
Article:
Dubash, S, Bridgewood, C, McGonagle, D et al. (1 more author) (2019) The advent of IL-17A blockade in ankylosing spondylitis: secukinumab, ixekizumab and beyond. Expert Review of Clinical Immunology, 15 (2). pp. 123-134. ISSN 1744-666X

https://doi.org/10.1080/1744666x.2019.1561281

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re 1.

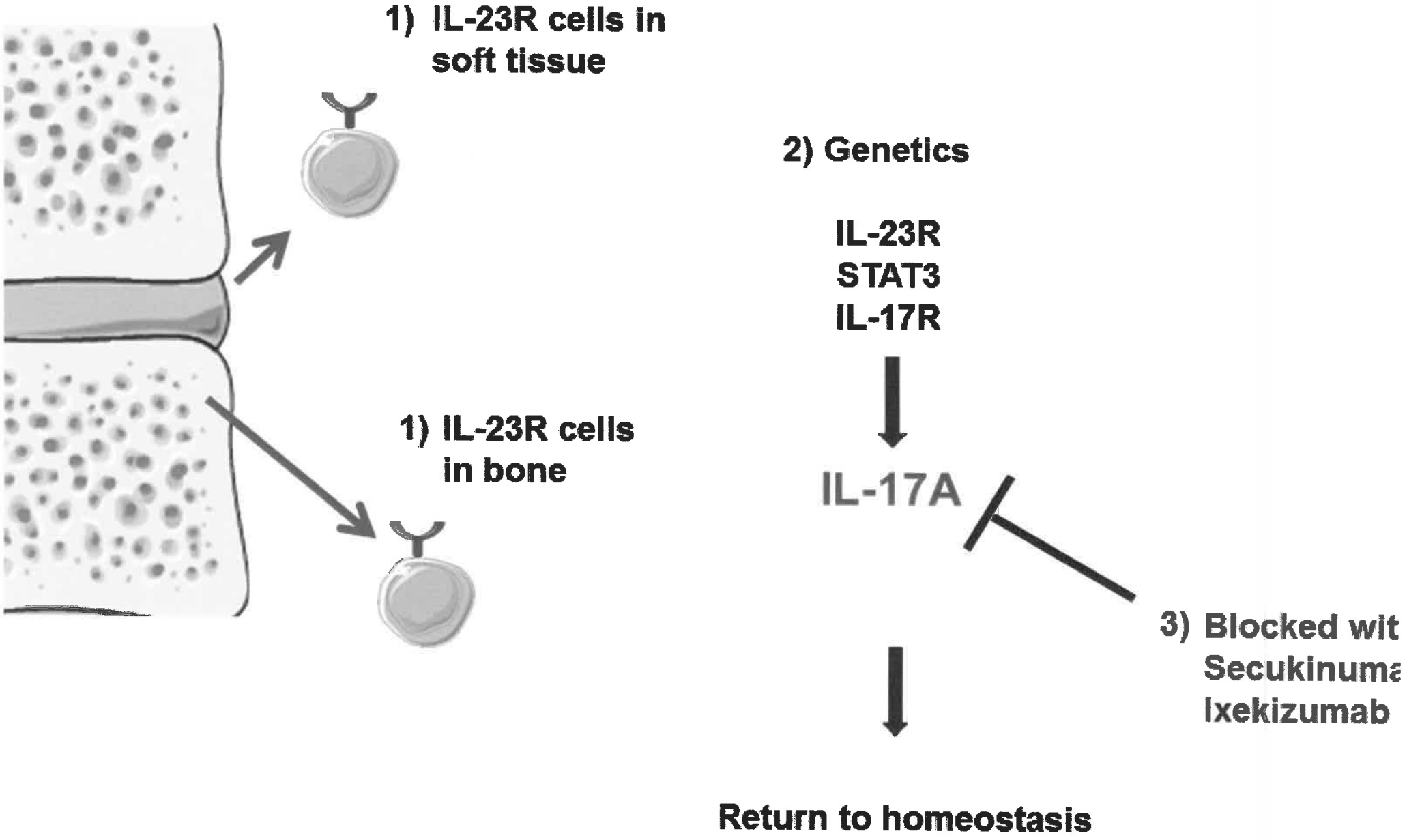
1) IL-23R cells in soft tissue
1) IL-23R cells in bone
2) Genetics
IL-23R
STAT3
IL-17R
IL-17A
3) Blocked wit
Secukinuma
Ixekizumab
Return to homeostasis

Figure 2.

Assessment of SpondyloArthritis international Society (ASAS) response criteria for clinical trials

ASAS response criteria definition
• The ASAS Response Criteria (ASAS 20) is defined as an improvement of at least 20% from baseline and an absolute improvement of at least 10 units on a 0-100 scale in at least three out of four of the following domains, and no worsening of >10 in the remaining one of four domains: 1. Patient global assessment, 2. Spinal pain score, 3. Physical function (BASFI), 4. Inflammation/ morning stiffness (last 2 questions of BASDAI).
• The ASAS Response Criteria (ASAS 40) is defined as an improvement of at least 40% from baseline and an absolute improvement of at least 20 units on a 0-100 scale in at least three out of four of the following domains, and no worsening in the remaining domain (listed above).
• ASAS partial remission is defined by a score of <20 in each of the four ASAS domains (above).

Figure 3.

Summary of MEASURE 1-3 trials and clinical improvement of patients seen in all groups 300mg, 150mg, and Placebo (PBO).

	MEASURE 1[7]	MEASURE 2[7,50]	MEASURE 3[51]
Total number of subjects	371	219	226
Induction regimen	i.v, 10mg/kg, weeks 0,2,4	s/c, 150mg or 75mg at weeks 0,1,2,3,4 then every 4 weeks	i.v, 10mg/kg, weeks 0,2,4
Maintenance Regimen	150mg or 75mg or matched PBO, s/c injection every 4 weeks	150mg or 75mg or matched PBO, s/c injection every 4 weeks	300mg or 150mg or matched PBO, s/c injection every 4 weeks
Achieved primary outcome: ASAS20 at 16 weeks	60% (150mg)* 61% (75mg)* 29% (PBO)	61% (150mg)* 41% (75mg) 28% (PBO)	60.5%(300mg)* 58.1% (150mg)** 36.8% (PBO)
Secondary outcomes: ASAS40 at 16 weeks	42% (150mg)* 33% (75mg)* 13% (PBO)	36% (150mg)* 26% (75mg) 11% (PBO)	42.1% (300mg)** 40.5% (150mg)** 21.1% (PBO)
ASAS partial remission	15% (150mg)* 16% (75mg)* 3% (PBO)	14% (150mg)* 15% (75mg)* 4% (PBO)	21.1% (300mg)** 9.5% (150mg) 1.3% (PBO)

Legend: i.v: intravenous, s/c: subcutaneous, PBO: placebo, *P<0.01, ** P<0.05

Figure 4.

Subgroup analyses for secukinumab and placebo with 2 years of follow up (MEASURE 2)[50]

	Anti-TNF naïve			**TNFi-IR**		
Dose	150mg	75mg	PBO	150mg	75mg	PBO
16 weeks	68.2%*	51.1%	31.1%	50%**	25%	24%
52 weeks	82.1%	71.4%		59.1%	47.4%	
104 weeks	76.9%	80%		85.0%	68.8%	

Legend: TNF-IR: TNF inadequate responders, PBO: placebo, *P<0.01, ** P<0.05.

P values are versus placebo at 16 weeks and demonstrate statistical significance. Missing data were imputed as non-responses at week 16 (non-responders imputation). Observed data are shown at weeks 52 and 104.

Figure 5.

Ixekizumab (COAST-V, COAST-W) and secukinumab (MEASURE 1) ASAS20 and ASAS40 data summary from clinical trials.

	COAST-V (TNFi naïve)[13]	COAST-W (TNFi-IR)[82]	MEASURE 1[7] (74% were TNF naïve, see legend below)***
Total number of subjects	341	316	371
Drug regimen (weeks 0-16)	80mg Q2W or Q4W	Loading dose at week 0 of either 80mg or 160mg respectively then 80mg Q2W or Q4W thereafter.	10mg/kg i.v. at weeks 0, 2, 4, then 150mg or 75mg s/c injection Q4W starting at week 8.
ASAS40 at 16 weeks	52% (IXE 80mg Q2W) † 48% (IXE 80mg Q4W) † 36% (ADA 40mg Q2W) 18% (PBO)	30.6% (IXE 80mg Q2W) ‡ 25.4% (IXE 80mg Q4W) ‡ 12.5% (PBO)	42% (150mg) *** 33% (75mg) *** 13% (PBO)
ASAS20 at 16 weeks	69% (IXE 80mg Q2W)* 64% (IXE 80mg Q4W)* 59% (ADA 40mg Q2W) 40% (PBO)	46.9% (IXE 80mg Q2W)** 48.2% (IXE 80mg Q4W)** 29.8% (PBO)	60% (150mg) *** 61% (75mg) *** 29% (PBO)

Legend: TNF-IR: TNFi inadequate responders, IXE: ixekizumab, i.v: intravenous route, s/c: subcutaneous route, PBO: placebo, ADA: adalimumab, SEC: secukinumab, Q2W: every 2 weeks, Q4W: every 4 weeks, †P<0.0001(Q2W and Q4W), ‡P=0.003 (Q2W), P=0.017 (Q4W), *P= 0.002 (Q2W), *P=0.0015 (Q4W), ** P<0.05 (Q2W), P<0.01 (Q4W), ***P<0.01. P values are versus placebo and demonstrate statistical significance. (MEASURE1 is taken from figure 3. Direct comparison with COAST trials is not possible due to different primary endpoints and mixed TNFi naïve and TNFi-IR in MEASURE1 study.)