Disclaimer: These responses are for general informational purposes only. These responses are not intended to be a substitute for medical advice,diagnosis or treatment by a physician who is aware of your medical history and has had an opportunity to examine you. Do not rely on these responses in place of seeking professional medical advice.

Question: How are the trials with Rapamycin and Gleevec progressing?

Answer: Rapamycin is being tested as a drug treatment for plexiform neurofibromas in a Phase II trial. This has been one of the first clinical trials commenced through the Department of Defense Congressionally Directed Medical Research Program for Neurofibromatosis (CDMRP NFRP). Nine clinical centers across the country have participated. This trial recruited all of the patients it needed quite quickly, and the study is now in late stages. We are hoping that the results of the trial will be available soon, certainly by spring 2011.

Gleevec is being tested as a drug treatment for plexiform neurofibromas in a Phase II trial. This study began a couple of years ago at Indiana University and has recently expanded to other centers. The results have not been published but we have heard that it looks promising at least in some patients. If you are interested in participating in this trial you can find more information here
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Question: Are there any studies that show vitamin D might be harmful to people with NF?

Answer: People with NF1 seem to metabolize Vitamin D differently than the rest of the population. The result is that individuals with NF1 effectively can have a Vitamin D 'deficiency' in the body, even if they are taking normal doses of Vitamin D (in food and supplements). The

main negative effect of this is believed to be detrimental effects on bone health. Bone is a tissue that turns over throughout life and it needs Vitamin D to do maintain healthy. The good news is that ongoing studies are pointing to the possibility that individuals with NF1 who take additional high amounts of Vitamin D supplements see a positive effect on bone health. There is no evidence that Vitamin D can be harmful for someone with NF1.

Question: How is NF related to mental & emotional challenges?

Answer: There is a well established link between NF1 and cognition problems (learning disabilities), as around two-thirds of individuals with NF1 will have some form of learning disability ranging from mild to severe. In the last few years doctors have started gaining a better understanding of the range of mental and emotional issues that can occur in NF1. It is emerging that individuals with NF1 can develop a broad spectrum of mental problems that can include, for example, elements of attention deficit and hyperactivity disorder or autism. In positive news from clinical trials, Lovastatin looks promising as a treatment for NF1 learning disabilities; and doctors are now bringing in further drugs for testing that have previously been used in ADHD or other conditions. The more we can learn about connections between NF1, ADHD, autism and other conditions, the faster we can identify new drugs to treat this.

Question: What are the dangers of birth control for women with NF? Are there any issues that may be more difficult for women with NF1 during the menstrual cycle?

There is some evidence that NF tumors can grow in response to major hormonal fluctuations in women. For this reason doctors will monitor women with NF1 particularly closely in puberty and pregnancy. Birth control is essentially a type of hormonal fluctuation; however there is no firm evidence that birth control promotes tumor growth. Women with NF1 will, however, have the same risks as women in the general population do in taking birth control; so for example if you have elevated blood pressure or other cardiovascular problems, you should discuss the risk with your doctor before commencing birth control. Women with NF1 should not face any further challenges during menstruation than women in the general population unless specific manifestations of NF are causing problems, e.g. a plexiform neurofibroma growing on the uterus or cervix causes additional discomfort or issues. Every case will be different, and it is critically important for every woman with NF1 to discuss all issues relating to their case of NF1 with their OB/GYN.

Question: Is there an NF sleep pattern that is unique to NF?

Answer: Disrupted sleep patterns in children with NF1 have been reported in at least one clinical study. Also, interestingly, if you delete the NF1 gene function in flies, the flies show disrupted circadian rhythm (sleep patterns). Unfortunately not much work has been published in this area.

Question: What is the relationship between NF and other cancers?

Answer: The cell signalling pathways that are disrupted in NF are also disrupted in a number of cancers. In fact, the NF1 gene is actually mutated in a number of cancers, including lung cancer. The good news is, this means NF can potentially benefit by drawing on what is learned from the development of treatments for other cancers, and see if any of those treatments could also be used in NF.

It is important to note that though NF is caused by mutations in what are called 'tumor suppressor genes', most cases of NF are NOT cancer. Cancer is defined as a malignant condition; in NF, this would include any tumor that transforms from benign to malignant, such as MPNSTs which can occur in NF1.

Question: What is the advantage of having a volumetric magnetic resonance imaging (MRI) verses a regular MRI? Should I be looking for a facility that offers volumetric MRI?

Answer: Volumetric (three-dimensional) MRI has been pioneered for use in NF really only in the past few years. It requires a 'recalibration' of the way doctors think about changes in tumor size and what they mean – for example a tiny change seen in regular MRI (two dimensions) might appear as a 300% change in volumetric MRI, but the clinical significance may be the same – it is just that volumetric is more sensitive. However, volumetric MRI does have advantages over regular MRI for large or complex tumors, especially those that may be infiltrating organs, and are hard to accurately measure in two dimensions. Volumetric MRI also has high value in NF clinical trials as it is a sensitive way to measure change in tumor size/response to drug. Volumetric MRI is gradually being introduced into standard NF clinical care. One of the main centers doing this routinely, at Harvard/ MGH, will accept scans from

around the country for analysis, and has been trying to overcome all of the challenges associated with insurance coverage. In 2011, CTF hopes to expand the MGH service through our NF Clinic Network to cover the cost for clinics to submit scans of complex NF cases to MGH for analysis.

Question: Is there any proven chemotherapy or radiation treatment that can have treat neurofibromas?

Answer: It is now recognized that chemotherapy is not the best treatment to use for the majority of NF tumors. Chemotherapy is used in cancer because it targets the tumor cells that are dividing rapidly. (This is why people on chemotherapy can also lose their hair and suffer from gastrointestinal problems, because both hair follicles and the GI tract lining are made up of rapidly dividing cells). The majority of NF tumors (including NF1 plexiform neurofibromas and NF2 vestibular schwannomas) are actually quite SLOW growing. However chemotherapy can be used as a therapy in NF tumors that have undergone malignant transformation - e.g. NF1 MPNSTs. However as candidate drugs emerge, more and more individuals with NF1 are being placed on experimental biological therapies instead of chemotherapy.

As for chemotherapy, radiation has more application in fast growing cancer tumors than slow growing NF tumors. However use of radiation therapy is a very controversial topic in the NF medical community. Some centers will offer this, and others will not. The controversy has arisen from a belief by some that radiotherapy might promote malignancy. Where radiotherapy is employed, it is often for a tumor that is in a hard to reach spot. Interestingly the tide may be turning on the use of radiotherapy. At the Foundation's NF2 Las Vegas Workshop in May, the consensus reached was that the role of radiotherapy could be for small tumors (to avoid conventional surgery) or hard to reach tumors e.g. spinal tumors.

One thing that is poorly understood is what actually happens inside the tumor after radiotherapy. For example post-irradiated tumors often increase in size before they shrink; is this due to inflammation or something else? To address this, CTF has just funded a Young Investigator Award to Dr. Nicolas Bonne at House Ear Institute to study the biology of post-irradiated NF2 tumors in mice.

[Ed Note: Thanks to everyone for your questions! We'll be conducting Q&A sessions with Dr. Hunter-Schaedle every few months so feel free to post questions here and/or follow us on Facebook for notices about when we'll be doing the next Q&A.]