10 al 14 de
noviembre
2024
Ciudad San Diego
(USA)

Sociedad Española de Reumatología

ACRreview 23

#ACReview23

AstraZeneca

ACRreview 23

#ACReview23

Sociedad Española de Reumatología

Espondiloartritis Tratamiento

Dr. Javier Rueda Gotor

Servicio de Reumatología
Hospital Sierrallana. Cantabria

AstraZeneca

ACRreview 23

#ACReview23

Tratamiento de Espondiloartritis (EspA axial y Artritis Psoríasica)

APs y EspAax

EFICACIA FARMACOLÓGICA Y ESTRATEGIAS TERAPEUTICAS

- Comparaciones entre fármacos (ECAs H2H y en vida real)
- Eficacia sobre manifestaciones extraarticulares
- Factores predictores de respuesta
- Swtiching Vs Cycling
- Tratamiento combinado
- Optimización

SEGURIDAD

- Seguridad a largo plazo (LTE)
- Seguridad cardiovascular

NOVEDADES TERAPÉUTICAS

- Fármacos en desarrollo clínico
- Fármacos con aprobación pero no comercializados
- Nuevas vías de administración de fármacos en uso

APs

EFICACIA FARMACOLÓGICA Y ESTRATEGIAS TERAPEUTICAS

- Comparaciones entre fármacos (ECAs H2H y en vida real)
- Eficacia sobre manifestaciones extraarticulares
- Factores predictores de respuesta
- Swtiching Vs Cycling
- Tratamiento combinado
- Optimización

SEGURIDAD

- Seguridad a largo plazo (LTE)
- Seguridad cardiovascular

NOVEDADES TERAPÉUTICAS

- Fármacos en desarrollo clínico
- Fármacos con aprobación pero no comercializados
- Nuevas vías de administración de fármacos en uso

1. Ixekizumab Significantly Improves Nail Disease and Adjacent Joint Tenderness and Swelling in Psoriatic Arthritis. McGonagle D, et al (2231, Poster session)

Psoriatic arthritis

CLINICAL SCIENCE

A head-to-head comparison of the efficacy and safety of ixekizumab and adalimumab in biological-naïve patients with active psoriatic arthritis: 24-week results of a randomised, open-label, blinded-assessor trial

Mease PJ, *et al*. *Ann Rheum Dis* 2020;**79**:123–131.

- Similar respuesta articular (ACR 50)
- IXE → superior en PsO cutánea (PASI 100) y ungueal (NAPSI)

º dedos)

- El presente estudio: IXE vs ADA en artritis asociada a onicopatía PsO

1. Ixekizumab Significantly Improves Nail Disease and Adjacent Joint Tenderness and Swelling in Psoriatic Arthritis. McGonagle D, et al (2231, Poster session)

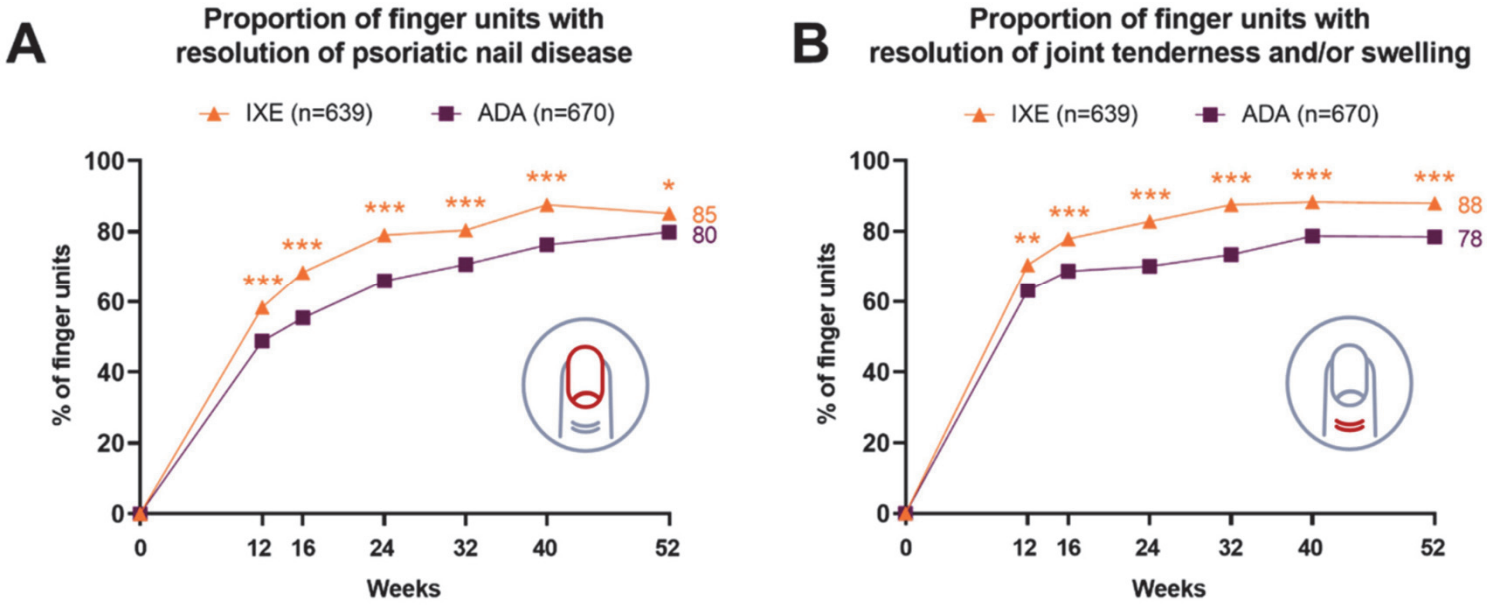
MÉTODOS

- Análisis post-hoc SPIRIT-H2H
- 354 APs con onicopatía PsO + dolor y/o inflamación articulación adyacente (unidad digital)
  - IXE (N=186)
  - ADA (N=168)
- Análisis individual de cada unidad digital (uña + articulación adyacente) afectada en semanas 12,16,24, 32 40 y 52

1. Ixekizumab Significantly Improves Nail Disease and Adjacent Joint Tenderness and Swelling in Psoriatic Arthritis. McGonagle D, et al (2231, Poster session)

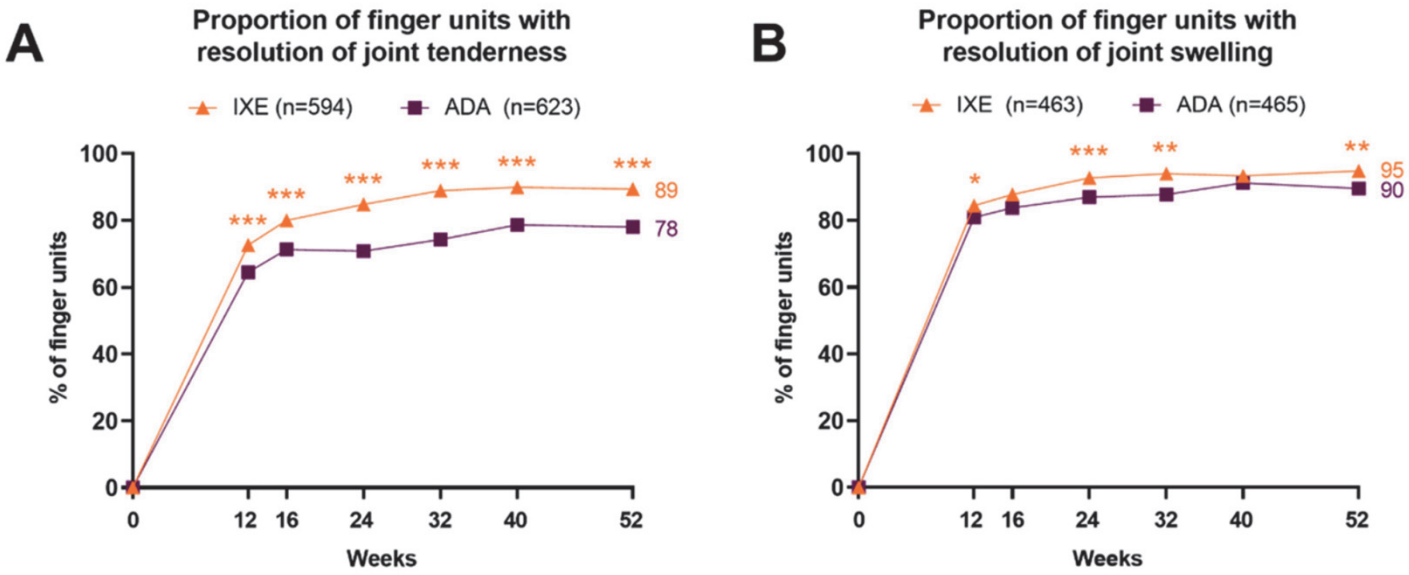
RESULTADOS

- 1309 unidades digitales afectadas (IXE=639, ADA=670)



1. Ixekizumab Significantly Improves Nail Disease and Adjacent Joint Tenderness and Swelling in Psoriatic Arthritis. McGonagle D, et al (2231, Poster session)

RESULTADOS



Conclusiones

- Ixe → opción preferencial en artritis IFDs asociadas a onicopatía psoríasica?

INTRODUCCIÓN

- JAK-i superior a ADA en mejoría del dolor articular en AR (de forma independiente de la inflamación) [1,2]
- JAK-i VS ADA en APs? (entesopatía, dolor axial...)
- EL presente estudio: comparación de UPA Vs ADA Vs Placebo en el control del dolor (subanálisis SELECT-PsA 1)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Upadacitinib and Adalimumab for Psoriatic Arthritis

McInnes IB, et al. N Engl J Med. 2021 Apr 1;384(13):1227-1239.

- ECA fase 3 randomizado, doble ciego, n= 1740 pacientes
- Objetivo 1º: Respuesta ACR 20 sem 12
  - UPA 15 mg: 70.6%
  - UPA 30 mg : 78.5%
  - ADA: 65.0%
  - Placebo: 36.2%
- Análisis de PtGA, articulaciones dolorosas (TJC 28) en UPA 15, ADA y placebo en APs

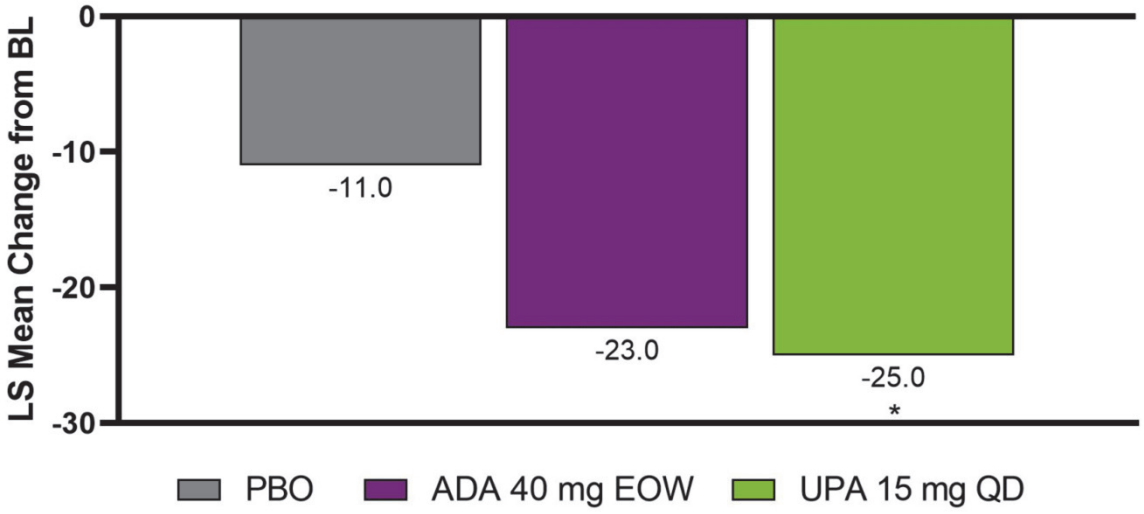
1. Intern Emerg Med. 2023 Sep;18(6):1735-1746.
2. Taylor PC, et al. J Clin Med. 2019 Jun 12;8(6):831.

2. Direct and Indirect Effects of Upadacitinib or Adalimumab on Pain in Psoriatic Arthritis/ Results from a Randomized Phase 3 Study. Taylor P, et al (2251, Poster session)

RESULTADOS

- n=1281 (UPA=429, ADA=429, PBO=423)

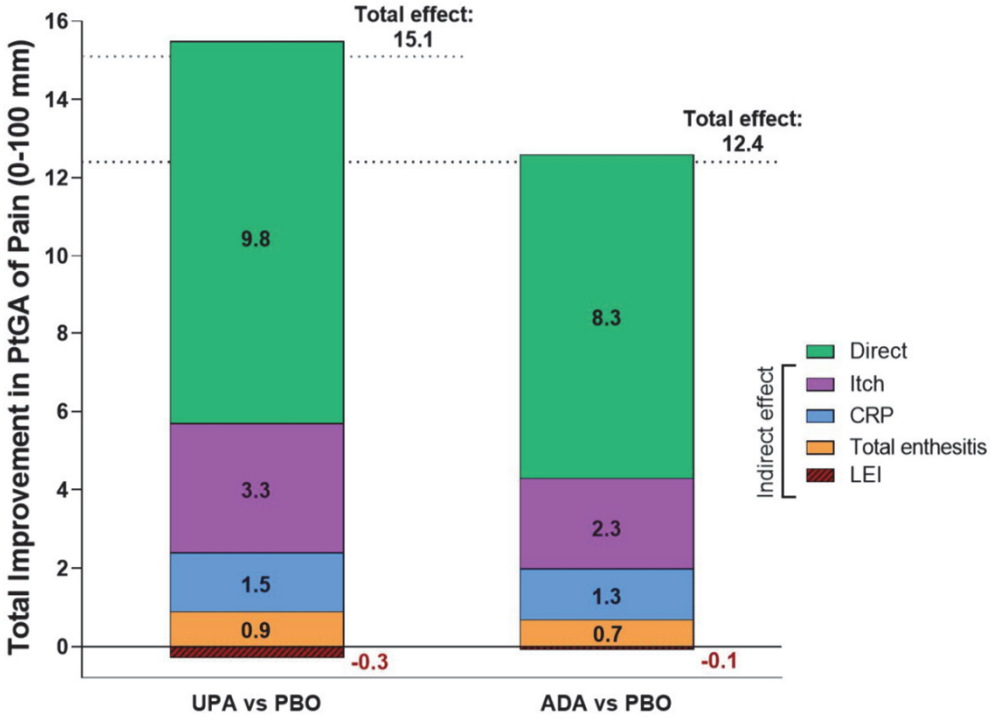
Figure 1. Change from Baseline in PtGA of Pain (mm) at Week 16



2. Direct and Indirect Effects of Upadacitinib or Adalimumab on Pain in Psoriatic Arthritis/ Results from a Randomized Phase 3 Study. Taylor P, et al (2251, Poster session)

RESULTADOS

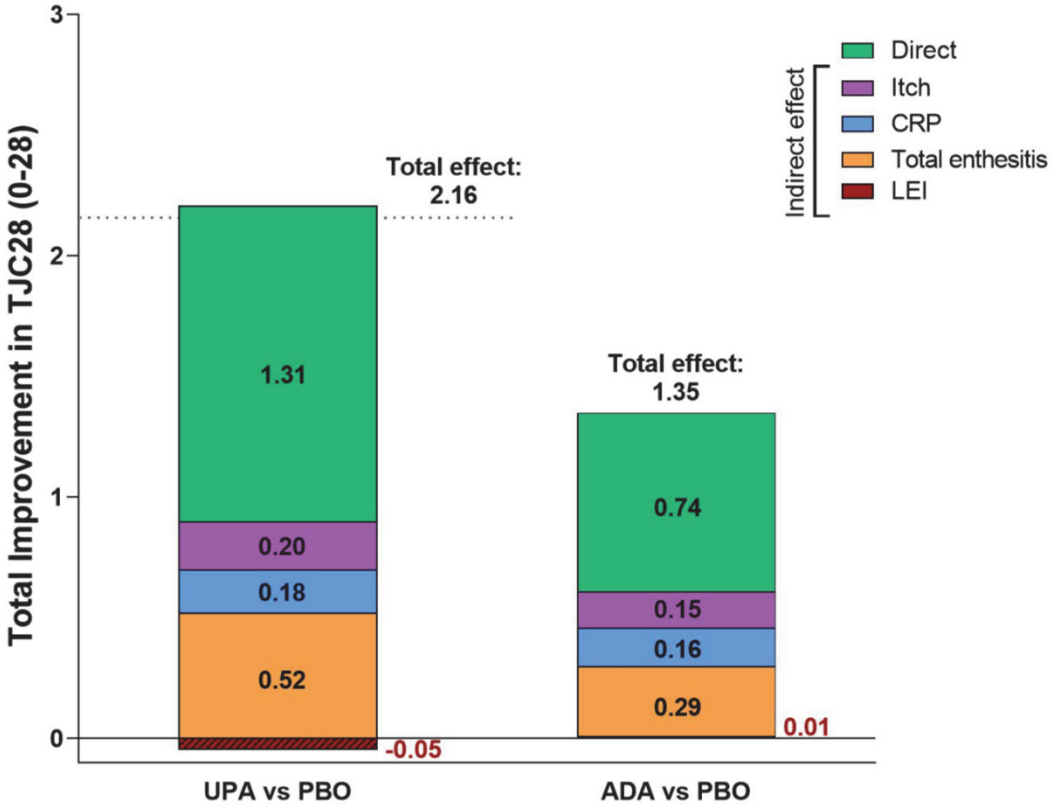
Figure 2. Direct and Indirect Effects of Treatment on Pain Assessed as Improvement in PtGA of Pain at Week 16



2. Direct and Indirect Effects of Upadacitinib or Adalimumab on Pain in Psoriatic Arthritis/ Results from a Randomized Phase 3 Study. Taylor P, et al (2251, Poster session)

RESULTADOS

Figure 3. Direct and Indirect Effects of Treatment on Pain Assessed as Improvement in TJC28 at Week 16



2. Direct and Indirect Effects of Upadacitinib or Adalimumab on Pain in Psoriatic Arthritis/ Results from a Randomized Phase 3 Study. Taylor P, et al (2251, Poster session)

CONCLUSIONES

- UPA y ADA → disminución del dolor global del paciente y de las articulaciones dolorosas en APs
- 2 vías difereciadas
  - Directa
  - Indirecta (inflamatoria)
- La mejoría del dolor → numéricamente superior con UPA...valor añadido?

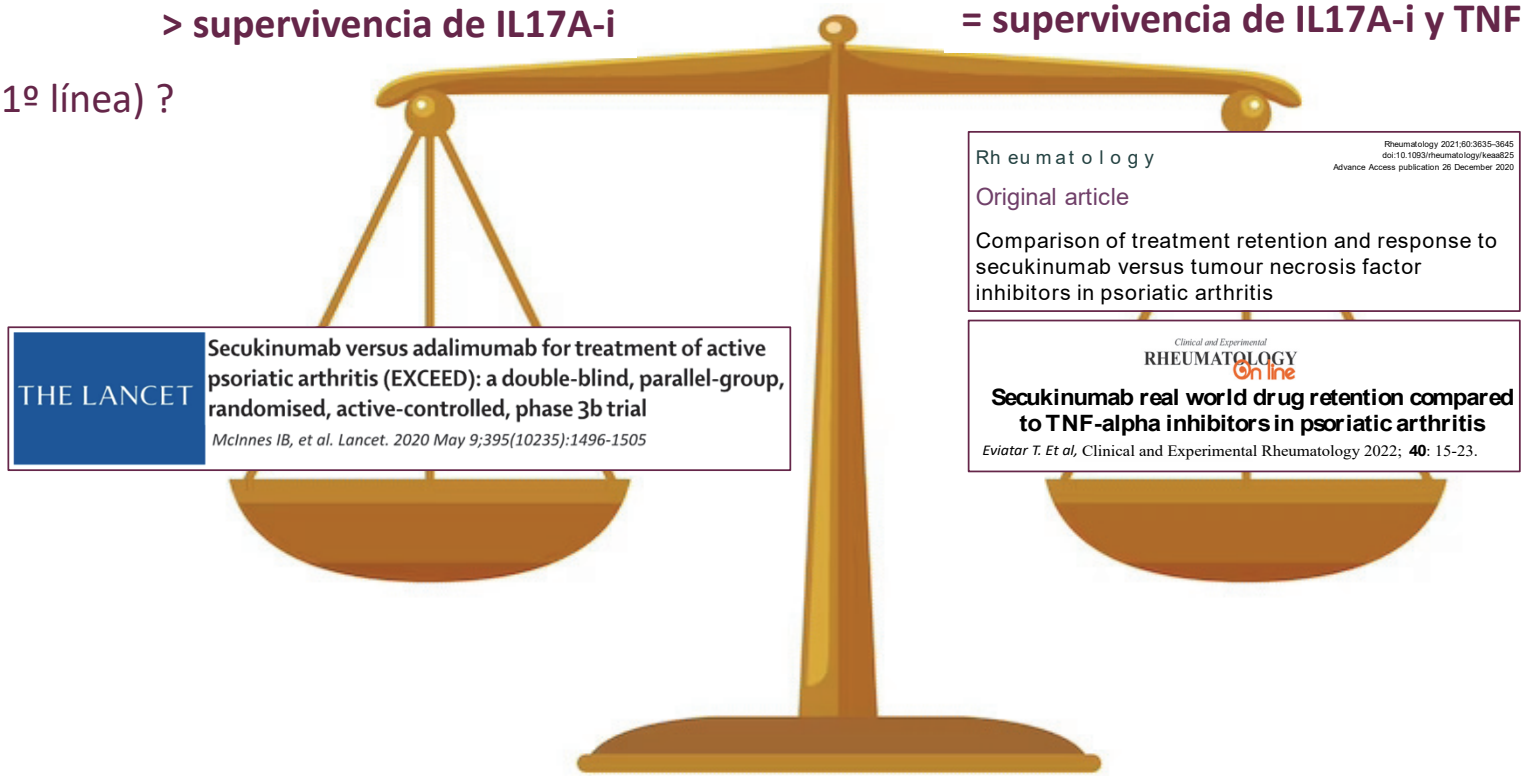
3. Better Drug Retention on anti-IL17A Compared to Anti-TNF Therapy Despite Its Inferior Effect on Composite Joint Indexes and Quality of Life in Patients with PsA–analysis from the Czech Biologics Registry ATTR. Zavada J, et al (1439, Poster session)

INTRODUCCIÓN

- IL17-i Vs TNF-i en APs (1º línea) ?

> supervivencia de IL17A-i

= supervivencia de IL17A-i y TNF



- Análisis de eficacia, supervivencia del fármaco y seguridad en APs que inician TNF-i o IL17A-i en 1º línea (vida real)

3. Better Drug Retention on anti-IL17A Compared to Anti-TNF Therapy Despite Its Inferior Effect on Composite Joint Indexes and Quality of Life in Patients with PsA–analysis from the Czech Biologics Registry ATTR. Zavada J, et al (1439, Poster session)

MÉTODOS

- Registro checo de TB ATTRA (longitudinal prospectivo)
- Criterios de inclusión:
  - inicio de IL17A-i o TNF-i entre 2016-2022
  - ≥ 1año de seguimiento
- Propensity score (PS) matching

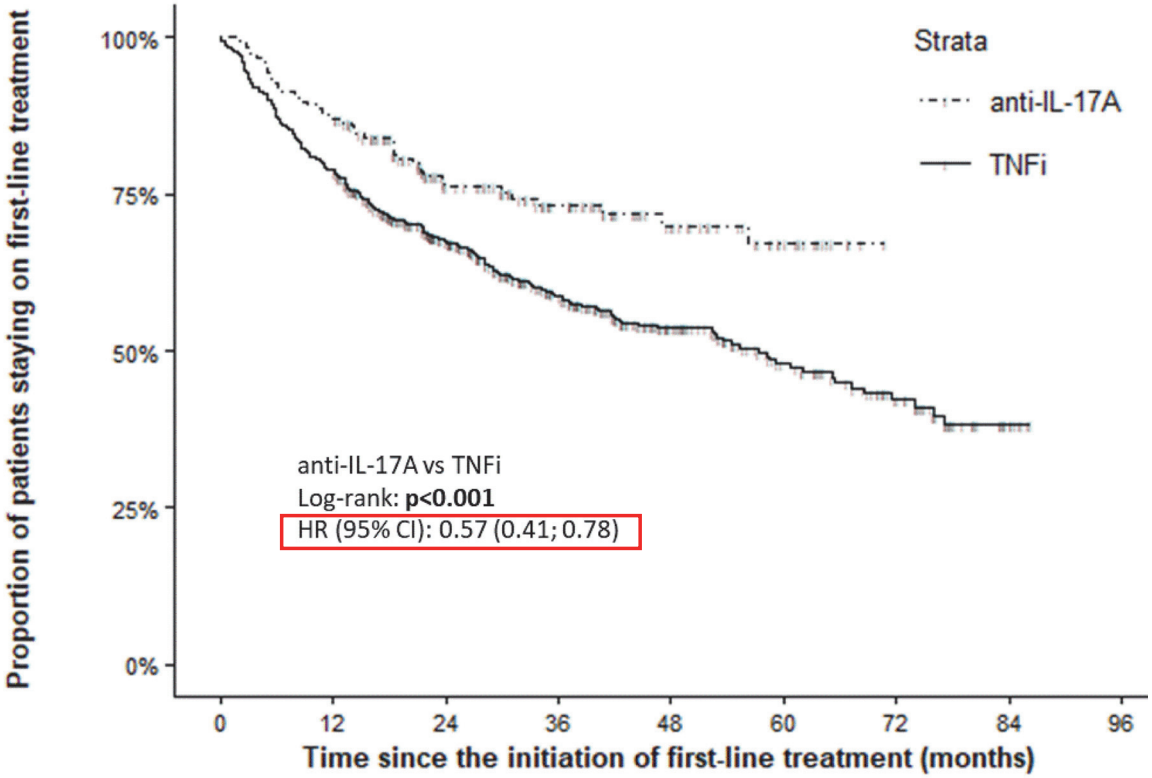
RESULTADOS

Characteristics		anti-IL17A (n=177)	anti-TNF (n=577)	p-value
Female		85 (48.0%)	289 (50.1%)	0.631
Age at diagnosis, yrs		41.0 (33.0–52.0)	43.0 (34.0–51.0)	0.377
Age at start of 1st line, yrs		49.0 (42.0–57.0)	51.0 (42.0–58.0)	0.697
BMI		28.7 (25.3–33.1)	28.3 (25.3–32.5)	0.741
Tender joint count (66 joints)		12.0 (8.0–20.0)	12.0 (7.0–19.0)	0.439
Swollen joint count (68 joints)		7.0 (3.0–12.0)	8.0 (4.0–12.0)	0.329
ESR (mm/h)		24.0 (11.0–38.0)	26.0 (12.0–40.0)	0.206
CRP (mg/dl)		9.5 (3.9–19.0)	12.0 (5.1–22.0)	0.052
Patient global assessment of disease activity (VAS: 0–100)		70.0 (60.0–80.0)	75.0 (58.0–85.0)	0.671
Physician global assessment of disease activity (0–100)		70.0 (52.0–80.0)	67.0 (50.0–80.0)	0.285
Physician global assessment of psoriasis (scale 0–5: no psoriasis – very severe)	0–1	39 (22.0%)	146 (25.3%)	0.458
	2–3	116 (65.5%)	348 (60.3%)	
	4–5	22 (12.4%)	83 (14.4%)	
Patient assessment of pain (VAS: 0–100)		70.0 (50.0–80.0)	70.0 (55.0–80.0)	0.482
HAQ		1.3 (1.0–1.8)	1.3 (0.9–1.8)	0.668
Nail involvement	No	68 (39.8%)	232 (40.8%)	0.920
	Mild	43 (25.1%)	146 (25.7%)	
	Medium	50 (29.2%)	164 (28.9%)	
	Severe	10 (5.8%)	26 (4.6%)	
Enthesitis		23 (13.0%)	67 (11.6%)	0.620
DAS28-ESR		5.3 (4.6–5.9)	5.4 (4.5–6.1)	0.380
DAPSA		35.0 (26.8–47.6)	36.0 (27.3–45.4)	0.900

3. Better Drug Retention on anti-IL17A Compared to Anti-TNF Therapy Despite Its Inferior Effect on Composite Joint Indexes and Quality of Life in Patients with PsA–analysis from the Czech Biologics Registry ATTR. Zavada J, et al (1439, Poster session)

RESULTADOS

Kaplan-Meier curves of drug survival on first-line treatment – anti-IL_17A vs TNFi



Number at risk:

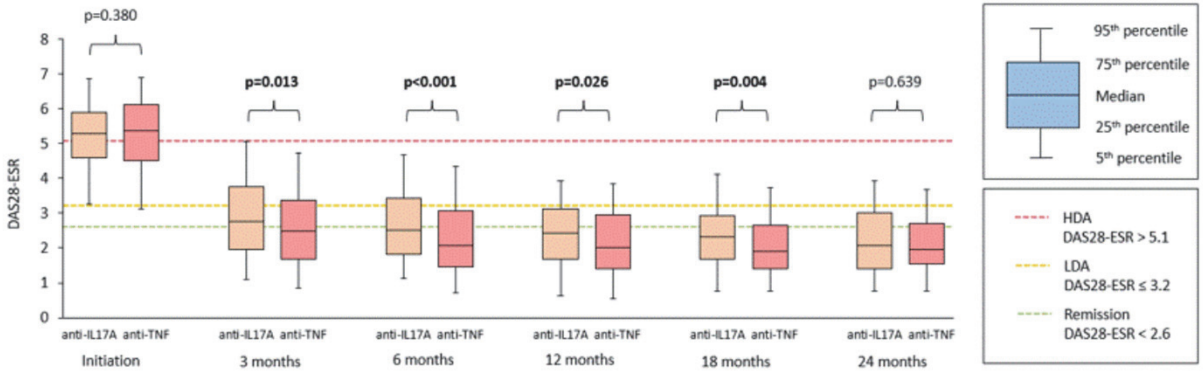
anti-IL-17A	177	154	93	64	36	15	0	0	0
TNFi	577	455	311	204	120	71	40	7	0

3. Better Drug Retention on anti-IL17A Compared to Anti-TNF Therapy Despite Its Inferior Effect on Composite Joint Indexes and Quality of Life in Patients with PsA–analysis from the Czech Biologics Registry ATTR. Zavada J, et al (1439, Poster session)

RESULTADOS

TNF-i

- < Fallo 1º (16% vs 32%)
- < valores DAS 28 y DAPSA
- > valores de EQ5D



IL17A-i

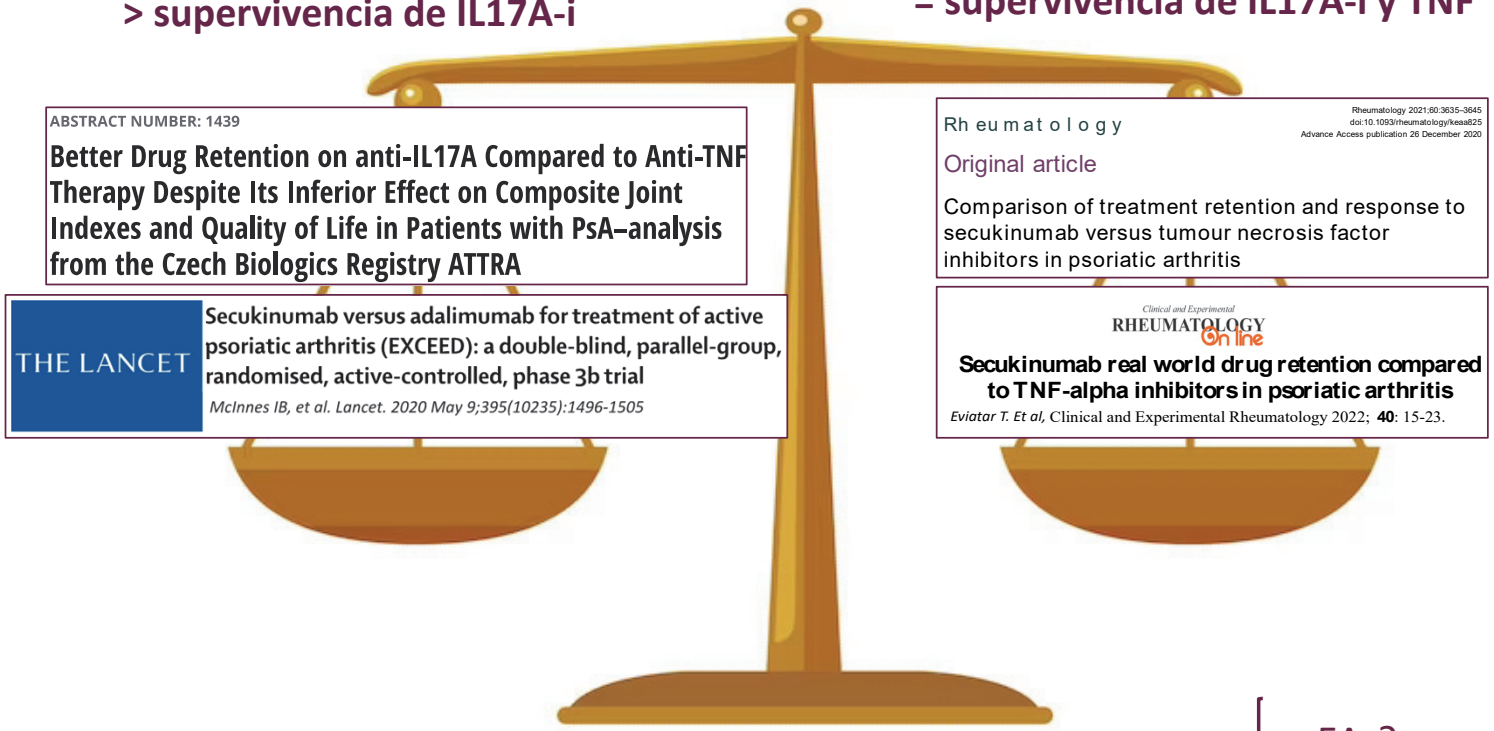
- < suspensión por EAs (9% vs 17%) o razones no especificadas (13% Vs 21%)
- > respuesta cutánea (PGApso en meses 3 y 12)
- < incidencias de EAs
  - Totales: 93 vs 168/1000 p-yrs, p< 0.001
  - Graves: 7 vs 18 /1000 p-yrs, p=0.079

3. Better Drug Retention on anti-IL17A Compared to Anti-TNF Therapy Despite Its Inferior Effect on Composite Joint Indexes and Quality of Life in Patients with PsA–analysis from the Czech Biologics Registry ATTR. Zavada J, et al (1439, Poster session)

CONCLUSIONES

> supervivencia de IL17A-i

= supervivencia de IL17A-i y TNF



- > retención de SECU Vs ADA a pesar de < respuesta en índices articulares y QoL
- Análisis supervivencia de ≈ 5 años, n elevada, emparejamiento de pacientes

< EAs?

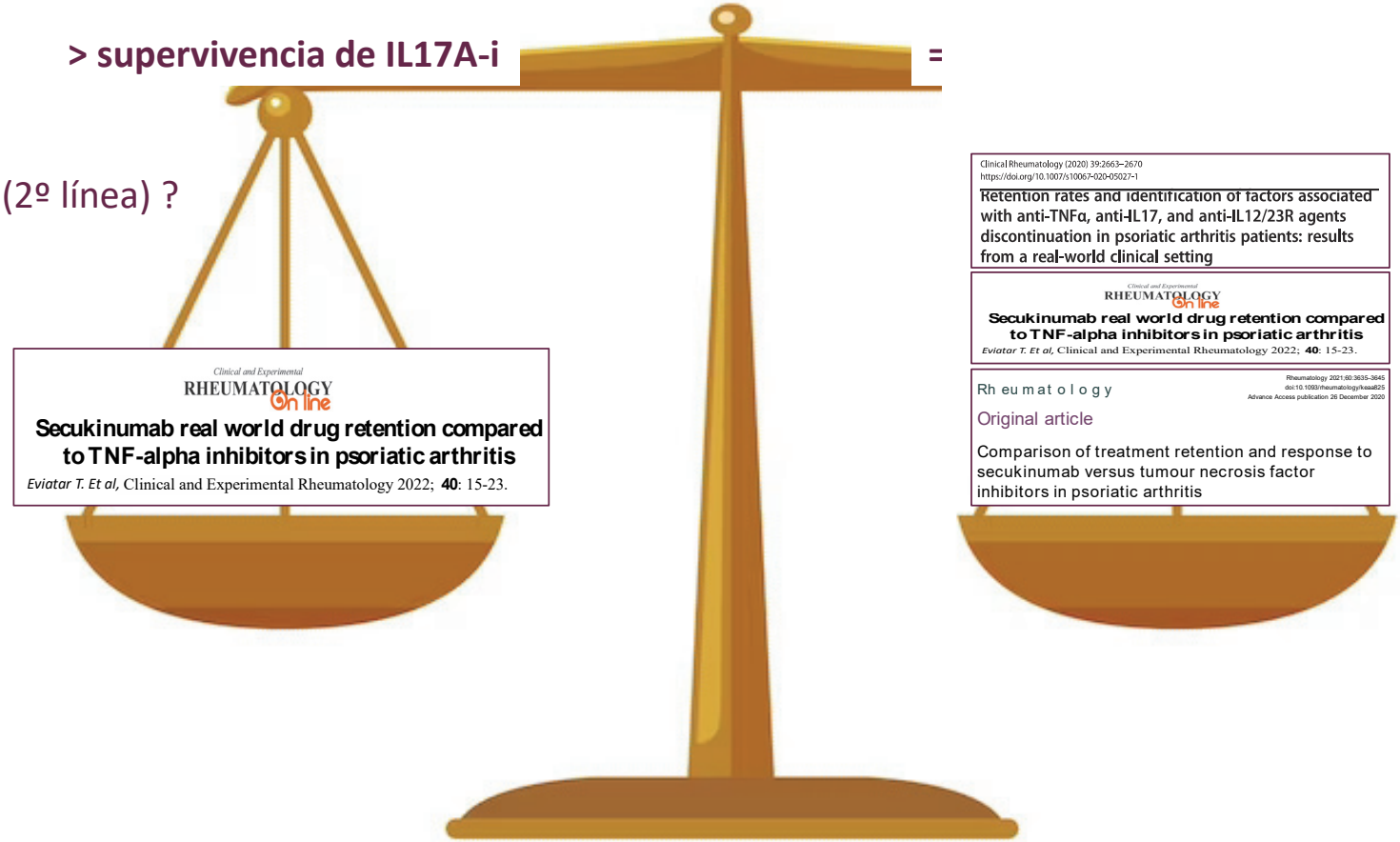
> Eficacia en PsO?

4. Persistence to Therapy Among Patients with Psoriatic Arthritis Treated with IL-17A or TNFα Inhibitors (IL-17Ai or TNFi). Vadhariya A, et al (2240, Poster session)

INTRODUCCIÓN

- IL17-i Vs TNF-i en APs (2º línea) ?

> supervivencia de IL17A-i **=**



- Análisis de eficacia, supervivencia del fármaco en APs que inician ADA o SECU en vida real

4. Persistence to Therapy Among Patients with Psoriatic Arthritis Treated with IL-17A or TNFα Inhibitors (IL-17Ai or TNFi). Vadhariya A, et al (2240, Poster session)

MÉTODOS

- Base de datos de seguros EEUU MArketScan → APs (2006-2021)
- Criterios de inclusión:
  - inicio de IL17A-i o TNF-i entre 2016-2021
  - ≥ 1año de seguimiento

RESULTADOS

	IL-17Ai N = 4,338		TNFi N = 7,753	
	N/Mean	%/SD	N/Mean	%/SD
Age (Mean, SD)	49.72	10.25	48.52	10.88
Age category (N, %)				
18-34	335	7.7%	910	11.7%
35-44	892	20.6%	1,659	21.4%
45-54	1,543	35.6%	2,664	34.4%
55-64	1,421	32.8%	2,247	29.0%
65+	147	3.4%	273	3.5%
Sex (N, %)				
Male	1,813	41.8%	3,410	44.0%
Female	2,525	58.2%	4,343	56.0%

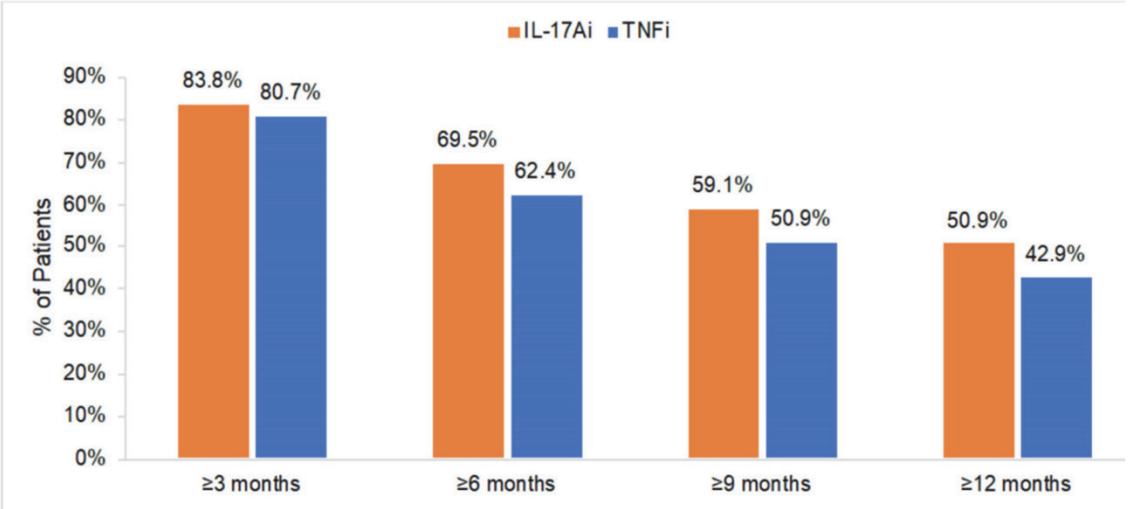
	IL-17Ai N = 4,338		TNFi N = 7,753	
	N/Mean	%/SD	N/Mean	%/SD
Charlson Comorbidity Index (Mean, SD)	0.7	1.2	0.5	1.0
Comorbidities and related conditions (N, %)				
Alcohol abuse	17	0.4%	43	0.6%
Anxiety	621	14.3%	1,039	13.4%
Depression	523	12.1%	886	11.4%
Dyslipidemia	1,063	24.5%	1,697	21.9%
Elevated transaminase	40	0.9%	104	1.3%
Cardiovascular diseases	303	7.0%	448	5.8%
Atherosclerosis	30	0.7%	34	0.4%
Peripheral arterial disease	93	2.1%	133	1.7%
Cerebrovascular disease	63	1.5%	109	1.4%
Coronary artery disease	168	3.9%	243	3.1%
Cirrhosis of the liver	27	0.6%	31	0.4%
Lymphoma	8	0.2%	4	0.1%
Metabolic syndrome	29	0.7%	55	0.7%
NAFL/NASH	100	2.3%	183	2.4%
Obesity[1]	1,082	24.9%	1,745	22.5%
Osteoarthritis	938	21.6%	1,718	22.2%
Osteoporosis	78	1.8%	104	1.3%
Psoriasis	3,041	70.1%	4,587	59.2%
Skin cancer	42	1.0%	67	0.9%
Type 2 diabetes	639	14.7%	924	11.9%
Pre-Index Medication Use (N, %)				
Biologic utilization	2,681	61.8%	2,248	29.0%
cDMARD utilization	1,114	37.6%	2,350	43.3%

4. Persistence to Therapy Among Patients with Psoriatic Arthritis Treated with IL-17A or TNFα Inhibitors (IL-17Ai or TNFi). Vadhariya A, et al (2240, Poster session)

RESULTADOS

	IL-17i	TNF-i
Persistencia de tratamiento (días), media±SD	261±126	243±127

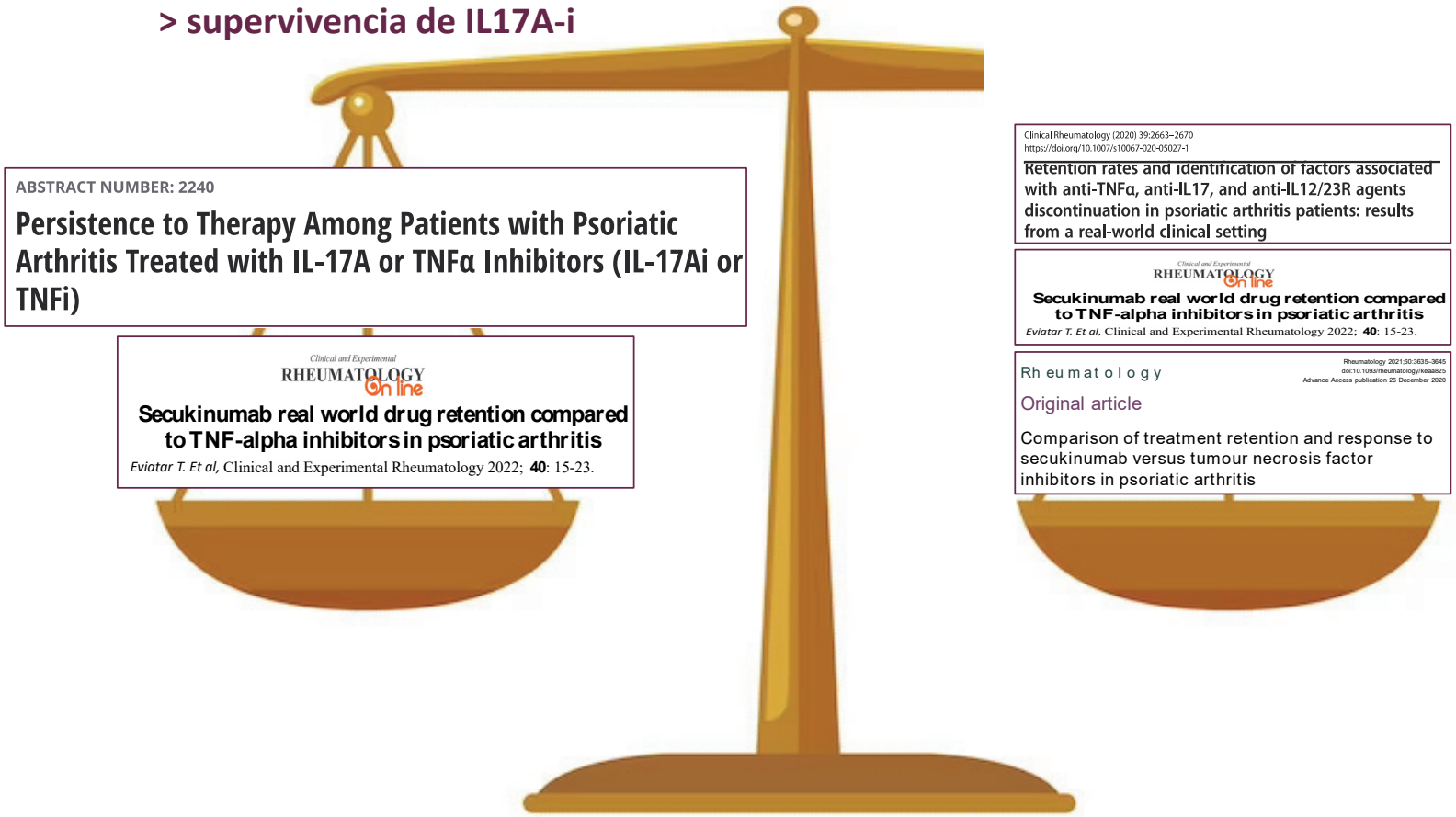
Figure 2. Persistence to Index Biologic Over the 12-Month Post-period



4. Persistence to Therapy Among Patients with Psoriatic Arthritis Treated with IL-17A or TNFα Inhibitors (IL-17Ai or TNFi). Vadhariya A, et al (2240, Poster session)

CONCLUSIÓN

> supervivencia de IL17A-i



- > supervivencia a pesar de ser pacientes más refractarios

APs

EFICACIA FARMACOLÓGICA Y ESTRATEGIAS TERAPEUTICAS

- Comparaciones entre fármacos (ECAs H2H y en vida real)
- Eficacia sobre manifestaciones extraarticulares
- Factores predictores de respuesta
- Swtiching Vs Cycling
- Tratamiento combinado
- Optimización

SEGURIDAD

- Seguridad a largo plazo (LTE)
- Seguridad cardiovascular

NOVEDADES TERAPÉUTICAS

- Fármacos en desarrollo clínico
- Fármacos con aprobación pero no comercializados
- Nuevas vías de administración de fármacos en uso

5. Primary Non-response in Psoriatic Arthritis Treated with Biologics and Targeted Synthetic Therapies in Daily Clinical Practice. Abasolo I, et al (2248, Poster session)

INTRODUCCIÓN

- Fallo a TNF: switching o cycling?

Annals of the Rheumatic Diseases
Recommendation
OPEN ACCESS

EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update

Gossec L, et al. Ann Rheum Dis. 2020 Jun;79(6):700-712.

Recommendation 11: In patients who fail to respond adequately to, or are intolerant of a bDMARD, switching to another bDMARD or tsDMARD should be considered, including one switch within a class.

the SLR.[88] Trials performed in TNFi insufficient responders have demonstrated efficacy of bDMARDs with another mode of action when TNFi has failed.[56] However, another TNFi can also be used, since no head-to-head trial data are available that suggest switching between classes is different from switching within class. Finally, the taskforce agreed that while switching within class was a viable option, it would be logical to change class after a second failure within a given class (expert opinion). Studies addressing the best possible strategy after failure(s) of bDMARDs other than TNFi are lacking to date, and this topic was added to the research agenda.

Arthritis & Rheumatology
Vol. 71, No. 1, January 2019, pp 5–32
DOI 10.1002/art.40726

American College of Rheumatology
EDUCATION • TREATMENT • RESEARCH

SPECIAL ARTICLE

2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis

Active PsA despite treatment with a TNFi biologic agent as monotherapy or in combination therapy (Table 3 and Figure 5). *All recommendations for patients with*

Figure 5). An IL-12/23i biologic, IL-17i biologic, abatacept, or tofacitinib may be used instead of a different TNFi biologic monotherapy in the case of a primary TNFi biologic failure or a serious adverse event due to the TNFi biologic. An IL-17i

5. Primary Non-response in Psoriatic Arthritis Treated with Biologics and Targeted Synthetic Therapies in Daily Clinical Practice. Abasolo I, et al (2248, Poster session)

MÉTODOS

- Estudio monocéntrico, longitudinal, retrospectivo.

Pacientes APs (CASPAR) tratados con TB/JAK-i desde 2016-2022

↓

Pacientes que habían requerido cambio de tratamiento por fallo 1º → tasa de incidencia de fallos 1º

↓

Pacientes con fallo terapéutico posterior → Análisis de factores asociados fallo terapéutico (switching Vs cycling)

5. Primary Non-response in Psoriatic Arthritis Treated with Biologics and Targeted Synthetic Therapies in Daily Clinical Practice. Abasolo I, et al (2248, Poster session)

RESULTADOS

- n=146 APS, seguimiento máximo de 16 años

Table 1: Incidence rate of switching due to primary non-response rate by covariables.

	Patients/year	N	IR	95%CI
Total	893.62	48	5.37	4.05-7.12
By gender				
Female	432.75	40	9.24	6.78-42.605
Male	460.87	8	1.73	0.86-3.47
By age at first ts/bDMARD, years				
< 40	228.12	9	3.94	2.05-7.58
40-50	262.77	12	4.56	2.59-8.04
50-60	222.56	13	5.84	3.39-10.06
60-70	129.68	12	9.25	5.25-16.29
>70	50.49	2	3.96	0.99-15.83
By year of ts/bDMARD start				
2007-2012	478.24	12	2.51	1.42-4.41
2013-2017	206.21	4	1.93	0.73-5.16
2018-2022	209.17	32	15.30	10.82-21.63
By bDMARDs				
TNF-alpha	793.69	31	3.90	2.74-5.55
IL-17	69.67	11	15.78	8.74-28.51
IL-23	10.28	4	38.87	14.59-103.58
JAKi	14.05	1	7.11	1.0-50.49
Abatacept	5.93	1	16.94	2.38-120.28

Tasa de incidencia de fallo 1º inicial: 5.37

- Mujeres
- Anti IL-17/23/ABA

5. Primary Non-response in Psoriatic Arthritis Treated with Biologics and Targeted Synthetic Therapies in Daily Clinical Practice. Abasolo I, et al (2248, Poster session)

RESULTADOS

Table 2: In those with primary non-response, incidence rate of subsequent failure by covariables

	Patients/year	N	IR	95%CI
Total	117.69	26	22.09	15.04-32.44
By gender				
Female	87.75	22	25.07	16.50-38.07
Male	29.94	4	13.36	5.01-35.58
By age at first ts/bDMARD, years				
< 40	10.13	4	39.49	14.82-105.21
40-50	44.84	10	22.30	11.99-41.44
50-60	11.34	5	44.07	18.34-105.87
60-70	27.51	6	21.80	9.79-48.54
>70	23.87	1	4.19	0.59-29.74
By year of ts/bDMARD start				
2007-2012	56.57	7	12.37	5.89-25.95
2013-2017	31.24	4	12.80	4.80-34.11
2018-2022	29.88	15	50.19	30.26-83.27
By bDMARDs switching				
Within class	73.71	14	18.99	11.25-32.06
Between class	43.98	12	27.28	15.49-48.04

- Tasa de fallo posterior: 22.09
  - Mujeres

Asociación de cycling-fallo terapéutico en pacientes con fallo 1º previo: HR:3.26 [1.23-8.62], p=0.017

5. Primary Non-response in Psoriatic Arthritis Treated with Biologics and Targeted Synthetic Therapies in Daily Clinical Practice. Abasolo I, et al (2248, Poster session)

INTRODUCCIÓN

Annals of the Rheumatic Diseases

Recommendation

OPEN ACCESS

EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update

Gossec L, et al. Ann Rheum Dis. 2020 Jun;79(6):700-712.

Recommendation 11: In patients who fail to respond adequately to, or are intolerant of a bDMARD, switching to another bDMARD or tsDMARD should be considered, including one switch within a class.

the SLR.[88] Trials performed in TNFi insufficient responders have demonstrated efficacy of bDMARDs with another mode of action when TNFi has failed.[56] However, another TNFi can also be used, since no head-to-head trial data are available that suggest switching between classes is different from switching within class. Finally, the taskforce agreed that while switching within class was a viable option, it would be logical to change class after a second failure within a given class (expert opinion). Studies addressing the best possible strategy after failure(s) of bDMARDs other than TNFi are lacking to date, and this topic was added to the research agenda.

Arthritis & Rheumatology
Vol. 71, No. 1, January 2019, pp 5–32
DOI 10.1002/art.40726

American College of Rheumatology
EDUCATION • TREATMENT • RESEARCH

SPECIAL ARTICLE

2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis

Active PsA despite treatment with a TNFi biologic agent as monotherapy or in combination therapy (Table 3 and Figure 5). *All recommendations for patients with*

Figure 5). An IL-12/23i biologic, IL-17i biologic, abatacept, or tofacitinib may be used instead of a different TNFi biologic monotherapy in the case of a primary TNFi biologic failure or a serious adverse event due to the TNFi biologic. An IL-17i

10 al 14 de
noviembre
2024
Ciudad San Diego
(USA)

Sociedad Española de Reumatología

ACRreview 23

#ACReview23

AstraZeneca