2017 ANNUAL MEETING
SUMMARY OF PRESENTATIONS

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John Tourtelot, MD, a specialist in the endocrinology program at Moffitt Cancer Center, introduced some background information on VHL. He also discussed the importance and value of regular surveillance for patients with VHL.

Von Hippel-Lindau Disease, or VHL, involves several different organs in the body and multiple different types of tumors. These tumors are treatable, but require a logical approach in order to find, follow, and address them as they develop. When you first suspect VHL, you must think about the diagnostic criteria and the organs and glands which are affected.

VHL is inherited from a parent that already has the mutation in their sperm or eggs and (except for mosaic cases) every other cell in their body. In de novo cases, VHL is acquired by a mutation that randomly occurs in one sperm or one egg, in which case the child will have VHL, but the parents will not. In patients with a positive family history, a clinical diagnosis of VHL disease can be made by the finding of a single VHL-associated tumor. On the other hand, approximately 20% of cases result from de novo, or first-in-family, mutations and therefore do not have a positive family history. In these cases, the presence of at least two VHL-associated tumors is required for a clinical diagnosis.

There are several components to the initial evaluation. The evaluation should include a complete physical examination by a physician who is experienced and informed about VHL. An eye/retinal examination should be conducted by an ophthalmologist familiar with VHL, using a dilated exam. A quality ultrasound and at least every other year, an abdominal MRI scan with and without contrast, should be performed to assess kidneys, pancreas, and adrenals (except during pregnancy). A blood and/or 24-hour urine test should be performed to look for fractionated metanephrines. If any abnormalities are found, it should be followed up with an abdominal MRI or MIBG scan. MRI scans should be ordered, with and without contrast, of brain, cervical, thoracic, and lumbar spine, with attention paid to the inner ear to rule out both ELST and hemangioblastomas of the central nervous system (CNS).

VHL is a disease with many possible manifestations including: brain and spine hemangioblastomas, retinal hemangioblastomas, endolymphatic sac tumors (ELST), benign, asymptomatic lung lesions, pancreatic cysts and tumors, pheochromocytomas (pheos) and paragangliomas (paras), kidney cysts, kidney tumors, cystadenomas (epididymal in men and broad ligament in women) and benign, asymptomatic liver lesions. Dr. Tourtelot emphasized the importance of regular screenings and referred to the VHLA recommended active surveillance guidelines, which can be found at: vhl.org/active-surveillance.

Dr. Tourtelot concluded by describing the average age of onset and frequency in patients, by manifestation:

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Average age of onset (age range of diagnosis), Years</th>
<th>Frequency in Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central Nervous System</strong></td>
<td></td>
<td></td>
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<tr>
<td>Retinal Hemangioblastomas</td>
<td>25 (0-68)</td>
<td>25-60</td>
</tr>
<tr>
<td>Endolymphatic sac tumors</td>
<td>22 (12-50)</td>
<td>10-25</td>
</tr>
<tr>
<td>Cerebellar hemangioblastomas</td>
<td>33 (9-78)</td>
<td>44-72</td>
</tr>
<tr>
<td>Brain stem hemangioblastomas</td>
<td>32 (12-46)</td>
<td>10-25</td>
</tr>
<tr>
<td>Spinal cord hemangioblastomas</td>
<td>33 (11-66)</td>
<td>13-50</td>
</tr>
<tr>
<td><strong>Visceral</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal cell carcinoma or cysts</td>
<td>39 (13-70)</td>
<td>25-75</td>
</tr>
<tr>
<td>Pheochromocytomas &quot;Includes the 20% of these tumors that occur outside the adrenal gland, a.k.a. paragangliomas; frequency depends on VHL subtype.&quot;</td>
<td>27 (5-58)</td>
<td>10-25</td>
</tr>
<tr>
<td>Pancreatic Neuroendocrine Tumor (PNET)</td>
<td>36 (5-70)</td>
<td>11-17</td>
</tr>
<tr>
<td>Pancreatic cyst</td>
<td>36 (5-70)</td>
<td>&lt;=75</td>
</tr>
<tr>
<td>Epididymal cystadenomas</td>
<td>Unknown (17-43)</td>
<td>25-60 (of males)</td>
</tr>
<tr>
<td>APMO or broad ligament cystadenomas</td>
<td>Unknown (16-46)</td>
<td>10 (estimated, of males)</td>
</tr>
</tbody>
</table>
**WHY IS A REGULAR OPHTHALMOLOGICAL EXAM CRITICAL IN VHL**

Brian Madow, MD, PhD, a specialist in the Department of Ophthalmology at the University of South Florida, discussed the importance of regular eye exams as part of the surveillance process.

The surveillance guidelines for people who are at risk for or have VHL, but do not yet have visual symptoms include an annual eye/retinal examination for those ages 1 – 4, by an ophthalmologist skilled in the diagnosis and management of retinal disease. This is especially important for children known to carry a VHL mutation. For those ages 5 and older, an annual dilated eye/retinal examination should be performed.

Dr. Madow pointed out that during pregnancy, women with VHL should undergo more frequent retinal examinations to anticipate the potential of more rapid growth of lesions. Dr. Madow shared that the ophthalmologist is looking for retinal capillary hemangioblastomas, which look like a “ball of small pipes”. The occurrence of retinal capillary hemangioblastomas in VHL has been reported to vary from 50% to 80%. This means that in every 10 people with VHL, 5-8 people will have the “ball”. The average age at diagnosis of retinal capillary hemangiomas in VHL patients is approximately 25 years. Most patients present between the ages of 10 and 40 years. The probability of developing a retinal capillary hemangioblastoma increases progressively with age. The ophthalmologist may use diagnostic photography tools, such as color fundus photos, red-free fundus photos, fluorescein angiography, and fundus autofluorescence. These tools, as part of a comprehensive exam, will help to identify a variety of issues that may be tied to VHL.

Dr. Madow emphasized that early, timely, and continuous periodic retinal examination by a retinal specialist with knowledge of VHL can prevent vision loss.

**ENDOCRINOLOGICAL ADVANCES IN THE MANAGEMENT OF VHL**

John Tourtelot, MD, a specialist in the endocrinology program at Moffitt Cancer Center, discussed the endocrine manifestations of VHL and current updates. VHL is an autosomal dominant disorder caused by mutations in the *VHL* gene and is characterized by the occurrence of multiple endocrine and non-endocrine lesions.

The endocrinological manifestations of VHL are pancreatic neuroendocrine tumors (pNETs), pheos, and paras. They frequently display characteristics that can suggest VHL as the underlying issue. Accurate recognition and classification of these tumors is important in order to determine treatment and follow-up strategies for affected patients.

It is important to note that pNETs are rare, occurring in only about 9% of VHL patients. When they do occur, pNETs are often multiple and can be located throughout the pancreas. Regardless of their size or grade, pNETs can be malignant tumors. Research has shown that signs of local aggressiveness are present in about 60% of VHL patients with pNETs. The identification of local aggressiveness in these tumors is important as it can lead to life-threatening complications.

A pheo is a tumor arising from specific cells in the adrenal glands that commonly produces one or more specific types of hormones. These tumors are rarely biochemically silent, producing hormones known as catecholamines (dopamine, norepinephrine and epinephrine). A para is another tumor derived from specific cells in the thorax, abdomen or pelvis. Evidence has demonstrated that hereditary pheos and paras are characterized by a distinct clinical presentation and differences in biological behavior. About 80 to 85% of these tumors are pheos. Paras are rarer and represent about 15 to 20% of these tumors. Paras can also arise along certain nerves in the neck and at the base of the skull. These tumors do not produce hormones.

It is important to note that not all pheos and paras are alike. Recognizing the distinct presentations of hereditary pheos and paras, it is recommended to take a personalized approach to patient management. This includes biochemical testing, imaging, surgery, and follow-up. Initial biochemical testing for pheos and paras should include blood and 24-hour urine tests.

There are different types of VHL mutations that can increase the chances of having a pheo. Type 1 patients are generally unlikely to have pheos as one of their manifestations. Type 1 is characterized by a whole or partial gene deletion or a nonsense mutation. Type 2 patients also have a lower likelihood of developing pheos. Type 2 is associated with missense mutations. Type 2 is further subdivided in type 2A (low risk for RCCs), type 2B (high risk for kidney tumors), and type 2C (generally pheos only).

Dr. Tourtelot described the importance of preparing for any surgery. All VHL patients should be tested for pheos prior to surgery. Patients with a hormonally functional pheo or para should take medication to prevent cardiovascular complications. Studies show that adrenergic receptor blockers should be started at least 7 days prior to surgery to normalize blood pressure. Taking phenoxybenzamine, an alpha blocker, intravenously for 5 hours per day for 3 days before surgery, has been reported as one...
effective approach. Studies have also found that initiation of a high-sodium diet a few days after the start of adrenergic receptor blockers can prevent low blood pressure upon standing from a seated position, before surgery. It can also reduce the risk of significant low blood pressure after surgery. A target blood pressure of less than 130/80 mm Hg while seated and greater than 90 mm Hg systolic while standing is reasonable, with a target heart rate of 60 –70 bpm seated and 70 – 80 bpm standing.

MINIMALLY INVASIVE MANAGEMENT OF KIDNEY TUMORS IN THE VHL PATIENT

Wade Sexton, MD, a specialist in the Department of Genitourinary Oncology at Moffitt Cancer Center, discussed detection and treatment of tumors of the kidneys. He described that a patient is suspected to have VHL when they have multiple hemangioblastomas in their brain, spine, and/or eye, or have one hemangioblastoma and at least one of the following: kidney tumors, pancreatic cysts, pheos, ELST, or an epididymal cyst.

Dr. Sexton noted that in young patients, VHL is also suspected when there are multiple kidney tumors in both kidneys. He also noted that not every VHL patient develops renal tumors. In fact, for a type 2A patient, there is generally a low incidence and almost no incidence in patients with type 2C. Approximately 25-45% of VHL patients will develop kidney tumors and up to 63% will develop kidney cysts. The average age at presentation is about 39 years old and there are equal rates in both male and female VHL patients. VHL-related renal cell carcinoma (RCC) comprises about 4% of the total kidney cancer incidence.

When treating renal tumors in VHL patients, it is important to preserve as much kidney function as possible. This is accomplished by performing surgery once tumors reach 3 cm, known as the “3 cm rule”. The average growth rate of solid kidney tumors in VHL patients is 4.4 mm/year, which is similar to the growth rate of sporadic RCC. The growth rate depends on several factors, including the type of mutation. Tumors in VHL patients with certain mutations grow at a faster rate than those with other mutations. Faster growing tumors have a higher probability for becoming metastatic. In these cases, physicians should consider more frequent imaging and may even consider surgery at a smaller tumor size.

The majority of VHL-related renal cysts grow slowly. Kidney tumors can occur alone, or in combination with complex cysts. Studies have shown that VHL kidneys comprised 39% tumor volume and 16% cyst volume in relation to total kidney volume.

Renal tumors are addressed in several ways. The goals for managing kidney tumors in VHL patients are to minimize risk of kidney cancer metastasis, preserve renal function, minimize the total lifetime number of surgeries, and to monitor small lesions until they reach 3 cm. Active surveillance allows for the identification of troublesome tumors. When they meet the criteria for surgical removal, partial nephrectomy is recommended, in order to preserve kidney function. Radical nephrectomy should be avoided, if possible. There are a variety of surgical approaches for partial nephrectomy including traditional open incisions, as well as laparoscopic and robotic-assisted procedures. Surgery should be followed by a post-op renal function test.

Another treatment option is ablation, which is generally reserved for tumors less than 2.5-3 cm. Ablation is usually a secondary procedure. Some presentations making ablation not recommended include cystic tumors, tumors adjacent to ureter, intestines, or major kidney vessels, and extensive multifocal tumors. Radiofrequency ablation (RFA) has a 12-21% failure rate, while cryoablation has an 8-10% failure rate. There are concerns about using RFA that include increased local recurrence rates when compared to surgical removal, controversy about metrics for success, and difficulty with future surgeries, if required. The most common complication reported with cryoablation is hemorrhage, usually due to renal fracture. Studies also report pancreatic injury and ureteral obstruction. Cryoablation is associated with good renal function preservation, in the absence of complications. Rarely renal loss has been reported in the presence of complications.

Dr. Sexton concluded by stating that the purpose of kidney sparing procedures in VHL is not to “eradicate” tumors, but rather to “reset the clock”, emphasizing that the best approach is partial nephrectomy.

LIVER AND PANCREATIC MANIFESTATIONS OF VHL

Mokenge Malafa, MD, a specialist in the Department of Genitourinary Oncology at Moffitt Cancer Center, discussed the liver and pancreatic manifestations of VHL. Seventy-seven percent of VHL patients have pancreatic lesions. Most have simple cysts, while 9% have serous cystadenomas (SCA) and 9% have pNETs. Survival rates and quality of life in patients with VHL can be improved by better understanding of the biology of VHL-associated pancreatic and liver tumors. This can be accomplished through improved diagnostics and surveillance, as well as individualized treatments. The management of pancreatic cystic lesions in VHL consists of observation, until the lesions become symptomatic.

For VHL-related pNETs, surveillance is indicated because 40% of patients with pNETs will have no tumor growth or decrease in tumor size over 4 years. Surveillance includes annual CT and MRI scans. In addition, less than 20% of these tumors are malignant. In the case of localized disease, surgical management is indicated when:

- pNETs are greater than or equal to 3cm in the body or tail of the pancreas
- pNETs are greater than or equal to 2cm in the head of the pancreas
The clinical diagnostic criteria for VHL are:

- The tumor doubling time is less than 500 days
- There is a mutation in exon 3 of the VHL gene

In the case of locally advanced, or metastatic disease, surgical management is indicated, if feasible and if greater than 90% of the entire tumor can be removed.

Treatment options for pNET liver metastasis include surgical removal, microwave ablation, selective- intra- arterial –radiotherapy, chemoembolization or bland embolization, and medical therapy. There are a variety of available medical therapies including somatostatin analogues, targeted therapy (mTOR inhibitors), chemotherapy, and peptide-receptor radionuclide therapy.

Dr. Malafa summarized by saying that pancreatic manifestations occur in more than two-thirds of patients with VHL and that any cystic lesions are almost always benign. The presentation of pNETs is different from patient to patient. There are currently better diagnostic tools and more management options than ever before. Ongoing surveillance and individualized interventions can help to ensure optimal outcomes.

### NEUROLOGICAL MANIFESTATIONS OF VHL

Arnold Etame, MD, PhD, a neurological surgeon and scientist specializing in Neuro-Oncology at Moffitt Cancer Center, discussed the neurological manifestations of VHL. Hemangioblastoma tumors are benign and are classified as Grade 1 tumors by the World Health Organization.

Hemangioblastoma tumors are very common in VHL patients and can be seen in the brain and spine. These tumors are monitored using MRI scans of the brain and spine. They are often nodular (solid) and can have a cyst. In the brain, hemangioblastomas are usually found in the cerebellum and brainstem. They can also be seen in the other areas of the brain. Symptoms depend on location, tumor size, tumor bleeding, and swelling. Tumors in the cerebellum can bleed and block the flow of spinal fluid. This can result in nausea, loss of coordination, and feeling tired. Brainstem lesions can cause difficulties in swallowing, breathing, seeing, and feeling tired. Spinal lesions can cause weakness (paralysis), balance issues with walking, sensory symptoms, and bowel and bladder problems.

The vast majority of VHL hemangioblastomas will remain asymptomatic and will never require treatment. Close surveillance with MRI scans of the brain and spine is advised. Surgery is the primary treatment option, particularly when dealing with symptomatic lesions. Surgical removal of non-symptomatic lesions is highly controversial and not generally recommended. Stereotactic radiosurgery (SRS) is another emerging radiation therapy treatment option. Evidence has shown that SRS in the brain is much more effective for small and solid tumors, as compared to large and cystic tumors. Furthermore, SRS is ideal for patients who are deemed high risk for surgery, those with multiple lesions, or those with tumors not amenable to surgical removal.

Dr. Etame summarized by saying that hemangioblastomas that are symptomatic, or demonstrate worrisome radiographic features, warrant surgical removal if safely feasible. However, most hemangioblastoma patients will never need treatment. Close MRI surveillance with a neurosurgeon is very important. When treated appropriately, excellent long-term outcomes can be expected with surgery, as well as radiation therapy in the right setting.

### THE GENETICS OF VHL

Xia Wang, MD, PhD, a specialist in the Department of Genetics at Moffitt Cancer Center, discussed the genetics of VHL. Normal tissue growth is regulated by many genetic factors. Each cell in the human body has the same set of genomic blueprints of ~20,000 genes with which we are born. The VHL gene is a tumor suppressor and VHL mutations predispose individuals to developing tumors. VHL affects approximately 1 in 36,000 births. Active surveillance can find VHL-related tumors before they cause symptoms. Finding the tumors early leads to early intervention, which results in better outcomes.

Dr. Wang then explained that anybody with a family history of VHL should be screened. Approximately 20% of the individuals affected with VHL did not inherit it from the parents and are known as de novo (new) cases. VHL follows an autosomal dominant inheritance pattern. There are a variety of types of VHL gene mutations, including deletion of a segment of the chromosome, base pair (DNA code) changes, and the deletion of a segment of the gene.

The clinical diagnostic criteria for VHL are:

- Simplex case with two or more of the following:
  - Two or more hemangioblastomas
  - A single hemangioblastoma with multiple kidney or pancreatic cysts
  - Kidney tumors
  - Pheos
  - ELSTs, cystadenomas of the epididymis (men) or broad ligament (women), or pNETs
- VHL diagnosis based on VHL gene testing
The technology for genetic testing has changed dramatically in the past 10 years. While it may take some time for results to be accurately read and reported, results can often be given within days or weeks. Sanger sequencing reading the raw sequences of the VHL gene can take 3-4 days to perform. Large deletions detection by Southern Blot can take 4-5 days to perform. Next-generation sequencing can detect a single code change, small/large deletions or duplications. It can take as little as 3 days for the raw sequences of the entire human genome. The type of genetic testing performed and the amount of time is takes to receive results is dependent on the lab performing it. Types of VHL variations include: disease causing variations, resulting in loss of function/dysfunction; benign variations, resulting in normal function; and variations of unknown significance (VUS).

Dr. Wang noted that the interpretation of a variation is not always straight forward. Genetic testing of skin or blood cells can be used to find the germline mutation, while genetic testing of tumor tissue may reveal the germline and/or the somatic mutation.

**APPLICATIONS OF PERSONALIZED MEDICINE IN THE CARE OF PATIENTS WITH VHL AND OTHER HEREDITARY RENAL MALIGNANCIES**

Howard McLeod, PharmD, Chairman of the Department of Personalized Medicine at Moffitt Cancer Center, discussed the clinical dilemma in which as the number of choices of treatments increases, so does the difficulty in making a decision on appropriate course of action. There are multiple types of treatment for most cancers. There is also a variation in response to therapy and unpredictable toxicity. This demonstrates the importance of deciding on a course of action that is appropriate for the individual patient.

Many clinical interventions are based on the increased probability of a problem occurring. As risk for the patient increases, so does the necessity of staging an intervention. There are many reasons why there is a focus on drugs. Adverse drug events are fifth leading cause of death in the United States. Adverse drugs events are heavily litigated and often predictable. Cancer chemotherapy is also very expensive, which increases the importance of choosing the appropriate course of action. In addition, there are opportunities to improve the value of treatments, with new research and tailored interventions.

Dr. McLeod described how cancer care is changing rapidly and how it presents an opportunity, as well as a threat. There are practical choices to be made. Doctors have to select treatments among “equals”. They have to decide what is an acceptable level of toxicity to the patient. Every doctor has to perform an assessment of the benefit to risk ratio, in order to avoid risk and assure the best chance of a benefit.

Dr. McLeod concluded that using a clinical risk panel can help in providing clinical pathway-driven care. By adhering to cancer risk guidelines, identifying underlying susceptibility to severe toxicity, reducing risk of negative drug effects, improving probability of benefit, and studying the growing number of ‘actionable’ genes, doctors can individualize the treatment to the specific patient and expect the best possible outcome.

**CARING FOR YOUNG PATIENTS WITH VHL: INSURING NEEDS AND DEMANDS ARE MET**

Damon Reed, MD, Director of the Adolescent and Young Adult Program at Moffitt Cancer Center, discussed the adolescent and young adult program at Moffitt for young adults with cancer, and those predisposed to cancer. Dr. Reed stressed the importance of a comprehensive program that addresses the medical, psychosocial, reproductive, educational, survivorship, and research needs of this population.

At Moffitt, 12% of all new patients are adolescents or young adults. They represent about 125 outpatient visits per day and occupy about 10% of inpatient beds. Every clinic at Moffitt sees at least one adolescent or young adult patient each week.

Dr. Reed described how traditionally, hospitals are set up with individual “silos” by department, location and training. He went on to detail how Moffitt is making efforts to coordinate care across “silos” for this special population by using patient navigators. Dr. Reed also noted that information about fertility and family planning is an important part of providing care to this population. In addition, financial and insurance counseling should be offered because adolescent and young adults have reported that lack of health insurance was the biggest barrier to receiving medical care during the first few years after diagnosis. Research is ongoing on types of treatments and best practices for treating adolescents and young adults.

**THE PAST, PRESENT AND FUTURE OF VHL: A CLINICAL PERSPECTIVE**

Eric Jonasch, MD, Professor in Genitourinary Medical Oncology at the University of Texas MD Anderson Cancer Center described the past, present, and future of clinical research into VHL. He stated that many layers of knowledge are needed to develop a cure for VHL, including:

- Identification of the VHL Gene
- Description of VHL protein Function
- Identifying and Characterizing Additional genes Disrupted in VHL Disease
- Generate real-world patient databases
- Development of relevant model systems
Detection -> followup -> treatment

New and ongoing research studies are adding to our wealth of knowledge by addressing unmet needs in areas of basic science, screening tools, models of disease, imaging technology and data collection. There is a number of promising new therapies being tested that block the consequences of VHL loss, including pazopanib and a new drug by Peloton called PT2977. PT2977 is a next-generation HIF-2 alpha blocker that is administered in pill form. A study will be launched in early 2018 to test the effect of PT2977 on kidney and other manifestations in individuals with VHL. The primary goal of the study will be to see whether kidney tumors shrink. It will also assess impact in other sites.

The VHL Alliance has awarded nearly two million dollars in research grants to date. Grants are chosen by a review committee consisting of world leaders in VHL research. There is a strong emphasis placed on translational research which will benefit patients sooner rather than later.

VHLA grants come in two sizes: a one-year $25,000 pilot grant and a two-year $100,000 research grant. Each research proposal is evaluated on rationale, approach, and significance.

2014 Full Grant Awardee: Dr. Othon Iliopoulos, Massachusetts General Hospital
Dr. Iliopoulos’ team uses zebrafish with VHL to screen drugs that may help treat people with VHL. Zebrafish with the VHL gene deleted display a number of VHL lesions similar to those seen in people. Since these tiny fish are relatively transparent, you can actually “see” the effect that potential drugs have on the VHL manifestations. Work is almost complete and will be published soon.

2015 Pilot Grant Awardee: Dr. A.N.A. van der Horst-Shrivers, University Medical Center in Groningen, Netherlands
Dr. Horst-Shrivers’ team is trying to understand if hormones produced by pheochromocytomas can be reliably measured in saliva. If successful, this would enable VHL patients to screen for pheos using a “spit in cup” method instead of the 24-hour urine test or the blood test which requires you to rest for 30 minutes before the blood draw.

2015 Full Grant Awardee: Dr. Ian J. Frew, University of Zurich
Dr. Frew’s team is using a mouse model to test drugs that may be able to treat clear cell renal cell carcinoma (ccRCC), a type of kidney cancer that frequently affects VHL patients. This research will be used to guide new trials in people with VHL or other patients with noninherited ccRCC.

2016 Pilot Grant Awardee: Dr. Raymond Kim, University of Toronto
Dr. Kim will head the international VHL-IT Sharing International Consortium (VISIon) with the goal of developing a more efficient approach to collect information on VHL mutations and the way that VHL manifests in these individuals. This will help us better understand genotype-phenotype patterns (ie: which mutations cause which manifestations).

2016 Full Grant Awardee: Dr. Michael Gorin, University of California Los Angeles
Dr. Gorin is developing two new models to study VHL retinal lesions. One model will use inducible pluripotent stem cells. This means that undifferentiated somatic cells (ie: undifferentiated skin cells, blood cells) can be trained to act as a cell in the eye. The other model involves a VHL knockout mouse which will allow us to better understand how retinal hemangioblastomas form and develop new strategies for blocking the formation of these retinal tumors.

VHL Patient Natural History Study
This gives VHL patients an opportunity to contribute their own information. With more people participating longitudinally, we can better understand the natural history of the disease. One finding from the databank is that dry mouth, canker sores, and other oral health issues are seen at a higher incidence in VHL patients than they are in the general population. Another finding that is being further investigated is the association between VHL and thyroid issues. For more information, go to: vhl.org/databank.

We anticipate that all of these studies will help move the field of VHL research forward substantially in the next few years.

Dr. Jonasch concluded by saying that, with regard to VHL research, in the past we identified the VHL gene, currently we are determining how VHL deficiency affects patients, and in the future we can expect the development of new ways to treat VHL.