

# The North American Neuroendocrine Tumor Society (NANETS) Guidelines

## *Mission, Goals, and Process*

Larry K. Kvols, MD\* and Kari L. Brendtro†

The North American Neuroendocrine Tumor Society (NANETS) had its initial organizational meeting in Portland, Oregon on September 28, 2006 to establish a professional society with the primary purpose to improve neuroendocrine tumor disease management through increased research and educational opportunities. This founding group was comprised of scientists, physicians, and surgeons representing a variety of specialties, all with a particular interest in neuroendocrine tumors (NETs).

During this initial assembly, by-laws were adopted, officers were elected, and specific objectives were prioritized. The NANETS was registered and granted nonprofit 501(c)(3) status by the Internal Revenue Service on February 21, 2007. The first project decided by the organization was to develop an authoritative consensus guideline containing appropriate NET disease management to serve as a practical resource for health care providers. These guidelines would incorporate early detection procedures for a definitive diagnosis, various aspects of imaging, histopathology, biochemical evaluation, surgical interventions, and evidence-based treatments with emphasis on a multidisciplinary team-based approach to patient care.

To begin the development of the guidelines, we reviewed all the evidence-based literature published on the management of NETs and evaluated the practice guidelines developed by other academic societies such as the European Neuroendocrine Tumor Society, World Health Organization, and National Comprehensive Cancer Network. In addition, we determined the best working format and procedures to develop the NANETS standards.

The next and most important step in the writing process was to assemble various recognized authorities representing a wide range of disciplines from the United States, Canada, and Europe specializing in these challenging diseases (Table 1). This was done at a separate assembly in Bermuda on October 2, 2008 before the beginning of the NANETS first annual symposium.

This entire group was challenged to not merely summarize other consensus papers but to enhance the already published data and assure the NANETS standards are “distinctive” and applicable to available and approved treatments in North America. Therefore, the main objective for each of the specialty panels was to assess and compare supporting publications and formulate draft position papers for their working subgroup. Each writing chair was given the responsibility for the coordination of communication and exchanging of information within their subgroup.

After the Bermuda meeting, it was determined that the manuscripts would address key aspects of neuroendocrine tumor diagnosis and treatment by organ site. The position papers from all subgroups were then completed and the contributions compiled and distributed to all participants for additional input. Two lead

authors volunteered to assimilate the submitted data, edit, and complete one of each of the following manuscripts. These primary authors reviewed the material to determine what information was still needed and obtained additional contributions regarding their topics from each of the writing group chairs.

The manuscripts and lead authors are as follows:

1. The NANETS Consensus Guideline for the Pathologic Classification of Neuroendocrine Tumors: A Review of Nomenclature, Grading and Staging Systems—Klimstra/Suster
2. The NANETS Consensus Guideline for the Diagnosis and Management of Neuroendocrine Tumors: Well-Differentiated NETs of the Stomach and Pancreas—Kulke/Jensen
3. The NANETS Consensus Guideline for the Diagnosis and Management of Neuroendocrine Tumors: Well-Differentiated NETs of the Jejunum, Ileum, Appendix, and Cecum—Yao/Boudreaux
4. The NANETS Consensus Guideline for the Diagnosis and Management of Neuroendocrine Tumors: Well-Differentiated NETs of the Distal Colon and Rectum—Pommier/Anthony
5. The NANETS Consensus Guideline for the Diagnosis and Management of Neuroendocrine Tumors: Well-Differentiated NETs of the Thorax (Includes Lung and Thymus)—Phan/Maples
6. The NANETS Consensus Guideline for the Diagnosis and Management of Neuroendocrine Tumors: Pheochromocytoma, Paraganglioma, and Medullary Thyroid Cancer—Chen/Pacak
7. The NANETS Consensus Guideline for the Diagnosis and Management of Neuroendocrine Tumors: Poorly Differentiated (High Grade) Extrapulmonary Neuroendocrine Carcinomas—Strosberg/Kvols
8. The NANETS Consensus Guideline for the Diagnosis and Management of Neuroendocrine Tumors: Diagnostic Approach to NETs—Woltering/Vinik

Once the draft copies of each paper were complete, they were posted on a secure page on the NANETS website for all writing group members to review and make comments. All input was then collected and forwarded to the appropriate lead authors for evaluation and inclusion of applicable remarks. The revised manuscripts were then reviewed by select NANETS officers to assure the content was in the required format and complete for all sections. Finally, the last draft of each guideline was circulated to the NANETS Board of Directors, Executive Committee, Advisory Board, and Writing Group chairs for consensus and approval for publication. The final review was completed in May 2010.

In closing, the following 8 manuscripts are the result of a cooperative project beginning in 2008 and involving numerous experts who have committed an enormous amount of time and energy with enthusiasm, dedication, and patience. Each individual's contributions have been valuable in creating the final product. Our hope is that these guidelines will provide the practical information necessary for professionals from a variety of

From the \*Department of Gastrointestinal Oncology, H. Lee Moffitt Cancer Center, Tampa, FL; and †Department of Executive Director, North American Neuroendocrine Tumor Society, Vancouver, WA.

Reprints: Larry K. Kvols, MD, Department of Gastrointestinal Oncology, H. Lee Moffitt Cancer Center, 12902 Magnolia Dr, FOB-2, Tampa, FL 33612 (e-mail: larry.kvols@moffitt.org).

Copyright © 2010 by Lippincott Williams & Wilkins

**TABLE 1.** The NANETS Guidelines Working Group

| <b>Epidemiology and Genetics</b>            | <b>Pathology</b>           | <b>Radionuclide Therapies</b> |
|---|----------------------------|-------------------------------|
| Steve Marx*                                 | Cesar Moran*               | Dave Bushnell*                |
| Manal Hassan                                | Domenico Coppola           | Eric Krenning                 |
| Sue O'Dorisio                               | Rick Lloyd                 | Karel Pacak                   |
|   | Saul Suster                |                               |
|   | Mark Wick                  |                               |
| <b>Biochemistry</b>                         | <b>Symptomatic Control</b> | <b>Surgery</b>                |
| Aaron Vinik*                                | Gene Woltering*            | Phil Boudreaux*               |
| Martyn Caplin                               | Wouter de Herder           | Herb Chen                     |
| Bill Go                                     | Bob Jensen                 | Lynn Harrison                 |
| Richard Warner                              | Larry Kvols                | Chris Hughes                  |
|   | Bill Maples                | Janice Pasieka                |
| <b>Imaging and Liver-Directed Therapies</b> | <b>Systemic Treatments</b> | <b>Follow-up</b>              |
| Rod Pommier*                                | James Yao*                 | Lowell Anthony*               |
| Greg Wiseman*                               | Matt Kulke                 | Al Benson                     |
| J.C. Choi                                   | Kjell Oberg                | Walter Kocha                  |
| Stan Goldsmith                              | Jon Strosberg              | Tom O'Dorisio                 |
| Charlie Nutting                             |                            |                               |

\*Writing Group Chair.

specialties to reach a proper diagnosis and develop a treatment plan for their NET patients. In particular, we anticipate that these will be useful resources for busy clinicians who may only encounter these tumors infrequently. The NANETS anticipates continued interactions with professionals from all areas of medicine to update and enhance the guidelines throughout the upcoming years when new evidence-based studies are available. The NANETS also looks forward to and encourages collaboration with all providers managing NET patients to develop the most effective management strategies by using a multidisciplinary approach that will improve patients' quality of life, optimize survival, and lead to the most positive outcomes.

Finally, we want to acknowledge our European colleagues, European Neuroendocrine Tumor Society officers, and consensus guideline committees for their time and expertise during this collaborative endeavor. The experiences they shared about development and execution of the guideline process were invaluable.

We look forward to further input from the membership of NANETS and other professional groups and health care providers for updating the NANETS Guidelines in the near future.

**Lowell B. Anthony**, Louisiana State University Health Sciences Center, New Orleans, LA

**Al B. Benson III**, Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL

**J. Philip Boudreaux**, Louisiana State University Health Sciences Center, New Orleans, LA

**David L. Bushnell**, University of Iowa Hospitals, Iowa City, IA

**Martyn E. Caplin**, Royal Free Hospital, London, UK

**Herbert Chen**, University of Wisconsin, Madison, WI

**Junsung Choi**, H. Lee Moffitt Cancer Center, University of South Florida, Tampa, FL

**Domenico Coppola**, H. Lee Moffitt Cancer Center, University of South Florida, Tampa, FL

**Wouter W. de Herder**, Erasmus Medical Center, Rotterdam, The Netherlands

**Vay Liang W. Go**, David Geffen School of Medicine, UCLA, Los Angeles, CA

**Stanley J. Goldsmith**, New York Presbyterian Hospital/Weill Cornell Medical Center, New York, NY

**Lynn H. Harrison Jr.**, Baptist Health Cardiac and Thoracic Surgical Group, Miami, FL

**Manal Hassan**, The University of Texas MD Anderson Cancer Center, Houston, TX

**Christopher B. Hughes**, Emory University School of Medicine, Atlanta, GA

**Robert T. Jensen**, National Institute of Diabetes and Digestive and Kidney Diseases/National Institutes of Health (NIH), Bethesda, MD

**David S. Klimstra**, Memorial Sloan-Kettering Cancer Center, New York, NY

**Walter Kocha**, London Regional Cancer Centre, Toronto, Canada

**Eric P. Krenning**, Erasmus Medical Center Rotterdam, The Netherlands

**Matthew H. Kulke**, Dana Farber Cancer Institute, Boston, MA

**Ricardo V. Lloyd**, University of Wisconsin School of Medicine and Public Health, Madison, WI

**William J. Maples**, Mayo Clinic, Jacksonville, FL

**Stephen J. Marx**, Institute of Diabetes and Digestive and Kidney Diseases/NIH, Bethesda, MD

**Irvin R. Modlin**, Yale University School of Medicine, New Haven, CT

**Charles Nutting**, Skyridge Medical Center, Denver, CO

**Kjell Öberg**, Uppsala University Hospital, Uppsala, Sweden

**M. Sue O'Dorisio**, University of Iowa, Iowa City, IA

**Thomas M. O'Dorisio**, Holden Comprehensive Cancer Center, University of Iowa, Iowa City, IA

**Karel Pacak**, MD, PhD, DSc, Senior Investigator, Chief, Section on Neuroendocrinology, Reproductive and Adult Endocrinology Branch, The Eunice Kennedy Shriver National Institute of Child Health and Human Development/NIH, Bethesda, MD

**Janice L. Pasieka**, University of Calgary, Calgary, Canada

**Alexandria T. Phan**, The University of Texas MD

Anderson Cancer Center, Houston, TX

**Rodney F. Pommier**, Oregon Health and Science University, Portland, OR

**Guido Rindi**, Università Cattolica del Sacro Cuore, Rome, Italy

**Rebecca S. Sippel**, University of Wisconsin, Madison, WI

**Jonathan R. Strosberg**, H. Lee Moffitt Cancer Center, University of South Florida, Tampa, FL

**Saul Suster**, Medical College of Wisconsin, Milwaukee, WI

**Aaron I. Vinik**, Eastern Virginia Medical School, Strelitz Diabetes Center for Endocrine and Metabolic Disorders, Norfolk, VA

**Richard R. P. Warner**, The Mount Sinai School of Medicine, New York, NY

**Bertram Wiedenmann**, University Medicine Berlin, Charité Berlin, Germany

**Mark R. Wick**, University of Virginia Hospital,

Charlottesville, VA

**Gregory A. Wiseman**, Mayo Clinic, Rochester, MN

**Eugene A. Woltering**, Louisiana State University Health Sciences Center, New Orleans, LA

**James C. Yao**, The University of Texas MD Anderson Cancer Center, Houston, TX