The impact of different DMARDs on mortality in patients with rheumatoid arthritis and prevalent interstitial lung disease

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Conclusion

In accordance with the few existing recommendations and studies, all non-TNFi-biologics as well as JAKi showed a protective signal compared to TNFi in all three regression models. Furthermore, patients who did not receive any DMARD had an increased risk of mortality. However, the study sample size was small, the results should thus be interpreted with caution.

Background

Interstitial lung disease (ILD) is one of the most common extra-articular manifestations of rheumatoid arthritis (RA) with a high mortality risk. Only few studies examined the association between RA treatment and mortality in patients with RA-ILD. These studies do not include all available DMARDs and had small sample sizes [1].

Reference: [1] PMID: 36064885

Objectives

To investigate the impact of treatment on all-cause mortality in patients with RA-ILD taking inflammation, traditional risk factors and comorbidities into account.

Methods

- Data source: Biologics register RABBIT
- Enrolment: RA patients between 01/2007 and 06/2021 with an ILD, reported either at enrolment or during follow-up
- Observation started at the time of ILD reporting (= baseline) and ended at death, dropout or end of follow-up, whichever came first
- Data analysis:
  - Time-varying cox regression (= main model) was applied with monthly information
  - Sensitivity analyses comprised two alternative treatment exposures:
    - Cumulative model (cumulative exposure in months for every treatment divided by total months of observation)
    - Intention-to-treat model (treatment exposure at baseline)

Missing data was imputed 10 times. All models were adjusted by inverse probability weighting and number of comorbidities as covariate.

Results

Out of 15,566 cohort participants, 381 patients were identified as prevalent ILD cases, of whom 97 patients (25 %) died. The total observed time for RA-ILD patients was 1,258 person years.

Patients exposed to:

- csDMARD / TNFi - are less affected overall
- IL6i - are younger but have a comparable number of comorbidities as patients with csDMARDs / TNFi
- T cell / B cell / JAKi – have the highest disease activity, the worst functional level and the most comorbidities
- No DMARD – are different from the other groups and most likely a mixture of a variety of patients: low disease activity on one hand, but higher number of comorbidities and more prior treatments on the other

The main Cox regression model showed a 2.8-fold higher mortality risk for patients receiving no DMARD treatment compared to TNFi (Figure).

Numerically, hazard ratios < 1 for mortality were observed for IL6i, T cell, B cell, JAKi and csDMARD in reference to TNFi but without statistical significance. The results of the sensitivity analyses pointed in the same direction.

Abbreviations: *B cell: B cell targeted therapy, csDMARD: conventional synthetic disease-modifying anti-rheumatic drugs, IL6i: interleukin-6 inhibitors, JAKi: Janus kinase inhibitors, T cell: T cell costimulation modulator, TNFi: tumour necrosis factor inhibitor*

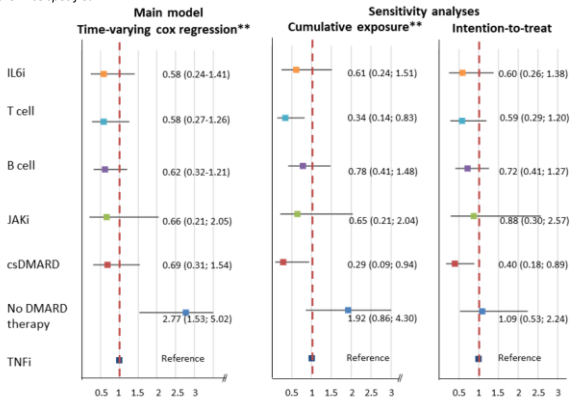
Table: Characteristics by treatment group at time of ILD reporting

	csDMARD	TNFi	IL6i	T cell	B cell	JAKi	No DMARD
N	61	114	33	60	64	19	30
Patient-years	147	345	140	179	308	78	109
Age, years	64.6	66.4	63.7	67.1	64.6	65.3	66.6
Female, %	52.5	50.0	48.5	58.3	57.8	36.8	63.3
Disease duration, years	11.0	11.6	9.5	11.8	12.9	14.2	11.1
Rheumatoid factor, %	75.4	85.1	81.8	83.3	92.2	84.2	76.7
DAS28-ESR	4.6	4.6	4.9	5.1	5.0	5.2	4.0
% of physical function	70.0	64.0	60.4	54.4	54.4	59.4	63.3
CRP, mg/l	10.6	12.8	12.9	17.0	18.6	8.0	12.3
No. of comorbidities	4.0	3.6	3.9	5.2	4.6	5.4	5.0
Glucocorticoid ≥10 mg/d, %	9.8	19.3	21.2	18.3	15.6	10.5	13.3
No. of prior biologics or JAKi	1.0	0.7	1.8	1.4	2.0	1.5	2.2

Values are means unless otherwise specified

Figure: Hazard ratios for mortality, calculated with inverse probability weighted* Cox regression models

**Includes: age, CRP, disease duration, categorized glucocorticoids (< 10 vs. ≥10), % of physical function, rheumatoid factor, sex, year of inclusion*
*** An additional six months were added as risk window*



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