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5 Současnost a novinky v léčbě roztroušené sklerózy
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Imunoterapie inhibitory kontrolních bodů imunity – průlom v léčbě pokročilých „trojitě“ negativních karcinomů prsu

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1 **Hammond, M. E. – Hayes, D. F. – Dowsett, M., et al.**: American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer (unabridged version). *Arch Pathol Lab Med*, 2010, 134, s. e48.

2 **Hammond, M. E. – Hayes, D. F. – Dowsett, M., et al.**: American Society of Clinical Oncology/College Of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. *J Clin Oncol*, 2010, 28, s. 2784.

3 **Wolff, A. C. – Hammond, M. E. – Hicks, D. G., et al.**: Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. *J Clin Oncol*, 2013, 31, s. 3997.

4 **Livasy, C. A. – Karaca, G. – Nanda, R., et al.**: Phenotypic evaluation of the basal-like subtype of invasive breast carcinoma. *Mod Pathol*, 2006, 19, s. 264.

5 **Gonzalez-Angulo, A. M. – Timms, K. M. – Liu, S., et al.**: Incidence and outcome of BRCA mutations in un selected patients with triple receptor-negative breast cancer. *Clin Cancer Res*, 2011, 17, s. 1082.

6 **Navrátil, J. – Fabián, J. – Palácová, M., et al.**: Triple negativní karcinom prsu. *Klin Onkol*, 2015, 28, s. 405–415.

7 NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk assessment: Breast and Ovarian. Version 4.2013. Dostupné z: http://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf, vyhledáno 6. 2. 2020.

8 **Phipps, A. I. – Chlebowski, R. T. – Prentice, R., et al.**: Reproductive history and oral contraceptive use in relation to risk of triple-negative breast cancer. *J Natl Cancer Inst*, 2011, 103, s. 470.

9 **Pierobon, M. – Frankenfeld, C. L.**: Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. *Breast Cancer Res Treat*, 2013, 137, s. 307.

10 **Dent, R. – Trudeau, M. – Pritchard, K. I., et al.**: Triple-negative breast cancer: clinical features and patterns of recurrence. *Clin Cancer Res*, 2007, 13, s. 4429.

11 **Schmid, M. – Wang, Y. – Zhang, Y., et al.**: Subtypes of breast cancer show preferential site of relapse. *Cancer Res*, 2008, 68, s. 3108.

12 **Lin, N. U. – Claus, E. – Sohl, J., et al.**: Sites of distant recurrence and clinical outcomes in patients with metastatic triple-negative breast cancer: high incidence of central nervous system metastases. *Cancer*, 2008, 113, s. 2638.

13 **Hicks, D. G. – Short, S. M. – Prescott, N. L., et al.**: Breast cancers with brain metastases are more likely to be estrogen receptor negative, express the basal cytokeratin CK5/6, and overexpress HER2 or EGFR. *Am J Surg Pathol*, 2006, 30, s. 1097.

14 **Lin, N. U. – Vanderplas, A. – Hughes, M. E., et al.**: Clinicopathologic features, patterns of recurrence, and survival among women with triple-negative breast cancer in the National Comprehensive Cancer Network. *Cancer*, 2012, 118, s. 5463.

15 **Amir, E. – Clemons, M. – Freedman, O. C., et al.**: Tissue confirmation of disease recurrence in patients with breast cancer: Pooled analysis of two large prospective studies. *J Clin Oncol*, 2010, 28S, ASCO #1007.

16 **Simmons, C. – Miller, N. – Geddie, W., et al.**: Does confirmatory tumor biopsy alter the management of breast cancer patients with distant metastases? *Ann Oncol*, 2009, 20, s. 1499.

17 **Amir, E. – Clemons, M.**: Should a biopsybere commended to confirm metastatic disease in women with breast cancer? *Lancet Oncol*, 2009, 10, s. 933.

18 **Khasraw, M. – Brogi, E. – Seidman, A. D.**: The need to examine metastatic tissue at the time of progression of breast cancer: is re-biopsy a necessity or a luxury? *Curr Oncol Rep*, 2011, 13, s. 17.

19 **Le Du, F.**: Is the future of personalized therapy in triple-negative breast cancer based on molecular subtype? *Oncotarget*, 2015, 6, s. 12890–12908.

20 **McGhan, L. J. – McCullough, A. E. – Protheroe, C. A., et al.**: Androgen receptor-positive triple negative breast cancer: a unique breast cancer subtype. *Ann Surg Oncol*, 2014, 21, s. 361–367.

21 **Robson, M. – Im, S.-A. – Senkus, E., et al.**: Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. *N Engl J Med*, 2017, 377, s. 523–533.

22 **Robson, M. – Tung, N. – Conte, P., et al.**: OlympiAD final overall survival and tolerability results: olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer. *Ann Oncol*, 2019, 30, s. 558– 566.

23 **Litton, J. K. – Rugo, H. S. – Ettl, J., et al.**: Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. *N Engl J Med*, 2018, 379, s. 753–763.

24 **Schmid, P. – Adams, S. – Rugo, H. S., et al.**; IMpassion130 Trial Investigators: Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. *N Engl J Med*, 2018, 379, s. 2108– 2121.

25 **Emens, L. A. – Loi, S. – Rugo, H. S., et al.**: IMpassion130: efficacy in immune biomarker subgroups from the global, randomized, double-blind, placebo-controlled, phase III study ofatezolizumab + nab-paclitaxel in patients with treatment-naïve, locally advanced or metastatic triple-negative breast cancer. *Cancer Res*, 2019, 79, suppl. 4, abstrakt GS104.

26 **Schmid, P. – Cortés, J. – Dent, R., et al.**: KEYNOTE-522: phase 3 study of pembrolizumab + chemotherapy vs. placebo + chemotherapy as neoadjuvant treatment, followed by pembrolizumab vs placebo as adjuvant treatment for early-stage high-risk triple-negative breast cancer. Prezentováno na European Society for Medical Oncology Congress 2019, abstrakt LBA8_PR.

27 **Esteva, F. J. – Hubbard-Lucey, V. M. – Tang, J. – Pusztai, L.**: Immunotherapy and targeted therapy combinations in metastatic breast cancer. *Lancet Oncol*, 2019, 20, s. e175–e186.

28 **Marra, A. – Viale, G. – Curigliano, G.**: Recent advances in triple negative breast cancer: the immunotherapy era. *BMC Medicine*, 2019, 17, s. 90.

29 **Liedtke, C. – Mazouni, C. – Hess, K. R., et al.**: Response to neoadjuvant therapy and long-term survival in patients with triple-negative breast cancer. *J Clin Oncol*, 2008, 26, s. 1275–1281.

30 **Anders, C. K. – Carey, L. A.**: ER/PR negative, HER2-negative (triple-negative) breast cancer. Dostupné z: https://www.uptodate.com/contents/er-pr-negative-her2-negative-triple-negative-breast-cancer, vyhledáno 14. 3. 2020.

Význam biologické léčby v terapii karcinomu prsu

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1 Národní onkologický registr 2016. Karcinom prsu – incidence a mortalita. Dostupné z: www.svod.cz.

2 **Cardoso, F. – Senkus, E. – Costa, A., et al.**: 4th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC4). *Ann Oncol*, 2018, 29, s. 1634–1657.

3 **Schmid, P. – Adams, S. – Rugo, H. S., et al.**: Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. *N Engl J Med*, 2018, 379, s. 2108–2121.

4 **Schmid, P.**: IMpassion130: updated overall survival (OS) from a global, randomized, double-blind, placebo-controlled, phase III study of atezolizumab (atezo) + nab-paclitaxel (nP) in previously untreated locally advanced or metastatic triple-negative breast cancer (mTNBC). ASCO 2019. Abstract 1003. *J Clin Oncol*, 2019, 37, suppl., s. 1003.

5 **Schmid, P. – Rugo, H. S. – Adams, S., et al.**: Atezolizumab plus nab-paclitaxel as first-line treatment for unresectable, locally advanced or metastatic triple-negativebreast cancer (IMpassion130): updated efficacy results from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*, 2020, 21, s. 44–59.

6 **Gianni, L.**: Combining atezolizumab with neoadjuvant chemotherapy does not improve pathologic complete response rates for patients with triple-negativne breast cancer. SABCS 2019. Abstr GS3–04. Dostupné z: https://clinicaltrials.gov.

7 **Miller, K. – Wang, M. – Gralow, J., et al.**: Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. *N Engl J Med*, 2007, 357, s. 2666–2676.

8 **Cardoso, F. – Kyriakides, S. – Ohno, S., et al.**: Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*, 2019, 30, s. 1194–1220.

9 **Earl, H. M. – Hiller, L. – Vallier, A. L., et al.**: PERSEPHONE: 6 versus 12 months (m) of adjuvant trastuzumab in patients (pts) with HER2 positive (+) early breast cancer (EBC): Randomised phase 3 non-inferiority trial with definitive 4-year (yr) disease-free survival (DFS) results. *J Clin Oncol*, 2018, 36, suppl., abstrakt 506.

10 SPC Perjeta. Dostupné z: https://www.ema.europa.eu/en/documents/product-information/perjeta-epar-product-information_cs.pdf, vyhledáno 21. 2. 2020.

11 Perjeta, ceny a úhrady. Dostupné z: http://www.sukl.cz/modules/medication/detail.php?code=0193870&tab=prices, vyhledáno 21. 2. 2020.

12 **von Minckwitz, G. – Procter, M. – de Azambuja, E., et al.**: Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. *N Engl J Med*, 2017, 377, s. 122–131.

13 **Piccart, M., et al.**: Interim overall survival analysis of APHINITY (BIG 4-11): A randomized multicenter, double-blind, placebo-controlled trial comparing chemotherapy plus trastuzumab plus pertuzumab versus chemotherapy plus trastuzuamb plus placebo as adjuvant therapy in patients with operable HER2-positive early brest cancer. SABCS 2019. Abstrakt GS1–04.

14 **Von Minckwitz, G. – Huang, C. S. – Mano, M. S., et al.**: Trastuzumab emtansin for residual invasive HER2-positive breast cancer. *N Engl J Med*, 2019, 380, s. 617–628.

15 **Martin, M. – Holmes, F. A. – Ejlertsen, 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.

16 **Swain, S. M. – Kim, S. B. – Cortés, J., et al.**: Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet Oncol*, 2013, 14, s. 461–471.

17 **Krop, I. E. – Lin, N. U. – Blackwell, K., et al.**: Trastuzumab emtansine (T-DM1) versus lapatinib plus capecitabine in patients with HER2-positive metastatic breast cancer and central nervous system metastases: a retrospective, exploratory analysis in EMILIA. *Ann Oncol*, 2015, 26, s. 113–119.

18 **Geyer, C. E. – Forster, J. – Lindquist, D., et al.**: Lapatinib plus capecitabine for HER-2 positive advanced breast cancer. *N Engl J Med*, 2006, 355, s. 2733–2743.

19 Trastuzumab. Dostupné z: www.sukl.cz.

20 **Krop, I. E., et al.**: [Fam-] trastuzumab deruxtecan (T-DXd; DS-8201a) in subjects with HER2-positive metastatic breast cancer previously treated with T-DM1: A phase 2, multicenter, open-label study (DESTINY-Breast01). SABCS 2019. Abstrakt GS1–03.

21 **Murthy, R., et al.**: Tucatinib vs placebo, both combined with capecitabine and trastuzumab, for patients with pretreated HER2-positive metastatic breast cancer with and without brain metastases (HER2CLIMB). SABCS 2019. Abstrakt GS1–01.

22 **Finn, R. S. – Crown, J. P. – Lang, I., et al.**: The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomized phase 2 study. *Lancet Oncol*, 2015, 16, s. 25–35.

23 **Finn, R. S. – Martin, M. – Rugo, H. S., et al.**: Palbociclib and letrozole in advanced breast cancer. *N Engl J Med*, 2016, 375, s. 1925–1936.

24 **Hortobagyi, G. N. – Stemmer, S. M. – Burris, H. A., et al.**: Ribociclib as first-line therapy for HR-positive, advanced breast cancer. *N Engl J Med*, 2016, 375, s. 1738–1748.

25 **Hortobagyi, G. N. – Stemmer, S. M. – Burris, H. A., et al.**: Updated results from MONALEESA-2, a phase III trial of first-line ribociclib plus letrozole versus placebo plus letrozole in hormone receptor-positive, HER2-negative advanced breast cancer. *Ann Oncol*, 2018, 29, s. 1541–1547.

26 **Goetz, M. P. – Toi, M. – Campone, M., et al.**: MONARCH 3: Abemaciclib as initial therapy for advanced breast cancer. *J Clin Oncol*, 2017, 35, s. 3638–3646.

27 **Slamon, D. J. – Neven, P. – Chia, S., et al.**: Phase III randomized study of ribociclib and fulvestrant in hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced brest cancer: MONALEESA-3. *J Clin Oncol*, 2018, 36, s. 2465–2472.

28 **Cristofanilli, M. – Turner, N. C. – Bondarenko, I., et al.**: Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind-phase 3 randomised controlled trial. *Lancet Oncol*, 2016, 17, s. 425–439.

29 **Sledge, G. W. Jr. – Toi, M. – Neven, P., et al.**: MONARCH 2: Abemaciclib in combination with fulvestrant in women with HR+/HER2– advanced breast cancer who had progressed while receiving endocrine therapy. *J Clin Oncol*, 2017, 35, s. 2875–2884.

30 **Slamon, D. J.**: Overall survival (OS) results of the phase III MONALEESA-3 trial of postmenopausal patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor 2-negative (HER2-) advanced breast cancer (ABC) treated with fulvestrant (FUL) ± ribociclib (RIB). ESMO 2019 Congress. Abstrakt LBA7_PR. *Ann Oncol*, 2019, 30, suppl. 5, s. v851–v934.

31 Společné stanovisko VZP a ČOS: Doporučené podmínky použití CDK 4/6 inhibitorů při léčbě žen s hormonálně pozitivním HER2 negativním neresekovatelným lokálně pokročilým nebo metastatickým

karcinomem prsu a síť indikujících specializovaných center ze dne 6. 11. 2019. Dostupné z: https://media.vzpstatic.cz/media/Default/dokumenty/spolecna-stanoviska/2019_11_06_spolecnestanovisko_ibrancekisqaliverzenios.pdf, vyhledáno 21. 2. 2020.
32 **Verret, B. – Cortes, J. – Bachelot, T., et al.**: Efficacy of PI3K inhibitors in advanced breast cancer. *Ann Oncol*, 2019, 30, suppl. 10, s. 12–20.
33 **André, F. – Ciruelos, E. M. – Rubovszky, G., et al.**: Alpelisib (ALP) + fulvestrant (FUL) for advanced breast cancer (ABC): results of the Phase 3 SOLAR-1 trial. ESMO 2018 Congress, 19.–23. 10. 2018, Mnichov, Německo (LBA3_PR).
34 **Baselga, J. – Campone, M. – Piccart, M., et al.**: Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. *N Eng J Med*, 2012, 366, s. 520–529.
35 **Kim, S. B. – Dent, R. – Seock-Ah, I., et al.**: Ipatasertib plus paclitaxel versus placebo plus paclitaxel as first-line therapy for metastatic triple-negative breast cancer (LOTUS): a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet Oncol*, 2017, 18, s. 1360–1372.
36 **Dent, R. – Im, S. A. – Espie, M., et al.**: Overall survival (OS) update of the double-blind placebo (PBO)-controlled randomized phase 2 LOTUS trial of first-line ipatasertib (IPAT) + paclitaxel (PAC) for locally advanced/metastatic triple-negative breast cancer (mTNBC). *J Clin Oncol*, 2018, 36, suppl., s. 1008.
37 **Robson, M. – Im, S. A. – Senkus, E., et al.**: Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. *N Engl J Med*, 2017, 377, s. 523–533.
38 **Robson, M. E. – Tung, N. – Conte, P., et al.**: OlympiAD final overall survival and tolerability results: Olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER-2 negative metastatic breast cancer. *Ann Oncol*, 2019, 30, s. 558–566.
39 **Litton, J. K. – Rugo, H. S. – Ettl, J., et al.**: Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. *N Engl J Med*, 2018, 379, s. 753–763.
40 **Im, S. A. – Lu, Y. S. – Bardia, A., et al.**: Overall survival with ribociclib plus endocrine therapy in breast cancer. *N Eng J Med*, 2019, 381, s. 307–316.
41 **Sledge, G. W. jr – Toi, M. – Neven, P., et al.**: The effect of abemaciclib plus fulvestrant on overall survival in hormone receptor-positive, ERBB2-negative breast cancer that progressed on endocrine therapy – MONARCH 2. *JAMA Oncol*, 2020, 6, s. 116–124.

Ramucirumab u karcinomu žaludku

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1 **Dušek, L. – Mužík, J. – Kubásek, M., et al.**: *Epidemiologie zhoubných nádorů v České republice*. Masarykova univerzita, 2005. Dostupné z: http://www.svod.cz.
2 **Japanese Gastric Cancer Association**: Japanese gastric cancer treatment guidelines 2014 (ver. 4). *Gastric Cancer*, 2017, 20, s. 1–19.
3 **Pappas, A. L. – Hanna, S.**: Cyramza [package insert US]. Eli Lilly and Company, Indianapolis, IN. 2015, 2015-03-23 08:25:40.
4 **Fuchs, C. S. – Tomasek, J. – Yong, C. J., et al.**: Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. *Lancet*, 2014, 383, s. 31–39.
5 **Wilke, H. – Muro, K. – Van Cutsem, E., et al.**: 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.
6 **De Vita, F. – Borg, C. – Farina, G., et al.**: Ramucirumab and paclitaxel in patients with gastric cancer and prior trastuzumab: subgroup analysis from RAINBOW study. *Future Oncol*, 2019, 15, s. 2723–2731.
7 **Fuchs, C. S. – Shitara, K. – Di Bartolomeo, M., et al.**: Ramucirumab with cisplatin and fluoropyrimidine as first-line therapy in patients with metastatic gastric or junctional adenocarcinoma (RAINFALL): a double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet Oncol*, 2019, 20, s. 420–435.
8 **Yoon, H. – Bendell, J. C. – Braiteh, F. S., et al.**: Ramucirumab combined with FOLFOX as front-line therapy for advanced esophageal, gastroesophageal junction, or gastric adenocarcinoma: a randomized, double-blind, multicenter Phase II tr. *Ann Oncol*, 2016, 27, s. 2196–2203.
9 **Arnold, D. – Fuchs, C. S. – Tabernero, J., et al.**: Meta-analysis of individual patient safety data from six randomized, placebo-controlled trials with the antiangiogenic VEGFR2-binding monoclonal antibody ramucirumab. *Ann Oncol*, 2017, 28, s. 2932–2942.
10 **Hara, H. – Shoji, H. – Takahari, T., et al.**: Phase I/II study of ramucirumab plus nivolumab in patients in second line treatment for advanced gastric adenocarcinoma (NivoRam study). *J Clin Oncol*, 2019, 37, suppl, abstrakt 129.

Imunoonkologická léčba karcinomů plic – současnost a perspektivy

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1 **Antonia, S. J. – Borghaei, H. – Ramalingam, S. S., et al.**: Four-year survival with nivolumab in patients with previously treated advanced non-small-cell lung cancer: a pooled analysis. *Lancet Oncol*, 2019, 20, s. 1395–1408.
2 **Borghaei, H. – Paz-Ares, L. – Horn, L., et al.**: Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. *N Engl J Med*, 2015, 373, s. 1627–1639.
3 **Brahmer, J. – Reckamp, K. L. – Baas, P., et al.**: Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer. *N Engl J Med*, 2015, 373, s. 123–135.
4 **Hellmann, M. D. – Paz-Ares, L. – Bernabe Caro, R., et al.**: Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. *N Engl J Med*, 2019, 381, s. 2020–2031.
5 Tisková zpráva dostupná z: https://news.bms.com/press-release/corporatefinancial-news/bristol-myers-squibb-withdraws-european-application-opdivo-niv, vyhledáno 17. 3. 2020.
6 **Horn, L. – Spigel, D. R. – Vokes, E. E., et al.**: Nivolumab versus docetaxel in previously treated patients with advanced non-small-cell lung cancer: Two-year outcomes from two randomized, open-label, phase III Trials (CheckMate 017 and CheckMate 057). *J Clin Oncol*, 2017, 35, s. 3924–3933.
7 **Vokes, E. E. – Ready, N. – Felip, E., et al.**: Nivolumab versus docetaxel in previously treated advanced non-small-cell lung cancer (CheckMate 017 and CheckMate 057): 3-year update and outcomes in patients with liver metastases. *Ann Oncol*, 2018, 29, s. 959–965.
8 **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, 37, 15, suppl., s. 9013.
9 **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.
10 **Herbst, R. S. – Baas, P. – Kim, D. W., et al.**: Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet*, 2016, 387, s. 1540–1550.
11 **Paz-Ares, L. – 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.
12 **Paz-Ares, L. – Vicente, D. – Tafreshi, A., et al.**: Pembrolizumab (pembro) + chemotherapy (chemo) in metastatic squamous NSCLC: Final analysis and progression after the next line of therapy (PFS2) in KEYNOTE-407. *Ann Oncol*, 2019, 30, suppl. 5, mdz394.080.
13 **Reck, M. – Rodriguez-Abreu, D. – Robinson, A. G., et al.**: Pembrolizumab versus chemotherapy for PD-L1-positive non-small cell lung cancer. *N Engl J Med*, 2016, 375, s. 1823–1833.
14 **Reck, M. – Rodriguez-Abreu, D. – Robinson, A. G., et al.**: Updated analysis of KEYNOTE-024: Pembrolizumab versus platinum-based chemotherapy for advanced non-small-cell lung cancer with PD-L1 tumor proportion score of 50% or greater. *J Clin Oncol*, 2019, 37, s. 537–546.
15 **Reck, M., et al.**: *J Clin Oncol*, 8. 1. 2019, JCO1800149 (Epub před tiskem): [a] Effective crossover rate from chemotherapy to anti-PD-L1 therapy, 62.3% (82 patients crossed over to pembrolizumab during the study and 12 received anti-PD-L1 therapy outside of crossover). [b] Nominal P value. NR, not reached. NCCW 7.019, www.nccw.org.
16 **Roy, S. – Baas, H. P. – Kim, D-W. – Felip, E., et al.**: Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet*, 2016, 387, s. 1540–1550.
17 **Herbst, R. S. – Garon, E. B. – Kim, D.-W., et al.**: Long-term outcomes and retreatment among patients with previously treated, programmed death-ligand 1-positive, advanced non-small-cell lung cancer in the KEYNOTE-010 study. *J Clin Oncol*, 20. 2. 2020, JCO1902446.
18 **Barlesi, F., et al.**: Updated efficacy and safety from the global phase II NP28673 study of alectinib in patients (PTS) with previously treated ALK+ non-small-cell lung cancer (NSCLC). ESMO 2016 (Abs LBA 44). *Annals of Oncology*, 2016, 27, s. 416–454.
19 **Cortinovis, D., et al.**: Immune-related adverse events (IRAES) in advanced NSCLC patients treated with atezolumab: safety population analyses from the PH III study OAK. ESMO 2017 (Abs 1313P). *An Oncol*, 2017, 28, suppl. 5, s. v460–v496.
20 **Fehrenbacher, L., et al.**: Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, phase 2 randomised controlled trial. *Lancet*, 2016, 387, s. 1837–1846.
21 **Horn, L. – Mansfield, A. S. – Szczęsna, A., et al.**: First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *N Engl J Med*, 2018, 379, s. 2220–2229.
22 **Kowanetz, M., et al.**: IMpower150: Efficacy of atezolizumab (atezo) plus bevacizumab (bev) and chemotherapy (chemo) in 1L metastatic nonsquamous NSCLC (mNSCLC) across key subgroups. *Cancer Research*, 2018, 78, suppl. 13, AACR 2018, abstrakt CT076, dostupné z: https://cancerres.aacrjournals.org/content/78/13_Supplement/CT076, vyhledáno 17. 3. 2020.
23 **Von Pawel, et al.**: Association between immune-related adverse events (IRAES) and atezolimumab efficacy in advanced NSCLC: analyses from the Ph III study OAK.ESMO 2017 (Abs 1314P). *An Oncol*, 2017, 28, suppl. 5, s. v460–v496.
24 **Reck, 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.
25 **Rittmayer, A. – Barlesi, F. – Waterkamp, D., et al.**: Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. *Lancet*, 2017, 389, s. 255–265.
26 **Socinski, M. A. – Jotte, R. M. – Cappuzzo, F., et al.**: Atezolizumab for first-line treatement of metastatic nonsquamous NSCLC. *N Engl J Med*, 2018, 378, s. 2288–2301.
27 **Spigel, D. – de Marinis, F. – Giaccone, G., et al.**: IMpower110: Interim overall survival (OS) analysis of a phase III study of atezolizumab (atezo) vs platinum-based chemotherapy (chemo) as first-line (1L) treatment (tx) in PD-L1–selected NSCLC. *Ann Oncol*, 2019, 30, suppl. 5, s. v851–934.
28 **West, H. – McCleod, M. – Hussein, M., et al.**: Atezolizumab in combination with carboplatin plus nab-paclitaxel chemotherapy compared with chemotherapy alone as first-line treatment for metastatic non-squamous non-small-cell lung cancer (IMpower130): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol*, 2019, 20, s. 924–937.
29 **Antonia, S. J. – Villegas, A. – Daniel, D., et al.**: Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. *N Engl J Med*, 2017, 377, s. 1919–1929.
30 **Antonia, S. J. – Villegas, A. – Daniel, D., et al.**: Overall survival with durvalumab after chemoradiotherapy in stage III NSCLC. *N Engl J Med*, 2018, 379, s. 2342–2350.
31 **Gray, J. E. – Villegas, A. – Daniel, D., et al.**: Durvalumab. Three-year overal survival update from the PACIFIC trial. ASCO 2019, poster 8526.
32 **Fessas, P. – Hassal, L. – Shinji, I., et al.**: A molecular and preclinical comparison of the PD-1 – targeted T-cell checkpoint inhibitors nivolumab and pembrolizumab. *Semin Oncol*, 2017, 44, s. 136–140.
33 **Hyun, T. L. – Sang, H. L. – Heo, Y.-S.**: Molecular interactions of antibody drugs targeting PD-1, PD-L1, and CTLA-4 in immuno-oncology. *Molecules*, 2019, 24, s. 1190.
34 **Lee, J. Y. – Lee, H. T. – Shin, W., et al.**: Structural basis of checkpoint blockade by monoclonal antibodies in cancer immunotherapy. *Nat Commun*, 2016, 7, s. 13354.
35 **Lepir, T. – Zaghouani, M. – Stéphane, P., et al.**: Nivolumab to pembrolizumab switch induced a durable melanoma response. A case report. *Medicine*, 2019, 98, s. 2 (e13804).
36 **Tan, S. – Zhang, H. – Chai, Y., et al.**: An unexpected N-terminal loop in PD-1 dominates binding by nivolumab. *Nature Communications*, 2017, 8, 14369.
37 **Sun, X. – Roudi, R. – Dai, T., et al.**: Immune-related adverse events associated with programmed cell death protein-1 and programmed cell death ligand 1 inhibitors for non-small cell lung cancer: a PRISMA systematic review and meta-analysis. *BMC Cancer*, 2019, 19 , s. 558.
38 **Planchard, D. – Popat, S. – Kerr, K., et al.**: Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Updated 18 September 2019. *Ann Oncol*, 2018, 29, suppl. 4, s. iv192–iv237.
39 **Planchard, D., et al.**: Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*, 2018, 29, suppl. 4, s. iv192–iv237.

Osimertinib jako preferovaný standard první linie léčby nemalobuněčného karcinomu plic s pozitivní mutací EGFR

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1 **Midha, A. – Dearden, S. – McCormack, R.**: EGFR mutation incidence in non-small-cell lung cancer of adenocarcinoma histology: A systematic review and global map by ethnicity (mutMap II). *Am J Canc Res*, 2015, 5, s. 2892–2911.

2 **Kultan, J. – Kolek, V. – Fiala, O., et al.**: Frequency of EGFR gene mutations in patients with NSCLC in Czech Republic. In: 14th Central European Lung Cancer Conference, 2014, ISSN 2218–6751.

3 **Wu, Y.-L. – Zhou, C. – Liam, C.-K., et al.**: First-line erlotinib versus gemcitabine/cisplatin in patients with advanced EGFR mutation-positive non-small-cell lung cancer: analyses from the phase III, randomized, open-label, ENSURE study. *An Oncol*, 2015, 26, s. 1883–1889.

4 **Park, K. – Tan, E.-H. – O'Byrne, K., et al.**: Afatinib versus gefitinib as first-line treatment of patients with mutation-positive non-small-cell lung cancer (LUX-Lung 7): a phase 2B, open-label, randomised controlled trial. *Lancet Oncol*, 2016, 17, s. 577–589.

5 **Soria, J.-C. – Ohe, Y. – Vansteenkiste, J., et al.**; FLAURA Investigators: Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. *N Engl J Med*, 2018, 378, s. 113–125.

6 **Vansteenkiste, J. – Reungwetwattana, T. – Nakagawa, K., et al.**: CNS response to osimertinib vs standard-of-care EGFR-TKI as first-line treatment in patients with EGFRm advanced NSCLC: FLAURA. *An Oncol*, 2017, 28, suppl. 10, s. x186–x195, 10.1093/annonc/mdx729.

7 **Ramalingam, S. S. – Cheng, Y. – Zhou, C., et al.**: Mechanisms of acquired resistance to first-line osimertinib: preliminary data from the phase III FLAURA study. *An Oncol*, 2018, 29, suppl. 9, s. ix173-ix178, 10.1093/annonc/mdy483.

8 NCCN Guidelines in Oncology, Version 3.2020, 11. 2. 2020, dostupné z: https://www.nccn.org/profesionals/physicians_gls.pdf/nscl_blocks.pdf, https://www.nccn.org/professionals/physician_gls/default.aspx, vyhledáno 19. 2. 2020.

9 ESMO Guidelines. *Ann Oncol*, 2018, 29, suppl. 4, s. iv192–iv237, dostupné z: https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer, vyhledáno 18. 3. 2020.

10 SPC Tagrisso, dostupné z: https://www.ema.europa.eu/en/documents/product-information/tagrisso-epar-product-information_en.pdf, vyhledáno 18. 3. 2020.

Novinky v léčbě maligního melanomu

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1 **Hodi, F. S. – O'Day, S. J. – McDermott, D. F., et** al.: Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med*, 2010, 363, s. 711–723.

2 **Robert, C. – Thomas, L. – Bondarenko, I., et al.**: Ipilimumab plus dacarbazine for previously untreated metastatic melanoma. *N Engl J Med*, 2011, 364, s. 2517–2526.

3 **Robert, C. – Long, G. V. – Brady, B., et al.**: Nivolumab in previously untreated melanoma without BRAF mutation. *N Engl J Med*, 2015, 372, s. 320–330.

4 **Larkin, J. – Lao, C. D. – Urba, W. J., et al.**: Efficacy and safety of nivolumab in patients with BRAF V600 mutant and BRAF wild-type advanced melanoma: a pooled analysis of 4 clinical trials. *JAMA Oncol*, 2015, 1, s. 433–440.

5 **Ribas, A. – Hamid, O. – Daud, A., et al.**: Association of pembrolizumab with tumor response and survival among patients with advanced melanoma. *Jama*, 2016, 315, s. 1600–1609.

6 **Larkin, J. – Ascierto, P. A. – Dreno, B., et al.**: Combined vemurafenib and cobimetinib in BRAF-mutated melanoma. *N Engl J Med*, 2014, 371, s. 1867–1876.

7 **Long, G. V. – Stroyakovskiy, D. – Gogas, H., et al.**: Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma. *N Engl J Med*, 2014, 371, s. 1877–1888.

8 **Robert, C. – Karaszewska, B. – Schachter, J., et al.**: Improved overall survival in melanoma with combined dabrafenib and trametinib. *N Engl J Med*, 2015, 372, s. 30–39.

9 **Liszkay, G. –Gogas, H. – Mandalà, M., et al.**: Update on overall survival in COLUMBUS: A randomized phase III trial of encorafenib (ENCO) plus binimetinib (BINI) versus vemurafenib (VEM) or ENCO in patients with BRAF V600-mutant melanoma. *J Clin Oncol*, 2019, 37, suppl., s. 9512–9512.

10 **Schadendorf, D. – Hodi, F. S. – Robert, C., et al.**: Pooled analysis of long-term survival data from Phase II and Phase III Trials of ipilimumab in unresectable or metastatic melanoma. *J Clin Oncol*, 2015, 33, s. 1889–1894.

11 **Maio, M. – Grob, J. J. – Aamdal, S., et al.**: Five-year survival rates for treatment-naive patients with advanced melanoma who received ipilimumab plus dacarbazine in a phase III trial. *J Clin Oncol*, 2015, 33, s. 1191–1196.

12 **Long, G. V. – Flaherty, K. T. – Stroyakovskiy, D., et al.**: Dabrafenib plus trametinib versus dabrafenib monotherapy in patients with metastatic BRAF V600E/K-mutant melanoma: long-term survival and safety analysis of a phase 3 study. *Ann Oncol*, 2017, 28, s. 1631–1639.

13 **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.

14 **Dreno, B. – Ascierto, P. A. – McArthur, G. A., et al.**: Efficacy and safety of cobimetinib (C) combined with vemurafenib (V) in patients (pts) with BRAFV600 mutation-positive metastatic melanoma: analysis from the 4-year extended follow-up of the phase 3 coBRIM study. *J Clin Oncol*, 2018, 36, suppl., s. 9522–9522.

15 **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.

16 **Larkin, J. – Chiarion-Sileni, V. – Gonzalez, R., et al.**: Five-year survival with combined nivolumab and ipilimumab in advanced melanoma. *New Eng J Med*, 2019, 381, s. 1535–1546.

17 **Robert, C. – Ribas, A. – Schachter, J., et al.**: Pembrolizumab versus ipilimumab in advanced melanoma (KEYNOTE-006): post-hoc 5-year results from an open-label, multicentre, randomised, controlled, phase 3 study. *Lancet Oncol*, 2019 20, s. 1239–1251.

18 **Grob, J. J. – Amonkar, M. M. – Karaszewska, B., et al.**: Comparison of dabrafenib and trametinib combination therapy with vemurafenib monotherapy on health-related quality of life in patients with unresectable or metastatic cutaneous BRAF Val600-mutation-positive melanoma (COMBI-v): results of a phase 3, open-label, randomised trial. *Lancet Oncol*, 2015, 16, s. 1389–1398.

19 **Petrella, T. M. – Robert, C. – Richtig, E., et al.**: Patient-reported outcomes in KEYNOTE-006, a randomised study of pembrolizumab versus ipilimumab in patients with advanced melanoma. *Eur J Cancer*, 2017, 86, s. 115–124.

20 **Long, G. V. – Atkinson, V. – Ascierto, P. A., et al.**: Effect of nivolumab on health-related quality of life in patients with treatment-naive advanced melanoma: results from the phase III CheckMate 066 study. *Ann Oncol*, 2016, 27, s. 1940–1946.

21 **Balch, C. M. – Gershenwald, J. E. – Soong, S. J., et al.**: Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol*, 2009, 27, s. 6199–206.

22 **Weber, J. – Mandala, M. – Del Vecchio, M., et al.**: Adjuvant nivolumab versus ipilimumab in resected stage III or IV melanoma. *N Engl J Med*, 2017, 377, s. 1824–1835.

23 **Eggermont, A. M. M. – Blank, C. U. – Mandala, M., et al.**: Adjuvant pembrolizumab versus placebo in resected stage III melanoma. *N Engl J Med*, 2018, 378, s. 1789–1801.

24 **Long, G. V. – Hauschild, A. – Santinami, M., et al.**: Adjuvant dabrafenib plus trametinib in stage III BRAF-mutated melanoma. *N Engl J Med*, 2017, 377, s. 1813–1823.

Atezolizumab v léčbě nemalobuněčného karcinomu plic u předléčených pacientů

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1 **Horn, L. – Spigel, D. R. – Gettinger, S. N., et al.**: Clinical activity, safety and predictive biomarkers of the engineered antibody MPDL3280A (anti-PDL1) in non-small cell lung cancer (NSCLC): update from a phase la study. *J Clin Oncol*, 2015, 33, suppl., abstrakt 8029.

2 **Fehrenbacher, L. – Spira, A. – Ballinger, M., et al.**: Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, phase 2 randomised controlled trial. *Lancet*, 2016, 387, s. 1837–1846.

3 **Smith, D. A. – Vansteenkiste, J. F. – Fehrenbacher, L., et al.**: Updated survival and biomarker analyses of a randomized phase II study of atezolizumab vs docetaxel in 2L/3L NSCLC (POPLAR). *J Clin Oncol*, 2016, 34, suppl, abstrakt 9028.

4 **Rittmeyer, A. – Barlesi, F. – Waterkamp, D., et al.**: Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. *Lancet*, 2017, 389, s. 255–265.

5 **von Pawel, J. – Bordoni, R. – Satouchi, M., et al.**: Long-term survival in patients with advanced non-small-cell lung cancer treated with atezolizumab versus docetaxel: Results from the randomised phase III OAK study. *Eur J Cancer*, 2019, 107, s. 124–132.

Cílená onkologická léčba v éře komplexního genomického profilování

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1 **Horstmann, E. – McCabe, M. S. – Grochow, L., et al.**: Risks and benefits of phase 1 oncology trials, 1991 through 2002. *N Engl J Med*, 2005, 352, s. 895–904.

2 **Kurzrock, R. – Benjamin, R. S.**: Risks and benefits of phase 1 oncology trials, revisited. *N Engl J Med*, 2005, 352, s. 930–932.

3 **Tsimberidou, A. M. – Iskander, N. G. – Hong, D. S., et al.**: Personalized medicine in a phase I clinical trials program: the MD Anderson Cancer Center initiative. *Clin Cancer Res*, 2012, 18, s. 6373–6383.

4 **Khozin, S. – Blumenthal, G. M. – Zhang, L., et al.**: FDA approval: ceritinib for the treatment of metastatic anaplastic lymphomakinase-positive non-small cell lung cancer. *Clin Cancer Res*, 2015, 21, s. 2436–2439.

5 **Falchook, G. S. – Millward, M. – Hong, D., et al.**: BRAF inhibitor dabrafenib in patients with metastatic BRAF-mutant thyroid cancer. *Thyroid*, 2015, 25, s. 71–77.

6 **Wheler, J. – Janku, F. – Naing, A., et al.**: Cancer therapy directed by comprehensive genomic profiling: a single center study. *Cancer Res*, 2016, 76, s. 3690–3701.

7 **Henary, H. – Hong, D. S. – Falchook, G. S., et al.**: Melanoma patients in a phase I clinic: molecular aberrations, targeted therapy and outcomes. *Ann Oncol*, 2013, 24, s. 2158–2165.

8 **Chabner, B. A.**: Approval after phase I: ceritinib runs the three-minute mile. *Oncologist*, 2014, 19, s. 577–578.

9 Foundation Medicine Inc.: FoundationOne CDx™ Technical Information. Dostupné z: https://www.foundationmedicine.com/genomic-testing/foundation-one-cdx, vyhledáno 20. 3. 2020.

10 **Morganti, S. – Tarantino, P. – Ferraro, E., et al.**: Complexity of genome sequencing and reporting: next generation sequencing (NGS) technologies and implementation of precision medicine in real life. *Crit Rev Oncol Hematol*, 2019, 133, s. 171–182.

Bevacizumab v léčbě k platině rezistentního karcinomu ovaria/vejcovodu a primárně peritoneálního karcinomu – kazuistika

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1 **Fínek, J. – Zikán, M., et al.**: *Karcinom ovaria*. Farmakon Press, 2019.
2 **Pignata, S. – Pisano, C., et al.**: Treatment of recurrent epithelial ovarian cancer. *Cancer*, 2019, 125, s. 4609–4615.
3 **Pujade-Lauraine, E. – Hilpert, F. – Weber, B., et al.**: Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer – The AURELIA open – label randomised phase III trial. *J Clin Oncol*, 2014, 32, s. 1302–1308.
4 *Modrá kniha České onkologické společnosti*. Masarykův onkologický ústav, Brno, 2019.

Bevacizumab v léčbě recidivujícího karcinomu ovaria – předčasné ukončení úspěšné léčby – kazuistika

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1 **Fischerová, D. – Novotný, J. – Vítek, P., et al.**: Karcinom tuby, ovarií a primární peritoneální karcinom. In: Novotný, J. – Vítek, P. – Klebl, Z., et al.: *Onkologie v klinické praxi*. Praha, Mladá Fronta, 2016, s. 399–416.
2 **Chovanec, J.**: Cílená (biologická) léčba a její využití u karcinomu ovaria. *Acta Medicinae*, 2016, 1, s. 13–17.
3 **Pujade-Laurante, E. – Hilpert, F. – Weber, B., et al.**: Bevacizumab combinate with chemotherapy for platinum-resistantre current ovarian cancer: the AURELIA open-label randomised phase III trial. *J Clin Oncol*, 2014, 32, s. 1302–1308.
4 **Rooth, C.**: Ovarian cancer: risk factors, treatment and management. *Br J Nurs*, 2013, 22, s. 523–530.
5 *Modrá kniha České onkologické společnosti*. MOÚ Brno, aktualizace 25 (1. 3. 2019).

Biologická a cílená léčba mnohočetného myelomu

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1 **Nishimura, K. K. – Barlogie, B. – van Rhee, F., et al.**: Long-term outcomes after autologous stem cell transplantation for multiple myeloma. *Blood Adv*, 2020, 4, s. 422–431.
2 **Usmani, S. Z. – Hoering, A. – Cavo, M., et al.**: Clinical predictors of long-term survival in newly diagnosed transplanteligible multiple myeloma – an IMWG Research Project. *Blood Cancer J*, 2018, 8, s. 123.
3 **Palumbo, A. – Chanan-Khan, A. – Weisel, K., et al.**; CASTOR Investigators: Daratumumab, bortezomib, and dexamethasone for multiple myeloma. *N Engl J Med*, 2016, 375, s. 754–766.
4 **Dimopoulos, M. A. – Oriol, A. – Nahi, H., et al.**; POLLUX Investigators: Daratumumab, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*, 2016, 375, s. 1319–1331.
5 **Moreau, P. – Attal, M. – Hulin, C., et al.**: Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study. *Lancet*, 2019, 394, s. 29–38.
6 **Mateos, M. V. – Dimopoulos, M. A. – Cavo, M., et al.**; ALCYONE Trial Investigators: Daratumumab plus bortezomib, melphalan, and prednisone for untreated myeloma. *N Engl J Med*, 2018, 378, s. 518–528.
7 **Facon, T. – Kumar, S. – Plesner, T., et al.**; MAIA Trial Investigators: Daratumumab plus lenalidomide and dexamethasone for untreated myeloma. *N Engl J Med*, 2019, 380, s. 2104–2115.
8 **Martin, T. – Baz, R. – Benson, D. M., et al.**: A phase 1b study of isatuximab plus lenalidomide and dexamethasone for relapsed/refractory multiple myeloma. *Blood*, 2017, 129, s. 3294–3303.
9 **Attal, M. – Richardson, P. G. – Rajkumar, S. V., et al.**; ICARIA-MM study group: Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study. *Lancet*, 14. 11. 2019, pii: S0140-6736(19)32556–32555.
10 **Špička, I.**: Léčba mnohočetného myelomu – současné možnosti. *Acta medicinae*, 2017, 6, s. 56–62.
11 **Kazandjian, D. – Korde, N. – Mailankody, S., et al.**: Remission and progression-free survival in patients with newly diagnosed multiple myeloma treated with carfilzomib, lenalidomide, and dexamethasone: five-year follow-up of a phase 2 clinical trial. *JAMA Oncol*, 2018, 4, s. 1781–1783.
12 **Roussel, M. – Lauwers-Cances, V. – Robillard, N., et al.**: Frontline therapy with carfilzomib, lenalidomide, and dexamethasone (KRd) induction followed by autologous stem cell transplantation, Krd consolidation and lenalidomide maintenance in newly diagnosed multiple myeloma (NDMM) patients: primary results of the Intergroupe Francophone Du MyéLome (IFM) Krd phase II study. *Blood*, 2016, 128, s. 1142. Předneseno na ASH 2016 Annual Meeting, San Diego, CA, 3.–6. 12. 2016.
13 **Sonneveld, P. – Asselbergs, E. – Zweegman, S., et al.**: Phase 2 study of carfilzomib, thalidomide, and dexamethasone as induction/consolidation therapy for newly diagnosed multiple myeloma. *Blood*, 2015, 125, s. 449–456.
14 **Ali, S. A. – Shi, V. – Maric, I., et al.**: T cells expressing an anti-B-cell maturation antigen chimeric antigen receptor cause remissions of multiple myeloma. *Blood*, 2016, 128, s. 1688–1700.

Současnost a novinky v léčbě roztroušené sklerózy

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1 **Polman, C. H. – Reingold, S. C. – Banwell, B., et al.**: Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol*, 2011, 69, s. 292–302.
2 **Thompson, A. J. – Banwell, B. L. – Barkhoff, F., et al.**: Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*, 2018, 17, s. 162–173.
3 **Kappos, L. – Li, D. – Calabresi, P. A., et al.**: Ocrelizumab in relapsing-remitting multiple sclerosis a phase 2, randomised, placebo-controled, multicentre trial. *Lancet*, 2011, 378, s. 1779–1787.
4 **Brück, W.**: The pathology of multiple sclerosis is the reset of focalin flamatory demyelination with axonal damage. *J Neurol*, 2005, 252, suppl. 5, s. v3–v9.
5 **Milo, R.**: Therapeutic strategies targeting B-cells in multiple sclerosis. *Autoimmun Rev*, 2016, 15, s. 714–718.
6 **Krejsek, J.**: Biologická terapie ocrelizumabem (anti-CD20) je překvapivě klinicky účinná u nemocných s roztroušenou sklerózou mozkomíšní. *Neurol Praxi*, 2017, 18, s. 403–407.
7 **Winger, R. C. – Zamvil, S. S.**: Antibodies in multiple sclerosis oligoclonal bands target debris. *Proc Natl Acad Sci U.S.A*, 2016, 113, s. 7696–7698.
8 **Lehmann-Horn, K. – Kronsbein, H. C. – Weber, M. S.**: Targeting B cells in the treatment of multiple sclerosis: recent advances and remaining challenges. *Ther Advneurol Disord*, 2013, 6, s. 161–173.
9 **Hauser, S. L. – Bar-Or, A. – Giovannoni, G., et al.**; for the OPERA I and OPERA II Clinical Investigators: Ocrelizumab versus interferon beta-1a in relapsing multiple sclerosis. *N Engl J Med*, 2017, 376, s. 221–234.
10 **Motalban, X. – Hauser, S. L. – Kappos, L., et al.**; for the ORATORIO Clinical Investigators: Ocrelizumab versus placebo in primary progressive multiple sclerosis. *N Engl J Med*, 2017, 376, s. 209–220.
11 **Kubala Havrdová, E.**: Ocrelizumab v léčbě roztroušené sklerózy. *Neurol Praxi*, 2017, 18, s. 287–290.
12 **Sorensen, P. S. – Blinkenberg, M.**: The potencial role for ocrelizumab in the treatment of multiple sclerosis: current evidence and future prospects. *Ther Adv Neurol Disord*, 2016, 9, s. 44–52.
13 **Winkelmann, A. – Loebermann, M. – Reisinger, E. C., et al.**: Disease modifying therapies and infectious risks in multiple sclerosis. *Nat Rev Neurol*, 2016, 12, s. 217–233.
14 **Hawker, K. – O'Connor, P. – Freedman, M. S., et al.**: Rituximab in patiens with primary progresive multiple sclerosis: results of a randomised double-blind placebo-controled multicenter trial. *Ann Neurol*, 2009, 66, s. 460–471.
15 **Margulis, A. V. – Andrews, E. B. – Hernandez-Diaz, S., et al.**: Designs of a multi-source post-marketing study to evaluate pregnancy and infant outcomes in women with multiple sclerosis who exposed to ocrelizumab during, or within 6 months before, pregnancy. *AAN*, 2018, P372.
16 **Wormser, D. – Engel, P. – Hahn, K., et al.**: Design of the Ocrelizumab Pregnancy Registry to assess maternal, fetal and infant outcomes in women with multiple sclerosis who were exposed to ocrelizumab during, or within 6 months before, pregnancy. *AAN*, 2018, P367.
17 **Chitnis, T. – Arnold, D. L. – Banwell, B., et al.**; PARADIGMS Study Group: Trial of fingolimod versus interferon beta-1a in pediatric multiple sclerosis. *N Engl J Med*, 2018, 379, s. 1017–1027.
18 **Selmaj, K. – Li, D. K. – Hartung, H. P., et al.**: Siponimod for patients with relapsing-remitting multiple sclerosis (BOLD): an adaptive, dose-ranging, randomised, phase 2 study. *Lancet Neurol*, 2013, 12, s. 756–767.
19 **Kappos, L. – Bar-Or, A. – Cree, B. A. C., et al.**: Siponimod versus placebo in secondary progressivve multiple sclerosis (EXPAND); a double-blind, randomised, phase 3 study. *Lancet*, 2018, 391, s. 1263–1273.
20 **Al-Salam, Z. T.**: Siponimod: first global approval. *Drugs*, 2019, 79, s. 1009–1015.
21 **Gold, R. – Kappos, L. – Bar-Or, A., et al.**: Efficacy of siponimod in secondary progressive multiple sclerosis patients with active disease: the EXPAND Study subgroup analysis. Stockholm, ECTRIMS Online Library, Gold R. 09/12/19, 279110; P750.
22 OCREVUS, SPC. Dostupné z: https://www.ema.europa.eu/en/documents/product-information/ocrevus-epar-product-information_cs.pdf, vyhledáno 14. 2. 2020.

Diagnostika a léčba sekundárně progresivní roztroušené sklerózy

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1 **Lassmann, H.**: Targets of therapy in progressive MS. *Multiple Scler J*, 2017, 23, s. 1593–1599.
2 **Lublin, F. D.**: New multiple sclerosis phenotypic classification. *European Neurology*, 2014, 72, suppl. 1, s. 1–5.
3 **Tremlett, H. – Zhao, Y. – Devonshire, V.**: Natural history of secondary-progressive multiple sclerosis. *MJS*, 2008, s. 314–324.
4 **Lorscheider, J. – Buzzard, K. – Jokubaitis, V., et al.**: Defining secondary progressive multiple sclerosis. *Brain*, 2016, 139, s. 2395–2405.
5 **Bergsland, N. – Horakova, D. – Dwyer, M. G.**: Subcortical and cortical gray matter atrophy in a large sample of patients with clinically isolated syndrome and early relapsing-remitting multiple sclerosis. *Am J Neuroradiol*, 2012, 33, s. 1573–1578.
6 **Bhatia, R. – Singh, N.**: Can we treat secondary progressive multiple sclerosis now? *Ann Indian Acad Neurol*, 2019, 22, s. 131–136.
7 **Gentile, A. – Musella, A. – Bullitta, S.**: Siponimod (BAF312) prevents synaptic neurodegeneration in experimental multiple sclerosis. *J Neuroinflammation*, 2016, 13, s. 207.
8 **Kappos, L. – Bar-Or, A. – Cree, B. A. C.**: Siponimod versus placebo in secondary progressive multiple sclerosis (EXPAND): a double-blind, randomised, phase 3 study. *Lancet*, 2018, 391, s. 1263–1273.

Biologická léčba migrény

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1 Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3. vydání. *Cephalalgia*, 2018, 38, s. 1–211.
2 **Kotas, R.**: Současný pohled na patofyziologii migrény. *Cesk Slov Neurol N*, 2011, 74/107, s. 654–661.
3 **Cameron, C.**: Triptans in the acute treatment of migraine: a systematic review and network meta-analysis. *Headache*, 2015, 55, suppl. 4, s. 221–235.
4 **Tepper, S. J.**: History and review of anti-calcitonin gene-related peptide (CGRP) therapies: From translational research to treatment. *Headache*, 2018, 58, suppl. 3, s. 238–275.
5 **Cameron, C. – Kelly, S. – Hsieh, S. C., et al.**: Triptans in the acute treatment of migraine: a systematic review and network meta-analysis. *Headache*, 2015, 55, suppl. 4, s. 221–235.
6 **Kotas, R.**: *Bolest hlavy v klinické praxi*. Praha, Maxdorf, 2015.
7 **Nežádal, T.**: Moderní léčba migrény. *Remédia*, 2018, 28, s. 1–5.
8 **Dodick, D. W. – Ashina, M. – Brandes, J. L., et al.**: ARISE: A phase 3 randomized trial of erenumab for episodic migraine. *Cephalalgia*, 2018, 38, s. 1026–1037.
9 **Tepper, S. J. – Diener, H.-Ch. – Ashina, M., et al.**: Efficacy of erenumab for the treatment of patients with chronic migraine in presence of medication over use. *Cephalalgia*, 2017, 37, suppl. 1, s. 33–34.
10 **Silberstein, S. D. – McAllister, P. – Ning, X., et al.**: Safety and tolerability of fremanezumab for the prevention of migraine: a pooled analysis of phases 2b and 3 clinical trials. *Headache*, 2019, 59, s. 880–890.

JAK/STAT inhibitory u revmatoidní artritidy

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1 **Šenolt, L.**: Rheumatoid arthritis. *Vnitr Lek*, 2018, 64, s. 98–106.
2 **Romano, S. – Salustri, E. – Ruscitti, P., et al.**: Cardiovascular and metabolic comorbidities in rheumatoid arthritis. *Curr Rheumatol Rep*, 2018, 20, s. 81.
3 **Taylor, P. C. – Balsa Criado, A., et al.**: How to get the most from methotrexate (MTX) treatment for your rheumatoid arthritis patient? MTX in the treat-to-target strategy. *J Clin Med*, 2019, 8, pii: E515.
4 **Šenolt, L. – Mann, H. – Závada, J. – Pavelka, K. – Vencovský, J.**: Doporučení České revmatologické společnosti pro farmakoterapii revmatoidní artritidy 2017. *Česká revmatologie*, 2017, 25, s. 3–18.
5 **Smolen, J. S. – Breedveld, F. C. – Burmester, G. R., et al.**: Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. *Ann Rheum Dis*, 2016, 75, s. 3–15.
6 **Okada, Y. – Wu, D. – Trynka, G., et al.**: Genetics of rheumatoid arthritis contributes to biology and drug discovery. *Nature*, 2014, 506, s. 376–381.
7 **Šenolt, L.**: Emerging therapies in rheumatoid arthritis: focus on monoclonal antibodies. F1000Res, 30. 8. 2019, 8. pii: F1000 Faculty Rev-1549.
8 **Wu, J. – Zhu, Z. – Yu, Q., et al.**: Tyrosine kinase inhibitors for the treatment of rheumatoid arthritis: phase I to II clinical trials. *Expert Opin Investig Drugs*. 2019, 28, s. 1113–1123.
9 **Hirahara, K. – Schwartz, D. – Gadina, M., et al.**: Targeting cytosine signaling in autoimmunity: back to the future and beyond. *Curr Opin Immunol*, 2016, 43, s. 89–97.
10 **D'Aura Swanson, C. – Paniagua, R. T. – Lindstrom, T. M., et al.**: Tyrosine kinases as targets for the treatment of rheumatoid arthritis. *Nat Rev Rheumatol*, 2009, 5, s. 317–324.
11 **Davis, M. I. – Hunt, J. P. – Herrgard, S., et al.**: Comprehensive analysis of kinase inhibitor selectivity. *Nat Biotechnol*, 2011, 29, s. 1046–1051
12 **Genovese, M. C. – van der Heijde, D. M. – Keystone, E. C., et al.**: A phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group study of 2 dosing regimens of fostamatinib in patients with rheumatoid arthritis with anadequate response to a tumor necrosis factor-α antagonist. *J Rheumatol*, 2014, 41, s. 2120–2128.
13 **Shuai, K. – Ziemiecki, A. – Wilks, A. F., et al.**: Polypeptide signalling to the nukleus through tyrosine phosphorylation of Jak and Stat proteins. *Nature*, 1993, 366, s. 580–583.
14 **Briscoe, J. – Guschin, D. – Müller, M.**: Signal transduction. Just another signalling path way. *Curr Biol*, 1994, 4, s. 1033–1035.
15 **Yamaoka, K. – Saharinen, P. – Pesu, M., et al.**: The Janus kinases (Jaks). *Genome Biol*, 2004, 5, s. 253.
16 **Walker, J. G. – Smith, M. D.**: The Jak-STAT pathway in rheumatoid arthritis. *J Rheumatol*, 2005, 32, s. 1650–1653.
17 **Migita, K. – Izumi, Y. – Torigoshi, T., et al.**: Inhibition of Janus kinase/signal transducer and activator of transcription (JAK/STAT) signalling pathway in rheumatoid synovial fibroblasts using small molekule compounds. *Clin Exp Immunol*, 2013, 174, s. 356–363.
18 **Gadina, M. – Le, M. T. – Schwartz, D. M., et al.**: Janus kinases to jakinibs: from basic insights to clinical practice. *Rheumatology* (Oxford), 2019, 58, suppl. 1, s. i4–i16.
19 **O'Shea, J. J. – Husa, M. – Li, D., et al.**: Jak3 and the pathogenesis of severe cosine immunodeficiency. *Mol Immunol*, 2004, 41, s. 727–737.
20 **Walker, J. G. – Ahern, M. J. – Coleman, M., et al.**: Changes in synovial tissue Jak-STAT expression in rheumatoid arthritis in response to successful DMARD treatment. *Ann Rheum Dis*, 2006, 65, s. 1558–1564.
21 **Yamaoka, K.**: Janus kinase inhibitors for rheumatoid arthritis. *Curr Opin Chem Biol*, 2016, 32, s. 29–33.
22 **Westhovens, R.**: Clinical efficacy of new JAK inhibitors under development. Just more of the same? *Rheumatology* (Oxford), 2019, 58, suppl. 1, s. i27–i33.
23 **Taylor, P. C.**: Clinical efficacy of launched JAK inhibitors in rheumatoid arthritis. *Rheumatology* (Oxford), 2019, 58, suppl. 1, s. i17–i26.
24 **Changelian, P. S. – Flanagan, M. E. – Ball, D. J., et al.**: Prevention of organ allograft rejection by a specific Janus kinase 3 inhibitor. *Science*, 2003, 302, s. 875–878.
25 **Biggioggero, M. – Becciolini, A. – Crotti, C., et al.**: Upadacitinib and filgotinib: the role of JAK1 selective inhibition in the treatment of rheumatoid arthritis. *Drugs Context*, 2019, 8, s. 212595.
26 **Ogata, A. – Kato, Y. – Higa, S., et al.**: IL-6 inhibitor for the treatment of rheumatoid arthritis: A comprehensive review. *Mod Rheumatol*, 2019, 29, s. 258–267.
27 **Lee, E. B. – Fleischmann, R. – Hall, S., et al.**: Tofacitinib versus methotrexate in rheumatoid arthritis. *N Engl J Med*, 2014, 370, s. 2377–2386.
28 **Fleischmann, R. – Mysler, E. – Hall, S., et al.**; ORAL Strategy investigators: Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy): a phase 3b/4, double-blind, head-to-head, randomised controlled trial. *Lancet*, 2017, 390, s. 457–468.
29 **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 Rheumatol*, 2017, 69, s. 506–517.
30 **Taylor, P. C. – Keystone, E. C. – van der Heijde, D., et al.**: Baricitinib versus placebo or adalimumab in rheumatoid arthritis. *N Engl J Med*, 2017, 376, s. 652–662.
31 **Strand, V. – Lee, E. B. – Fleischmann, R., et al.**: Tofacitinib versus methotrexate in rheumatoid arthritis: patient-reported outcomes from the randomised phase III ORAL Start trial. *RMD Open*, 2016, 2, e000308.
32 **Keystone, E. C. – Taylor, P. C. – Tanaka, Y., et al.**: Patient-reported outcomes from a phase 3 study of baricitinib versus placebo or adalimumab in rheumatoid arthritis: secondary analyses from the RA-BEAM study. *Ann Rheum Dis*, 2017, 76, s. 1853–1861.
33 **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.
34 **Harigai, M.**: Growing evidence of the safety of JAK inhibitors in patients with rheumatoid arthritis. *Rheumatology* (Oxford), 2019, 58, suppl. 1, s. i34–i42.
35 **Atzeni, F. – Masala, I. F. – di Franco, M., et al.**: Infections in rheumatoid arthritis. *Curr Opin Rheumatol*, 2017, 29, s. 323–330.
36 **Blum, A. – Adawi, M.**: Rheumatoid arthritis (RA) and cardiovascular disease. *Autoimmun Rev*, 2019, 18, s. 679–690.
37 **Taylor, P. C. – Weinblatt, M. E. – Burmester, G. R., et al.**: Cardiovascular safety during treatment with baricitinib in rheumatoid arthritis. *Arthritis Rheumatol*, 2019, 71, s. 1042–1055.
38 **Desai, R. J. – Pawar, A. – Weinblatt, M. E., et al.**: Comparative risk of venous thromboembolism in rheumatoid arthritis patients receiving tofacitinib versus those receiving tumor necrosis factor inhibitors: an observational cohort study. *Arthritis Rheumatol*, 2019, 71, s. 892–900.
39 **Liang, H. – Danwada, R. – Guo, D. – Curtis, J. R., et al.**: Incidence of in patient venous thromboembolism in treated patients with rheumatoid arthritis and the association with switching biologicor targeted synthetic disease-modifying anti rheumatic drugs (DMARDs) in the-real-worldsetting. *RMD Open*, 2019, 5, e001013.
40 **Fragoulis, G. E. – McInnes, I. B. – Siebert, S.**: JAK-inhibitors. New players in the field of immune-mediated diseases, beyond rheumatoid arthritis. *Rheumatology* (Oxford), 2019, 58, suppl. 1, s. i43–i54.

Nízký výskyt intersticiální plicní nemoci u pacientů s revmatoidní artritidou: souhrnná post hoc analýza dat z programu klinického vývoje tofacitinibu

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1 **Curtis, J. R. – Sarsour, K. – Napalkov, P., et al.**: Incidence and complications of interstitial lung disease in users of tocilizumab, rituximab, abatacept and anti-tumor necrosis factor α agents, a retrospective cohort study. *Arthritis Res Ther*, 2015, 17, s. 319.
2 **Furukawa, H. – Oka, S. – Shimada, K., et al.**: Genetics of interstitial lung disease: vol de nuit (night flight). *Clin Med Insights Circ Respir Pulm Med*, 2015, 9, suppl. 1, s. 1–7.
3 **Citera, G. – Mysler, E. – Madariaga, H., et al.**: Low interstitial lung disease event rate in patients with rheumatoid arthritis: pooled post hoc analysis of data from the Tofacitinib Clinical Development Program. 2018 ACR/ARHP Annual Meeting, abstrakt 525.

Bezpečnost etanerceptu u starších osob s revmatoidní artritidou: data z reálné klinické praxe

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1 **Taylor, P. C. – Moore, A. – Vasilescu, R., et al.**: A structured literature review of the burden of illness and unmet needs in patients with rheumatoid arthritis: a current perspective. *Rheumatol Int*, 2016, 36, s. 685–695.
2 **Smolen, J. S. – Aletaha, D. – McInnes, I. B.**: Rheumatoid arthritis. *Lancet*, 2016, 388, s. 2023–2038.
3 **Nam, J. L. – Takase-Minegishi, K. – Ramiro, S., et al.**: Efficacy of biological disease modifying antirheumatic drugs: a systematic literature review informing the 2016 update of the EULAR recommendations for the management of rheumatoid arthritis. *Ann Rheum Dis*, 2017, 76, s. 1113–1136.
4 **Dougados, M. – Soubrier, M. – Antunez, A., et al.**: Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, crosssectional study (COMORA). *Ann Rheum Dis*, 2014, 73, s. 62–68.
5 **Taylor, P. C. – Feldmann, M.**: Anti-TNF biologic agents: still the therapy of choice for rheumatoid arthritis. *Nat Rev Rheumatol*, 2009, 5, s. 578–582.
6 **Humphreys, J. – Hyrich, K. – Symmons, D.**: What is the impact of biologic therapies on common co-morbidities in patients with rheumatoid arthritis? *Arthritis Res Ther*, 2016, 18, s. 282.
7 **Edwards, C. J. – Roshak, K. – Bukowski, J. F., et al.**: Efficacy and safety of etanercept in elderly patients with rheumatoid arthritis: a post-hoc analysis of randomized controlled trials. *Drugs Aging*, 2019, 36, s. 853–862.
8 **Edwards, C. J. – Bukowski, J. F. – Burns, S. M., et al.**: An analysis of real-world data on the safety of etanercept in older patients with rheumatoid arthritis. *Drugs Aging*, 2020, 37, s. 35–41.
9 **Bathon, J. M. – Fleischmann, R. M. – Van der Heijde, D., et al.**: Safety and efficacy of etanercept treatment in elderly subjects with rheumatoid arthritis. *J Rheumatol*, 2006, 33, s. 234–243.
10 **Galloway, J. B. – Hyrich, K. L. – Mercer, L. K., et al.**: Anti-TNF therapy is associated with an increased risk of serious infections in patients with rheumatoid arthritis especially in the first 6 months of treatment: updated results from the British Society for Rheumatology Biologics Register with special emphasis on risks in the elderly. *Rheumatology*, 2011, 50, s. 124–131.

Dna a použití febuxostatu v algoritmu léčby

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1 **Dalbeth, N. – Merriman, T. R. – Stamp, L. K.**: Gout. *Lancet*, 2016, 388, s. 2039–2052.
2 **Richette, P. – Doherty, M. – Pascual, E., et al.**: 2018 updated European League Against Rheumatism evidence-based recommendations for the diagnosis of gout. *Ann Rheum Dis*, 2020, 79, s. 31–38.
3 **Zhu, Y. – Pandya, B. J. – Choi, H. K.**: Comorbidities of gout and hyperuricemia in the US general population: NHANES 2007–2008. *Am J Med*, 2012, 125, s. 679–687 e671.
4 **Choi, H. K. – Curhan, G.**: Independent impact of gout on mortality and risk for coronary heart disease. *Circulation*, 2007, 116, s. 894–900.
5 **Richette, P. – Doherty, M. – Pascual, E., et al.**: 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis*, 2017, 76, s. 29–42.
6 **Saag, K. G. – Fitz-Patrick, D. – Kopicko, J., et al.**: Lesinurad combined with allopurinol: a randomized, double-blind, placebo-controlled study in gout patients with an inadequate response to standard-of-care allopurinol (a US-Based Study). *Arthritis & Rheumatology*, 2017, 69, s. 203–212.
7 **Becker, M. A. – Schumacher, H. R. Jr., – Wortmann, R. L., et al.**: Febuxostat, a novel nonpurine selective inhibitor of xanthine oxidase: a twenty-eight-day, multicenter, phase II, randomized, double-blind, placebo-controlled, dose-response clinical trial examining safety and efficacy in patients with gout. *Arthritis Rheum*, 2005, 52, s. 916–923.
8 **Schumacher, H. R. Jr., – Becker, M. A. – Lloyd, E., et al.**: Febuxostat in the treatment of gout: 5-yr findings of the FOCUS efficacy and safety study. *Rheumatology* (Oxford), 2009, 48, s. 188–194.
9 **Becker, M. A. – Schumacher, H. R. Jr., – Wortmann, R. L., et al.**: Febuxostat compared with allopurinol in patients with hyperuricemia and gout. *N Engl J Med*, 2005, 353, s. 2450–2461.
10 **Becker, M. A. – Schumacher, H. R. – Espinoza L. R., et al.**: The urate-lowering efficacy and safety of febuxostat in the treatment of the hyperuricemia of gout: the CONFIRMS trial. *Arthritis Res Ther*, 2010, 12, s. R63.
11 **Kimura, K. – Hosoya, T. – Uchida, S., et al.**: Febuxostat therapy for patients with stage 3 CKD and asymptomatic hyperuricemia: a randomized trial. *Am J Kidney Dis*, 2018, 72, s. 798–810.
12 **Tojimbara, T. – Nakajima, I. – Yashima, J., et al.**: Efficacy and safety of febuxostat, a novel nonpurine selective inhibitor of xanthine oxidase for the treatment of hyperuricemia in kidney transplant recipients. *Transplant Proc*, 2014, 46, s. 511–513.

Biosimilars: switch a lékové formy

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1 **Strojil, J.**: Biosimilars – specifika schvalovacího procesu v EU. *Klin Farmakol Farm*, 2014, 28, s. 14–18.
2 **Uhlig, T. – Goll, G. L.**: Reviewing the evidence for biosimilars: keyinsights, lessons learned and future horizons. *Rheumatology* (Oxford), 2017, 56, suppl. 4, s. iv49–iv62.
3 **Usach, I. – Martinez, R. – Festini, T. – Peris, J. E.**: Subcutaneous injection of drugs: literature review of factors influencing pain sensation at the injection site. *Adv Ther*, 2019, 36, s. 2986–2996.
4 **Erskine, D.**: Update on development of biosimilar versions of adalimumab with particular focus on excipients and injections interactions. Specialist Pharmacy Service NHS, publikováno 18. 1. 2019, update 25. 2. 2019. Dostupné z: https://www.sps.nhs.uk/articles/update-on-development-of-biosimilar-versions-of-adalimumab-with-particular-focus-on-excipients-and-injection-site-reactions/, vyhledáno 6. 2. 2020.

Biologická léčba systémového lupus erythematodes

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1 **Navarra, S. V. – Guzmán, R. M. – Gallacher, A. E., et al.**; BLISS-52 Study Group: Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial. *Lancet*, 2011, 377, s. 721–731.
2 **Furie, R. – Petri, M. – Zamani, O., et al.**; BLISS-76 Study Group: A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocytes timulator, in patients with systemic lupus erythematosus. *Arthritis Rheum*, 2011, 63, s. 3918–3930.
3 **Dooley, M. A. – Houssiau, F. – Aranow, C., et al.**: Effect of belimumab tratment on renal outcomes: results from the phase 3 belimumab clinical trials in patients with SLE. *Lupus*, 2013, 22, s. 63–72.
4 **Sheikh, S. – Scheinberg, M. – Wei, C. C., et al.**: Adverse events of special interest, SLE medication utilization, hospitalizations, and organ damage: results from a phase 4, randomized, double-blind, placebo controlled, 52 week study of belimumab in adults with active, auto antibody-positive SLE. Abstract. *Arthritis Rheumatol*, 2019, 71, suppl. 10, s. 858.
5 **Trentin, F. – Gatto, M. – Zen, M., et al.**: Effectiveness, tolerabilty and safety of belimumab in patients with refractory SLE: a review of observational clinical – practice – based studies. *Clin Rev Allergy Immunol*, 2018, 54, s. 331–343.
6 **Horák, P. – Tegzová, D. – Závada, J., et al.**: Doporučení ČRS pro léčbu nemocných se SLE. *Čes Revmatol*, 2013, 21, s. 110–122.
7 **Merrill, J. T. – Neuwelt, C. M. – Wallace, D. J., et al.**: Efficacy and safety of rituximab in moderately-to-severely active systemic lupus erythematosus: the randomized, double-blind, phase II/III systemic lupus erythematosus evaluation of rituximab trial. *Arthritis Rheum*, 2010, 62, s. 222–233.
8 **Rovin, B. H. – Furie, R. – Latinis, K., et al.**; LUNAR Investigator Group: Efficacy and safety of rituximab in patients with active proliferative lupus nephritis: the Lupus Nephritis Assessment with Rituximab study. *Arthritis Rheum*, 2012, 64, s. 1215–1226.
9 **Condon, M. B. – Ashby, D. – Pepper, R. J., et al.**: Prospective observational single-centre cohort study to evaluate the effectiveness of treating lupus nephritis with rituximab and mycophenolate mofetil but no oral steroids. *Ann Rheum Dis*, 2013, 72, s. 1280–1286.
10 **Roccatello, D. – Sciascia, S. – Baldovino, S., et al.**: A 4-year observation in lupus nephritis patients treated with an intensified V-lymphocyte depletion without immunosuppressive maintenance treatment – clinical response compared to literature and immunological re-assessment. *Autommunuty Rev*, 2015, 14, s. 1123–1130.
11 **Dall'Era, M. – Aranow, C. – Byron, M., et al.**: Phase 2 trial of induction therapy with anti-CD20 (rituximab) followed by maintenance therapy with anti-BAFF (belimumab) in patients with active lupus nephritis. Abstract. *Arthritis Rheumatol*, 2019, 71, suppl. 10, s. 1870.
12 **Wallace, D. J. – Gordon, C. – Strand, V., et al.**: Efficacy and safety of epratuzumab in patients with moderate/severe flaring systemic lupus erythematosus: results from two randomized, double-blind, placebo-controlled, multicentre studies (ALLEVIATE) and follow-up. *Rheumatology* (Oxford), 2013, 52, s. 1313–1322.
13 **Wallace, D. J. – Kalunian, K. – Petri, M. A., et al.**: Efficacy and safety of epratuzumab in patients with moderate/severe active systemic lupus erythematosus: results from EMBLEM, a phase IIb, randomised, double-blind, placebo-controlled, multicentre study. *Ann Rheum Dis*, 2014, 73, s. 183–190.
14 **Clowse, M. E. B. – Wallace, D. J. – Furie, R., et al.**: Efficacy and safety of epratuzumab in patients with moderate-to-severe systemic lupus erythematosus: results from two phase 3 randomized, placebo-controlled trials. *Arthritis Rheumatol*, 2015, 67, suppl. 10, s. 4L.
15 **Mysler, E. F. – Spindler, A. J. – Guzman, R., et al.**: Efficacy and safety of ocrelizumab in active proliferative lupus nephritis: results from a randomized, double-blind, phase III study. *Arthritis Rheum*, 2013, 65, s. 2368–2379.
16 **Isenberg, D. – Gordon, C. – Licu, D., et al.**: Efficacy and safety of atacicept for prevention of flares in patients with moderate-to-severe systemic lupus erythematosus (SLE): 52-week data (APRIL-SLE randomised trial). *Ann Rheum Dis*, 2015, 74, s. 2006–2015.
17 **Furie, R. A. – Leon, G. – Thomas, M., et al.**: PEARL-SC Study. A phase 2, randomised, placebo-controlled clinical trial of blisibimod, an inhibitor of B cell activating factor, in patients with moderate-to-severe systemic lupus erythematosus, the PEARL-SC study. *Ann Rheum Dis*, 2015, 74, s. 1667–1675.
18 **Merrill, J. T. – Strand, V. – Hislop, C., et al.**: AB0412 exploratory results from the Bliss and Illuminate trials support the design ofthe CHABLIS-SC1 trial, a randomized, double-blind, placebo-controlled phase 3 study to evaluace the efficacy and safety of blisibimod administration in subjects with systemic lupus erythematosus. *Ann Rheum Dis*, 2016, 75, suppl. 2, s. 1047.
19 **Isenberg, D. A. – Petri, M. – Kalunian, K., et al.**: Efficacy and safety of subcutaneous tabalumab in patients with systemic lupus erythematosus: results from ILLUMINATE-1, a 52-week, phase III, multicentre, randomised, double-blind, placebo-controlled study. *Ann Rheum Dis*, 2016, 75, s. 323–331.
20 **Merrill, J. T. – van Vollenhoven, R. F. – Buyon, J. P., et al.**: Efficacy and safety of subcutaneous tabalumab, a monoclonal antibody to B-cell activating factor, in patients with systemic lupus erythematosus:

results from ILLUMINATE-2, a 52-week, phase III, multicentre, randomised, double-blind, placebo-controlled study. *Ann Rheum Dis*, 2016, 75, s. 332–340.
21 The ACCESS Trial Group: Treatment of lupus nephritis with abatacept: The Abatacept and Cyclophosphamide Combination Efficacy and Safety Study. *Arthritis Rheumatol*, 2014, 66, s. 3096–3104.
22 **Illei, G. G. – Shirota, Y. – Yarboro, C. H., et al.**: Tocilizumab in systemic lupus erythematosus: data on safety, preliminary efficacy, and impact on circulating plasma cells from an open-label phase I dosage-escalation study. *Arthritis Rheum*, 2010, 62, s. 542–552.
23 **Szepietowski, J. C. – Nilganuwong, S. – Wozniacka A., et al.**: Phase I, randomized, double-blind, placebo-controlled, multiple intravenous, dose-ascending study of sirukumab in cutaneous or systemic lupus erythematosus. *Arthritis Rheum*, 2013, 65, s. 2661–2671.
24 **Rovin, B. H. – van Vollenhoven, R. F. – Aranow, C., et al.**: A multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of treatment with sirukumab (CNTO 136) in patients with active lupus nephritis. *Arthritis Rheumatol*, 2016, 68, s. 2174–2183.
25 **Khamashta, M. – Merrill, J. T. – Werth, V. P., et al.**; CD1067 study investigators: Sifalimumab, an anti-interferon-α monoclonal antibody, in moderate to severe systemic lupus erythematosus: a randomised, double-blind, placebo-controlled study. *Ann Rheum Dis*, 2016, 75, s. 1909–1916.
26 **McBride, J. M. – Jiang, J. – Abbas, A. R., et al.**: Safety and pharmacodynamics of rontalizumab in patients with systemic lupus erythematosus: results of a phase I, placebo-controlled, double-blind, dose-escalation study. *Arthritis Rheum*, 2012, 64, s. 3666–3676.
27 **Merrill, J. T. – Furie, R. – Werth, V. P., et al.**: Anifrolumab reduces disease activity in multiple organ domains in moderate to severe systemic lupus erythematosus (SLE). *Ann Rheum Dis*, 2016, 75, suppl. 2, s. 293.
28 **Furie, R. – Morand, E. – Bruce, I., et al.**: Abstract. A phase 3 randomized controlled trial of anifrolumab in patients with moderate to severe systemic lupus eythematosus. *Arthritis Rheumatol*, 2019, 71, suppl. 10, s. 1763.
29 **Werth, V. P. – Fiorentino, D. – Sullivan, B. A., et al.**: Brief report: Pharmacodynamics, safety, and clinical efficacy of AMG 811, a human anti-interferon-γ antibody, in patients with discoid lupus erythematosus. *Arthritis Rheumatol*, 2017, 69, s. 1028–1034.

Biologická léčba astmatu v roce 2020

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1 **Hekking, P.-P. W., et al.**: *J Allergy Clin Immunol*, 2015, 135, s. 896–902.
2 **Barnes, P. J. – Woolcock, A. J.**: Difficult asthma. *Eur Respir J*, 1998, 12, s. 1209–1218.
3 **Busse, W. W. – Banks-Schlegel, S. – Wenzel, S. E.**: Pathophysiology of severe asthma. *J Allergy ClinImmunol*, 2000, 106, s. 1033–1042.
4 **O'Byrne, P. M. – Naji, N. – Gauvreau, G. M.**: Severe asthma: future treatments. *Clin Exp Allergy*, 2012, 42, s. 706–711.
5 GINA (Global Initiative for Asthma). Global Strategy for Asthma Management and Prevention, 2019, https://ginasthma.org.
6 **Teřl, M. – Čáp, P. – Sedlák, V., et al.**: Doporučený postup diagnostiky a léčby astmatu. In: *Doporučené postupy v pneumologii*. Maxdorf, 2019.
7 **de Groot, J. C. – Brinke, A. – Bel, E.**: Management of the patient with eosinophilic asthma: a new era begins. *ERJ Open Res*, 2015, 1:00024-2015, DOI: 10.1183/23120541.00024-2015.
8 Dostupné z: http://www.sukl.cz/modules/medication/search.php.
9 **Noonan, M. – Korenblat, P. – Mosesova, S., et al.**: Dose-ranging study of lebrikizumab in asthmatic patients not receiving inhaled steroids. *J Allergy Clin Immunol*, 2013, 132, s. 567–574.
10 **Piper, E. – Brightling, C. – Niven, R., et al.**: A phase II placebo-controlled study of tralokinumab in moderate-to-severe asthma. *Eur Respir J*, 2013, 41, s. 330–338.