Publikujeme v zahraničí

Onkológia (Bratisl.), 2023;18(5):388-389

PODPORNÁ LIEČBA

Ciernikova S, Sevcikova A, Drgona L, Mego M.

Modulating the gut microbiota by probiotics, prebiotics, postbiotics, and fecal microbiota transplantation: An emerging trend in cancer patient care

Biochim Biophys Acta Rev Cancer. 2023 Sep 22;1878(6):188990.

Treatment resistance, together with acute and late adverse effects, represents critical issues in the management of cancer patients. Promising results from preclinical and clinical research underline the emerging trend of a microbiome-based approach in oncology. Favorable bacterial species and higher gut diversity are associated with increased treatment efficacy, mainly in chemo- and immunotherapy. On the other hand, alterations in the composition and activity of gut microbial communities are linked to intestinal dysbiosis and contribute to high treatment-induced toxicity. In this Review, we provide an overview of studies concerning gut microbiota modulation in patients with solid and hematologic malignancies with a focus on probiotics, prebiotics, postbiotics, and fecal microbiota transplantation. Targeting the gut microbiome might bring clinical benefits and improve patient outcomes. However, a deeper understanding of mechanisms and large clinical trials concerning microbiome and immunological profiling is warranted to identify safe and effective ways to incorporate microbiota-based interventions in routine clinical practice.

GENITOURINÁRNE MALIGNITY

Lauritsen J, Sauvé N, Tryakin A, Jiang DM, Huddart R, Heng DYC, Terbuch A, Winquist E, **Chovanec M,** Hentrich M, Fankhauser CD, Shamash J, Del Muro XG, Vaughn D, Heidenreich A, Sternberg CN, Sweeney C, Necchi A, Bokemeyer C, Bandak M, Jandari A, Collette L, Gillessen S, Beyer J, Daugaard G.

Outcomes of relapsed clinical stage I versus de novo metastatic testicular cancer patients: an analysis of the IGCCCG Update database

Br J Cancer. 2023 Sep 30.

Background: Active surveillance after orchiectomy is the preferred management in clinical stage I (CSI) germ-cell tumours (GCT) associated with a 15 to 30% relapse rate.

Patients and methods: In the IGCCCG Update database, we compared the outcomes of gonadal disseminated GCT relapsing from initial CSI to outcomes of patients with de novo metastatic GCT.

Results: A total of 1014 seminoma (Sem) [298 (29.4%) relapsed from CSI, 716 (70.6%) de novo] and 3103 non-seminoma (NSem) [626 (20.2%) relapsed from CSI, 2477 (79.8%) de novo] were identified. Among Sem, no statistically significant differences in PFS and OS were found between patients relapsing from CSI and de novo metastatic disease [5-year progression-free survival (5y-PFS) 87.6% versus 88.5%; 5-year overall survival (5y-OS) 93.2% versus 96.1%). Among NSem, PFS and OS were higher overall in relapsing CSI patients (5y-PFS 84.6% versus 80.0%; 5y-OS 93.3% versus 88.7%), but there were no differences within the same IGCCCG prognostic groups (HR = 0.89; 95% CI: 0.70-1.12). Relapses in the intermediate or poor prognostic groups occurred in 11/298 (4%) Sem and 112/626 (18%) NSem.

Conclusion: Relapsing CSI GCT patients expect similar survival compared to de novo metastatic patients of the same ICCCCG prognostic group. Intermediate and poor prognosis relapses from initial CSI expose patients to unnecessary toxicity from more intensive treatments.

Dubinsky P, Vojtek V, Belanova K, Janickova N, Balazova N, Tomkova Z.

Hypofractionated Post-Prostatectomy Radiotherapy in 16 Fractions: A Single-Institution Outcome

Life (Basel). 2023 Jul 23;13(7):1610.

Background: The optimal hypofractionated schedule of post-prostatectomy radiotherapy remains to be established. We evaluated treatment outcomes and toxicity of moderately hypofractionated post-prostatectomy radiotherapy in 16 daily fractions delivered with intensity-modulated radiotherapy. The treatment schedule selection was motivated by limited technology resources and was radiobiologically dose-escalated.

Methods: One hundred consecutive M0 patients with post-prostatectomy radiotherapy were evaluated. Radiotherapy indication was adjuvant (ART) in 19%, early-salvage (eSRT) in 46% and salvage (SRT) in 35%. The dose prescription for prostate bed planning target volume was 52.8 Gy in 16 fractions of 3.3 Gy. The Common Terminology Criteria v. 4 for Adverse Events scale was used for toxicity grading.

Results: The median follow-up was 61 months. Five-year biochemical recurrence-free survival (bRFS) was 78.6%, distant metastases-free survival (DMFS) was 95.7% and overall survival was 98.8%. Treatment indication (ART or eSRT vs. SRT) was the only significant factor for bRFS (HR 0.15, 95% CI 0.05-0.47, $p = 0.001$) and DMFS (HR 0.16, 95% CI 0.03-0.90; $p = 0.038$). Acute gastrointestinal (GI) toxicity grade 2 was recorded in 24%, grade 3 in 2%, acute genitourinary (GU) toxicity grade 2 in 10% of patients, and no grade 3. A cumulative rate of late GI toxicity grade ≥ 2 was observed in 9% and late GU toxicity grade ≥ 2 in 16% of patients.

Conclusions: The observed results confirmed efficacy and showed a higher than anticipated rate of early GI, late GI, and GU toxicity of post-prostatectomy radiobiologically dose-escalated hypofractionated radiotherapy in 16 daily fractions.

NÁDORY PĽÚC

Planchard D, Jänne PA, Cheng Y, Yang JC, Yanagitani N, Kim SW, Sugawara S, Yu Y, Fan Y, Geater SL, Laktionov K, Lee CK, Valdiviezo N, Ahmed S, Maurel JM, **Andrasina I,** Goldman J, Ghiorghiu D, Rukazenkov Y, Todd A, Kobayashi K; FLAURA2 Investigators.

Osimertinib with or without Chemotherapy in EGFR-Mutated Advanced NSCLC.

N Engl J Med. 2023 Nov 23;389(21):1935-1948.

Background: Osimertinib is a third-generation epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) that is selective for EGFR-TKI-sensitizing and *EGFR* T790M resistance mutations. Evidence suggests that the addition of chemotherapy may extend the benefits of EGFR-TKI therapy.

Methods: In this phase 3, international, open-label trial, we randomly assigned in a 1:1 ratio patients with *EGFR*-mutated (exon 19 deletion or L858R mutation) advanced non-small-cell lung cancer (NSCLC) who had not previously received treatment for advanced disease to receive osimertinib (80 mg once daily) with chemotherapy (pemetrexed [500 mg per square meter of body-surface area] plus either cisplatin [75 mg per square meter] or carboplatin [pharmacologically guided dose]) or to receive osimertinib monotherapy (80 mg once daily). The primary end point was investigator-assessed progression-free survival. Response and safety were also assessed.

Results: A total of 557 patients underwent randomization. Investigator-assessed progression-free survival was significantly longer in the osimertinib-chemotherapy group than in the osimertinib group (hazard ratio for disease progression or death, 0.62; 95% confidence interval [CI], 0.49 to 0.79; P<0.001). At 24 months, 57% (95% CI, 50 to 63) of the patients in the osimertinib-chemotherapy group and 41% (95% CI, 35 to 47) of those in the osimertinib group were alive and progression-free. Progression-free survival as assessed according to blinded independent central review was consistent with the primary analysis (hazard ratio, 0.62; 95% CI, 0.48 to 0.80). An objective (complete or partial) response was observed in 83% of the patients in the osimertinib-chemotherapy group and in 76% of those in the osimertinib group; the median response duration was 24.0 months (95% CI, 20.9 to 27.8) and 15.3 months (95% CI, 12.7 to 19.4), respectively. The incidence of grade 3 or higher adverse events from any cause was higher with the combination than with monotherapy - a finding driven by known chemotherapy-related adverse events. The safety profile of osimertinib plus pemetrexed and a platinum-based agent was consistent with the established profiles of the individual agents.

Conclusions: First-line treatment with osimertinib-chemotherapy led to significantly longer progression-free survival than osimertinib monotherapy among patients with *EGFR*-mutated advanced NSCLC. (Funded by AstraZeneca; FLAURA2 ClinicalTrials.gov number, NCT04035486.).

ABSTRAKTY Z KONFERENCIÍ

Taglialatela I, Giannatempo P, Nazzani S, Bernasconi V, **M. Mego**, Bimbatti D, Secondino S, Claps M, Biasoni D, Catanzaro M, Zimatore M, Torelli T, Stagni S, Macchi A, Tesone A, Pedrazzoli P, Basso U, Verzoni E, Procopio G, Nicolai N.

Primary Retroperitoneal germ-cell tumours (pR-GCT): Evaluation of Treatment Outcomes of an international collaboration (PRIMERE study-IGG05), ESMO, 2023