



Highlights from the IG Living Teleconference, February 21, 2018

Topic: Immune Globulin (IG) Updates for 2018 and General IG Questions

[This is an edited version of a live teleconference presentation.]

Guest Speaker: Leslie J. Vaughan, RPh, Senior Vice President of Clinical Programs, NuFACTOR Specialty Pharmacy

There's not a tremendous amount that's new today. However, there are a couple of things in the works with a couple of different IG brands that are being studied. We are expecting the announcement of two new subcutaneous IG (SCIG) products in 2018. There is an additional 5% product expected. Additionally, several manufacturers of current products are conducting disease-state specific studies. For instance, we're expecting an indication for an SCIG product to treat CIDP. And, several studies are being conducted in a variety of disease states, including myasthenia gravis and dermatomyositis. One manufacturer is even looking at utilizing intravenous immune globulin (IVIG) to treat some of the more rare autoimmune disorders such as encephalitis and PANS/PANDAS. As such, we have high hopes we're going to see a lot of advancement of indications in 2018 and some new products being released.

On the more distant horizon, there is a new grant that is being used to study the use of recombinant technologies to generate an antibody-specific type of IG. As most of you know, IG has a broad group of antibodies, so it doesn't target one specific antibody that might cause a condition. A recombinant IVIG (rIVIG) product, however, could be made with a specific antibody to product a lot of smaller rIVIG products that target particular disease states. In addition, those products could potentially reduce side effects cause by IG products produced with human plasma donations. Again, though, a rIVIG product is fairly far on the horizon.

Following are some answers to specific questions in general about IG:

Monitoring

What is the difference between blood pressure monitoring during IVIG vs. SCIG therapy?

Blood pressure is a common measurement during IVIG so that it doesn't become too elevated, which can increase the risk of serious side effects such as stroke. Most infusion centers have their own protocols on how blood pressure is monitored. Typically, blood pressure is taken before the infusion is started and is monitored with each ramp-up. So, if the infusion is started at a low rate and ramped up every 15 to 30 minutes, the nurse should check blood pressure before each ramp-up. Once the maximum tolerated infusion rate is reached, the nurse should check blood pressure every 30 minutes or every hour to be sure it's not elevated or it hasn't decreased too much. This is different with SCIG because it is typically self-administered at a much lower dose, so there is much lower chance of blood pressure issues.

Chronic Inflammatory Demyelinating Polyneuropathy (CID)

1) How does CIDP continue to progress? Does myelin ever regenerate?

Unfortunately with CIDP, patients have antibodies that are attacking the myelin sheath. The sheath doesn't regenerate once it has been restored. However, the good news is there are studies underway at Mayo Clinic and Cornell University evaluating therapies to help regenerate myelin.

If myelin doesn't regenerate, and a patient continues to have antibodies, CIDP can progress. Therefore, the goal of IVIG therapy is to make sure antibodies are in control to ensure patients improve. With IVIG, it's not necessarily that myelin is regenerating, but patients do have some reinnervation of nerve function.

2) Can diet help with CIDP?

Certainly. There's not a specific diet recommended. But, any time there is a chronic illness, a healthy diet will help with the disease state.

3) Has IVIG ever stopped being effective for CIDP?

Patients can be responsive to IVIG for many years, and then experience demyelination causing secondary axonal loss. When this happens, IVIG might start to lose its effectiveness requiring a higher dose or more frequent dosing.

4) Will stem cell replacement work for CIDP?

Right now, stem cell replacement is investigational. There is a current clinical trial at Northwest University that has 80 participants. But, no results are posted yet. We're all keeping our fingers crossed for a positive outcome.

5) Are there any new drugs on the horizon for CIDP?

There may be. There are some studies using disease-modifying drugs that are used for other types of immune conditions such as multiple sclerosis, which is also a demyelinating disease. Right now, there are no new drug indications, but there is definitely research underway. Many institutions are studying Rituxan (a monoclonal antibody) to see if it will help control CIDP and slow its progression.

Dosing

1) What is the right dose of IG, and how is it determined?

For disease states that have an FDA indication, the package insert shows the FDA's approved dosing regimen. For instance, for primary immunodeficiencies (PIs), it's a fairly broad dosing indication, and each package insert has its own dosing. But, typically, dosing is usually from 300 mg/kg to 800 mg/kg every three to four weeks. For CIDP, the approved dosing is 3 g/kg for the loading dose following by 1 g/kg every three weeks as a maintenance dose. For multifocal motor neuropathy (MMN), it's a little bit different because it's even broader than PI. Dosing for MMN is from 0.5 g/kg up to 2.4 g/kg on a monthly basis as the patient responds to therapy.

So, most physicians will start with package insert dosing recommendations and then evaluate how the patient is responding to therapy and then adjust accordingly. For PI patients, monitoring immunoglobulin levels is helpful, but that's not the sole basis for dosing. Rather, it's mostly whether the patient is having the expected response, which means they are getting sick less frequently and, when there is sickness, it is less severe than before starting treatment. For autoimmune diseases, physicians are looking for improvement in presenting symptoms. For instance, with CIDP, they are looking for improvements in weakness.

Hydration

1) Is it OK to run IVIG and normal saline concurrently vs. running them separately?

There are two ways to look at this. Hydration can help with side effects. Unfortunately, we're faced with a national shortage of hydration solutions. For instance, one manufacturer, Baxter, has a plant in Puerto Rico that, due to the hurricane, is not fully functional yet. Therefore, a lot of patients are asking to orally hydrate rather than getting intravenous hydration.

It is OK to concurrently hydrate with saline while infusing IG, as long as the saline and IG are being run through a separate infusion line. They should not be run through the same infusion line because there is a bit of an incompatibility.

While the incompatibility is not horrible, normal saline can cause the IVIG to form dimers that can make side effects worse. It's preferred that the saline be given before or after infusion of, if during the infusion through a separate infusion line. If there is a need to run the hydration solution through the same line, the only compatible solution is dextrose 5% in water.

IVIG vs. SCIG

1) Is SCIG as effective as IVIG?

Yes. The nice thing about SCIG is it is infused in smaller doses more frequently, so there are fewer side effects. Patients might experience local side effects, but there are fewer side effects such as headaches, nausea, chills and fatigue. On the other hand, the nice thing about IVIG is the full dose is received right away so IgG levels go way up, which great for PI and autoimmune conditions.

For autoimmune conditions, patients receive a large dose of IVIG and it binds up all antibodies fairly rapidly, versus smaller doses over a period of time. Interestingly, as noted earlier, we are expecting the first SCIG indication for CIDP. In the comparison trial of SCIG for CIDP, researchers found patients receiving SCIG did as well as those who received IVIG.

2) Is there a similar product to HyQvia that could be given once a month?

No. The only product indicated for once-monthly subcutaneous infusion is HyQvia. The reason it can be given in a large dose once a month is it is combined with another product called hyaluronidase that loosens the skin so it can take in a much larger volume of product. No other products have that additional product.

Shortages

Are there any current IG shortages?

We haven't seen shortages like we did 20 years. Currently, things are stabilizing, but there are definitely shortages. While we may be able to get product, sometimes we can't get it in the exact vial size we are looking for. For instance, if the dose is 20 grams, a 20-gram vial may not be available so we may have to prescribe four 5-gram vials. But, for the most part, IG products are relatively stable. One exception to this is Carimune (that is typically infused in a doctor office setting or hospital setting), which is on strict allocation right now. *[Editor's note: CSL Behring just announced it will discontinue the production of Carimune NF (immune globulin [human] nanofiltered) in the third quarter of 2018 due to the preference among healthcare professionals and patients for newer, more advanced immune globulin options.]*

The other shortage pertaining to IG is hydration solutions that are very difficult to obtain.

Side Effects

What are the side effects of IG, and how are they minimized?

Most common side effects with IVIG are headache, chills, nausea, rashes, back pain or leg pain. It runs the gamut, but headache is the most prevalent. With SCIG, the side effects are mostly local. The location of the needle set where the IG is administered can cause a large bump that is painful or swollen. But, local side effects tend to decrease over time.

There are ways to mitigate IVIG side effects. Hydration is best way. Patients should maintain good oral infusion before, during and after infusion. They should increase the amount of water they are drinking. Water is the best source. Stay away from caffeinated drinks that have a dehydration effect. Some sports drinks contain salt or electrolytes, so while it may be OK to add a little bit of those, it's best to hydrate with water.

There are other things patients can do to mitigate side effects. They can talk to their physician and pharmacist about taking premedications such as Tylenol, Benadryl and ibuprofen, which can mitigate side effects before they start. To reduce side effects during the infusion, the rate of infusion can be slowed down. If patients start to feel a headache coming on or if they just don't feel well, they should talk to the nurse about slowing the infusion rate. If side effects don't stop even with slowing the rate, the infusion should be stopped completely to see if the side effects go away and then restarted at that slower rate. If patients who receive their dose over several days experience really bad side effects on day two or four, they can try to infuse on nonconsecutive days to give their body some time to adjust.