Rheumatoid Arthritis: Challenges and Opportunities in the Evolving Treatment Landscape

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Therapy Selection for Patients with Rheumatoid Arthritis (RA)

- Disease duration*
  - Early RA: duration of disease/symptoms <6 mo
  - Established RA: duration of disease/symptoms of ≥6 mo

- Disease activity
  - Categorized as low, moderate, or high as per validated scales

*Denotes the length of time the patient has had symptoms/disease, not the length of time since RA diagnosis.

Therapy Selection for Patients with RA

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ACR, American College of Rheumatology; DMARD, disease-modifying antirheumatic drugs; MTX, methotrexate; TNF, tumor necrosis factor
Pathophysiology of RA and Targets for Biologics

OPGL, OPGL osteoprotegerin ligand; Th, T helper cell; TNF, tumor necrosis factor

Case Study: Janet

Personal and Family History

- Caucasian
- 42 years of age
- Family history of RA
- Diagnosed with RA at age 41
  - Moderate disease
- Initially started on MTX

Physical Exam and Lab Results

- BMI: 24 kg/m²
- BP: 130/82 mm Hg
- Sodium: 135 mEq/L
- Potassium: 4.3 mEq/L
- Blood glucose: 100 mg/dL
- A1C: 5.2%
- Hemoglobin: 13.6 g/dL
- Hematocrit: 40%
- RBC count: 5.03 million cells/mcL
- WBC count: 10,000 cells/mcL
- Platelet count: 280,000/mcL

BMI, body mass index; BP, blood pressure; RBC, red blood cell; WBC, white blood cell
Case Study: Janet (cont’d)

- Janet has had good resolution of her Clinical Disease Activity Index (CDAI) on initial MTX
- However, she now complains of increased pain and swelling in her joints
- There has been a gradual increase in her CDAI back to baseline levels
Disease Activity Measures

Clinical Disease Activity Index (CDAI)
Range: 0–76.0
Thresholds of disease activity
- Remission: ≤2.8
- Low: >2.8–10.0
- Moderate: >10.0–22.0
- High: >22

- Disease Activity Score with 28-joint counts (DAS28) erythrocyte sedimentation rate (ESR)
- Routine Assessment of Patient Index Data with 3 measures (RAPID3)
- Simplified Disease Activity Index (SDAI)

2015 ACR Recommendations for Established RA

- Moderate to high disease activity
  - DMARD monotherapy
  - TNF inhibitor ± MTX
  - Non-TNF biologic ± MTX
  - Tofacitinib ± MTX

- Continued disease activity
  - Add DMARD to monotherapy
  - Switch within TNF inhibitor class
  - Switch to non-TNF biologic or JAK inhibitor

- Disease remission
  - May consider tapering therapy on an individual basis

Monitoring and Follow-up

Active RA

Main Target*
Adapt therapy according to disease activity*
(Consider comorbidities and other patient factors)

Active RA

Alternative Target*
Adapt therapy according to disease activity*
(Consider comorbidities and other patient factors)

Use a composite measure of disease activity every 1-3 months

Remission
Assess disease activity about every 6 months

Low disease activity

Adapt therapy if state is lost*
(Consider comorbidities and other patient factors)

Sustained Remission

Sustained low disease activity

Adapt therapy if state is lost*
(Consider comorbidities and other patient factors)

*Shared decision with patient

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Monitoring and Follow-up (cont’d)

• Disease activity measures\(^1\)

• Laboratory follow-up\(^1\)
  – Complete blood count (CBC)
  – Liver transaminase
  – Serum creatinine

• Potential adverse events (AEs)\(^2\)
  – Biologics increase risk for serious infection

New and Emerging Biologic Agents

• JAK inhibitors\textsuperscript{1,2}
  – Tofacitinib JAK1/JAK3
  – Baricitinib JAK1/JAK2

JAK, Janus kinase; STAT, signal transducer and activator of transcription


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New and Emerging Biologic Agents (cont’d)

• IL-6/IL-6R inhibitors
  – Tocilizumab IL-6
  – Sarilumab IL-6R
  – Sirukumab IL-6

Case Study: Janet (cont’d)

• Inadequate response to initial MTX
• Receives TNF inhibitor in addition to MTX
• A few months later, Janet has:
  – Severe disease
  – Inadequate response to TNF inhibitor therapy
Considering Comorbidities

• Common comorbidities include renal dysfunction, diabetes mellitus, pulmonary disorders, liver dysfunction, and CVD\textsuperscript{1,2}
• Important not to exacerbate comorbidities with additional therapy and to ensure no new comorbidities have arisen\textsuperscript{2}

CVD, cardiovascular disease
Considering Comorbidities (cont’d)

The ACR recommends specific therapies for patients with certain high-risk comorbidities

• Non-TNF biologics or tofacitinib are preferred for patients with a history of or newly developed congestive heart failure (CHF)

• Abatacept or tofacitinib are preferred over TNF inhibitors for patients with a previously treated lymphoproliferative disorder

• Abatacept is recommended over TNF inhibitors for patients with a history of serious infection

• DMARDs/combination DMARDs are recommended over biologic agents for patients with CHF, hepatitis C, skin cancers, lymphoproliferative disorder, or a history of serious infection

Drug Selection

• In patients with insufficient response to TNF-inhibitor therapy, biologics that interfere with different target mechanisms are generally expected to be effective\(^1,2\)
  – However, all agents have lesser efficacy in TNF-experienced vs TNF-naïve patients

• Options include alternative TNF inhibitors\(^2\)
  – However, these agents seem to be less efficacious in RA patients who previously had inadequate response to TNF-inhibitor therapy compared with TNF-naïve patients

• JAK inhibitor (tofacitinib) may also be appropriate per the 2015 ACR recommendations\(^3\)

Monitoring and Follow-up (cont’d)

- Use of a validated composite measure of disease activity is needed in routine clinical practice to guide treatment decisions
- Measures of disease activity must be obtained and documented regularly, as frequently as:
  - Monthly for patients with moderate or high disease activity
  - About every 6 mo for patients in sustained low disease activity or remission
- Structural changes, functional impairment, and comorbidities should be considered when making additional clinical decisions
- Until the desired treatment target is reached, drug therapy should be adjusted at least every 3 mo

Key Takeaways

• The treatment of RA must be individualized
• The importance of disease activity measures (particularly the CDAI) in every RA patient at every visit cannot be understated
• Therapeutic decisions must be linked to disease activity scores
References