ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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Preparing for Biologic or Immunosuppressant Therapy

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G&H What factors should clinicians consider before initiating biologic or immunosuppressant therapy?

SVK First, clinicians should consider whether the patient's disease warrants such treatment: Is the patient sick enough that he or she needs biologic or immunosuppressant therapy? Also, is the patient healthy enough to tolerate these drugs? If the patient's disease makes him or her a good candidate for therapy, then clinicians should consider the patient's mindset and whether he or she will "buy into" the therapy. If a patient feels a therapy is too dangerous, he or she is likely to be noncompliant with the prescribed regimen, even if he or she does not directly express any objections to the therapy. Finally, the patient's economic status should be taken into consideration, as immunosuppressants and especially biologic agents can be very expensive. Depending on whether the patient has health insurance, clinicians may need to complete paperwork for the insurance company or research patient assistance programs for patients who do not have adequate insurance.

G&H When is use of biologic or immunosuppressant medications most appropriate? In which patients would you not consider these medications?

SVK Biologic agents and immunosuppressants are appropriate if patients have moderate-to-severe disease and have failed other standard therapies. These agents are also appropriate for patients who are steroid-dependent.

These agents are contraindicated in patients who have active, untreated infections; patients who have certain kinds of untreated cancers, including malignant melanoma, lymphoma, renal cell carcinoma, and possibly lung cancer; and patients who are being actively treated for certain kinds of tumors. In addition, biologic agents are contraindicated in patients who have uncontrolled heart failure or certain neurologic diseases, such as multiple sclerosis or an autoimmune neurologic problem. Immunosuppressants are contraindicated in patients who are already significantly immunosuppressed due to underlying conditions.

Finally, use of biologic agents or immunomodulators should only be considered if a recent evaluation has confirmed that the patient has active inflammatory bowel disease (IBD). A number of patients have pain and diarrhea, but some of these individuals may have irritable bowel syndrome or bacterial overgrowth. Likewise, patients who have pain, nausea, vomiting, and possibly diarrhea should be assessed for fibrostenotic strictures and are not candidates for biologic or immunomodulator therapy.

G&H What points should clinicians address when talking to patients about biologic or immunomodulator therapy?

SVK Clinicians need to explain to patients that their disease is aggressive and that their treatment needs to provide chronic immune suppression. The risks involved with these therapies should be discussed, but clinicians should also explain that, in the right setting, the benefit of these treatments can far outweigh the risks. Risks of biologic and immunomodulator therapy include infection, an immune-allergic phenomenon, anaphylaxis, and lymphoma.

When discussing the risk of lymphoma, clinicians should mention that this risk is equal for all agents in

a particular class, and that while all of these agents are associated with an increased risk for lymphoma, this risk is not as high as the risk of complications from untreated IBD. Finally, although the risk of lymphoma is 4 times greater for patients receiving these agents than for someone who is not taking these medicines, the absolute risk of lymphoma remains low in most patients.

One important point to note is that there is a much higher risk for certain kinds of lymphomas in males under the age of 30 years, and this risk seems to be even higher when these patients are receiving combination therapy. Unfortunately, clinicians cannot screen for this kind of cancer, so it is important to consider whether combination therapy is really necessary in these patients.

G&H Does pretherapy counseling affect the success of biologic or immunosuppresant therapy?

SVK Absolutely. If clinicians simply recommend therapy but do not talk to patients about the risks of treatment, then patients may not be properly adherent to therapy, which could increase their risk for adverse events. On the other hand, if patients receive proper counseling, then the risk of adverse events can be reduced. For example, if I tell patients that they are going to be at a higher risk for infections, then patients will be more vigilant about avoiding environments where they are likely to acquire an infection (such as a nursing home), less likely to visit someone who is known to be ill, and more vigilant about washing their hands. In addition, warning patients about the risk of infection may prompt them to call me sooner if they have a fever, instead of being admitted to the hospital 2 weeks later with a complication that might have been avoided. Similarly, explaining why biologic agents need to be taken on a regular basis can help to reduce patients' risk of immunologic reactions.

G&H Do patients need to be screened for latent infections prior to starting biologic therapy or immunosuppressants?

SVK Prior to starting biologic therapy, I screen patients for latent tuberculosis (TB), hepatitis B virus (HBV) infection, and usually hepatitis C virus (HCV) infection. Testing for TB and HBV is standard and should be performed in all patients who are preparing to start biologic therapy. There are no guidelines regarding HCV screening in this population, but testing is suggested. In addition, if a patient is having severe diarrhea, or diarrhea with fever and bleeding, then clinicians may want to check whether the patient is infected with *Clostridium difficile* or cytomegalovirus, as these infections could be driving symptoms in the absence of active IBD.

Appropriate screening prior to starting biologic therapy is very important, as reactivation of an infection could make the patient sicker. If a patient has recurrent TB, for example, administration of an immunosuppressant could exacerbate the infection and cause an overall worsening of the patient's condition.

G&H What can clinicians do before starting therapy to minimize the risks of side effects with biologic or immunosuppresant therapy?

SVK Discussing the therapy with patients and screening for infections are both essential steps. If counseling and screening are not performed before starting therapy, then the patient will not get the full effect of the drug, and the patient will also be at greater risk for adverse events. Patient education can consist of either a face-to-face discussion or the recommendation of educational materials that patients can study on their own. In addition to screening for infections, clinicians also need to make sure that patients do not have uncontrolled heart failure or neurologic disorders such as multiple sclerosis.

G&H Should clinicians perform any ongoing monitoring after therapy has been initiated?

SVK Gastroenterologists hold different opinions about the need for ongoing monitoring. For biologic therapy, there are currently no accepted monitoring guidelines. While some physicians feel that they need to do monthly blood work for these patients, I do not feel that such frequent monitoring is usually warranted. When a patient develops a new complaint, however, then a work-up is certainly necessary. There is also no set protocol regarding repeat TB screening, but my practice is to rescreen patients after 1 year if I plan to continue administering the biologic agent. Similarly, women who are sexually active should be monitored for human papillomavirus via Pap smear testing, and they should follow up with their gynecologist if the test shows an abnormal result.

For patients who are receiving immunomodulator therapy, frequent monitoring is necessary initially, but the frequency of monitoring decreases over time. Whether testing should be performed every month, every 6 weeks, or every 3 months depends on the clinician's comfort level and how he or she was educated. In my practice, we do blood work frequently within the first 2–3 months after starting a patient on an immunomodulator and every 3 months thereafter.

In the pediatric population, clinicians tend to perform blood work much more frequently, often on a monthly basis, regardless of which type of therapy the patient is receiving. Children are at a high risk for mal-

nutrition and growth retardation, so pediatric gastroenterologists strive to ensure that they are being sufficiently aggressive in eliminating inflammation; thus, they tend to treat patients aggressively and monitor them more closely.

G&H Overall, what are the most important steps clinicians should take to prepare patients for biologic or immunomodulator therapy?

SVK First, clinicians need to make sure that they have identified the right patient for the drug. Many patients have irritable bowel syndrome or a known stricture, but they are prescribed a biologic agent anyway; in these cases, patients are being exposed to all of the drug's risks and getting none of its benefits. Once the clinician has decided that a patient truly has active IBD, then he or she needs to educate the patient about the risk-to-benefit profile of the drug. Part of the educational process is to explain all the therapeutic options that are available; in addition, patients need to understand that the goal of biologic or immunosuppressant therapy is to make them feel better, that steroids and narcotics are associated with worse outcomes if they are used long term, and that withholding therapy and allowing the disease to remain active leads to worse outcomes.

Suggested Reading

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