Northwoods NETs Meeting
Burnsville, MN (near Minneapolis)

January 14, 2018

Purpose:
Presentations by 3 Mayo Clinic NETs specialists at the Fairview Ridges Hospital in Burnsville, MN.

Dr. Ayse T. Kendi
Department of Radiology
She is responsible for Ga-68 DOTATE scanning and PRRT

Dr. Thor Halfdanarson
Professor of Oncology

Rachel Eiring
Physician Assistant in the NETs Clinic

The presentations were recorded and will be on the Northwoods NETs site in a couple of weeks. www.northwoodsnets.org

Summary
Dr. Ayse Kendi

- PRRT works like a 'lock and key or 'Trojan horse'; it lets itself in, attaches to the enemy and kills it.
- Krenning Scoring. The Krenning score is used to grade the uptake intensity of neuroendocrine tumors on somatostatin receptor imaging such as octreotide scan. Typically, peptide receptor radionuclide therapy (PRRT) is considered when the Krenning score is greater than 2. High uptake is good; limited liver involvement.
- Reviewed eligibility requirements for PRRT (i.e. must be inoperable, not have kidney issues, have receptors).
- Must be off SSA's for 4-6 weeks (Octreotide / Lanreotide)
- The procedure is 8 hours. Mayo has 4 large, very nice rooms set up for PRRT.
- Different teams come into the room for different purposes - people to provide the line; Radiologist to review risks, benefits, side effects, the IV team, nausea meds (both oral and IV)

- There is a 4-hour solution feed of amino acid to protect the kidneys
- Lutetium for 1 hour (given 30 minutes after amino acid)
- Radiation safety is reviewed (contact with others, travel by plane
- Patients are dismissed 30 minutes after completion
- 4 cycles, every 8 weeks or so.
- On average, PRRT, provides 3 to 4 years of progression free survival.
- There is a post treatment scan and consult (check blood and kidneys)
- Side effects fatigue, diarrhea, nausea (usually mild), some hair loss 60% of the time (not to the point of balding).
- PRRT improves bone pain; 36% in trial had improved quality of life
- NETTER-1 trial - multicenter double blind study with two arms. One was PRRT, the other a double dose of Octreotide (60 mg vs 30). Mayo now has good experience with PRRT and if approved by FDA on January 28th, they will be ready to implement in a reasonably short time frame. Mayo had about 8 patients in the NETTER-1 clinical study.
- Australia is testing PRRT with chemotherapy.
- Their is work on alternative to Lu-77 (lutetium) which as a shorter, yet strong beam meaning it better focuses on tumor tissue and does so more aggressively.
- Mayo's PRRT team is comprised of 23 multidisciplinary team members.
- Those who have Y90 can also be candidates for PRRT.

Dr. Thor Halfdanarson, Professor of Oncology and recognized NETs specialist
Rachel Eiring - P.A. - C.

- Mayo see's about 400 NETs cases annually just in Rochester.
- The median age at diagnosis is 63.
- The incidence is growing from 1/100,000 to 6+ due to more scanning and awareness. PNET incidence is 4x higher now. NETs may lose its 'rare' status which could be good in terms of attracting more research funding.

- Dr. James Howe at University of Iowa is conducting a familial genetic testing study on NETs patients and their families. If you wish to participate, contact him.
- Its critical to have an accurate diagnosis for proper therapy. Pathology is very tricky. Dr. Thor commented that at Mayo they have two pathologist independently and sign off. If they have different findings, they bring in a third set of eyes. Ki-67 and differentiation are important.
- Origin of the primary is critical in order to develop a therapy plan.
- Tumor markers like CG-A or 5-HIAA are never sufficient alone for diagnosis. They only help you to know when the next scan should be. He mentioned that he was doing a study on CG-A and its predictive ability. He almost never makes therapy changes solely based on markers.
- Ga-68 DOTATATE PET/MRI is the best scan for certain NETs.
- In NETs, one size does not fit all. Therapy is individualized.
- Lexicon Pharmaceuticals has a drug to aid in reducing the occurrences of diarrhea among NETs patients. It doesn't work for everyone. From Lexicon… Elotristat Ethyl is an extremely significant introduction to the treatment of Carcinoid Syndrome diarrhea. The brand name is XERMELO®
- PNETs are a more homogenous group of NETs.
- Retrospective studies indicate that patients being seen at a high volume NETs specialty center like Mayo do better.
- Targeted therapy is the future.
- Immunotherapy hasn't worked well yet, for NETs.
- Personalized therapy - not yet for NETs patients.
- Always let your oncologist know of any alternative therapies you are trying.
- Mayo takes a team approach to NETs, including your 'home' oncologist. Dr. Thor reviewed all the members on the NETs team which is very diverse and numerous.
- They have a NETs tumor board which meets every two weeks with specialists having over 100 years experience. They have the largest NETs/Carcinoid team and see about 5 new NETs patients weekly.
- To date, Mayo has done 300 Netspot tests (Ga-68 DOTATATE).
- Ki-67 should be checked via biopsy if there is tumor growth.

- There can be major differences in scanning results at different centers even if both have the same, best in class equipment. If the technician doesn't apply the contrast at the right time (phase), the results can be very different.
- When to increase the dosage of SSA's versus changing the interval. Like most things NETs, it depends. If patients have syndrome before 28 days, increasing the interval to 28 days is the strategy. If they aren't responding to 30mg for tumor growth, increased dosage may make more sense. Insurance companies sometimes push back. If so, have your doctor who administers the SSA do a peer to peer with the insurance company.
- If not responding to Octreotide can go to 60 mg every 21 days.
- No difference in efficacy of Octreotide vs Lanreotide. Lanreotide can be more painful with some patients.
- Can you get PRRT with high liver tumor load? Yes. If can take a while for it to work. You may need 3 CT's to start noticing an effect.
- There can be false positives with Ga-68.
- Bladder and spleen always lights up on Ga-68. How do you know if there is an issue? In the bladder, get a cystostomy. With the spleen, do a PET/MRI.
- Ki-67 check. If the tumor is behaving differently, get another biopsy of the liver.
- Pain from PRRT when tumor begins to die. Some patients on the NETTER-1 trial had some abdominal pain for a week or so.
- Have a lot of experience 'treating' patients who have had PRRT, but haven't given a lot of it.
- PRRT - how long will you go progression free? Less than half of NETTER-1 clinical went 3-4 years, but they really don't know the end point. After 4-5 years, they do another round of 4 and after that 2 rounds.
- Improving Mayo's reputation as a center of excellence for NETs. Treating hundreds and hundreds of patients. Every NET patients should be linked to a specialist.
- Sloan Kettering - have the top 3 NET pathologists who individually read hundreds of high grade NETs and on ⅓ of the cases, they disagreed.
- Testing facility to facility. Yes. Biggest difference is in CT's. The most common mistake is the wrong timing in the contrast injection, even with the best equipment. This happens all the time. Its a training issue with the technologist. Mayo does high volume and uses

biphasic liver imaging - it helps when you know you looking for a NET. In an ER, they are looking for something else, most likely.