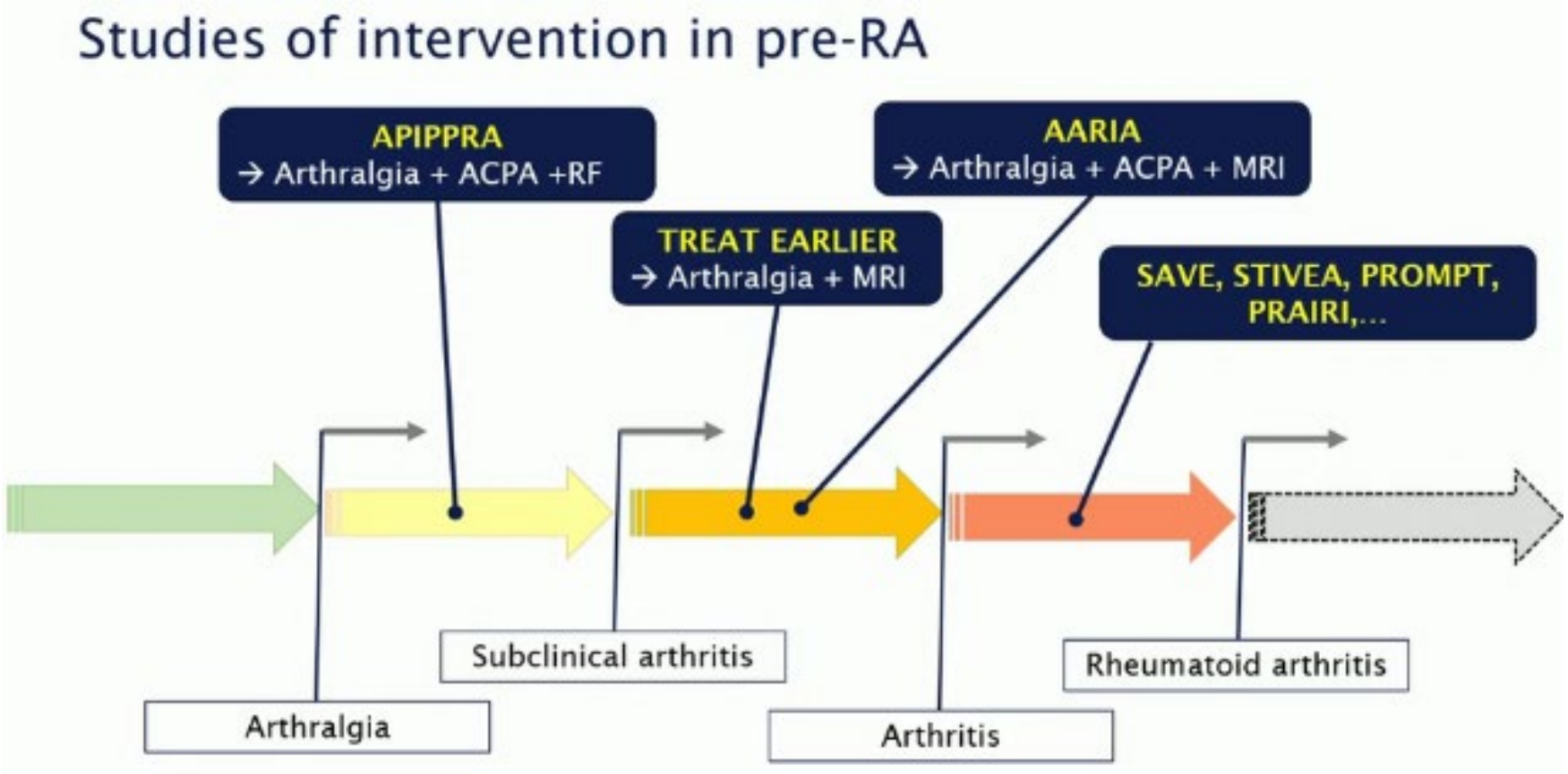
Universitätsspital Basel

Rheumatoide Arthritis

EULAR Highlights

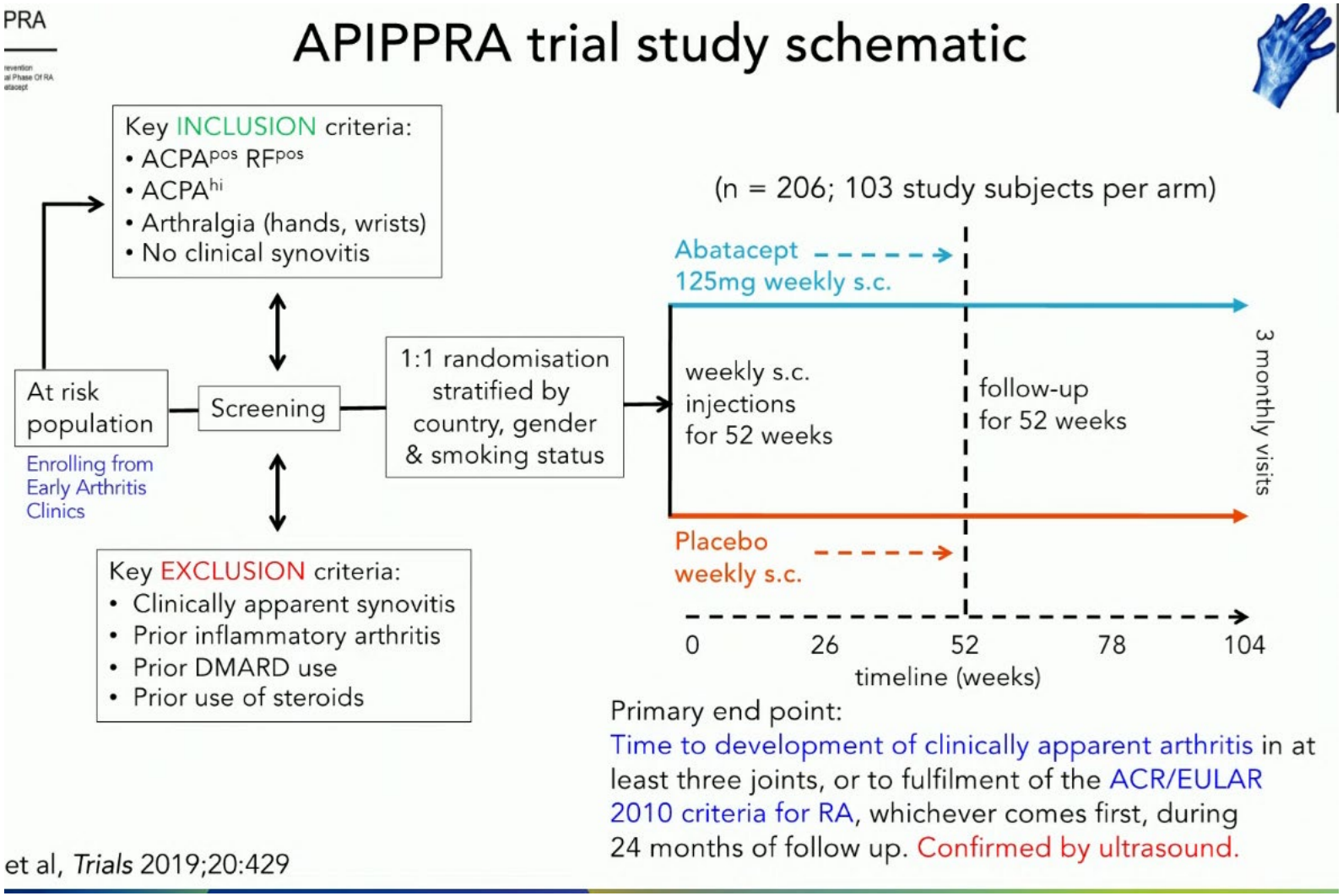
Diego Kyburz
Rheumatologie
Universitätsspital Basel

RA prevention



Aletaha, EULAR 2023 plenary lecture

RA prevention trials: APIPPRA

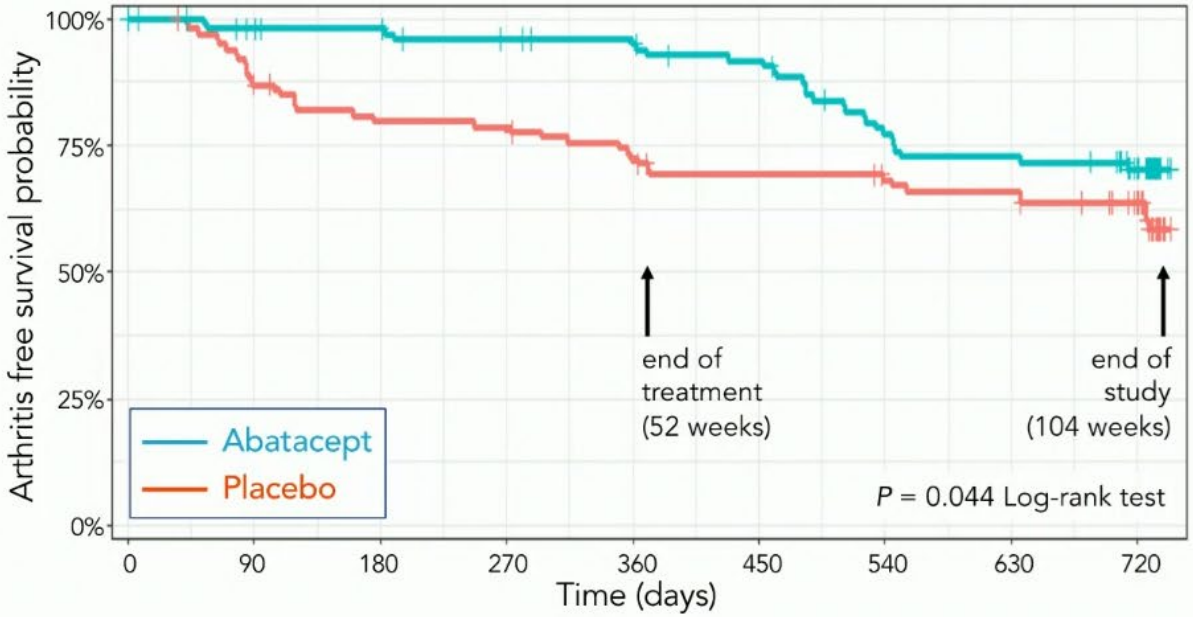


Cope et al, EULAR 2023 OP0130

RA prevention trials: APIPPRA

APIPPRA
Arthritis Prevention In The Pre-Clinical Phase Of RA With Abatacept

Time to event analysis: arthritis-free survival



Number at risk:	103	87	77	76	69	64	61	59	49
Cumulative events:		13	20	21	27	30	31	33	35
Cumulative censored obs:		3	6	6	7	9	11	11	19
Number at risk:	110	100	97	92	89	84	69	65	54
Cumulative events:		2	2	4	5	8	21	25	27
Cumulative censored obs:		8	11	14	16	18	20	20	29

Placebo

Abatacept

N=213

ITT analysis

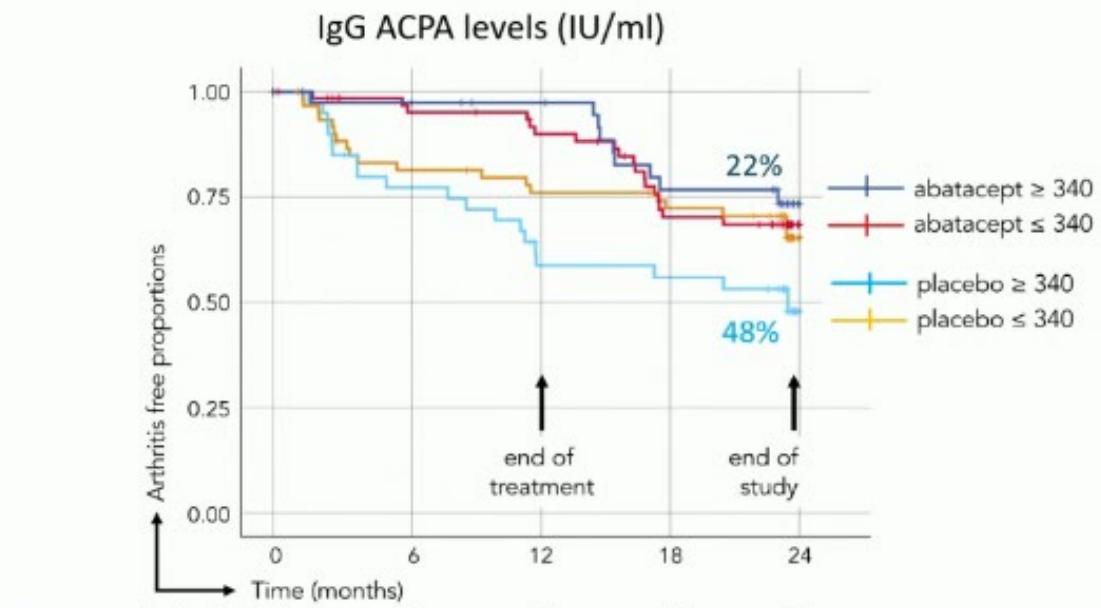
Cope et al, EULAR 2023 OP0130

Universitätsspital Basel

APIPPRA: post hoc analysis

eular 24
EUROPEAN CONGRESS OF RHEUMATOLOGY
VIENNA
12–15 JUNE 2024

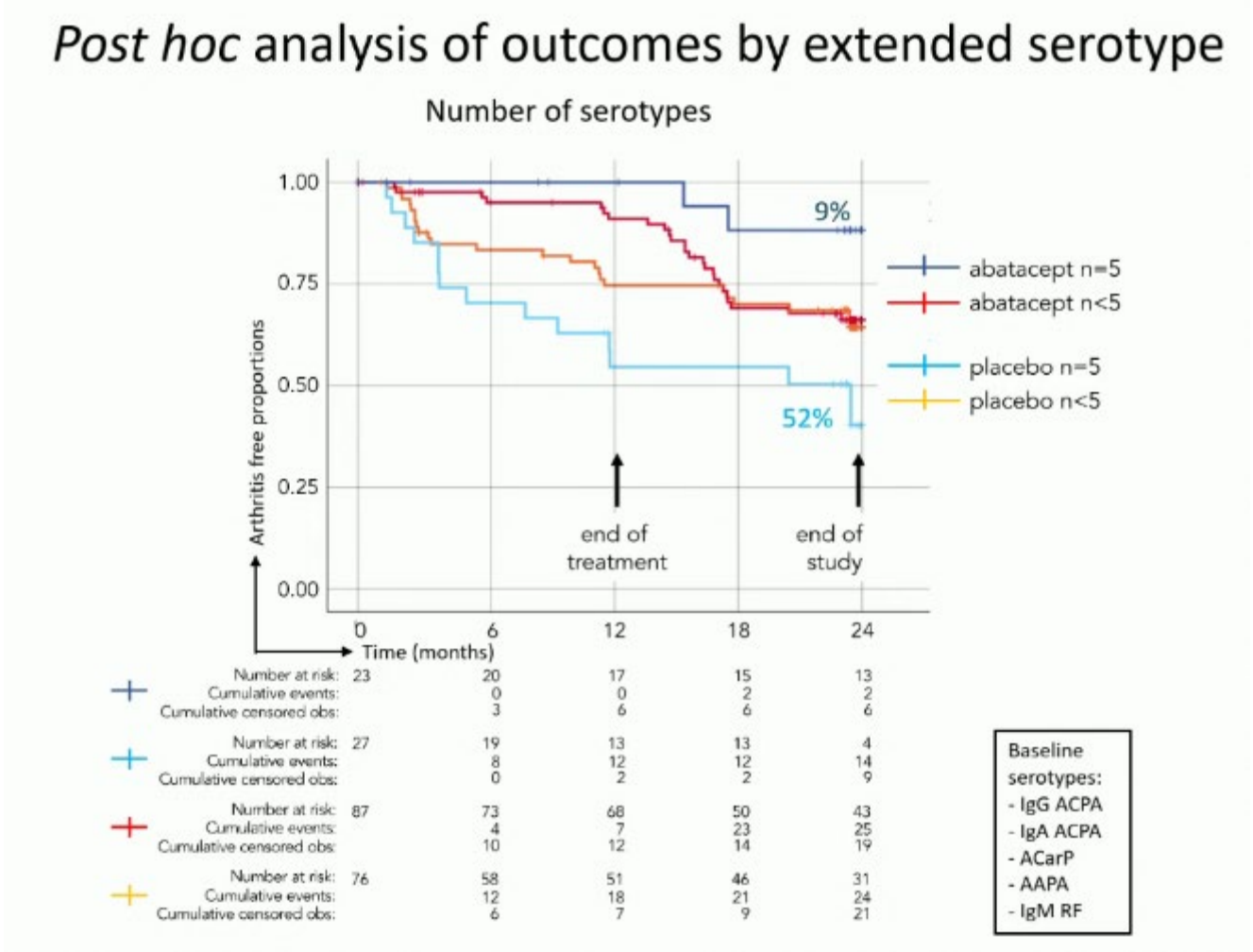
Post hoc analysis of outcomes stratified by ACPA level



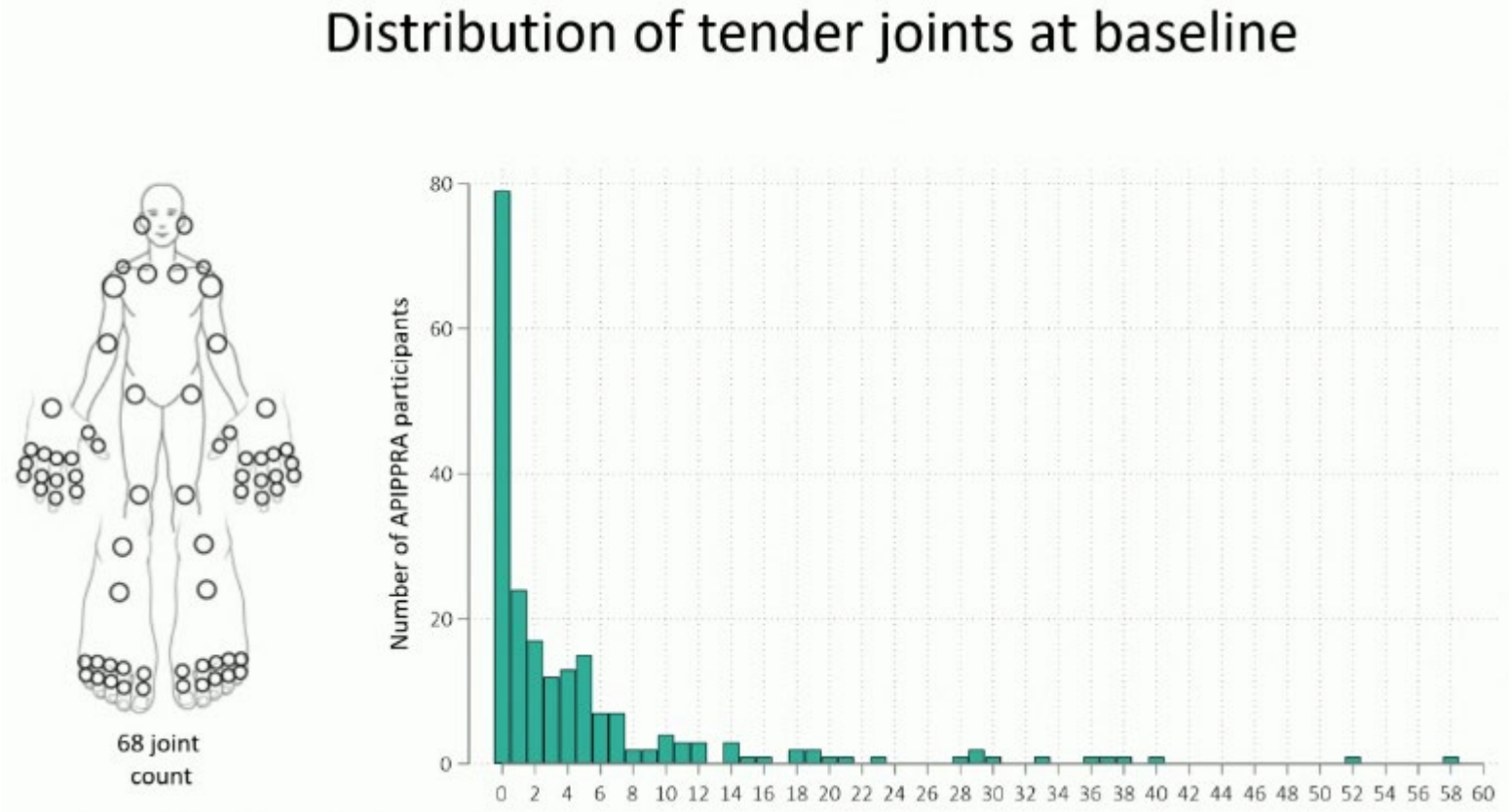
Cope EULAR 2024 OP

Universitätsspital Basel

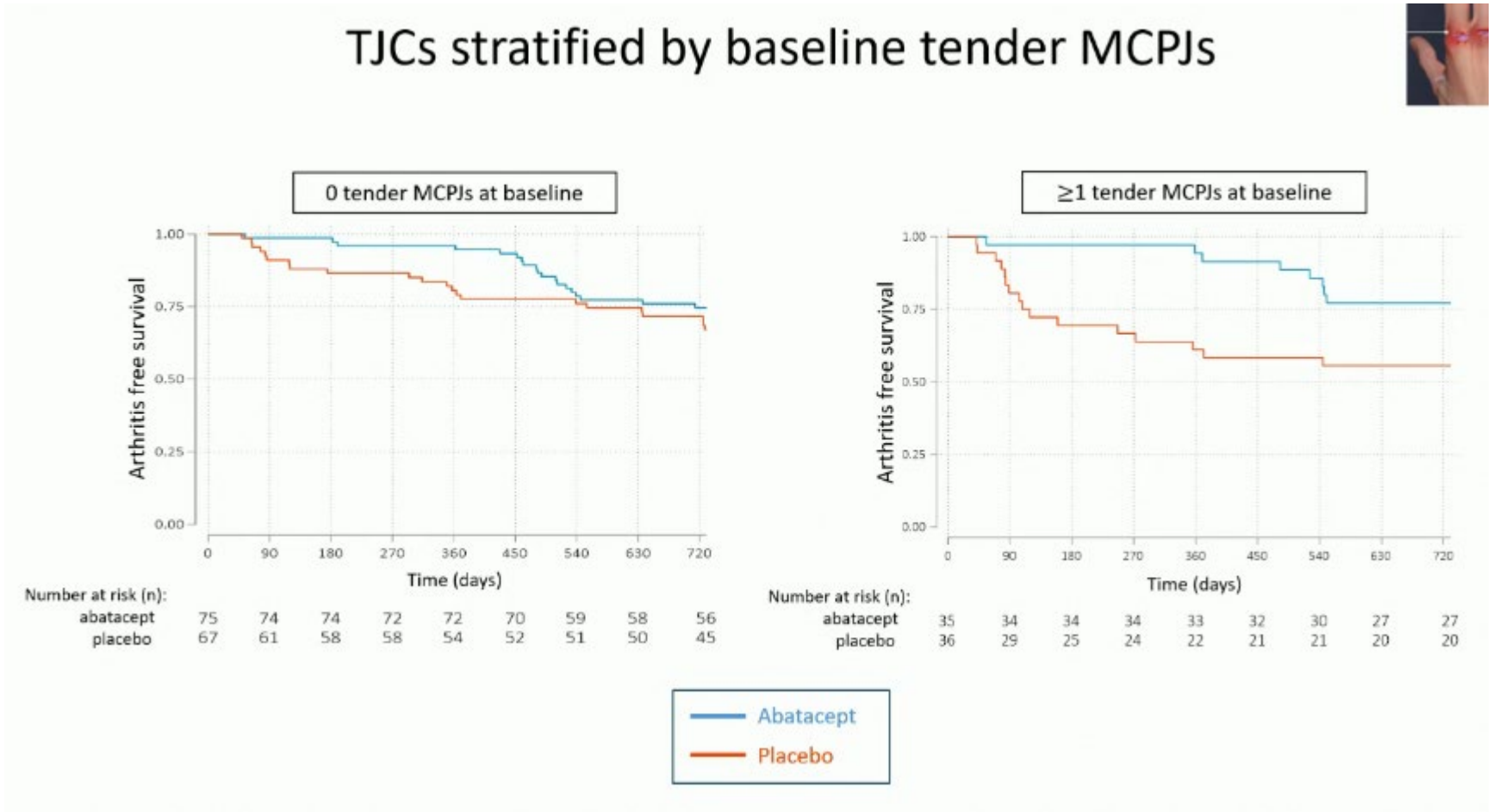
RA prevention trials: APIPPRA



RA prevention trials: APIPPRA

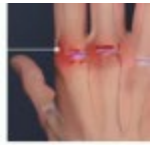


RA prevention trials: APIPPRA



RA prevention trials: APIPPRA

Arthritis-free survival stratified by serology and baseline tender MCPJs

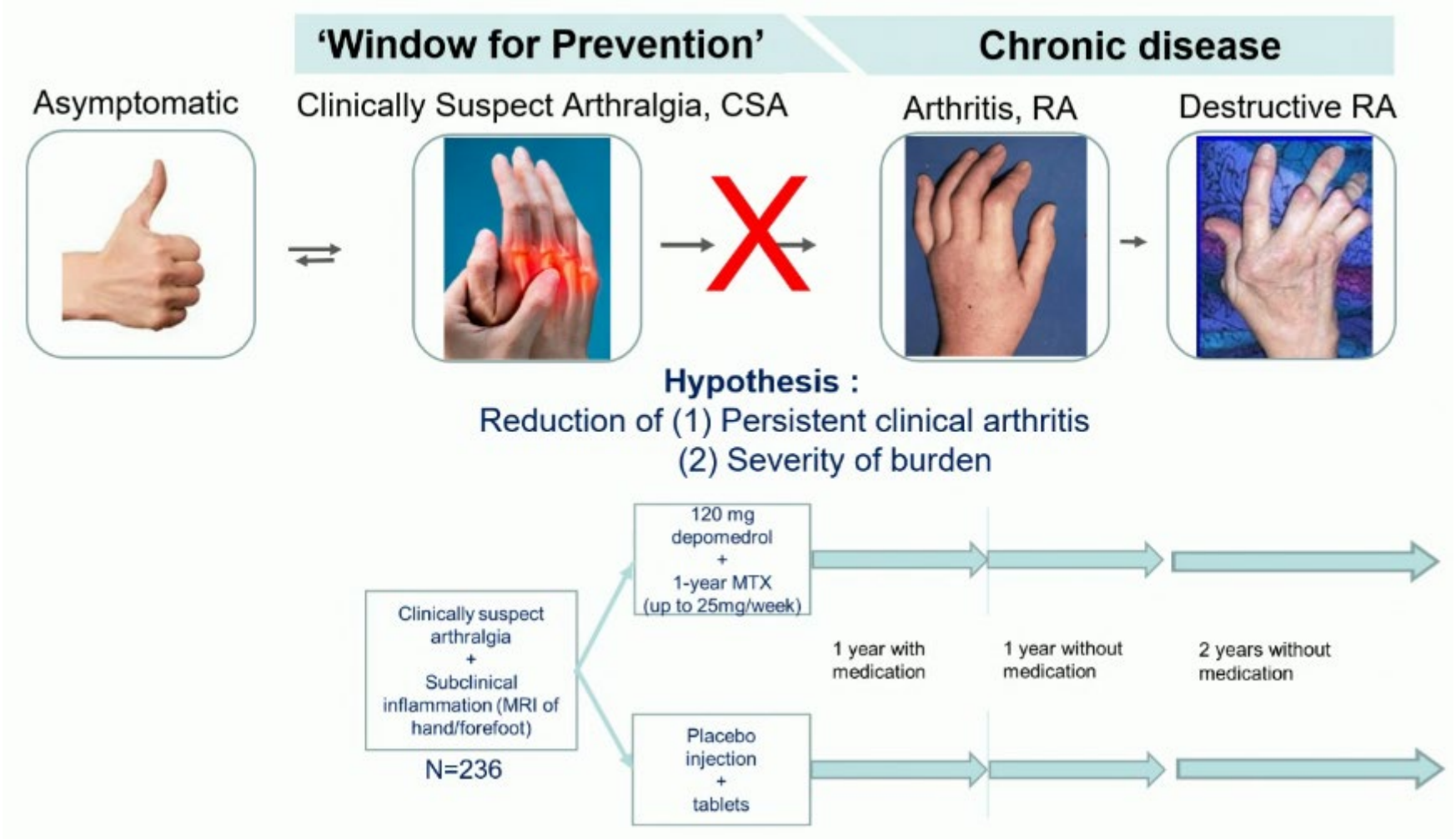


Cope EULAR 2024 OP

RA prevention trials: APIPPRA

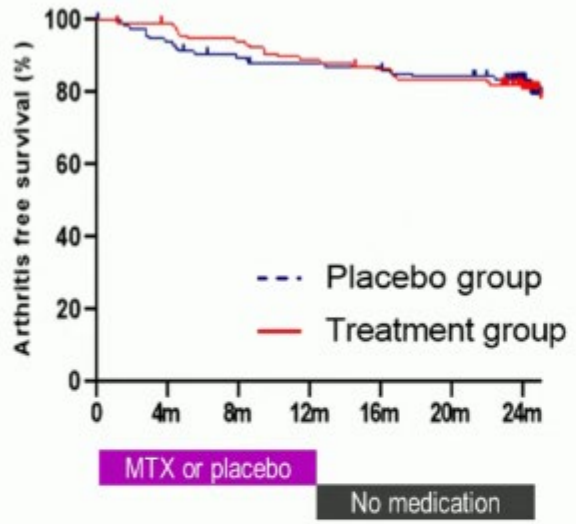
- Conclusions
  - Prevention trials are feasible
  - Prevention is possible (follow up 2 yrs) in a subset of patients with pre-RA
  - Predictors for arthritis free outcome
    - High level of ACPA
    - «mature» ACPA profile
    - Number of tender MCP joints

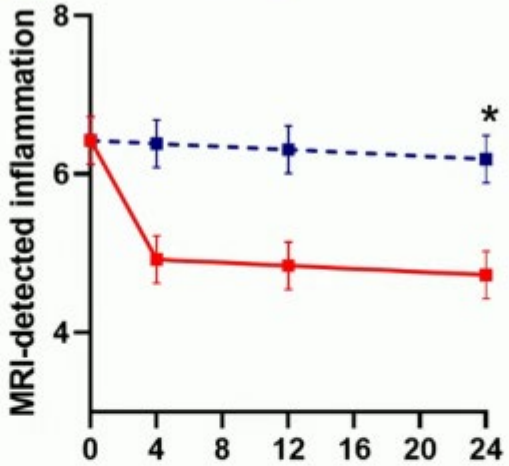
RA prevention trials: Treat earlier

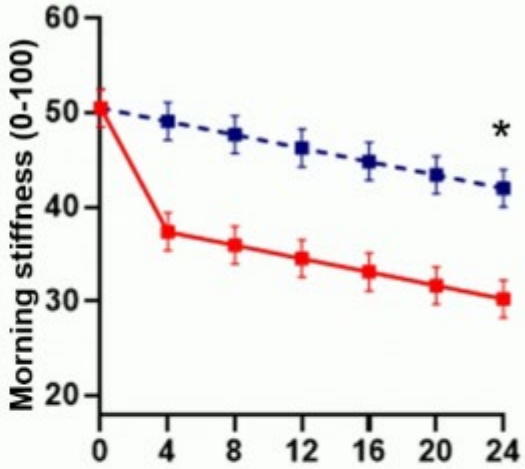


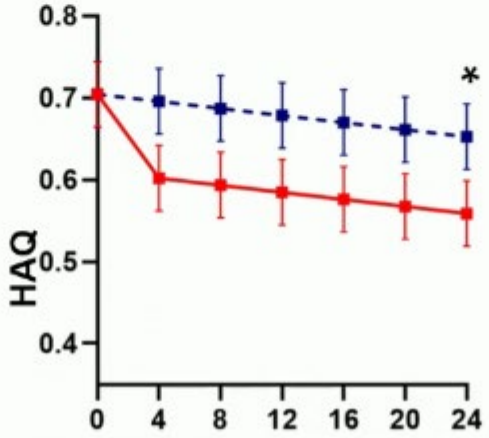
Van der Helm van Mil EULAR 2024 OP

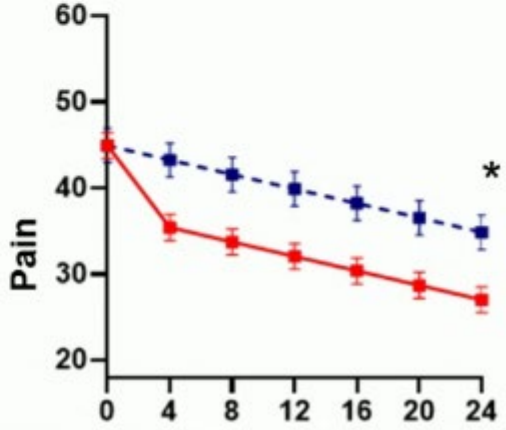
Total study population; 2 years follow-up



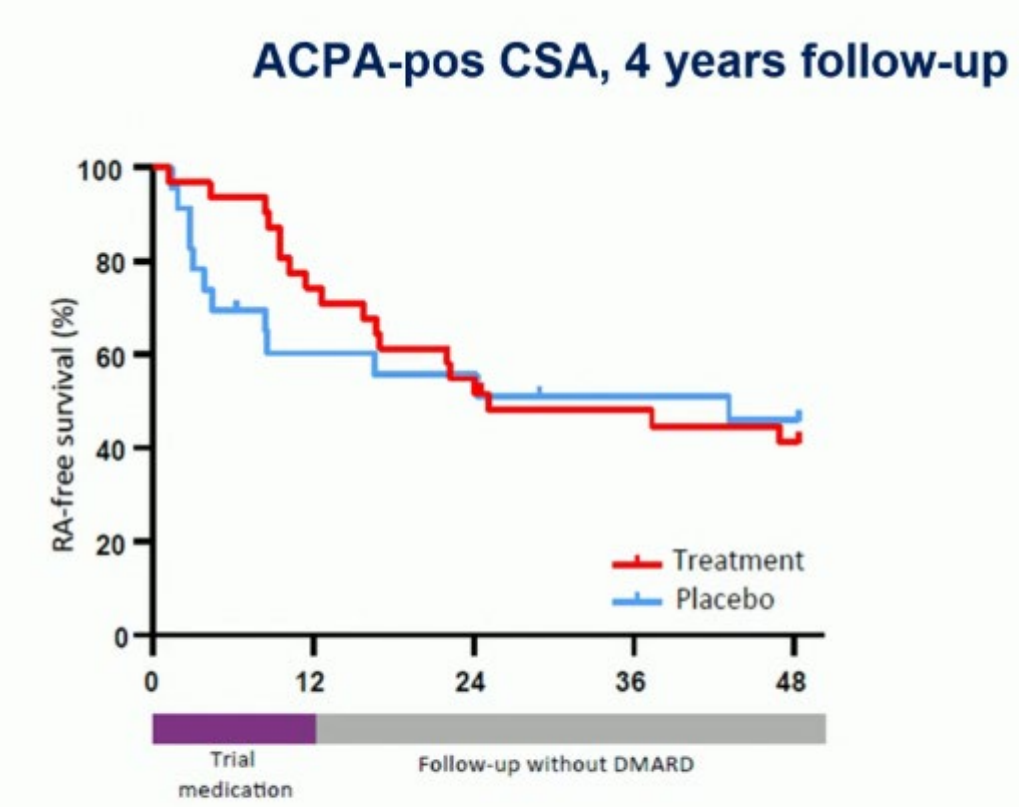


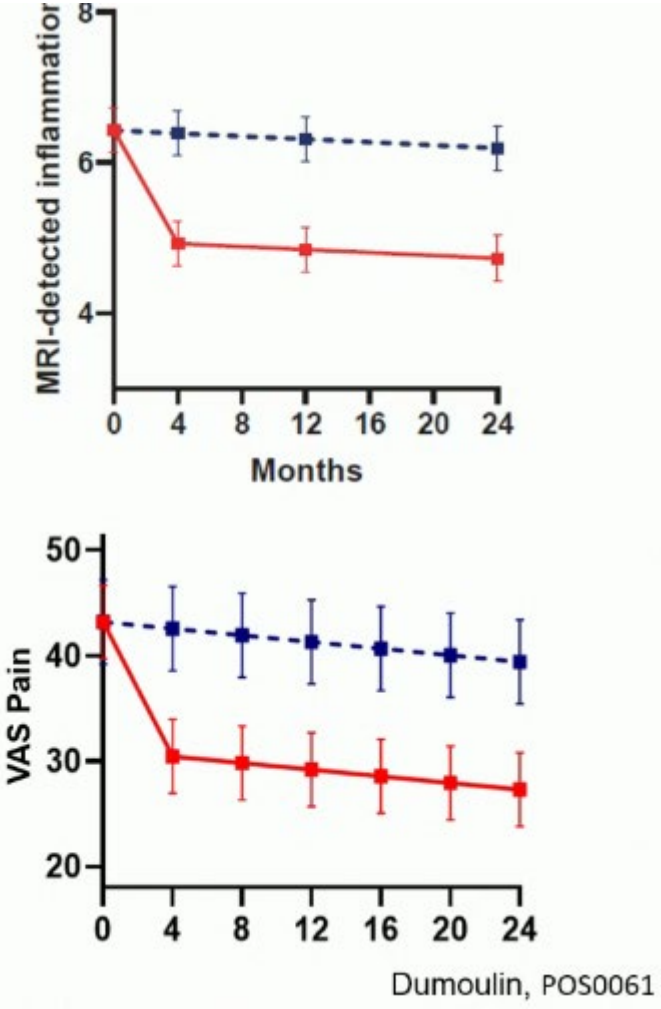




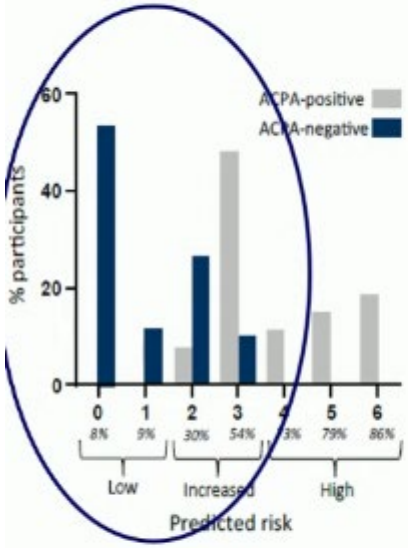


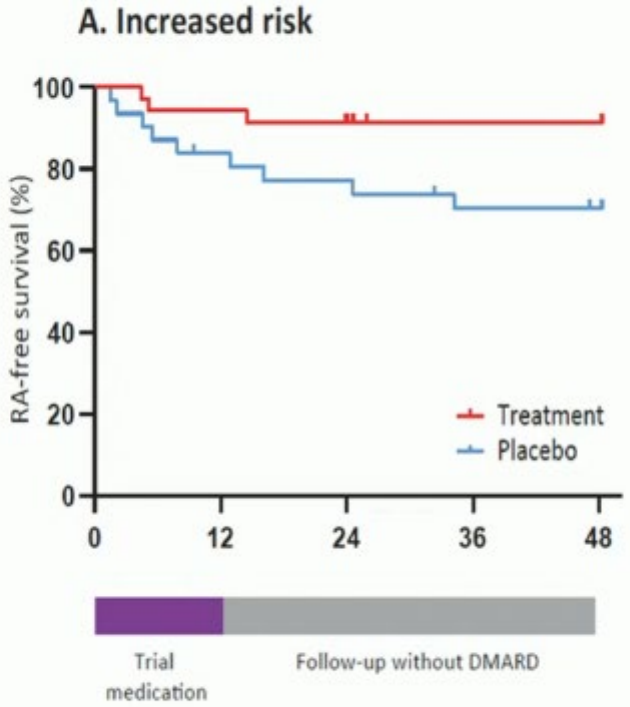
Krijbolder et al. The Lancet, 2022


ACPA-pos CSA, 4 years follow-up
RA-free survival (%)
100
80
60
40
20
0
0
12
24
36
48
Treatment
Placebo
Trial medication
Follow-up without DMARD

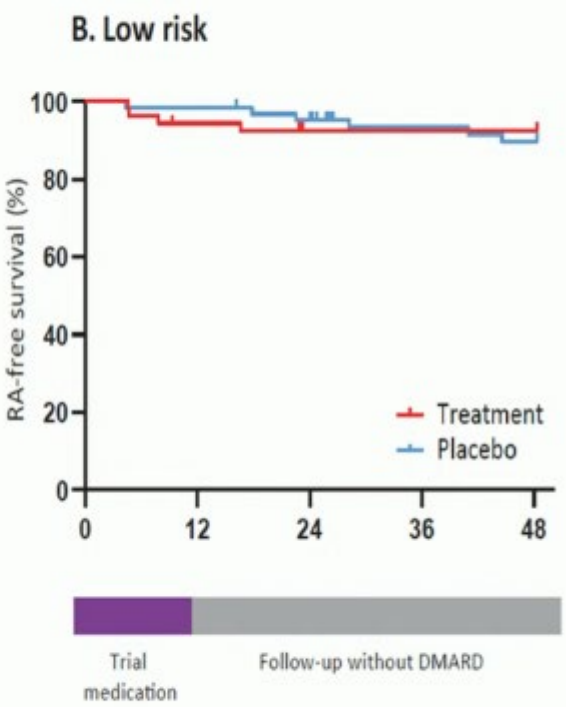

MRI-detected inflammation
8
6
4
0
4
8
12
16
20
24
Months
VAS Pain
50
40
30
20
0
4
8
12
16
20
24
Dumoulin, POS0061

ACPA-neg CSA, 4 years follow-up





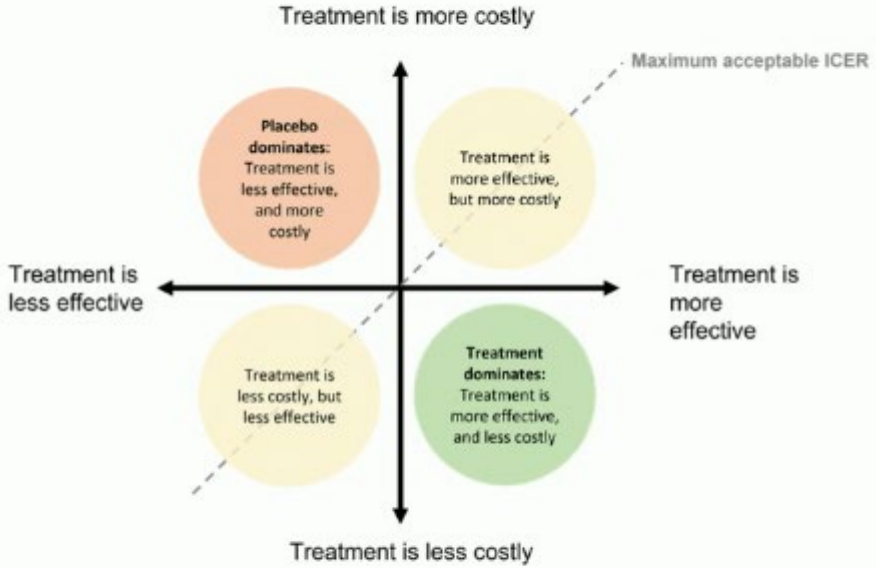
HR 0.27 (95%CI 0.07-0.99)

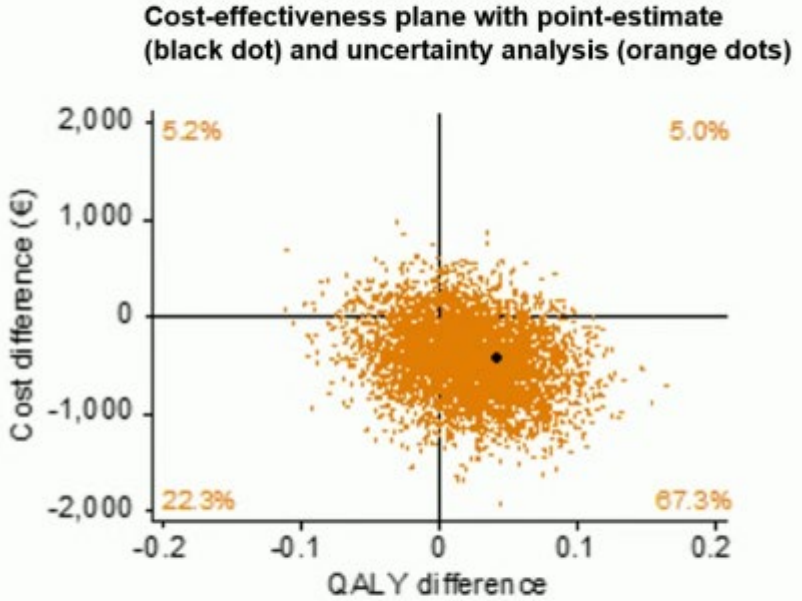


NS

Dumoulin, POS0061

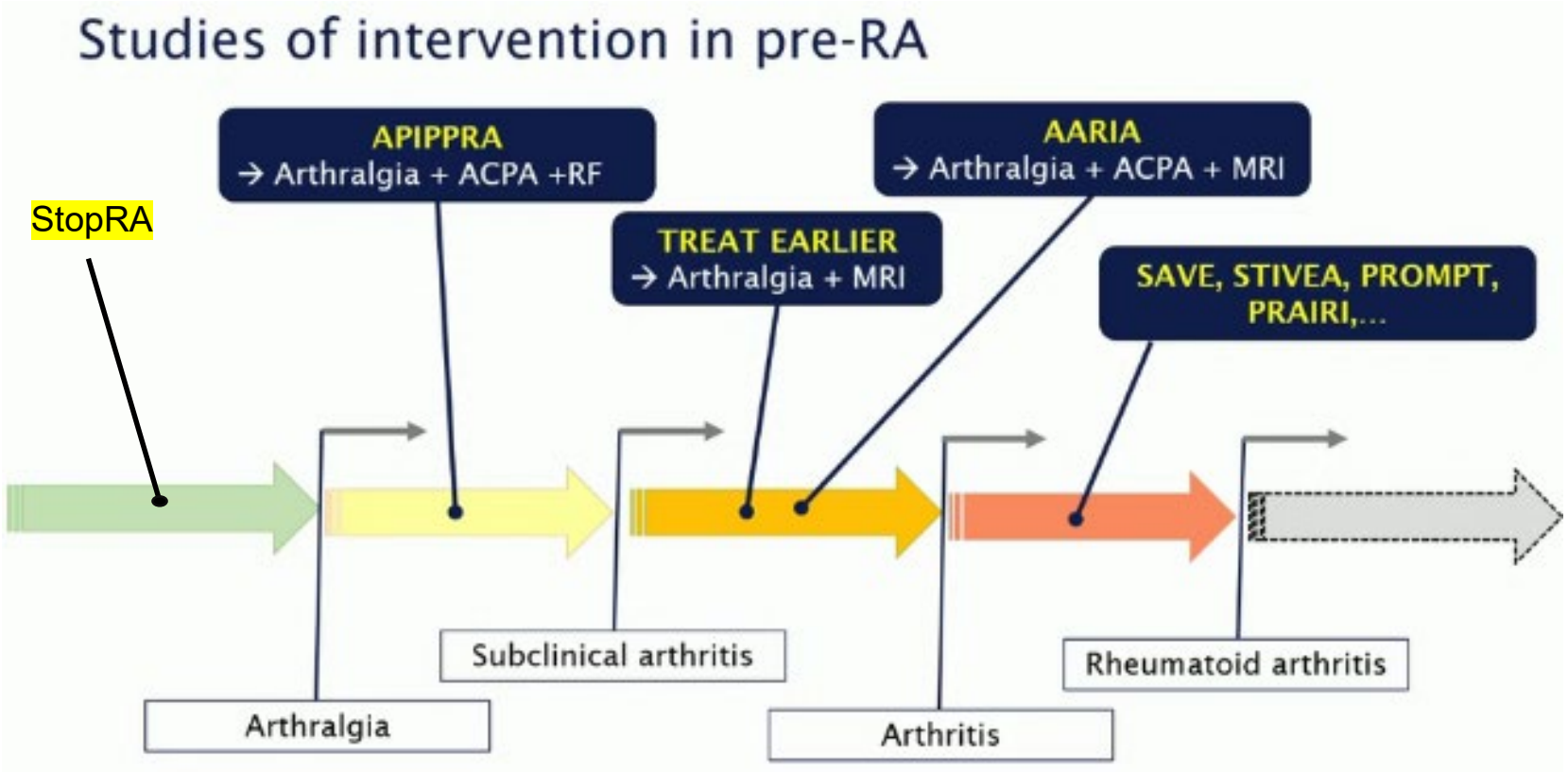
Cost effectiveness – 2 years data total trial population





Van Mulligen et al, POS0009

RA prevention



Aletaha, EULAR 2023 plenary lecture

Study Design

Phase 2 multicenter, randomized, double-masked, placebo-controlled, parallel group trial to evaluate the efficacy and safety of a 12-month course of HCQ to prevent future RA

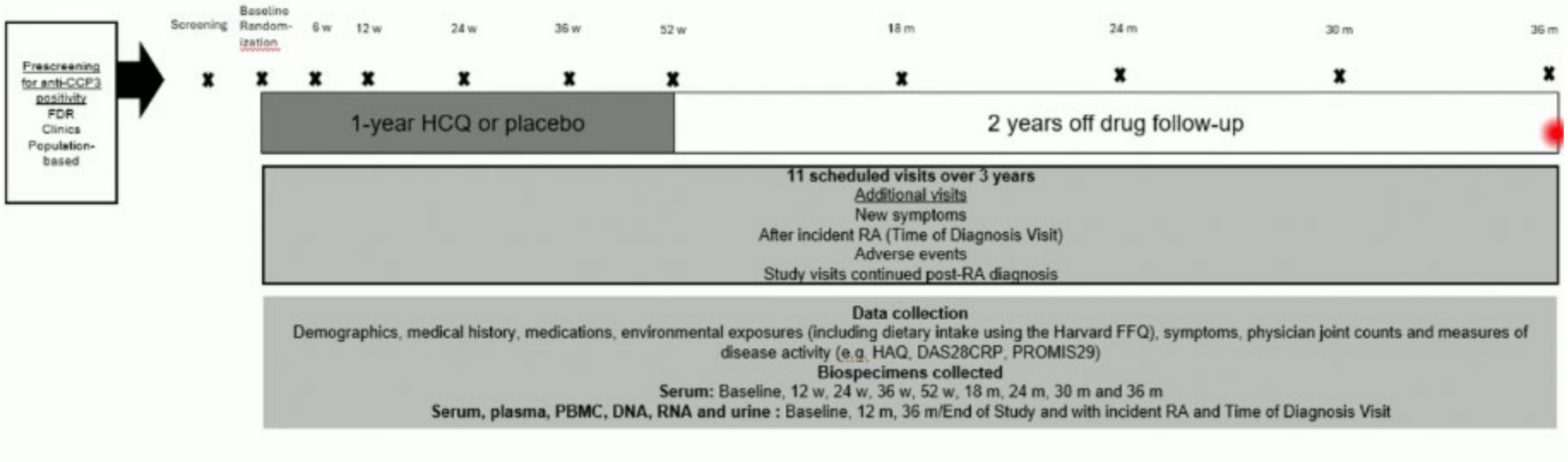
Target to randomize 200 (revised to 140) participants randomized 1:1 HCQ vs placebo

- Dose <=6.5 mg/kg/day (ideal body weight)
- Pre-drug eye evaluation to identify features that would preclude identifying HCQ toxicity in future (no follow-up examination)

Randomization was balanced between:

- Site
- Cigarette smoking (ever/never)
- Method of 'recruitment' (FDR, clinic, & general population)

Study Design



Key Inclusion/Exclusion Criteria

Anti-cyclic citrullinated peptide-3 (anti-CCP3) ≥40 units (2x the upper limit of normal)

IgG ELISA Inova/Werfen, San Diego, CA – all testing done at Exsera Biolabs, University of Colorado

No history or baseline physical examination findings of joint swelling consistent with RA-like synovitis

No prior or current DMARD/immunotherapy

Symptoms were not used to determine inclusion/exclusion

Imaging was not used to determine inclusion/exclusion

Recruitment

Individuals identified in clinics as CCP(+) without IA

'Targeted' first-degree relative (FDR) testing

- Approach clinic patients to access their FDRs
- Biobank testing targeting self-reported FDRs

'General population' testing (could include FDRs)

- Health-fairs
- Blood donors
- Biobank

Primary Endpoint

Development of clinically-apparent RA (Clinical RA) at 36 months

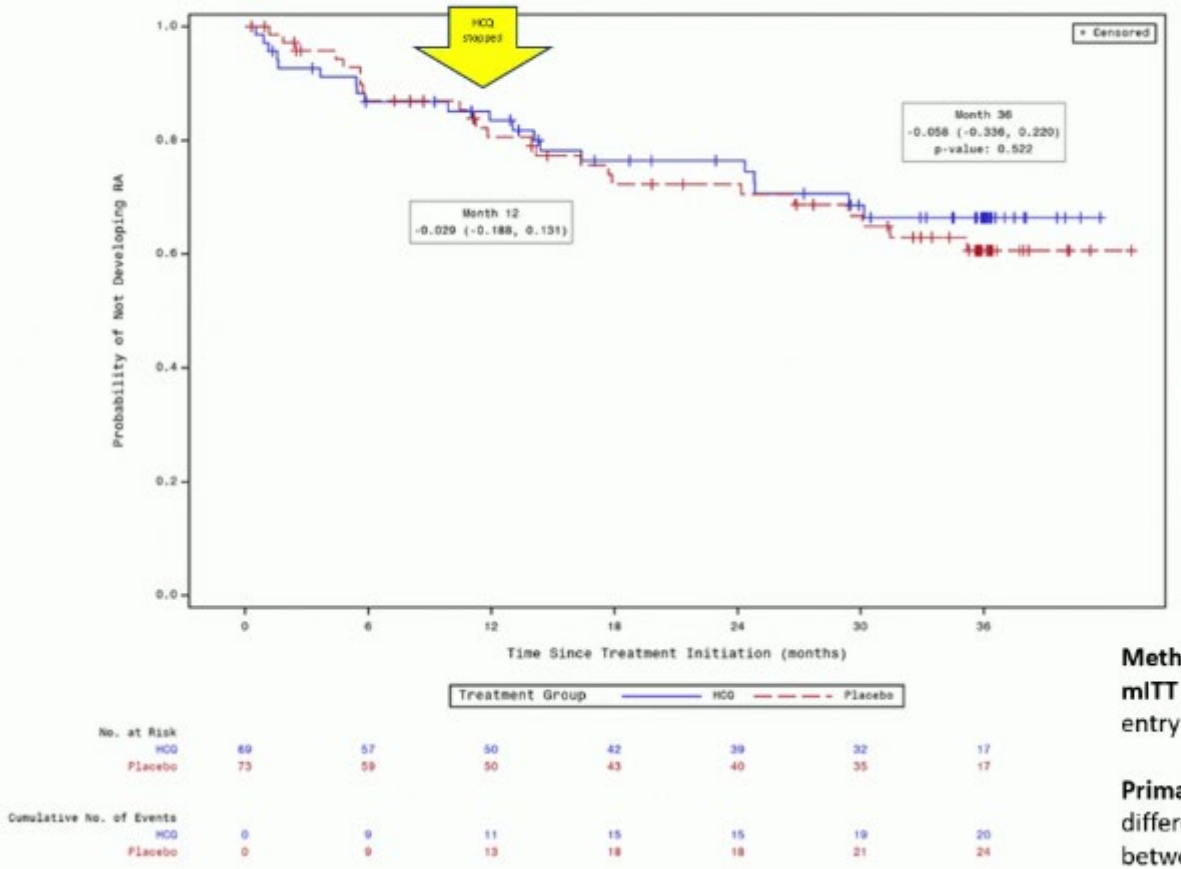
Clinical RA defined as:

>=1 swollen joint on physical examination consistent with RA-like synovitis and
2010 ACR/EULAR RA Classification Criteria score ≥6

Or

>=1 swollen joint on physical examination consistent with RA-like synovitis and
>=1 erosion identified via x-ray of the hands, wrists, and feet

Primary outcome



Clinical RA Development
HCQ ~29%
Placebo~33%

No difference observed between arms on estimated risk of development of RA at 36 months or 12 months

Methods
mITT population: all randomized participants who met entry criteria and received at least 1 dose of study drug

Primary Estimand: Kaplan-Meier based estimated difference in risk of development of RA at Month 36 between treatment groups

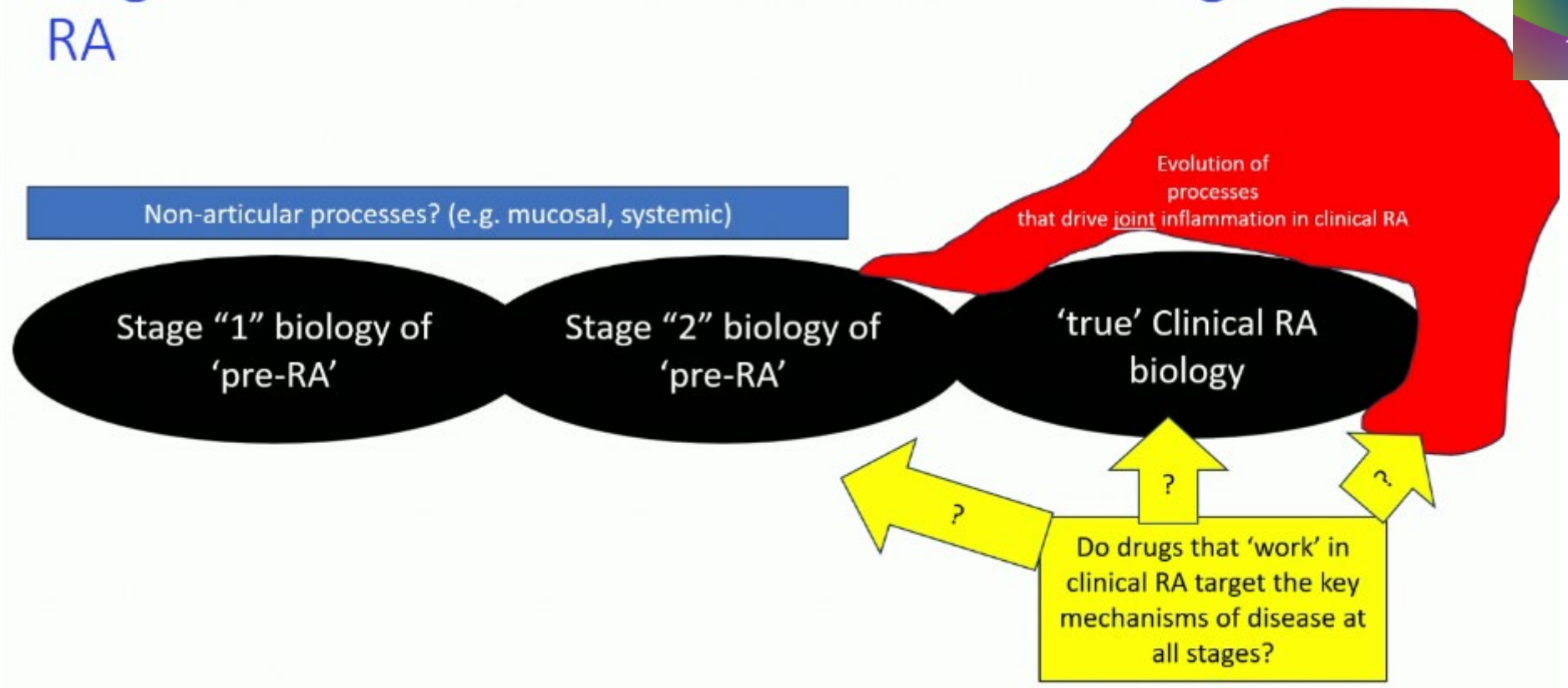
17

Conclusions

In individuals who are anti-CCP3(+) >=2 ULN without IA at baseline, 1 year of HCQ is not superior to placebo in preventing or delaying the development of clinical RA at 3 years

The study was halted due to futility

Next steps: understanding 'core' biology across the stages of RA will inform treatments at all stages of RA



eular 24
EUROPEAN CONGRESS OF RHEUMATOLOGY
VIENNA
12 – 15 JUNE 2024

3-YEAR RESULTS OF TAPERING TNFi TO WITHDRAWAL COMPARED TO STABLE TNFi AMONG RHEUMATOID ARTHRITIS PATIENTS IN SUSTAINED REMISSION: A MULTICENTER RANDOMIZED TRIAL

Kaja E. Kjørholt[1,2], Nina Paulshus Sundlisæter[1], Anna-Birgitte Aga[1], Joseph Sexton[1], Inge C. Olsen[3], Åse Lexberg[4], Tor M. Madland[5], Hallvard Fremstad[6], Christian A. Høili[7], Gunnstein Bakland[8], Cristina Spada[9], Hilde Haukeland[10], Inger M. Hansen[11], Ellen Moholt[1], Karen Holten[1,2], Till Uhlig[1,2], Tore K. Kvien[1,2], Daniel H. Solomon[12], Désirée van der Heijde[1,13], Espen A. Haavardsholm[1,2], **Siri Lillegraven**[1]

[1]Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Norway, [2]University of Oslo, Norway, [3]Oslo University Hospital, Norway, [4]Drammen Hospital, Vestre Viken HF, Norway, [5]Haukeland University Hospital, Norway,[6]Møre og Romsdal Hospital Trust, Norway, [7]Østfold Hospital Trust, Norway, [8]University Hospital of North Norway, Norway, [9]Revmatismesykehuset AS, Norway [10]Martina Hansens Hospital, Norway, [11]Helgelandssykehuset, Norway, [12]Brigham and Women's Hospital, USA, [13]Leiden University Medical Center, Netherlands

Lillegraven et al EULAR 2024 OP0021

Universitätsspital Basel

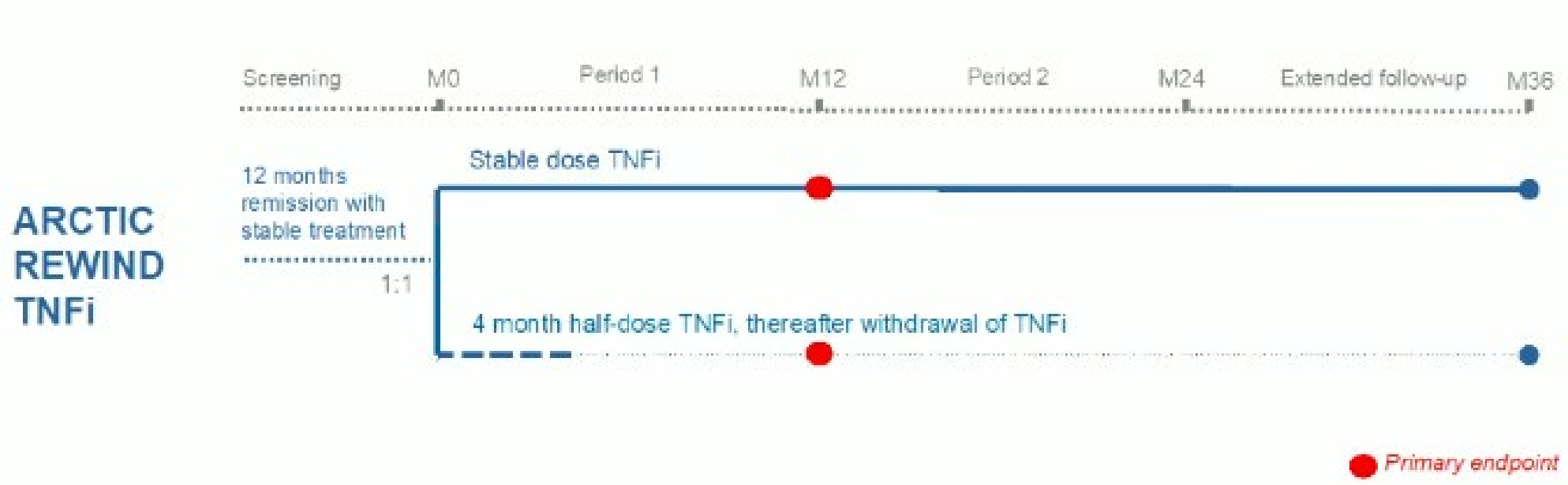
STUDY DESIGN

The ARCTIC REWIND TNFi trial

- Multicenter, open-label, non-inferior, randomized-controlled trial
- RA patients in sustained remission ≥12 months on stable treatment
- DAS remission and no swollen joints at inclusion
- **1:1 Randomization**
  1) Stable treatment
  2) Half-dose TNFi for 4 months, then withdrawal of TNFi

Lillegraven et al EULAR 2024 OP0021

- Study design



Lillegraven et al EULAR 2024 OP0021

PRIMARY ENDPOINT

Disease flare 0-36 months

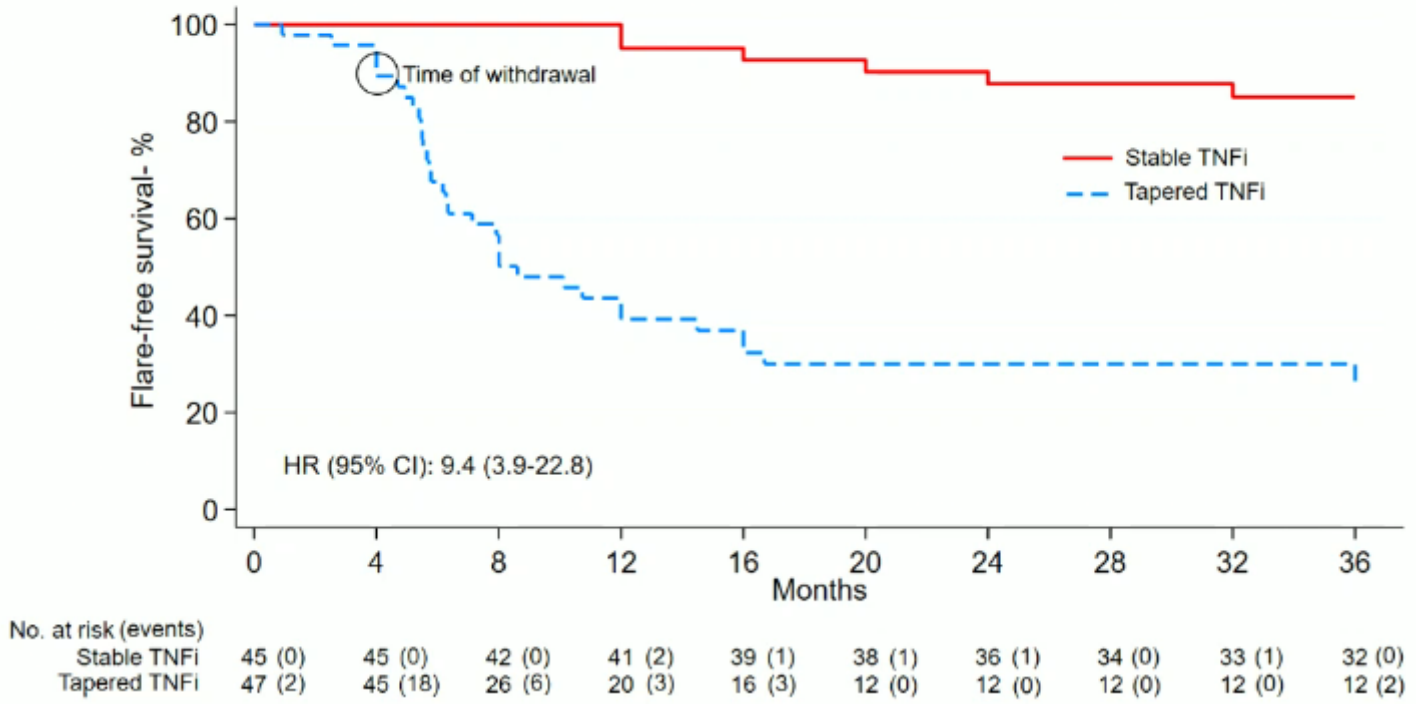
DAS>1.6 *(cut-off for remission)* **+**
ΔDAS ≥ 0.6 *(minimal detectable change)* **+**
Swollen joint count ≥2

or

Agreement between the physician and the patient that a clinically significant flare had occurred

Lillegraven et al EULAR 2024 OP0021

PATIENTS WITHOUT FLARE 0-36 MONTHS



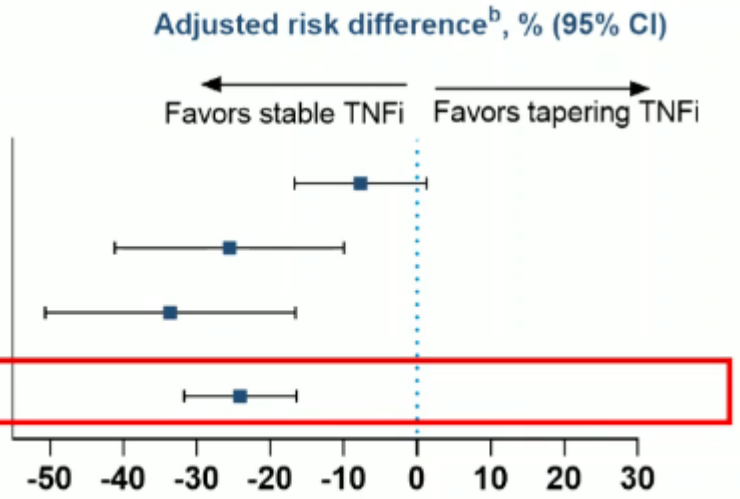
No. at risk (events)										
Stable TNFi	45 (0)	45 (0)	42 (0)	41 (2)	39 (1)	38 (1)	36 (1)	34 (0)	33 (1)	32 (0)
Tapered TNFi	47 (2)	45 (18)	26 (6)	20 (3)	16 (3)	12 (0)	12 (0)	12 (0)	12 (0)	12 (2)

Lillegraven et al EULAR 2024 OP0021

Universitätsspital Basel

ACR/EULAR BOOLEAN 2.0 REMISSION

	Patients in remission, unadjusted % (No./total No.)		
	Tapering TNFi	Stable TNFi	
12 months	67% (31/46)	72% (28/39)	12 months
24 months	73% (32/44)	85% (33/39)	24 months
36 months	60% (25/42)	76% (29/38)	36 months
0-36 months	**61% (N/A)***	**85% (N/A)***	**0-36 months**



Lillegraven et al EULAR 2024 OP0021

ADVERSE EVENTS 0-36 MONTHS

Table: Adverse events from month 0 to 36 months[a]

	Tapering TNFi (N=47)	Stable TNFi (N=45)
Total number of adverse events	162	133
Patients with ≥1 adverse event, % (N)	81% (38)	89% (40)
Patients with ≥3 adverse events, % (N)	47% (22)	53% (24)
Patients with serious adverse events, % (N)	21% (10)	11% (5)
Patients with adverse events of special interest[c]		
Leading to study discontinuation or major protocol violation, % (N)	4% (2)	11% (5)
Any type of infection, % (N)	60% (28)	62% (28)
Cancer, % (N)	9% (4)	4% (2)
Death, % (N)	4% (2)	0% (0)

JOINT DAMAGE 0-36 MONTHS

Median radiographic change (van der Heijde Sharp Score)

- Tapering group: 0.5 (95% CI: 0.0 to 2.0)
- Stable group: 0.5 (0.0 to 1.5)
- p-value for comparison = 0.6

Lillegraven et al EULAR 2024 OP0021

Universitätsspital Basel

MEDICATION AT 36 MONTHS

% (No./total No.)	Tapering TNFi	Stable TNFi
bDMARD/tsDMARD treatment at 3-year follow-up[a]:		
☐ No bDMARD/JAKi	29% (12/42)	0% (0/38)
☐ Same TNFi as baseline	62% (26/42)	89% (34/38)
☐ Other TNFi	10% (4/42)	5% (2/38)
☐ JAKi	0% (0/42)	5% (2/38)
csDMARD comedication increase at 3-years follow-up compared to baseline[1]	8% (3/42)	3% (1/38)
Glucocorticoids during the study:		
- ≥1 treatment period with systemic glucocorticoids	23% (11/47)	13% (6/45)
- ≥1 intraarticular glucocorticoids injections	46% (21/47)	23% (10/45)

Lillegraven et al EULAR 2024 OP0021

Universitätsspital Basel

SUMMARY

- If important to avoid flares: keep treatment stable
- Significant increase in flares when tapering medication
  - 59% risk increase in the ARCTIC REWIND TNFi study
- Research is needed to develop personalized tapering strategies
- **Any decision to taper should be based on shared decision making**

Lillegraven et al EULAR 2024 OP0021

Universitätsspital Basel

Universitätsspital Basel

Vielen Dank für die Aufmerksamkeit