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“Invited Perspective” for ^{68}Ga -DOTATOC Imaging of Neuroendocrine Tumors: A Systematic Review and Meta-Analysis.” - M.Graham et al.

Improving Tools and Options for the Management of Patients with Neuroendocrine Tumors - A patient perspective.

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It has been nearly nine years since I first saw a presentation on ^{68}Ga-DOTATOC Positron Emission Tomography Computed Tomography (PET/CT) given by a European physician at a patient education conference. I had just been diagnosed with a rare Neuroendocrine tumor and did not have many therapeutic options. I vividly remember Dr. Richard Baum from Germany addressing the audience on the third day of the conference after two days of lectures on surgery and long acting somatostatin analogue therapy, wondering how treatments were selected when the disease could not be accurately localized. Dr. Baum proceeded to talk about the benefits of imaging with ^{68}Ga PET/CT. I knew immediately that I would undergo this imaging procedure in order to have the clearest picture of the state of my disease. Little did I know that flying to Germany for a ^{68}Ga-DOTATOC PET/CT in December of 2008 would change the path of my disease management as well as my involvement in the nuclear medicine field. It is with this background that I am honored to write an introduction to “^{68}Ga-DOTATOC Imaging of Neuroendocrine Tumors: A Systematic Review and Meta-Analysis.” - M.Graham et al. (1)

As the authors point out, the standard of care for Neuroendocrine Tumors (NETs) whole body imaging had been the Octreoscan™ first approved in June 1994. At the time of my NET diagnosis in 2007, it was the last diagnostic or therapeutic agent approved for the treatment of NETs. The authors also state that NETs are a rare disease and while the incidence and

prevalence continue to increase as reported by A. Dasari et al (2), the standard of care had not progressed in several decades.

From a patient perspective, the Octreoscan is less than ideal. The entire process can take 2-3 days and may require use of a laxative (3). Due to the complexity of the scan and the resulting image quality, many treating physicians only order a single Octreoscan at the onset of diagnosis. The only perceived value of the Octreoscan was either to determine if the disease was somatostatin subtype 2 receptor positive for long acting octreotide therapy or to see if the disease had spread to regions not imaged by Computed Tomography or Magnetic Resonance Imaging.

At the time of my first ^{68}Ga-DOTATOC PET/CT in 2008, many US-based treatment providers were skeptical of the need for an additional imaging method for NETs. While Graham et al show that ^{68}Ga-DOTATOC PET/CT is a superior imaging method over the Octreoscan, many providers in 2008 felt it would not result in a change of management given the therapeutic treatment options available. I was personally convinced that ^{68}Ga DOTATOC PET/CT should continue to be studied. In addition to more precise imaging, it is a more convenient procedure for the patient requiring a single half-day visit to an imaging center and no use of a laxative.

My initial ^{68}Ga-DOTATOC PET/CT showed no additional disease and no change in my treatment course as my disease was stable. In three months this would change as I developed symptoms, while moderately controlled by somatostatin analogues, needed to be addressed with additional therapeutic options for control of my progression. With no approved treatment for my specific condition and no clinical trials available in the US for which I was eligible, I again turned to the facility that had imaged me with ^{68}Ga-DOTATOC PET/CT. The facility had been performing therapy for 10 years based using the same DOTATOC that I had been imaged with. In 2009/10,

I underwent three successful treatments of Peptide Receptor Radionuclide Therapy treatment using DOTATOC as a diagnostic and therapeutic pair. As Dr. Graham demonstrates, my personal experience of a change in treatment was not unique. Centers around the world using ^{68}Ga-DOTA agents were reporting changes in patient therapy management for ⅓ to ⅔ of patients who were undergoing the ^{68}Ga imaging. These therapy changes were due to a variety of reasons including discovery of cancers of unknown primary leading to surgery, existence of additional metastatic disease, and change in eligibility for Peptide Receptor Radionuclide Therapy.

This growing body of work was presented at the 1st Theranostics World Congress in Germany in 2011, bringing together nearly 400 members of the nuclear medicine community to discuss their work with Ga68 and other diagnostic/therapeutic pairs. Many of the referenced papers in this article were first presented at the Congress. The Congress continued to drive interest, and shortly thereafter the first US Investigational New Drug Applications were filed with the Food & Drug Administration for ^{68}GA-DOTATATE and ^{68}Ga-DOTATOC. Results from those trials and additional positive trials have been used to support a New Drug Application to the Food & Drug Administration for ^{68}Ga-DOTATATE which was approved in June 2016 for the imaging of NETs. As Graham et al mentions, The University of Iowa will soon be submitting a New Drug Application with the Food & Drug Administration for ^{68}Ga-DOTATOC.

A great deal has happened in the 23 years since the Octreoscan was approved. In addition to ^{68}Ga-DOTATATE's approval, four new therapeutics have been approved by the Food & Drug Administration this decade for the treatment of NETs (Sunitinib, Everolimus, Lanreotide, Telotristat) with an additional application currently under review (Lutathera). With the advent of low cost ^{68}Ga generators, many research institutions now have the capability to do research and clinical trials using targeted therapy with the same peptide by changing out the isotopes for

diagnostic or therapeutic use.

As a patient with a rare disease it has been encouraging to see the increase in the development of new imaging and treatment options. Reviewing Graham et al, reminds the entire patient community just how many researchers from around the world are vested in improving patient outcomes and quality of life. While it took 22 years to bring forward a new approval for an imaging agent for NETs, there is no reason to wait an additional 22 years for the next agent. DOTATOC and other targeted peptides will give clinicians new tools to work with in the management of Neuroendocrine Tumor patients. More tools will continue to increase access for patients to have diagnostics imaging and improved outcomes. I concur with the author's' closing statement "^{68}Ga-DOTATOC has shown that it is an excellent imaging agent to assess patients with known NET and frequently leads to a change in management."

REFERENCE

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