EULAR Highlights online

Rheumatoid arthritis

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Basistherapie bei RA und Covid-19

eular
EUROPEAN CONGRESS OF RHEUMATOLOGY
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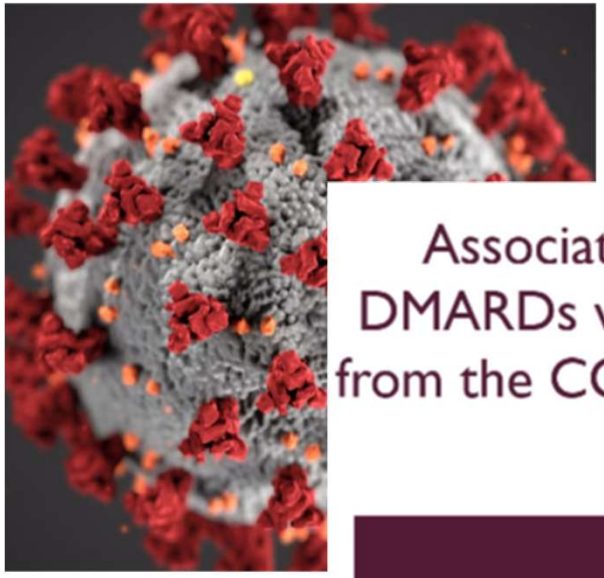

Associations of Baseline Use of Biologic or Targeted Synthetic DMARDs with COVID-19 Severity in Rheumatoid Arthritis: Results from the COVID-19 Global Rheumatology Alliance Physician Registry

Virtual EULAR Congress 2021

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COVID-19 Global Rheumatology Alliance

OP0006: DMARDs und Covid-19

- Ziel : Assoziation von bDMARD/tsDMARD Behandlung und Covid-19 Verlauf
- Daten: Covid-19 global rheumatology alliance
  - Patientenregister: 15’457 Patienten

    - Voluntarily reported cases of COVID-19 to the GRA physician registry
      - March 24, 2020 – April 12, 2021 (n=15,127)
        - Only analyzed patients reported to have RA (n=6,132)
        - Required treatment with b/tsDMARD at time of COVID-19 onset (baseline)
          - Minimize possible confounding by indication: similar disease state, opportunity to receive advanced treatment
          - Concomitant glucocorticoids and csDMARDs allowed
        - Excluded patients on IL-1 inhibitors due to small sample size (n=4)
        - All cases required to have resolved COVID-19 course

OP0006: DMARDs und Covid-19

- Statistische Analyse

  - Exposure: b/tsDMARD class
    - ABA, RTX, IL6i, JAKi, TNFi (reference group)
  - Outcome: ordinal COVID-19 severity scale
  - Primary analysis: multivariable ordinal logistic regression
    - Interpretation of effect size estimate: odds of being one level higher on the ordinal scale than the reference group

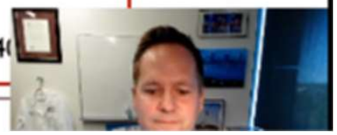
  - Sensitivity analyses:
    - Excluded ILD and cancer
    - Propensity score-matched: each b/tsDMARD class matched separately to TNFi
  - Binary outcomes at each level of the ordinal scale

OP0006: Resultate

- Hospitalisation und Tod durch Covid und b/ts DMARD

Results: COVID-19 outcomes by baseline b/tsDMARD (n=2,869)

COVID-19 severity scale level	Overall n=2869	ABA n=237	RTX n=364	IL6i n=317	JAKi n=563	TNFi n=1388
1) Not hospitalized	2256 (78.6%)	181 (76.4%)	210 (57.7%)	271 (85.5%)	409 (72.6%)	1185 (85.4%)
2) Hospitalized without oxygenation	137 (4.8%)	12 (5.1%)	20 (5.5%)	13 (4.1%)	28 (5.0%)	64 (4.6%)
3) Hospitalized with oxygen or ventilation	319 (11.1%)	26 (11.0%)	80 (22.0%)	24 (7.6%)	86 (15.3%)	103 (7.4%)
4) Death	157 (5.5%)	18 (7.6%)	54 (14.8%)	9 (2.8%)	4(	



OP0006: Resultate

- Assoziation von b/tsDMARD Therapie und Risiko für Hospitalisation/Tod

Results: Associations of baseline b/tsDMARD with binary COVID-19 outcomes (n=2,869)

OR (95%CI)	ABA	RTX	IL6i	JAKi	TNFi
Hospitalized	1.18 (0.76, 1.82)	**4.53 (3.32, 6.18)**	0.84 (0.53, 1.33)	**2.40 (1.78, 3.24)**	Ref
Hospitalized with oxygen or ventilation	1.12 (0.70, 1.81)	**2.87 (2.03, 4.06)**	0.72 (0.43, 1.20)	**1.55 (1.04, 2.18)**	Ref
Mechanical ventilation	1.41 (0.94, 2.10)	**4.05 (3.08, 5.33)**	0.75 (0.51, 1.10)	**2.03 (1.56, 2.62)**	Ref
Death	1.46 (0.72, 2.89)	**4.57 (3.32, 9.01)**	1.13 (0.50, 2.59)	**2.04 (1.58, 2**	

OP0006: Conclusions

- Unterschiede zwischen b/tsDMARDs und Covid 19 Verlauf

- Baseline use of RTX or JAKi use for RA associated with worse COVID-19 severity than TNFi use
  - RTX: 4-fold risk of ordinal COVID-19 severity
  - JAKi: 2-fold risk of ordinal COVID-19 severity
- No consistent associations of ABA or IL6i with COVID-19 severity compared to TNFi

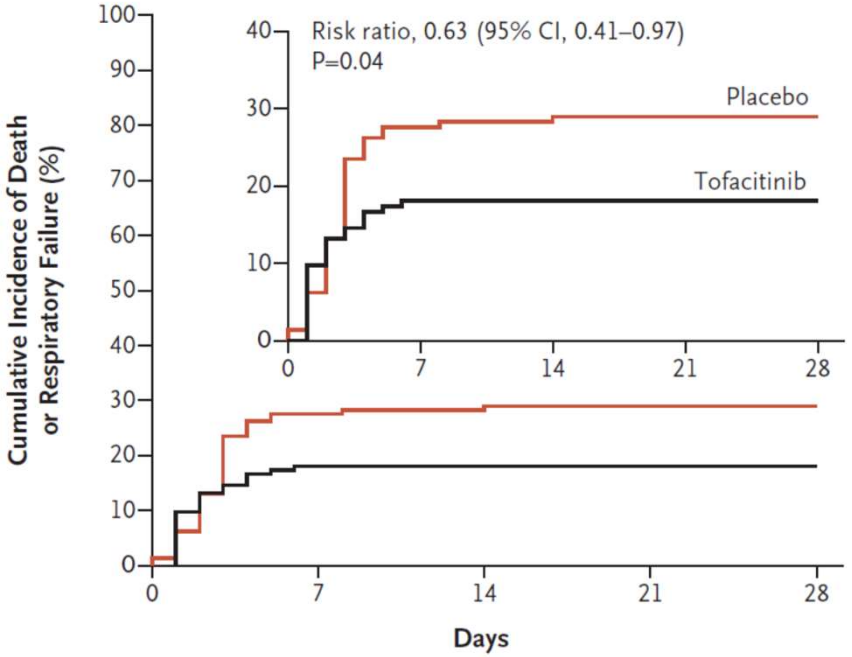
Vorsicht bei Pat. unter Rituximab und JAK-Inhibitoren

JAK Inhibitoren bei Covid-19 Pneumonie

N Engl J Med. 2021 Jun 16. doi: 10.1056/NEJMoa2101643. Online ahead of print.

Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia

Patrícia O Guimarães [1], Daniel Quirk [1], Remo H Furtado [1], Lilia N Maia [1], José F Saraiva Murillo O Antunes [1], Roberto Kalil Filho [1], Vagner M Junior [1], Alexandre M Soeiro [1], Alexandre P Tognon [1], Viviane C Veiga [1], Priscilla A Martins [1], Diogo D F Moia [1], Bruna S Sampaio [1], Silvia R L Assis [1], Ronaldo V P Soares [1], Luciana P A Piano [1], Kleber Roberta G R A P Momesso [1], Frederico Monfardini [1], Helio P Guimarães [1], Dario Ponce Majori Dulcine [1], Marcia R T Pinheiro [1], Levent M Gunay [1], J Jasper Deuring [1], Luiz V Ri Tamas Koncz [1], Otavio Berwanger [1], STOP-COVID Trial Investigators



Conclusions: Among patients hospitalized with Covid-19 pneumonia, tofacitinib led to a lower risk of death or respiratory failure through day 28 than placebo. (Funded by Pfizer; STOP-COVID

Guimaraes et al, NEJM 2021, Jun 16

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LB0003: Covid-19 Vakzinierung und Basistherapie

- Immunogenität der Pfizer/Biontech Covid-19 Vakzine bei RA unter DMARDs
- Prospektive multizentrische Studie, Israel
- 686 Patienten, RA, PsA, axSpA, SLE, ,CTD, Vaskulitis

Study population

- Inclusion criteria:
- Consecutive adult AIIRD patients (≥18 years of age)
  - rheumatoid arthritis (RA),
  - psoriatic arthritis (PsA), axial spondyloarthritis (axSpA)
  - systemic lupus erythematosus (SLE)
  - systemic vasculitis, idiopathic inflammatory myositis (IIM)
- Control group - a sample of the general population, without history of AIIRD and without immunosuppressive treatment.
- Exclusion criteria for all groups
  - pregnancy, history of past vaccination allergy, previous COVID-19 infection

Vaccination immunogenicity

- Tested 2 to 6 weeks after the 2nd vaccine dose
- LIASON (DiaSorin) SARS-CoV-2 IgG anti-trimeric S1/S2 spike glycoprotein Abs.
- FDA authorized assay with a clinical sensitivity and specificity > 98%.
- A value > 15 binding antibody units (BAU) was considered as a cutoff of seropositivity.

LB0003: Covid-19 Vakzinierung und Basistherapie

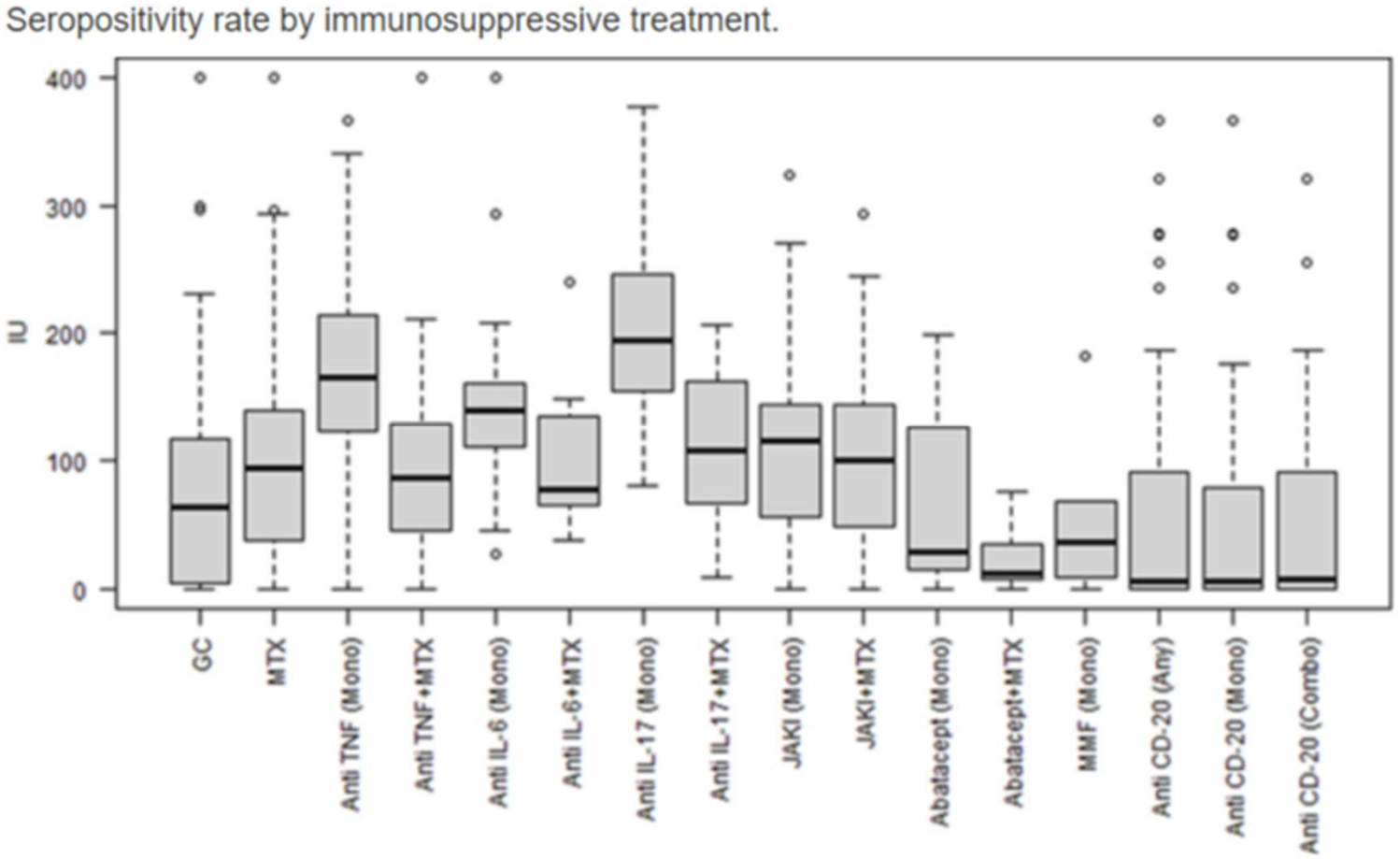
- Seropositivitätsrate

The seropositivity rate was 86% (n=590) in AIIRD patients vs 100% in controls (p <0.0001).

Study participants, n	Seropositivity rate, n (%)	Serum anti-S1/S2 IgG titer, mean±SD, BAU/ml
Controls, n=121	121 (100)	218.6±82.06
AIIRD (all), n=686	590 (86.0) *	132.9±91.7 *
RA, n=263	216 (82.1)	108.7±84.7
PsA, n=165	160 (96.9)	162.0±71.7
AxSpA, n=68	67 (98.5)	173.1±90.1
SLE, n=101	93 (92.1)	161.9±105.2
IIM, n=19	7 (36.8)	42.9±62.6
LVV, n=21	20 (95.2)	143.3±84.6
AAV, n=26	8 (30.8)	40.3±73.2
Other vasculitides, n=23	19 (86.6)	122.7±87.9

LB0003: Covid-19 Vakzinierung und Basistherapie

- Seropositivitätsrate nach Medikament

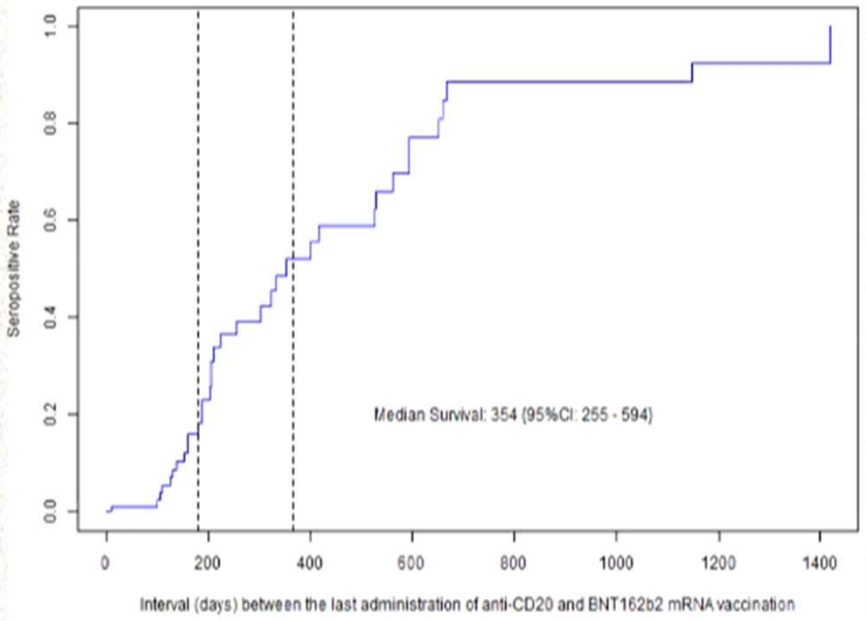


Reduziert bei

Rituximab
Abatacept
Glucocorticoide
MMF

LB0003: Covid-19 Vakzinierung und Basistherapie

- Rituximab mit tiefer Seropositivitätsrate

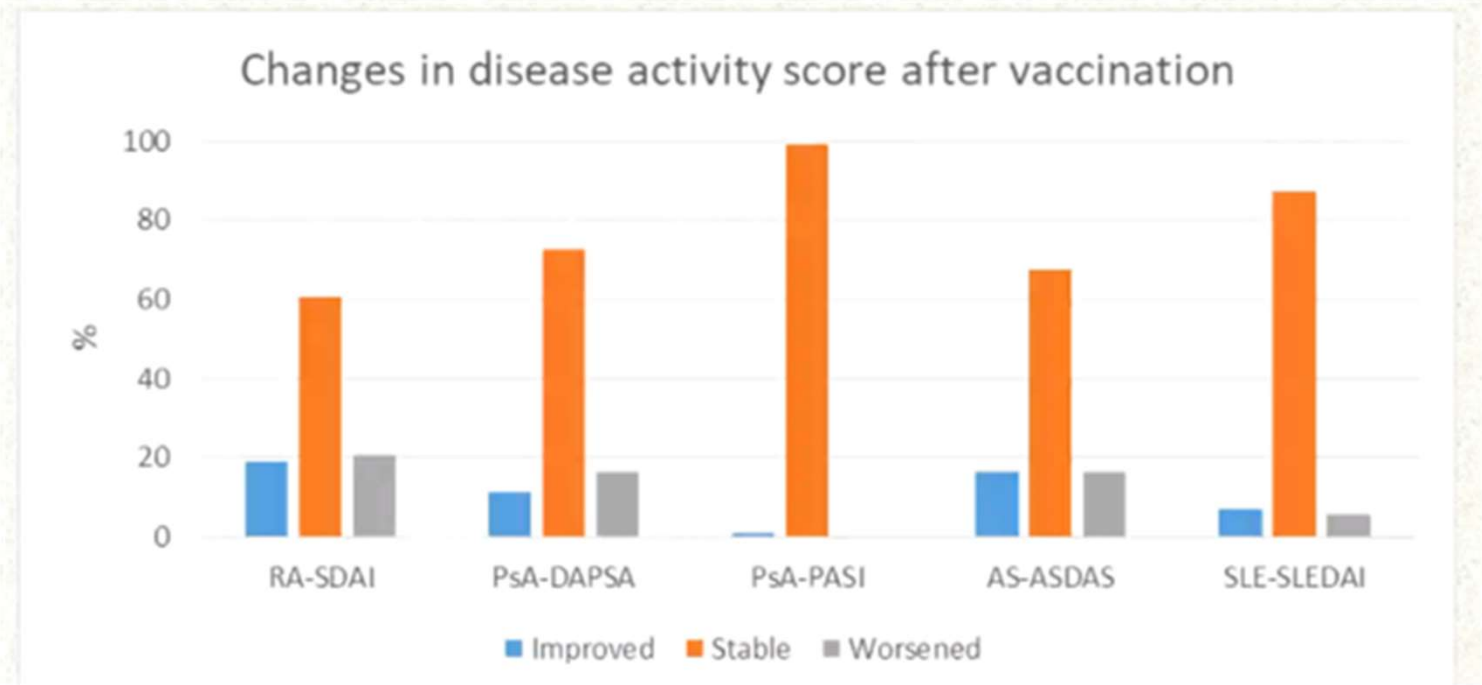


% Seropositive after 90 days	% Seropositive after 180 days	% Seropositive after 365 days
1.15%	18.39%	52.18%

The time interval between the pre-vaccination administration of rituximab and vaccination had a significant impact on the vaccine's immunogenicity.

LB0003: Covid-19 Vakzinierung

- Krankheitsaktivität stabil nach Covid Impfung (RA, PsA, AS)



LB0003: Conclusions

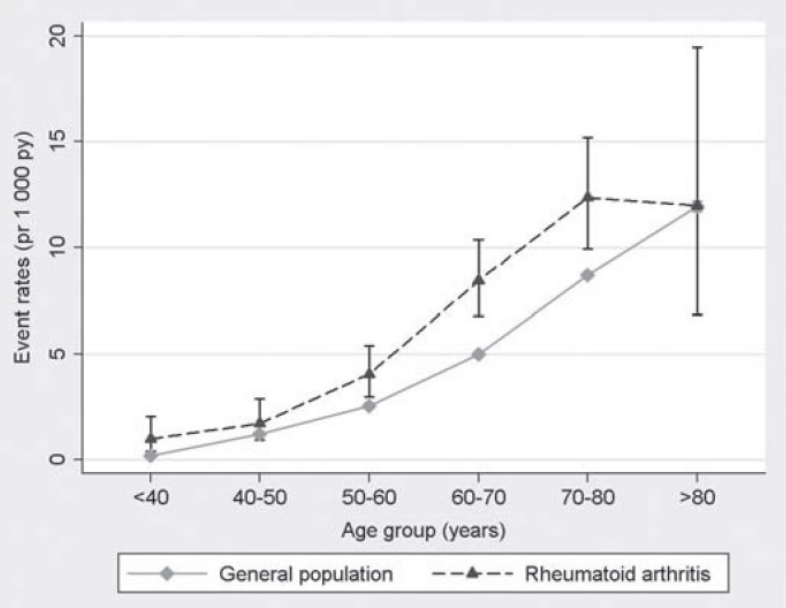
- Covid-19 Impfung bei entzündlich rheumatischen Erkrankungen

- Immunogenicity was severely impaired by rituximab; moderately impaired by glucocorticoids, abatacept, and mycophenolate mofetil; mildly impaired by methotrexate.
- The vaccine was generally safe in terms of adverse events.
- Post-vaccination disease activity remained stable in the majority of AIIRD patients.

Cardiovaskuläres Risiko bei RA

- Ca 1.5-fach erhöhtes CV Risiko bei RA
- Entzündung fördert die Entstehung einer Arteriosklerose

Myokardinfarktrate / 1000 Pat Jahre



Risiko vergleichbar mit Diabetes mellitus

Table 4 Risk of myocardial infarction (MI) associated with rheumatoid arthritis and diabetes mellitus. Results from conditional logistic regression analysis in nested case–control study*

	MI cases	Controls	OR*
	n=80 104	n=318 296	(CI)
Rheumatoid arthritis	265 (0.33%)	603 (0.19%)	1.9 (1.6 to 2.3)
Treatment duration strata (years)			
0–3	79 (0.10%)	216 (0.06%)	1.7 (1.3 to 2.2)
3–6	105 (0.13%)	207 (0.07%)	2.0 (1.4 to 2.9)
More than 6	81 (0.10%)	180 (0.06%)	1.7 (1.6 to 1.9)
Diabetes mellitus	3 948 (4.93%)	8 463 (2.66%)	1.9 (1.8 to 1.9)
Treatment duration strata (years)			
0–3	2 260 (2.82%)	4 743 (1.49%)	2.1 (1.6 to 2.7)
3–6	1 208 (1.51%)	2 685 (0.84%)	1.9 (1.8 to 2.1)
More than 6	480 (0.60%)	1035 (0.33%)	1.8 (1.6 to 2.1)

Lindhardsen et al, Ann Rheum Dis 2011

RA: Kardiovaskuläres Risiko

- EULAR Recommendations

	Level of evidence	Strength of recommendation
Overarching principles A. Clinicians should be aware of the higher risk for CVD in patients with RA compared with the general population. This may also apply to AS and PsA. B. The rheumatologist is responsible for CVD risk management in patients with RA and other IJD. C. The use of NSAIDs and corticosteroids should be in accordance with treatment-specific recommendations from EULAR and ASAS		
Recommendations		
1. Disease activity should be controlled optimally in order to lower CVD risk in all patients with RA, AS or PsA	2b-3	B
2. CVD risk assessment is recommended for all patients with RA, AS or PsA at least once every 5 years and should be reconsidered following major changes in antirheumatic therapy	3–4	C
3. CVD risk estimation for patients with RA, AS or PsA should be performed according to national guidelines and the SCORE CVD risk prediction model should be used if no national guideline is available	3–4	C–D
4. TC and HDLc should be used in CVD risk assessment in RA, AS and PsA and lipids should ideally be measured when disease activity is stable or in remission. Non-fasting lipids measurements are also perfectly acceptable	3	C
5. CVD risk prediction models should be adapted for patients with RA by a 1.5 multiplication factor, if this is not already included in the model	3–4	C

OP0103

- Cardiovaskuläres Risiko unter Therapie?

Methods

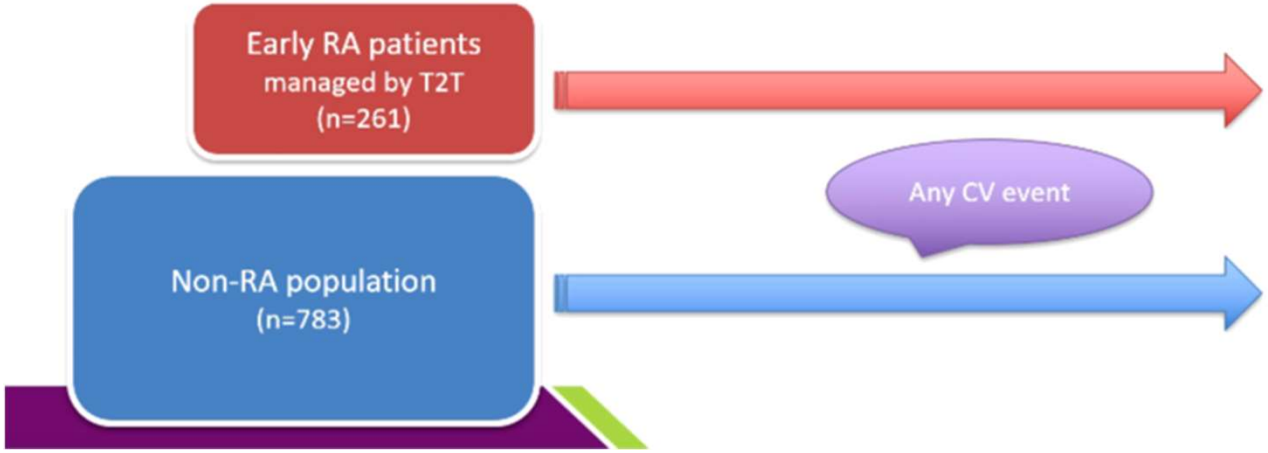
- Objective: to compare the **5-year** cardiovascular event rate among **early RA patients managed by a T2T** strategy with a CV risk factor-**matched non-RA population**

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

OP0103: CV Risko und T2T

Methods

- The 2 groups were followed-up for **5 years** from their baseline
- **Primary endpoint**: the first occurrence of an cardiovascular **event** defined by **acute coronary syndrome**, **ischaemic stroke**, or **heart failure**

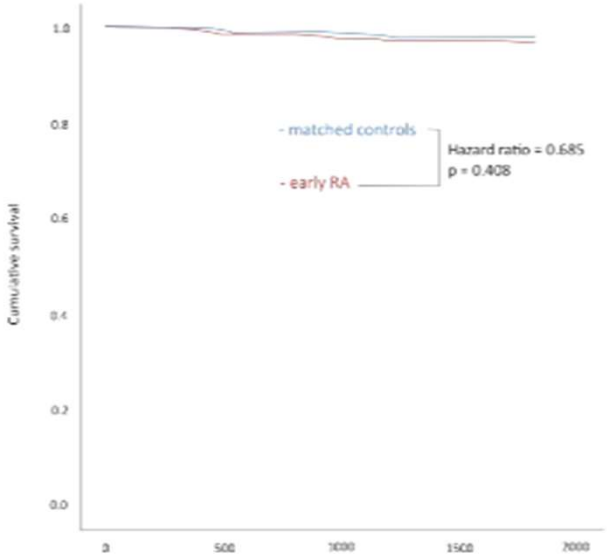


OP0103: CV Risko und T2T

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*



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OP0103: CV Risko und T2T

Predictors of Cardiovascular Event

In the entire cohort

- **Early RA** was **NOT** a significant predictor of CV event
  hazard ratio of 0.53 (95% CI: 0.15-1.79, p-value 0.304)

- **Age** was the most significant predictor of CV event
  hazard ratio of 1.14 (95% CI: 1.07-1.21, p-value <0.01)

OP0103: CV Risko und T2T

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

OP0103: CV Risko und T2T

Conclusions

- **ERA** patients managed by a **T2T** strategy did **NOT** develop excessive cardiovascular event compared to cardiovascular risk factor-matched controls over a period of 5 years.

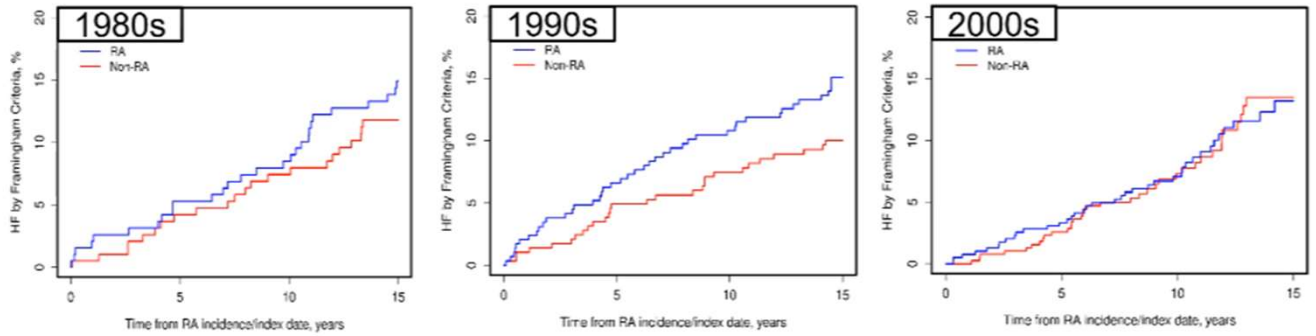
- *The 1.5X increased CV risk may **NOT** be applicable to **ERA** patients who have achieved remission or who have received effective T2T management*

However our ERA cohort might **UNDER-REPRESENT** the real world ERA patients' RA and CVD risk profile

OP0102

- Zeitlicher Trend des Riskos für Herzinsuffizienz bei RA

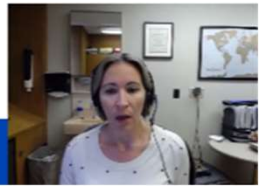
Results: Risk of HF in patients with vs without RA, by Decade



HR 2.20 (95%CI 1.44-3.34) HR 1.54 (95%CI 1.04-2.29) HR 1.14 (95%CI 0.73-1.78)

MAYO CLINIC

*Adjusted for Age, Sex, and CVD risk factors



RA und CV-Risiko

- Gute Kontrolle der entzündlichen Aktivität entscheidend
- Vergleichbares Risiko wie Individuen ohne RA erreichbar
- Trotzdem:
  - **CV Risikofaktoren beachten**

England et al, Brit Med J 2018

Besten Dank für die Aufmerksamkeit