• WEBINAR

Ανασκόπηση

ΕΤΗΣΙΟΥ ΣΥΝΕΔΡΙΟΥ

EULAR 2021

Ρευματοειδής Αρθρίτιδα

Χάρης Παπαγόρας

Επίκουρος Καθηγητής Ρευματολογίας

Τμήμα Ιατρικής ΔΠΘ

30 Ιουνίου 2021

ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΕΒΡΟΥ

ΦΟΡΕΑΣ ΑΛΕΞΑΝΔΡΟΥΠΟΛΗΣ

Δήλωση συμφερόντων

- Δεν υπάρχει κάποια σύγκρουση συμφερόντων για αυτήν την ομιλία

Εκπαιδευτικές-ερευνητικές-συμβουλευτικές επιχορηγήσεις την τελευταία διετία:

- Abbvie, Novartis, Genesis, Lilly, Aenosasis, GSK, Pfizer

Identification of a subgroup of people with rheumatoid arthritis characterised by high disability over 10 years, despite low inflammation

Results from two European prospective cohort studies

Dr James Gwinnutt

Medical Research Council

CfMR Centre for Musculoskeletal Research

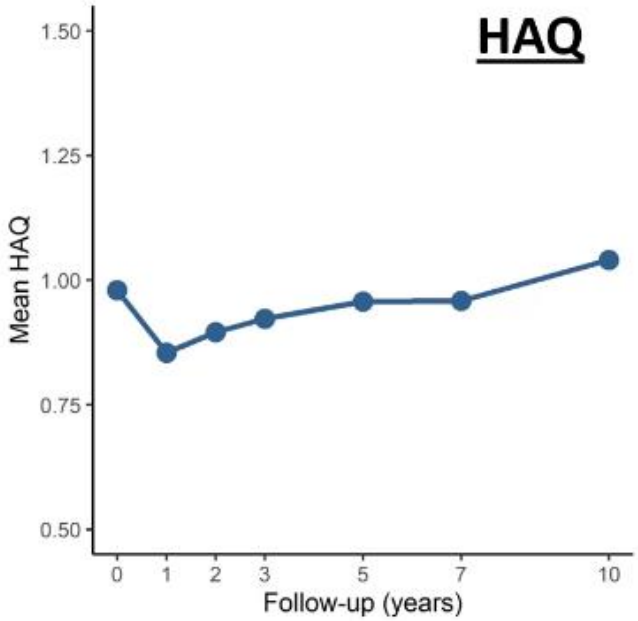
CENTRE FOR EPIDEMIOLOGY VERSUS ARTHRITIS

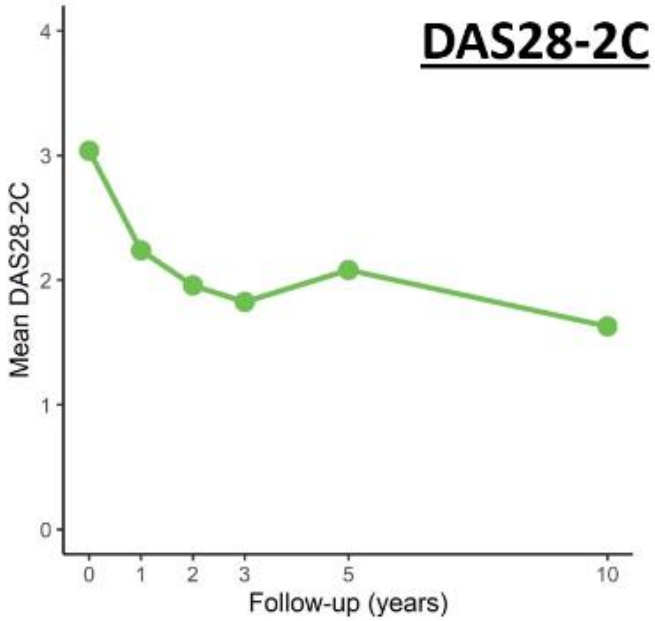
Datasets

- Norfolk Arthritis Register (NOAR)
  - Recruited people with ≥2 swollen joints lasting for ≥4 weeks in Norfolk, UK
  - Assessed regularly over subsequent 10 years

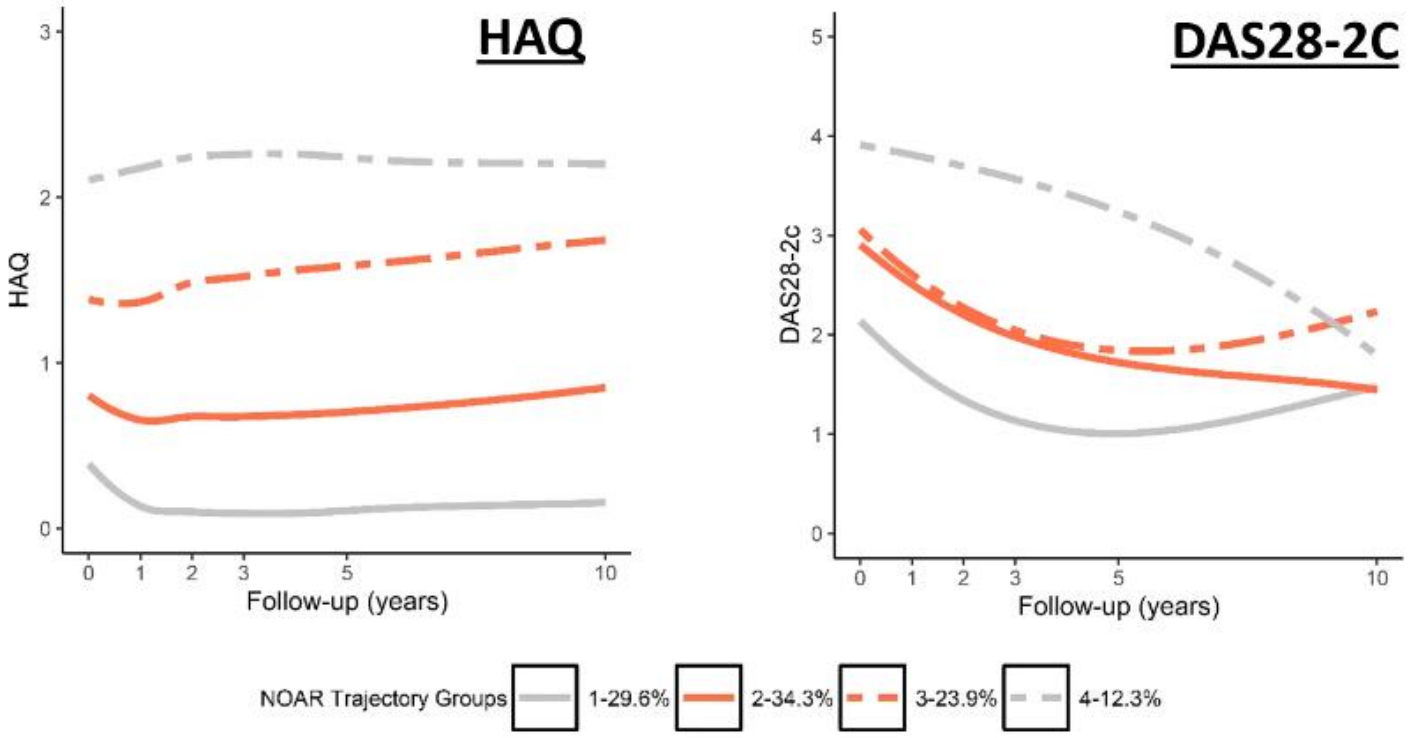
- Étude et Suivi des Polyarthrites Indifférenciées Récentes (ESPOIR)
  - Recruited people with >2 swollen joints lasting for >6 weeks from 14 regional centres across France
  - Also followed-up over 10 years

Outcomes over time - NOAR

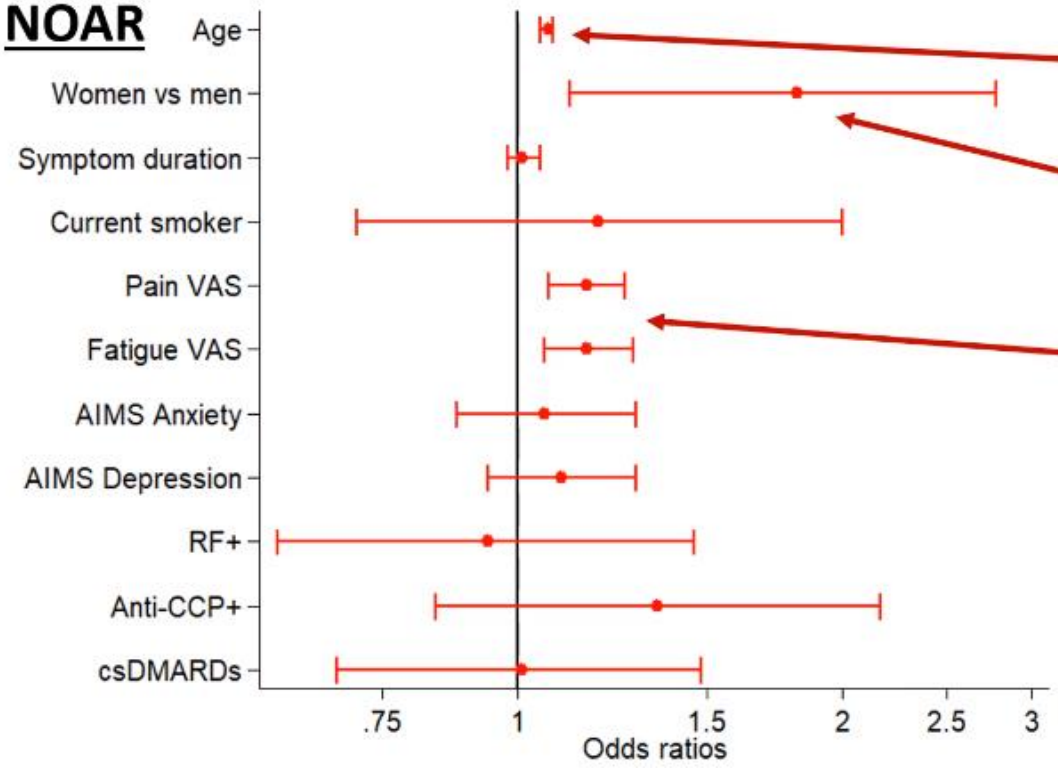




Trajectory groups - NOAR



Baseline predictors - NOAR



Age – OR 1.07

Women vs men – OR 1.82

Pain (per cm) – OR 1.16

Fatigue (per cm) – OR 1.16

Συμπέρασμα

- Υπάρχουν υποομάδες ασθενών με ΡΑ διαφορετικά επίπεδα λειτουργικότητας παρότι είχαν παρόμοια επίπεδα φλεγμονής
- Οι ασθενείς με χαμηλή λειτουργικότητα είχαν υψηλά επίπεδα πόνου και κόπωσης
- Χρειάζονται στρατηγικές αντιμετώπισης του πόνου και της κόπωσης, για να κλείσει το κλείσει το χάσμα ανάμεσα στη φλεγμονή και τη λειτουργικότητα

EULAR European Congress of Rheumatology 2021
2-5 June 2021 (Virtual)

Epidemiology and mortality of RA-associated interstitial lung disease: data from a French administrative healthcare database

Pierre-Antoine Juge,[1] Lidwine Wémeau-Stervinou,[2] Sébastien Ottaviani,[1] Guillaume Desjeux,[3] Joe Zhuo,[4] Bruno Bregman,[5] Virginie Vannier-Moreau,[5] Rene-Marc Flipo,[6] Bruno Crestani,[7] Philippe Dieudé[1]

[1]Service de Rhumatologie, Université de Paris, Hôpital Bichat-Claude-Bernard, APHP, Paris, France; [2]Service de Pneumologie, CHU Lille, Lille, France; [3]Sanoïa, Aubagne, France; [4]Bristol Myers Squibb, Princeton, NJ, USA; [5]Bristol Myers Squibb, Rueil-Malmaison, France; [6]Service de Rheumatologie, CHU Lille, Lille, France; [7]Service de Pneumologie A, Université de Paris, Hôpital Bichat-Claude-Bernard, APHP, Paris, France

Presentation Number OP0099

Σκοπός

- Να εκτιμηθεί η επιδημιολογία της κλινικής RA-ILD και να συγκριθεί η θνητότητα και τα θεραπευτικά πρότυπα μεταξύ ασθενών με PA με ή χωρίς ILD
- Δεδομένα από εθνική ασφαλιστική βάση δεδομένων (1/1/2013-31/12/2018)

Αποτελέσματα

- Ασθενείς με PA: 173132
- Ασθενείς με RA-ILD N=4330 (2,5%), άνδρες 39,8%
- Επιπολασμός: 6,52/10^5
- Επίπτωση 1,04/10^5
- **Η προσαρμοσμένη θνητότητα ήταν 3 φορές μεγαλύτερη στους ασθενείς με RA-ILD από τους ασθενείς με RA χωρίς ILD**
- Οι ασθενείς με RA-ILD λάμβαναν σπανιότερα MTX και TNFi και συχνότερα άλλα csDMARDs, bDMARDs και GC

Ηλικία	Επιπολασμός (x10^{-5})	Επίπτωση (x10^{-5})
<65	1,66	0,21
65-74	12,8	1,72
≥75	**14,8**	**2,07**

Effects of nintedanib in patients with progressive fibrosing interstitial lung disease associated with rheumatoid arthritis (RA-ILD) in the INBUILD trial

Clive Kelly,[1] Eric L Matteson,[2] Martin Aringer,[3] Gerd Burmester,[4] Heiko Mueller,[5] Lizette Moros,[6] Klaus B Rohr,[6] Martin Kolb[7] on behalf of the INBUILD trial investigators

[1]Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK; [2]Division of Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA; [3]Rheumatology, Medicine III, University Medical Center & Faculty of Medicine, TU Dresden, Dresden, Germany; [4]Department of Rheumatology and Clinical Immunology, Charité–University Medicine Berlin, Berlin, Germany; [5]Biostatistics and Data Sciences, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; [6]TA Inflammation Med, Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; [7]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, Ontario, Canada.

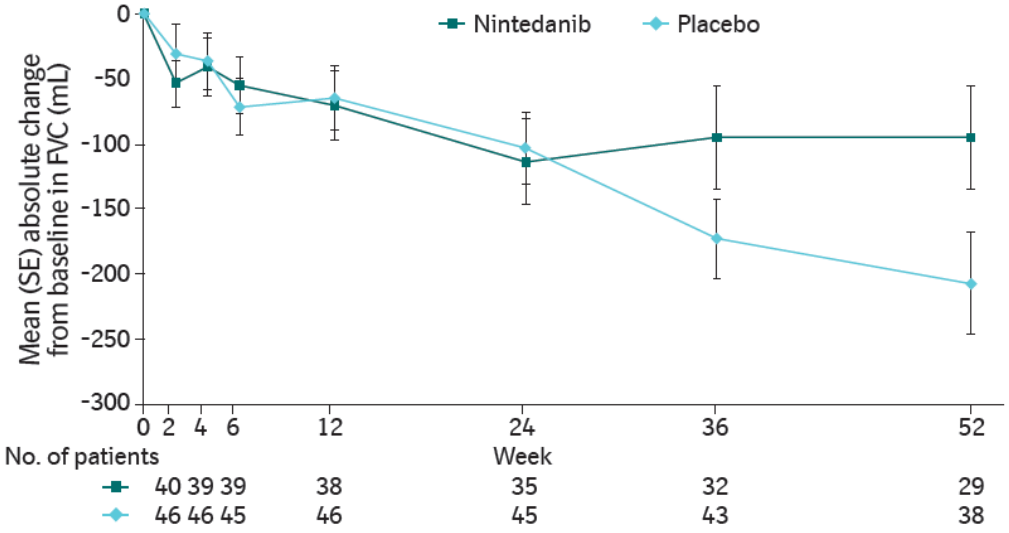
INTRODUCTION

- In the INBUILD trial in patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF), nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 57% compared with placebo.[1]
- Of the 663 patients in the INBUILD trial, 89 had RA-ILD.

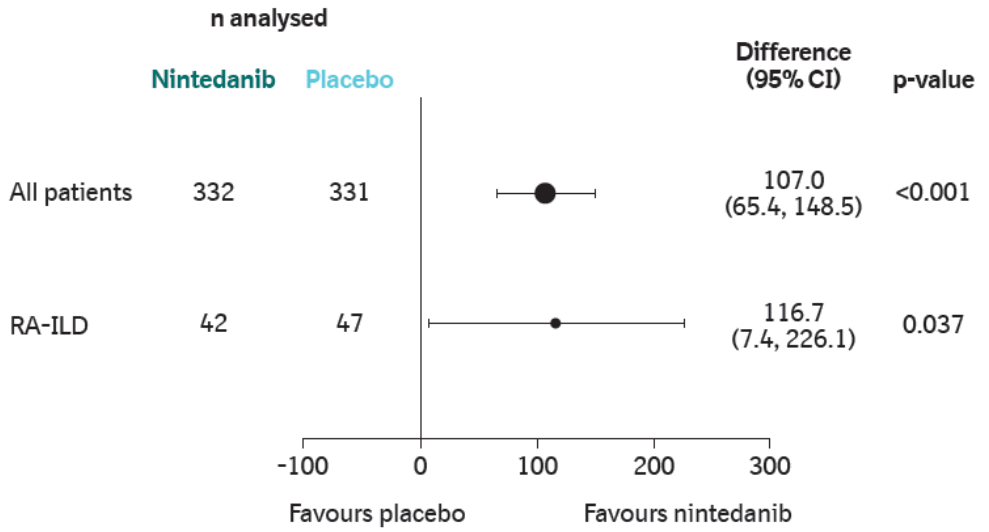
AIM

- To assess the efficacy and safety of nintedanib in patients with RA-ILD in the INBUILD trial.

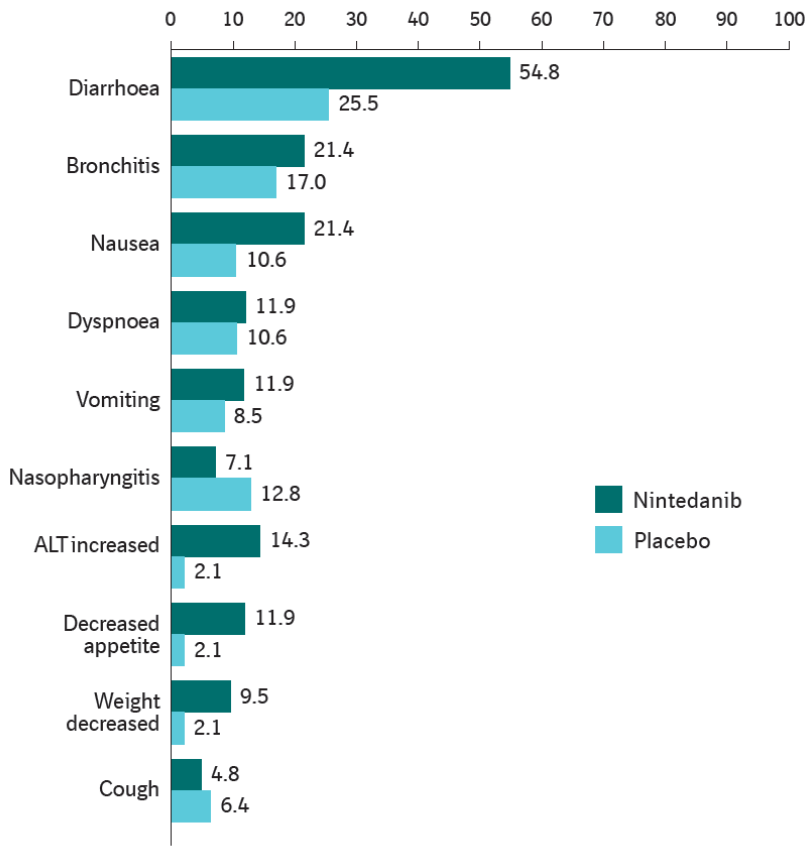
Absolute change from baseline in FVC (mL) over 52 weeks



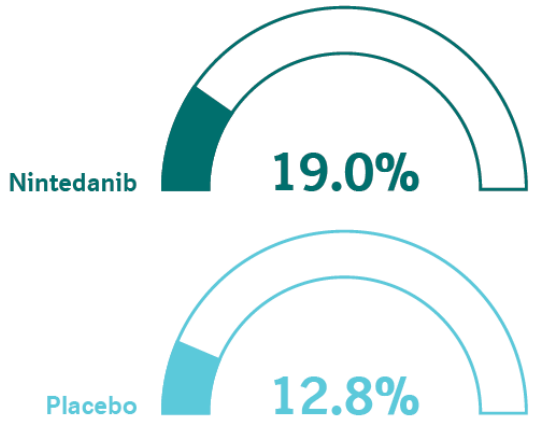
Rate of decline in FVC (mL/year) over 52 weeks with nintedanib versus placebo



Adverse events (reported irrespective of causality)



Adverse events leading to treatment discontinuation



Data are % of patients with ≥1 such adverse event reported over 52 weeks.

Συμπέρασμα

- Στη μελέτη INBUILD το nintedanib επιβράδυνε το ρυθμό μείωσης της FVC σε ασθενείς με PA και προοδευτική ινοποιό RA-ILD
- Οι AE ήταν διαχειρίσιμες στους περισσότερους ασθενείς
- Η αποτελεσματικότητα και ασφάλεια του nintedanib ήταν παρόμοια με το συνολικό πληθυσμό της μελέτης
- Τα συμπεράσματα της ανάλυσης υποομάδων περιορίζεται από το μικρό αριθμό ασθενών

香港中文大學
The Chinese University of Hong Kong

Faculty of Medicine

5-Year Cardiovascular Event Risk

in Early Rheumatoid Arthritis Patients who Received Treat-to-Target Management

a population-based cohort study

Dr. Tommy Lam T.O., Prof. Lai-Shan Tam
On behalf of the CRYSTAL group

The Department of Medicine & Therapeutics,
The Prince of Wales Hospital
The Chinese University of Hong Kong

Tsz On Lam

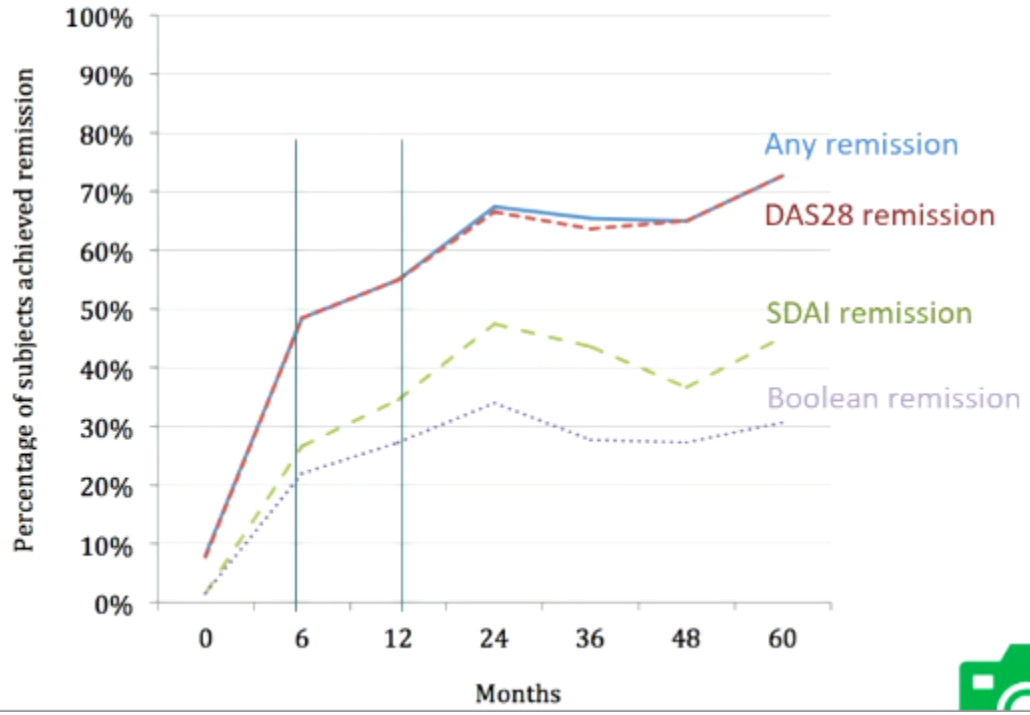
5-Year Cardiovascular Event Risk in Early Rheumatoid Arthritis Patients who received Treat-to-Target Management: a population-based cohort study

Methods

- Objective: to compare the **5-year** cardiovascular event rate among **early RA patients managed by a T2T** strategy with a CV risk factor-**matched non-RA population**

*Whether effective suppression of inflammation by the **treat-to-target** approach can reduce the excessive CVD risk associated with RA*

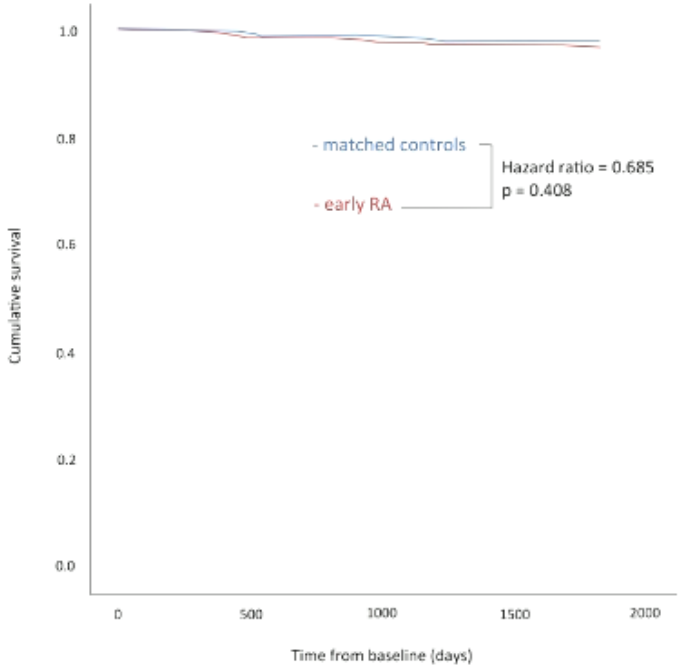
- Median disease duration **<6 months**
- Good proportion achieved remission
- 46% able to **sustain remission** for at least 3 years



Cardiovascular Event Outcome

- **No difference** in major or minor CV event risk over 5 years
- **ERA: 4.6** per 1000 persons-year vs. **non-RA: 6.6** per 1000 persons-year

	ERA (n=261)	Controls (n=783)	*p-value*
Major cardiovascular events in 5 years	3 (1.1%)	17 (2.2%)	*0.44*
Acute coronary syndrome	1 (0.4%)	4 (0.5%)	*1.00*
or percutaneous coronary intervention			
Heart failure	1 (0.4%)	8 (1.0%)	*0.464*
Stroke	1 (0.38%)	4 (0.51%)	*1.00*
Minor cardiovascular events in 5 years	3 (1.1%)	12 (1.5%)	*0.77*
Ischaemic heart disease	3 (1.1%)	9 (1.1%)	*1.00*
Transient ischaemic attack	0 (0%)	1 (0.1%)	*1.00*
Carotid stenosis	0 (0%)	2 (0.3%)	*1.00*



Predictors of Cardiovascular Event **in ERA**

Univariate analysis among the **ERA** cohort

- **Atherogenic index of plasma** (HR 10.7, p-value 0.02) and **Age** (HR 1.1, p-value 0.02) were the most significant **non-RA-specific** predictors for CV events

Multivariate analysis among the **ERA** cohort adjusted for **AIP** and **Age**

	Factor	Adjusted hazard ratio	95% CI	p-value
1st year disease activity	Year 1 DAS28-ESR	2.71	1.078-6.811	0.034
	Year 1 DAS28-CRP	3.01	1.377-6.558	0.006
Remission duration	Remission (any) duration	0.452	0.222-0.920	0.029
	DAS28-ESR remission duration	0.459	0.226-0.934	0.032
	SDAI remission duration	0.357	0.108-1.180	0.091
Baseline function	Baseline Health Assessment Questionnaire	5.196	1.169-23.098	0.030
	Hydroxychloroquine use	0.135	0.016-1.182	0.071

Συμπέρασμα

- Ασθενείς με πρώιμη PA που αντιμετωπίζονται με στρατηγική T2T δεν εκδήλωσαν περίσσεια καρδιαγγειακών συμβαμάτων στην 5ετία σε σχέση με την ομάδα ελέγχου
- Ο συντελεστής x1.5 ίσως δεν είναι κατάλληλος για ασθενείς με πρώιμη PA που έχουν επιτύχει ύφεση ή αντιμετωπίζονται με T2T

Department of Rheumatology,
Clinical Immunology
University Hospital of Heraklion

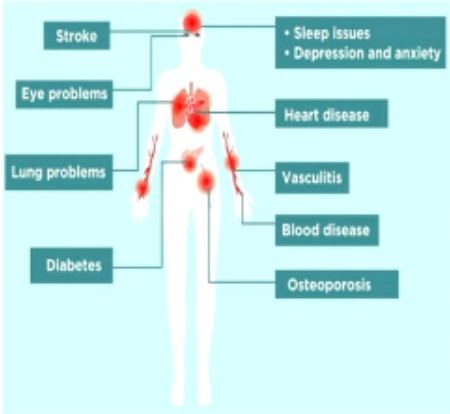
Medical School
University of Crete

IN RHEUMATOID ARTHRITIS PATIENTS HIGHER NUMBER OF COMORBIDITIES PREDICTS 6-MONTH INSUFFICIENT RESPONSE TO 1st BIOLOGIC THERAPY AND EVENTUAL CATEGORIZATION OF THE DISEASE AS DIFFICULT-TO-TREAT

Irini Flouri, Argyro Repa, Nestor Avgustidis, Nikolaos Kougkas, Anastasios Eskitzis, Ainour Molla Ismail Sali, Sofia Pitsigavdaki, Katerina Pateromichelaki, Eleni Kalogiannaki, Maria Terizaki, George Bertsias, Prodromos Sidiropoulos

University Hospital of Heraklion, Crete, Rheumatology Department, Heraklion, Crete, Gre

Aims



To evaluate the impact of comorbidities on:

1. Response to treatment at 6 months with the 1st bDMARD
2. Disease characterization as D2T

Methods – University of Crete Rheumatology Clinic Registry (UCRCR)

- ✓ Prospective registry for safety and effectiveness of bDMARDs in **inflammatory arthritis** (2004)
- ✓ Comorbidities (2011)
- ✓ **SLE** registry (2012)

Methods – Outcomes: Response / D2T

A. Response to therapy at 6 months with the 1st bDMARD:

- Simplified Disease Activity Index (**SDAI**): Low disease activity (>3.3-11) or remission (<=3.3)
- Health Assessment Questionnaire **(HAQ) improvement ≥ 0.25**

B. Contribution of comorbidities in D2T:

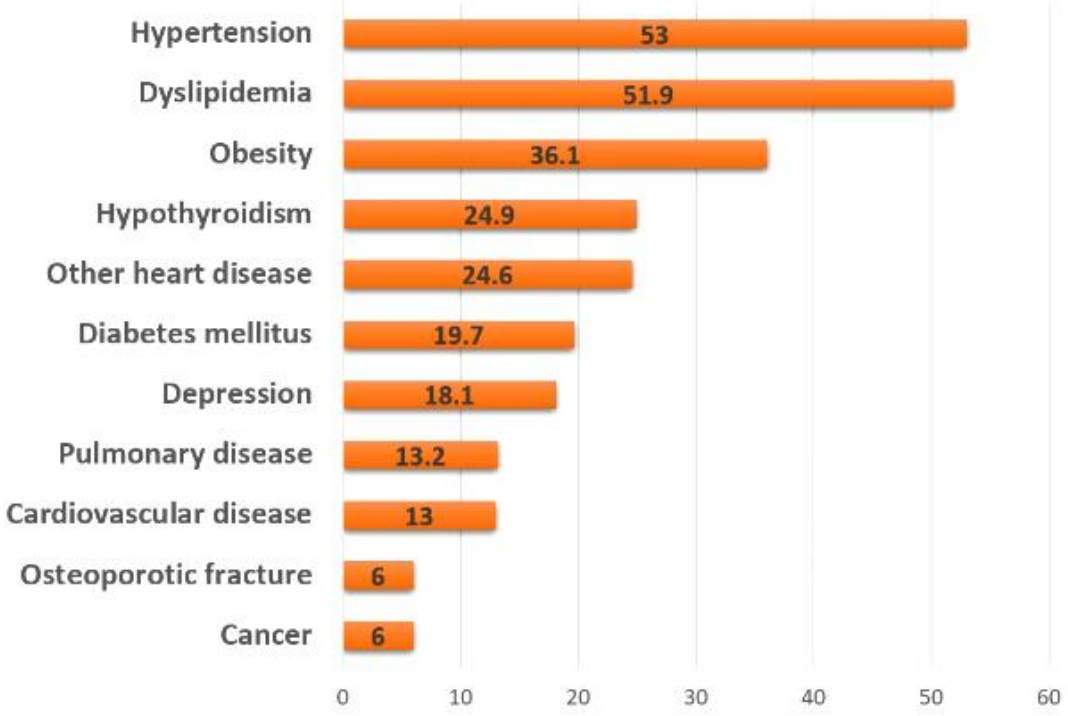
- D2T group (according to the EULAR study group definition[1]):
  - ✓ Failure of ≥2 bDMARDs/tsDMARDs with different mechanisms of action
  - ✓ At least moderate disease activity, or inability to taper glucocorticoid treatment
  - ✓ High global and/or physician visual analogue score of disease activity

- D2T group was compared at baseline of 1st bDMARD to:
  - ✓ "Non-D2T"
  - ✓ "Well-controlled": follow-up ≥2 years **AND** ≥2 visits in the last year in LDA/Rem.

[1] Nagy G, Roodenrijs NM, Welsing PM, et al. EULAR definition of difficult-to-treat rheumatoid arthritis. Annals of the Rheumatic Diseases 2021;80:

High baseline burden of comorbidities:

- ✓ Median comorbidities count =3
- ✓ Median RDCI =1



Number of comorbidities at baseline	
Comorbidities count (CC) median (IQR)	**3 (1-4)**
CC=0, N (%)	82 (11)
CC=1, N (%)	124 (16.5)
CC=2, N (%)	140 (19)
CC ≥ 3, N (%)	405 (54)
RDCI, median (IQR)	**1 (0-2)**
RDCI = 0, N (%)	205 (27)
RDCI = 1, N (%)	215 (28.5)
RDCI = 2, N (%)	
RDCI ≥ 3, N (%)	

Comorbidities negatively affect 6-month responses

(Logistic regression analysis)

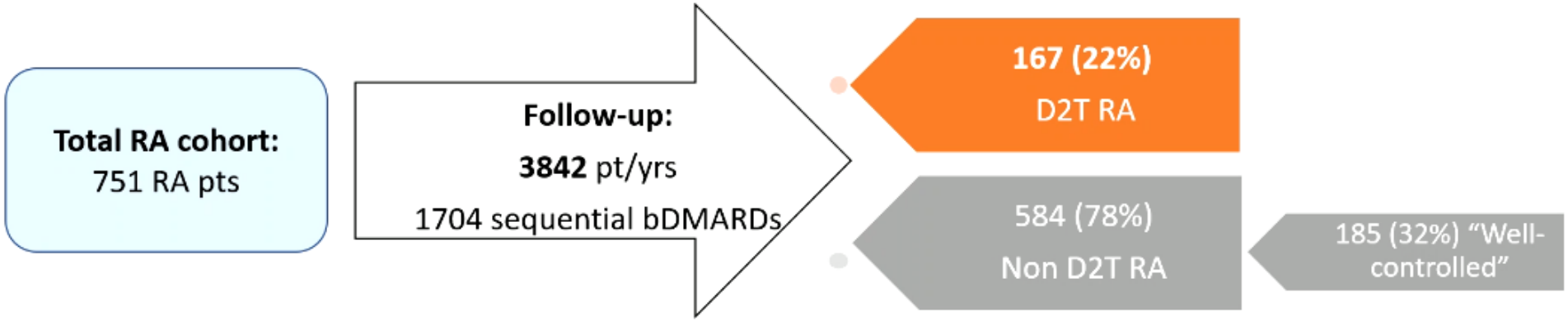
	SDAI LDA/Remission	
	*Adjusted OR**	
TNFi (vs. nonTNFi)	2.6 (1.1 - 5.8)[a]	2.8 (1.2 – 6.3)[a]
Seropositive (yes vs. no)	2.3 (1.3 – 4.0)[b]	2.2 (1.3 – 3.8)[b]
Baseline SDAI	0.93 (0.91 –0.96)[c]	0.93 (0.91-0.95)[c]
CC ≤ 1 (vs. ≥2)	**3.58 (2.0 - 6.4)[c]**	
RDCI =0 (vs. ≥1)		**2.0 (1.1 – 3.5)[a]**
a: p<0.05; b: p<0.01; c: p<0.001		

	HAQ improvement ≥ 0.25	
	*Adjusted OR**	
Age	0.96 (0.93-0.99)[b]	0.97 (0.94-0.99)[a]
Baseline HAQ	7.39 (4.2-13.1)[c]	7.83 (4.4-14.0)[c]
CC ≤ 1 (vs. ≥2)	1.40 (0.7-2.7)	
RDCI =0 (vs. ≥1)		**2.08 (1.1 - 4.0)[a]**
a: p<0.05; b: p<0.01; c: p<0.001		

* Variables entered in the analyses and removed from the final models with backward selection (p≥0.10) : sex, age, RF/anti-CCP seropositivity, disease duration since diagnosis, year of therapy start, number of previous csDMARDs, type of 1st bDMARD used (TNFi vs. non-TNFi), co-therapy v
methotrexate or corticosteroids (yes/no), baseline SDAI and HAQ

Substantial number of patients are characterized as D2T:

22% of the cohort



Comorbidity burden at baseline predicts disease characterization as D2T

compared to "non-D2T"

	D2T versus "non-D2T"	
At baseline	*Adjusted OR**	
Sex (male vs. female)	0.48 (0.2-0.9)[a]	0.48 (0.2-0.9)[a]
Seropositivity	0.65 (0.4-1.0)[a]	0.66 (0.4-1.0)[a]
Nr of previous csDMARDs	1.24 (1.02-1.5)[a]	1.24 (1.01-1.5)[a]
SDAI	1.02 (1.00-1.03)[b]	1.02 (1.00-1.03)[b]
CC ≥2 (vs. ≤1)	1.30 (0.8-2.2)	
RDCI ≥1 (vs. 0)		**1.78 (1.04-3.04)[a]**
a: p<0.05; b: p<0.01; c: p<0.001		

* Variables entered in the analyses and removed from the final models with backward selection (p≥0.10) : sex, age, RF/anti-CCP seropositi... diagnos... duration since diagnosis, year of therapy start, number of previous csDMARDs, type of 1st bDMARD used (TNFi vs. non-TNFi), co-therapy ... methotrexate or corticosteroids (yes/no), baseline SDAI and HAQ

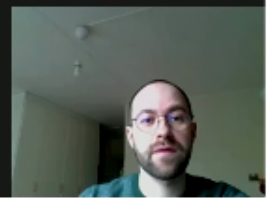
Συμπεράσματα

- Οι ασθενείς με PA που λαμβάνουν bDMARDs έχουν ένα σημαντικό φορτίο συννοσηροτήτων, ενώ 22% χαρακτηρίζονται τελικά ως D2T
- Οι συννοσηρότητες επηρεάζουν αρνητικά την απάντηση στη θεραπεία στους 6 μήνες (OR=2 για LDA/Rem)
- Οι συννοσηρότητες συνεισφέρουν σημαντικά στην εξέλιξη σε D2T (OR=2,2)
- Οι Ρευματολόγοι θα πρέπει να εστιάζουν στις συννοσηρότητες προκειμένου να βελτιώνουν τις βραχυ- και μακροπρόθεσμες εκβάσεις των ασθενών με PA υπό bDMARDs

Karolinska Institutet

Comparative effectiveness of Janus Kinase inhibitors versus biological Disease Modifying Anti-Rheumatic Drugs

Swedish RA patients experience



Andrei Barbulescu

Comparative effectiveness of JAKi versus bDMARDs; a nationwide study in RA

Aims

Aims

Compare **JAKi** with **bDMARDs** in terms of:

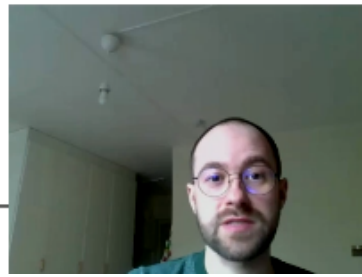
- Patient **characteristics** at treatment start
- Proportion of patients remaining **on therapy** at ~12m
- **Clinical Response** rate (5 dimensions) at ~12m

Study Period and **Data Sources**

Patient recruitment (treatment starts): 01-JAN-2017 to 30-SEP-2018

Secondary Data (linked Swedish national registers):

- Swedish Rheumatology Quality register (SRQ)
- National Patients register
- Prescribed Drugs register
- Causes of Death register
- Total Population register



Methods

Karolinska Institutet

Study Design

- Clinical treatment responses measured within [+275d to +455d] after start
- Patients were considered **non-responders** if they **stopped** treatment **before evaluation** due to **adverse effects** or **inefficacy**
- Treatments stopped for other reasons (e.g. death, pregnancy) were censored

Compared **Treatment Cohorts**

1. JAKi (tofacitinib 20%, **baricitinib 80%**)
2. TNFi (etanercept, infliximab, adalimumab, certolizumab, golimumab)
3. Rituximab
4. Abatacept
5. IL6i (tocilizumab, sarilumab)

Εκβάσεις: Καλή απάντηση κατά EULAR, DAS28 ύφεση, CDAI ύφεση, HAQ

Αποτελέσματα-Συμπέρασμα

- Η σύγκριση των JAKi με καθεμιά κατηγορία στοχευμένης θεραπείας (TNFi, ABA, IL-6i, RTX) δεν έδειξε στατιστικώς σημαντικές διαφορές αναφορικά με:
- Good EULAR response
- DAS28(ESR) ύφεση
- CDAI ύφεση
- ΔHAQ>2

Discontinuation rate of Tofacitinib is similar when compared to TNF inhibitors in Rheumatoid Arthritis Patients:

Pooled Data from two Rheumatoid Arthritis Registries in Canada

Mohammad Movahedi, Denis Choquette, Louis Coupal , Angela Cesta, Xiuying Li, Edward Keystone, Claire Bombardier on behalf of OBRI and RHUMADATA investigators

Presenter: Dr Mohammad Movahedi

INSTITUT de RHUMATOLOGIE de MONTRÉAL

OBRI ONTARIO BEST PRACTICES RESEARCH INITIATIVE
Shaping the Future of Arthritis Care

Annual European Congress of Rheumatology EULAR 2021
Virtual, 2-5 June 2021

Number OP0179

Dataset description

The Ontario Best Practice Research Initiative (OBRI) is a multicenter registry across Ontario, Canada, collecting data from both rheumatologists and patients with RA at enrolment and at follow-up. Enrolled patients are interviewed every 6 months by phone and are seen by their rheumatologist as per routine care.

The Rhumadata clinical database and registry monitors the clinical care of patients with inflammatory diseases seen at the *Institut de Rhumatologie de Montréal* (IRM) and the *Centre de l'ostéoporose et de rhumatologie de Québec* (CORQ), the largest rheumatologic clinics in the province of Québec, Canada. Rhumadata collects real-world observational data of patients since 1998. The database currently has the treatment history of more than 6000 patients with inflammatory disease (RA, AS, SpA).

Methods

- **Study design: Retrospective cohort study**

- **Population:** RA patients enrolled in the OBRI and RHUMADATA initiating their TOFA or TNFi between 1 June 2014 (TOFA approval date in Canada) and 31 Dec 2019 were included.

- **TNFi group:** adalimumab, certolizumab, etanercept, golimumab, infliximab, and biosimilars.

- **Dealing with missing data**
  Multiple imputation (Imputation Chained Equation method; n=20) was used to deal with missing data.

- **Dealing with Confounding by indication**
  In observational studies, two treated group may be different with respect to different factors (e.g. disease severity) other than treatment. Therefore, direct comparisons of two groups may be misleading and result in biased estimates of the treatment effect.

Results…

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Table 2. Discontinuation of TNFi vs. TOFA due to any reason – Cox Regression Model

	HRs (95% CI), p-Value TNFi vs. TOFA			
	Unadjusted Events/total=491/1318	**Complete case analysis** Events/total=237/689	**Stratification (propensity deciles)** Events/total=491/1318	**IPTW** Events/total=491/1318
Discontinuation due to any reason	**0.83 (0.69-1.00), 0.05**	0.82 (0.61-1.10), 0.19	0.96 (0.78-1.19), 0.74	0.96 (0.79-1.15), 0.64

Note:
- Thirteen covariates with more than 10% standard mean difference between two treatment groups were used to calculate propensity score: Age, disease duration, positive RF, number of prior biologic used, CDAI, SDAI, HAQ-DI, ESR, concomitant use of MTX, leflunomide, hydroxychloroquine, and steroids.

IPTW: Inverse Probability of Treatment Weight
Bold: statistically significant p-value

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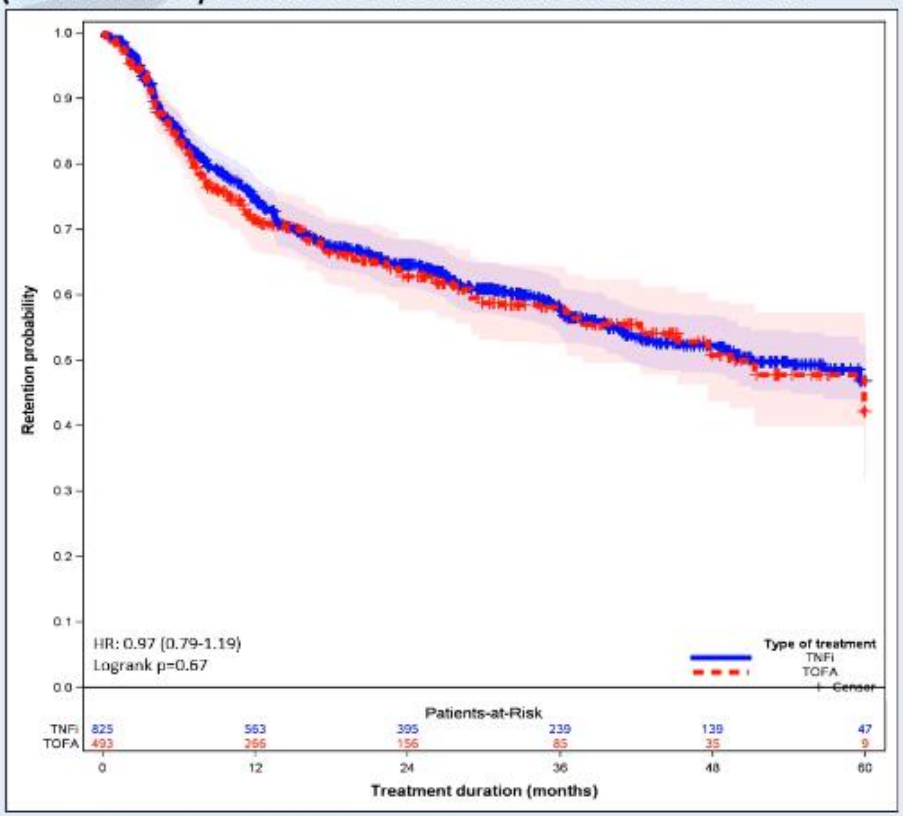
Fig 1. Propensity Score Adjusted Survival Curves (IPTW method) for Time to Discontinuation of TNFi vs. TOFA



IPTW: Inverse Probability of Treatment Weight

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Note:

- Propensity Score Adjusted (IPTW method) Survival Curves was performed using one imputed dataset.
- Thirteen covariates with more than 10% standard mean difference between two treatment groups were used to calculate propensity score:
  Age, disease duration, positive RF, number of prior bio
  SDAI, HAQ-DI, ESR, concomitant use of MTX, Leflunomi
  hydroxychloroquine, and steroids.

Συμπέρασμα: Σε αυτά τα registry η παραμονή στο tofacitinib και τους TNFi ήταν παρόμοια

Biobadaser 3.0

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2021 | 2–5 JUNE

OP0123: SAFETY PROFILE OF JAK INHIBITORS VERSUS TNF-INHIBITORS IN REAL-WORLD CLINICAL PRACTICE: DATA FROM A MULTICENTER REGISTER

B. Hernández-Cruz, C. Sánchez-Piedra, M. Freire, N. Busquets, J. García-González, M. Moreno[6], J M Blanco, S. Manrique, E. Perez-Pampín, F. Sánchez-Alonso, **Isabel Castrejón*** on behalf of BIOBADASER

Isabel Castrejon

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

OBJECTIVE

The aim of the present study is

1. to compare drug survival of JAKi versus anti-TNF
2. to evaluate the safety profile of approved JAKi –tofacitinib and baricitinib

in real world clinical practice

METHODS: BIOBADASER

February 2000

Drug safety registry launched

Dr. J. Gomez-Reino (PI)
Dr. L. Carmona (Co-I)
Objectives:
1. Identify adverse events (AE) in daily practice
2. Estimate the risk of AE
3. Assess long-term biologics retention

December 2015

PHASE III

Centres: 35
Patients: 2,664
- Biosimilars
- Small molecules
- Activity scores data

November 2020

PI: Dr. Castrejon

December 2020

Centres: 28
Drugs: 35
Patients: 7,485

RESULTS

Characteristics of patients included from BIOBADASER and medications used by diagnosis

	All patients	Rheumatoid Arthritis	Ankylosing spondylitis	Psoriatic arthritis
N (%)	4,532 (100%)	1,724 (38%)	1,032 (23%)	973 (21%)
Age	56.0 (13.2)	60.0 (12.8)	51.1 (13.1)	54.3 (12.1)
Women, n (%)	2182 (58.5)	1372 (79.6)	314 (30.4)	496 (51.0)
Disease duration, median (IQR)	6.5 [2.4-13.0]	7.1 [3.2-13.8]	6.9 [1.8-15.1]	5.2 [2.0-10.0]
Charlson index, mean (SD)	1.9 (1.3)	2.1 (1.4)	1.7 (1.2)	1.9 (1.3)
Anti-TNF				
Mean age start of first anti-TNF (SD)	50.8 (12.6)	53.0 (12.3)	47.3 (12.7)	49.9 (11.8)
First line anti-TNF, n (%)	2614 (49.3)	1110 (48.8)	782 (49.8)	722 (49.5)
JAKi				
Mean age start of JAKi (SD)	57.6 (11.9)	57.8 (12.0)	61.0 (7.4)	51.8 (9.2)
First line JAKi, n (%)	117 (23.7)	115 (24.5)	0 (0.0)	2 (9.5)

Fundación Española de Reumatología

RESULTS

Drug survival (95% confidence interval) by diagnosis for JAKi versus anti-TNF

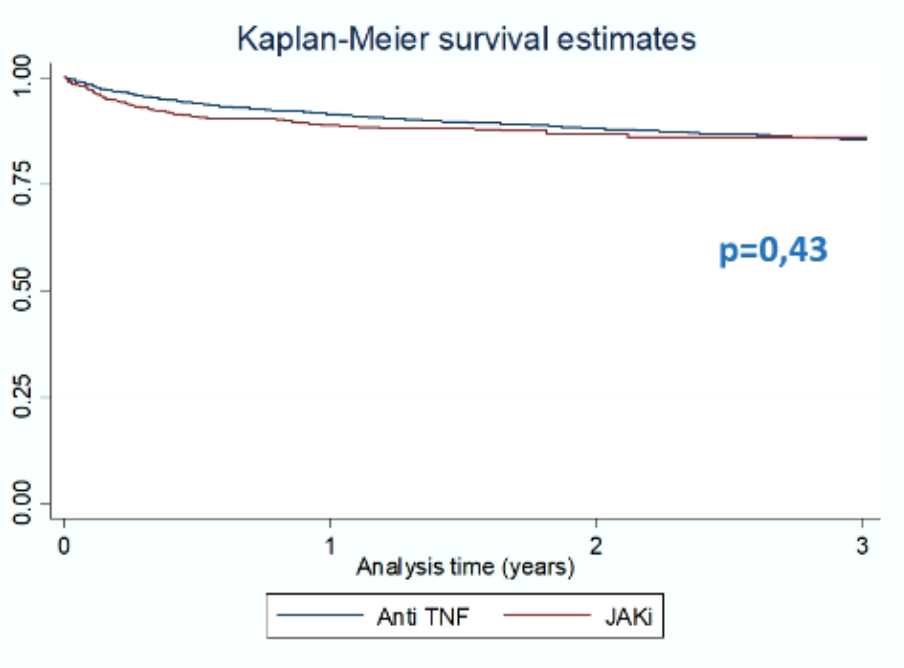
	One Year	Two years	Three years
Rheumatoid arthritis			
Anti-TNF	89.5 (88.2-90.7)	85.0 (83.3-86.5)	81.2 (79.3-83.1)
JAKi	89.1 (86.4-91.3)	87.4 (84.2-89.9)	86.6 (83.1-89.5)
Spondyloarthritis			
Anti-TNF	92.9 (91.9-93.7)	90.3 (89.1-91.3)	88.4 (87.0-89.6)
JAKi	86.5 (72.6-93.6)	75.7 (46.0-90.5)	-

Reasons to stop therapy, n (%)

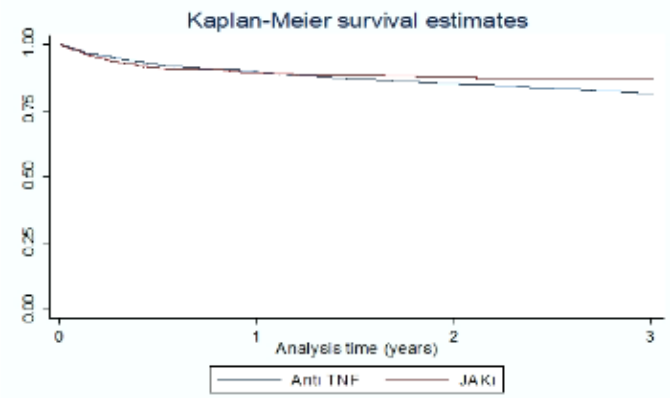
	Anti-TNF	JAKi
Lack of efficacy	1825 (53.2%)	142 (55.9%)
Adverse event	858 (25.0%)	86 (33.9%)

RESULTS

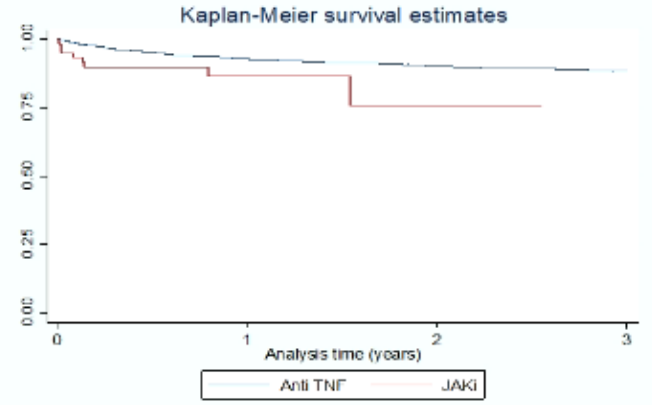
Survival of JAKi (red) and anti-TNF (blue)



Rheumatoid artrhitis



Spondyloarthritis



RESULTS

Adverse events in patients with RA and SpA treated with anti-TNF and JAKi

	Rheumatoid Arthritis		SpA	
	Anti-TNF	JAKi	Anti-TNF	JAKi
Total exposure (visits)	6270.7	378	8796.9	**13**
Type of adverse event				
All infections	136.5 (127.7-146.0)	166.7 (130.2-213.4)	92.4 (86.3-99.0)	230.0 (74.2-713.0)
Serious infections	20.3 (17.0-24.1)	34.4 (20.0-59.2)	9.9 (8.0-12.2)	0.0 (0.0-0.0)
Herpes Zoster	7.5 (5.6-10.0)	13.2 (5.5-31.8)	4.4 (3.2-6.1)	0.0 (0.0-0.0)
Tuberculosis	1.1 (0.5-2.3)	0.0 (0.0-0.0)	0.5 (0.2-1.2)	0.0 (0.0-0.0)
Malignancy/neoplasia	13.2 (10.7-16.4)	15.9 (7.1-35.3)	8.0 (6.3-10.1)	0.0 (0.0-0.0)
Thrombotic/vascular events	1.1 (0.5-2.3)	2.6 (0.4-18.8)	1.0 (0.5-2.0)	0.0 (0.0-0.0)
Gastrointestinal	42.3 (37.5-47.7)	145.5 (111.7-189.5)	43.8 (39.6-48.4)	153.3 (38.3-613.0)
Pulmonary	1.1 (0.5-2.3)	2.6 (0.4- 18.8)	0.1 (0.0-0.8)	-

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

RESULTS

Adverse events in patients with RA and SpA treated with anti-TNF and JAKi

After adjustment for:

- **Female sex** (HR = 1.40 [95% CI, 1.12–1.75])
- **Age at treatment initiation** (HR = 1.02 [95% CI, 1.01–1.03])
- **Disease duration** (HR = 1.07 [95% CI, 0.99–1.15])
- **Number of previous therapies** (HR = 1.09 [95% CI, 1.03–1.14])
- **Comorbidity** (HR = 1.00 [95% CI, 0.99–1.01])

HR for an AE in JAKi vs anti-TNF was 0.93 [95% CI, 0.72–1.21]

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

Συμπεράσματα

- Η επιβίωση των JAKi είναι παρόμοια με τους TNFi
- Οι λοιμώξεις και ο ζωστήρας τείνουν να είναι συχνότερα σε ασθενείς με JAKi
- Ωστόσο οι ασθενείς με JAKi ήταν μεγαλύτερης ηλικίας, είχαν μακρότερη διάρκεια νόσου και περισσότερες συννοσηρότητες

Pregnancy outcomes in relation to disease activity and anti-rheumatic treatment strategies in women with rheumatoid arthritis

- a matched cohort study from Sweden and Denmark

Karin Hellgren*, Anne Emilie Secher*, Bente Glintborg, Ane Lilleøre Rom, Bjorn Gudbjornsson, Brigitte Michelsen, Fredrik Granath*, Merete Lund Hetland*

a NordForsk collaboration on behalf of Sweden (SRQ) and Denmark (DANBIO)

* Shared authorship

Methods - Matched cohort study (Sweden and Denmark)

Exposed: RA-pregnancies by linking women with RA from Sweden (SRQ) and Denmark (DANBIO) to nationwide medical birth registers (MBR) to identify singleton pregnancies

Non-exposed: Non-RA pregnancies through MBR matched 1:10 on parity, birth year and maternal age at delivery

Outcomes:

Preterm birth: delivery <37 gestational weeks

Small for gestational age: birth weight below two standard deviations adjusted for gestational age and sex

Statistics Odds Ratios (OR) through logistic regression with generalized-estimation-equation method (GEE).

Adjusting for maternal age, parity, birth year, BMI, smoking, educational level and country (Sweden, Denmark)

Data on disease activity available
in 1095 (63%) of the RA pregnancies

From SRQ/DANBIO
Disease activity
(DAS28, HAQ)
9 months before and during pregnancy

From MBR and educational registers:
Maternal characteristics
(smoking, BMI, education)

1739 RA pregnancies
Sweden 1104, 63.5%
Denmark 635, 36.5%

17390 Non-RA pregnancies
Sweden 11040, 63.5%
Denmark 6350, 36.5%

From SRQ/DANBIO and Prescribed drug registers:
anti-rheumatic treatment
(csDMARD, bDMARD, and oral corticosteroids,
9 months before and during pregnancy

Results - Risk of preterm birth (PTB) and small for gestational age (SGA) overall

Outcomes, n (%)	RA-pregnancies n= 1739	Non-RA pregnancies n= 17390	Adjusted Odds Ratio* 95% CI
Preterm birth definition: < 37 gestational weeks	144 (8.3)	794 (4.6)	**1.92 (1.56-2.35)**
Small for gestational age definition: birth weight below 2 SD adjusted for gestational age and sex	75 (4.3)	418 (2.4)	**1.93 (1.45-2.57)**

*Adjusted for maternal age, parity, birth year, BMI, smoking, educational level and country (Sweden, Denmark) and applying generalized-estimation-equation method (GEE)

Results - Risk in relation to treatment in the 9 months before pregnancy

	Preterm birth		Small for gestational age	
	Events (%)	Adjusted OR[1] 95% CI	Events (%)	Adjusted OR[1] 95% CI
Non-RA pregnancies	794 (4.6)	REF	418 (2.4)	REF
Maternal anti-rheumatic treatment				
No treatment	33 (8.1)	**1.90 (1.28-2.82)**	12 (3.0)	1.34 (0.70-2.58)
Monotherapy				
Oral steroids	11 (7.6)	1.56 (0.79-3.08)	8 (5.6)	**2.44 (1.12-5.28)**
cDMARD	19 (5.8)	1.31 (0.80-2.16)	14 (4.3)	1.76 (0.98-3.15)
bDMARD	11 (6.0)	1.31 (0.65-2.65)	5 (2.7)	0.54 (0.14-2.11)
Combination therapy without bDMARD				
Oral steroids + cDMARD	15 (6.6)	1.48 (0.83-2.62)	9 (3.9)	**2.10 (1.06-4.18)**
Combination therapy with bDMARD				
Oral steroids + bDMARD	21 (12.9)	**3.34 (1.97-5.65)**	11 (6.8)	**3.22 (1.61-6.44)**
csDMARD + bDMARD	19 (14.3)	**3.45 (1.94-6.14)**	7 (5.3)	**2.40 (1.08-5.30)**
Oral steroids + csDMARD + bDMARD	15 (10.5)	**2.57 (1.41-4.69)**	9 (6.3)	**3.81 (1.90-7.65)**

[1] Adjusted for parity, maternal age, birth year, BMI, smoking, educational level and country (Sweden, Denmark) and applying GEE

Results - Risk in relation to disease activity *during* pregnancy

	Preterm birth		Small for gestational age	
	Adjusted OR[2] (95% CI)	Adjusted OR[3] (95% CI) also for treatment	Adjusted OR[2] (95% CI)	Adjusted OR[3] (95% CI) also for treatment
DAS28-CRPa[1]				
<3.2	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
3.2-4.1	2.12 (0.89-5.05)	1.75 (0.73-4.23)	2.56 (0.87-7.56)	2.16 (0.71-6.54)
>4.1	**3.38 (1.52-7.55)**	**2.47 (1.05-5.76)**	**3.90 (1.46-10.4)**	**3.23 (1.13-9.27)**
CRP (mg/L)				
≥10 vs. <10	**4.17 (2.13-8.18)**	**3.35 (1.66-6.75)**	**2.91 (1.26-6.73)**	**2.63 (1.10-6.29)**
HAQ-score				
≥1 vs. <1	1.53 (0.78-3.02)	1.09 (0.53-2.23)	**4.03 (1.73-9.40)**	**3.35 (1**

[1]DAS28-CRP without patient's global health assessment.

[2] Adjusted for maternal age, parity, birth year, BMI, smoking, educational level and country (Sweden, Denmark). No GEE was applied in this analysis

[3]Adjusted also for treatment (csDMARD yes/no oral corticosteroids yes/no, and bDMARD, yes/no) during pregnancy

Results - Risk in relation to type of treatment *during* pregnancy

	Preterm birth (PTB)		Small for gestational age (SGA)	
Treatment during pregnancy	Adjusted OR[2] (95% CI)	Adjusted OR[3] (95% CI) also for disease activity	Adjusted OR[2] (95% CI)	Adjusted OR[3] (95% CI) also for disease activity
csDMARD yes vs. no	1.19 (0.60-2.38)	1.09 (0.54-2.19)	0.77 (0.31-1.88)	0.70 (0.28-1.73)
Oral corticosteroids yes vs. no	**2.62 (1.23-5.59)**	2.11 (0.94-4.74)	2.31 (0.90-5.96)	1.49 (0.53-4.15)
bDMARD yes vs. no	1.44 (0.70-2.95)	1.38 (0.66-2.89)	0.81 (0.32-2.04)	0.

[1]DAS28-CRP without patient's global health assessment.

[2]Adjusted for maternal age, parity, birth year, BMI, smoking, educational level and country (Sweden, Denmark) and treatment (csDMARD yes/no,oral corticosteroids yes/no, and bDMARD, yes/no) during pregnancy. No GEE was app

[3] Adjusted also DAS28CRPa <3.2, ≥3.2-4.1, >4.1 during pregnancy.

Συμπεράσματα

- Ο κίνδυνος προωρότητας και χαμηλού βάρους γέννησης παραμένει υψηλός σε αυτήν τη σύγχρονη κοόρτη με ΡΑ και γεννήσεις 2006-2018
- Η εκτεταμένη αντιρρευματική θεραπεία τους 9 μήνες *προ* της κύησης σχετίστηκε με ακόμη μεγαλύτερο κίνδυνο προωρότητας και SGA-δείκτης ενεργής νόσου;
- **Η ενεργότητα της νόσου παρά η θεραπεία φαίνονται ως οι σημαντικότεροι παράγοντες κινδύνου για προωρότητα και SGA**
- Αυξημένος κίνδυνος προωρότητας με τα GC

• WEBINAR

Ανασκόπηση

ΕΤΗΣΙΟΥ ΣΥΝΕΔΡΙΟΥ

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