Cena České hematologické společnosti za nejlepší původní vědeckou práci a monografii v oboru hematologie v roce 2022

Výbor České hematologické společnosti udělil Cenu ČHS za nejlepší původní vědeckou práci v roce 2022 ve výši 30 000,- Kč

doc. MUDr. Tomáši Jelínkovi, Ph.D. z Kliniky hematoonkologie LF OU a FN Ostrava za práci:

Jelínek T, Bezděková R, Žihala D, Ševčíková T, Anilkumar Sithara A, Pospíšilová L, Ševčíková S, Poláčková P, Štork M, Knechtová Z, Venglář O, Kapustová V, Popková T, Muroňová L, Chyra Z, Hrdinka M, Šimíček M, Garcés JJ, Puig N, Cedena MT, Jurczyszyn A, Castillo JJ, Penka M, Radocha J, Mateos MV, San-Miguel JF, Paiva B, Pour L, Říhová L, **Hájek R.** More Than 2% of Circulating Tumor Plasma Cells Defines Plasma Cell Leukemia-Like Multiple Myeloma. **J Clin Oncol.** 2023 Mar 1;41(7):1383-1392. doi: 10.1200/JCO.22.01226. Epub 2022 Oct 31. IF 44,54.

SUMMARY: **Purpose:** Primary plasma cell leukemia (PCL) is the most aggressive monoclonal gammopathy. It was formerly characterized by ≥ 20% circulating plasma cells (CTCs) until 2021, when this threshold was decreased to ≥ 5%. We hypothesized that primary PCL is not a separate clinical entity, but rather that it represents ultra-high-risk multiple myeloma (MM) characterized by elevated CTC levels. **Methods:** We assessed the levels of CTCs by multiparameter flow cytometry in 395 patients with newly diagnosed transplant-ineligible MM to establish a cutoff for CTCs that identifies the patients with ultra-high-risk PCL-like MM. We tested the cutoff on 185 transplant-eligible patients with MM and further validated on an independent cohort of 280 transplant-ineligible patients treated in the GEM-CLARIDEX trial. The largest published real-world cohort of patients with primary PCL was used for comparison of survival. Finally, we challenged the current 5% threshold for primary PCL diagnosis. **Results:** Newly diagnosed transplant-ineligible patients with MM with 2%–20% CTCs had significantly shorter progression-free survival (3.1 v 15.6 months; P < 0.001) and overall survival (14.6 v 33.6 months; P = 0.023) than patients with < 2%. The 2% cutoff proved to be applicable also in transplant-eligible patients with MM and was successfully validated on an independent cohort of patients from the GEM-CLARIDEX trial. Most importantly, patients with 2%–20% CTCs had comparable dismal outcomes with primary PCL. Moreover, after revealing a low mean difference between flow cytometric and morphologic evaluation of CTCs, we showed that patients with 2%–5% CTCs have similar outcomes as those with 5%–20% CTCs. **Conclusion:** Our study uncovers that ≥ 2% CTCs is a biomarker of hidden primary PCL and supports the assessment of CTCs by flow cytometry during the diagnostic workup of MM.

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doc. MUDr. Petru Dulíčkovi, Ph.D. z IV. interní hematologické kliniky LF UK a FN Hradec Králové za monografii:

Poruchy hemostázy v klinické praxi. Grada Publishing 2022.

ANOTACE: Monografie se zabývá praktickými otázkami poruch hemostázy v reálné klinické praxi. Proto je obsah knihy tomu uzpůsoben. Po nezbytném úvodu o fyziologii a patofyziologii hemostázy se pak více zabýváme diferenciální diagnostickou poruch hemostázy. K tomu je nezbytná kapitola o laboratorním vyšetření, které je dostupné v České republice. Protože monografie je určena pro klinickou praxi, věnujeme se doporučeným postupům a podstatnou součástí je kapitola o antikoagulační terapii. Zde se zaměřujeme na monitorování, přípravu pacienta na intervenční zákrok a léčbu krvácení. Tyto otázky jsou nejčastěji kladeny na naše centrum. Závěr monografie tvoří 50 vybraných případů s položenými otázkami a volbou odpovědi tak, aby si čtenář mohl porovnat svůj postup s naším řešením. Věříme, že kniha si najde své čtenáře v pregraduálním vzdělávání, ale zejména postgraduálním, třeba i jako příprava na specializovanou atestaci. Pokud si čtenář z knihy odnese do praxe nějaké informace, které mu usnadní rozhodování, pak naše úsilí mělo smysl.

Výbor ČHS dále rozhodl o udělení Ceny ČHS ve výši 10 000,- Kč za publikaci v prvním decilu časopisů oboru třem původním pracím, které úspěšně reprezentují českou hematologii v mezinárodním srovnání. Nositeli jsou:

RNDr. Martina Fejtková, Ph.D. z Kliniky dětské hematologie a onkologie 2. LF UK a FN Motol za práci:

Fejtková M, Suková M, Hložková K, Škvárová Kramarzová K, Racková M, Jakubec D, Bakardjieva M, Bloomfield M, Klocperk A, Paráčková Z, Šedivá A, Aluri J, Nováková M, Kalina T, Froňková E, Hrušák O, Malcová H, Sedláček P, Liba Z, Kudr M, Starý J, Cooper MA, Svatoň M, Kanderová V. TLR8/TLR7 dysregulation due to a novel TLR8 mutation causes severe autoimmune hemolytic anemia and autoinflammation in identical twins. American Journal of Hematology 2022 Mar 1;97(3):338–351 doi: 10.1002/ajh.26452. IF 13.268 (1. decil).

SUMMARY: Our study presents a novel germline c.1715G>T (p.G572V) mutation in the gene encoding Toll-like receptor 8 (*TLR8*) causing an autoimmune and autoinflammatory disorder in a family with monozygotic male twins, who suffer from severe autoimmune hemolytic anemia worsening with infections, and autoinflammation presenting as fevers, enteritis, arthritis, and CNS vasculitis. The pathogenicity of the mutation was confirmed by in vitro assays on transfected cell lines and primary cells. The p.G572V mutation causes impaired stability of the TLR8 protein, cross-reactivity to TLR7 ligands and reduced ability of TLR8 to attenuate TLR7 signaling. This imbalance toward TLR7-dependent signaling leads to increased pro-inflammatory responses, such as nuclear factor-κB (NF-κB) activation and production of pro-inflammatory cytokines IL-1β, IL-6, and TNFα. This unique *TLR8* mutation with partial TLR8 protein loss and hyperinflammatory phenotype mediated by TLR7 ligands represents a novel inborn error of immunity with childhood-onset and a good response to TLR7 inhibition.

Mgr. Monika Kaisrlíková, Ph.D. z Ústavu hematologie a krevní transfuze v Praze za práci:

Kaisrlíková M, Veselá J, Kundrát D, Votavová H, Dostálová Merkerová M, Krejčík Z, Divoký V, Jedlička M, Frič J, Klema J, Mikulenková D, Šťastná Marková M, Lauermannová M, Mertová J, Soukupová Maaloufová J, Jonášová A, Čermák J, Beličková M. RUNX1 mutations contribute to the progression of MDS due to disruption of antitumor cellular defense: a study on patients with lower-risk MDS. Leukemia. 2022 Jul;36(7):1898–1906. doi: 10.1038/s41375-022-01584-3. IF 12.897 (1. decil).

SUMMARY: Patients with lower-risk myelodysplastic syndromes (LR-MDS) have a generally favorable prognosis; however, a small proportion of cases progress rapidly. This study aimed to define molecular biomarkers predictive of LR-MDS progression and to uncover cellular pathways contributing to malignant transformation. The mutational landscape was analyzed in 214 LR-MDS patients, and at least one mutation was detected in 137 patients (64%). Mutated *RUNX1* was identified as the main molecular predictor of rapid progression by statistics and machine learning. To study the effect of mutated *RUNX1* on pathway regulation, the expression profiles of CD34 + cells from LR-MDS patients with *RUNX1* mutations were compared to those from patients without *RUNX1* mutations. The data suggest that RUNX1-unmutated LR-MDS cells are protected by DNA damage response (DDR) mechanisms and cellular senescence as an antitumor cellular barrier, while RUNX1 mutations may be one of the triggers of malignant transformation. Dysregulated DDR and cellular senescence were also observed at the functional level by detecting γH2AX expression and β-galactosidase activity. Notably, the expression profiles of RUNX1-mutated LR-MDS resembled those of higher-risk MDS at diagnosis. This study demonstrates that incorporating molecular data improves LR-MDS risk stratification and that mutated RUNX1 is associated with a suppressed defense against LR-MDS progression.

prof. MUDr. Jan Zuna, Ph.D. z Kliniky dětské hematologie a onkologie 2. LF UK a FN Motol za práci:

Zuna J, Hovorková L, Krotká J, Koehrmann A, Bardini M, Winkowska L, Froňková E, Alten J, Koehler R, Eckert C, Brizzolara L, Trková M, Stuchlý J, Zimmermann M, De Lorenzo P, Valsecchi MG, Conter V, Starý J, Schrappe M, Biondi A, Trka J, Žaliová M, Cazzaniga G, Cario G. Minimal residual disease in BCR::ABL1-positive acute lymphoblastic leukemia: different significance in typical ALL and in CML-like disease. Leukemia. 2022 Dec;36(12):2793–2801. doi: 10.1038/s41375-022-01668-0. IF 12,897 (1.decil)

SUMMARY: Recently, we defined "CML-like" subtype of BCR::ABL1-positive acute lymphoblastic leukemia (ALL), resembling lymphoid blast crisis of chronic myeloid leukemia (CML). Here we retrospectively analyzed prognostic relevance of minimal residual disease (MRD) and other features in 147 children with BCR::ABL1-positive ALL (diagnosed I/2000–IV/2021, treated according to EsPhALL (n = 133) or other (n = 14) protocols), using DNA-based monitoring of BCR::ABL1 genomic breakpoint and clonal immunoglobulin/T-cell receptor gene rearrangements. Although overall prognosis of CML-like (n = 48) and typical ALL (n = 99) was similar (5-year-EFS 60% and 49%, respectively; 5-year-OS 75% and 73%, respectively), typical ALL presented more relapses while CML-like patients more often died in the first remission. Prognostic role of MRD was significant in the typical ALL (p = 0.0005 in multivariate analysis for EFS). In contrast, in CML-like patients MRD was not significant (p values > 0.2) and inapplicable for therapy adjustment. Moreover, in the typical ALL, risk-prediction could be further improved by considering initial hyperleukocytosis. Early distinguishing typical BCR::ABL1-positive ALL and CML-like patients is essential to enable optimal treatment approach in upcoming protocols. For the typical ALL, tyrosine-kinase inhibitors and concurrent chemotherapy with risk-directed intensity should be recommended; in the CML-like disease, no relevant prognostic feature applicable for therapy tailoring was found so far.

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