Quality of Life in Patients with Pituitary Tumors: A Preliminary Study

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Introduction

Pituitary tumors generally are treatable and, for practical purposes, benign in terms of morbidity and mortality. However, many individuals who have undergone treatment for these tumors report a number of persistent difficulties and delays in obtaining workup and treatment for symptoms due to the perception on the part of the medical community that long-term sequelae are infrequent or minor. We surveyed individuals in this group and other patients in contact with the group to understand the specificity and range of problems and symptoms. Within a large southeastern Michigan pituitary disorders support group, we observed a staggeringly high number of patient complaints, although many patients reported that laboratory testing indicated adequate medical and hormonal treatment.

Given the relatively high incidence of pituitary tumors in the general population and the fact that the majority of these tumors can be controlled, if

Clinical Trial

Are you a woman between 18-50 years of age with a pituitary problem? You may be eligible for our research study. In this study, we are replacing testosterone via an investigational patch to normal female levels to find out if women have improved energy levels, sex drive, weight, muscle, and bone density. This study includes 6 outpatient visits to Massachusetts General Hospital over 12 months and a stipend of $600 if you qualify. Travel reimbursement and accommodations will be provided. If you are interested in more information about this research study, please contact Julie Jones, Nurse Practitioner, in the Neuroendocrine Unit at Massachusetts General Hospital.

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not cured, the negative impact these problems have on patient outcomes is enormous and, unfortunately, largely unnoticed. As most of the complaints expressed by patients fall into the general category of HRQOL “Hormone Replacement Quality Of Life”, we chose to survey a group of patients undergoing treatment for pituitary tumors to understand the specificity and range of problems and symptoms. The goals in this study were twofold; first to determine whether the sickness-related quality of life reported by patients with pituitary tumors was poorer than that experienced by the general adult population and second, to know whether some complaints and areas of dysfunction were more troublesome than others.

Method

Through publication by announcement in meetings of the Pituitary Tumor Support Group and through an announcement on the website, 92 individuals requested a survey to participate in the study. We did not collect identifying data on the individuals who requested a survey or those who returned it. Of 92 surveys, 43 were returned for a response rate of 47%. On average, our respondents were 40 years old (SD = 9), but they ranged in age from 21 to 65. The average participant had a college education (M = 16 years; SD = 2; range = 9 to 21 years). Most individuals in the study were married. Of the participants, 30 were women, 12 were men, and 1 didn’t report gender.

Materials

Each participant completed two scales, one a list of symptoms and problems specific to patients with pituitary tumors and the other a very broad-based index of life quality, the Sickness Impact Profile “SIP”. The scale of symptoms was based on a list compiled by the leader of the Pituitary Tumor Support Group (T. Sullivan). Using a model developed by a colleague in studying neurobehavioral problems reported by athletes, as often as possible complaints were described in the words used by the support group members, and we asked respondents to rate each one on a 0 (none) to 6 (severe) scale. Symptoms were randomly ordered on the list. Each respondent also circled the single most troublesome complaint on the list and added major complaints not on the original list. Participants also indicated whether they had experienced difficulty in obtaining referrals for needed health care because of a professional’s inability to discern need.

The second measure was the Sickness Impact Profile SIP, designed to be a broadly- and behaviorally-based measure of life quality. The SIP yields an overall score, a Physical, Psychosocial, and Other dimension score, and 12 category scores. Each item endorsed by the respondent is weighted by a value meant to reflect the severity of the dysfunction. Each item endorsed adds to a particular Category and Dimension score as well as to the overall score. Symptom and Complaint List. As shown in Table 2, in which symptoms are listed in order of decreasing mean ratings for the whole group, respondents tend to agree on the ratings of the 20 symptoms and do not rate all symptoms as equally troublesome. The range of mean ratings falls from minimal to moderate. For the 38 participants who rated each symptom, the mean item rating was 2.58, suggesting that respondents do not uniformly rate all symptoms as present or severe. Mental or physical fatigue appeared to be the single most troublesome symptom for the sample as a whole, as well as for the prolactinoma, Cushing’s disease, and other/mixed subgroups. Sleep difficulties and libidinal changes also received fairly high mean ratings across the entire group. Responses to query about the single most troublesome complaint on the list also indicated that fatigue is especially vexing and salient for this group as a whole. Twenty-three percent of respondents identified fatigue as the most
troublesome symptom, followed by 11.8% of the sample endorsing one of the following symptoms: mood disorder, sleep problems, or unexplained pain. Thirty-four respondents in all followed instructions to identify the most troublesome symptom.

Like the analyses with the Symptom Lambda = .35, F (2, 40) = 37.42, p = .000, but there was no significant interaction between the SIP Dimensions and the tumor type (pure prolactinoma versus everything else). Within-subjects contrasts further demonstrated that the Psychosocial Dimension mean score diverged significantly both from the Physical Dimension (F (1, 41) = 55.76, p = .000) and from the Other Dimension (F (1,41) = 16.52, p = .000). Mean Dimension scores (% impaired) for the whole sample were 7.1 (SD = 9.7) for the Physical Dimension, 15.6 for the Other Dimension(SD = 13.2), and 24.0 (SD = 19.6) for the Psychosocial Dimension. Post hoc contrasts confirmed that the mean percent of dysfunction on the Psychosocial Dimension was significantly higher than for the Physical Dimension (F (1,41) = 55.8, p=.000) and than for the Other Dimension (F (1,41) = 16.52, p = .000). In other words, although the pure prolactinoma group reported less impairment on each dimension, the relative dysfunction in these three different areas was similar for the two tumor groups. There appears to be considerable consistency in the areas of difficulty related.

The category scores also show that the average individual in our sample also reports dysfunction in a number of other categories, including Emotional Behavior and Sleep and Rest, categories that may relate more specifically to the Mood Disorders and Fatigue complaints of many in our sample on the Symptom Checklist. There is no overall category on the SIP that relates specifically to sickness-related sexual dysfunction. However, a single item on the Social Interaction subscale relates specifically to a decline in sexual function. In our sample of 43 individuals, 29 endorsed this statement.

**Discussion**

Although the actual incidence rates of HRQOL complaints in patients with pituitary tumors have not been documented, a study of 116 patients with pituitary insufficiency ranging in age from 18-38 years revealed that the rate of unemployment was approximately 3 times higher than expected and the percentage of married individuals less than 30% of that expected.

Other reports point to a decreased psychosocial functioning in young adults with childhood-onset pituitary insufficiency even after presumably adequate treatment with growth hormone (until they reached normal height). Scrutiny of other populations with the SIP reveals that the present participants are reporting especially great difficulty in the cognitive area. Comparison of the overall SIP score, Psychosocial Dimension, and Alertness Behavior score with those of other groups suggested more marked difficulties in all three areas than those reported by samples of individuals with multiple sclerosis before an exercise intervention. For a sample of COPD patients and a sample of frail home-bound elderly, the mean Alertness Behavior percent impairment was lower than in the pituitary patients, even though the mean overall SIP percent was higher in both studies.

The kinds of difficulties endorsed have all been mentioned in the literature on patients with pituitary tumors, although the hope has been that these symptoms usually remit with treatment. In contrast, we find that even individuals with the mildest of pituitary tumors on average experience significant dysfunction in day-to-day life.
Conclusions

This preliminary study provides a basis for further studies to document these problems, to understand the neurobehavioral basis of these complaints, and to devise interventions. A significant limitation to the interpretation of results in this data set is the inability to validate the patient demographics or clinical disease status. This investigation served to confirm our general clinical impression relative to treated patients with pituitary tumors but the next iteration of the survey will have to focus on a subgroup of pituitary tumor patients whose demographic and medical data have been documented, thereby enabling more critical evaluation of the patient responses. This, in turn, may allow better investigations of the medical and psychosocial bases of these complaints.

Note. Whole = whole sample (N = 43); Prolact = prolactinoma (N = 22); Cushing’s = Cushing’s disease (N = 3); Acromeg = acromegaly (N = 4); Null = null or nonfunctioning tumor (N = 5); Other = tumor type other than above or mixed tumor type (N = 8). Symptoms are listed in table in order of decreasing average ratings for the whole sample. Fatigue = Fatigue, physical or mental; Sleep problems = Sleep problems, including insomnia and increased urge to sleep; Change in libido = Change in libido or sex drive; Apathy = Apathy, including excessive submissiveness; Visual problems = Visual problems, including trouble focusing and double vision.

Note. There were 43 individuals who completed the Sickness Impact Profile (Total category above). Twenty-two individuals had prolactinomas only (Prolactinoma category). The other 21 participants had prolactinoma and one or more other pituitary tumor types or another pituitary tumor type alone or in combination (Other category).
The following article is composed of excerpts from a manuscript published by D.M. Cook, W.H. Ludlam, and M.B. Cook in Advances in Internal Medicine, Volume 45, pages 297-315 (2000). The adult growth hormone (GH) deficiency syndrome has been defined recently and separated from the childhood deficiency syndrome. With the availability of potentially unlimited supplies of recombinant engineered human GH for clinical use, endocrinologists must learn how to diagnose and treat this syndrome. However, diagnosis remains controversial and arbitrary, dosing guidelines have yet to be defined, and realistic expectations for patients receiving GH must be further delineated. The potential for abuse of this hormone must be kept in mind, both for improper indications such as performance-enhancing aids for athletes and for clinically unproven indications such as obesity and prevention or delaying of the aging process.

**Symptoms**

Symptoms of the adult GH deficiency syndrome are non-specific and in general cannot be separated from other debilitating illnesses such as depression, hypogonadism, or hypothyroidism. Two symptoms have stood out in several studies: a decrease in energy and feeling of social isolation. The former symptom can best be ascertained by asking the patients what hobbies or pastime activities they have enjoyed and if they are continuing to do so. Feelings of social isolation can be exposed by asking patients if they get out and meet their friends as much as they used to. Two important points should be made concerning symptoms. The first is that patients may not realize they have symptoms until they are treated and experience unexpected improvements. The second is that a spouse or partner can often be more objective about the patient’s changing behavior and thus can offer a better assessment of those changes. This is true for deficiency symptoms as well as for their resolution after successful therapy.

Just as the primary focus of childhood GH deficiency remains linear growth; in adults the primary focus is symptoms. To successfully interact with patients during GH therapy, the endocrinologist must anticipate four sets of symptoms, which include: symptoms of the syndrome itself, "start-up” symptoms related to the impact of initiating therapy, symptoms related to too much GH, and lastly, symptoms of improvement. Symptoms occurring at therapy initiation include muscle or joint pain, headaches, and blurred vision. Presumably these symptoms are created by the sudden retention of sodium and water. These important symptoms should be anticipated in susceptible individuals, such as the elderly and those more severely deficient. Symptoms of excess GH include musculoskeletal pain, peripheral edema, and carpal tunnel syndrome. The patient’s tolerance of therapy often will determine the final dose of GH, even though serum IGF-1 concentrations do not suggest the dose is excessive. Increasing the dose slowly, that is, every 6 to 8 weeks, helps to minimize side effects. Patients often report carpal tunnel symptoms after each dose increment. These symptoms disappear after 3 or 4 days of therapy. Others will have persistent carpal tunnel signs and symptoms and will wish to have this problem surgically repaired rather than discontinuing therapy and relapsing to deficient syndrome status.

Improvement symptoms include return of energy and an increase in alertness. Many times, spouses or children of the patient will notice these improvements first. Return of energy is the symptom most often reported and is the main reason patients want to continue therapy. Many times this is confirmed by interruption of the drug, either voluntarily or involuntarily (i.e., forgetting the medicine for a few days). The patient quickly realized that he or she is not functioning as well without the drug. Thereafter, patients will seldom interrupt therapy.

**Diagnosis**

Sampling random serum GH is of no value, because normal individuals have random GH levels that are low throughout most of the day. A stimulation test is necessary to confirm the diagnosis.
The Food and Drug Administration (FDA) has established criteria for a normal response after a standard provocative stimulus. It is > 5 ng/mL when using a nonspecific radioimmunoassay that measures most of the circulatory molecular species of GH and > 2.5 ng/mL when using the more specific immunoradiometric assay (IRMA), one that quantitates the major biologically active molecular species of GH, which is the 22,000 molecular weight (22K) molecule.

**Signs of GH Deficiency**

The physical signs of GH deficiency consist of body composition changes, including an increase in fat and a decrease in lean body mass. The fat deposition is predominantly in visceral fat but also occurs in subcutaneous fat. Lean body mass changes include a decrease in both muscle and bone mass. The latter has been associated with an increase in fracture rates. Deficiency of GH also leads to increased total cholesterol and triglycerides, and a decrease in high-density lipoprotein (HDL) cholesterol. This profile of an increase in visceral fat and other cardiovascular risk features has presumably led to an increase in cardiovascular mortality.

**Dosing**

It has become increasingly clear that doses once thought to be reasonable for adults were excessive and associated with side effects and elevated IGF-1 concentrations. Original studies by Ho and others have suggested that normal postmenopausal women secrete more GH when given oral vs. transdermal estrogen. Using IGF-1 concentrations and symptoms tolerance, we have translated these original observations to GH replacement therapy. We have found that it takes more GH to bring IGF-1 into the normal range when a woman is taking oral, rather than transdermal, estrogen. The dosage for men is similar as for women receiving transdermal estrogen, but men require less than women who are taking also oral estrogen.

Patients should be monitored with IGF-1 concentrations every 6 to 8 weeks until the IGF-1 is in the mid to high normal range for age and sex. Symptom tolerance also may dictate final dose. Patients with musculoskeletal pain and carpal tunnel symptoms or aggravation of hypertension may wish to cut back on their dose. Many times these symptoms are associated with initiation of therapy or a change to a higher dose. If symptoms appear within the first 10 days of either of these clinical situations, we suggest patients continue taking their dose because these symptoms will usually disappear. Symptoms that persist beyond 2 weeks probably will not resolve and should be corrected by reducing to the previously acceptable dose. Some patients will “settle” for an IGF-1 that is not in the normal range, yet feel so much better while taking a sub therapeutic dose that they retain it as their final dose. Patients should be cautioned that it usually requires two to three dose changes before a final plateau dose is reached. Also, patients should be advised that complete resolution of the syndrome may take 8 to 12 months.

**Interaction with other hormones**

Panhypopituitary patients are frequently taking other hormones in addition to GH. These usually include testosterone or estrogen, thyroxin, and cortisol. Of these hormones, none except cortisol appear to be affected by GH therapy. Although clinically there have not been reports of adrenal insufficiency with GH therapy, there is a theoretical concern. One report suggests that cortisol metabolites in urine increase during GH therapy. There is an increase in cortisone metabolites. This line of evidence suggests an increase in the enzyme 11 hydroxysteroid dehydrogenase, which is biologically inactive. Another hormonal impact is on glucose control. Patients, especially those with type 2 diabetes, frequently have aggravation of their diabetic control during the first 6 months of therapy. Eventually their diabetic control improves as they lose fat and accumulate muscle and lose weight.

**Summary**

The diagnosis of the adult GH deficiency syndrome from a clinical and laboratory standpoint has been reviewed. Therapy guidelines and monitoring should focus on the patient’s symptoms and IGF-1 concentrations from a laboratory standpoint. Successful patient/physician interaction depends on physician awareness of the symptoms of the deficiency syndrome and symptoms associated with therapy. Successful therapy with GH almost always results in an extremely satisfied patient, family, and physician. The full text and references can be found in: Advances in Internal Medicine, Volume 45, pages 297-315. These excerpts are printed with permission of Mosby, Inc.
How to find a qualified Surgeon

Many readers either have had or will have surgery to remove a pituitary tumor. This operation is called a Transsphenoidal Adenectomy, so named because it involves removing the tumor (adenoma) by going through (trans) the sphenoid sinus (sphenoidal). Despite the superior safety characteristics of Transsphenoidal surgery, there are some risks. In addition, any time one undergoes surgery, there are some risks. Patients and their loved ones rightly worry about the outcome of the surgery. And, as one might expect, the experience of the surgeon makes a big difference in outcomes. In 1997, a team led by Ivan Ciric, M.D., at Northwestern University’s Evanston Hospital, published the results of a survey of nearly 1,000 neurosurgeons practicing in the U.S. This article can be found on the Web at www.c3.hu/~mavideg/ns/ciric2-97.html. In their report, first published in the journal Neurosurgery, Ciric and company discuss their findings based on the responses of 958 neurosurgeons who had performed transsphenoidal surgeries on pituitary tumors. The authors concluded, “Transsphenoidal surgery seems to be a reasonably safe procedure, with a mortality rate of less than 1%.“ On the other hand, the article indicates that a significant number of complications do occur with less-experienced surgeons. Surgeons who have performed 200 and even 500 transsphenoidal operations show significant improvement in successful operations. As you can see from the survey by Ciric and company, a surgeon’s experience says a lot about the outcome of a transsphenoidal operation. The article is a great source of information, but the question for most patients is “how do I make use of all this?” For this article, we asked three members of the PDES Medical Advisory Board to help understand what sort of questions to ask a neurosurgeon to help gauge his/her experience.

Getting off to a good start

To begin, many patients will ask, “How many of these surgeries have you performed?” It is possible that some physicians do not immediately recall the exact number of pituitary surgeries they have performed. Questions worded this way usually only leave room for two types of responses – either a flat number or an evasion. It may be more helpful to ask how many times a month a surgeon performs transsphenoidals, and how long he or she has been in practice. After that, a patient might ask if that surgeon has performed more of these procedures over the past few years than earlier in his/her career. Given that approach, patients might discover that Dr. Jones, a surgeon with 10 years’ experience, typically performs one transsphenoidal a month. You can surmise that Dr. Jones has performed about 120 transsphenoidals. This discussion points out one unavoidable conclusion: you have to do your homework. Though it is a stressful time for gathering information and decision-making we hope this interview with three qualified surgeons will help you feel more confident in the process.

Q. What do you think are the three most important questions a patient can ask a neurosurgeon?

Dr. Chandler:
How long has the surgeon been in practice? How many transsphenoidal operations does the surgeon perform each year? Does the surgeon work closely with an endocrinologist?

Dr. Rock:
A patient can determine a physician’s experience by asking how many cases the surgeon would see in a year and how many operations he/she has performed. I would think that a surgeons doing about 10 cases/year for a few years would have sufficient experience to handle most tumors but, in determining experience regarding patients with Cushing’s disease, the number ought to be higher and an experienced endocrinologist should be involved as well.

Dr. Vance:
Patients should ask the neurosurgeon how many of these operations he/she has performed and the outcome rates and complication rates.

Q. What sort of preparation should a patient undertake before the first appointment with a neurosurgeon?

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The use of this newsletter is not a substitute for medical, legal, or other professional services. Consult a competent professional for answers to your specific questions.
Dr. Chandler:
The patient needs to have in hand all images, such as MRI scans (not just the reports), and also copies of all endocrine blood tests. They should ask the referring doctor exactly what has been diagnosed and why they are being referred to a neurosurgeon.

Dr. Rock:
A patient should have all hormonal results (especially prolactin) or the reports from an endocrinologist, and, if visual problems are occurred, the results of an ophthalmologist consultation. Additionally, an MRI of the pituitary region (i.e., sella) must be available.

Dr. Vance:
It is of utmost importance that the patient sees an endocrinologist who has taken care of patients with pituitary tumors before an appointment with a neurosurgeon. The patient may need vital hormone replacements before surgery and if the tumor is a prolactin-producing tumor, surgery may not be necessary.

Q. Many in the healthcare industry feel that the experience of the institution is as important as that of the surgeon in predicting outcomes. Do you agree?

Dr. Chandler:
The experience of the surgeon is the most important issue. However, the quality of the institution is important for postoperative care and also tells the person something about the surgeons who would be hired to work there.

Dr. Rock:
If we are discussing surgical outcomes, the experience of the surgeon is paramount. “The experience of the institution” is a nebulous concept and is more often promoted by inexperienced physicians. The successful management of patients with pituitary tumors boils down to the expertise of the primary care doctor (realization of the clinical problem), endocrinologist (determination of the hormonal details) and the surgeon (when a surgeon is necessary which is not the case in many cases).

Dr. Vance:
If a person is to have pituitary surgery, the most important issue is the experience and expertise of the neurosurgeon. The “institution” has nothing to do with the outcome, but it is important to have a close collaboration between the neurosurgeon and the endocrinologist for optimal perioperative and postoperative management.

Q. In some instances, a patient has no choice but to go with a surgeon with very limited experience. Do you feel that more experienced surgeons would be willing to consult with those who are less experienced prior to an operation to pass along some helpful advice?

Dr. Chandler:
It is not realistic to pass on advice for a single operation. Experienced surgeons should be involved in teaching courses at national or regional meetings for less experienced surgeons. It is certainly advisable for the less experienced surgeon to show the films to another surgeon to ask his or her opinion about an approach or the advisability of surgery, but not for advice on how to do the surgery. I think every surgeon should be very open to the idea of a second opinion for the patient. The less-experienced surgeon may want to go watch the expert do several cases.

Dr. Rock:
Although this sounds good in concept, the verbal consultation is not likely to change the outcome very much. Surgeons who are less experienced can always consult with more experienced surgeons, but to give advice over the phone is less than optimal. I doubt that, in practice, this process would work for long.

Dr. Vance:
This is not a practical question because the “experienced” surgeons can’t be there to give advice. Advice on the phone is not practical and is not good medical practice. Surgery is taught in the operating room with the experienced surgeon directing the trainee.
The PDES and all our members would like to thank Michelle Hildebrant, a professional web developer and graphic designer, who dedicated several months to build a Web site that is easy to navigate, educational and engaging. New features on the site include our wellness center, a new survey, and graphics of the pituitary gland and endocrine system.

PDES has grown by leaps and bound since 2002. We have two new sponsors to thank this year: We obtained donations from OHSU, Oregon Health Science University Pituitary Center, and Massachusetts General Hospital Neuroendocrine Center. Our deepest gratitude to these centers for their support. It is just this kind of backing that allows the PDES to bring support and education to all. These donations, we hope, are a sign of good things to come, and we hope to earn the support of many more centers as we continue to grow.

Our Board of Directors has grown and is made up of a team that is not only dedicated and knowledgeable, but who also have our mission at heart. Thanks to Chairman Sharon Cini, our new bylaws have been adopted. We also have applied for a 501-c3 tax status to allow all contributions to be tax deductible. This new status will enable us to raise funds for research and education.

Many of our readers have contributed to the Henry Ford Pituitary Disorders Center Quality of Life Study (www.henryfordhealth.org/body.cfm?id=45110). We are pleased to bring you the results of the preliminary study in this issue. The responses we obtained gave us a superb base of data from which to proceed further in this area.

In our next issue—and on our new Web site—we will bring you a survey that will help us build a database of doctors who are dedicated to treating pituitary tumors and pituitary disorders. This survey also will give us a contact list for doctors to inform them of educational seminars and the latest information and breakthroughs in pituitary care.

In this edition of Pituitary News, we offer an article on how a patient can evaluate if a neurosurgeon is really qualified to perform a transsphenoidal surgery. One member of our Board of Directors, Mark McCarty, has two transsphenoidals under his belt and drew the inspiration for this article from a published survey on the intersection of surgeon experience and surgical outcomes. He also obtained some very valuable feedback from three members of our Medical Advisory Board, namely Drs. William Chandler, Jack Rock and Mary Lee Vance, all of whom are very distinguished practitioners.

In this issue, we also offer an update on the ins and outs of growth hormone replacement “GH”. GH replacement for adults is a notion that provoked a lot of controversy in times gone by. While much of that noise has faded, a few physicians still have reservations. This article will give you an idea of where medical science currently stands on the issues surrounding replacement of this vital hormone. We hope you enjoy this issue of Pituitary News. Please feel free to send any suggestions to pdes@comcast.net.

Best regards,

President

We would like to thank Eli Lilly for sponsoring this newsletter. Thank you again for your support of PDES.
US FOOD AND DRUG ADMINISTRATION APPROVES SOMAVERT® FOR THE TREATMENT OF ACROMEGALY

First in a new class of medicines treats debilitating hormone disease

Peapack, N.J. (March 26, 2003) ¾ Pharmacia Corporation (NYSE:PHA) announced today that the US Food and Drug Administration (FDA) has approved SOMAVERT® (pegvisomant for injection) for the treatment of acromegaly in patients who have had an inadequate response to surgery and/or radiation therapy and/or other medical therapies, or for whom these therapies are not appropriate. The goal of treatment is to normalize serum IGF-I levels.

Acromegaly is a serious, life-shortening disease triggered by over-secretion of growth hormone, most often caused by a pituitary tumor. This excess of growth hormone leads to overproduction of a second hormone, IGF-I (insulin-like growth factor-I), which contributes to the disabling symptoms and the long-term health problems associated with the disorder. Patients with acromegaly often suffer from headache, excessive sweating, soft-tissue swelling, joint disorders and, perhaps most striking, a progressive coarsening of facial features and enlargement of the hands, feet and jaw. Patients with acromegaly face a mortality rate two to four times higher than the average person, due to such serious long-term complications as heart and respiratory disease, diabetes mellitus and some forms of cancer.

SOMAVERT is the first in a new class of medicines called growth hormone receptor antagonists and the only medicine designed to specifically block the effects of excess growth hormone in acromegaly. It will be available in the US by prescription within the next few weeks. SOMAVERT was approved by the European Commission in November 2002.

"SOMAVERT is an important medical advance that offers new hope to patients with acromegaly," said Ariel Barkan, MD, Professor of Internal Medicine, Professor of Neurosurgery and Co-director of the Pituitary and Neuroendocrine Center, University of Michigan Health Systems, and clinical investigator for SOMAVERT. "We are very encouraged by the introduction of SOMAVERT, an important new treatment option for those who are suffering the ravages of this disease," said Robert Knutzen, acromegaly patient and CEO/Chairman of the Pituitary Network Association, an international non-profit organization dedicated to providing support and information to patients with pituitary disorders.

SOMAVERT was studied in a fixed-dose, randomized clinical trial and in a long-term, open-label, dose-adjusted study in patients with acromegaly. In the pivotal study, SOMAVERT normalized IGF-I levels in up to 82 percent of patients, and in the long-term study, SOMAVERT normalized concentrations of IGF-I in 92 percent of patients. IGF-I level is a biochemical measure of the severity of acromegaly.

"We are excited to bring to market a new treatment for patients with acromegaly," said Peter Rost, MD, Vice President, Endocrine Care, Pharmacia Corporation. "The addition of SOMAVERT to our portfolio of products to treat pituitary disorders further strengthens our commitment to global leadership in endocrine care."

The number of patients diagnosed with acromegaly in the US, Europe and Japan is in the tens of thousands. Experts believe the prevalence may be higher, as diagnosis is often delayed for up to 15 years after symptoms begin.2 Traditional treatments for acromegaly include surgery to remove the pituitary tumor, radiation therapy and pharmaceutical treatments.

In clinical studies, elevations of liver tests (ALT and AST) greater than ten times the upper limit of normal were reported in two patients (0.8%) exposed to SOMAVERT. Serial monitoring of liver tests is necessary when beginning and during therapy with SOMAVERT. The most commonly reported adverse events with SOMAVERT occurring in at least ten percent of patients and at frequencies greater than placebo were infection, pain, diarrhea, nausea, flu syndrome, abnormal liver function tests, and injection-site reactions. The majority of reported adverse events were of mild to moderate intensity and limited duration. SOMAVERT is contraindicated in patients with hypersensitivity to any of its components. The stopper on the vial of SOMAVERT contains latex. For additional patient product information, please contact 1-888-691-6813. For physician/pharmacist information, please contact 1-800-323-4204.

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For additional patient product information, please contact 1-888-691-6813. or visit our Web Site at www.somavert.com

New Treatments, Continued on Page 11
2003 Calendar

Patient Events

Event: Seminar on Growth Hormone Replacement
Date: Saturday - Oct 18, 2003
Time: 10:00 a.m. to 1:00 p.m.
Place: Oakwood Hospital Auditorium
18101 Oakwood Blvd P.O. Box 2500
Dearborn, MI 48124
Fee: No Fee
RSVP: For more information Contact Teresa Sullivan at 810-227-5615
or email: PDES@comcast.net

Event: The Neuroscience Center at UVA present Pituitary Days
Date: Friday, April 2-Saturday, April 3rd
Time: Brochures will be available in December
Place: University of Virginia Health System Charlottesville, Virginia

For Physicians

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