Current Rheumatoid Arthritis Treatment Options: Update for Managed Care and Specialty Pharmacists

1. Which of the following matches of biologic targets that contribute to rheumatoid arthritis (RA) and drugs that affect these targets is INCORRECT:
   
   A. Tumor Necrosis Factor (TNF) Alpha: Etanercept  
   B. Interleukin (IL)-2: Anakinra***  
   C. Immunologic B Cells: Rituximab  
   D. IL-6: Tocilizumab  

   **Answer B.** Anakinra blocks IL-1 not IL-2. The other choices are correct

2. The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) both recommend in their practice guidelines for RA that the goal with modern therapy should be which of the following:

   A. Avoiding all surgeries related to RA  
   B. Curing RA  
   C. Use biologic disease-modifying antirheumatic drugs (DMARDs) only as a last resort  
   D. Complete remission or low disease activity in all patients***

   **Answer D.** Both guidelines explicitly state that with modern DMARD therapy complete remission is an achievable goal for most patients. This does not mean patients may not require surgery for joint damage done prior to DMARD initiation or that remission is a cure. DMARDs can and should be considered earlier, especially in patients with poor prognostic factors.

3. Which of the following statements concerning methotrexate is correct:

   A. Folic acid supplementation reduces the effectiveness of treatment  
   B. Higher weekly doses may be more effective for the treatment of RA than lower weekly doses***  
   C. Methotrexate should always be used in combination with other DMARDs  
   D. Methotrexate can only be given intramuscularly or orally weekly
**Answer:** **B.** Recent studies have suggested that higher weekly doses may achieve higher disease remission scores than lower doses. Folic acid should be added to any regimen of methotrexate and does not impair effectiveness. Methotrexate can (and should) be used as monotherapy by many patients with RA and it can be given subcutaneously.

4. **Which of the following medications is recommended, in combination with methotrexate, according to the EULAR guidelines, to hasten time to symptom resolution if used for a short period of time:**

A. Lefunomide  
B. Sulfasalazine  
C. Hydroxychloroquine  
D. Corticosteroids***

**Answer D.** The EULAR guidelines specifically state that a short course of corticosteroids is reasonable to add to methotrexate. Although combinations of synthetic DMARDs have been shown to have a somewhat additive effect, only corticosteroids have been recommended to hasten symptom resolution.

5. **A patient was diagnosed last week with RA after roughly 1 month of progressive finger joint pain and low fever. Her rheumatoid factor is highly positive and she has a rheumatoid nodule on one finger. According to ACR guidelines, what DMARD regimen should she be started on?**

A. Methotrexate  
B. Methotrexate, Sulfasalazine, Corticosteroids, Hydroxychloroquine***  
C. Methotrexate and Leflunomide  
D. Methotrexate and Infliximab

**Answer B.** The ACR guidelines recommend triple therapy with synthetic DMARDs for patients first diagnosed with RA and poor prognostic signs (of which she has 2, positive rheumatoid factor and rheumatoid nodules). The largest study that examined this strategy also included a short course of corticosteroids with triple therapy, thus the correct answer is B.

6. **What is the major difference between the current ACR and EULAR guidelines as it relates to the initiation of biologic DMARD therapy?**

A. ACR suggests that biologic DMARDs should be initiated immediately upon diagnosis of RA; EULAR does not
B. ACR suggests that patients fail 2 synthetic DMARDs before starting biologic DMARDs; EULAR suggests that patients fail 3 synthetic DMARDs before starting biologic therapy

C. ACR suggests that patients with high disease activity after 3 months of treatment with methotrexate, should consider biologic DMARDs; EULAR suggests that an additional 3 to 6 months should elapse in order to discuss and prepare for biologic DMARD therapy

D. ACR suggests that infliximab is the preferred first biologic DMARD to use; EULAR suggests that adalimumab is the preferred first biologic DMARD

**Answer C.** The major difference between current RA guidelines is that EULAR suggests that an additional 3 to 6 months of treatment with methotrexate, or another synthetic DMARD, be considered before initiating biologic therapy. EULAR also recommends that, during this time, the benefits and risks of these drugs should be discussed.

7. Which of the following statements is TRUE regarding the use of anti-TNF biologic DMARDs for the treatment of RA:

A. One large meta-analysis suggested that etanercept may be better tolerated than other TNF biologics

B. Combination treatment with 2 TNF medications is a reasonable approach for patients who no longer respond to treatment with 1 TNF medication

C. There is no benefit to adding methotrexate to a treatment regimen for patients who have lost a response to TNF medications

D. Newer TNF medications, such as golimumab, are much less likely to cause infections compared with traditional formulations, such as infliximab

**Answer A.** A large meta-analysis, done in 2012, that compared trial data with all 5 available TNF medications in the United States did find that response rates for those with RA were relatively similar, but etanercept was less likely to be discontinued as a result of adverse effects compared with other TNF medications. Adding methotrexate is a reasonable approach to recapture patient response in patients who have lost response to a TNF medication, but combining 2 TNF medications has no additional benefit. All TNF medications pose a similar risk of infection.

8. A patient with severe RA has experienced treatment failure with several synthetic and biologic DMARDs, including etanercept, methotrexate, and rituximab. Her medical history is significant for hypertension and hyperlipidemia. Her rheumatologist is discussing tofacitinib therapy with the patient. Which of the following statements is TRUE regarding this case:

- A large meta-analysis, done in 2012, that compared trial data with all 5 available TNF medications in the United States did find that response rates for those with RA were relatively similar, but etanercept was less likely to be discontinued as a result of adverse effects compared with other TNF medications. Adding methotrexate is a reasonable approach to recapture patient response in patients who have lost response to a TNF medication, but combining 2 TNF medications has no additional benefit. All TNF medications pose a similar risk of infection.
A. Tofacitinib must be administered as a 4-hour intravenous infusion every 4 weeks

B. Tofacitinib seems to be more effective than TNF medications for the treatment of RA

C. Her cholesterol levels should be monitored closely while taking tofacitinib because it can raise these levels***

D. Serious infections have not been reported with tofacitinib

**Answer C.** Tofacitinib is a tablet that should be administered orally. In a large phase III study, this medication was shown to be about as effective as adalimumab (a TNF medication). During the study, 2 patients developed tuberculosis in the tofacitinib arm. This drug can increase cholesterol levels and because this patient already has hyperlipidemia, cholesterol should be monitored closely.

9. **A patient with moderate RA has been well controlled on etanercept for about 5 years, but has recently complained of an increase in her joint swelling, pain, and fatigue. Her rheumatologist would like to switch to another therapy to recapture her remission. According to a recent pharmacoeconomic study, which strategy would likely be the most cost-effective?**

A. Infliximab

B. Tofacitinib

C. Tocilizumab

D. Abatacept***

**Answer D.** A large pharmacoeconomic analysis has suggested that using abatacept after treatment failure with a TNF medication instead of cycling to another TNF medication, such as rituximab, was the most cost-effective approach. Both tofacitinib and tocilizumab have relatively little or no pharmacoeconomic data supporting their use for the treatment of RA.

10. **Which of the following statements concerning medication adherence for patients with RA is correct:**

A. A comprehensive medication therapy management (MTM) program has been shown to improve patient reported outcomes for those with RA receiving DMARDs***

B. As patients understand the consequences of nonadherence to medication regimens, rates of medication adherence for patients with RA becomes relatively high

C. Studies have found no modifiable risk factors that may improve adherence to medication for those with RA
D. MTM programs for patients with RA would only be cost-effective if delivered by a nonpharmacist health care provider

**Answer A.** A large MTM program for those with RA has been initiated by a pharmacy benefits manager and this program has effectively improved adherence and patient-reported RA outcomes. It has been proven that patients with RA exhibit poor adherence to prescribed medication regimens and, so, the lack of a belief in the need for medication has proven to be a strong risk factor for adherence. To date, the only data about MTM programs for patients with RA has been with pharmacists.