

Factors Guiding Optimal Management Approaches in Rheumatic Diseases

Developed by the
Coalition of Rheumatology Educators (CORE™)





Learning Objectives

- Discuss practical approaches for application of clinical measurement tools to monitor tight control of RA
- Institute individualized treatment strategies in patients with RA to achieve LDA or remission
- Incorporate strategies for biologic switching following an inadequate response to RA therapy
- Evaluate early and preclinical assessment of SpA
- Assess efficacy data of biologic therapy in SpA



Audience Response

If RA is present for 3 to 6 months in a patient who has an inadequate response to MTX monotherapy, then a TNF inhibitor should be initiated.

1. Strongly agree
2. Agree
3. Somewhat agree
4. Somewhat disagree
5. Disagree
6. Strongly disagree



Audience Response

In patients who fail to respond to a TNF inhibitor and are switched to a second TNF inhibitor, the reasons for failing the first agent may impact the likelihood of successful response to the second agent.

1. Strongly agree
2. Agree
3. Somewhat agree
4. Somewhat disagree
5. Disagree
6. Strongly disagree



Audience Response

How confident are you that objective clinical measurements accurately reflect disease activity in your patients with RA?

1. Very confident
2. Confident
3. Somewhat confident
4. Not confident
5. Unsure

Current Management Strategies for New RA

- Early diagnosis
 - Get the message to PCPs
- Early aggressive management
 - DMARD therapy for all patients
 - MTX remains appropriate first option
- Measure activity, then treat to a goal

Clinical Measurement of Disease Activity in RA

Instruments Used to Measure RA Disease Activity

Instrument	Score Range	Thresholds of Disease Activity			
		Remission	Low	Moderate	High
DAS in 28 Joints	0-9.4	≤ 2.6	> 2.6 and ≤ 3.2	> 3.2 and ≤ 5.1	> 5.1
SDAI	0.1-86	≤ 3.3	> 3.3 and ≤ 11	> 11 and ≤ 26	> 26
CDAI	0-76	≤ 2.8	> 2.8 and ≤ 10	> 10 and ≤ 22	> 22
RADAI	0-10	≤ 1.4	> 1.4 and < 2.2	≥ 2.2 and ≤ 4.9	$> 4.9^*$
PAS or PASII	0-10	≤ 0.5	> 0.5 and < 1.9	≥ 1.9 and ≤ 5.3	> 5.3
RAPID	0-30	≤ 1	> 1 and < 6	≥ 6 and ≤ 12	> 12

*Median.

DAS = Disease Activity Score 28-defined remission; SDAI = Simplified Disease Activity Index; CDAI = Clinical Disease Activity Index; RADAI = Rheumatoid Arthritis Disease Activity Index; PAS = Patient Activity Scale; RAPID = Routine Assessment Patient Index Data.

Saag KG, et al. *Arthritis Rheum.* 2008;59(6):762-784. Mierau M, et al. *Rheumatology (Oxford).* 2007;46(6):975-979. Rintelen B, et al. *Rheumatol.* 2009;36(5):918-924.

Wolfe F, et al. *Arthritis Rheum.* 2007;57(6):935-942. Pincus T, et al. *Rheumatol.* 2008;35(11):2136-2147.

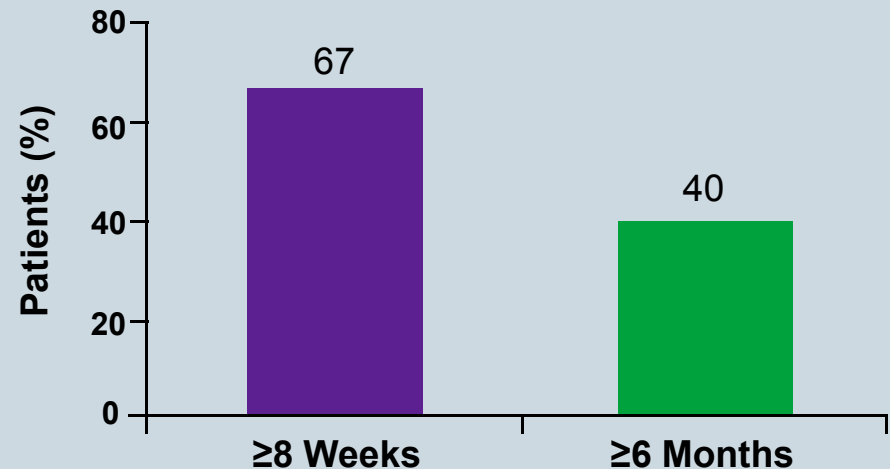
DREAM Registry: Reaching and Maintaining Remission

- 330 patients from DREAM registry with early RA (≤ 1 year)
- Examined ability to maintain remission (from January 2006 and October 2008)
- Tight control and step-up treatment strategy
 - Stable remission defined as DAS28 < 2.6
- **Conclusion:**
 - Stable remission achieved in almost 90% of patients on traditional DMARDs
 - Remission was maintained in patients with RA using tight control and treatment through protocol

Treatment Protocol Based on Response

Week 1	→	MTX 15 mg/week
Week 8	→	MTX 25 mg/week
Week 12	→	MTX 25 mg/week + SSZ 2 g/day
Week 20	→	MTX 25 mg/week + SSZ 3 g/day
Week 24	→	MTX 25 mg/week + ADA 40 mg/2 weeks
Week 36	→	MTX 25 mg/week + ADA 40 mg/week

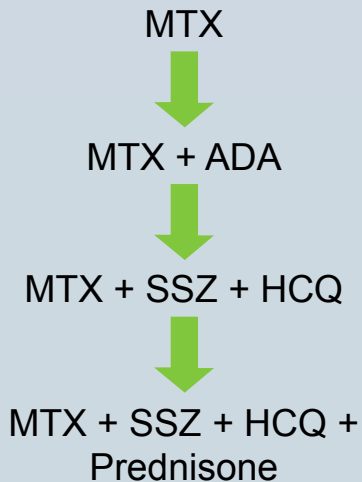
Patients Achieving and Maintaining Remission



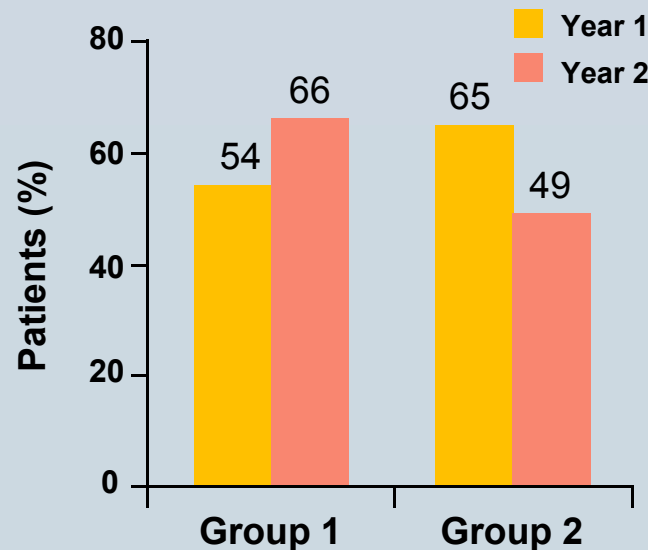
STREAM Study: Aggressive Treatment Prevents Joint Damage and Increases Remission in Early RA

- DAS-driven therapy vs physician judgment-directed therapy in patients with early RA (N=82)
- Group 1: step-up therapy adjusted to DAS ≤ 1.6
- Group 2: traditional DMARDs adjusted by physician judgment

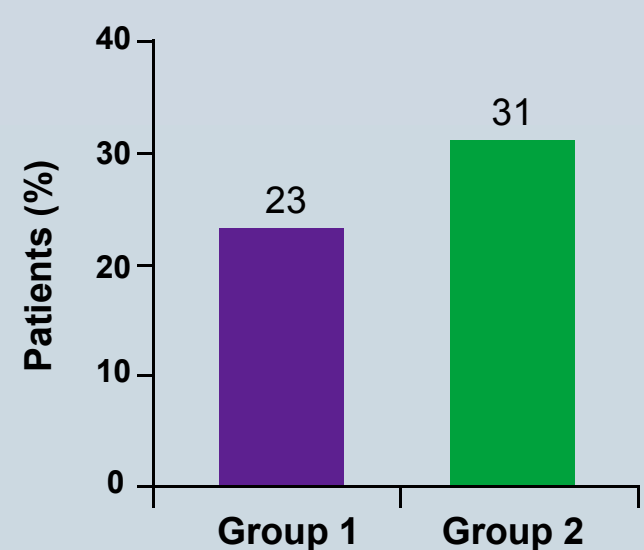
Step-up Therapy Treatment Protocol



Patients Reaching Remission*



Development of Erosions at Year 2*



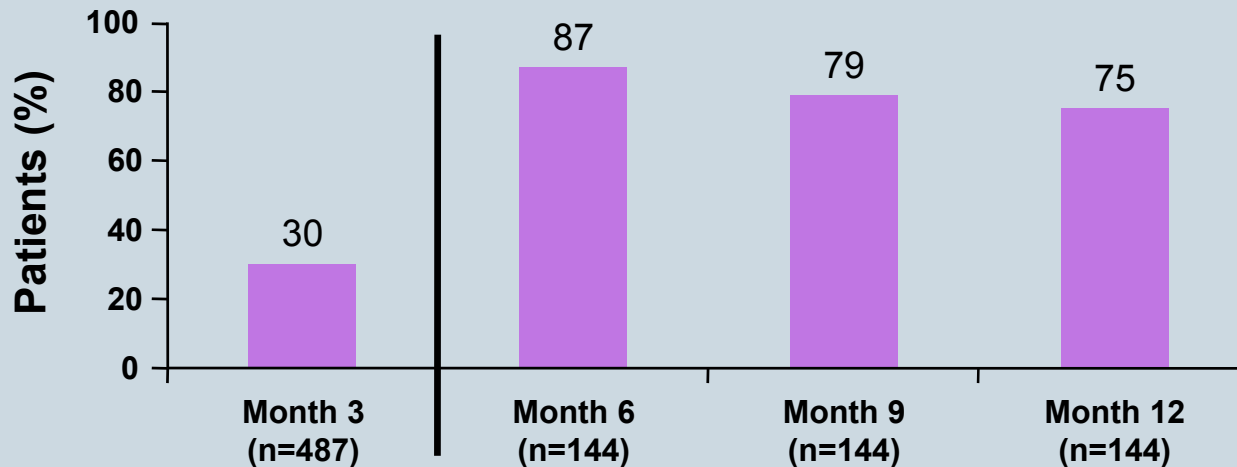
Conclusion:

- Fewer erosions and higher number of patients in remission for step-up therapy group
- Full disease control, including arrest of radiographic damage, not possible in all patients

SWEFOT Subanalysis: Effectiveness of MTX Monotherapy in Reaching LDA

- SWEFOT study
 - 487 patients with early RA (<1 year) started MTX monotherapy (rapid increases up to at least 20 mg/week)
- SWEFOT subanalysis
 - 144 patients continued on MTX monotherapy with LDA measure by DAS28 <3.2 after 3-4 months
 - Examined clinical course of therapy

Patients on MTX Monotherapy with DAS28 <3.2



- **Conclusion: a high proportion of patients continued on MTX monotherapy exhibited an LDA as measured by a DAS28 <3.2**

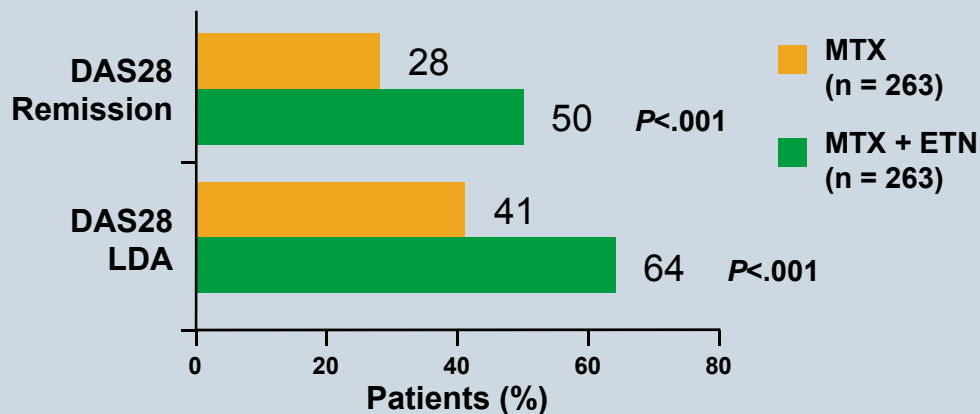
COMET Study: Reaching Remission with MTX or MTX + ETN

- 542 MTX-naïve outpatients with early moderate-to-severe RA
- Assessed DAS28 remission and amount of patients achieving radiographic nonprogression over 52 weeks
- Patients treated with either MTX monotherapy or MTX + ETN combination therapy

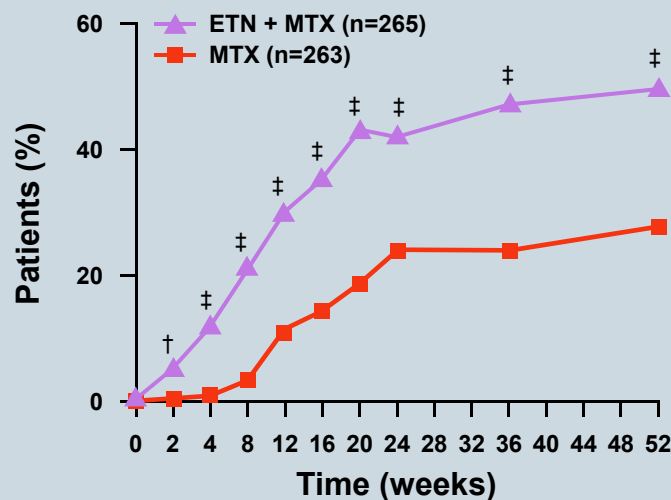
• Conclusions:

- MTX + ETN therapy: substantial number of patients achieved remission (50%) or LDA (64%)
- MTX therapy: high number of patients achieved remission (28%) or LDA (41%)
- Maximum response to MTX achieved by 6 months

DAS28 Remission and LDA



DAS28 Remission Over Time



What Agent to Add to MTX Monotherapy?

- Additional DMARDs
- TNF inhibitors: Any particular order?
- ABA
- RTX

Recommendations for the Use of Biologic Therapy in RA

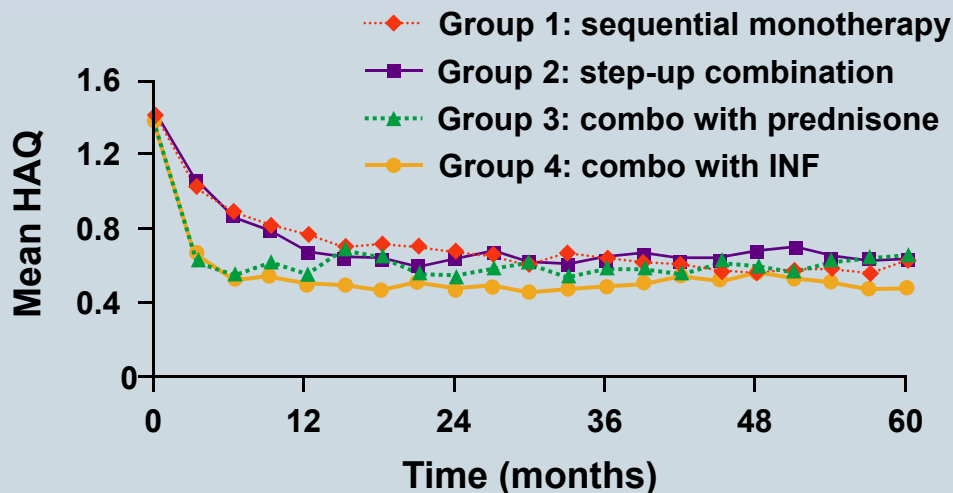
- If RA is present for ≥ 6 months in a patient who has an inadequate response to MTX monotherapy with high disease activity, then a TNF inhibitor should be initiated
- If RA is present for ≥ 6 months in a patient who has an inadequate response to MTX combination with other DMARDs, then either a TNF inhibitor, or ABA, or RTX can be initiated
- ADA and ETN are both FDA approved as first agent for RA
 - INF is sometimes used as a first agent in RA (not FDA approved)

BeSt Study

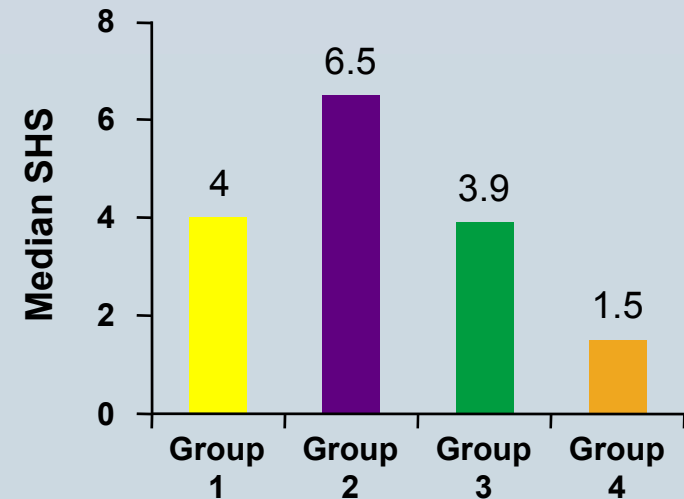
Effect of Disease-modifying Therapy on Functional Outcomes

- 5-year study of 508 patients with early RA
 - Randomized to receive sequential monotherapy (group 1), step-up combination therapy (group 2), initial combination with prednisone (group 3), or initial combination with INF (group 4)
- Primary end points were functional ability measured by HAQ score and joint damage progression measured by SHS

Mean HAQ at Year 5



Median SHS at Year 5

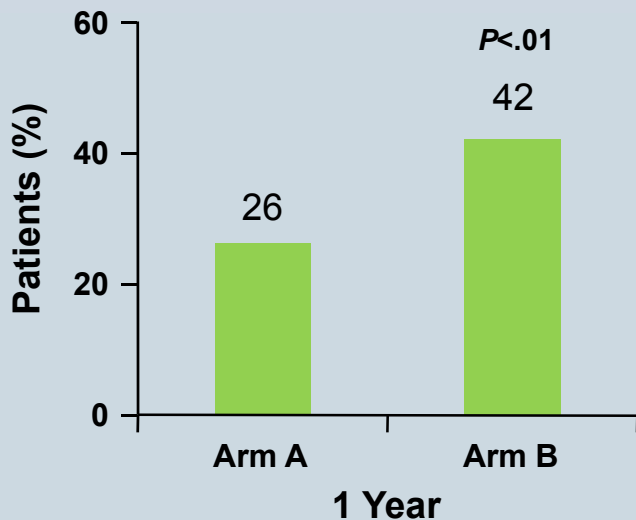


- **Conclusion: early combination therapy with INF sustained functional improvement and reduced progression of joint damage**

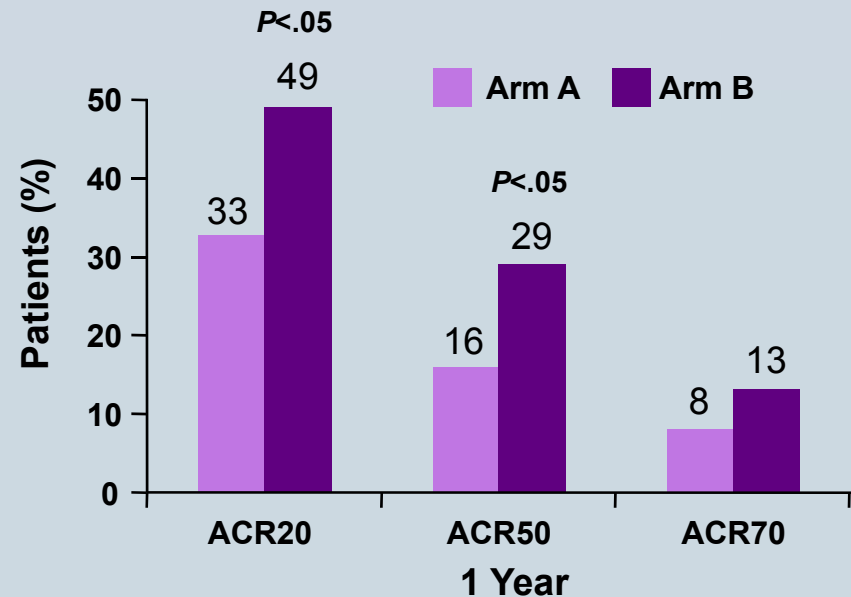
SWEFOT Study: Addition of INF to MTX Monotherapy

- Open, randomized, controlled study of 258 patients with inadequate response to MTX monotherapy
- Examined efficacy of INF in patients with early RA
- Patients separated into arm A (SSZ and HCQ added to MTX) and arm B (INF added to MTX)

Achieving EULAR Good Response



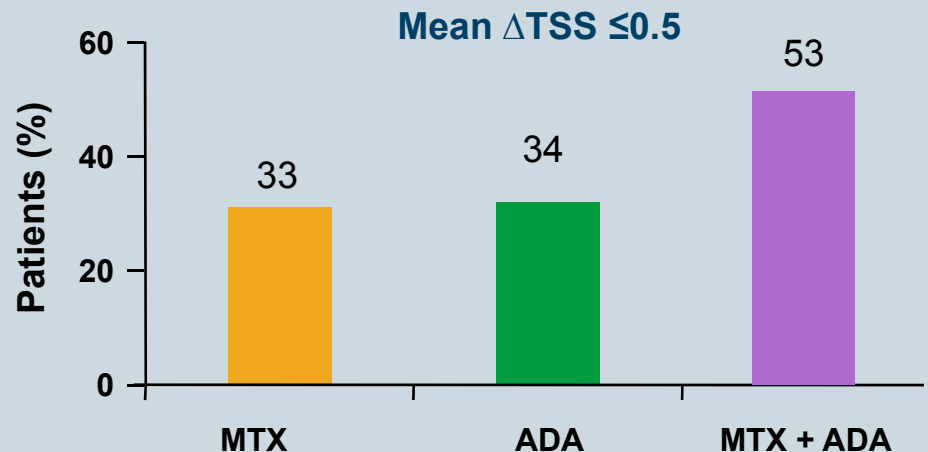
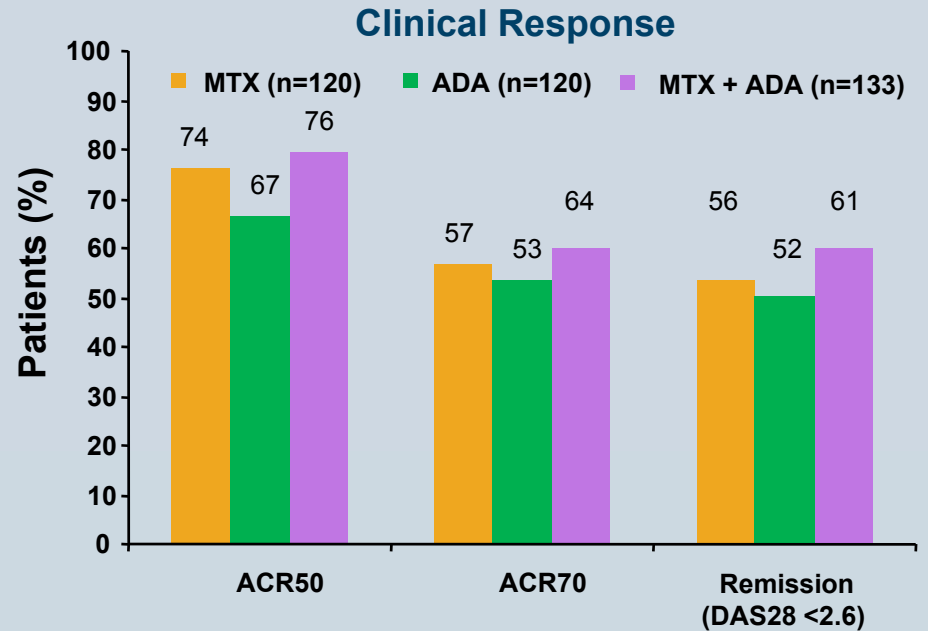
ACR Response



- **Conclusion: significantly greater EULAR, ACR20, and ACR50 responses in MTX + INF group compared to SSZ + HCQ group**

PREMIER Study Year 5: ADA + MTX Therapy in Early RA

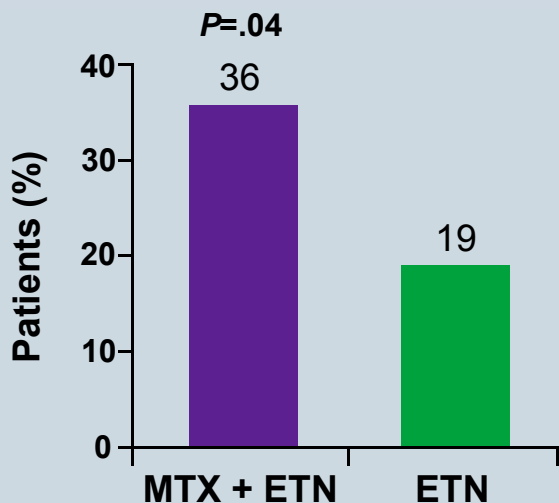
- 3-year OLE of a previous 2-year, multicenter, double-blind, comparator-controlled study
- Assessed clinical improvement through ACR response criteria and evaluated radiographic progression
- Patients treated with either MTX monotherapy, ADA monotherapy, or MTX + ADA combination therapy
- **Conclusion: initial combination therapy with MTX + ADA led to better ACR responses and less radiographic progression in this patient population**



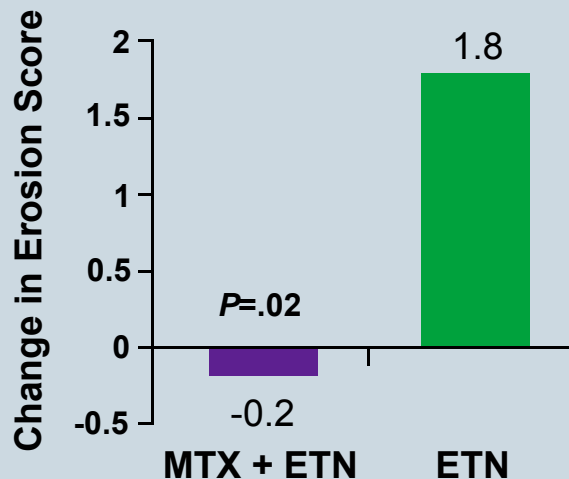
JESMR Study: Should MTX be Continued after Addition of ETN?

- Assessed efficacy and safety of either continuing or discontinuing MTX therapy at the initiation of ETN therapy in patients with RA who were treated with MTX for 2 years
- 151 patients randomized to continue MTX (6-8 mg/week) + ETN or ETN monotherapy
- Primary end point included radiographic progression at week 52
- Significantly higher rates of EULAR good response in patients treated with ETN + MTX compared to ETN monotherapy at week 52 (52.1% and 33.3%, respectively; $P < .0001$)

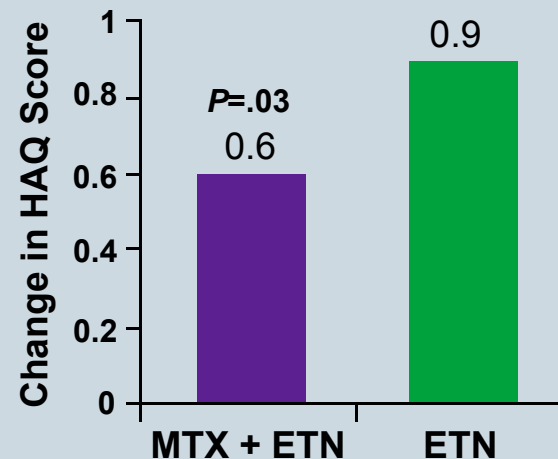
Patients in DAS Remission



Erosion Score



Mean Change HAQ Score

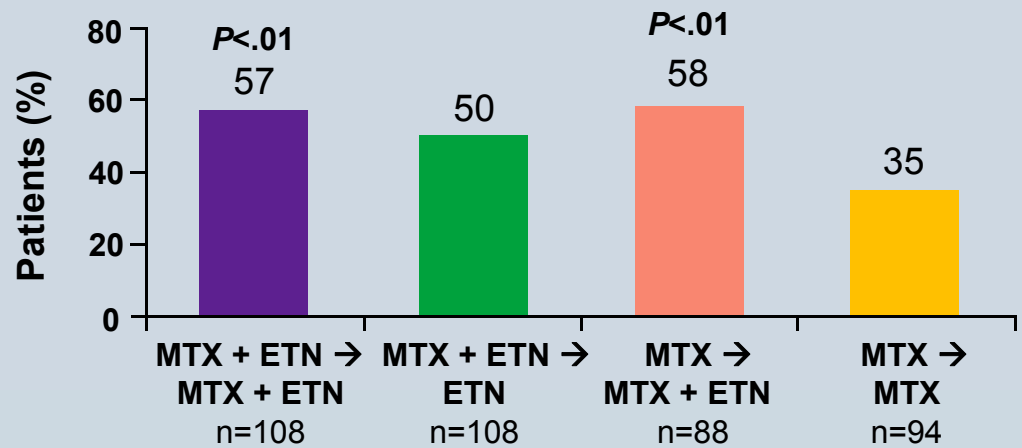


- **Conclusion: patients who continued MTX with ETN therapy did better based on significantly lower erosion and HAQ scores**

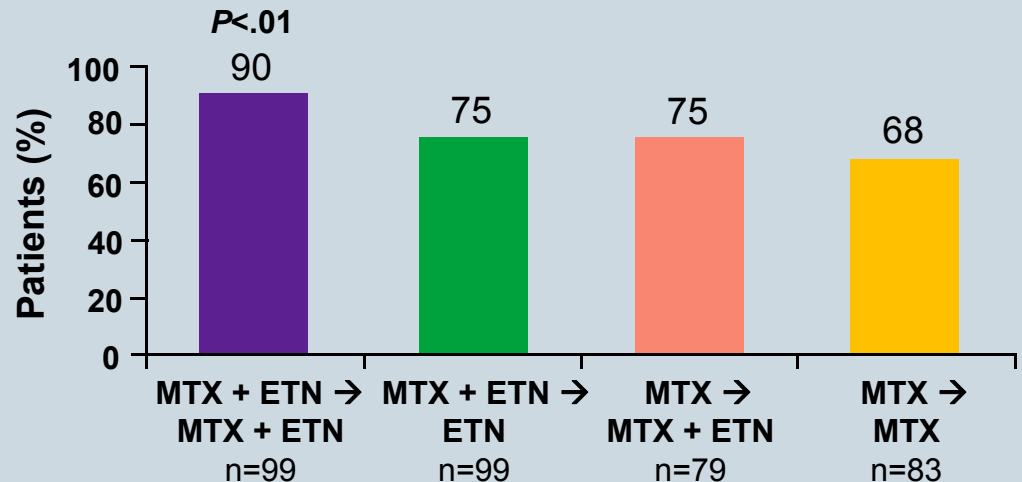
COMET Study: Reaching Clinical Remission and Radiographic Nonprogression at Year 2

- Following 1-year period:
 - MTX + ETN group continued or received ETN monotherapy
 - MTX group continued or received MTX + ETN combination therapy
- End points included clinical remission of DAS28 <2.6 and radiographic nonprogression of change in mTSS ≤ 0.5 at year 2
- **Conclusion: sustained combination of MTX + ETN through year 2 resulted in significantly higher rates of clinical remission and had less radiographic progression**

Clinical Remission at Year 2



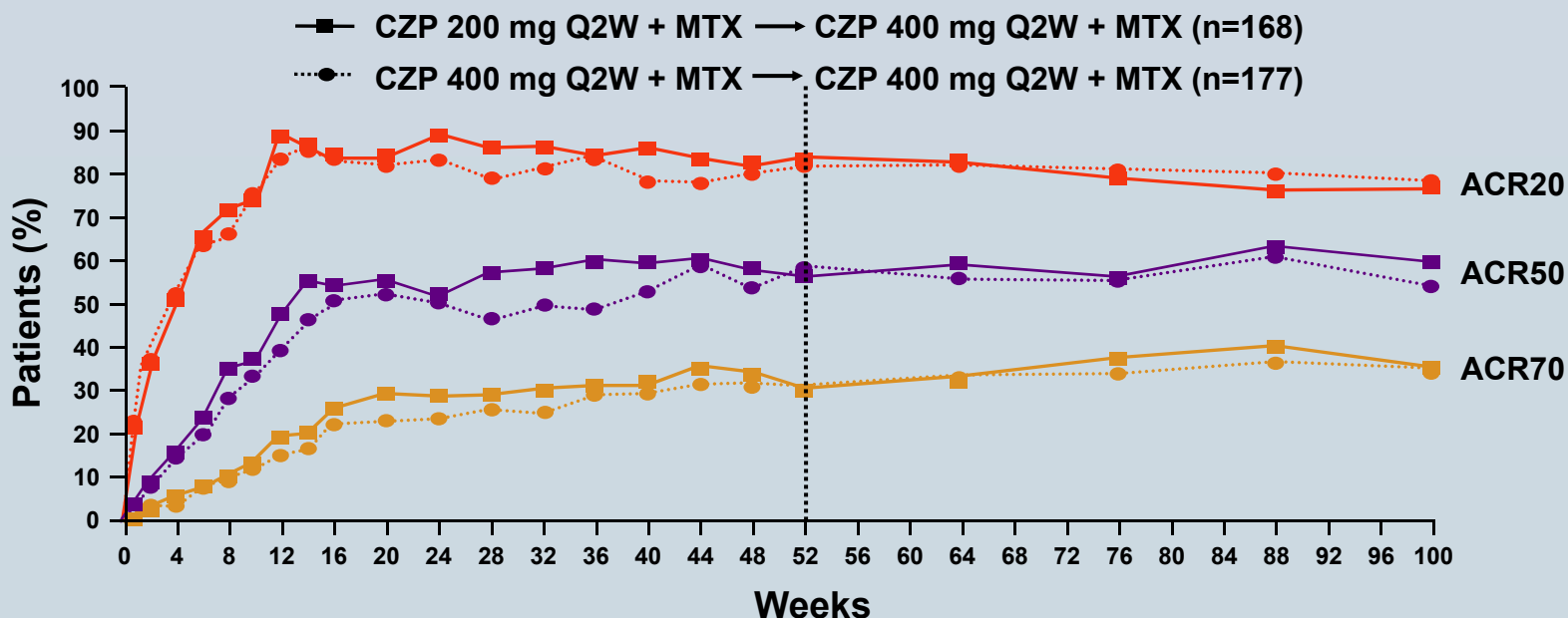
Radiographic Nonprogression at Year 2



RAPID 1 Study: CZP Therapy in MTX-Inadequate Responders with RA

- CZP is a PEGylated, Fc-free TNF inhibitor
- 52-week randomized phase followed by a 48-week open-label phase (2-year study)
- Evaluated efficacy of CZP 200 mg SC + MTX therapy vs CZP 400 mg SC + MTX therapy

ACR Responses over 52 Weeks—Completers

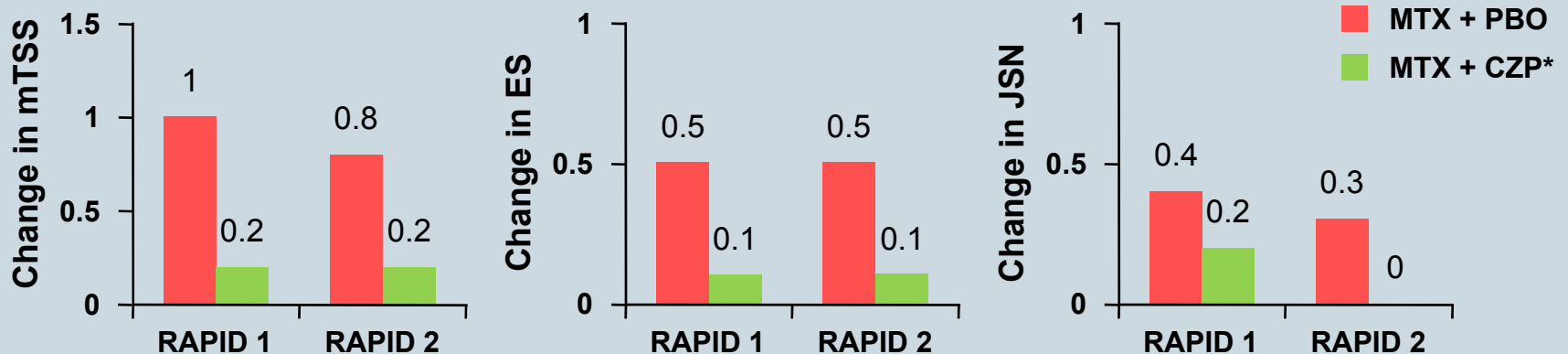


- **Conclusion: ACR20, 50, and 70 rates maintained over 2 years in patients treated with CZP**

Effect of CZP on Structural Damage in RA

- Post-hoc analysis of RAPID 1 and 2 studies
- Determined whether inhibition of structural damage was evident at week 16 in clinical nonresponders
- Patients (N = 982 RAPID 1, and N = 619 RAPID 2) randomized 2:2:1 to CZP (200 mg or 400 mg) or PBO added to MTX
- Radiographs taken at baseline, week 24 (both trials) and week 52 (RAPID 1) or at withdrawal

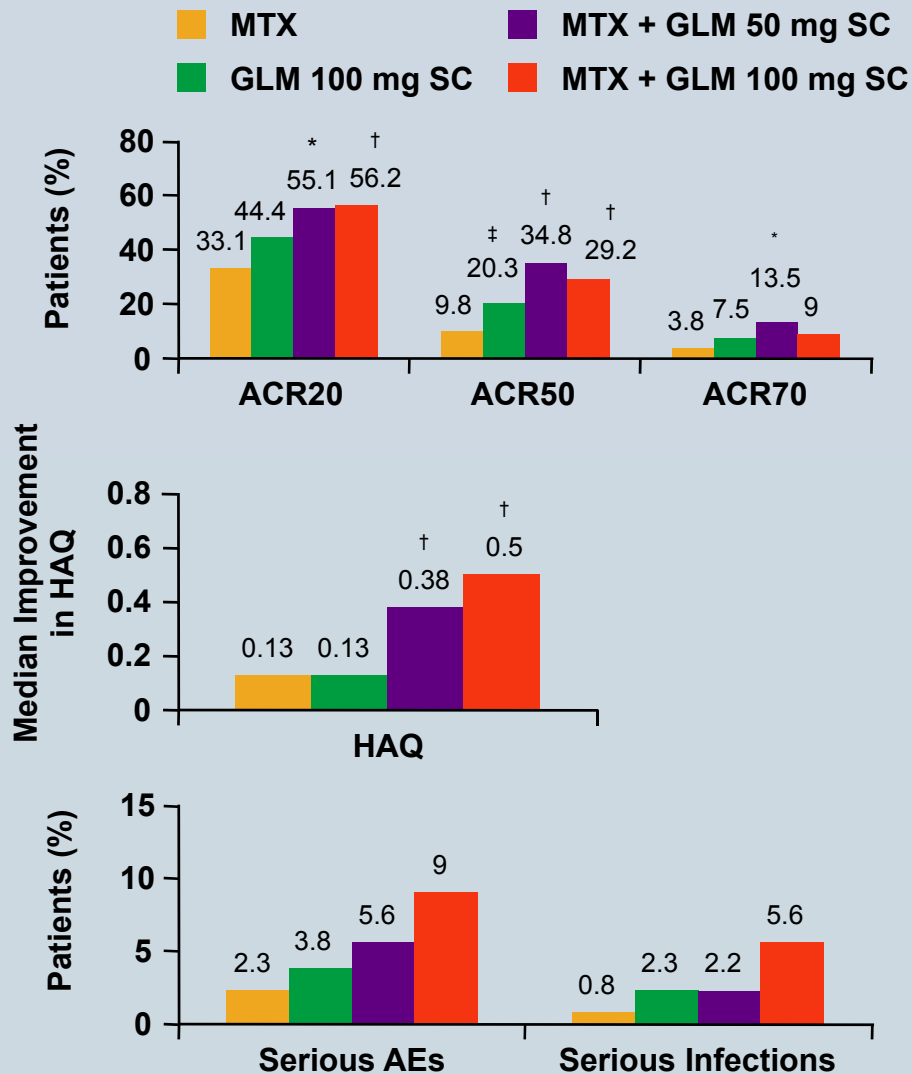
Radiographic Results in Patients Withdrawn at Week 16



- **Conclusion: less change in mTSS, ES, and JSN in patients treated with CZP + MTX therapy who were withdrawn at week 16 from RAPID 1 and 2 for not fulfilling ACR20 response criteria**

GO-FORWARD Study: GLM Therapy in MTX Inadequate Responders with RA

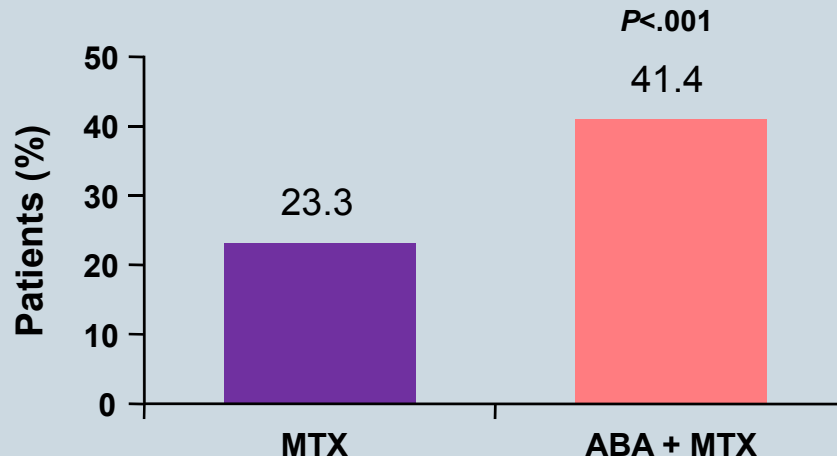
- Multicenter, randomized, double-blind, PBO-controlled study of patients with RA treated with GLM (N = 444)
- Co-primary end points: proportion of patients achieving ACR20 at week 14 and improvement from baseline in HAQ at week 24
- Assessment between:
 - MTX monotherapy
 - GLM monotherapy
 - MTX + GLM 50-mg combination
 - MTX + GLM 100-mg combination
- **Conclusion: patients treated with GLM had significantly higher responses for both ACR20 and median improvement in HAQ**



ABA Therapy in Early RA

- 2-year, randomized, double-blind study of 509 MTX-naïve patients with early RA
- Determined efficacy of ABA + MTX combination therapy vs MTX monotherapy
- Co-primary end points were proportion of patients reaching DAS28-defined remission and joint damage progression measured by the TS at year 1
- Significantly more radiographic progression in MTX group vs ABA + MTX group (mean change in TS 1.06 vs 0.63, respectively; $P = .04$)

Reaching DAS28-Defined Remission at Year 1



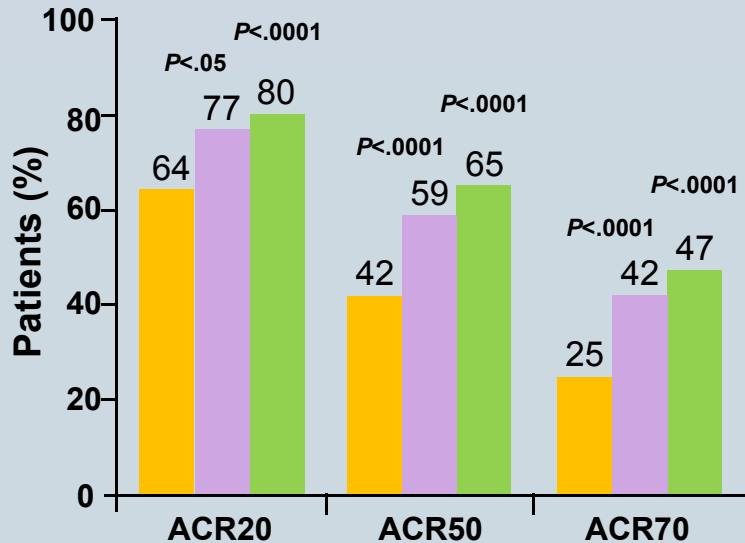
- **Conclusion: Significantly higher proportion of patients treated with ABA achieved DAS28-defined remission and had significantly less radiographic progression**

Efficacy of MTX + RTX Therapy in MTX-Naïve Patients with Early RA: IMAGE

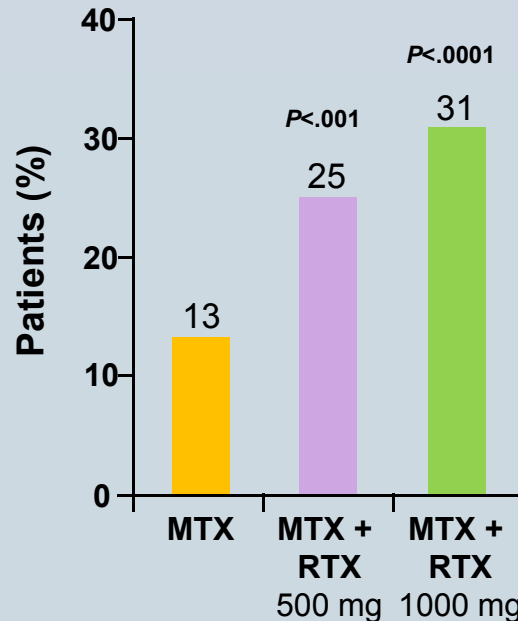
- 52-week, randomized, PBO-controlled study of DMARD- and biologic agent-naïve patients
- Examined radiographic and clinical outcomes among patients with early RA treated with MTX monotherapy or MTX + RTX (2 doses)
- Primary end point was the change in mTSS; secondary endpoint was ACR responses

■ MTX (n=232)
 ■ MTX + RTX 500mg (n=239)
 ■ MTX + RTX 1000mg (n=244)

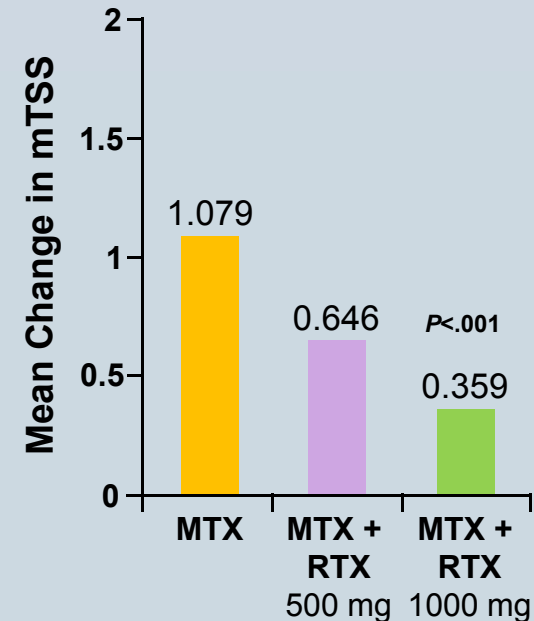
ACR Responses



DAS28 Remission



ΔmTSS



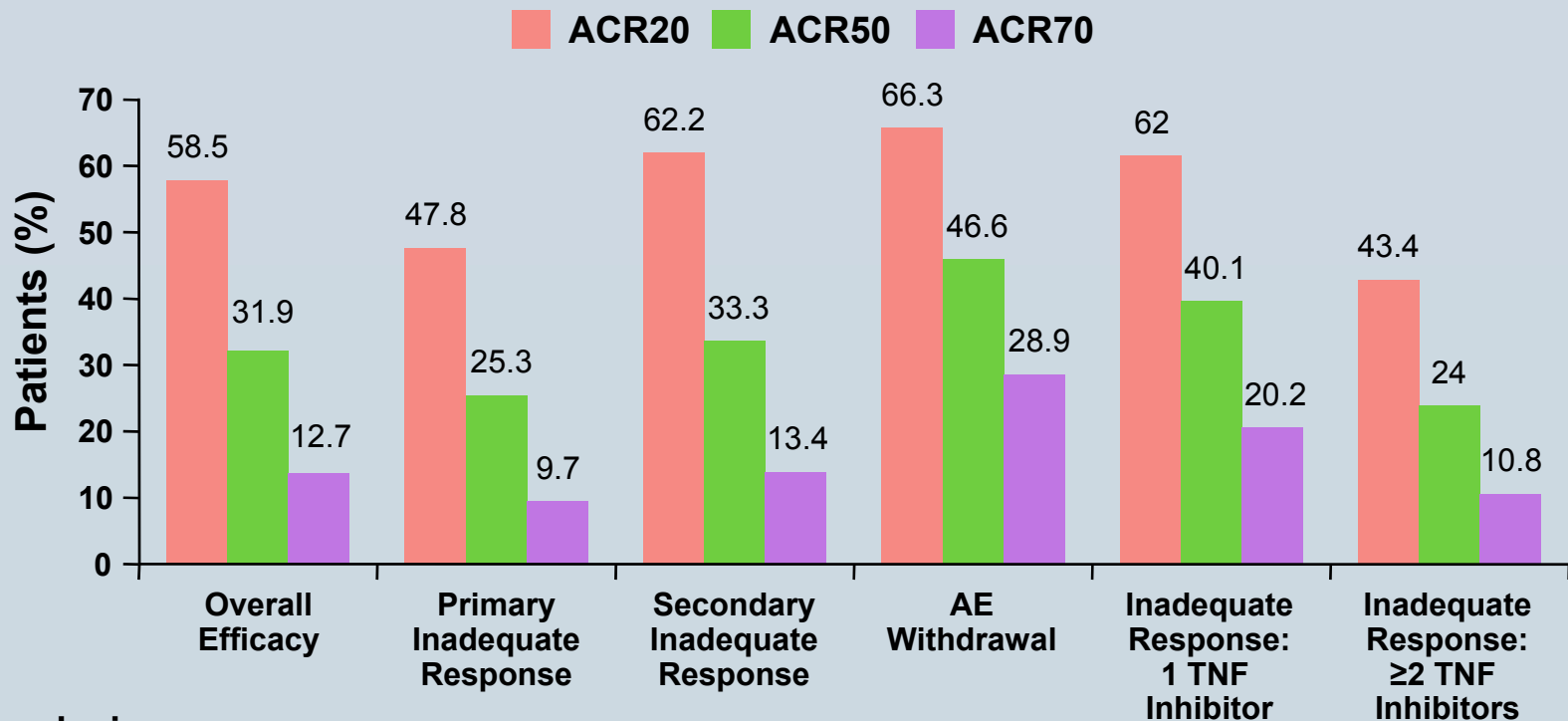
- **Conclusion: MTX + RTX in high doses exhibited significantly better radiographic and clinical outcomes**

What Agent Should be Added for a Patient Experiencing a Partial Response to a TNF Inhibitor?

- Cycle through TNF inhibitors
- Change mechanism of action

TNF Switching: Meta-analysis

- Meta-analysis of 31 studies (16 articles, 15 abstracts); 5306 patients with RA
 - 1 controlled trial; 77% were prospective cohort studies; 81% of studies conducted in Europe
- Examined efficacy of second and third TNF inhibitors after inadequate response to first TNF inhibitor



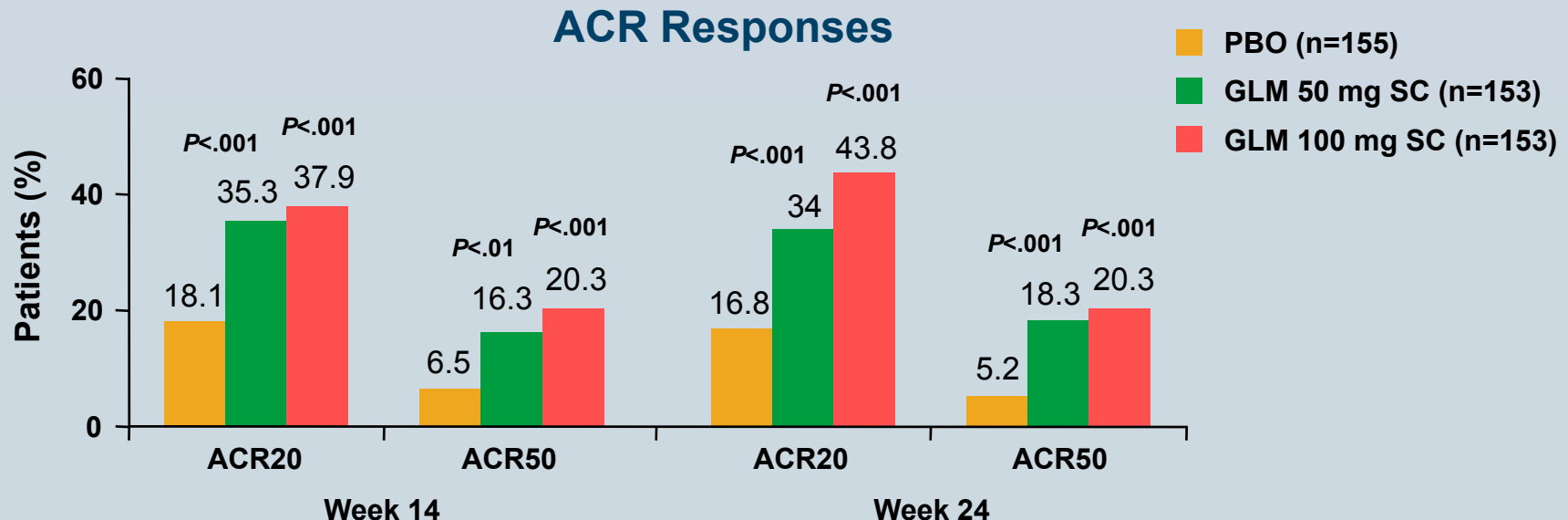
Conclusions:

- Efficacy after switching between TNF inhibitors lower after primary inadequate response and inadequate response to ≥ 2 agents
- Patients who switch due to primary failure with first TNF inhibitor have lower response compared to those switching due to secondary failure

GO-AFTER Study:

GLM Therapy in TNF Inhibitor Inadequate Responders

- Multicenter, randomized, double-blind, PBO-controlled study (N = 461)
- Evaluated GLM efficacy with ≥ 1 TNF-inhibitor—inadequate response (baseline MTX)
- Primary end point was the proportion of patients achieving an ACR20 at week 14
- Efficacy of GLM vs PBO observed for prior use of 1 TNF inhibitor (39% vs 20%, $P=.002$, respectively) and 2 TNF inhibitors (38% vs 16%, $P=.014$)



- **Conclusion: patients treated with GLM therapy experienced significantly greater ACR responses after switching from 1 or 2 (or even 3) TNF inhibitors**

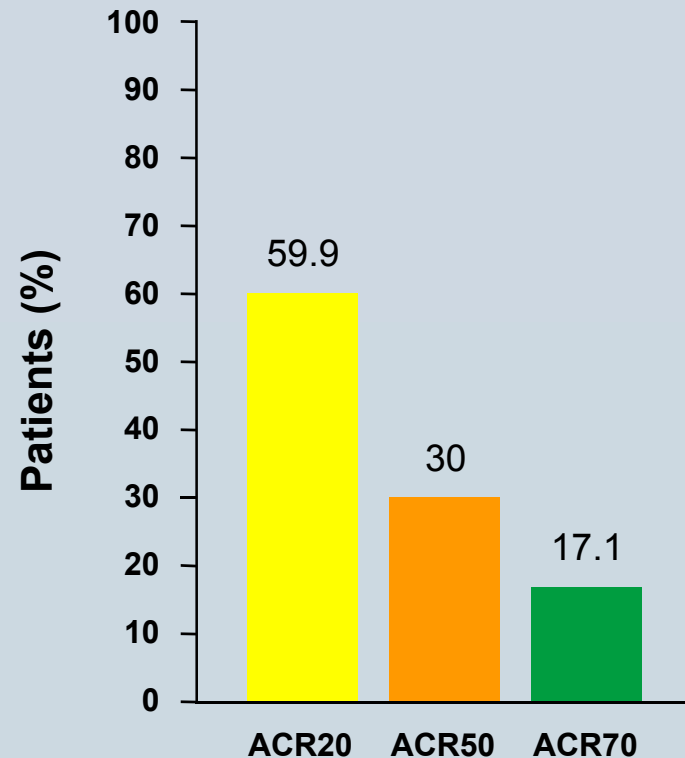
GO-AFTER = GOLimumab After Former anti-TNF Therapy Evaluated in RA.

Smolen J, et al. Presented at: 2008 EULAR Annual Meeting; June 11-14, 2008; Paris, France. Abstract OP-0010. Smolen J, et al. Presented at: 2009 EULAR Annual Meeting; June 10-13, 2009; Copenhagen, Denmark. Abstract THU0209.

ATTAIN Study: ABA Therapy in TNF-Inhibitor–Inadequate Responders

- Randomized, double-blind, PBO-controlled trial (317 patients with RA) followed by long-term extension (222 patients with RA)
- Examined efficacy of ABA in patients with inadequate response to >1 TNF inhibitor
- Patients on a DMARD (MTX)
- **Conclusion: Patients treated with ABA achieved ACR20, ACR50, and ACR70 responses**

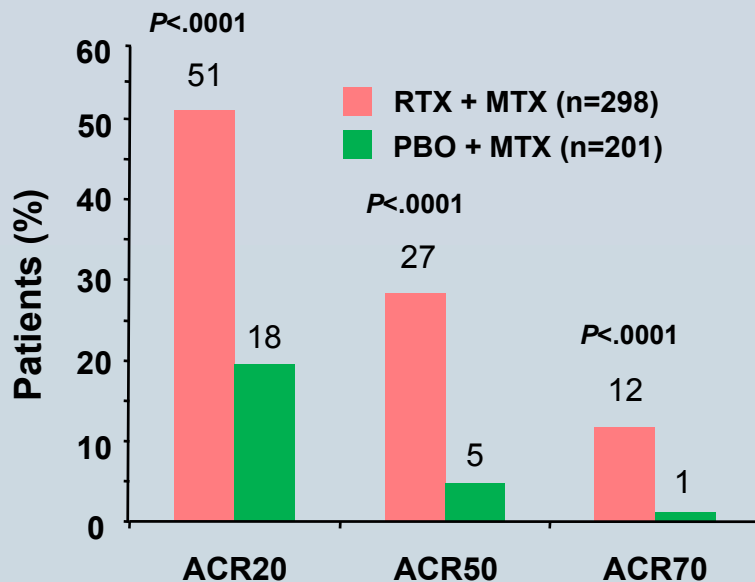
ACR Response at Month 12



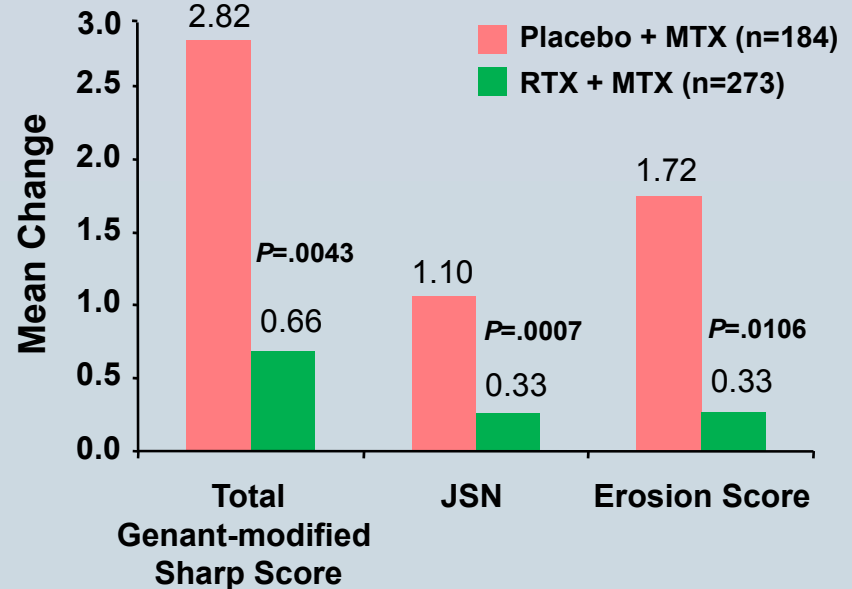
REFLEX Study: RTX Therapy in TNF Inhibitor Inadequate Responders

- 2-year, multicenter, randomized, double-blind, PBO-controlled, phase 3 study of RTX therapy in TNF-inhibitor—inadequate responders

ACR Response at Week 24



Change in Radiographic End Points at Week 56

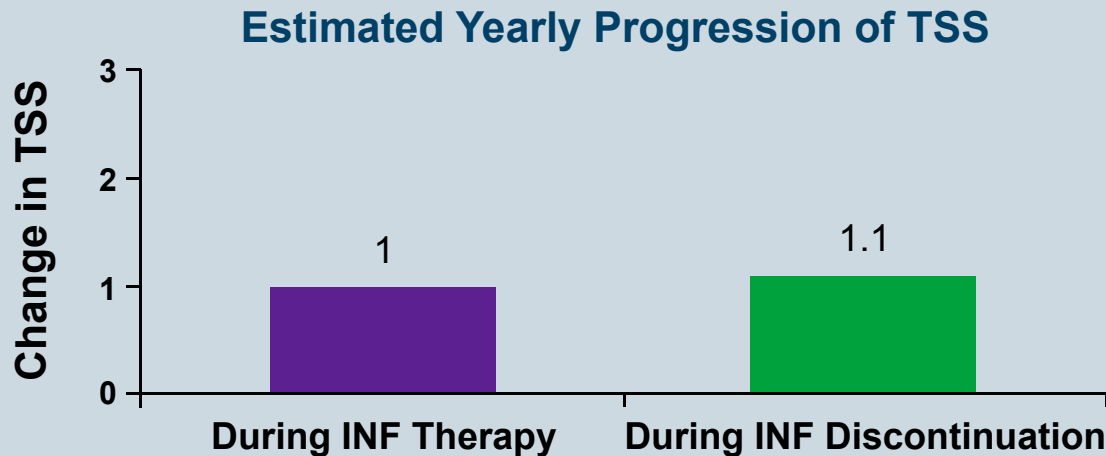


Primary analysis: radiographs within time window, linear extrapolation from week 24 for missing values

- Conclusion: RTX exhibited significant improvements in clinical and radiographic response**

Following the Use of Disease Modifying Therapy, Can Drug-Free Remission in RA be Achieved?

- Examined possibility of discontinuing INF in patients with RA with LDA and determined the risk of articular destruction during INF discontinuation
- 100 patients received INF and had DAS28 <3.2 for 24 weeks
- No restrictions on duration of disease, history of traditional DMARDs, degree of articular destruction, and MTX dose level (patients excluded if steroid dose was over 5 mg/day)
- 27 patients restarted INF therapy after 7.2 months; discontinuation of INF lasted more than 1 year in 38 patients



- **Conclusion: INF therapy was discontinued and remission maintained for greater than 12 months in 38 patients without significant radiographic progression**



Does Clinical Remission Prevent Structural Damage?

- 102 patients with RA judged to be in remission by their physician
- Patients followed prospectively for 1 year
- Radiographic joint damage developed in 19% of patients
- Damage correlated with US and MRI evidence of synovitis at baseline
- **Conclusions**
 - Clinical assessment of remission may not be sufficient to identify patients at risk of disease progression
 - **Should MRI and/or US be used to identify patients at low risk of progression?**



RA Treatment Strategies: Conclusions

- Early use of DMARD therapy and treatment to a goal leads to better outcomes
- TNF inhibitors are commonly used as a next step in MTX-inadequate responders
- No comparative data to identify the best option in patients with inadequate response to TNF inhibitors
- Early use of biologic therapy may lead to improved outcomes
 - Identifying appropriate patients for this approach remains difficult
- Current goal of therapy is remission
 - Definition? Imaging?



Audience Response

If RA is present for 3 to 6 months in a patient who has an inadequate response to MTX monotherapy, then a TNF inhibitor should be initiated.

1. Strongly agree
2. Agree
3. Somewhat agree
4. Somewhat disagree
5. Disagree
6. Strongly disagree



Audience Response

In patients who fail to respond to a TNF inhibitor and are switched to a second TNF inhibitor, the reasons for failing the first agent may impact the likelihood of successful response to the second agent.

1. Strongly agree
2. Agree
3. Somewhat agree
4. Somewhat disagree
5. Disagree
6. Strongly disagree



Audience Response

How confident are you that objective clinical measurements accurately reflect disease activity in your patients with RA?

1. Very confident
2. Confident
3. Somewhat confident
4. Not confident
5. Unsure



Patient Case Presentation 1

- 32-year-old female is referred to your office by a PCP after complaining of pain in her hands and feet
 - 3 hours of morning stiffness
 - Mild relief with OTC naproxen
 - PMH: Hypothyroidism controlled with levothyroxine
- On exam, she has obvious synovitis, with 14 swollen and 18 tender joints (of 28)
 - Remainder of her physical exam is normal
- Labs show mild anemia, normal chemistries, ESR 56 mm/hr, RF negative, CCP positive
- Medication history
 - Started on MTX monotherapy 9 months ago
 - Started on MTX and ETN combination therapy 6 months ago due to MTX inadequate response

What would be your recommendation for therapy after giving the patient an IM corticosteroid injection for acute relief of symptoms?

1. Maintain ETN therapy and increase MTX dose
2. Maintain MTX therapy and increase ETN dose
3. Maintain MTX therapy and switch to another TNF inhibitor
4. Maintain MTX therapy and switch to ABA
5. Maintain MTX therapy and switch to RTX



SpAs

GRAPPA: PsA Severity Criteria

	Mild	Moderate	Severe
Peripheral Arthritis	<p><5 joints</p> <p>No damage on X-ray</p> <p>No LOF</p> <p>Minimal impact on QOL</p> <p>Patient evaluation mild</p>	<p>≥5 joints (T/S)</p> <p>Damage on X-ray</p> <p>IR to mild treatment</p> <p>Moderate LOF</p> <p>Moderate impact on QOL</p> <p>Patient evaluation moderate</p>	<p>≥5 joints (T/S)</p> <p>Severe damage on X-ray</p> <p>IR to mild-moderate treatment</p> <p>Severe LOF</p> <p>Severe impact on QOL</p> <p>Patient evaluation severe</p>
Skin Disease	<p>BSA <5, PASI <5, asymptomatic</p>	<p>Nonresponse to topicals, DLQI, PASI <10</p>	<p>BSA >10, DLQI >10, PASI >10</p>
Spinal Disease	<p>Mild pain</p> <p>No LOF</p>	<p>LOF or BASDAI >4</p>	<p>Failure of response</p>
Enthesitis	<p>1 to 2 sites</p> <p>No LOF</p>	<p>>2 sites or LOF</p>	<p>LOF or >2 sites and failure of response</p>
Dactylitis	<p>Pain absent to mild</p> <p>Normal function</p>	<p>Erosive disease or functional loss</p>	<p>Failure of response</p>

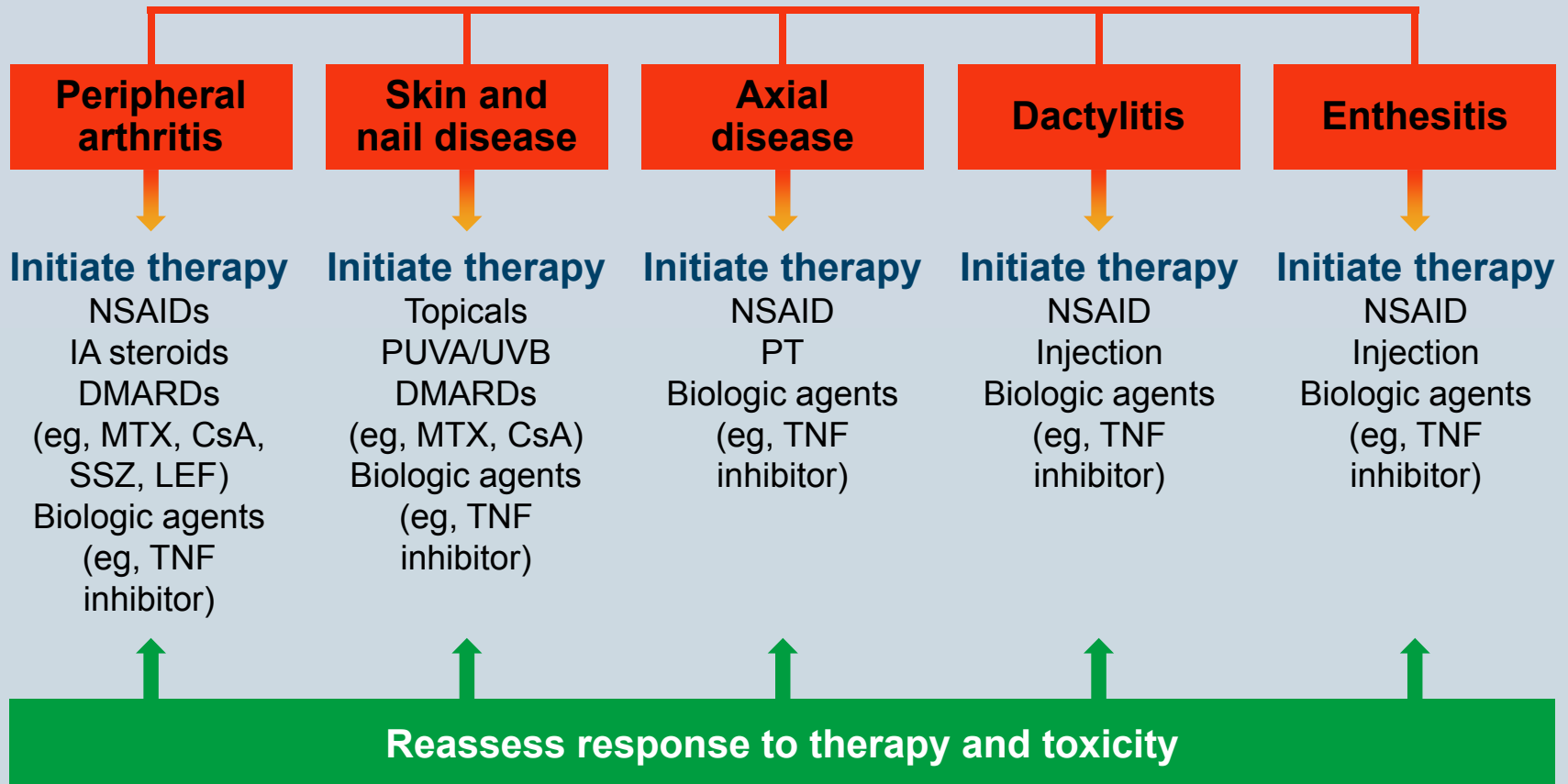
GRAPPA = Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; PsA = psoriatic arthritis; LOF = loss of physical function; QOL = quality of life; T/S = tender/swollen; IR = inadequate response; BSA = body surface area; PASI = Psoriasis Activity Severity Score; DLQI = Dermatology Life Quality Index; BASDAI = Bath Ankylosing Spondylitis Disability Activity.

Ritchlin CT, et al. *Ann Rheum Dis*. 2008. [Epub ahead of print]

GRAPPA:

Recommendations for Treatment of PsA

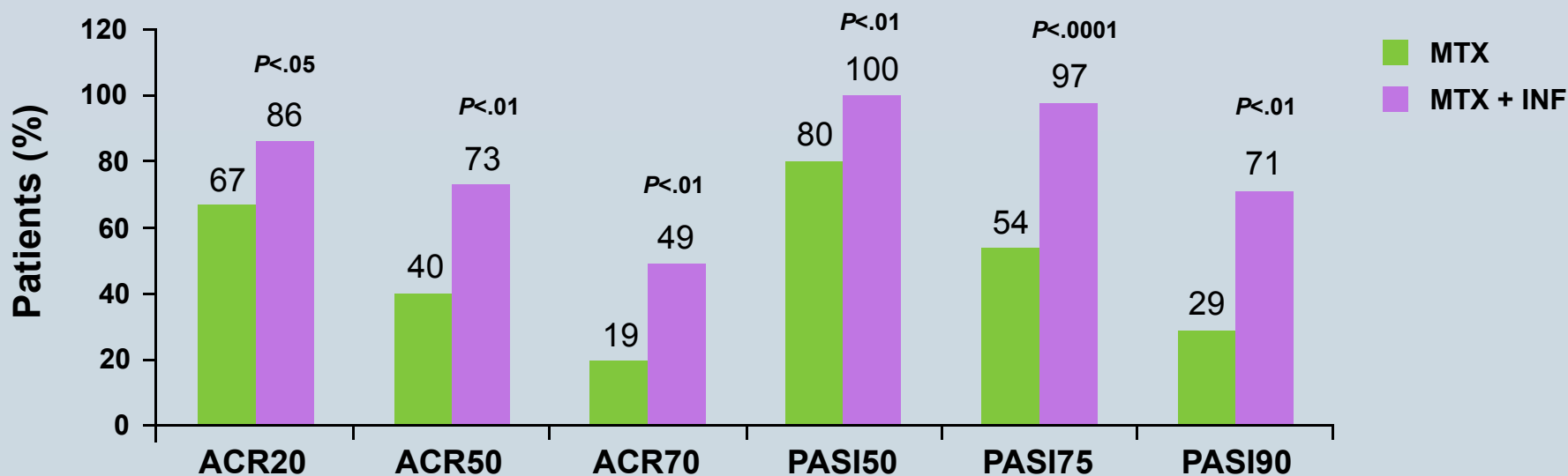
Establish Diagnosis of PsA



RESPOND Study: MTX + INF Therapy in Patients with PsA

- Prospective, randomized, open-label, multicenter, multinational study (N=115)
- Evaluated efficacy of MTX + INF vs MTX monotherapy MTX-naïve patients with early, polyarticular PsA
- Primary outcome: ACR20 response at week 16

Efficacy Results at Week 16

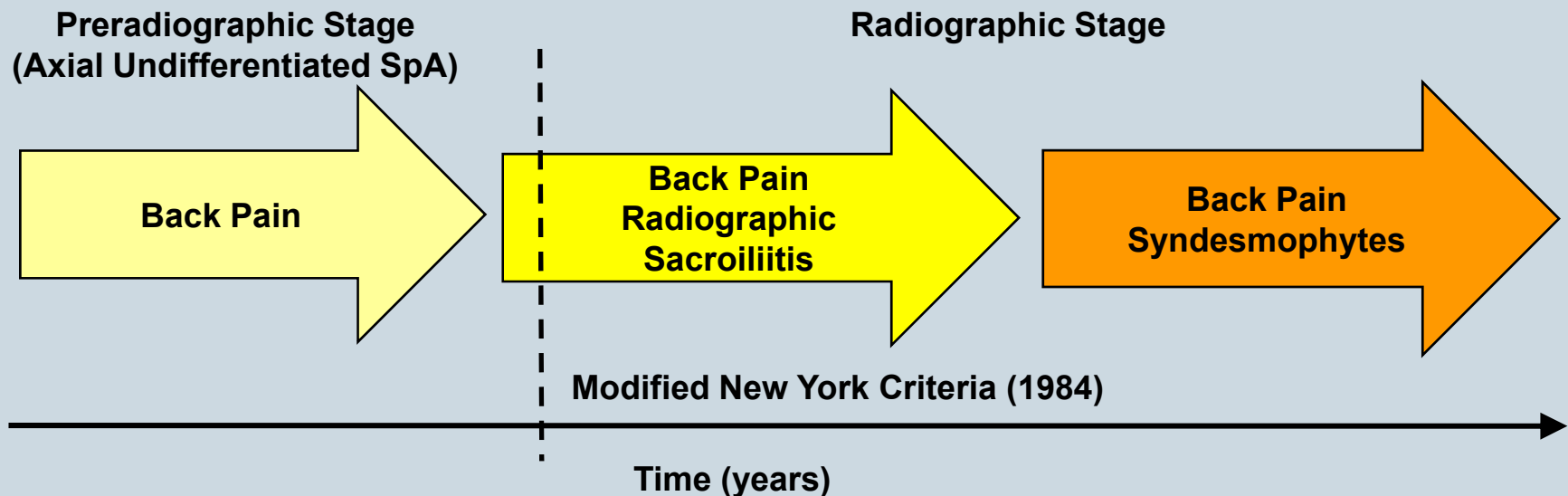


Conclusions:

- MTX-naïve patients with early, polyarticular PsA treated with MTX + INF achieved significantly greater ACR20 and PASI >5 responses
- First controlled trial to compare initial therapy with MTX or TNF inhibitor in this population

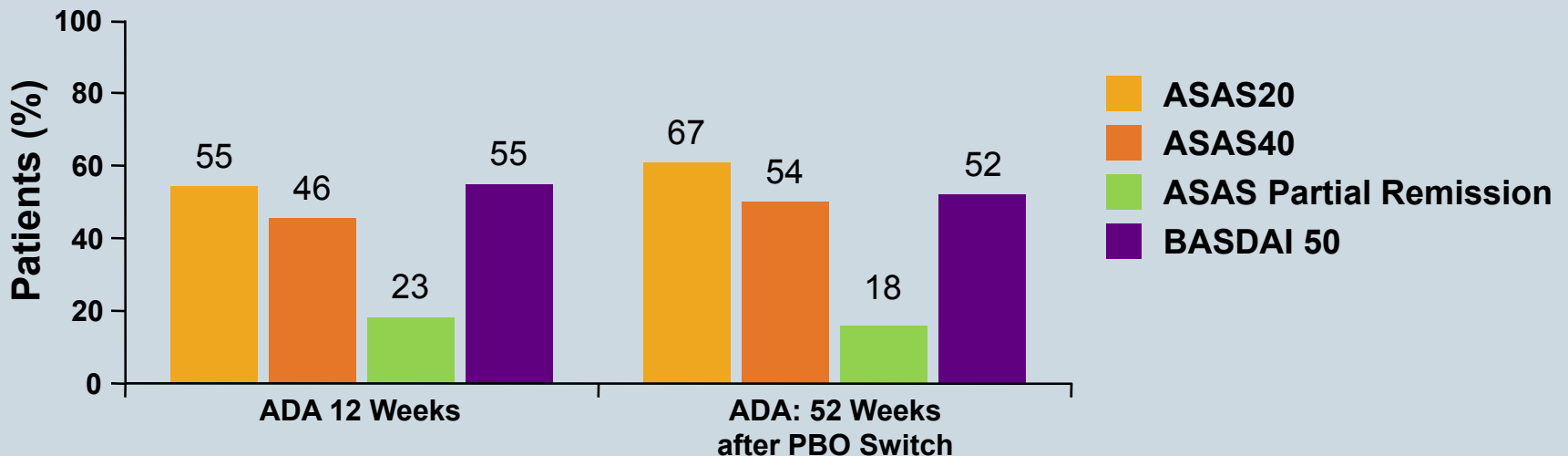
Diagnostic Standard for AS: Modified New York Criteria

- Clinical criteria:
 - Low back pain and stiffness for >3 months that improves with exercise but is not relieved by rest
 - Limitation of motion of the lumbar spine in both the sagittal and frontal planes
 - Limitation of chest expansion relative to normal values correlated for age and sex
- Radiologic criterion: sacroiliitis (grade ≥ 2 bilaterally or grade 3-4 unilaterally)
- Definite AS = radiologic criterion present + ≥ 1 clinical criterion
- Probable AS = 3 clinical criteria present or radiologic criteria present without clinical criteria



ADA Therapy for “Pre-radiographic” AS

- 46 patients with chronic low back pain (duration >3 months, age <50 years)
- At least 3 of the following, including at least 2 of the first 3
 - Inflammatory back pain
 - HLA-B27 positive
 - MRI with acute inflammatory lesions in spine or SI joints
 - Good response to NSAIDs
 - Extraspinal manifestations: uveitis, peripheral arthritis, enthesitis
 - Positive family history
- BASDAI ≥ 4 despite NSAIDs



- **Conclusion: patients with “pre-radiographic” AS treated with ADA therapy had sustained ASAS and BASDAI responses**

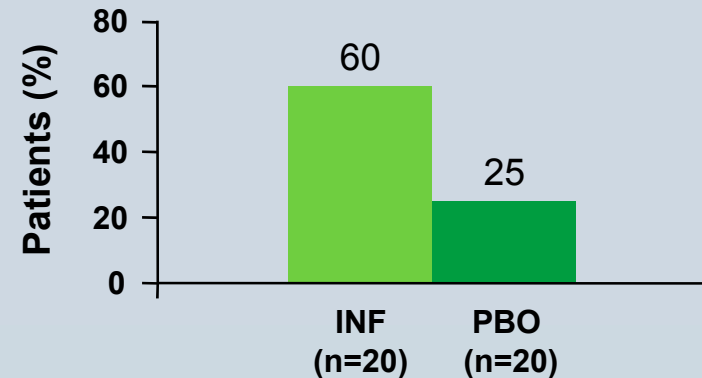
SI = sacroiliac; ASAS = Assessments in Ankylosing Spondylitis.

Haibel H, et al. Presented at: 2007 ACR Annual Scientific Meeting; November 6-11, 2007; Boston, MA. Abstract 753. Amtenbrink AL, et al. Presented at: 2008 ACR Annual Scientific Meeting; October 24-29, 2008; San Francisco, CA. Abstract 1108.

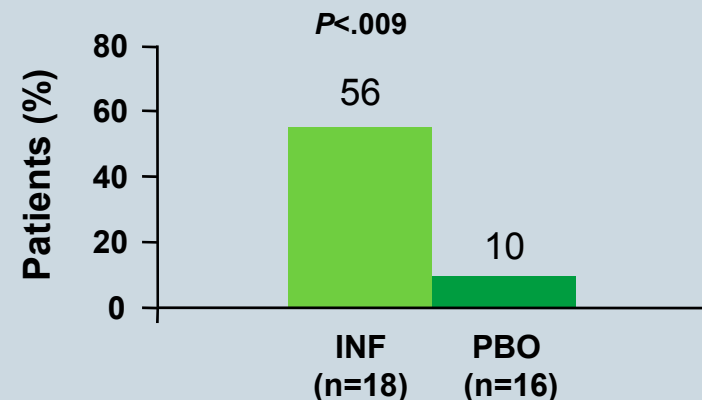
INF Treatment in “Very Early” AS

- Assessed INF-induced changes in osteitis and enthesitis of spine and SI joints
- Inclusion
 - Inflammatory back pain (Calin)
 - 3 months to 3 years duration
 - HLA-B27 positive
 - MRI scan showing edema at SI joints
- Arm 1: blinded INF 5 mg/kg infusions (standard regimen)
- Arm 2: blinded PBO infusions
- **Conclusion: greater proportion of patients treated with INF in “very early” AS exhibited resolution of spinal lesions and reached ASAS partial remission**

Spinal Lesions Resolved at Week 16



ASAS Partial Remission at Week 16



Physical Function in Patients with AS

- Sub-analysis of ASSERT database at baseline in patients with AS (N=214)
- Examined relationship between disease activity (measured by ASDAS-CRP or BASDAI), spinal mobility (measured by BASMI-lin), and physical function (measured by BASFI)
- BASFI correlated moderately with BASMI-lin (Spearman's rho=0.4) and ASDAS (Spearman's rho=0.32)

Best-fit Model for BASFI

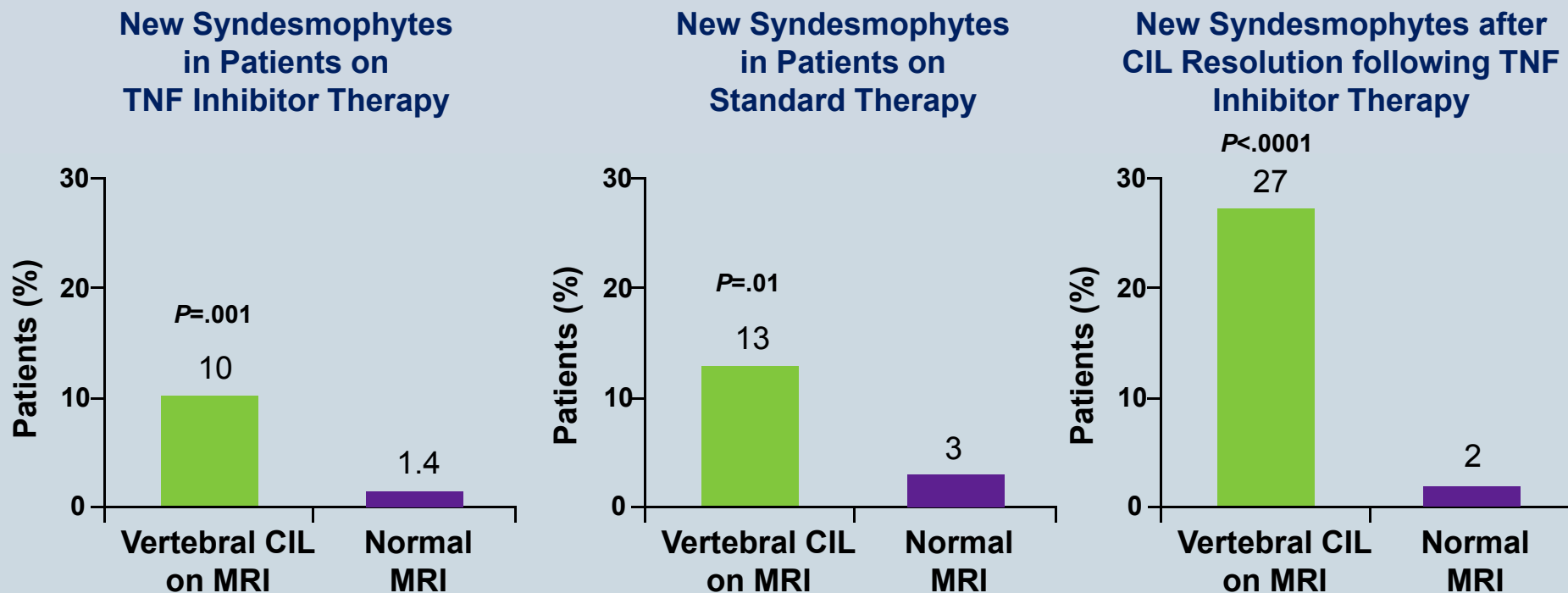
Measure	B	95% CI	P value
BASMI-lin	0.498	0.358, 0.638	<.001
ASDAS	0.636	0.421, 0.852	<.001

Conclusions:

- Physical function in these patients with AS was independently determined by disease activity and spinal mobility
- As seen in RA, both inflammation and structural damage can contribute to loss of function in AS

TNF Brake Hypothesis: New Bone Formation Following Resolution of Inflammation

- 2-year, prospective cohort study of 51 patients with AS (28 on standard therapy, 23 on TNF inhibitor therapy)
- Examined if vertebral CIL resolving after treatment is more likely to develop into a de novo syndesmophyte visible on radiographs than vertebral corner with no prior CIL visible on MRI



- **Conclusion: increased likelihood of syndesmophyte development following resolution of inflammation**

TNF Inhibitor Therapy and Radiographic Progression in AS

- No PBO-controlled trials of sufficient duration to show whether TNF inhibitors slow disease progression
- RCT radiographic data for available TNF inhibitors, compared with historical data from the OASIS cohort, does not show any effect on lumbar spine radiographic progression
 - Results unchanged when including only OASIS subjects who would have met inclusion criteria for RCTs
- In a small study of 33 patients with AS treated for 4 years with TNF, the mean change in mSASSS score was 1.6 ± 2.6
 - Published OASIS data predicts a 4-year change of 4.4 units
 - Change between baseline and year 2 was significant, but change between years 2 and 4 was not significant
- Do TNF inhibitors slow radiographic progression with sufficient duration of therapy?



Patient Case Presentation 2

- 24-year-old male presents to your office complaining of low back pain
 - Back pain since college, but it has worsened in the past several years
 - Quit his local softball league 2 years ago because of pain
- His left ankle, which does not bother him right now, has been swollen and painful at times
- On exam, he has normal peripheral joints, including his ankles
 - Schober's test goes from 10 to 12.5 cm
- Laboratory studies are all normal
 - CRP is 0.5 (<0.8)
- Radiographs show bilateral grade 3 sacroiliitis, but lumbar spine appears normal

What is Your Treatment Recommendation for this Patient at this Time?

1. Indomethacin
2. Low-dose prednisone
3. SSZ
4. MTX
5. TNF inhibitor

What treatment would you recommend if the patient's history and physical were unchanged, but his radiographs were normal?

1. Indomethacin
2. Low-dose prednisone
3. Sulfasalazine
4. MTX
5. TNF inhibitor