The Changing Landscape in the Treatment of Rheumatoid Arthritis: An Update for Pharmacists

EDUCATIONAL OBJECTIVES

Upon completion of this activity, participants will be better able to:

1. Evaluate current and emerging therapies used in rheumatoid arthritis (RA);
2. Describe the epidemiology of and risk factors associated with RA;
3. List specific adverse effects reported with RA therapy;
4. Recommend appropriate monitoring parameters for RA; and
5. Counsel patients on expectations of therapeutic benefits of different RA therapies.

Post-Test/Rationale:

1. Which of the following statements is TRUE regarding risk factors for rheumatoid arthritis (RA)?

A. Patients over 40 years old rarely develop RA
B. Women are more likely than men to develop RA***
C. Cigarette smoking has a neutral effect of the risk of developing RA
D. Patients with chronic obstructive pulmonary disease are likely to develop RA

Correct Answer: B
As with other autoimmune-type diseases, RA is more common in women, affecting them approximately three times more frequently than men. It usually begins in individuals between 25 and 55 years of age. Women who smoke cigarettes have a 2.5 times higher risk of developing RA than women who do not smoke. Patients with chronic obstructive pulmonary disease are not at increased risk for developing RA, but they may be at increased risk for adverse effects of certain medications used to treat RA.

2. What percentage of the United States population is thought to have rheumatoid arthritis?

A. 0.1%
B. 1%***
C. 3%
D. 5%

Correct Answer: B
Rheumatoid arthritis is a chronic inflammatory form of arthritis that affects approximately 1% of the population of the United States.

3. A patient with rheumatoid arthritis presents to your pharmacy with a new prescription for methotrexate. She mentions that her rheumatologist explained that he was using a treat-to-target
approach for her therapy, but she was a bit unsure of what that meant. Which of the following statements best explains this concept to her?

A. Treat-to-target means using frequent assessments and therapy adjustments to reach a goal of low or no disease activity***
B. Treat-to-target means using biologic disease modifying antirheumatic drugs in all patients to achieve disease remission
C. Treat-to-target means using aggressive therapy to achieve remission regardless of the safety profiles of the drugs used
D. Treat-to-target means asking the patient what therapeutic target he/she wants to achieve and then using therapies to achieve only that goal

Correct Answer: A
The central theme of treat-to-target recommendations is aggressive therapy that is frequently monitored with a goal of low or no disease activity in patients with rheumatoid arthritis. In other words, total remission of disease activity is the goal for most patients.

4. Which of the following is TRUE regarding synthetic disease-modifying antirheumatic drugs?

A. Vitamin D should be given to patients receiving methotrexate to prevent adverse effects
B. Sulfasalazine is not used in rheumatoid arthritis patients
C. The major toxicity associated with leflunomide is acute kidney injury
D. Hydroxychloroquine does not usually cause ocular toxicity at clinically used doses***

Correct Answer: D
Ocular toxicity has been reported with high doses of hydroxychloroquine, but this effect is rare at clinically used doses. Folic acid can ameliorate some of the side effects of methotrexate therapy. Sulfasalazine is included in a “triple therapy” approach to treating rheumatoid arthritis. Adverse effects of leflunomide include hepatotoxicity, pancytopenia, and agranulocytosis.

5. You sit on the Pharmacy and Therapeutics committee of a large pharmacy benefits management plan. In this role, you have been asked to review information about the tumor necrosis factor inhibitors (TNFis) for efficacy and safety and to choose a primary agent for formulary inclusion. According to a recent large meta-analysis in rheumatoid arthritis (RA), what conclusion is most accurate?

A. Approximately 50% of RA patients will achieve a 50% improvement in symptoms with any TNFi agent***
B. Only etanercept has been shown to halt joint destruction in RA patients
C. Golimumab should be reserved for patients who have failed previous TNFi therapy due to is poor safety profile
D. Only infliximab puts patients at risk of reactivation of tuberculosis

Correct Answer: A
A recent network analysis concluded that, regardless of the TNFi used with methotrexate, roughly half of patients can expect a 50% improvement in signs of symptoms of RA with the use
of any TNFi agent. All TNFis contribute to halting joint destruction. Tofacitinib should be reserved for patients who have failed previous TNFi therapy. All TNFis increase the risk of new or reactivated infection, including tuberculosis.

6. A rheumatologist approaches you for help in initiating a therapeutic drug monitoring program for her patients receiving infliximab for rheumatoid arthritis. Which of the following statements is TRUE concerning this subject?

A. No relationship between serum trough infliximab levels and effectiveness of the drug has been found
B. High levels of anti-infliximab antibodies have been associated with poor outcomes***
C. Serum peak and trough levels of infliximab must be used to calculate an appropriate dose
D. Infliximab is the only tumor necrosis factor inhibitor for which serum trough levels can be measured

Correct Answer: B
Therapeutic drug monitoring is an emerging strategy to appropriately dose tumor necrosis factor inhibitors (TNFis), particularly infliximab and adalimumab. Patients receiving infliximab may develop anti-infliximab antibodies (sometimes called human anti-chimeric antibodies, [HACA]). These antibodies develop in a significant minority of patients and are associated with both a loss of efficacy over time and an increased risk for adverse effects. Monitoring of serum trough levels (not peak levels) of TNFis and HACA levels are associated with prolonged efficacy of infliximab in rheumatoid arthritis patients. As testing for TNFi levels and antibodies becomes more widely available, pharmacists may assist in the interpretation of these values and corresponding dose adjustments.

7. Which of the following statements is TRUE concerning rituximab use in rheumatoid arthritis (RA)?

A. Studies suggest it is only effective in patients with a positive rheumatoid factor level
B. It needs to be given monthly to achieve successful results in RA
C. It may increase the risk of lymphomas in RA patients
D. Infusion reactions are the most feared adverse effect with this drug***

Correct Answer: D
Among the most feared adverse effects of rituximab are infusion reactions, which can be fatal. Rituximab is administered less frequently than other biologic disease-modifying antirheumatic drugs: patients usually only receive 2 doses per year of rituximab. Rheumatoid factor denotes general inflammation in many, but not all, RA patients. A recent review did not find an increased risk of solid tumor malignancies or lymphoma in RA patients receiving tumor necrosis factor inhibitor therapy.

8. Which of the following unique adverse effects has been reported for tofacitinib but not other biologic disease-modifying antirheumatic drugs?
A. Increased risk of bacterial infections
B. Reactivation of tuberculosis
C. Intestinal perforation**
D. Dyslipidemia

Correct Answer: C
The product information for tofacitinib lists intestinal perforation as a possible adverse effect that was reported in the Phase III studies of the drug, but the role of tofacitinib is not clear.

9. Baricitinib is a janus kinase (JAK) inhibitor in late-stage trials for rheumatoid arthritis. Which of the following statements concerning this drug is TRUE?

A. It is more specific for certain JAK pathways than tofacitinib***
B. Head-to-head studies between baricitinib and tofacitinib have found no clinical differences between the 2 agents
C. Baricitinib will be given subcutaneously, but tofacitinib is an oral tablet
D. Baricitinib should only be used with methotrexate

Correct Answer: A
Tofacitinib blocks JAK-1 and JAK-3 preferentially. Other JAK inhibitors being studied for rheumatoid arthritis include decernotinib and baricitinib, which are more selective for a single JAK isoform than tofacitinib. JAK inhibitors are given orally. Currently approved JAK inhibitors can be given with or without methotrexate.

10. A 54-year-old male with long-standing rheumatoid arthritis has failed multiple disease-modifying antirheumatic drugs for his disease. His rheumatologist is now considering starting tofacitinib. He has received all normal vaccinations for his age, with the exception of herpes zoster. His QuantiFERON-TB Gold-In-Tube is negative for tuberculosis. He has a family history of colon cancer but a screening colonoscopy was normal 4 years ago. Which of the following is MOST important to complete before proceeding with tofacitinib in this patient?

A. Hepatitis A screening
B. Herpes zoster vaccination***
C. Follow-up colonoscopy
D. Repeat tuberculosis testing

Correct Answer: B
The risk of herpes zoster reactivation is concerning with tofacitinib, with one trial finding twice the risk of this viral infection occurring with tofacitinib compared to other biologic drugs. Herpes zoster vaccination should be considered before starting tofacitinib therapy.