Comparative risk of cancer associated with first-line DMARDs use in rheumatoid arthritis: real world evidence from the OHDSI network

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Talita Duarte-Salles[1], Martina Recalde[1],Yesika Díaz[1], Ben Illigens[2,3], David Vizcaya[4]; James Weaver[5,6], Edward Burn[1,7], Katerina Chatzidionysiou[6], Patrick Ryan[5,6,7], Daniel Prieto-Alhambra[1,9], and the EHDEN RA Research Group

[1]IDIAPJGol, Spain; [2]Harvard Medical School, US, [3]Odysseus Inc, [4]Bayer Pharma, Spain; [5]Janssen R&D, US, [6]Observational Health Data Sciences and Informatics, US, [7]Department of Biomedical Informatics, Columbia University, US, [8]Karolinska Institutet, Sweden, [9]NDORMS, University of Oxford, UK

Background

- **Rationale**: Conventional synthetic disease-modifying antirheumatic drugs (csDMARD) are recommended as first line treatment for rheumatoid arthritis (RA) patients. The effect of csDMARD on the immune system may increase long-term cancer risk. Whether the risk of cancer differs by csDMARD treatments is still unclear.
- **Objective**: To compare the risk of incident overall (excluding non-melanoma skin) and site-specific cancers (colorectal, lung, lymphoma, leukaemia) associated with first-line use of csDMARD in patients with RA.

Methods

- **Study design**: Multinational network cohort from 2005 to 2018.
- **Data sources**: 7 healthcare databases (claims and electronic medical records) part of the Observational Health Data Sciences and Informatics (OHDSI) network:
  - Spain: SIDIAP
  - US: Optum, MDCR, CCAE, AMBEMR-IQVIA
  - Germany: GERMANY-IQVIA
  - UK: THIN
- **Participants**: Initiators aged ≥18 years of one of the following first-line monotherapies after a diagnosis of RA:
  - methotrexate (MTX)
  - hydroxychloroquine (HCQ)
  - sulphasalazine (SSZ)
  - leflunomide (LEF)
- **Exclusion criteria**: a prior diagnosis of another inflammatory arthropathy or cancer, or <1 year of follow-up.
- **Follow-up**: 1-year after treatment initiation to the earliest of incident cancer, loss to follow-up, or 5-years.
- **Analysis**: Cox proportional-hazard models for each csDMARD against MTX after propensity score stratification. Negative control outcomes were analysed to empirically calibrate hazard ratios (cHRs).

Results

- We included 127,547 RA patients initiating csDMARD therapy (MTX: 73,996, HCQ: 36,381 SSZ: 9,383 LEF: 7,787).
- Estimates for overall cancer risk are shown below in Figure 1.
- Compared to MTX, LEF was consistently associated with a reduced overall cancer risk (cHRs ranged from 0.53 (0.36 to 0.80 in CCAE-US to 0.84 [0.58 to 1.22] in SIDIAP-Spain). Small differences were observed for HCQ and SSZ compared to MTX.
- For most databases, there were too few cancer cases to investigate site-specific cancers separately. When compared with MTX, LEF was associated with lower colorectal cancer risk in Optum-US and AMBEMR-IQVIA-US (cHRs of 0.46 [0.13 to 1.58] and 0.53 [0.18 to 1.54], respectively).

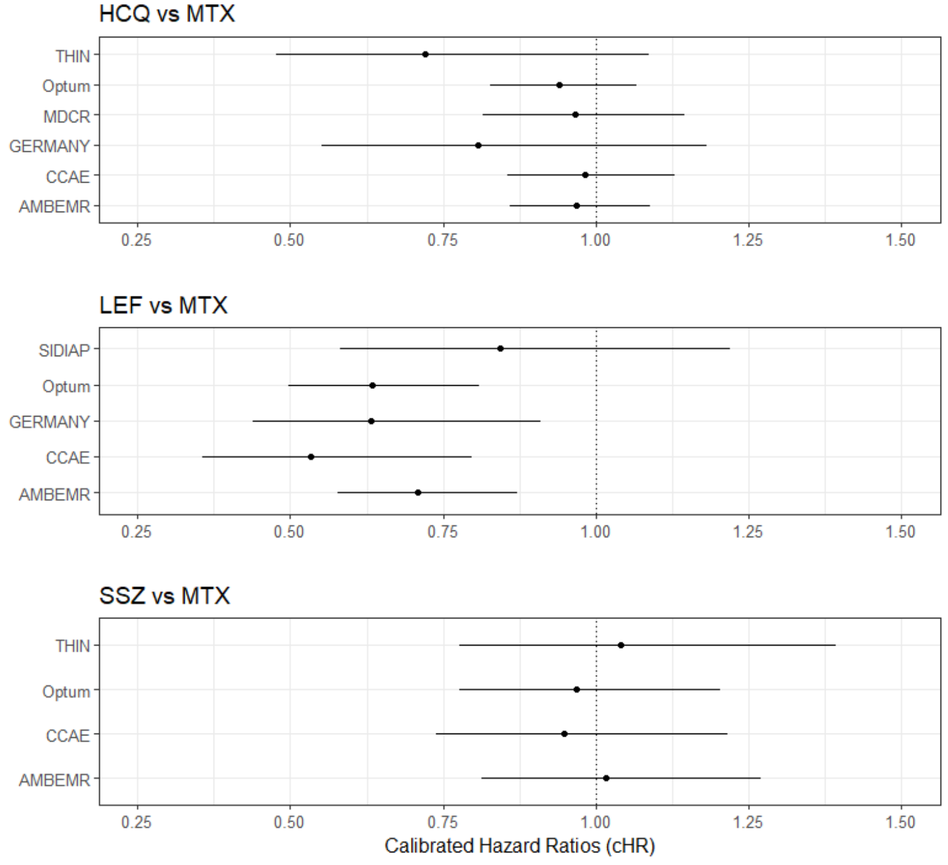

Figure 1. Overall cancer risk and first line csDMARD treatment during 1year after RA diagnosis

Conclusions

- Compared to MTX users, RA patients treated with LEF had lower risk of overall cancer in most databases.
- There was insufficient statistical power to investigate specific cancer types except for colorectal cancer in two US databases, where no significant associations were observed.

Contact: tduarte@idiapjgol.org

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