

review and meta-analysis. A comprehensive search was conducted across MEDLINE, EMBASE, and CENTRAL databases. The search strategy included the following terms: “Breast cancer” AND “Radium-223”. The selection criteria encompassed both single-arm and randomized controlled trials (RCT). MedCalc® Statistical Software was used. Hazard ratios (HR) were preferred. Odds ratios (OR) or Relative risk (RR) were used when HR was not disponible. For single-arm studies, a proportion meta-analysis was performed. Random-effects methods were used. The initial search yielded 349 articles, 28 articles were reviewed with full-text, and 5 were considered eligible (3 RCT and 2 single-arm studies). SC therapy included: capecitabine, paclitaxel, exemestane plus everolimus and hormonal therapy. Overall, the group submitted to Ra-223 showed a trend to have better symptomatic skeletal event-free survival – SSEFS - (HR: 0.855, CI: 0.643-1.138) and pain improvement (OR: 1.308, CI: 0.780-2.196), but without statistical significance. The pooled analysis showed no difference between arms for serious adverse effects (RR: 0.836, CI: 0.331-2.112). The proportion of SAE in patients submitted to Ra-223 plus SC was 20.1% (CI: 3.6-45.3%). **Conclusão:** Ra-223 plus SC in bone metastatic breast cancer patients showed a trend to better SSEFS and pain improvement. However, the low number of RCT studies and the high heterogeneity of SC are great limitations. Results from ongoing RCT (everolimus and avelumab) can change this scenario.

Keywords: Breast cancer, Meta-analysis., Radium-223, Systematic review.

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EPSTEIN-BARR VIRUS AND LYMPHOMA IN RHEUMATOID ARTHRITIS: PREVALENCE AND ASSOCIATION WITH METHOTREXATE. RESULT OF SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES

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Summary: Introduction: rheumatoid arthritis (RA) is an autoimmune, inflammatory, and systemic disease, whose pathogenesis involves both the innate and adaptive immune systems. Its global prevalence varies from 0,4% to 1,3%, and the incidence increases with age. Given the increase in the general life expectancy of the population, the number of elderly patients with RA is growing, as are the complications of the disease. Several studies have demonstrated that patients with RA are at increased risk of developing lymphoproliferative diseases when compared to the general population. Some theories have emerged to explain this association, with emphasis on the role of the Epstein-Barr virus (EBV) and immunosuppressive drugs, especially methotrexate (MTX), the medication most frequently used to treat the disease. Methodology: Pubmed, Cochrane, Lilacs, Scopus, Embase and

Web of Science databases were systematically reviewed in September 2023, without language or publication date restrictions. We searched for observational studies that associated EBV, RA, methotrexate and lymphoma. The recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Cochrane Collaboration were used. **Results:** the analysis of 10 studies published between 2001 and 2022, involving 674 patients with RA and lymphoma, demonstrated that 77,3% used MTX and 27,4% were positive for EBV. The most common lymphoma was diffuse large B-cell lymphoma (DLBCL). The prevalence of EBV in DLBCL patients ranges from 5-15%, compared to 27,4% in the present study. This histological subtype was also associated with lower rates of spontaneous remission and worse outcomes. The prevalence of EBV in RA patients not treated with MTX was 7,7%, compared to 46% in patients who used the drug. Spontaneous remission rates (sRR) after MTX suspension (without associated immunochemotherapy) were variable (22,9% to 69,2%), but higher in the EBV-positive group. **Discussion:** in RA patients treated with MTX, EBV is expected to be activated through 3 mechanisms. The first of these involves AR itself. Patients with the disease have a deficiency of CD8+ T cells and, consequently, a high EBV burden due to immunodeficiency. The second mechanism is the suppression of T cell activation and adhesion by MTX. The third mechanism is direct reactivation of latent EBV by MTX. Thus, MTX withdrawal appears to result in recovery of immune surveillance and interruption of the EBV-induced tumor pathway. sRR with MTX withdraw were higher in EBV-positive group and could indicate that the virus is associated with a better outcome. The different prognosis of EBV-negative cases suggests that these tumors have a distinct biology. **Conclusão:** Conclusion: our systematic review found a high prevalence of EBV positivity in patients with RA and lymphoma, suggesting an important role for the virus in lymphomagenesis in this specific population. Due to the frequent use of MTX in the RA population, data from the systematic review alone are not capable of attributing the drug's causality to other confounding factors.

Keywords: Epstein-Barr, Lymphoma, Methotrexate, Rheumatoid arthritis.

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TRENDS IN RADIOISOTOPES AND RADIOLABELING METHODS

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Summary: Radiopharmaceutical research and bioscience or medical applications have changed during the decades in the function of available technologies for radioisotope production and imaging detection technologies. In the 1940s to 1960s year, radioisotopes were supplied by reactor production, such as ¹³¹I for thyroid uptake study, ¹⁹⁷Hg, ²⁰³Hg-chlormerodrin for brain scans, ¹⁹⁸Au-colloid for liver scans, and ⁸⁵Sr-chloride for the bone scans. In the late 1960s, with the