



CARING FOR CARCINOID FOUNDATION

Dedicated to discovering a cure for carcinoid cancer

Ask the Doctor January 2009

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1. I am a carcinoid patient diagnosed in 2003. I have had ileum surgery to remove the primary but it has metastasized to the liver and now the bones. Can you tell me the effectiveness of MIBG for bone tumors? I currently get 120LAR of sandostatin and zometa monthly.

We have treated patients with I-131 MIBG who have liver and bone metastases and have seen responses to the therapy. Bones metastases are generally considered to be less responsive to radionuclide therapies, but we have seen responses.

2. Can you tell me if the Cyberknife is a viable option for carcinoid tumors? I have a liver tumor that needs attention and I am trying to avoid another surgery.

I am not aware of any data on the use of the Cyberknife for treating liver metastases from carcinoid tumors.

3. What was the MTD (maximum tolerated dose) that was determined by the Phase I trial of I-131 MIBG? Where will the Phase II trials for I-131 MIBG "Azedra" that are due to begin in early 2009 be held? Will Duke be one of the sites? Do you know if these trials will be open to carcinoid patients?

The maximum tolerated dose in the Phase I trial was 8mCi/kg. There are several sites that will be participating in the Phase II trial. I know that Duke and Cornell University Medical Centers will be participating but I do not know any of the other centers that will be participating at this time. There may be a small trial in carcinoid patients in a limited number of sites, but that decision has not been finalized at this time.

4. What is the difference between LU-177 & Y - 90?

Those are 2 different radionuclides that have been used to radiolabel somatostatin-like agents for therapeutic purposes. Studies with these agents have been performed primarily in European countries.

5. What is your opinion on Selective Internal Radiation Therapy using Y-90 ?

There are some patients who have liver metastases from carcinoid tumor who have quite good responses to the use of this therapy. The studies published recently are quite promising on the results of this therapy.

6. Could you please comment on the radiographic appearance of dipnechs. I am a 47 year old physician who had an asymptomatic 1.8 cm typical pulmonary carcinoid removed several months ago. On CT, I also have a 3 cm area of clustered nodules that look like old granulomatous disease and a 1 cm area of what looks like scarring. I am wondering if these are carcinoid related.

I am not sure what "dipnechs" is. It is unlikely that the clustered nodules or the scarring are related to your typical pulmonary carcinoid that was removed. When nodules are identified in the lung, they are typically followed for 2 years to document that they are benign since they are not growing.

7. My 22 year old son was diagnosed in April, 2007 with atypical thymic carcinoid which had metastasized to other parts of his chest and back. He is currently being treated at Memorial Sloan Kettering. He went through five rounds of chemotherapy (cisplatin and etoposide) followed by two surgeries to remove the tumors. All evidence of cancer was gone, however, the margins were not clean for the large tumor of the chest. Recently, in October, 2008, followed by a clean chest CT scan, he noticed swelling under his eye. An MRI revealed a carcinoid under his left eye and small lesions in his brain. He experienced no symptoms other than swelling under the eye. He has just finished 10 days of WBRT. It also appears that the lesion under the eye was present in May, 2007 but was thought to be a fatty deposit. We will have a follow up MRI in mid January to see how the radiation worked. Do you know of any medication, trials, etc. that might be beneficial to my son?

Your son has a very unusual presentation of a very unusual tumor. I have no experience treating tumors like you describe with MIBG and am not familiar with any trials for tumors behaving like this one.

8. Can you give me an overview of MIBG therapy? Does this therapy work to reduce/stabilize tumors? What are the pros and cons of the procedure?

MIBG is an analogue of norepinephrine that localizes in several types of neuroendocrine tumors because of the presence of the norepinephrine transporter in the tumors. If the MIBG is labeled with an imaging radionuclide such as I-123, the images can detect the distribution of the MIBG avid tumor. And if labeled with a therapeutic radionuclide such as I-131(which can also be imaged), it can be used to treat the MIBG avid tumors. The best way to treat patients with MIBG avid tumors(i.e., amount of radioactivity and frequency of administering the therapy) is still being worked out. It has been demonstrated that some patients with MIBG avid tumors respond to the therapy with some of the tumor sites "cured." Some other patients have stabilization of the disease for months/years. Thus, the pros are that some patients respond to the therapy and some quite well, and the cons are that not all patients respond to the therapy. There are some side effects of the therapy at the time of the therapy as well as some long-term effects, but these risks seem to be outweighed by the benefits.

9. Could you please explain the effects of radiopeptide therapy on the kidney? What are the risk factors for a patient who only has one kidney? Would dialysis or a amino acid infusion help to protect the kidneys?

Previous studies have shown that radiopeptide therapy may cause decrease renal function in some patients that can be avoided by the use of amino acid infusion. I am not aware of a study that documents the risk factors that predicts subsequent renal toxicity. Lutetium-177 labeled agent seems to have less renal toxicity than the Y-90 labeled agent.

10. Is the MIBG therapy for Carcinoid at Duke the same as the LU 177 therapy used at Erasmus Medical Center and other sites in Europe? I have had Yttrium 90 treatments (Therspheres to right lobe and Sir Spheres to left lobe) with minimal efficacy. Does the LU 177 seem to have better results? Which type of radiopeptides seems to have the best results? Which type is offered at Duke?

The MIBG therapy is different from the Lu-177 DOTATOC therapy and the Y-90 sphere therapies. Both the MIBG and DOTATOC therapies are systemic therapies, whereas the Y-90 sphere therapy is limited to treatment of liver metastases. There are no comparative studies to determine that one type of therapy is better than the other. At Duke we offer the Y-90 sphere therapy and will be offering the MIBG therapy in a Phase II study.

11. What, in your opinion, is the most promising development in radiopeptide therapy in the US?

Several agents are now under testing, and I do not have enough experience with all of these therapies to determine that one is better than any other.

12. What specific test(s), scans, etc. direct/determine the most successful treatment option(s) and follow up?

The scans that best predict the response to treatment depends on the therapeutic agent being used. An MIBG scan is necessary before MIBG therapy, and an Octreoscan or other similar agent is used before radiopeptide therapy. We still have a lot to learn how predictive these scans are related to response to therapy and what scans are most important in following the effect of therapy.

13. Do certain treatments preclude others? Is there an order that would allow the most options?

Since these therapies work on different mechanisms in the tumors, combinations of these therapies may be appropriate. However, these combinations or serial treatments have not been evaluated yet to determine if there is increased efficacy.

14. This obviously isn't a medical question, but I hear more and more about insurance denying treatment...for one example...Y-90 treatments for carcinoid as "off label/experimental". This is certainly true of other treatments discussed here. As a physician who has most likely encountered these time consuming, excruciating and exhausting battles, what specific tool(s) has proved successful for you and your patients in the appeal process?

This is a difficult problem. Specifically for the Y-90 therapies, if the patient has other than metastatic colon cancer or hepatoma, it is considered off label. We have had some success getting the procedure covered by talking to the medical directors of the insurance company

and providing them with more recent literature on the results in patients with neuroendocrine tumor metastasized to the liver.

15. What are all of the current radiopeptide trials at Duke which relate to neuroendocrine tumors?

We do not presently have any radiopeptide trials at Duke.

16. Are Lu-177, γ -90, I-131 MIBG indicated for both primary tumors and liver metastasis or are some of them just for liver metastasis? Are any effective against bone metastasis? Are there peer-reviewed publications demonstrating efficacy against primary or metastatic legions? The Y-90 microspheres are used for liver metastases. Lu-177 DOTATOC and I-131 MIBG are used to treat tumors that are avid for these agents and located anywhere in the body.

I am not aware of any publication that has focused on bone metastases only, but we have had several patients with metastatic neuroendocrine tumors to bone respond to MIBG therapy.