



## Coping with 3F8 Antibodies

There are currently several clinical trials using intravenous 3F8 monoclonal antibodies being conducted at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City. Factual information about the purpose and scientific aspects of 3F8 treatment, and its role in various frontline, refractory, or relapse treatments, will be discussed elsewhere in this Handbook. The focus of this section is *coping with the side effects* of 3F8 treatment.

Regardless of which clinical trial a child is treated on, the side effects of 3F8 protocols are similar and are managed in the same ways. (Intrathecal 8H9 treatment is discussed separately in another section of this chapter.)

### **How is 3F8 administered and how long does it take?**

Ten to twelve children receive 3F8 treatments each week -- one group in the morning and another group in the afternoon. Antibody treatments are administered in a series of adjacent one- and two-patient rooms in the bed area of the MSKCC Pediatric Day Hospital (PDH). Patients who do not have a port or central line receive the treatments through a peripheral intravenous catheter (PIV) which is inserted for the week. As PIVs are not as stable as central lines, it is possible that the child will need it replaced.

Actual administration of the treatment takes about 90 minutes: 30 minutes for pre-meds, 30 minutes to administer the antibody, and 30 minutes for a flush. Patients often sleep for a few hours afterwards, so a child could be in the clinic anywhere from 3 to 6 hours.

On a typical treatment day, patients arrive at about 8:30 a.m. if they are on the "first shift" or 11:30 a.m. if they are on the "second shift" for antibody treatments that week. If you prefer to be on the earlier or later shift, let the staff know. Although they may not be able to accommodate your request that week, adjustments can usually be made for future rounds of treatment.

After checking in at the front desk, patients usually go to the area outside the IV room and wait to be called for a finger stick or other lab draws. After any required blood work is completed, patients may be "hooked up" to pre-treatment hydration, but they are usually free to stay in the clinic playroom or waiting area, attend class in the clinic school, or even go to the cafeteria while the fluids are running. Patients on 3F8 trials using GM-CSF may receive the shot at this time if they have not received it before coming to the PDH.

Patients are called to the bed area when it is time to administer pre-treatment medications. It is a good idea to have your child use the restroom before the pre-meds are administered, as some children feel a strong urge to urinate during the actual 3F8 treatment.

Once all of the pre-meds have been administered, a pre-treatment dose of pain medication is administered before the 3F8 infusion begins. The infusion begins when the research nurse pushes the syringe of 3F8 antibodies into the IV soluset, mixing it with saline solution. Often the patient is situated comfortably, watching TV or otherwise distracted, so the nurse may let the parent know the infusion is starting without announcing it to the child.

At sometime during the infusion the child will begin to experience pain and possibly other side effects (see discussion below). Because every child's experience is different, it is imperative that a parent stay with the child, since parents know their child best and can pick up on early signs of distress.

When the infusion and flush are finished, the treatment itself is complete. Patients usually are in a drug-induced sleep for a while after treatment as a result of the pain and allergy medications received. During the rest time after treatment, nurses continue to monitor the child for any adverse or late effects of the treatment. Patients are not released to leave the PDH until the medical staff is satisfied that they no longer need medical supervision.

### **What are the side effects of 3F8?**

Although there definitely are side effects, these have all been short-lived, lasting (with rare exception) only during the week of the treatment. The common side effects are described below.

#### ***Pain***

The most common and pronounced side effect of 3F8 is pain, which is controlled with narcotics (dilaudid or morphine) (see below). Pain occurs because the 3F8 antibody attaches to the GD2 antigen found on the surface of neuroblastoma cells. However, the GD2 antigen is also found on some normal nerve cells. When the antibody attaches to the GD2 antigen on a nerve cell, a message is sent to the brain, and the patient feels pain.

For most children the pain is severe, at least in the early rounds of treatment, and witnessing a child in pain can be extremely difficult for parents. As with everything in neuroblastoma treatment, the degree of pain experienced varies with each child. Many a mother watching her child experience 3F8 treatment has concluded that the pain seems similar to the pain of childbirth—although fortunately of much shorter duration--yet other parents have observed, “it’s really not that bad.”

Most patients seem to experience pain during the “flush” received during the last 30 minutes of the 90-minute treatment. However, for some the pain may start at the very beginning of the 3F8 infusion, and others may not experience pain until after the infusion is completed. The pain is generally localized to a certain area, such as the back, neck, abdomen, arms, hands, legs, knees, feet, or ankles, but some patients feel pain in more than one place. The pain tends to last 20-30 minutes for many patients, but other patients, especially older ones, continue to have residual symptoms of pain into the evening hours, often localized in hands, feet, knees, back, or other places. In general, the residual pain seems more severe for teenagers and young adults. If it is a continuing problem, additional medications can be prescribed.

Recovery time varies from patient to patient. Although some will sit up and feel totally recovered shortly after completing the treatment, many others, depending on the amount of pain medication, will sleep for an hour or so afterwards. Some parents find this an excellent time to crawl into their child’s treatment bed to provide physical comfort and catch a nap themselves. Most patients will have some after-effects from the pain medications when they awake, and young children will generally be “fussy” and/or demanding until it wears off, so the after-treatment rest time provides a good opportunity for parents to recharge their own reserves. Some patients are back to normal by early evening, whereas others have residual pain and/or moodiness until late in the night. Many children do not remember the pain and return cheerfully to the clinic for the next day.

#### ***Allergic Reactions***

The second most common side effects are allergic reactions, usually hives, with or without itching. This side effect is controlled with Benadryl (diphenhydramine) or Vistaril (hydroxyzine).

From time to time, children have been known to experience hives in the mouth or throat that cause swelling and result in breathing difficulties. All patients receiving 3F8 wear a pulse-oximeter to measure oxygen absorption. If a child’s oxygen level drops, oxygen is on hand to be administered if needed.

As frightening as these rare events are, they can usually be resolved in the outpatient clinic, although sometimes a patient will be admitted to the hospital for overnight observation. In very rare

cases, a reaction is life-threatening and the doctors conclude that the risks of continuing treatment outweigh the benefits.

### ***High Blood Pressure***

Children can also experience high blood pressure during and, very occasionally after, 3F8 treatment. High blood pressure is usually caused by increased heart rates that are a normal response to pain. Blood pressure is monitored periodically throughout the 3F8 treatment and afterward, and patients are not released from clinic until their vital signs are within normal ranges.

### ***Fever, Vomiting, Intestinal Distress***

Patients may experience these side effects in varying degrees during treatment. Fever can be concerning if the patient has a central line or port, as it can be difficult to determine if the fever is treatment related, or a result of blood-borne infection. Blood cultures may be drawn and parents may need to watch the child closely after treatment and notify the clinic if fever returns. Aloxi (palonosetron) or Zofran (ondansetron) are usually administered before treatment to prevent nausea. Some children experience diarrhea, which generally resolves after treatment, while a few others have had difficulty due to the constipating effect of the pain medications used.

There is no denying that 3F8 is a difficult treatment. Yet few patients object to returning the next day for treatment. In comparison to the pain, nausea, neuropathy, and debilitation of chemotherapy treatments, most children and parents seem to find 3F8 considerably more manageable.

### **More on Managing Pain and Other Side Effects of 3F8**

Naturally it is difficult going into a treatment for the first time knowing it will be painful, yet not knowing specifically what to expect.

MSKCC employs specially trained nurses that administer the antibody treatments, and the clinic nurses are very experienced in caring for patients receiving antibodies. Before beginning the infusion, each patient receives an antihistamine for allergic reactions (Benadryl or Vistaril), an antiemetic for nausea (Aloxi or Zofran), Tylenol for fever, and, just before the infusion, a narcotic (Dilaudid or morphine) for pain. Some children also receive Ativan to relieve any anxiety. Children that seem prone to breathing difficulties may receive a nebulizer treatment with Xopenex (levalbuterol) to relax and open up the airways before receiving 3F8.

At the first indication of pain, a “rescue” dose of the child’s most effective painkiller—already drawn up and waiting at the bedside—is administered. Additional rescues of pain medication are available to be administered at 10 minute intervals if needed, up to a maximum of 5 during the infusion and flush. It’s generally important to administer a rescue at the first indication of pain, otherwise the pain can be difficult to control.

Unfortunately it is difficult to manage the child’s pain as effectively during the first few 3F8 treatments, because everyone is learning—the patient, medical staff, and parents—how the child reacts to treatment and what medicines and other measures are most effective in bringing relief. However, often a pattern emerges in later rounds of treatment that allows parents and staff to quickly address the child’s needs.

In addition to medications, there are a number of non-medicinal palliative measures that may be used to relieve or lessen the side effects of 3F8 treatment. Each family will learn through trial and error which techniques work best for their child. For example, some find applying ice packs helps with the pain, while others prefer heat packs. Some children will use both ice and heat at different stages of the treatment.

Distraction can be effective for some children, who simply prefer to watch TV. Teens may opt to listen to a favorite CD or their iPod during treatment. Other children like the feel of the cool air from

the blow-by oxygen on their face, while still others may use massage or guided imagery to take their mind off the physical experience.

There are several complementary techniques available through MSKCC's Integrative Medicine Service for addressing the pain of antibody treatment. Success usually depends on a patient's (or parent's) willingness to try these approaches with an open mind. Families interested in complementary approaches can ask a nurse practitioner, one of the research nurses, or the Child Life staff for information on available options. The integrative medicine department will set up a time to teach visualization to the patient. All integrative medicine services are free of charge.

After a round or two of treatment the pain is almost always more manageable, because the child and the parents know what to expect, and because the parents and the medical staff have learned what techniques are best for managing the individual child's side effects. While some parents have observed that pain definitely diminished over the course of numerous rounds of 3F8, others have seen a less marked difference.

Once the last day of a week of 3F8 treatment is completed, it is extremely rare for a child to have any side effects. Blood counts are generally not affected, though children may lose a bit of weight if they do not eat much during the week of treatment. However, no long-term effects from 3F8s have been seen over the past twenty-plus years.

### **Anxieties over the Presence/Lack of Pain and HAMA**

As hard as it is to watch one's child in pain, most parents *want* their child to have pain through at least four cycles of 3F8 treatment, to get the most benefit from the antibodies before the body forms the immune response known as Human Anti-Mouse Antibody (HAMA) that blocks the effect of the treatments. You will hear parents and sometimes even nurses discussing the fact that if the child is experiencing pain, then he is *not* forming HAMA—or if the child is experiencing *no* pain, then the child *may be* forming HAMA. However, it seems that there simply is no single rule. While it is true that patients with an existing HAMA do not have pain during 3F8 treatment, nonetheless, patients *without* side effects sometimes do *not* develop HAMA, and patients often *do* form HAMA during a round of 3F8s in which they *did* have pain.

Try not to agonize over whether your child is having too little or too much pain, and try to resist the temptation to compare your child's experience with others. Every child is different, and there appears to be no correlation between long-term survival and the degree of pain experienced, or the lack thereof, during antibodies.

Generally one or more of the NB doctors makes rounds of the 3F8 treatment rooms and speaks individually with each family, at least once during the 3F8 treatment week. In addition to any scheduled meetings with the docs, this tends to be a good opportunity to ask questions about the 3F8 protocol and discuss your child's case with one of the NB doctors—the only ones other than you who understand all the facts of your child's particular case and his or her 3F8 history.

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