Rheumatoid arthritis - non biologic treatment and small molecules

OP0122

COMPARATIVE EFFECTIVENESS OF JAKI VERSUS bDMARDs; A NATIONWIDE STUDY IN RA

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Background: The Janus kinase inhibitors (JAKi) have been increasingly used for the treatment of rheumatoid arthritis (RA) in Sweden, with baricitinib representing ~80% of prescriptions. Evidence regarding the comparative effectiveness of JAKis versus biologics (bDMARDs), and in particular non- tumour-necrosis-factor inhibitor (TNFi) bDMARDs, in real-life is limited.

Objectives: To compare RA patients treated with bDMARDs and JAKi in Sweden, in terms of: (1) patient characteristics at treatment start; (2) proportions of patients remaining on therapy, and response rates, at 12 months.

Methods: RA patients starting treatment in 2017 and 2018 with either a TNFi, rituximab, abatacept, interleukin 6 inhibitors (IL6i) or a JAKi as different lines of treatment were identified in the Swedish Rheumatology Quality Register. One patient could contribute with more than one treatment episode.

Treatment response at 12 months was measured as EULAR good response, HAQ improvement >0.2 units, DAS28 and CDAI remission, and as 0 tender and swollen joint counts (28JC). Patients were classified as non-responders if they stopped treatment before evaluation due to safety or inefficacy. Responses for patients who stopped treatment due to pregnancy or death and patients on treatment but with missing response were imputed using multiple imputation.

Proportions of responders and differences in proportions between treatment groups, adjusted using inverse probability of treatment weighting, were estimated using linear regression with robust standard errors.

Results: JAKi were often used after bDMARDs, and less frequently prescribed in combination with methotrexate. Measured comorbidities were less frequent among JAKi initiators than among non-TNFi biologic initiators, but RA activity was similar (Table).

Table 1. Patient characteristics at treatment initiation

Characteristic	Abatacept	IL6i	Rituximab	TNFi	JAKi
Treatment Starts	694	534	692	3497	905
Age	63 (53-71)	59 (48-70)	65 (54-73)	59 (47-68)	60 (51-70)
Female	543 (78)	441 (83)	519 (75)	2739 (78)	759 (84)
RA duration (years)	13 (5-21)	10 (5-18)	12 (6-22)	9 (3-17)	13 (7-22)
Rheum. factor	535 (79)	385 (73)	588 (87)	2405 (70)	686 (77)
DAS28	4.8 (3.9-5.6)	4.9 (4.0-5.7)	4.7 (3.8-5.5)	4.4 (3.4-5.3)	4.7 (3.9-5.7)
HAQ	1.3 (0.8-1.6)	1.3 (0.8-1.8)	1.3 (0.8-1.8)	1.0 (0.5-1.4)	1.3 (0.8-1.8)
Tender joints	5 (2-9)	6 (3-10)	5 (2-9)	4 (2-8)	6 (2-10)
Swollen joints	4 (2-6)	4 (2-7)	4 (2-7)	3 (1-6)	4 (2-7)
ts/bDMARD line	3 (2-4)	3 (2-4)	2 (1-4)	1 (1-2)	4 (2-6)
At least one prev. TNFi	539 (78)	442 (83)	457 (66)	1448 (41)	770 (85)
At least one prev. non-TNFi	271 (39)	220 (41)	243 (35)	441 (13)	584 (65)
Methotrexate co-treatment	264 (50)	172 (40)	286 (53)	1708 (62)	296 (40)
Glucocorticoids co-treatment	247 (47)	186 (43)	275 (51)	1126 (41)	389 (53)
Cancer*	90 (2.8)	64 (2.3)	363 (7.7)	410 (1.8)	20 (2.2)
Cardio-vascular dis.*	245 (75)	123 (4.4)	322 (6.8)	749 (3.4)	41 (4.4)
Chronic respiratory dis.*	303 (9.3)	140 (5.0)	473 (10.0)	721 (3.2)	50 (5.4)
Diabetes*	324 (9.9)	216 (7.7)	456 (9.7)	1479 (6.7)	69 (7.5)

* any diagnosis within 5 years before start Adjusted differences in proportion with each response outcome

In a crude comparison, 65% (61%-68%) of JAKi, 62% (59%-66%) of abatacept, 58% (53%-62%) of IL6i, 80% (77%-83%) of rituximab and 68% (67%-70%) of TNFi initiators remained on treatment at 12 months after start. Also, JAKi showed lower overall responder proportions than TNFi, rituximab and IL6i.

After adjustment for demographic and socio-economic factors, RA disease activity, previous use of ts/bDMARDs, co-medication with glucocorticoids and methotrexate and comorbidities at baseline, no significant differences in responder proportions between JAKi and bDMARDs remained (Figure). Furthermore, the adjusted proportions of patients on treatment were higher for JAKi and rituximab than for the other bDMARDs.

Conclusion: This preliminary analysis of patients treated in clinical practice found no statistically significant difference in effectiveness between JAKi and bDMARDs.

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OP0123

SAFETY PROFILE OF JAK-INHIBITORS VERSUS TNF-INHIBITORS IN REAL-WORLD CLINICAL PRACTICE: DATA FROM A MULTICENTER REGISTER

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Background: JAK-inhibitors (JAKi) are small molecules emerging as a promising treatment for immune mediated diseases. Data from clinical trials are very promising. But long-term observational studies, with patients with diverse clinical backgrounds are required to confirm safety profile.

Objectives: To compare the safety profile of JAKi versus TNF antagonists (anti-TNF) in a multicenter real world dataset.

Methods: Data of patients enrolled in BIOBADASER 3.0 up to November 2020 with the start of anti-TNF or JAKi were analysed. Adverse events (AE) were classified according to Meddra dictionary (v19.0). For each group, demographic, clinical variables and incidence rate ratios of AE per 1000 patients-year (PYs) and 95% confidence interval were estimated.

Results: A total of 3,729 patients on anti-TNF (5,306) or JAKi (493) were analyzed. Patients on JAKi were older and with a mean disease duration of 10 years. JAKi were prescribed as first line treatment only in 24% of patients. The main reason of stopping treatment was ineffectiveness (53-59%) followed by adverse events (25-34%) in both groups. Survival during first year was similar between groups.

Table 1. Patient characteristics and adverse events by treatment group

	Anti-TNF	JAKi
Mean age start of treatment (SD), yrs	50.8 (12.6)	57.6 (11.9)
Female, n (%)	3122 (58.8)	392 (79.5)
Disease duration, median (IQR)	7.0 (2.7-13.7)	9.9 (4.9-16.8)
First line biologic, n (%)	2614 (49.3)	117 (23.7)
Rheumatoid Arthritis	1385 (41.1)	339 (95.2)
Ankylosing Spondylitis	1031 (30.6)	1 (0.3)
Psoriatic Arthritis	957 (28.4)	16 (4.5)
DAS28-ESR	4.3 (1.4)	4.7 (1.4)
Survival first year (IC 95%)	73.3 (71.9-74.6)	69.7 (66.0-73.0)
Charlson Index, mean (SD)	1.9 (1.3)	2.3 (1.6)
Reason to stop therapy (n)*:		
Lack of efficacy	1534 (53.2)	57 (58.8)
Adverse event	723 (25.1)	33 (34.0)
Adverse events (AE)*		
Serious infections	14.2 (12.4-16.2)	33.2 (19.3-57.3)
Herpes zoster	5.7 (4.6-7.1)	12.8 (5.3-30.7)
Tuberculosis	0.7 (0.4-1.3)	0.0 (0.0-0.0)
Malignancy/Neoplasia	10.2 (8.7-11.9)	15.3 (6.9-34.2)
Cardiac events	13.9 (12.2-16.0)	30.7 (17.4-54.0)
GI perforation	1.2 (0.8-1.9)	10.2 (3.8-27.3)
Vascular events	9.8 (8.3-11.5)	25.6 (13.8-47.5)

*Data show the incidence rate ratio per 1000 patient-years (PYs; 95% CI)

Conclusion: Serious infections and herpes zoster tend to be more frequent in patients on JAKi. However patients on JAKi were older, presented higher comorbidity and have a longer disease duration.

Disclosure of Interests: None declared

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OP0124

EFFECTS OF NINTEDANIB IN PATIENTS WITH PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS (RA-ILD) IN THE INBUILD TRIAL

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Background: In the INBUILD trial in subjects with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF), nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks by 57% compared with placebo.

Objectives: To assess the rate of decline in FVC in subjects with RA-ILD in the INBUILD trial.

Methods: Subjects in the INBUILD trial had a chronic fibrosing ILD other than IPF, reticular abnormality with traction bronchiectasis (with or without honeycombing) of >10% extent on high-resolution computed tomography (HRCT), forced vital capacity (FVC) ≥45% predicted, diffusing capacity of the lungs for carbon monoxide ≥30%–<80% predicted, and met criteria for progression of ILD within the 24 months before screening, despite management deemed appropriate in clinical practice. Patients taking stable doses of approved medications to treat RA or connective tissue disease could participate, except that the protocol excluded those taking azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, rituximab, cyclophosphamide, or oral glucocorticoids >20 mg/day. We analysed the rate of decline in FVC (mL/year) over 52 weeks and adverse events in subjects with RA-ILD.

Results: Of 663 subjects who received trial medication, 89 had RA-ILD (42 nintedanib, 47 placebo), of whom 60.7% were male, 64.0% were current or former smokers, 86.5% had a usual interstitial pneumonia (UIP)-like pattern on HRCT; 93.3% had received confirmation of their RA diagnosis from a rheumatologist. At baseline, 21.3% of subjects were taking biologic disease-modifying anti-rheumatic drugs (DMARDs), 53.9% were taking non-biologic DMARDs and 73.0% were taking glucocorticoids (≤20 mg/day prednisone or

equivalent). At baseline, mean (SD) age was 66.9 (9.6) years, time since RA diagnosis was 9.9 (9.4) years, time since ILD diagnosis was 3.6 (3.2) years, FVC was 71.5 (16.2) % predicted and C-reactive protein was 13.7 (22.5) mg/L. The adjusted mean (SE) rate of decline in FVC over 52 weeks was -82.6 (41.3) mL/year in the nintedanib group versus -199.3 (36.2) mL/year in the placebo group (difference 116.7 mL/year [95% CI 7.4, 226.1]; nominal p=0.037), consistent with findings in the overall trial population (Figure). As in the overall trial population, the most common adverse event in subjects with RA-ILD was diarrhoea (reported in 54.8% of the nintedanib group and 25.5% of the placebo group). Adverse events led to permanent discontinuation of trial drug in 19.0% of subjects in the nintedanib group and 12.8% of subjects in the placebo group.

Conclusion: In the INBUILD trial, nintedanib slowed the rate of decline in FVC in patients with progressive fibrosing RA-ILD, with adverse events that were manageable for most patients. The efficacy and safety of nintedanib in subjects with RA-ILD were consistent with those observed in the overall trial population.

Figure. Rate of decline in FVC (mL/year) over 52 weeks with nintedanib versus placebo in all subjects and in subjects with RA-ILD in the INBUILD trial.

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OP0125

TOFACITINIB IN RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: EFFICACY AND SAFETY ANALYSIS FROM TREASURE REAL-LIFE DATA

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