The iQ&A Interactive Medical Intelligence Zone for Rheumatoid Arthritis

Focus on Established and Novel Immune-Modulating Agents: Mechanisms of Action, Optimizing Efficacy, and Safety Considerations for Management of RA

An International Experts‘ Rheumatology Forum Focused on New Frontiers and Evidence-Based Therapy for Rheumatoid Arthritis

**Michael H. Schiff, MD**
Professor of Medicine
Rheumatology Division
University of Colorado School of Medicine
Denver, Colorado
Medical Director
Denver Arthritis Clinic Research Unit

**Question # 1:**
What is the rationale for, and what are the minimal triggers for initiating early therapy with DMARDs in rheumatoid arthritis?

**Question # 2:**
What should our therapeutic approach be to primary versus secondary non-responders who are failing with TNF-directed agents?

**Question # 3:**
What is the foundation role of the T-cell co-stimulation modulator, abatacept, across the risk spectrum of RA? And what do comparative trials vs TNF inhibitors teach us?

**Question # 4:**
How successful is switching from a TNF inhibitor to the T-cell co-stimulation modulator, abatacept? What do clinical trials and evidence show?

**Question # 5:**
What are the predictors of poor clinical response in patients with RA and how should we use these markers to trigger, switch, or accelerate biologic therapy?

**Question # 6:**
Are new, more sensitive modalities (MRI, ultrasound) available that can lower barriers to initiate or accelerate biologic therapy in RA?

**Question # 7:**
What is the most important performance gap in community-based care of patients with RA? Treat to target mandates?

**Question # 8:**
How aggressively and how quickly should we deploy biologic agents to achieve remission or low disease activity in patients with RA?
Yusuf Yazici, MD
Assistant Professor of Medicine
New York University School of Medicine
Director, Seligman Center for Advanced Therapeutics
NYU Hospital for Joint Diseases
New York, New York

Question # 9:
What are the key elements of the new European (EULAR) guidelines for treatment of RA, and what are the implications for use of T-cell co-modulating inhibitors?

Question # 10:
How long should biologic agents be continued in RA patients who have achieved remission? Should they ever be stopped?

Question # 11:
What are the implications of monitoring RA disease activity measures with objective scoring systems and clinical disease activity metrics?

Question # 12:
Despite the favorable legacy of TNF inhibitors for treating RA, based on the available evidence, how does this class compare to results reported for T cell co-stimulating modulating agents?

Question # 13:
Are there significant differences on the onset of action between TNF inhibitors and abatacept? What are the implications?

Question # 14:
What are the practical issues surrounding the use of infusions vs. subcutaneous injections for biologics, and how do you address them with your patients?

Question # 15:
Is there meta-analysis evidence to suggest different safety profiles/signal among biologic agents used for RA? TNF inhibitors versus T-cell co-stimulation modulators?

Question # 16:
Is there a subgroup of patients in whom biologic agents in the TNF inhibitor class should not be used, or would be considered problematic? Are there alternative biologic approaches?

Question # 17:
How long should we be treating RA patients with biologic therapy? Are there indications for drug cessation? If so, what are they?

Question # 18:
When in the natural “treatment history” of RA are changes in DMARD therapy usually made, and what switching strategies appear to be most effective and safe?

Question # 19:
What is the evolving role of MRI in RA management and treatment decisions?

Mark C. Genovese, MD
Associate Professor of Medicine
Co-Chief, Division of Immunology and Rheumatology
Stanford University School of Medicine
Palo Alto, California

Question # 20:
What are the core, first-line agents currently available in our biologic arsenal for RA?

Question # 21:
What are the therapeutic implications and strategies for managing RA patients who manifest an inadequate response to an initial biologic agent?

Question # 22:
What is the mechanism of action (MOA) for the T-cell co-stimulatory modulating agent, abatacept?
Question # 23:
What percentage of primary and secondary non-responders to TNF-inhibiting agents go on to respond to agents with alternative mechanisms of action?

Question # 24:
What future advances in RA therapy can we look forward to re: magnitude of clinical response, and percentage of patients responding to biologic therapy?

Question # 25:
Based on treat-to-target mandates for RA, what should we accept as a truly adequate treatment response in patients on biologic therapy for RA?

Question # 26:
Based on evidence available in landmark clinical trials, how do approach the problematic non-responder?

Allan Gibofsky, MD, JD
Professor of Medicine and Public Health
Weill Medical College
Cornell University, New York, NY
Attending Rheumatologist
Hospital for Special Surgery
New York, New York

Question # 27:
How are evolving guidelines for RA, as they relate to treatment target goals and other metrics, shaping our clinical decisions for RA?

Question # 28:
How should rheumatologists use the Clinical Disease Activity Index (CDAI) and Treat-to-Target goals to guide their therapeutic decisions?

Question # 29:
Based on the Treat-to-Target initiative for RA, how should we navigate among DMARDs and other treatment options for RA?

Question # 30:
What is the rationale for using an alternative mechanism of action (MOA), such as the T-cell co-stimulatory modulator, abatacept, following failure or poor response to a TNF inhibitor?

Question # 31:
How does T-cell co-stimulatory modulation/inhibition work to produce therapeutic effects in patients with RA?

Question # 32:
What are the efficacy and remission rates for T cell co-stimulatory modulators compared to other biologic agents?

Question # 33:
Is individualizing therapy for RA a reasonable goal and, if so, how do we get there?

Question # 34:
How should we employ objective metrics, including patient-report outcomes (PROs) to guide therapy in RA?

Question # 35:
What are the practical implications of the Treat-to-Target initiative for RA?

Question # 36:
What specific metric, clinical score, or structural marker should we be using to implement Treat-to-Target guidance?

Joel M. Kremer, MD
Pfaff Family Professor of Medicine
Director of Research
The Center for Rheumatology
Albany Medical Center
Albany, New York
**Question # 37:**
What is the evidence for early employment of DMARD therapy in rheumatoid arthritis?

**Question # 38:**
What is the currently approved armamentarium for RA therapy, including those biologic agents indicated for first-line therapy after poor response to methotrexate?

**Question # 39:**
How do you approach first-agent TNF failures and identify patients optimally treated with agents possessing alternative mechanisms of action (MOA)?

**Question # 40:**
Can you compare the side effect and adverse event profiles reported for the biologics, and identify any potential differences among the classes or specific agents?

**Question # 41:**
What aggregate or specific clinical criteria to you employ to accelerate and/or optimize therapy (i.e. Treat to Target) using biologic agents approved for RA?

**Question # 42:**
Based on clinical trial data, would we be wedded to TNF inhibitors as platform therapy for RA, if all the currently available agents had been evaluated, approved, and available simultaneously?

**Question # 43:**
What kind of clinical advances should we expect to see in RA management over the next few years?

**Question # 44:**
What is the mechanism of action for the Janus kinase (JAK) inhibitors?

**Question # 45:**
Can you explain the mechanism of action (MOA) for the T-cell co-stimulatory modulator, abatacept?

**Question # 46:**
What is the side effect and adverse event profile of abatacept, and how does it compare to other biologics used for RA?

**Question # 47:**
What in your view is the single greatest controversy surrounding RA treatment today?

**Eric Ruderman, MD**
Associate Professor of Medicine
Division of Rheumatology
Northwestern University
Feinberg School of Medicine
Chicago, Illinois

**Question # 48:**
Once the diagnosis of RA is confirmed clinically and/or with biomarkers, where should our initial therapeutic intervention be?

**Question # 49:**
What criteria should the rheumatologist employ to confirm there has been a methotrexate failure requiring intensification of therapy with a biologic agent?

**Question # 50:**
What classes of biologic agents are available for treatment of RA, and can you summarize their mechanisms of actions (MOA)?

**Question # 51:**
How should we be sequencing such biologics as the T-cell co-stimulatory modulators within the overall framework of RA therapy?

**Question # 52:**
How does identify poor clinical response (primary or secondary) to a biologic agent and what triggers do you employ for switching biologic agents?
Question # 53:
How long after initiating treatment should one expect to see a maximal clinical response with the T-cell co-stimulatory modulator abatacept?

Daniel E. Furst, MD
Professor of Rheumatology
Carl M. Pearson Chair of Rheumatology
Director of Interventional Therapeutics for RA
University of California
Los Angeles Medical Center for Health Sciences
Los Angeles, CA

Question # 54:
What are the various types of TNF failures and how should the type of TNF failure affect our clinical decision-making?

Question # 55:
What criteria should we employ to determine what alternative mechanism of action (MOA) we should employ following primary non-response to a TNF inhibitor?

Question # 56:
How should the side effect and adverse event profiles observed with TNF inhibitor guide our clinical decision-making for RA patients?

Question # 57:
What are the specific triggers and considerations rheumatologists should evaluate when intensifying or switching among biologic therapies?

Question # 58:
How many TNF inhibitors do you recommend cycling through before moving on to a T-cell co-stimulatory modulation agent?

Yvonne Sherrer, MD
Medical Director and Director of Clinical Research
Center for Rheumatology, Immunology and Arthritis
Fort Lauderdale, Florida

Question # 59:
How do we substantiate the diagnosis of rheumatoid arthritis?

Question # 60:
What is your approach to sequencing DMARDs in patients with RA? Where do you start? What do follow up with? When and how do you switch biologics?

Question # 61:
Based on what specific clinical responses, or lack thereof, do you add a biologic to methotrexate in poorly responding patients with RA?

Question # 62:
What is the current evidence-based role for biologic agents as foundation therapy for RA?

Question # 63:
What biologic agent do you first deploy in your RA patients? Why? And what response rates do you observe in your patient population?

Question # 64:
What is your strategy following an inadequate response or failure with a first TNF inhibiting agent? And what time frame do you use to judge failure?

Question # 65:
In practical terms and mechanistic terms, how do you employ a T-cell co-stimulating modulator such as abatacept for a TNF failure?

Question # 66:
What is your evidence-based rationale for escalating to a T-cell, co-stimulatory modulator after failure with a TNF inhibitor?
**Question # 67:**
Once started on a biologic agent, should RA patients be on them in perpetuity?

**Question # 68:**
What are the critical compliance and regimen adherence issues as they relate to biologic therapy for RA?

**Theresa A. Lawrence Ford, MD**
Rheumatologist
Lawrenceville, Georgia

**Question # 69:**
What do we and our patients gain from early, aggressive treatment with DMARDs and biologic therapy for RA?

**Question # 70:**
How should we administer methotrexate to achieve optimal clinical response, and how do we identify inadequate responders?

**Question # 71:**
What criteria do you use to accelerate therapy and/or switch from a TNF inhibitor?

**Question # 72:**
What are the target goals for using DMARDs in RA? ACR 20? CDAI scores?

**Question # 73:**
When and how do you measure whether a biologic is achieving treatment targets?