11. Folate Supplementation and Cancer Risk in Rheumatoid Arthritis Patients Exposed to Methotrexate.

Giordano Egiziano[1], Dr. Ines Colmegna[1], Maria E. Suarez-Almazor[2], Louis Bessette[3], Sasha Bernatsky[1].
[1]Department of Medicine, McGill University Health Center (MUHC), Montreal, QC; [2]Department of Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Department of Medicine, Centre Hospitalier de l'Université Laval (CHUL) , Université Laval, Québec, QC.

Background: Potential adverse effects of methotrexate use in rheumatoid arthritis (RA) can be diminished with folic acid. However, some literature in the general population suggests that folic acid may promote cancer progression, while other evidence suggests it may prevent certain malignancies.

Objective: To determine, in RA patients initially free of cancer and exposed to methotrexate, if folate supplementation affects later risk of any cancer.

Methods: Using physician billing codes from the Quebec public health insurance program (RAMQ) databases from 2002-2011, we identified a cohort of new-onset RA patients exposed to methotrexate (on the basis of at least one methotrexate prescription filled after RA diagnosis). Patients with a history of any cancer within 3 years prior to cohort entry were excluded. Time zero for cohort entry was date of first methotrexate exposure. Folate use (ever/never, time dependent) was based on first prescription filled. Adjusting for baseline demographic and clinical factors (age, sex, socioeconomic status, concurrent medications, comorbidities and correlates of RA severity), we performed multivariate Cox proportional hazard regression to assess for an association between folate use and time to event. The outcome event was defined by a first-time hospitalization featuring a diagnostic code (primary or non-primary) for any cancer.

Results: During the study period, we identified 11,046 new-onset RA patients, and of these 6,575 were prescribed methotrexate, and thus were followed in our cohort. The cohort was 71% female and the average age at cohort entry was 63.2 years (standard deviation 14.4 years). The methotrexate-exposed RA cohort provided 31,421 patient-years of follow-up. The majority (85%) of methotrexate-exposed patients filled at least one prescription for folate. Of those patients exposed to methotrexate, we identified 487 patients with any cancer diagnosis hospitalization codes. In the multivariate model, there was no clear effect of folate supplementation on total cancer risk (adjusted hazard ratio 0.85, 95% confidence interval 0.68-1.05).

Conclusions: In this large cohort of new-onset RA patients without a recent cancer diagnosis, we were unable to clearly document an increased risk of malignancy in patients taking folate with methotrexate, versus those taking methotrexate without folate. Further analyses should consider specific cancer types, longer follow-up, more complex exposure definitions, and assess the association of folate supplementation in RA patients with a prior cancer diagnosis.