Evaluating Newer Targeted Therapies for Patients with Rheumatoid Arthritis: Addressing Unmet Needs in the Primary Care Practice
Faculty Affiliation

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Denver, Colorado
Faculty Disclosures

- Barbara Goldstein, MD, MMSc, has no conflicts of interest to report.
Learning Objectives

- Proper work-up to improve the early and accurate diagnosis of rheumatoid arthritis (RA)
- Apply guideline recommendations for treating to remission in patients with RA
- Review the underlying pathophysiology of RA and the role of emerging targeted therapies, including cytokine inhibition, for patients with RA
- Implement strategies that promote early identification of important comorbidities and their management in patients with RA
RA Epidemiology and Burden

- Affects ~1.5 million US adults
- 2 to 3 times more prevalent in women vs men
- Prevalence increases with age (~1% in women >55 years of age)
- Presents at any age, but most common in the third to sixth decade of life
- Causes substantial disability and reduced QOL
- Is associated with multiple comorbid conditions, including CVD, which leads to shortened life expectancy

CVD, cardiovascular disease; QOL, quality of life.

Available at: http://www.cdc.gov/arthritis/basics/rheumatoid.htm
RA Pathophysiology

- Chronic autoimmune disease characterized by inflammation and synovial joint damage
- Inflammation of the synovial membrane
  - Leukocyte infiltration into normally sparsely populated synovial compartment

Altering Disease Progression


Increased disability, morbidity, and mortality going up the axis

High disease activity

Remission

Natural history

Late treatment

Early treatment

Treatment Delays Reduce the Likelihood of Achieving and Sustaining Remission

The likelihood of remission and sustained remission are reduced by 10% to 15% with every 5-year increase in disease duration prior to treatment initiation.

CDAI, Clinical Disease Activity Index; DAS28, Disease Activity Score; DMARD, disease-modifying antirheumatic drug; TNF, tumor necrosis factor.

Beneficial Impact of Early RA Treatment on Patient Function

Patients initiating treatment with adalimumab at ≤2 years disease duration were more likely to achieve ACR50, ACR70, low disease activity, and normal function.

ACR, American College of Rheumatology; ACR50, improvement of at least 50% in both tender and swollen joint counts; ACR70, improvement of at least 70% in both tender and swollen joint counts; LDA, low disease activity.

Current Areas of Focus in Clinical Practice

- Early identification and treatment to:
  - Alter disease course to prevent long-term joint damage
  - Control pain
  - Improve time to clinical remission
  - Restore/preserve function and regain/retain QOL

- Definition of:
  - Inadequate response
  - Remission

- Establishment of criteria for:
  - Monotherapy vs combination therapy
  - Switching treatment
  - Halting biologic treatment

Overarching Goals of Patient Care

- Early identification and treatment
- Effective management of comorbidities
- Optimal safety

Full function and high QOL
Evaluation and Diagnosis of RA
Case Study 1: Jane, 45-Year-Old Woman with Early RA

- 3-month history of pain and inflammation in her bilateral MCPs, PIPs, wrists and MTPs
- Stiffness every morning accompanied by fatigue
- Loss of appetite in recent weeks
- Physical exam
  - Bilateral symmetrical synovitis
  - Joint tenderness
  - Erythema
  - Warmth
Screening and Diagnosis

- RA is a **clinical diagnosis**
- Lab tests may aid in monitoring and ruling out other types of arthritis:
  - C-reactive protein (CRP)
  - Erythrocyte sedimentation rate (ESR)
  - Rheumatoid factor latex test
  - Anti-cyclic citrullinated peptide (anti-CCP) antibody testing
  - X-rays
  - Joint aspiration: WBC count, gram stain/cx and crystals
  - Would not get other autoantibodies or other tests at this point

Cx, culture; WBC, white blood cell.
Available at: [https://www.guideline.gov/summaries/summary/39244](https://www.guideline.gov/summaries/summary/39244)
## ACR/EULAR Criteria for Classification of RA

<table>
<thead>
<tr>
<th>Joints Involved</th>
<th>Score</th>
<th>Serology‡</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 large joint</td>
<td>0</td>
<td>Negative RF and negative ACPA</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low-positive RF or low-positive ACPA</td>
<td>2</td>
</tr>
<tr>
<td>2-10 large joints</td>
<td>1</td>
<td>High-positive RF or high-positive ACPA</td>
<td>3</td>
</tr>
<tr>
<td>1-3 small joints*</td>
<td>2</td>
<td>Normal CRP and normal ESR</td>
<td>0</td>
</tr>
<tr>
<td>4-10 small joints*</td>
<td>3</td>
<td>Abnormal CRP or abnormal ESR</td>
<td>1</td>
</tr>
<tr>
<td>&gt;10 joints†</td>
<td>4</td>
<td>&lt;6 weeks</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥6 weeks</td>
<td>1</td>
</tr>
</tbody>
</table>

### Acute-Phase Reactants‡

<table>
<thead>
<tr>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

### Duration of Symptoms

<table>
<thead>
<tr>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

*A total score ≥6 indicates definite RA.*

*With or without large joint involvement; † ≥1 small joint involved; ‡ ≥1 test required for classification. ACPA, anti-citrullinated protein antibodies; EULAR, European League Against Rheumatism; RF, rheumatoid factor.

## Case Study 1: Lab Results

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF</td>
<td>50 IU/mL (normal: &lt;20 IU/mL)</td>
</tr>
<tr>
<td>CCP</td>
<td>80 U (normal: &lt;20 U)</td>
</tr>
<tr>
<td>ESR</td>
<td>50 mm/hr (normal: &lt;20 mm/hr for women &lt;50 YOA)</td>
</tr>
<tr>
<td>CRP</td>
<td>5.0 mg/dL (normal: &lt;3.0 mg/dL)</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>Normal range</td>
</tr>
<tr>
<td>BUN</td>
<td>Normal range</td>
</tr>
<tr>
<td>Liver enzymes</td>
<td>Normal range</td>
</tr>
</tbody>
</table>

BUN, blood urea nitrogen; YOA, years of age.
Case Study 1: Diagnosis

- Based upon her ACR/EULAR classification score, the patient is diagnosed with RA:

<table>
<thead>
<tr>
<th>Category</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint involvement</td>
<td>4</td>
</tr>
<tr>
<td>Serology</td>
<td>2</td>
</tr>
<tr>
<td>Acute-phase reactants</td>
<td>1</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total score</strong></td>
<td><strong>8</strong></td>
</tr>
</tbody>
</table>
What are your primary treatment goals for Jane?
What are her goals?
What is the level of her disease activity (ie, is the RA impacting her life)?
ACR-endorsed Measures of Disease Activity

- DAS28 CRP/DAS28 ESR
- CDAI
- SDAI
- RAPID 3
- PAS
- PAS II

PAS, patient activity scale; RAPID, routine assessment of patient index data; SDAI, simplified disease activity index.

# Evaluating Disease Activity: RAPID 3

1. **PLEASE CHECK THE ONE BEST ANSWER FOR YOUR ABILITIES AT THIS TIME:**

<table>
<thead>
<tr>
<th>OVER THE LAST WEEK, WERE YOU ABLE TO:</th>
<th>WITHOUT ANY DIFFICULTY</th>
<th>WITH SOME DIFFICULTY</th>
<th>WITH MUCH DIFFICULTY</th>
<th>UNABLE TO DO</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Dress yourself, including tying shoelaces and doing buttons?</td>
<td>X 0</td>
<td>_ 1</td>
<td>_ 2</td>
<td>_ 3</td>
</tr>
<tr>
<td>b. Get in and out of bed?</td>
<td>_ 0</td>
<td>X 1</td>
<td>_ 2</td>
<td>_ 3</td>
</tr>
<tr>
<td>c. Lift a full cup or glass to your mouth?</td>
<td>_ 0</td>
<td>_ 1</td>
<td>_ 2</td>
<td>X 3</td>
</tr>
<tr>
<td>d. Walk outdoors on flat ground?</td>
<td>X 0</td>
<td>_ 1</td>
<td>_ 2</td>
<td>_ 3</td>
</tr>
<tr>
<td>e. Wash and dry your entire body?</td>
<td>_ 0</td>
<td>X 1</td>
<td>_ 2</td>
<td>_ 3</td>
</tr>
<tr>
<td>f. Bend down to pick up clothing from the floor?</td>
<td>_ 0</td>
<td>X 1</td>
<td>_ 2</td>
<td>_ 3</td>
</tr>
<tr>
<td>g. Turn regular faucets on and off?</td>
<td>_ 0</td>
<td>_ 1</td>
<td>X 2</td>
<td>_ 3</td>
</tr>
<tr>
<td>h. Get in and out of a car, bus, train, or airplane?</td>
<td>_ 0</td>
<td>_ 1</td>
<td>_ 2</td>
<td>X 3</td>
</tr>
<tr>
<td>i. Walk two miles or three kilometers, if you wish?</td>
<td>_ 0</td>
<td>X 1</td>
<td>_ 2</td>
<td>_ 3</td>
</tr>
<tr>
<td>j. Participate in recreational activities and sports as you would like, if you wish?</td>
<td>_ 0</td>
<td>X 1</td>
<td>_ 2</td>
<td>_ 3</td>
</tr>
<tr>
<td>k. Get a good night’s sleep?</td>
<td>X 0</td>
<td>_ 1.1</td>
<td>_ 2.2</td>
<td>_ 3.3</td>
</tr>
<tr>
<td>l. Deal with feelings of anxiety or being nervous?</td>
<td>_ 0</td>
<td>_ 1.1</td>
<td>_ 2.2</td>
<td>X 3.3</td>
</tr>
<tr>
<td>m. Deal with feelings of depression or feeling blue?</td>
<td>_ 0</td>
<td>_ 1.1</td>
<td>X 2.2</td>
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2. **HOW MUCH PAIN HAVE YOU HAD BECAUSE OF YOUR CONDITION OVER THE PAST WEEK?**

Example pain scale:

- NO PAIN
- PAIN AS BAD AS IT COULD BE

3. **CONSIDERING ALL THE WAYS IN WHICH ILLNESS AND HEALTH CONDITIONS MAY AFFECT YOU AT THIS TIME, PLEASE INDICATE BELOW HOW YOU ARE DOING:**

Example health scale:

- VERY WELL
- VERY POORLY

Available at: [http://www.rheumatology.org/Portals/0/Files/RAPID3%20Form.pdf](http://www.rheumatology.org/Portals/0/Files/RAPID3%20Form.pdf)
Case Study 1: RAPID 3 Scoring

**RAPID 3 Scoring Table**

<table>
<thead>
<tr>
<th>Over the Last Week, Were You Able To?</th>
<th>Without Any Difficulty</th>
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<td>___ 2.2</td>
<td>___ 3.3</td>
</tr>
</tbody>
</table>

**Pain Over the Past Week**

Please indicate below how severe your pain has been:

- No Pain
- Pain as Bad as it Could Be

**Illness and Health Conditions**

CONVERSION TABLE

**Near Remission (NRM) (0-3); 3=1.0**

**Low Severity (LS) (3-5); 5=1.0**

**Moderate Severity (MS) (5-7); 7=1.0**

**High Severity (HS) (8-11); 11=3.7**

RAPID 3 = 3.7

*Moderately active RA*
Pharmacologic Management of RA
Overarching Treatment Principles

**Shared Decision-making**
Between patient and physicians

**Abrogation of Inflammation**
(Not just control)

**Maximization of Long-term QOL**
Controlling symptoms, preventing joint damage, and normalizing function

**Treat-to-Target**
Measuring disease activity regularly and adjusting therapy to achieve clinical remission/LDA

Synthetic DMARDs Approved for RA

- Hydroxychloroquine (HCQ)
- Sulfasalazine (SSZ)
- Methotrexate (MTX)
- Leflunomide (LEF)
- Tofacitinib*

*The Janus kinase (JAK) inhibitor tofacitinib is a targeted synthetic DMARD.

Methotrexate: Cornerstone of RA Treatment

- First-line therapy
- Efficacy as monotherapy or combination therapy:
  - Superior to placebo
  - Comparable to other drugs, including anti-TNF therapy
- One-third of patients have no radiographic progression at one year with MTX
- Greater efficacy when combined with targeted biologics
- Reduces immunogenicity of biologic DMARDs
- GI toxicity is the most common (bone marrow, lung, and liver toxicity are rare)

GI, gastrointestinal.

### Biologic DMARDs Previously Approved for RA

<table>
<thead>
<tr>
<th>Class</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF inhibitor</td>
<td>• Adalimumab</td>
</tr>
<tr>
<td></td>
<td>• Certolizumab pegol</td>
</tr>
<tr>
<td></td>
<td>• Etanercept</td>
</tr>
<tr>
<td></td>
<td>• Golimumab</td>
</tr>
<tr>
<td></td>
<td>• Infliximab</td>
</tr>
<tr>
<td>Selective co-stimulation modulator</td>
<td>• Abatacept</td>
</tr>
<tr>
<td>B-cell inhibitor</td>
<td>• Rituximab</td>
</tr>
<tr>
<td>IL-6 Inhibitor</td>
<td>• Tocilizumab</td>
</tr>
</tbody>
</table>

IL-6, interleukin 6.

## Efficacy of Combination Therapy vs MTX Monotherapy

<table>
<thead>
<tr>
<th></th>
<th>MTX-Naive Patients</th>
<th>MTX-IR Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACR50</strong></td>
<td>Combination superior to MTX monotherapy</td>
<td>Combination superior to MTX monotherapy:</td>
</tr>
<tr>
<td></td>
<td>• Triple therapy (SSZ + HCQ)</td>
<td>• Triple therapy (SSZ + HCQ)</td>
</tr>
<tr>
<td></td>
<td>• MTX + biologics or tofacitinib</td>
<td>• MTX + HCQ, leflunomide, most biologics, or tofacitinib</td>
</tr>
<tr>
<td><strong>Inhibition of</strong></td>
<td>Combination superior to MTX monotherapy (except with tofacitinib)</td>
<td>No treatments clinically superior to MTX monotherapy (radiographic superiority for MTX plus biologic)</td>
</tr>
<tr>
<td><strong>radiographic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>progression</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MTX-IR, inadequate response to methotrexate.

## Comparison of DMARDs

<table>
<thead>
<tr>
<th></th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| **sDMARDs** | • Alleviate symptoms to some degree  
• Long track record of use | • May have lower efficacy  
• Tolerability  
• Toxicity concerns |
| **tsDMARDs** | • Target specific molecular structures  
• Oral bioavailability | • Less evidence about impact on long-term disease progression  
• Potential for immunosuppression |
| **bDMARDs** | • Potential for inducing and maintaining remission | • Shorter track record of use compared with traditional synthetic DMARDs  
• Potential for immunosuppression |

bDMARDs, biologic DMARDs; sDMARDs, synthetic DMARDs; tsDMARDs, targeted synthetic DMARDs.

# New and Emerging Agents for RA Treatment

<table>
<thead>
<tr>
<th>DMARD</th>
<th>Class</th>
<th>Agent</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>bDMARD</td>
<td>Anti-GM-CSF receptor</td>
<td>Mavrilimumab</td>
<td>Phase 2</td>
</tr>
<tr>
<td></td>
<td>Anti-IL-6</td>
<td>Sarilumab</td>
<td>Approved May 2017</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Olokizumab</td>
<td>Phase 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sirukumab</td>
<td>Phase 2</td>
</tr>
<tr>
<td></td>
<td>Anti-IL-17</td>
<td>Secukinumab</td>
<td>Phase 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ixekizumab</td>
<td>Phase 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Brodalumab</td>
<td>Phase 2</td>
</tr>
<tr>
<td>tsDMARD</td>
<td>JAK inhibitor</td>
<td>Baricitinib*</td>
<td>Phase 3</td>
</tr>
</tbody>
</table>

*FDA has extended action date to allow time to review additional data submitted in response to information requests. GM-CSF, granulocyte macrophage colony-stimulating factor.

Targeting IL-6: Sarilumab for Mod-to-Severe RA with Inadequate Response to MTX

*\( P < .0001 \) vs placebo plus MTX (results based on nonresponder imputation).

q2w, every 2 weeks.
Treatment with Sarilumab and MTX Reduces Signs of Radiographic Progression


*P<.001; †P<.01.
Secukinumab Reduces Disease Activity in Patients with RA and Inadequate Response to TNF inhibitors

Note: All footnote symbols above the lines indicate significant differences versus placebo at P≤.05.

Targeting JAK1/2: Baricitinib for Mod-to-Severe RA with Inadequate Response to Anti-TNFs

A  ACR20 response

B  DAS28-CRP

C  HAQ-DI

D  SDAI ≤3.3

*P ≤.05; †P ≤.01; ‡P ≤.001; §P ≤.001 for 4-mg dose baricitinib vs placebo

ACR20, improvement of at least 20% in both tender and swollen joint counts; HAQ-DI, health assessment questionnaire disability index.

Pharmacologic Management

Safety Considerations
Overview of Safety with Biologic and Nonbiologic DMARDs

<table>
<thead>
<tr>
<th>DMARD</th>
<th>Safety Concerns</th>
</tr>
</thead>
</table>
| MTX     | • Hepatotoxicity  
         | • Cytopenias  
         | • Pneumonitis                                                      |
| Anti-TNFs| • Increased risk of infection (including serious infections) by bacterial pathogens,  
|         | atypical fungi, and opportunistic pathogens  
         | • Reactivation of latent tuberculosis (screening is recommended)  
         | • CHF  
         | • Malignancy (evidence suggests no increased risk of solid tumors though nonmelanoma skin cancers are more common) |
| Tocilizumab| • GI perforation, transaminitis and hypercholesterolemia                        |
| Rituximab| • Progressive multifocal leukoencephalopathy                                    |
| Abatacept| • Pulmonary infection                                                          |

CHF, congestive heart failure.

## Comparison of Biologic Therapy vs Placebo

- Biologic therapy* vs placebo in patients with any disease except HIV/AIDS
- 163 RCTs (N=50,010; mean duration=6 months)
- 46 OLEs (N=11,954; mean duration=13 months)

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>NNTH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total AEs</strong></td>
<td>1.19 (1.09-1.30)</td>
<td>30 (21-60)</td>
</tr>
<tr>
<td><strong>Withdrawals due to AEs</strong></td>
<td>1.32 (1.06-1.64)</td>
<td>37 (19-190)</td>
</tr>
<tr>
<td><strong>TB reactivation†</strong></td>
<td>4.68 (1.18-18.60)</td>
<td>681 (143-14706)</td>
</tr>
</tbody>
</table>

- Serious AEs, serious infections, lymphoma,† and CHF† did not differ significantly between biologic vs control groups

*Etanercept, adalimumab, infliximab, golimumab, certolizumab, anakinra, tocilizumab, abatacept, and rituximab.
†Limited data.

OLE, open-label extension; OR, odds ratio; NNTH, number needed to treat to harm; RCT, randomized controlled trial; TB, tuberculosis.

Treatment of Early RA
Based upon Jane’s clinical profile, what initial treatment would you prescribe for her?

How do the relative safety concerns associated with the different treatment options impact your decision?

How would your treatment decision differ if she demonstrated signs indicative of poor prognosis (e.g., extra-articular symptoms) or a higher initial level of disease activity?
Treatment of Early RA

DMARD-Naïve Early RA

- Low Disease Activity
  - DMARD monotherapy
- Moderate/High Disease Activity
  - DMARD monotherapy

DMARD-Naïve Early RA

- Combination Traditional DMARDs or
- Anti-TNF ± MTX or
- Non-TNF Biologic ± MTX

Target Remission or LDA

Jane is initiated on oral MTX (10 mg/week) plus a folic acid supplement

What type of monitoring would you implement for Jane?

– How frequently would you recommend that she be reevaluated?
– At what point would you refer her to a specialist for follow-up?
Monitoring During sDMARD Treatment

Recommended Laboratory Monitoring Intervals for CBC, Liver Transaminase Levels, and SCr levels*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Monitoring Interval Based on Duration of Therapy†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;3 Months</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>None after baseline</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>2-4 weeks</td>
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<tr>
<td>Methotrexate</td>
<td>2-4 weeks</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>2-4 weeks</td>
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</tbody>
</table>

*More frequent monitoring recommended within first 3 months of therapy or after increasing dose, and the outer bound of monitoring interval is recommended beyond 6 months of therapy.

†Patients with comorbidities, abnormal laboratory results, and/or multiple therapies may require more frequent laboratory testing than generally for DMARDs in the table.

CBC, complete blood count; SCr, serum creatinine.

Defining Treatment Failure

- Inadequate initial response (primary treatment failure)
- Attenuation of response over time (secondary treatment failure)
- Definition of “inadequate response”
  - Clinical outcomes or ACR or DAS criteria
  - Radiographic disease activity
  - Patient-reported outcomes
  - QOL

Treatment of Established RA
Case Study 2: John, a 50-Year-Old Male with Established RA

- Overweight (BMI 29 kg/m2)
- Prediabetic (HbA1c: 6.5%)
- Previous diagnosis of RA
  - Persistent symmetric polyarthritis (synovitis) of hands
  - Progressive articular deterioration
  - Extra-articular involvement
  - Associated difficulty with ADLs
- Current medications
  - MTX
  - Sulfasalazine

ADLs, activities of daily living; BMI, body mass index; HbA1c, glycated hemoglobin.
How would you characterize John’s level of disease activity?

What alterations to his current treatment regimen would you recommend?
Treatment of Established RA

DMARD-Naïve Established RA

- Low Disease Activity
  - DMARD monotherapy

- Moderate/High Disease Activity
  - Combination Traditional DMARDs or
  - Anti-TNF ± MTX or
  - Non-TNF Biologic ± MTX
  - Tofacitinib ± MTX

DMARD monotherapy

Target Remission or LDA

Treatment of Established RA Following Single Anti-TNF Failure

- Single anti-TNF failure
  - Non-TNF biologic + MTX or anti-TNF + MTX
    - Mod/High Disease Activity
      - Non-anti-TNF biologic & anti-TNF failure
        - Other non-TNF biologic + MTX or Tofacitinib + MTX
      - Mod/High Disease Activity
        - Multiple anti-TNF failure
          - Non-TNF biologic + MTX or Tofacitinib + MTX

Treatment of Established RA Following Single Non-Anti-TNF Biologic Failure

Management of Comorbidities
Long-term Complications of RA

Dkk-1, Dickkopf-1 protein factor; HDL, high-density lipoprotein; HPA, hypothalamic–pituitary–adrenal; LDL, low-density lipoprotein; RANKL, receptor activator of nuclear factor kappa-B ligand; SERT, serotonin transporter.

Comorbidities of RA

- Cardiovascular disease
- Metabolic disorders
- Pulmonary disease
- Osteoporosis
- Malignancy
- Depression
Role of Inflammation in CVD

John: Case Study Discussion

- How is your treatment recommendation influenced by John’s risk for CVD?
- Is his prediabetic status also an influencing factor?
- What type of monitoring would you recommend for him and how often would you reevaluate him?
CVD Prevention in Patients with RA: Screening and Monitoring

- Consider RA as an independent CV risk factor
- Routinely screen for symptomatic and silent CVD
- Monitor modifiable CV risk factors annually and during intensified antirheumatic therapy, at least from 40 to 50 years of age
- Adjust intensity of monitoring according to CV risk
- Maintain a low threshold for cardiologic investigation (CVD clinical profile in RA may be atypical)
- Consider causes other than atherosclerosis (eg, vasculitis)

CV, cardiovascular.
Additional Strategies for Reducing CV Risk in Patients with RA

- Routine VS
- Lipid screening
- Screening and/or counseling for poor diet, physical inactivity, overweight, and stress
- Screening and/or management of psychosocial factors
- Smoking cessation
- Dental hygiene and treatment
- Vitamin D deficiency treatment
- Folic acid supplementation during MTX treatment
- Aspirin as recommended for general CVD prevention

BP, blood pressure; LDL, low-density lipoprotein; PG, plasma glucose; TC, total cholesterol; VS, vital signs.

Interstitial Lung Disease in RA

Predisposed host (HLA-DRB1 SE+)

Environmental/epigenetic factors

Lung injury/RA-ILD

Protein citrullination in the lungs

ACPA generation

HLA-DRB1 SE, human leukocyte antigen DRB1 shared epitope; ILD, interstitial lung disease.

### Clinical Factors Associated with RA-ILD

<table>
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<tr>
<th>Study</th>
<th>Age</th>
<th>Male sex</th>
<th>Later Onset RA</th>
<th>RA Duration</th>
<th>RF Titer</th>
<th>Anti-CCP</th>
<th>DAS 28</th>
<th>HLA-DRB1 SE</th>
<th>Cigarette Smoking</th>
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Considerations for RA Patients with High-risk Comorbidities

- Specialist collaboration and monitoring
- Management of polypharmacy
- Avoidance of anti-TNFs or other biologics depending on clinical circumstance

CHF
Hepatitis
Malignancy
Serious infections

Case Study: John’s Treatment Plan

- Based upon John’s current level of disease activity despite combined therapy with MTX and SSZ, along with his risk for CVD, he is switched to adalimumab (40 mg SC q2w)
- What type of monitoring, if any, would be appropriate for John given the switch to a biologic treatment? (ie, tuberculosis screening)

SC, subcutaneously.

Needs-based Patient Education in RA

- Consideration of patient beliefs
- Understandable information
- Frequent clinician-patient interaction

Needs-based Patient Education: Impact on Health Outcomes in RA


Note: Lower AIMS2-SF score indicates better health status.

*P=.013; †P=.006.
Summary

- Early diagnosis is crucial to achieving remission, preserving function, and preventing long-term complications in patients with RA
- Many efficacious disease-modifying treatment options are currently available and continue to emerge
- Patients being treated should be monitored for clinical and radiographic indicators of disease activity, and any adverse effects, as part of a treat-to-target algorithm
- Management strategies must take into consideration that patients with RA are at increased risk for comorbidities, especially CVD
- Optimal management of RA requires adequate communication and needs-based patient education to facilitate shared decision-making
Questions & Answers
Thank You!