Development of a Multidisciplinary, Multicampus Subspecialty Practice in Endocrine Cancers

By Keith C. Bible, MD, PhD, Robert C. Smallridge, MD, John C. Morris, MD, Julian R. Molina, MD, Vera J. Suman, PhD, John A. Copland, PhD, Joseph Rubin, MD, Michael E. Menefee, MD, Kostandinos Sideras, MD, William J. Maples, MD, Bryan McIver, MD, PhD, Vahab Fatourehchi, MD, Ian Hay, MD, PhD, Robert L. Foote, MD, Yolanda I. Garces, MD, Jan L. Kasperbauer, MD, Geoffrey B. Thompson, MD, Clive S. Grant, MD, Melanie L. Richards, MD, Thomas Sebo, MD, Ricardo Lloyd, MD, Norman L. Eberhardt, PhD, Honey V. Reddi, PhD, John D. Casler, MD, Nina J. Karlin, MD, Sydney A. Westphal, MD, Ronald L. Richardson, MD, Jan C. Buckner, MD, and Charles Erlichman, MD

Mayo Clinic, Rochester, MN; Mayo Clinic, Jacksonville, FL; Mayo Clinic, Scottsdale, AZ

Abstract

Purpose: Relative to more abundant neoplasms, endocrine cancers have been historically neglected, yet their incidence is increasing. We therefore sought to build interest in endocrine cancers, improve physician experience, and develop innovative approaches to treating patients with these neoplasms.

Methods: Between 2005 and 2010, we developed a multidisciplinary Endocrine Malignancies Disease Oriented Group involving all three Mayo Clinic campuses (Rochester, MN; Jacksonville, FL; and Scottsdale, AZ). In response to higher demand at the Rochester campus, we sought to develop a Subspecialty Tumor Group and an Endocrine Malignancies Tumor Clinic within the Division of Medical Oncology.

Results: The intended groups were successfully formed. We experienced difficulty in integration of the Mayo Scottsdale campus

resulting from local uncertainty as to whether patient volumes would be sufficient to sustain the effort at that campus and difficulty in developing enthusiasm among clinicians otherwise engaged in a busy clinical practice. But these obstacles were ultimately overcome. In addition, with respect to the newly formed medical oncology subspecialty endocrine malignancies group, appointment volumes quadrupled within the first year and increased seven times within two years. The number of active therapeutic endocrine malignancies clinical trials also increased from one in 2005 to five in 2009, with all three Mayo campuses participating.

Conclusion: The development of subspecialty tumor groups for uncommon malignancies represents an effective approach to building experience, increasing patient volumes and referrals, and fostering development of increased therapeutic options and clinical trials for patients afflicted with otherwise historically neglected cancers.

Introduction

The importance of ensuring quality of care in oncology practice has reached national prominence. In particular, quality measures are now being developed with emphasis placed on ensuring availability of expertise and standardization within specialized tumor groups in oncology¹; board certification and maintenance of certification by the American Board of Internal Medicine now require participation in practice quality projects. This issue of quality is, in our view, especially important for uncommon and rare cancers such as endocrine neoplasms, wherein the experience of medical oncologists and other specialists is often extremely limited as a result of low patient volumes.

Illustrative of this situation is that the number of full-time equivalent medical oncologists in the United States is about 3,600² whereas the number of patient deaths resulting from thyroid cancer is only about 1,800 annually.³ Even fewer (less than 900 annually) patients with adrenal cancer are threatened by their neoplasms.³ Consequently, assuming that these patients are uniformly distributed among all US medical oncologists,

any given medical oncologist would be expected to see only about one such patient annually on average, clearly insufficient exposure to maintain optimal expertise. In addition, endocrinologists and endocrine surgeons (rather than medical oncologists) have historically presided over the care of most patients with endocrine cancer, further limiting the experience of medical oncologists in managing such patients. As a result, it is extremely difficult for medical oncologists to gain and maintain sufficient experience with endocrine cancers to ensure that they are up-to-date on progress and adept at presiding over care. Moreover, unless specialized programs are developed and interest cultivated in these cancers, the rarity of endocrine malignancies makes it extremely unlikely that any given individual or center would see sufficient volumes of these patients to develop innovative therapies tailored to these cancers. Similar problems exist in other subspecialties (eg, endocrinology, surgery, radiation oncology) with respect to treating patients with rare cancers.

In response to the impediments to optimizing care for patients afflicted with endocrine cancers, efforts have been under-

taken in selected oncology practices to bolster expertise and improve outcomes with encouraging preliminary results. In particular, Agada et al⁴ have shown that development of a subspecialty surgical clinic leads to improved outcomes from thyroid cancer surgery. White et al⁵ similarly reported improved care as well as progressively increasing patient referrals as a result of the formation of a multispecialty clinic for patients with multiple endocrine neoplasia type 1 disease. Reports on the development of specialized programs in endocrine cancers, however, remain distinctly unusual, making it difficult for many centers to determine whether the investment in such initiatives would be worthwhile.

In the current report, we describe our experience at Mayo Clinic in developing what we feel is a more integrated and responsive approach to the care of patients with endocrine cancers and in the parallel development of innovative approaches to treating them. This effort has faced challenges, including integrating the effort across three campuses located in three different states. Although, historically, Mayo Clinic has had strong endocrine surgery and endocrinology referral practices dating back to the days of Charles Mayo and Henry Plummer,⁶ the Department of Oncology and Mayo Clinic Cancer Center had not developed a subspecialty clinic and specialized programs related to endocrine cancers until recently. In addition, there had been no deliberate or structured mechanism to coordinate efforts across disciplines and campuses to specifically target practice improvements and to develop innovative clinical trials designed to improve outcomes in this patient population, prompting the current initiatives.

Methods

Beginning in January 2005, we undertook a quality project specifically targeted toward improving the care of patients afflicted with endocrine cancers. We approached this initiative in several ways. First, so as to be expeditious and pilot the feasibility of the initiative, we developed an ad hoc multidisciplinary interest group involving and coordinating experts in endocrinology, surgery, medical oncology, radiation oncology, pathology, medical genetics, nuclear medicine, statistics, and related research disciplines. As this group solidified and coordinated efforts, it matured into a formal Disease Oriented Group within the Mayo Clinic Cancer Center in 2008, with a specific mission statement, scheduled monthly meetings, and participation in Mayo Clinic Cancer Center activities. This group has served not as a tumor board but as a means for the exchange of clinical, translational and basic research, and ideas related to endocrine malignancies with the primary goal of improving the care of patients afflicted with endocrine cancers.

Appreciating the problem of a lack of endocrine cancer subspecialization and in response to clinical demand, we next formed subspecialty tumor groups within the Divisions of Medical Oncology at the Mayo Clinics in Rochester and Jacksonville to direct the limited number of patients to a subset of interested medical oncologists in our practices. In addition, we targeted the development of a series of innovative therapeutic single-institution and multicenter clinical trials. This effort was

intended primarily to focus on thyroid cancers (given that they are the more incident and prevalent of endocrine cancers), but in parallel we sought to develop trials for less common endocrine cancers including adrenocortical carcinoma and pheochromocytoma/paraganglioma. This inclusive approach increased referrals, bolstering the experience of involved medical oncologists as well as of other members of the endocrine malignancies group. This in turn improved the feasibility of piloting additional novel therapies through the development of external networks with other cancer centers. These actions have allowed us to develop highly specialized expertise in the care of patients with rare endocrine cancers, and to begin to develop innovative approaches to treating these patients that have positively impacted outcomes.^{7,8} We herein discuss the approaches used, problems encountered, results realized, and lessons learned in hopes of encouraging similar initiatives elsewhere.

Results

Implementation

Implementation has overall gone smoothly, we believe in part as a result of our incremental approach, including the formulation of an ad hoc interest group as an initial maneuver to demonstrate clinician interest and buy-in as well as feasibility. Development of clinician interest within medical oncology was especially simple at the Rochester and Jacksonville sites, in part because medical oncologists with interest and expertise in endocrine cancers predated formulation of our innovations. At the Scottsville site, however, no analogous medical oncologist with endocrine cancer experience existed, and the participation of this site was delayed until 2009 for identification of interested medical oncologists and endocrinologists at that site.

The formation of a subspecialty endocrine cancer group within the Rochester Division of Medical Oncology was facilitated not only by demonstrated interest in endocrine cancer among several staff but also by the availability of an ongoing clinical trial in thyroid cancer and by sympathetic division and department chairs (J.C.B. and C.E., respectively). The formation of an endocrine malignancies clinic in response to demand to accommodate patients participating in our clinical trials was conducted on a conditional/interim basis with a single staff member (K.C.B.) agreeing to staff the clinic as a supplement to his existing clinical assignments, thus prohibiting a negative impact on other parts of the practice in the start-up period. Additionally, five core medical oncologists at the Rochester site were identified to care for patients with endocrine cancer outside of the designated clinic times so as to expand appointment availability when needed, accommodate overflow, and concentrate the care of such patients within a subgroup of oncologists specifically interested in endocrine cancers. Again, flexibility and dedication were required to develop the program.

Patient care and communication with referring physicians were facilitated by use of preexisting infrastructure rather than creation of processes specific to our initiatives. In particular, correspondence was generated through use of the assigned medical secretaries of physicians participating in the effort, with

correspondence sent out in hard-copy form within one week of patient visits and via fax when more expeditious communication was appropriate. Imaging and patient testing were also accomplished using preexisting personnel and processes without duplication of infrastructure. Similarly, desk personnel were those already in place and assisting involved physicians. This approach had no adverse impact on other clinical initiative, in large part because of the small incremental workloads imposed by the endocrine clinics relative to preexisting/baseline workloads—a critical issue in implementation—as an initiative of larger relative magnitude would have stressed preexisting infrastructure and impaired our ability to develop the program.

Development of therapeutic clinical trials for endocrine cancers has also proceeded relatively smoothly, largely as a result of the preexisting infrastructures of the Mayo Clinic Cancer Center and the Mayo phase II consortium, laboratory researchers interested in endocrine cancers, and sympathetic leadership (including at the National Cancer Institute and involved pharmaceutical companies). Without this fertile and receptive preexisting environment, implementation would have been much more challenging.

The development of clinical trials within the Mayo phase II consortium importantly allowed referral of suitable patients desiring clinical trial enrollment with affiliated institutions closer to their homes, thereby minimizing travel and patient inconvenience and expense and, importantly, facilitating a sort of outreach initiative developed in parallel with internal initiatives. As a part of these outreach initiatives, clinic staff have availed themselves to external physicians and patients to assist in administration of care both on and off study not only at Mayo sites but also at other locations.

Impediments

Impediments to implementation have been several. The motivation for formation of the group—the relative rarity of endocrine cancers—was also an obstacle. In particular, there was skepticism at various levels as to whether a successful group and program could be developed with its sole focus on rare cancers. This has been an impediment to the approval of clinical trials as well as a result of the inherent uncertainties related to rates of accrual to trials involving rare cancers. However, after our pazopanib phase II consortium thyroid trial became the most rapidly accruing clinical trial in the Mayo phase II consortium, concerns over trial accrual have somewhat attenuated. Among the most challenging issues was that of integration of Scottsdale site into the initiative, arising as a consequence of the lack of preexisting interested and motivated medical oncology staff at that campus and skepticism on the part of leaders of clinical trials at that as to whether trials confined to the therapy of patients with rare cancer would be cost-effective and accrue patients. These obstacles, however, were ultimately overcome, although they required several years of development; integration of the Scottsdale campus came only in 2009.

Patient Visits

From January 2007 through December 2009, the numbers of patient visits with endocrine oncology subspecialty medical oncologists in our Rochester practice increased substantially, as indicated in Figure 1. Volumes quadrupled from approximately 20 to approximately 80 patients per quarter within the first year of initiation, and increased about seven times (from approximately 20 to more than 140 patients per quarter) by the end of year two (Figure 1A). Although new referrals both internal and external to the Mayo Clinic system increased steadily during this interval, return appointments accounted for the majority of all visits (Figure 1B), resulting at least in part from initiation of systemic therapies in many patients, including enrollment of patients onto therapeutic clinical trials on which recurring follow-up was mandatory. However, many patients were referred elsewhere so as to facilitate their care closer to their homes whenever feasible and/or desired, as we strove for a collaborative model of care centered as close to patient's home as possible. Despite dramatic increases in patient volumes and demand over time as indicated in Figure 1, attained patient volumes were still modest overall in comparison to those in groups caring for patients with much more common tumor types. Hence, all clinicians participating in the newly formed clinic also maintain practices encompassing other tumor types.

The majority of all patients seen in the medical oncology endocrine tumor groups (more than 80%) were afflicted with thyroid malignancies. However, patients with adrenal cancers (adrenal cortical carcinoma, pheochromocytoma), parathyroid cancers, paraganglioma, and non-GI origin neuroendocrine cancers were/are also seen. Overall, the clinic enriched the exposure of participating physicians to endocrine cancers by a factor of five- or 10-fold in comparison with the prior system of more indiscriminately distributing such patients to oncology staff.

Therapeutic Clinical Trial Development

Beginning in 2005, implementation of a series of innovative therapeutic clinical trials for patients with all major types of endocrine cancer was undertaken (Table 1), the majority of which were initiated by Mayo Clinic investigators. The development of investigator-initiated trials was greatly aided by the acquisition of informative pilot preclinical data by laboratory investigators in our group, coupled with support from our phase II consortium chair (C.E.). Moreover, referral of trial-appropriate patients by endocrinologists, surgeons, and radiation oncologists—most of whom were participants in the endocrine malignancies group—was crucial to success. Without this preexisting infrastructure, the process would have been much more challenging. Hence, although many centers will be well positioned to similarly develop subspecialty oncology practices in endocrine cancers, fewer might be expected to be able to have the existing infrastructure to expeditiously mount an analogous portfolio of investigator-initiated trials.

Figure 1. Effects of practice innovations on patient volumes for endocrine cancer during innovation period. (A) Total patient volumes for endocrine cancer in the Division of Medical Oncology, Mayo Clinic (Rochester, MN) by quarter during the initial implementation period. (B) Patient volumes for endocrine cancer in the Division of Medical Oncology, Mayo Clinic (Rochester, MN) by year and appointment type during the first 3 years of innovation.

Additional Initiatives

Initiatives (beyond the development of dedicated subspecialty clinics) with potential to improve the care of patients with rare cancers have also been undertaken by our group. In particular,

we commonly provide remote consultation services to patients and physicians related to the care of patients with endocrine cancers to assist in the optimization of care locally whenever possible. Additionally, we also engage in outreach efforts, including through advocacy groups and continuing medical education programs. We believe that these efforts enhance the care provided at other institutions while building the referral base for clinical trials administered by our group.

Institutional Economic Impact

Net operating income (NOI) generated by the endocrine malignancies group of the Mayo Clinic Division of Medical Oncology at the Rochester site was specifically analyzed and compared with NOIs generated by other tumor groups within the division. NOIs for the endocrine tumor group were consistently within the top three of 12 assessed tumor groups, attesting to the economic sustainability of the newly formed endocrine tumor group. Similar analyses were undertaken at the Jacksonville site, where NOIs for patients with thyroid cancer in particular were also consistently in the top three NOIs generated across all tumor types seen at that site.

Lessons Learned

Key to the success of our initiatives has been the enthusiasm of involved clinicians; without this, the group would have failed. It has been our experience that enthusiasm can be fostered but not so easily created. In developing the program, we have emphasized identification/recruitment of group members who have had at least nascent interest in endocrine cancers, providing mentoring and encouragement to inspire them to become active contributors to the group. Vigilance in identifying potentially interested individuals is critical, in our experience, to building and sustaining such a group. Our practice begins identifying and nurturing individuals while they are in fellowship training or newly on staff, which results in recruitment of individuals to the group at times when their careers can still be influenced.

Dedicated time is required for individuals to participate in such a newly formed group. If an institution wishes to foster such an effort, protected time specifically designated to enable participation of key group contributors should be provided.

Table 1. Clinical Trials in Endocrine Cancer Developed During the Innovation Period

Agent	Disease	Sponsor	Phase	Activation	Status	Investigator Initiated (Y/N)
17-AAG	DTC, MTC	NCI	II	August 2005	Completed	Y
Vandetanib	MTC	Industry	III	May 2007	Completed	N
Pazopanib	DTC, MTC, ATC	NCI	II	February 2008	Enrolling	Y
CS7017 + paclitaxel	ATC	Industry	I/II	June 2008	Completed	Y
AT-101	ACC	NCI	II	March 2009	Completed	Y
XL184	MTC	Industry	III	June 2009	Completed	N
VB-111	DTC	Industry	II	February 2011	Enrolling	Y
Pazopanib + paclitaxel	ATC	NCI/RTOG	I/II	May 2011	Enrolling	Y
Pazopanib	PC, PG	NCI	II	January 2012	Enrolling	Y
E7080	DTC	Industry	III	Pending	Approved	N

Abbreviations: ACC, adrenal cortical carcinoma; ATC, anaplastic thyroid cancer; DTC, differentiated thyroid cancer; MTC, medullary thyroid cancer; NCI, National Cancer Institute; PC, pheochromocytoma; PG, paraganglioma; RTOG, Radiation Therapy Oncology Group.

That said, participation in a group can and should also be incentivized by ensuring that key contributors are cited in articles. In addition, contributors should also be acknowledged at the institutional level with the creation of titles and formal designations in acknowledgment of the group and its members. These incentives cost an institution little, but in our experience are at least as important as funded time.

Development of collaborative cross-disciplinary interactions is also critical to group success in our experience. We have therefore developed group meetings that are cross-cultural and not imbedded in only a single division or department but instead superimposed on existing meetings and groups. This approach is formulated so as not to threaten individuals already invested in their own intradivisional/intradepartmental efforts but to credit individuals for their expertise and acknowledge them as key contributors. Networking with extra-institutional groups can also help build a program. With increased visibility achieved through networking comes increased opportunity to expand a group's patient referral base and become involved in broader initiatives including multicenter clinical trials. In the case of rare/uncommon tumors, networking is critical to sustain the mission of the group and accrue needed patients to trials. When new initiatives arise, there is also a need to enhance awareness; this can be accomplished by featuring the innovations in existing newsletters and bulletins, something that we have taken advantage of in our group. For example, our innovations and clinical trials have been repeatedly featured in endocrinology newsletters distributed to referring physicians. Networking should also ideally encompass not only professional groups but also patient advocacy groups and industry groups to optimize opportunities to enhance the group in the broadest possible context—building relationships with patients themselves and with pharmaceutical companies with the potential to assist in clinical trial development.

Discussion

With effort, coordination, and dedication, our experience indicates that it is possible to develop a thriving specialized program that achieves success in optimizing patient care. We feel that such programs are particularly necessary for rare tumors, given that it is in the care of patients with rare tumors that general clinicians most lack experience and therefore require the greatest support. On the

basis of our experience in developing an Endocrine Malignancies Disease Oriented Group at Mayo Clinic campuses, we feel that such efforts at other institutions should be encouraged toward the common goal of improving outcomes in patients afflicted not only with more common tumors but also with rare tumor types whose scarcity has left them most commonly neglected.

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Author Contributions

Conception and design: Keith C. Bible, Robert C. Smallridge, John C. Morris, Vera J. Suman, Ian Hay, Robert L. Foote, Jan L. Kasperbauer, Clive S. Grant, Norman L. Eberhardt, Ronald L. Richardson

Provision of study materials or patients: Keith C. Bible, Robert C. Smallridge, John C. Morris, Julian R. Molina, John A. Copland, Joseph Rubin, Michael E. Menefee, Kostandinos Sideras, William J. Maples, Bryan McIver, Vahab Fatourehchi, Robert L. Foote, Yolanda I. Garces, Jan L. Kasperbauer, Geoffrey B. Thompson, Clive S. Grant, Melanie L. Richards, Thomas Sebo, Ricardo Lloyd, John D. Casler, Nina J. Karlin, Sydney A. Westphal, Jan C. Buckner, Charles Erlichman

Collection and assembly of data: Keith C. Bible, Robert C. Smallridge, John C. Morris, Joseph Rubin, Michael E. Menefee, Kostandinos Sideras, Honey V. Reddi

Data analysis and interpretation: Keith C. Bible, Robert C. Smallridge, John C. Morris, Vera J. Suman

Manuscript writing: Keith C. Bible, Robert C. Smallridge, John C. Morris, Vera J. Suman, Ian Hay

Final approval of manuscript: All authors

Corresponding author: Keith C. Bible, MD, PhD, Mayo Clinic, 200 First Street SW, Rochester, MN 55905; e-mail: bible.keith@mayo.edu.

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