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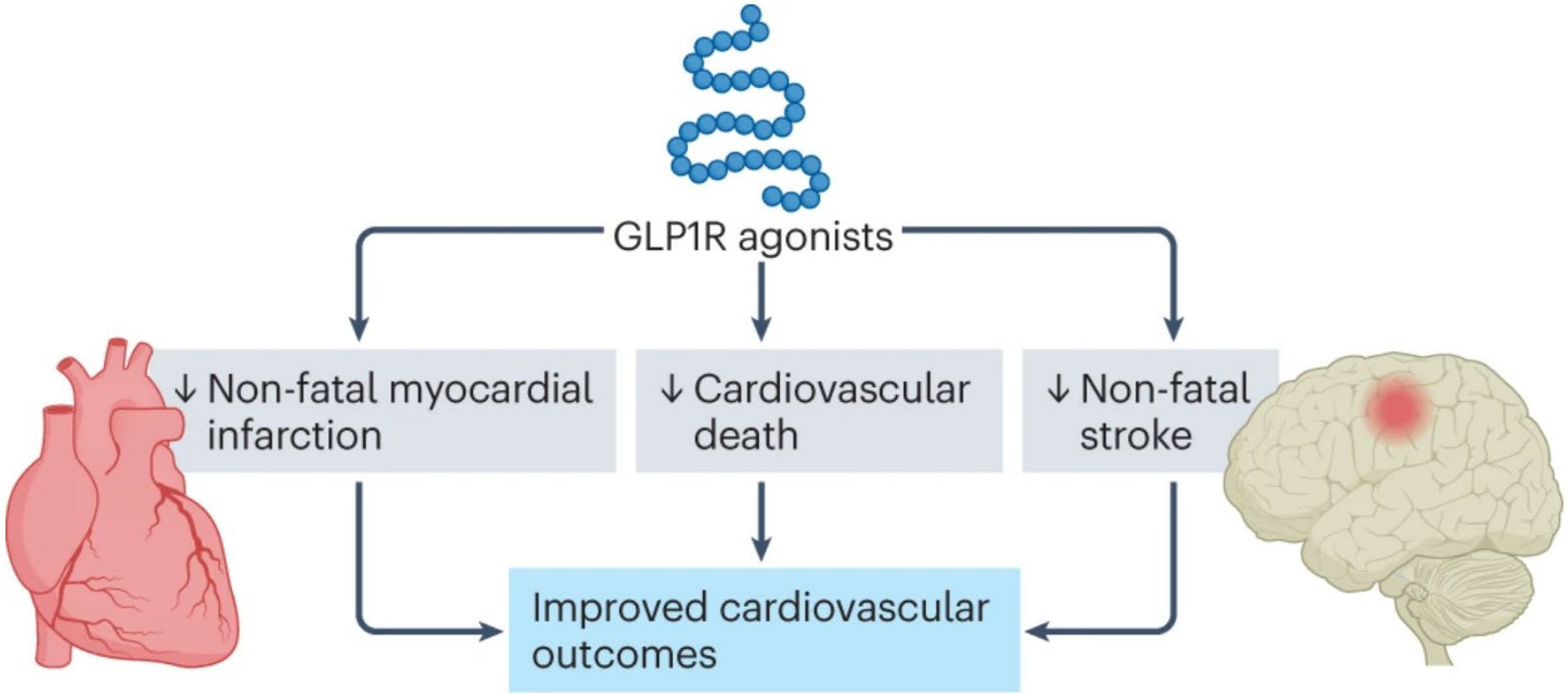
11–14 JUNE

EULAR Highlights: Rheumatoid arthritis

Diego Kyburz
Rheumatologie
Universitätsspital Basel

Cardiovascular risk in RA

- Reduced CV risk with GLP1R agonists in D.m.II but also non-diabetic individuals



Ussher & Drucker, Nat Rev Cardiol 2023

GLP1 agonists and CV risk in RA

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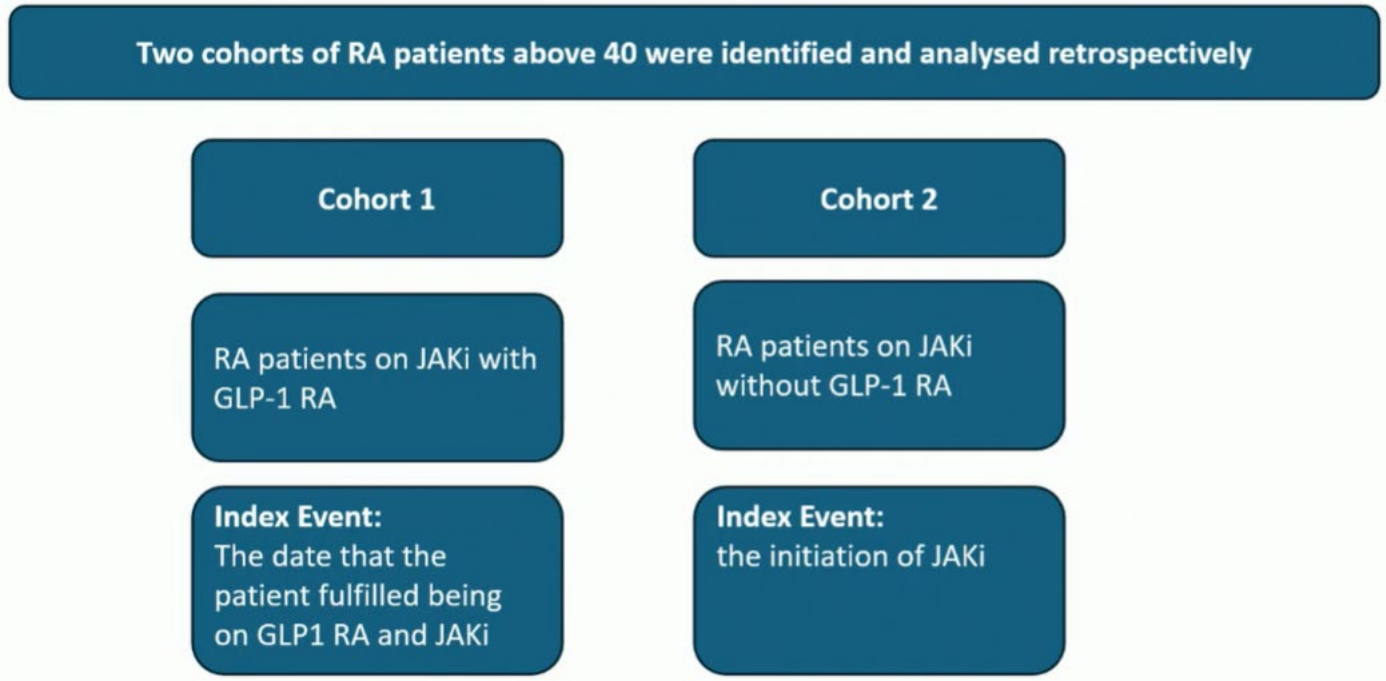
GLP1 agonists mitigate the risk of cardiovascular events in Rheumatoid Arthritis patients treated with JAK inhibitors

Dr. Asmaa Beltagy
Rheumatology Unit, Faculty of Medicine
Alexandria University, Egypt



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GLP1 agonists and CV risk in RA

- Retrospective analysis of data from the TriNetX platform

- **Propensity score matching** was performed to balance baseline characteristics, including age, sex, diabetes mellitus, hypertension, obesity, hyperlipidemia, primary thrombophilia, smoking, glucocorticoid use, and anticoagulant/antiplatelet use.
- **Each group included 2,449 patients** after propensity score matching

- Patients with outcomes before the index event were excluded from the analysis.

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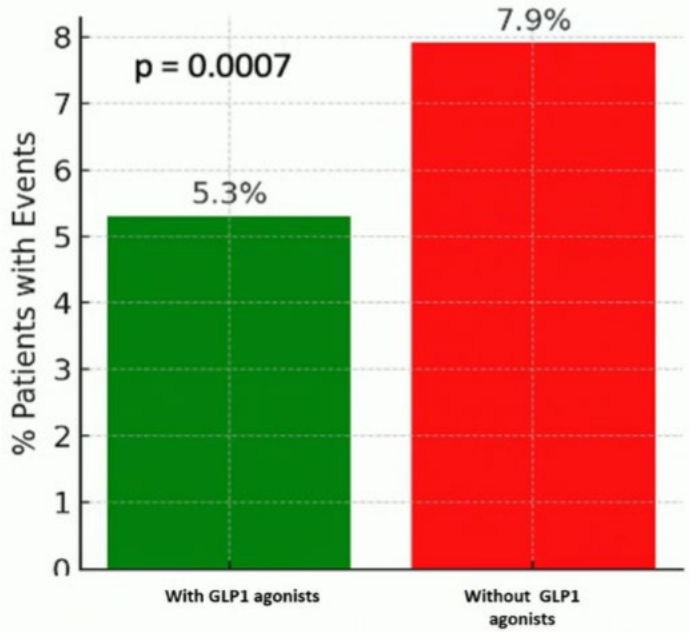
GLP1 agonists and CV risk in RA

- **Follow up:** 5 years after the index event
- **Primary outcomes were incidence of:**
  - ✓acute coronary syndromes
  - ✓cerebral infarction
  - ✓acute peripheral arterial thrombosis
  - ✓deep venous thrombosis/ pulmonary embolism
  - ✓and overall arterial CV events

Overall CV events in RA patients on JAKi with and without GLP1



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GLP1 agonists and CV risk in RA

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Cardiovascular and venous events in RA patients treated with JAK inhibitors with and without GLP1 agonists

	Number of patients	Patients with acute CV events	Risk	Risk ratio	P value
Acute Coronary Syndromes					
Group 1	2,198	88	4.0%	0.645	0.0009
Group 2	2,191	136	6.21%		
Acute Cerebral Infarction					
Group 1	2369	50	2.1%	0.753	0.12
Group 2	2355	66	2.8%		
Peripheral arterial thrombotic events					
Group 1	2,443	<10	0.41%	0.711	0.41
Group 2	2,433	14	0.58%		
Acute Deep Venous Thrombotic Events and pulmonary embolism					
Group 1	2,270	84	3.7%	0.69	0.007
Group 2	2,257	121	5.4%		

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GLP1 agonists and CV risk in RA

Conclusion

- GLP-1 receptor agonists may reduce cardiovascular and venous thrombotic risks in RA patients treated with JAK inhibitors.

- Controlled research is needed to verify the results of our preliminary study.
- Can GLP-1 RA co-medication support the prescription of JAKi in patients older than 50 or with more than one cardiovascular risk factor?
- Can GLP-1 RA co-medication add synergism to the anti-inflammatory effect of JAKi in RA patients?

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RA new drugs

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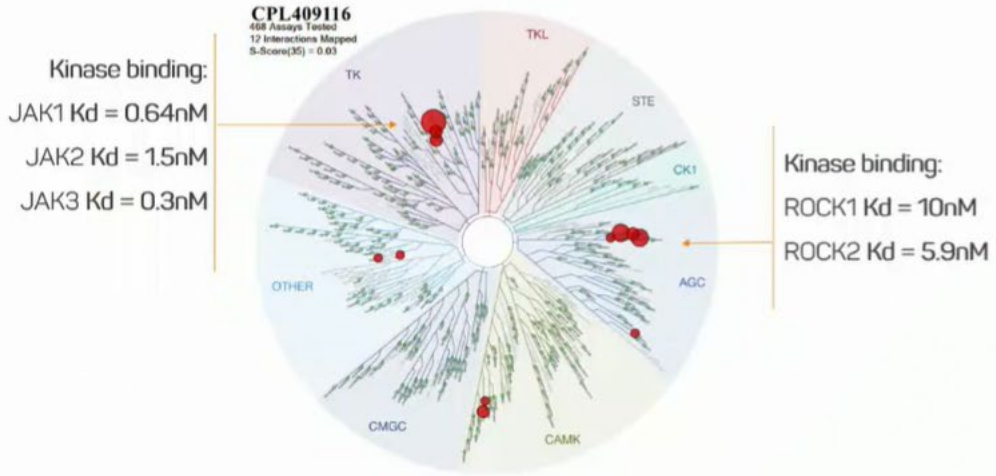
Dual JAK/ROCK inhibition in Rheumatoid Arthritis – results of a phase 2 study of CPL'116

Bartłomiej Kisiel, MD, PhD
Military Institute of Medicine - National Research Institute, Clinical Research Support Center, Warszawa, Poland

Dual JAK/ROCK inhibitor - an overview

KinomeScan™ for CPL'116 activity towards 403 kinases
High selectivity for JAKs and ROCKs families



CPL'116 is:

- Celon Pharma's novel asset
- orally administered
- small molecule

CPL'116 targets:

- cytokines signaling network through JAK-STAT
- regulation of the balance Th17/regulatory T cells and control of profibrotic pathways.

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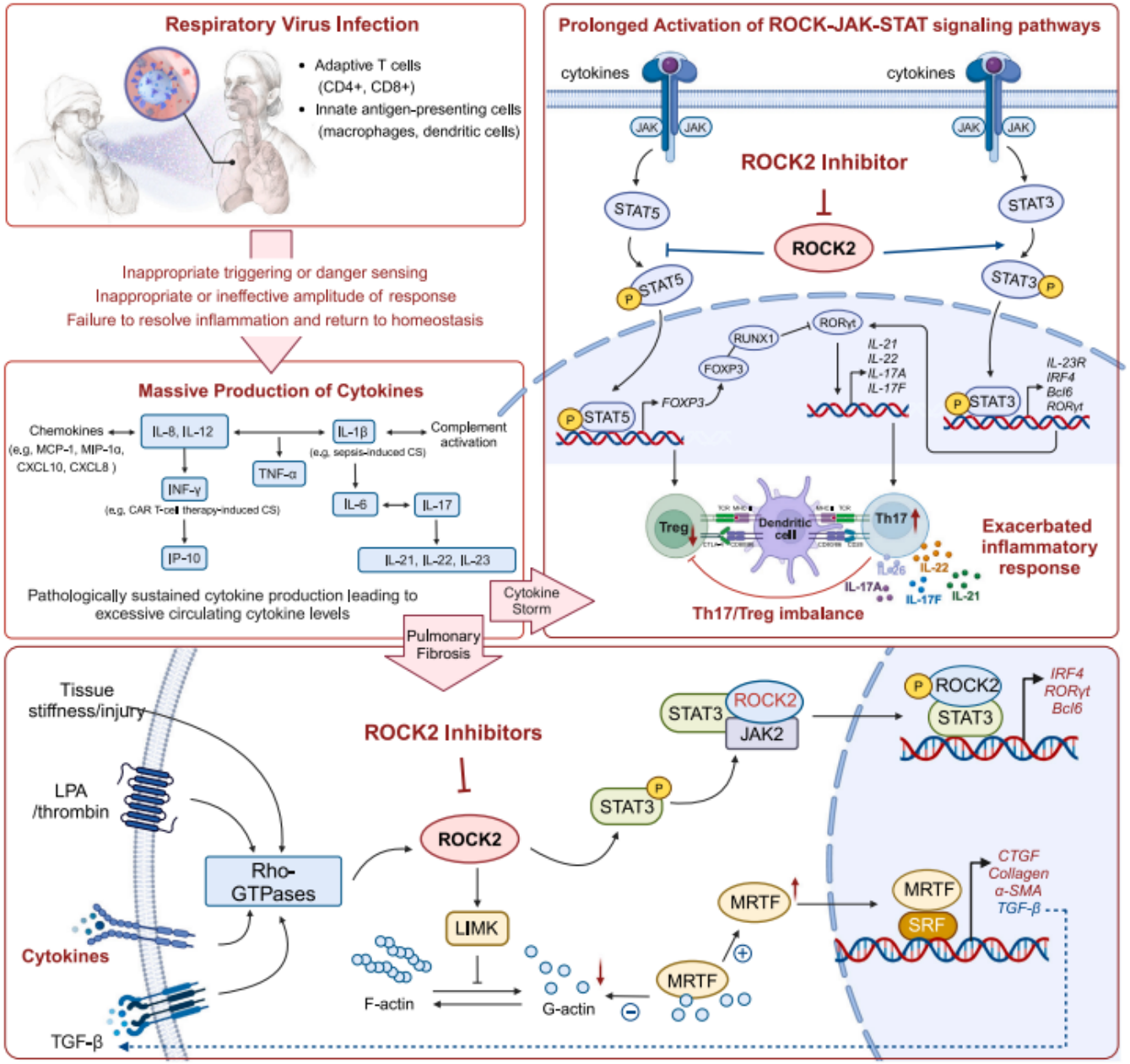
RA new drugs



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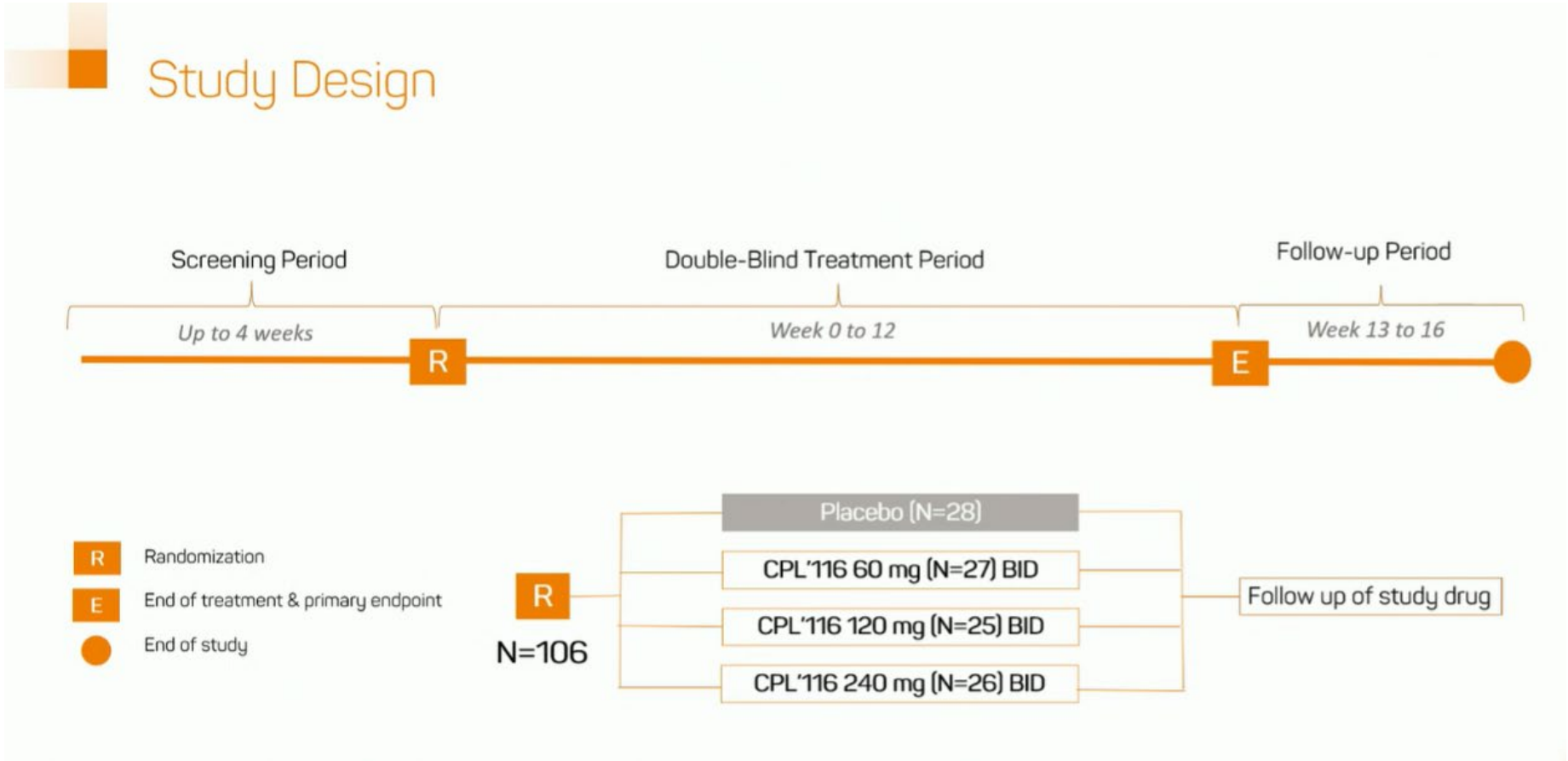
RA new drugs



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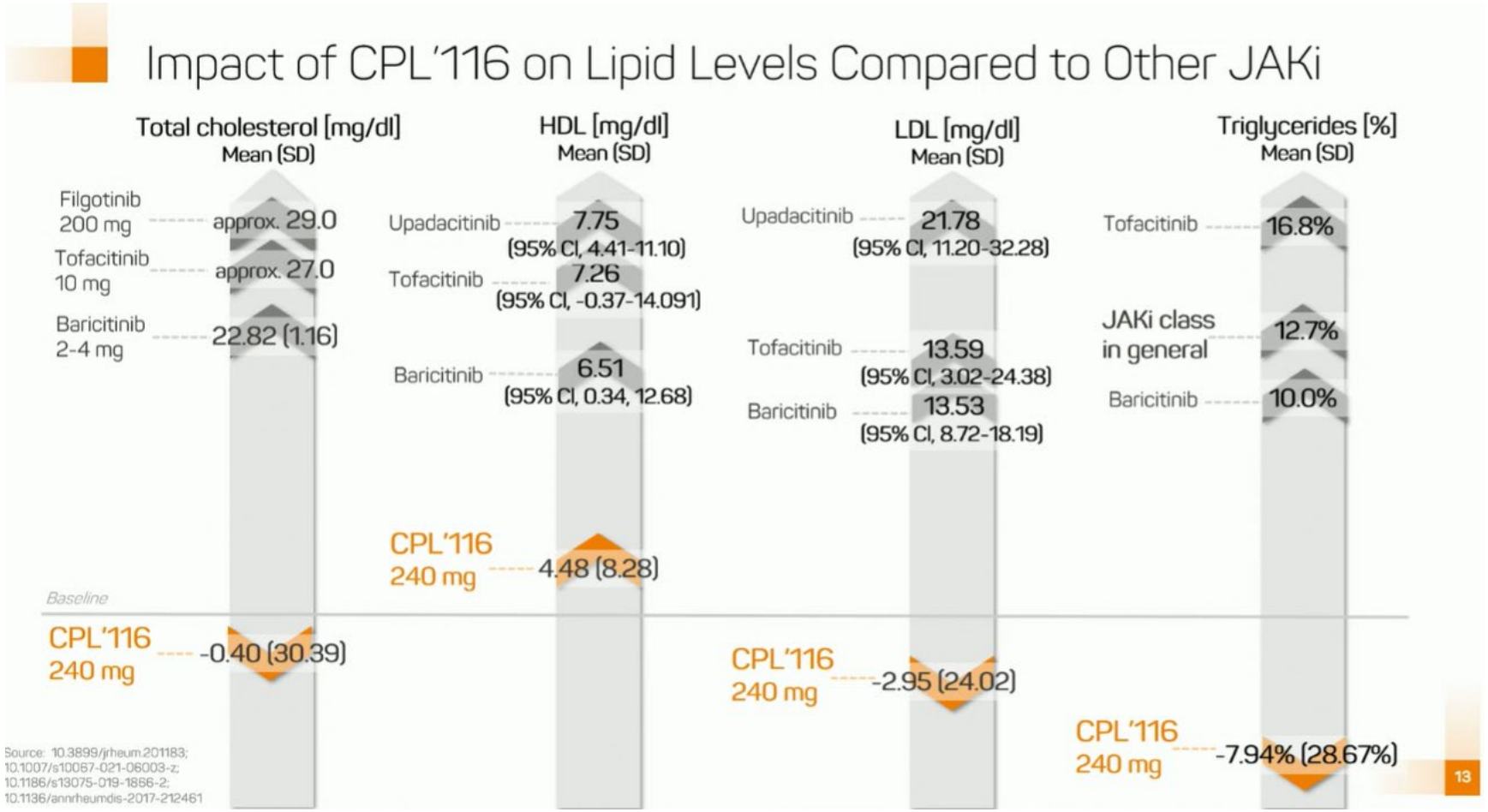
RA new drugs



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RA new drugs

- Double specific JAK / ROCK inhibitor

CPL'116 holds potential therapeutic benefits beyond JAK inhibition. In vitro and in vivo studies showed that blocking ROCK signaling pathway had a beneficial effect on endothelial function and also inhibited profibrotic pathways. In addition, the influence of ROCK kinase pathway on lipid metabolism has been demonstrated.

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JAK inhibitors: cancer risk

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Cancer incidence among rheumatoid arthritis patients treated with JAK-inhibitors compared to bDMARDs: data from an international collaboration of registers (the "JAK-pot" study)

Kim Lauper for the JAK-pot investigators
Geneva University Hospital, Switzerland

Hôpitaux Universitaires Genève

OP0232
EULAR 2025 Congress
Barcelona, 12 June 2025

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JAK inhibitors: cancer risk

MATCHED DATA (JAKi / TNFI)	**JAKi** (tofacitinib (29%), baricitinib (38%), upadacitinib (26%), filgotinib (7%)) **n = 12'916**	**TNFi** (etanercept (34%), adalimumab (35%), golimumab (9%), certolizumab (9%), infliximab (5%), unspecified (8%)) **n = 12'916**
Past malignancy (%)	3.2	3.2
Female (%)	81.4	81.4
Treatment duration, years (median [IQR])	1.5 [0.6, 3.1]	1.1 [0.5, 2.7]
Age, years (mean (SD))	57.7 (12.1)	56.2 (13.3)
Disease duration, years (median [IQR])	10.4 [5.0, 17.4]	7.9 [3.5, 14.7]
Seropositivity (%)	79.0	74.2
Previous b/ts DMARD (%)		
0	23.9	32.0
1	21.4	34.1
2	20.1	16.2
≥ 3	34.7	17.7
Concomitant csDMARD (%)	51.2	61.3
Concomitant GC (%)	44.0	42.8
CRP, mg/L (mean (SD))	11.0 (20.9)	11.6 (20.4)
CDAI (mean (SD))	26.8 (13.5)	27.6 (13.6)
DAS 28 (mean (SD))	26.8 (13.5)	27.6 (13.6)
HAQ (mean (SD))	1.2 (0.7)	1.2 (0.7)
BMI (mean (SD))	26.8 (5.6)	27.0 (5.7)
Tobacco (ever) (%)	33.0	34.9

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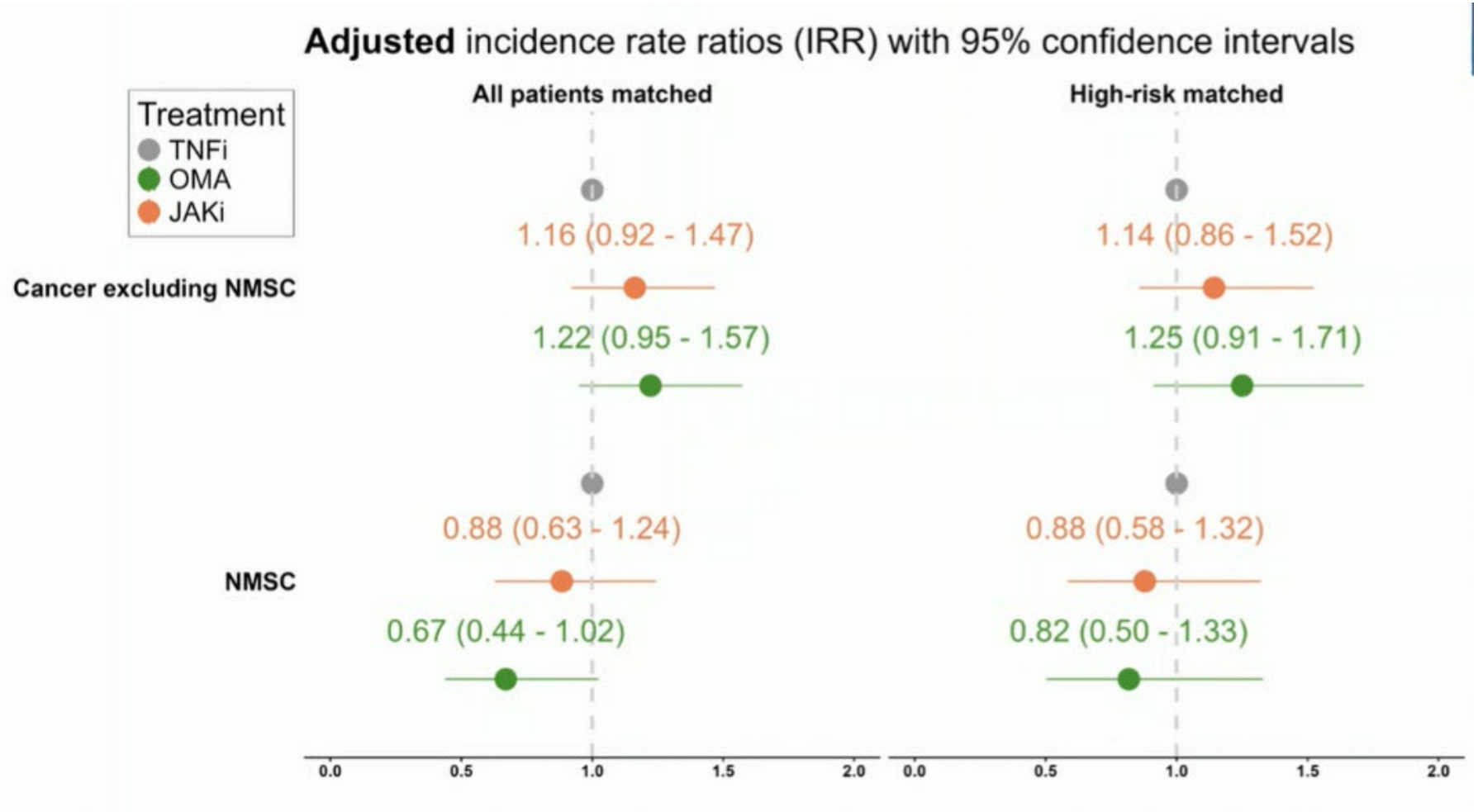
JAK inhibitors: cancer risk

- No significantly increased cancer risk in JAKi treated RA patients



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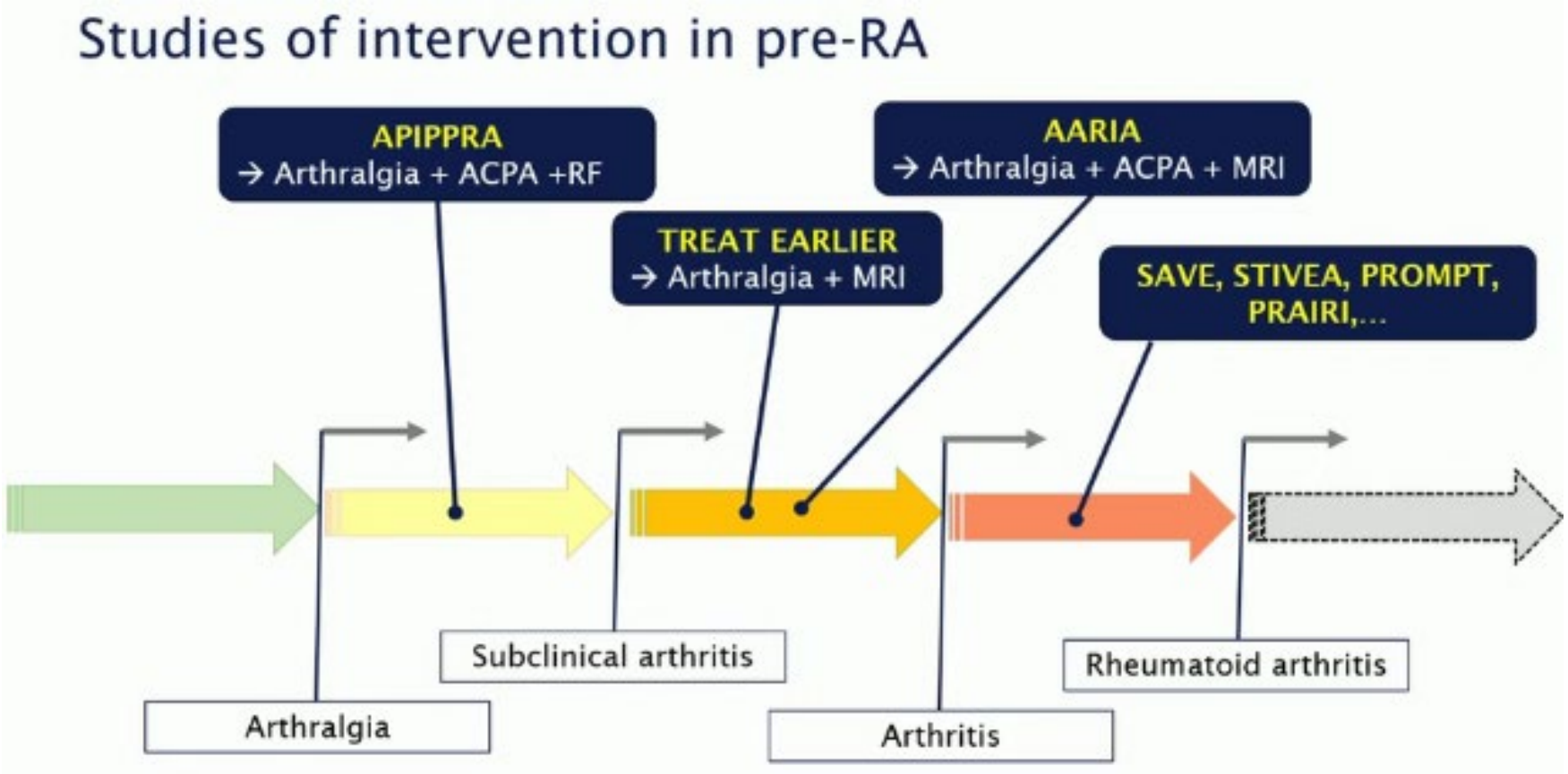
RA prevention



Aletaha, EULAR 2023 plenary lecture

RA prevention

The ALTO study

Study goals

To capture the long-term impact of disease interception with 12 months treatment with abatacept

To collect safety data:
- severe adverse events
- events of special interest
  infection, cancer, cardiovascular

Study design

A long-term outcome study

Recruiting participants who enrolled in the APIPPRA trial
- ACPA+
- arthralgia

Follow up for up to 6 years to January 2023, regardless of outcome in APIPPRA

No study specific intervention

Primary endpoint

Time to development of clinically apparent synovitis in ≥3 joints,

Time to development of RA according to the ACR/EULAR 2010 classification criteria,

Time to starting first DMARD, excluding corticosteroids,

..... whichever is met first

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RA prevention

Characteristics of the study population

	Randomised in APIPPRA (N=213)			Followed up in ALTO period (N=143)		
	Abatacept N=110	Placebo N=103	Total N=213	Abatacept N=71	Placebo N=72	Total N=143
Age Mean (SD)	48.3 (11.6)	48.8 (10.9)	48.5 (11.2)	47.2 (12.6)	49.1 (9.5)	48.2 (11.2)
Sex						
Male	24% (26)	21% (22)	23% (48)	24% (17)	19% (14)	22% (31)
Female	76% (84)	79% (81)	77% (165)	76% (54)	81% (58)	78% (112)
Smoking						
Current	19% (21)	20% (21)	20% (42)	11% (8)	21% (15)	16% (23)
Previous	40% (44)	46% (47)	43% (91)	45% (32)	43% (31)	44% (63)
Never	41% (45)	34% (35)	38% (80)	44% (71)	36% (26)	40% (57)
Previous event during APIPPRA YES				31% (22)	32% (23)	31% (45)
Previous event during APIPPRA NO				69% (49)	68% (49)	69% (90)

Median follow up time was 66 months (Q25-Q75: 54 – 78)

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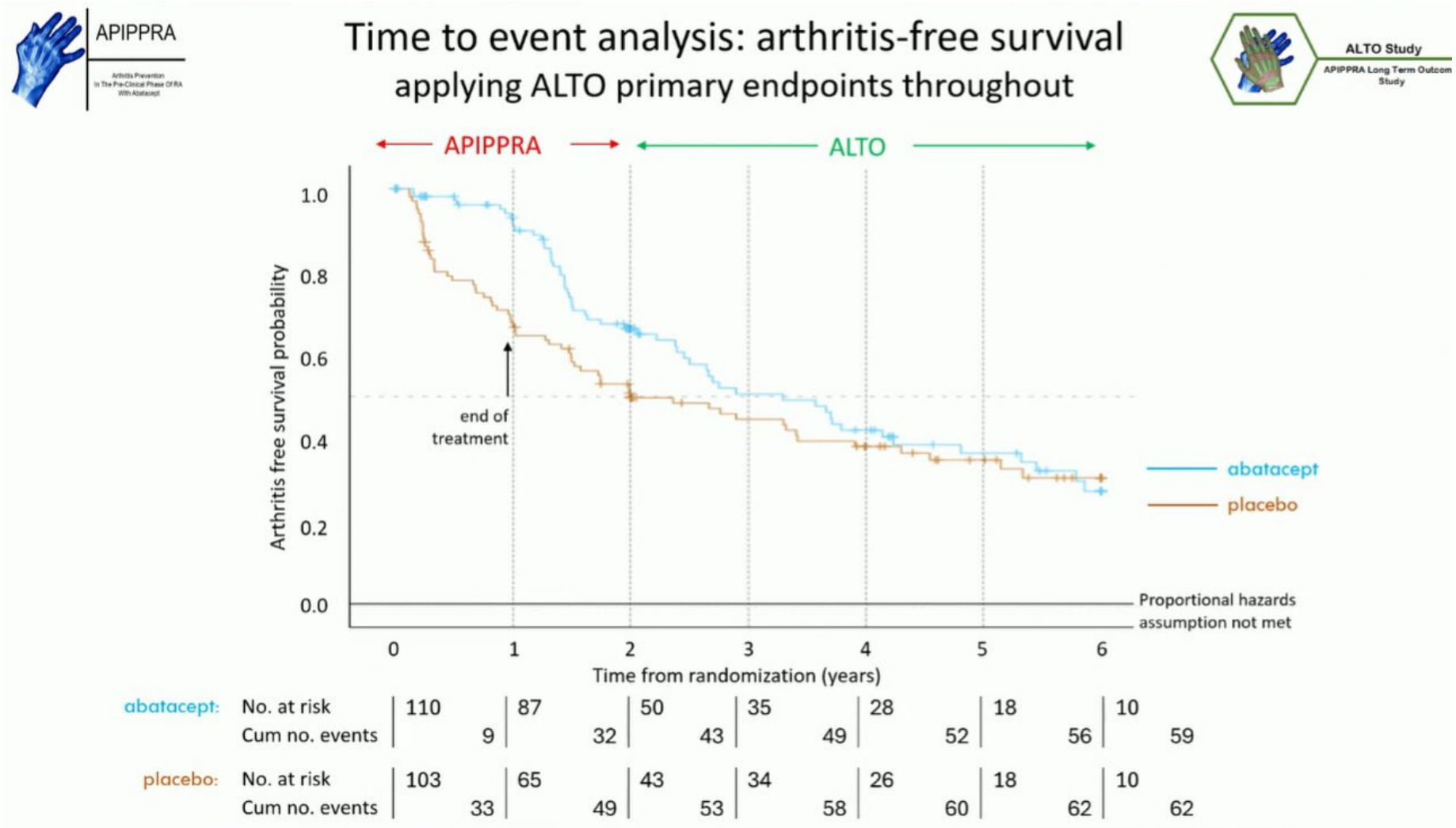
RA prevention



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RA prevention

ALTO study: summary of events by arm

APIPPRA ← → ALTO

	End of treatment Year 1		End of study Year 2		Year 3		Year 4		Year 5		Year 6	
	N	%	N	%	N	%	N	%	N	%	N	%
Placebo	29/103	28.2	39/103	37.9	51/103	49.5	56/103	54.4	59/103	57.3	61/103	59.2
Abatacept	6/110	5.5	27/110	24.5	42/110	38.2	48/110	43.6	51/110	46.4	55/110	50.0
Total Events (%)	35/213 (16%)		66/213 (31%)		93/213 (44%)		104/213 (49%)		110/213 (52%)		116/213 (54%)	
NNT	4		7		9		9		9		11	
Difference in restricted mean survival times p-value			p=0.001		p=0.008		p=0.039		p=0.102		p=0.171	

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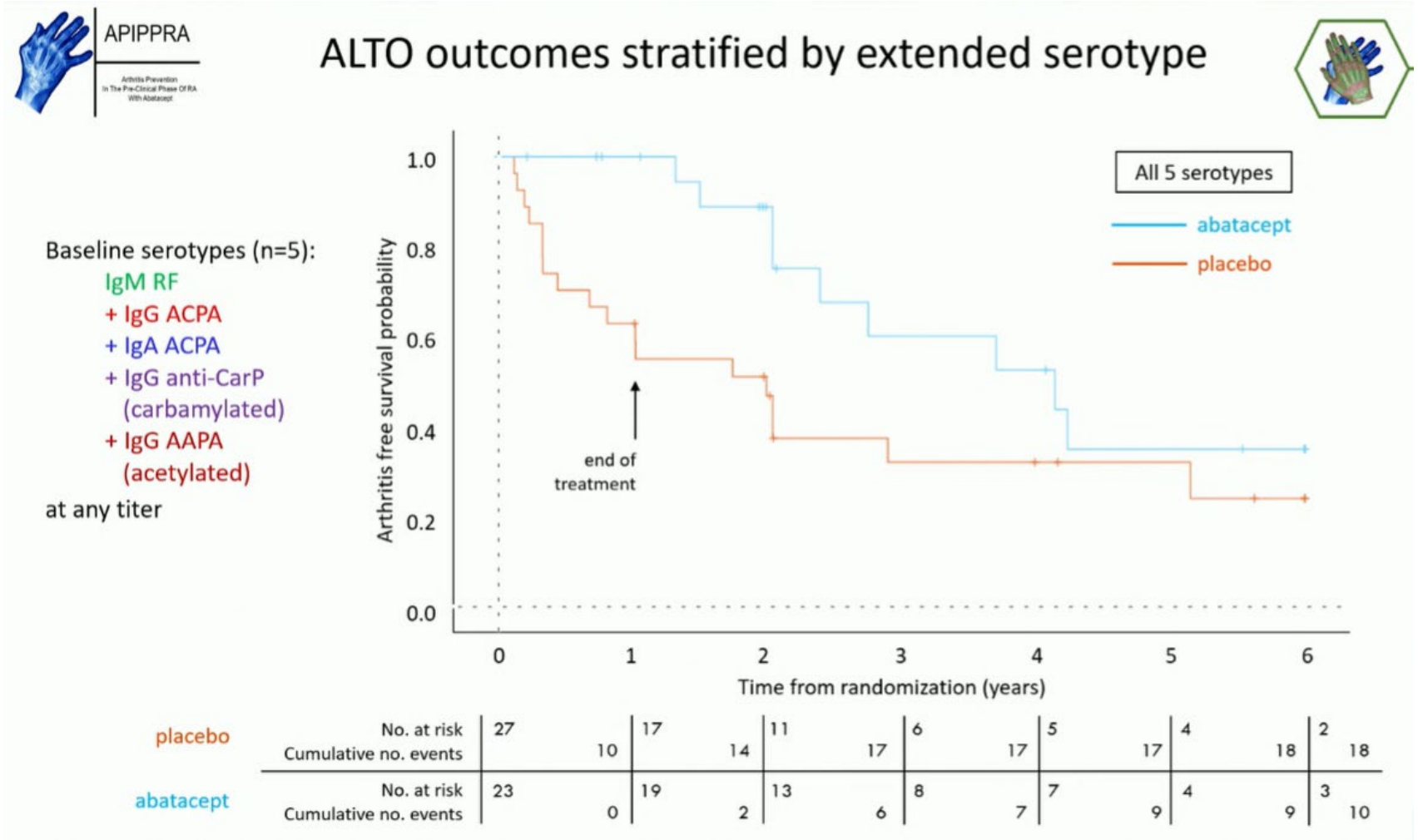
RA prevention



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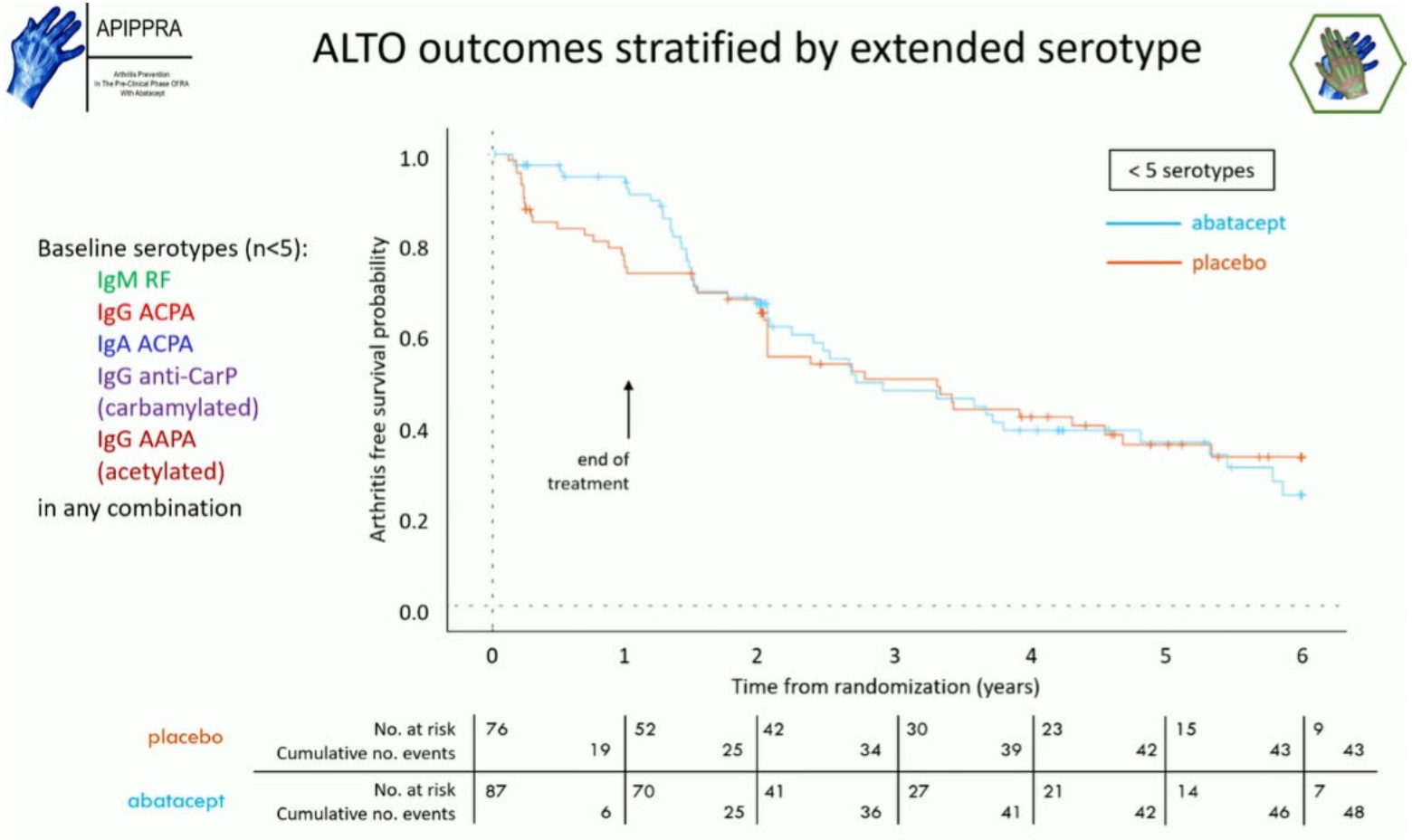
RA prevention



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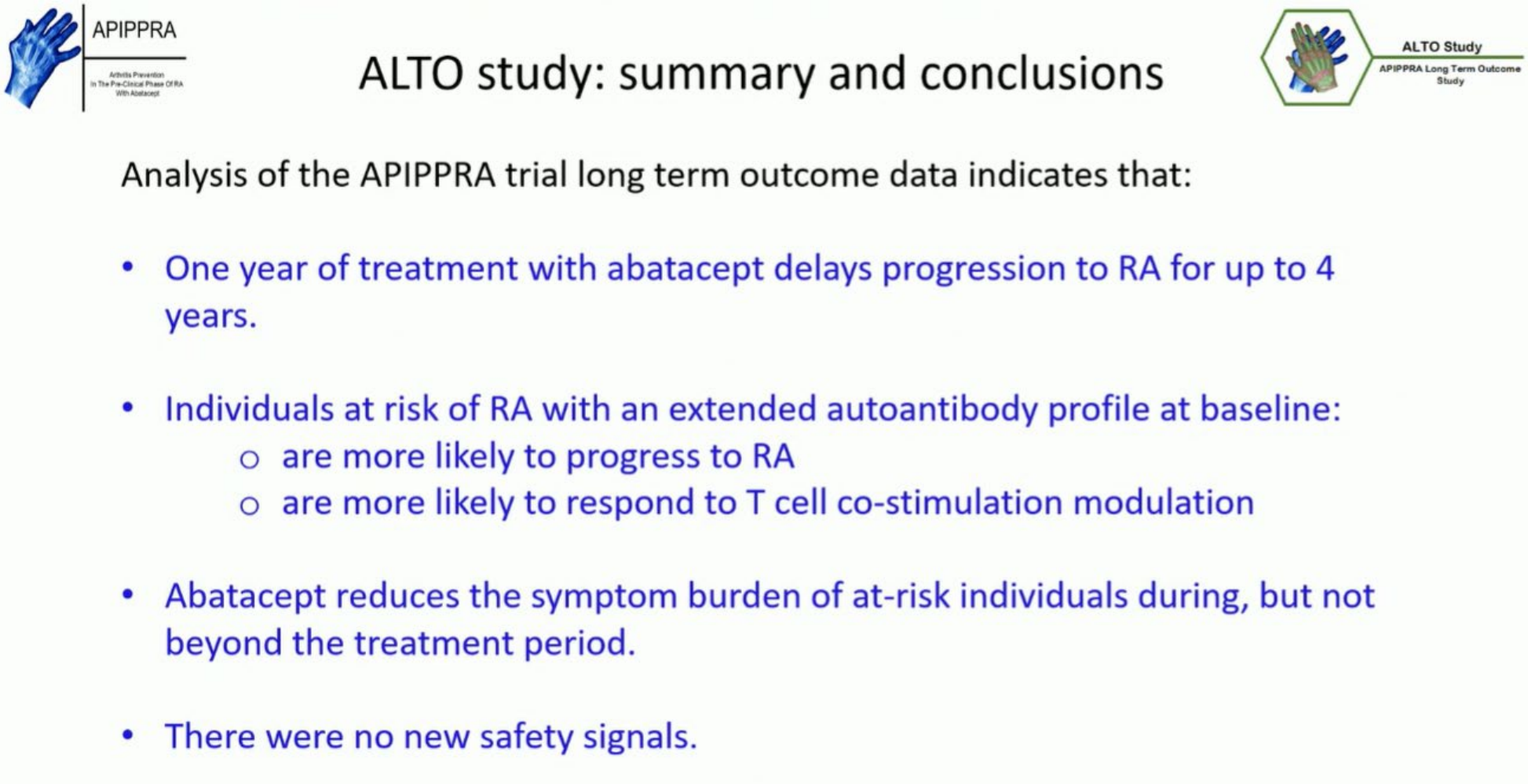
RA prevention

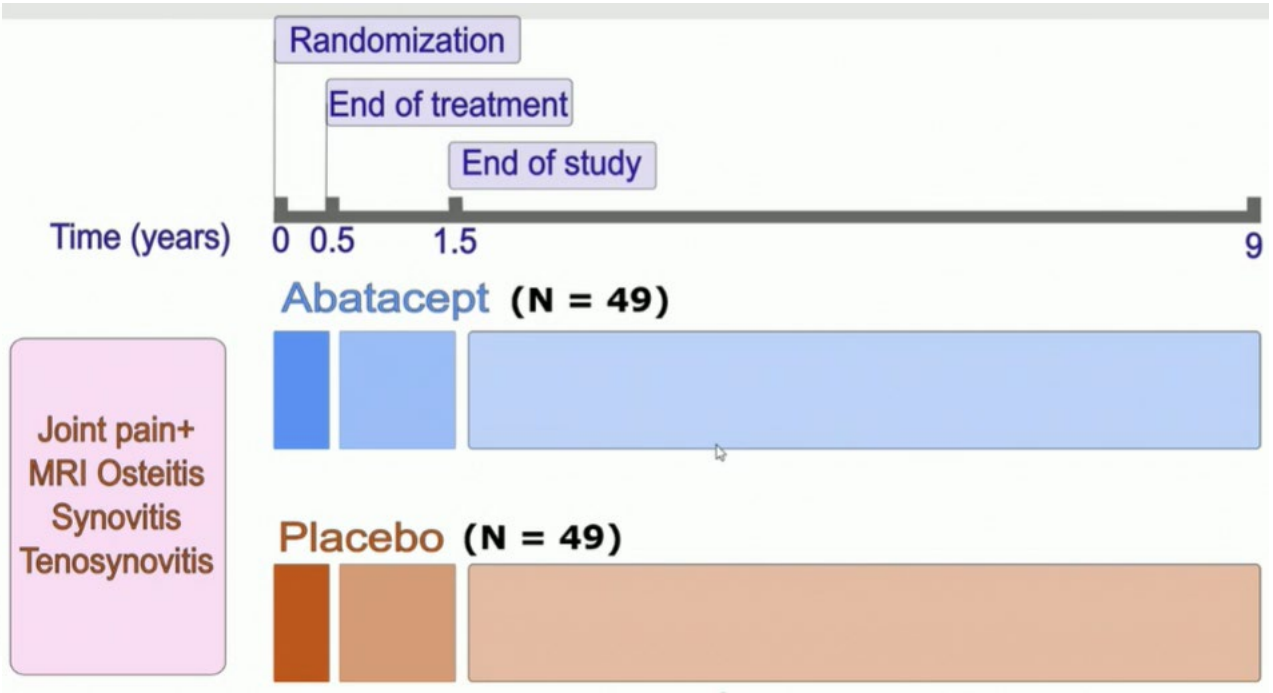


RA prevention

- ARIAA Trial

ARIAA Trial Overview:

- ACPA+ individuals with
  - joint pain
  - subclinical inflammation on hand MRI.
- Randomized to a 6-month treatment:
  - Abatacept (125 mg/w sc)
  - Placebo.
- Followed 12 months post-treatment (no therapy)



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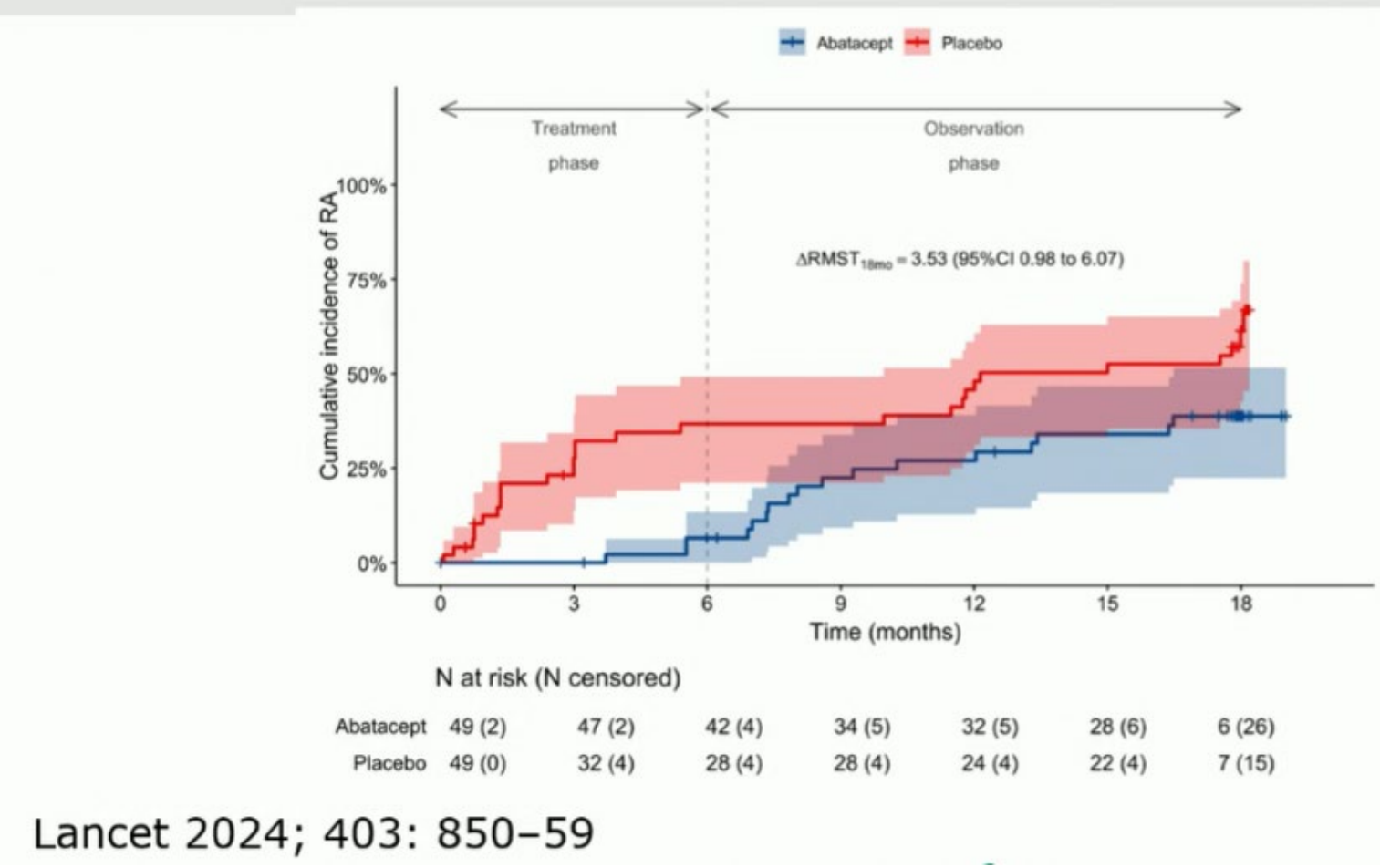
RA prevention

- RA (percentage) over study duration of 18 months



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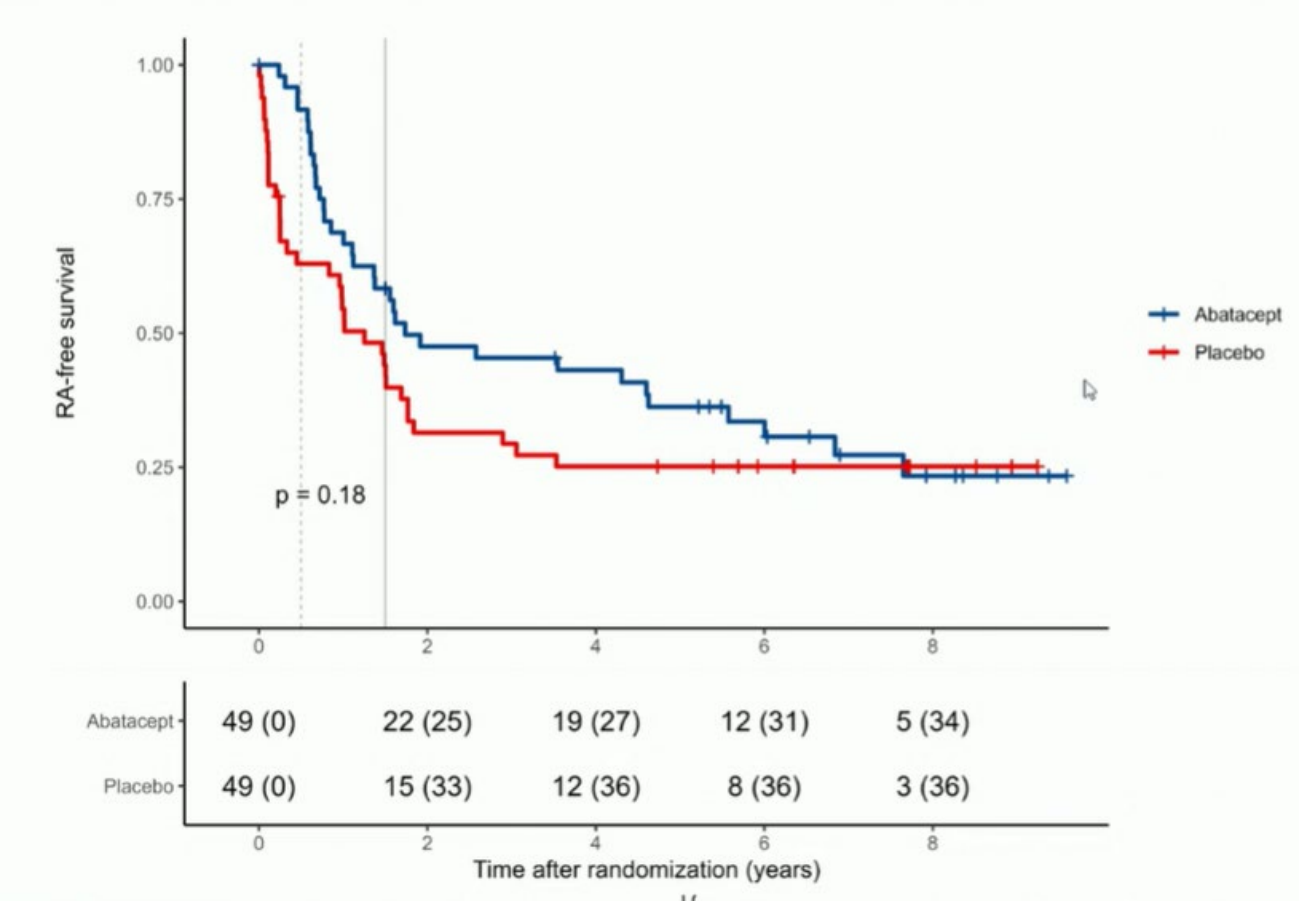
RA prevention

- RA free survival



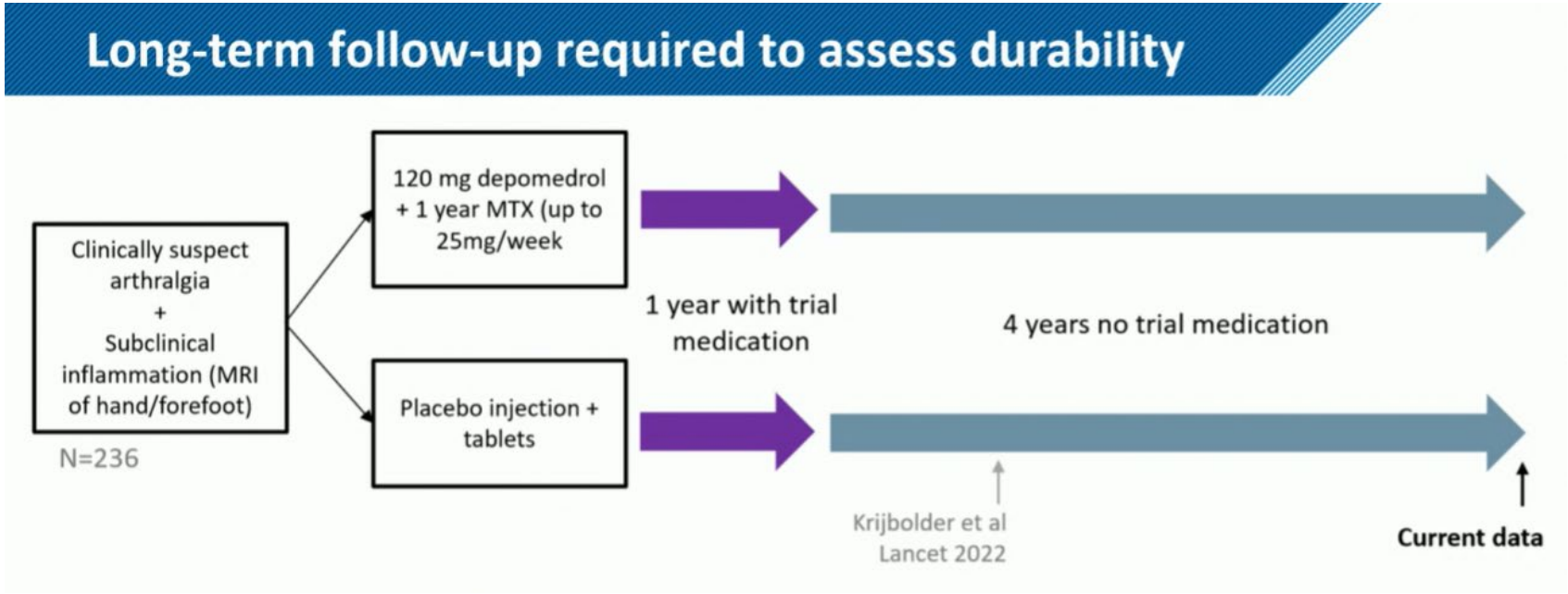
OP0325, EULAR 2025

RA prevention

OP0324, EULAR 2025

RA prevention

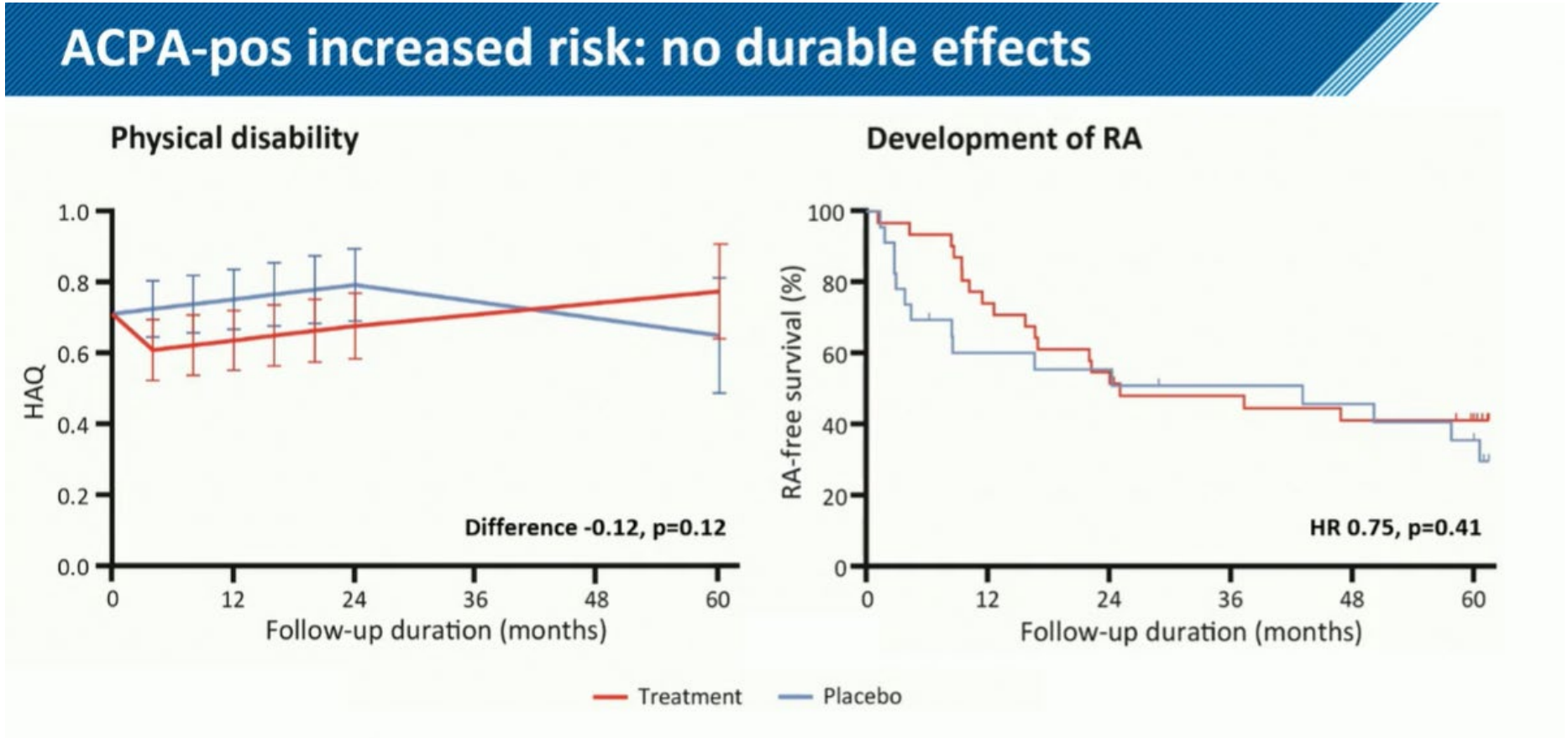
- Treat earlier trial



OP0324, EULAR 2025

RA prevention

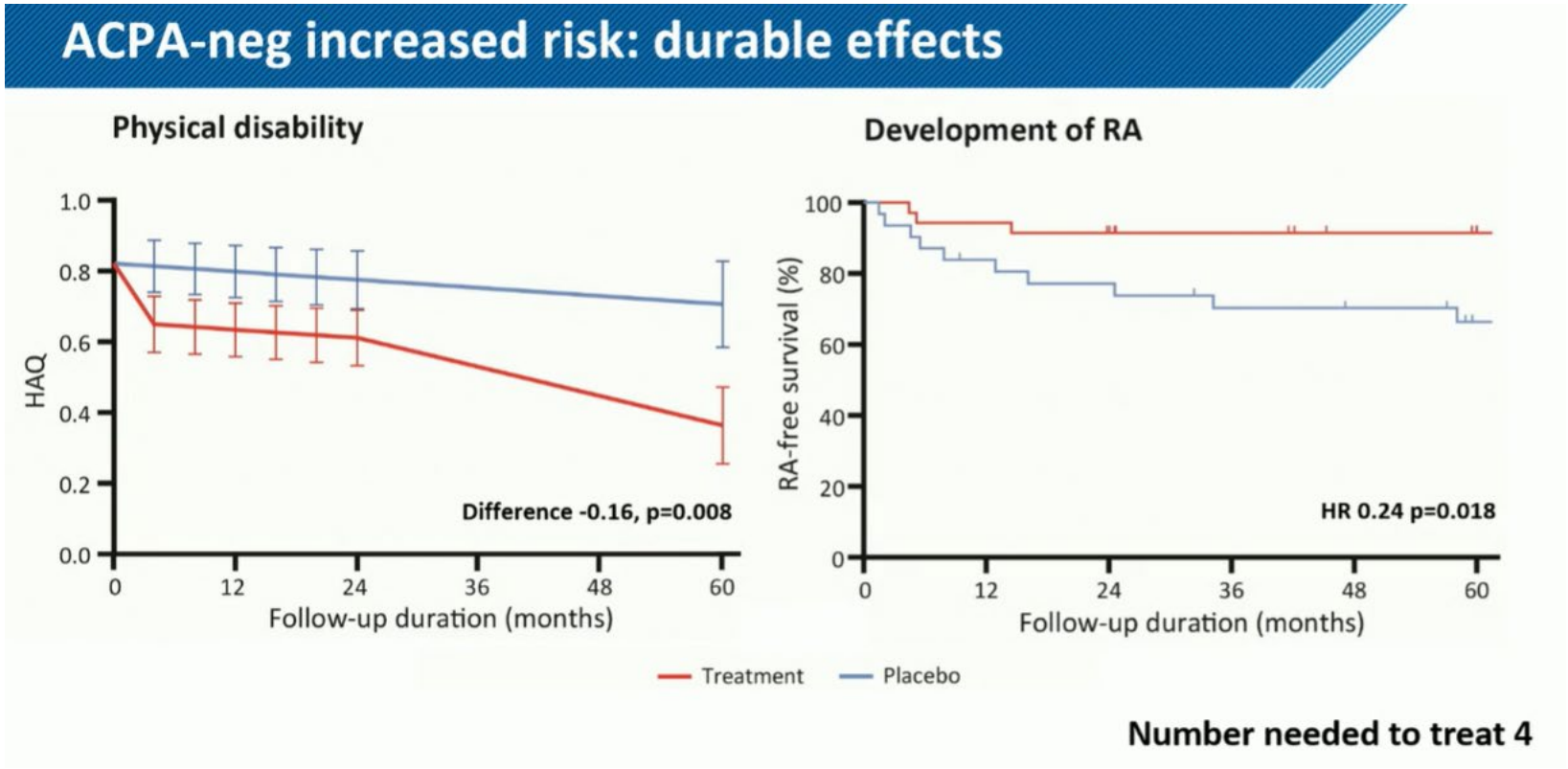
- ACPA+ individuals with increased risk for RA



OP0324, EULAR 2025

RA prevention

- ACPA – individuals with increased risk for RA



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RA prevention

Conclusions on long-term efficacy

- MTX: different long-term effects on developing ACPA-pos and ACPA-neg RA
- Different treatment strategies needed for ACPA-pos and ACPA-neg at-risk patients
- ACPA-neg increased risk: durable improvement in burden & less RA development

OP0324, EULAR 2025

RA prevention

- APIPPRA/ALTO (abatacept)
  - Delay of RA of 4 years, no durable effect
- ARIAA (abatacept)
  - Delay of RA of 5 years, no durable effect
- TREAT EARLIER (MTX)
  - No effect in ACPA + individuals
  - Durable effect in ACPA - individuals

ACPA + arthralgia patients

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OP0110

Results of a 10-year prospective follow-up of patients with musculoskeletal pain and anti-citrullinated protein antibodies -not every arthritis is rheumatoid arthritis, despite criteria fulfilment.

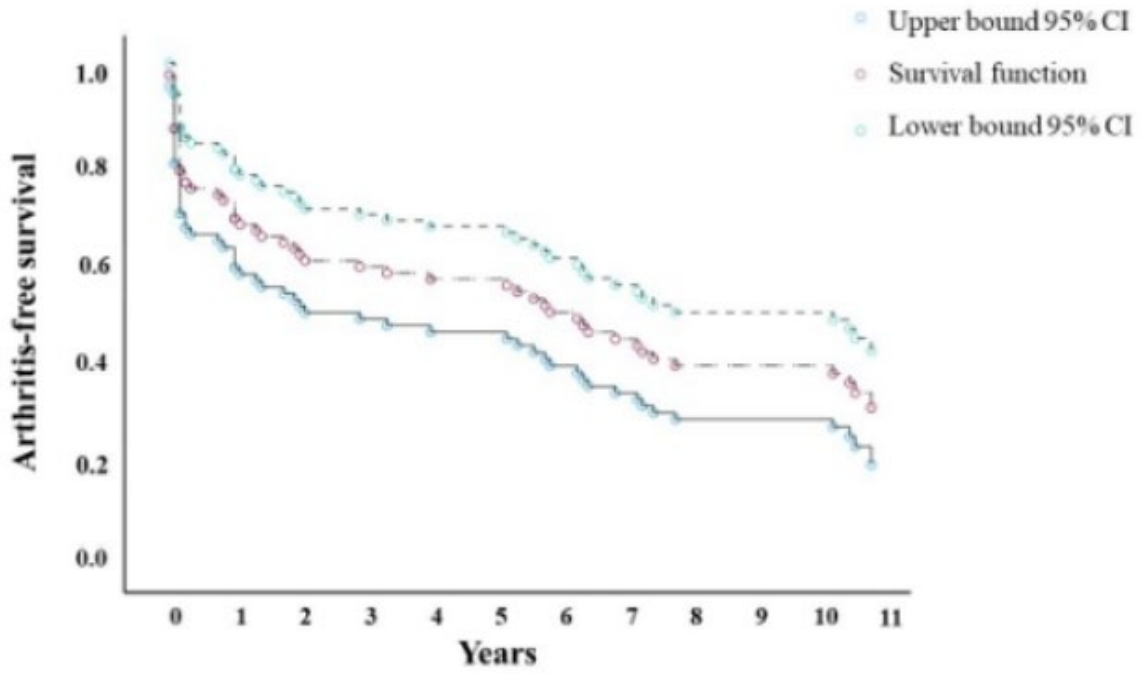
Keywords: Prognostic factors , Autoantibodies

Simon Åhammar* [1, 2], Klara Martinsson [1], Michael Ziegelasch [1, 2], Jan Cedergren [2], Alf Kastbom [1, 2]

[1] Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden [2] Department of Rheumatology in Östergötland, Linköping, Sweden

ACPA + arthralgia patients

- Single center study in Sweden
- 82 patients with muskuloskeletal symptoms and pos. ACPA
- Follow up 10 years
- Primay outcome: arthritis development (by rheumatologist)



60% developed arthritis

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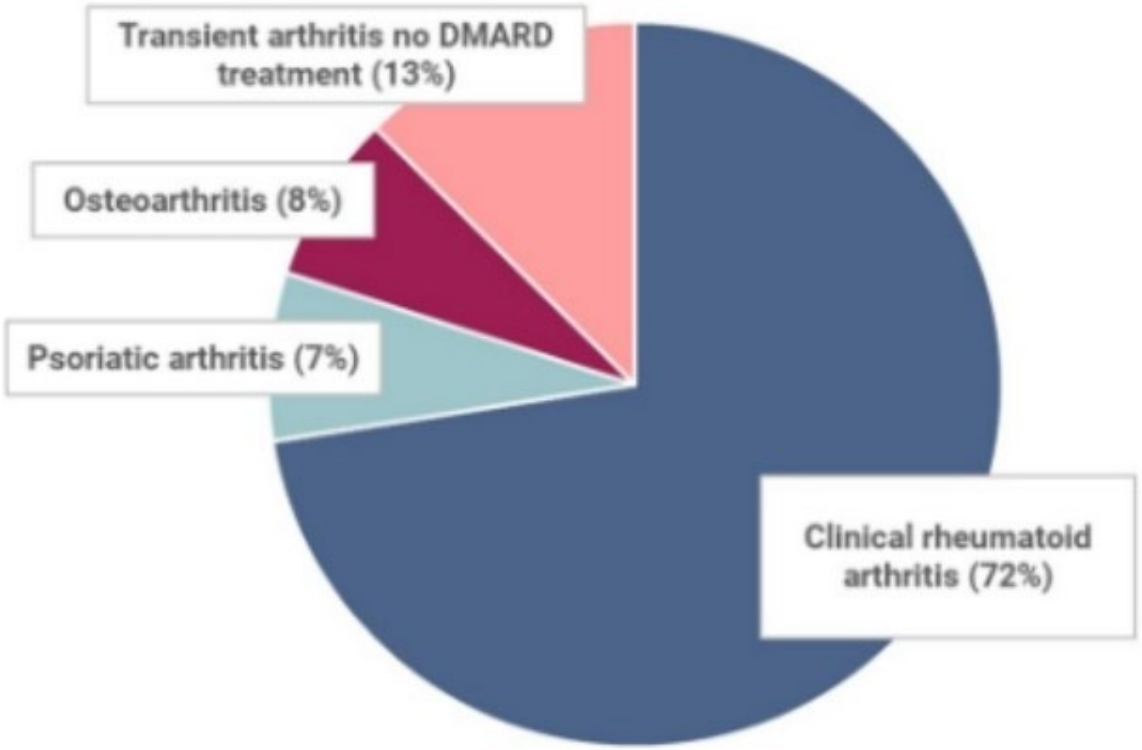
ACPA + arthralgia patients

- Not all patients who developed arthritis classified as RA



OP0110, EULAR 2025

The impact of social frailty and physical function on laughter frequency in rheumatoid arthritis patients from a multicenter observational study (T-FLAG)

Mochihito Suzuki1, 2, Yoshifumi Ohashi3, 4, Yasumori Sobue5, Kenya Terabe1, Shuji Asai1, Shiro Imagama1
1 Nagoya University Graduate School of Medicine, Department of Orthopedic Surgery and Rheumatology, Nagoya, Japan, 2 Jcho Kani Tono Hospital, Department of Orthopedic Surgery, Kani, Japan
3 Aichi Medical University Hospital, Department of Orthopedic Surgery, Nagakute, Japan, 4 Yokkaichi Municipal Hospital, Department of Orthopedic Surgery, Yokkaichi, Japan
5 Japanese Red Cross Nagoya Daiichi Hospital, Department of Orthopedic Surgery and Rheumatology, Nagoya, Japan

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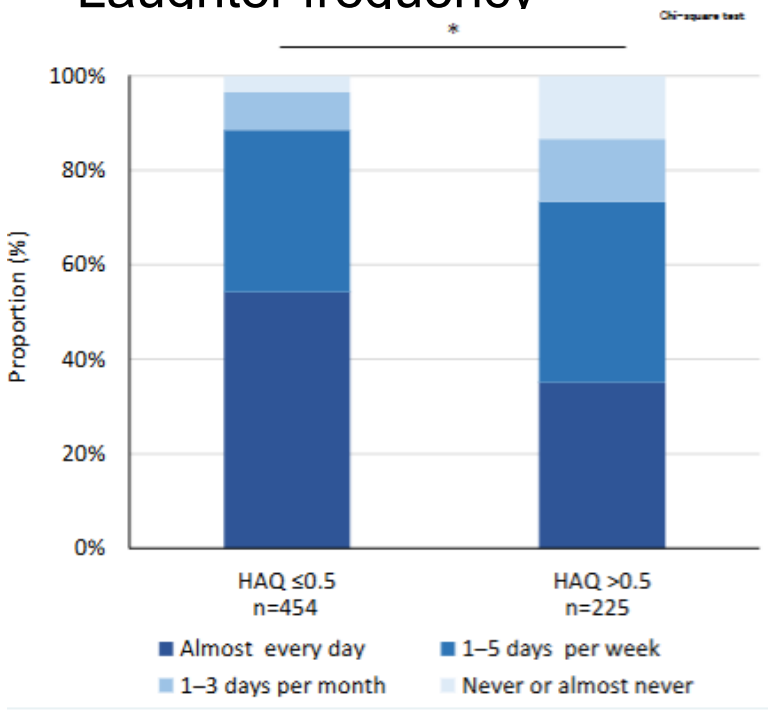
- Recent studies suggest laughter may reduce stress, boost immunity, and improve mental health (1), yet its role in RA remains understudied.

AIM

The aim of this study is to investigate the association between laughter frequency, disease activity, physical function, frailty, and social frailty in RA patients.

Laughter frequency



CONCLUSIONS

- This study is the first to thoroughly clarify the associations between laughter frequency and frailty, physical function, and social frailty in patients with RA.
- The findings indicate that laughter could serve as a beneficial approach to enhancing the QOL for RA patients. Beyond managing disease activity, integrated interventions that address physical and social dimensions may promote more frequent laughter, thereby supporting QOL improvements.

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Summary

- CV risk in RA modifiable with GLP1 agonists
- New signal transduction inhibitors with improved CV risk profile
- Cancer risk in RA treated with JAKi not increased in real-world studies

- RA prevention studies: no prevention of ACPA + RA possible
- RA prevention: exception ACPA – RA: durable effect of MTX/GC
- Prognosis of ACPA + arthralgia: 50% do not develop arthritis requring DMARD Tx

- Regular laughter is good for the quality of life

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Vielen Dank für die Aufmerksamkeit