley-Price, P. – Shovlin, C. – Chao, D.:** Interferon for metastatic renal cell cancer causing regression of hereditary hemorrhagic telangiectasia. *J Clin Gastroenterol*, 2005, 39, s. 344–345.

125 **Massoud, O. I. – Youssef, W. I. – Mullen, K. D.**: Resolution of hereditary hemorrhagic telangiectasia and anemia with prolonged alpha-interferon therapy for chronic hepatitis C. *J Clin Gastroenterol*, 2004, 38, s. 377–379.

126 **Brančíková, D.**: Přínos nových inhibitorů angiogeneze (bevacizumab a aflibercept) pro léčbu mnohočetné angiomatózy: kazuistika. *Vnitř Lék*, 2017, 63, s. 672–678.

127 **Ohji, M. – Takahashi, K. – Okada, A. A., et al.**: Efficacy and safety of intravitreal aflibercept treat-and-extend regimens in exudative age-related macular degeneration: 52- and 96-week findings from ALTAIR: a randomized controlled trial. *Adv Ther*, 2020, 37, s. 1173–1187.

128 **Geisthoff, U. W – Nguyen, H.-L. P. – Hess, D.**: Improvement in hereditary hemorrhagic telangiectasia after treatment with the phosphoinositide 3-kinase inhibitor BKM120. *An Hematol*, 2014, 93, s. 703–704.

129 **Faughnan, M. E. – Gossage, J. R. – Chakinala, M. M., et al.**: Pazopanib may reduce bleeding in hereditary hemorrhagic telangiectasia. *Angiogenesis*, 2019, 22, s. 145–155.

130 **Parambil, J. G. – Woodard, T. D. – Koc, O. N.**: Pazopanib effective for bevacizumab unresponsive epistaxis in hereditary hemorrhagic telangiectasia. *Laryngoscope*, 2018, 128, s. 2234–2236.

131 **Kovacs-Sipos, E. – Holzmann, D. – Scherer, T., et al.**: Nintedanib as a novel treatment option in hereditary haemorrhagic telangiectasia. *BMJ Case Rep*, 2017, bcr2017219393.

132 **Droege, F. – Thangavelu, K. – Lang, S., et al.**: Improvement in hereditary hemorrhagic telangiectasia after treatment with the multi-kinase inhibitor sunitinib. *Ann Hematol*, 2016, 95, s. 2077–2078.

133 **Dupuis-Girod, S. – Fargeton, A. E. – Grobost, V., et al.**: Efficacy and safety of a 0.1% tacrolimus nasal ointment as a treatment for epistaxis in hereditary hemorrhagic telangiectasia: a double-blind, randomized, placebo-controlled, multicenter trial. *J Clin Med*, 2020, 9, s. 1262.

134 **Sommer, N. – Droege, F. – Gamen, K. E., et al.**: Treatment with low-dose tacrolimus inhibits bleeding complications in a patient with hereditary hemorrhagic telangiectasia and pulmonary arterial hypertension. *Pulm Circ*, 2019, 9, doi: 10.1177/2045894018805406.

135 **Albiñana, V. – Cuesta, A. M. – Rojas-P, I., et al.**: Review of pharmacological strategies with repurposed drugs for hereditary hemorrhagic telangiectasia related bleeding. *J Clin Med*, 2020, 9, s. 1766.

136 **Ruiz, S. – Chandakkar, P. – Zhao, H., et al.**: Tacrolimus rescues the signaling and gene expression signature of endothelial ALK1 loss-of-function and improves HHT vascular pathology. *Hum Mol Genet*, 2017, 26, s. 4786–4798.

137 **Robert, F. – Desroches-Castan, A. – Bailly, S., et al.**: Future treatments for hereditary hemorrhagic telangiectasia. *Orphanet J Rare Dis*, 2020, 15, s. 4.

138 **Dupuis-Girod, S. – Chesnais, A. L. – Ginon, I., et al.**: Long-term outcome of patients with hereditary hemorrhagic telangiectasia and severe hepatic involvement after orthotopic liver transplantation: a single-center study. *Liver Transpl*, 2010, 16, s. 340–347.

139 **Salloum, R. – Fox, C. E. – Alvarez-Allende, C. R., et al.**: Response of blue rubber bleb nevus syndrome to sirolimus treatment. *Pediatr Blood Cancer*, 2016, 63, s. 1911–1914.

140 **Yesil, S. – Tanyildiz, H. G. – Bozkurt, C., et al.:** Single-center experience with sirolimus therapy for vascular malformations. *Pediatr Hematol Oncol*, 2016, 33, s. 219–225.

141 **Gran'Maison, A.**: Hereditary hemorrhagic telangiectasia. *Canadian Medical Association Journal Praktice*, 2009, 180, s. 833–835.