

NEWSLETTER

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ERECTILE DYSFUNCTION DEBATE

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MESSAGE FROM THE SIU PRESIDENT

Jack W. McAninch

It is a great honour for me to have been entrusted with this function, and I hope not only to meet the expectations of our members, but to do justice to my predecessors as well.

I wish to convey my gratitude to all our colleagues whose efforts made the Hawaii Congress such a memorable experience: Michael Rochford, SIU President; Luc Valiquette, Congress Organizing Committee Chair; Mostafa Elhilali, SIU General Secretary; Hugh Whitfield, Scientific Programme Chair; Richard Fourcade, Treasurer, dozens of other members who gave of their time generously, as well as our staff at the SIU Central Office. Their combined dedication allowed us, for the very first time in SIU history, to put on a very successful event completely independently.

The Society has evolved and grown over the past decade, adding new members, expanding

the reach of urological education to specialists in the developing world, facilitating regional, topical meetings that are more easily accessible to local urologists, sponsoring SIU lecturers to attend National meetings, maintaining the commitment to the Fellowship programme.

Yet in today's rapidly-changing world, it is not enough to rest on our past achievements. We must look towards the future and the trends that will shape it, and consider the direction in which we wish to see our organization go. And I see the future of the Society also resting on its members: their interests, their concerns, their priorities. During my tenure, I would like to hear about what the SIU can do for you – its members – and how you feel that you can contribute.

This is an important society to belong to. We have developed into an inclusive, international

organization with roots in 107 countries. We want to continue to fulfill our mission and meet the challenges that await us. I urge you all to consider the importance of your commitment to this Society.

I encourage those of you interested in diseases of the prostate to attend the SIU Meeting in Bariloche in September 2005. I also remind you all that our 2006 Congress will be hosted by our friends and colleagues in Cape Town, with Chris Heyns at the helm of the Local Organizing Committee.

I look forward to the challenges of the next two years, as we approach our Society centennial and continue to strive to build a stronger and more united international network to promote excellence in urological care.

NEW BOARD OF CHAIRMEN ELECTED AT HONOLULU

As is customary during the biennial Congress, the election of the new Board of Chairmen (2004-2006) was finalized. We take this opportunity to introduce the Board to our membership and welcome new Board members. We also wish to thank our departing Board members for their contributions, their commitment and their dedicated hard work for the Society.

President

Jack W. McAninch (USA)

President-elect

Alain Jardin (France)

Past President

Michael J. Rochford (Australia)

General Secretary

Mostafa M. Elhilali (Canada)

Treasurer

Richard O. Fourcade (France)

Congress Organization

Luc Valiquette (Canada)

Scientific Programme

Martin I. Resnick (USA)

Consensus and Education

Paul Abrams (UK)

Institutes and Scholarships

Joachim Thüroff (Germany)

Publications

Reynaldo Gómez (Chile)

Internet and Communications

Eiji Higashihara (Japan)

Long-range Strategic Planning

Christopher Woodhouse (UK)

International Relations

Ismail Khalaf (Egypt)

Sub-specialties

Mahesh Desai (India)

Fundraising

Shiro Baba (Japan)

National Delegate Representative

Christopher Cheng (Singapore)

National Delegate Representative

Arnaud Villers (France)

General Assembly Representative

William J. Lynch (Australia/New Zealand)

General Assembly Representative

Narmada P. Gupta (India)

SIU Award Winners

In a well-attended ceremony, Past President Michael Rochford awarded in Honolulu the very first SIU **Félix-Guyon Medal**, for outstanding service to the Society, to Professor René Küss of France.

In addition, four long-time SIU members received **Distinguished Career Awards**, honouring members who have contributed significantly to the field of urology over the course of their careers: Dr. Yoshio Aso (Japan), Dr. John P. Donohue (USA), Prof. Dr. Rudolf Hohenfellner (Germany), and Prof. Sami Arap (Brazil).

Finally, at the first plenary session on October 3, 2004, Prof. Dr. Michael Marberger was granted the **2004 Yamanouchi Award**, as a scientist of excellent professional and ethical standing and in recognition of his contribution to the international development of urology.



Highlights from the 27th Congress in Honolulu, Hawaii

Facts and Figures

Total number of participants: 2,858

Number of countries represented: 102

Top 6 countries: USA, Japan, UK, Spain, Poland, Canada

Total abstracts received: 1,325 (*record number*)

Countries represented: 55

Top 5 countries: Japan, USA, UK, South Korea, Iran

Number of exhibiting companies: 44

Number of square feet occupied by exhibition: 26,000

HIGHLIGHTS FROM SIU GENERAL SECRETARY'S REPORT AT GENERAL ASSEMBLY

The General Assembly of the SIU convened at Honolulu on Wednesday, October 6, 2004. General Secretary Mostafa Elhilali reported on a number of activities, including the major decisions enacted by the Board of Chairmen during its meeting on Saturday, October 2, 2004.

During the GA, 403 Candidate members were voted in as Active members. The top 6 countries represented were Australia, Canada, Egypt, India, Iran and Pakistan.

Dr. Elhilali presented the membership report, stating that the SIU had 2,441 Active members and 841 Senior members. With the addition of the 403 newly-elected Candidate members, the total membership now stands at 3,685.

The SIU Lectureships, wherein SIU lecturers speak at national annual meetings (as well as at organizations such as the AUA and the EAU), are becoming one of the Society's most high-profile activities, stated Dr. Elhilali. From 4 such Lectureships in 2003, the number rose to 7 in 2004. Continuing to promote these Lectureships is one of the SIU's objectives.

The success of the 2003 Sharm El-Sheikh Meeting demonstrated that this regional and topic-specific format is of great interest to urologists. The SIU continues the series with the 2005 Meeting on Prostatic Disease in Bariloche, Argentina, hosted by Dr. Leon Bernstein Hahn and his local committee.

The General Secretary also informed the GA of a recent Board of Chairmen decision, whereby a significant budget was approved to support the successful fellowship and scholarship programmes already in place, as well as for specific training projects in addition to the current 20 SIU-accredited training institutes throughout the world. For the 2002-2003 period, 22 fellowships were awarded. Fifteen were approved for 2004, and the field is still open for 2005.

In awarding the fellowships, priority is given to those applicants who are interested in training regionally in order to facilitate the transfer of knowledge and skills once they return home.

The Board of Chairmen also agreed to the creation of a special task force that will consider the feasibility of an SIU Office of Education. Coordinating this initiative will be Scientific Programme Chairman Martin Resnick, who will lead a triangular consultation with the Consensus and Education Committee, the Institutes and Scholarships Committee, and the International Relations Committee. The results of this process will help direct the SIU towards a more comprehensive educational office to promote teaching and continuing education.

Dr. Elhilali also touched upon the introduction of new awards for SIU members, the Félix-Guyon Medal which acknowledges major contributions to urology and to the SIU, as well as the Distinguished Career Awards, created to honour members who have contributed to urology and to the development of the SIU in a significant manner.

Another important item brought to the attention of members concerns the Society's journal. Indeed, after five years of cooperation, the contractual agreement between the SIU and the *BJUI* expired, and *Urology (The Gold Journal)* was chosen as the official journal of the SIU. *Urology* will also produce special supplements for the abstracts accepted for presentation at Congresses and Meetings.

Finally, Dr. Elhilali commented that for the first time, the SIU had planned its Congress in-house through its Montreal-based Central Office. This proved to be a success on many levels, and will thus be the way of the future. Apart from its initial function of providing membership services, the Central Office now manages the organizational/logistical/scientific/sponsorship/exhibits for the biennial Congresses, the off-year Meetings and ongoing industry relations.

Special Lecture: Drug availability in the developing world

Kenneth G. Watson, MD, Vice President, Head of Global Marketing, Yamanouchi

From the developing world's point of view, not all new drugs are essential. In 1997 the WHO published its first Essential Drug List, which is revised every two years. The last update (April 2002) contained 325 active substances. Worldwide, 135 countries have developed corresponding treatment guidelines and formularies. They offer specific training in rational prescription, centred on a problem-based rather than a choice-based approach.

In 2003 patents expired on more than 30 so-called blockbuster drugs, representing a huge loss of corporate income. Ninety-five percent of the drugs in the WHO's Essential Drug List no longer enjoy patent protection. Patents do not exclude access to essential medicines. Either the patents have expired or have yet to be filed in 65 Asian, African and Latin American countries with a total population of four billion people.

Non-signatories to trade agreements do provide better access to medicines. India is an example. In Africa 320 million people have access to less than 50 percent of listed medicines. A shortage of hospitals and clinics means that even available drugs fail to reach patients. Where the industry releases drugs and the infrastructure is poorly developed, patients are also denied access. As well as trade agreements, poverty and politics determine accessibility.

Counterfeiting is another major issue. Counterfeiters violate quality guidelines. Either they supply an incorrect ingredient or an incorrect amount of an essential ingredient. Mostly, they offer placebo. Counterfeiting is one of the biggest threats to an industry accused of offering drugs that do not work, are too expensive, and unsuitable for Africa or Asia. Counterfeit drugs comprise 6 percent of the world pharmaceutical market – a percentage rapidly escalating in third-world countries.

The industry – and governments and universities – must work together to improve delivery networks, to train people locally to provide better healthcare, and also to improve the infrastructure. Here, the SIU should be applauded for initiatives in training urologists on-site, for providing educational materials to developing countries, and for improving local practices.

Finally, an often-overlooked item: the industry's health-spending in developing countries equals the WHO's annual budget.

AWARD LECTURE: THE CHALLENGE OF CHANGE

Michael Marberger, MD, Professor & Chairman, Dept. of Urology, University of Vienna, Austria

Thirty years ago, open kidney surgery was the topic in urology. Using a variety of surgical and reconstructive techniques, urologists excelled at extracting staghorn stones – and we did wonderful things removing these daunting stones and putting the kidneys back together.

In the early 1980s percutaneous nephroscopy led to improved surgical techniques. Ten months after our initial account of 21 patients (three of whom we had to convert to open surgery) at the AUA (1981), we presented a retrospective comparison between 100 percutaneous cases and 100 open surgical cases. Compared to the latter, the former had reduced surgical trauma, lower complication rates, and required shorter hospitalisation.

Within four years we had moved to 75-percent percutaneous surgery, and in another four years urologists were doing extracorporeal surgery, using lithotripsy and lithoclasty to extract most stones. By 1997, a review of lithotripsy in Germany showed a complication rate of 0.66 percent in approximately 12,000 treatments, only three of which resulted in nephrectomy. Today, we can disintegrate even the hardest of stones using a holmium laser, with little peripheral soft-tissue damage.

Laparoscopic radical nephrectomy, now the standard procedure for removing tumour-bearing kidneys, offers the same oncological results as open surgery depending on tumour stage and metastasis.

Partial laparoscopic nephrectomy remains a daunting procedure, with a complication rate of between 13 and 16 percent, comparable to that in radical laparoscopic nephrectomy. Thirty years ago we used trans-arterial perfusion cooling in open partial nephrectomy, a technique now being revived for partial laparoscopic nephrectomy.

Cryoablation has been around for some time. With laparoscopy this requires anaesthesia, but has an acceptable recurrence rate of less than 2.8 percent. This has been attempted percutaneously with the new cryoneedles, a technique that is still evolving.

At the other end of the scale, heat ablation could almost be described as an easier way to destroy kidney tumours. We can now reach temperatures in the 100-degree range without major problems. Percutaneous radioablation techniques have also existed for a considerable time, with good results. However, they have a higher recurrence rate of around 10 percent, and there is some risk of leaving residual tumour.

High intensity focused ultrasound is the latest development, but this is still experimental. It is difficult to say which technique will provide a breakthrough. It could come from genetics. One thing is certain: change will be there. And the only way we can cope with it is to observe the transitions in an open-minded manner, adopting new techniques where they appear favourable to the patient.

FIRST GLOBAL GU ONCOLOGY CONFERENCE: CO-CHAIRMEN'S REPORT

by Laurence Klotz, MD and Yves Fradet, MD

The management of prostate cancer varies substantially between different regions in the world. This reflects many factors, including resource issues, differences in prevalence and mortality rates, access to specific treatment modalities, the influence of opinion leaders, and local traditions.

The Global GU Oncology Conference, held in conjunction with the SIU, brought together urologists with an interest in oncology from around the world. The Conference was organized around regional working groups, who were given the task of developing a consensus around several specific controversial subjects in prostate cancer management.

This consensus development process represented a unique opportunity to determine the range of approaches to prostate cancer by the urological community, and to identify areas of agreement and disagreement. The questions were deliberately constructed to draw out the range of practice, and to identify common clinical scenarios in which the greatest differences of opinion exist.

Approximately **450 attendees** participated in this process. Participants were informed in advance that they would be expected to participate actively in these working groups. Attendees were divided into 9 groups according to geographic regions and number of attendees, as follows :

- 1) United States
- 2) Canada
- 3) Asia-Pacific: Bangladesh, China, India, Malaysia, Myanmar, Pakistan, Philippines, Singapore, Taiwan, Vietnam
- 4) Africa
- 5) South and Central America
- 6) Central Europe: Austria, Belarus, Bosnia, Bulgaria, Czech Republic, Estonia, Germany, Hungary, Latvia, Lithuania, Poland, Russia, Slovakia, Switzerland
- 7) Southern Europe: Greece, Italy, Portugal, Spain, Turkey
- 8) Western Europe: Belgium, Denmark, France, Iceland, Ireland, Netherlands, Sweden, United Kingdom
- 9) Japan, South Korea

Each regional group was provided with common prostate cancer scenarios related to a) screening b) management of good risk disease and c) management of high-risk localized disease. Attendees were divided into regional groups of between 5 and 50 participants. Each group was provided with the scenarios listed below. Where a consensus did not exist, the variation in views was recorded.

The responses are fascinating. The variation in the degree of consensus is particularly striking. The responses to selected questions are presented here, while full results will be published in an upcoming issue of the *Canadian Journal of Urology*.

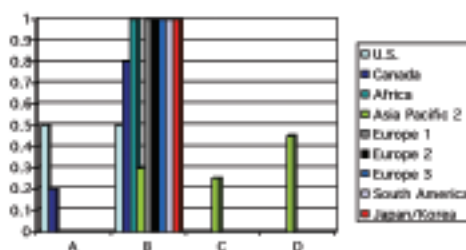
Results

Screening and Early Detection

Question 1: Regarding screening and early detection in my region, the following most closely reflects my views:

- a) All men above age 40 should have an annual PSA test
- b) All men between 50 and 70, and men over 40 with positive risk factors, should have an annual PSA test
- c) PSA screening is warranted only for high risk patients (with a strong family history or Black)
- d) PSA screening should not be carried out routinely

Question 1



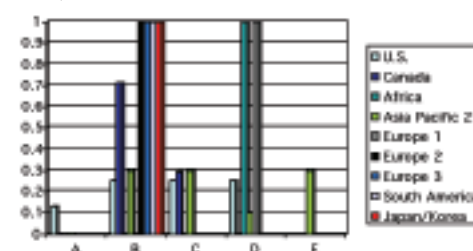
Comment : Considering the uncertainty in the literature over the benefits of screening, there was a remarkable degree of consensus. With the exception of Asia-Pacific, most regions supported the traditional approach to screening, i.e., men between 50 and 70. In North America, there was a trend to early initiation of screening. In Asia, there was support for a restricted approach to screening. Regions with historically low prostate cancer mortality rates report a dramatic increase in the last decade; prostate cancer is now the

third most common malignancy in the Philippines, and the fifth most common in Singapore.

Question 2: Assuming that a decision has been made to perform PSA screening:

- a) All men between 40-80 years of age, annually
- b) Men between 50 and 75, annually
- c) Men between 50 and 75, every 2 years
- d) Men between 50 and 75, every 5 years (assuming baseline value is low)

Question 2

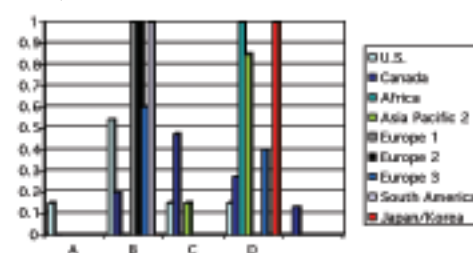


In contrast, there is wide variation in the recommended screening interval globally. Some propose increasing the screening interval if the initial PSA is low (< 1.0)

Question 3*: A 55 year-old man has an elevated PSA. He has a benign, 30cc prostate by DRE. Currently, the indication for the biopsy is a PSA of:

- a) > 2.0
- b) > 2.5
- c) > 3.5
- d) > 4.0
- e) Other

Question 3

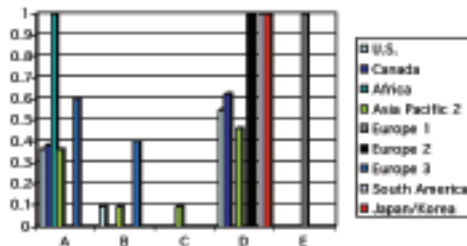


In addition, there is wide variation globally in the optimal PSA threshold for biopsy. Several confounding factors were identified, including differences in prostatic volume between Asian regions and Western countries, and the need for PSA reference ranges based on Asian patients.

Question 4: A 65 year-old healthy male has a PSA of 4.5. DRE reveals a 35cc benign prostate. Biopsy reveals a single microfocus (1mm) of Gleason 3+3=6 adenocarcinoma. Optimal management is:

- a) Active surveillance
- b) Brachytherapy
- c) External beam irradiation
- d) Radical prostatectomy

Question 4

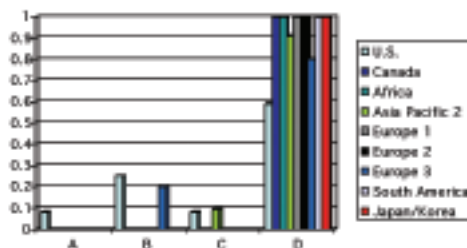


Comment : There is a diversity of opinions on the management of very good risk cancer. This was seen both within and between regions. Unavailability of brachytherapy restricted this choice in some areas.

Question 5: A 65 year-old healthy male has a PSA of 4.5. DRE reveals a 35cc benign prostate. Biopsy reveals 3/10 cores (all on the right) positive for Gleason 3+3=6 adenocarcinoma. 10% of each core is involved. Optimal management is:

- a) Active surveillance
- b) Brachytherapy
- c) External beam irradiation
- d) Radical prostatectomy

Question 5



With more extensive disease, there is a definite worldwide consensus for radical prostatectomy for good risk patients.

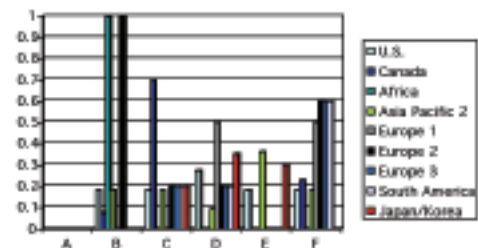
High-Risk Prostate Cancer

A 55 year-old healthy male develops moderate voiding symptoms over a 6-month period. He has a PSA of 22. DRE reveals a T2b nodule involved about 50% of the gland on the left. TRUS shows a 1.5 x 2 cm hypoechoic nodule in the left base. Seminal vesicles appear normal. Biopsy shows Gleason 8 prostate cancer involving 4/10 cores on the left. There is involvement of 40% of the surface area. A staging workup, including bone scan and CT pelvis, is negative.

Optimal management is:

- a) External beam irradiation
- b) External beam irradiation plus adjuvant androgen deprivation
- c) Radical prostatectomy, with surveillance until PSA progression (regardless of margins)
- d) Radical prostatectomy with adjuvant radiation for positive margins
- e) Radical prostatectomy with adjuvant or neoadjuvant hormone therapy for positive margins
- f) Radical prostatectomy with androgen deprivation and adjuvant radiation for positive margins

High-risk Question 1



This question revealed a marked diversity of views, both within and between regions. Many throughout the world believe surgery has a role for high-risk patients, particularly in combination with adjuvant therapy.

Conclusion: This exercise provided a unique opportunity to examine the range of opinion on the management of localized prostate cancer. Despite a diversity of views regarding optimal treatment strategies, the exercise revealed broad agreement in some areas. The degree of diversity itself was diverse; in some regions a consensus exists regarding a specific approach, and in other regions there is a complete lack of consensus on the same issue. This range of approaches undoubtedly reflects local epidemiologic factors, resource issues, and the influence of opinion leaders and regional treatment patterns. International consensus development based on regional patterns of practice provides an opportunity for practitioners to broaden their perspective on the management of common clinical scenarios.

DEBATES

The debate format developed for Honolulu by Scientific Chairman Hugh Whitfield was a successful addition to the 27th Congress. Debates were held on the topics of BPH, ED and the overactive bladder.

Overactive Bladder Debate

Moderator : Martin van der Weyden, MD,
Editor, *Australian Medical Journal*

Anticholinergics in the treatment of overactive bladder

Peter Herbison, PhD, Department of Preventive and Social Medicine, Dunedin School of Medicine, New Zealand

Our statistical review (*BMJ*, April 2003) looked at different anticholinergics used to treat OAB in 53 randomized controlled trials conducted between 1978 and 2001. We compared only studies with placebo and anticholinergic arms.

Meta-analysis showed that 40% of patients receiving anticholinergics reported subjective cure and improvement, with approximately one fewer leakage episode every 48 hours in the anticholinergic arm compared to the placebo arm. Only two of the studies included quality-of-life issues.

We found no evidence that anticholinergics caused increased residual volume, and no difference in withdrawal risk between the placebo and anticholinergic arms. Twenty of the included 34 studies found dry mouth the most significant side effect, with patients in the anticholinergic arm about 2.5 times more likely to get dry mouth than patients in the placebo arm.

Trospium chloride, tolterodine, and oxybutynin had much the same effects. Most results were measured at 12 weeks. Drug companies funded many of the trials, which had fairly restrictive inclusion criteria. There are no cost-effectiveness data on anticholinergics. It may be doubtful whether the minimally significant clinical results apply to patients seen in the urologist's office.

Large, pragmatic trials with long follow-ups are needed to measure the effectiveness of anticholinergics in the treatment of patients with OAB.

Meta-analysis questioned

Paul Abrams, MD, University of Bristol Medical School, UK

Meta-analysis cannot show how individuals will respond to anticholinergics. It can reveal mean data trends, but little of real-life patient experiences. A patient's clinical profile (plus his

or her responsiveness to specific drug or surgical therapy) determines the outcome more than any statistical analysis.

Clinical experience shows that patients do not improve by one micturition every 24 hours, or by one less leakage episode every 48 hours. Manufacturers' analyses of the data confirm a huge range of observable clinical differences. They also confirm that over a seven-day period about a quarter of patients will be dry on three different drugs.

The placebo effect is a complicating factor in OAB trials. Patients who participate in such trials believe they will do well. Screening out optimists would further skew the data. No randomized control trial could inform patients they were taking placebos. And it would be expensive to reproduce the placebo effect in clinical practice.

While there may be a need for large-scale, long follow-up trials, anticholinergics currently offer patients a one-in-four chance of a more than 90% improvement. OAB is a lifelong disease with no known cause or cure. However, good methodology and management can improve quality-of-life issues for OAB patients.

Erectile Dysfunction Debate

Framing the data

Moderator: Edwin Chan, PhD, Clinical Trials and Epidemiology Research Unit, Ministry of Health, Singapore

Most randomized clinical trials (RCTs) of PDE5 inhibitors have good internal validity. While the efficacy of PDE5 inhibitors is unquestionable, many RCTs have poor external validity due to a highly selected study population and short follow-up times.

Although several RCTs exist of difficult-to-treat ED patients, some methodological problems remain. Flexible versus fixed doses, treatment of naïve or experienced populations, drop-out rates, exaggerated placebo effects, and excluded non-responders enriching the population of PDE5 inhibitor-responders – all these, if unacknowledged, fail to give comparative measures with the confidence intervals that clinicians require from such studies.

Much depends on how the raw data are framed. With binary comparisons, an absolute risk difference against a relative risk difference may produce seemingly different results even for the same drug. If different PDE5 inhibitors show big percentage differences, then it is because the relative risk difference is being used to promote product marketability.

Continuous comparison scores present similar problems. For example, the IIEF validated scores are treated as continuous scores, while Q3 and Q4 item scores are often not presented as differences from placebo but as differences from the baseline. This is potentially even more deceptive if presented as a percentage difference, because it exaggerates the treatment effect. A publication on sildenafil in diabetics reports the Q4 outcome score as a 93% change from baseline versus a 14% change for the placebo. However, the actual mean difference is 1.2 and the baseline score is 1.3; hence the absolute change or improvement is not nearly so great.

Another study claims that sildenafil (84%) is slightly more effective than vardenafil (80%) and tadalafil (81%). Sampling and measurement error may make treatments appear to differ in effect when they in fact do not. Every estimate of treatment benefit should be accompanied by an estimate of the margin of error.

Sildenafil citrate – six years of ED treatment

Culley Carson III, MD, University of North Carolina, Chapel Hill

In 1997, urologists used the pejorative term "impotence" instead of erectile dysfunction. Injections, MUSE, or penile implants were the conventional – and invasive – treatments. All that changed with the revolutionary introduction of the first clinically available, safe PDE5 inhibitor, sildenafil citrate, about six years ago.

Since then there have been more than 130 completed and ongoing trials, with over 13,000 patient-years of exposure in more than 8,000 men – many more in clinical practice. The studies of diverse populations include more than 2,000 peer-review publications in such journals as *NEJM* and *JAMA* demonstrating Viagra's efficacy and safety, with 500 peer-reviewed papers and over 90 papers on the cardiovascular effects of sildenafil and new research on its efficacy in such problems as pulmonary hypertension and Raynaud's phenomenon.

Our study (Carson et al., *Urology* 2002) examined Viagra in a variety of co-morbid conditions: diabetes, radical retropubic prostatectomy, ischemic heart disease, hypertension (treated and untreated), depression, and peripheral vascular disease. All had statistically significant improvements in erectile function compared to placebo.

ED is difficult to treat in patients with radical prostatectomy. Sildenafil is more effective in patients with bilateral nerve-sparing than unilateral nerve-sparing prostatectomy, and is

significantly better than in non-nerve-sparing prostatectomy (Zippe et al., *Urology* 2000). The study also measured spousal satisfaction.

Because of significant vascular risk factors, diabetics are another group of difficult-to-treat ED patients. Studies show statistically significant improvement in erectile function with sildenafil compared to placebo, but not quite as significant as in non-diabetics. Diabetic patients need to control their diabetes to have the best response to sildenafil.

An open-label extension study confirms sildenafil's long-term safety (ISSIR Montreal 2002). The data on almost 1,000 patients show that satisfaction with erections continued to be the same at one to four years, and clearly demonstrate no tachyphylaxis or efficacy loss. Only 1.2% of patients discontinued due to adverse events. While 6 percent discontinued because of efficacy loss, that probably reflected progression of the underlying diseases that initially caused their ED.

Harin Padma-Nathan studied 220 sildenafil responders in a double-blind, placebo-controlled, 100 mg PRN design using a stopwatch (*Urology* 2003). Onset of action was statistically significantly better than placebo at about 13 to 14 minutes. Patients with mild to moderate ED showed rapid onset of action. Patients with severe vascular morbidity needed to wait longer.

Adverse events are significantly more probable than with placebo. Headache and vasodilation decrease with time.

Sildenafil has a large body of evidence – probably greater than for tadalafil and vardenafil – showing its fast action and broad and long-term effectiveness regardless of age, severity or underlying ED etiology. Sildenafil does not have an alpha-blocker contraindication in the US, and is not associated with tachyphylaxis. Well tolerated, sildenafil has set the world standard for ED treatment.

Levitra – vardenafil HCl

Ken Sprenger, Bayer HealthCare, USA

All three PDE5 inhibitors treat ED effectively. Tadalafil is long-acting, sildenafil and vardenafil short-acting. Physicians may want to consider this when prescribing these drugs.

Another factor is sexual ecology. This still-evolving concept may be defined as the pattern of relations between an individual's sexuality and the aggregate of biological and socio-cultural conditions that influence an individual's life.

The MALES study examined some 28,000 patients in eight countries, to determine the prevalence of ED and co-morbid conditions. A

follow-up questionnaire of approximately 2,400 ED patients asked for their behavioural approaches to ED and its pharmacotherapy. The patients judged safety, tolerability, and therapeutic reliability as essential.

Is rapid onset important? Bayer-GSK studied about 708 men who received either 10 mg or 20 mg of vardenafil or placebo. These patients were either naïve or sildenafil-responsive, so many had never taken PDE5 inhibitors. At 10 minutes, 21% of the patients who had taken 10 mg of vardenafil had erections sufficient for penetration and went on to have successful intercourse. The 20-mg group showed a similar response after 11 minutes. After 25 minutes, 53 percent of the men had erections sufficient for penetration and successful intercourse.

Is first-time success important for men? Bayer looked at first-time and subsequent success in two studies. They show 75% of moderate ED patients succeeded, the first time on vardenafil, in achieving sufficient erection. In SEP-2, the men plateaued with the second or third dose, and by then the cumulative probability was that they would know whether or not they would succeed. In SEP-3 (successful completion of intercourse), it took about four tablets before the plateau was reached.

In hard-to-treat populations, our studies showed positive results in both diabetic and post-prostatectomy groups that usually have severe endothelial dysfunction and other co-morbid conditions. Compared to placebo where the ED-EF domain score was 13 on 20 mg of vardenafil, these patients achieved an EF domain score of nearly 20 (26 and above would be normal).

Levitra is contraindicated with alpha-blockers in the US. Other regulatory authorities allow simultaneous administration of alpha-blockers with vardenafil, capping the dose and allowing a six-hour interval between the alpha-blocker and vardenafil for drugs other than Flomax.

One of our recent studies showed that patients on 20 mg vardenafil and tamsulosin experienced reductions of about 4 mm in standing systolic blood pressure compared to placebo. We now have a database of about 10,000 patients in clinical trials, and we're finishing two large simple safety studies, one in Europe and one in the US, of 30,000 patients each, with no evidence of significant cardiovascular effects. In fact, we can show that vardenafil may be protective.

If your patient needs a rapid-onset drug with high first-time success after the first couple of doses, or if he is a difficult-to-treat patient, then Levitra may be the drug of choice.

What differentiates Cialis from other PDE5 inhibitors?

Enrique Leñero MD, Lilly-ICOS, Mexico

New molecules in tadalafil differentiate Cialis from other PDE5 inhibitors. The best representation is an integrated analysis of 11 multi-centre, randomized double-blind, 12-week efficacy studies, in which the analysis included a large number of patients: 321 men randomized to tadalafil 10 mg, 1,143 men randomized to tadalafil 20 mg, and 638 men randomized to placebo.

The medication was taken without restrictions on time to intercourse or food consumption. The broad population included men with mild, moderate or severe ED. However, the trials excluded men with unstable cardiovascular disease.

At the end of the treatment, the mean IIEF scores were 23.2 and 21.1 respectively for the 10- and 20-mg groups – a statistically significant difference from the placebo group. The mean for successful intercourse was 68 percent in the 20-mg group, 58% in the 10-mg group – also a statistically significant difference from the placebo group.

Another way to look at the results of SEP-3 is the mean per attempted intercourse of patients enrolled in clinical trials – 72 for the 20-mg group, 61 for the 10-mg group – again, statistically significant compared to placebo.

Tadalafil achieves comparable response rates within the first 4 hours, but it is the only PDE5 inhibitor with response rates lasting up to 36 hours. Its adverse-event profile resembles those of other PDE5 inhibitors, as does its low discontinuation rate.

One double-blind cross-over study evaluated patient preference for tadalafil and sildenafil. This study randomized 219 patients to either sildenafil 50 mg or tadalafil 20 mg. The study included a sham placebo arm to maintain the double blind. After four weeks, patients in the sildenafil arm were offered titration up to 100 mg. Patients requesting upward titration received additional capsules in a double-blind fashion, and up to 35% of the titration requests were granted to patients taking sildenafil in each treatment period in each country, to mimic dosing observed in clinical practice.

After 12 weeks, patients in both arms were crossed over. Tadalafil was the preferred treatment of choice; even those patients to whom titration was granted showed a 69% preference for tadalafil over sildenafil.

Compared to other PDE5 inhibitors, tadalafil's longer half-life provides efficacy for up to 36 hours. Men in clinical trials, and in a randomized double-blind multi-centre trial, took advantage its 36-hour-long efficacy – and 69% of patients preferred tadalafil 20 mg over sildenafil 100 mg.

UPCOMING SIU MEETINGS AND CONGRESSES



Bariloche 2005
September 29-October 1, 2005

The SIU has chosen the city of San Carlos de Bariloche, in the spectacular Patagonian region of Argentina, to host its second off-year Meeting. Make plans to join us at the SIU Meeting on Prostatic Disease: Recent Advances and New Technologies. For details and registration, visit the Website at www.siu-urology.org/bariloche

Deadline for abstract submission is April 15, 2005



Cape Town 2006
November 12-16, 2006

The 28th Congress of the SIU will be hosted by our South African colleagues in beautiful Cape Town, South Africa. Visit our constantly-evolving Website at www.siu2006.com

Following the success of the Hawaii experience, the 2nd GU Oncology Conference will pursue its work in Cape Town (November 11 and 12).

Deadline for abstract submission is April 15, 2006



Paris 2007 : The SIU Centennial
September 2-6, 2007

The 29th Congress marks a century for the SIU, and it returns to its Paris birthplace to celebrate. Don't miss this truly unique opportunity to reflect on the past and shape the future of the SIU.



Beijing 2009
September 20-24, 2009

Nearly a decade later, the SIU returns to Asia, this time to commemorate its 30th Congress in ancient, exotic Beijing.

Call for SIU Congress and Meeting Venues

Groups wishing to explore the possibility of hosting the biennial SIU Congress or an off-year SIU Meeting are invited to submit an expression of interest to the SIU Central Office.

Society Publications

Official SIU Journal

The SIU is pleased to announce to its members that, as of January 2005, *Urology (The Gold Journal)* will be its official journal. If you are up-to-date in your dues payments but have not yet received your January and February issues of *Urology*, you may contact the SIU Central Office by e-mail at the following address: central.office@siu-urology.org

SIU/WHO/ICUD Bladder Cancer Supplement

Members who participated in the Hawaii Congress surely attended some part of the SIU/WHO/ICUD Consultation on Bladder Cancer, under the responsibility of Professor Saad Khoury (France) and spearheaded by Dr. Mark Soloway (USA).

A clear indication of the success of the Consultation is the publication of two supplements. The first, which will be available in August 2005, will feature chapters on Diagnosis, Molecular Biology, Low-Grade Ta Tumors, High-Grade Ta Tumors and CIS, and T1 Tumors. The second, which will print in late 2005, will include Muscle-Invasive Tumors and Surgery, Urinary Diversion, Urothelial Carcinoma Involving the Prostate, Chemotherapy, Radiation, and Non-urothelial Carcinoma of the Bladder. Authors are listed below.

Diagnosis, Imaging, Epidemiology: Ziya Kirkali

Epidemiology: Bart Kiemeneij

New Markers: TBA

Low Grade Ta, Intravesical Therapy: Willem Oosterlinck and Eduardo Solsona

High Grade Ta and CIS: Adrian van der Meijden and Richard Sylvester

T1: Michael Jewett

Muscle-Invasive Urothelial Cancer, Surgery: Bruce Malkowicz

Radiation: Mary Gospodarowicz and Michael Milosevic

Urinary Diversion: Richard Hautmann

Chemotherapy: Cora Sternberg

Molecular Biology, Markers, Cytology: Vinata Lokeshwar

Urothelial Carcinoma of the Prostate: Joan Palou

Non-urothelial Carcinoma of the Prostate:

Hassan Abol-Enein

GU Trauma Supplement

SIU members in good standing will have by now received their issue of the *Consensus on Genitourinary Trauma*, a collection of articles covering evaluation and management of renal injuries (Santucci et al.); a consensus statement on urethral trauma (Chapple et al.); a consensus statement on bladder injuries (Gomez et al.); the diagnosis and management of ureteric injury (Brandes et al.); and a consensus of genitourinary trauma to the external genitalia (Morey et al.).

New SIU Roster

SIU members in good standing will have by now received their 2004-2005 roster. Should you not yet be in possession of a copy, please contact the SIU Central Office. In order for the roster to be a useful tool, we ask for your cooperation in notifying us of any address or e-mail changes, or incorrect listings in the current roster.