HAIR TRANSPLANT forum INTERNATIONAL

INTERNATIONAL SOCIETY OF HAIR RESTORATION SURGERY

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Finasteride and prostate cancer

Edwin S. Epstein, MD *Virginia Beach, Virginia, USA* esehairmd@gmail.com

5-alpha reductase inhibitors (5ARIs) have been effective in the treatment of benign prostatic hyperplasia (BPH) and androgenetic alopecia (AGA). Proscar® (finasteride 5mg) was approved for the treatment of symptomatic BPH in 1992, and Propecia® (finasteride 1mg) for AGA in 1997. Since FDA approval, 20.5 million and 6.7 million patient years of exposure using Proscar and Propecia, respectively, are recorded with a low adverse event profile. Avodart® (dutasteride 0.5mg) was approved in 2003, with 5.5 million patient years of exposure and similar adverse events profiles. The efficacy of 5ARIs in the prevention of prostate cancer remains controversial, with proponents emphasizing the reduction in low-grade prostate cancer, while others share concerns about the increased incidence of high-grade cancer. Recently, the Food and Drug Administration (FDA) rejected Merck and Co.'s request for a product label change reflecting that Proscar was safe and effective for the reduction in the risk of prostate cancer in healthy men over 55, and GlaxoSmithKline's (GSK) proposed indication for Avodart in the reduction of prostate cancer in men at risk of developing prostate cancer. It is important for hair transplant surgeons to understand this issue to better advise our patients and other physicians.

Prostate Cancer Facts

Prostate cancer is the second leading cause of cancer death, behind lung cancer, in men in the United States. The American Cancer Society is projecting 240,000 new cases of prostate cancer diagnosis and over 33,020 prostate cancer-specific deaths in 2011. About one-sixth of men in the United States will be diagnosed during their lifetime, with Gleason grade 6 as the most commonly diagnosed.

Prognostic Factors

Prostate cancer is detected by PSA (prostatic specific antigen) and DRE (digital rectal examination), but diagnosed by needle biopsy (NBP). The original Gleason system graded the histological patterns of the two largest cancerous areas, with grades from 1-5 based on histologic differentiation patterns. The current or modified Gleason system uses the tertiary pattern instead of the secondary most predominant pattern. (See reference below for further discussion.) Gleason 6 or less is low grade or well differentiated, and 8-10 is high grade or poorly differentiated. If untreated, 20% of Gleason 6 patients will die from their disease and if treated by definitive prostate surgery, 10-15% will recur. Prostate cancer tends to be slow growing, and many men will die with their disease and not from it. Routine PSA screening remains somewhat controversial because reduction in death rates from early detection has not been consistently shown. Because of the potential morbidity with radical prostate surgery or definitive radiation therapy, some advocate "watchful waiting," or surveillance, with low Gleason grades. However, 90% of men with Gleason grade 6 will seek definitive therapy.

Prostate Cancer Screening

The American Cancer Society and the American Urological Association recommend the following screening ages:

- Age 50 for men who are at average risk of prostate cancer and are expected to live at least 10 more years.
- Age 45 for men at high risk of developing prostate cancer: African American men and men who have a first-degree relative (father, brother, or son) diagnosed with prostate cancer younger than age 65.
- Age 40 for men at even higher risk (those with several first-degree relatives who had prostate cancer at an early age).
- Regardless of age, yearly screening for PSA level if 2.5ng/ml or higher, and every 2 years for less than 2.5ng/ml.

Chemoprevention Studies

The two landmark studies evaluating 5ARIs in prostate cancer were the Prostate Cancer Prevention Trial (PCPT) using finasteride 5mg, and the Reduction by Dutasteride of Prostate Cancer (REDUCE) using dutasteride

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President's Message

Jerry E. Cooley, MD *Charlotte, North Carolina, USA* jcooley@haircenter.com

We have made steady progress as a society this year. First, I want to recognize the tremendous job our executive director, Victoria Ceh, does in providing organization leadership. Victoria and the entire ISHRS staff work hard behind the scenes to keep our Society functioning from day to day, and our success as we approach our 20th year is testament in large part to their efforts. They provide continuity from year to year as we members rotate through volunteer posts on committees, the Board of Governors, and the Executive Committee. Despite a bad world economy, the financial health of the ISHRS is strong and stable. Those of us in leadership positions take our stewardship responsibilities seriously, and we carefully weigh the costs and benefits to members of each new project.

Looking over the past year, there are several tangible accomplishments to note. We met in January as part of our periodic Strategic Planning to chart a course for the next 3 years. During this meeting, we began formulating a new mission and vision statement, which I discussed in my last message. We discussed how the ISHRS can continue to be the "Mother Ship" in a changing world where rapid growth is occurring in our field outside of North America. Other issues included getting the ISHRS involved in social media, providing resources for member physicians to train new assistants, and the possibility of adding a fellow category to our membership to identify experienced members who have distinguished themselves.

Over the past year, we have faced several "hot topics" including persistent sexual side effects from finasteride and the physician's role in automated FUE; we appointed committees to study these issues. After news reached us of pending regulation in Europe that would affect who can perform hair restoration procedures, we applied for and were granted liaison status with this regulatory body to ensure that our voice is heard. There are a surprising number of day-to-day issues that come up in the course of running our Society that must be dealt with; I have managed these the best I can with Victoria's able assistance.

During my time as president, my respect and admiration for the ISHRS has grown. What a marvelous organization we have. I encourage all of you who may have been watching from the sidelines to get more involved. Opportunities abound including committees, teaching at our meetings, and/or writing for the *Forum,* all of which can lead to further leadership posts. You will make friendships with colleagues from around the world and add to your career satisfaction in this wonderful field.◆

Co-editors' Messages

Nilofer P. Farjo, MBChB *Manchester, United Kingdom* editors@ISHRS.org

In the past few years, there has been a great volatility in the economic climate and this has been mirrored in many areas including cosmetic procedures. Hair transplantation in some countries has definitely followed a downward trend. Over the past year, though, the media seems to have taken a fascination to all things hair related, so perhaps the new boom is on its way. From Naomi Campbell's traction alopecia to soccer players such as Wayne Rooney's transplant, there seems to be a story of celebrities and their hair in the news all the time. The great thing is that they are talking about having hair rather than the type of procedure that puts the focus back where I feel it should be: on moving hair. The only matter of concern in all this is that celebrities such as Wayne Rooney, who are very young and destined for more hair loss, may give the impression to young men with early stage hair loss that hair restoration is always okay for this age group. In this edition three of our most experienced surgeons, Drs. Bill Parsley, Bill Rassman, and Walter Unger give their opinions and raise some interesting points of debate on this topic. Personally, I don't like operating on patients under age 30, but this does not mean that I NEVER operate on these younger men. There is a considered approach that must be made based on each individual case, but it does take experience to choose the right candidate. I do get patients who have been given very low hairlines at a young age who come in for remedial work, which, as we know, will never give a "great" result, rather only one that is better than they have now.◆

William H. Reed, MD *La Jolla, California, USA* editors@ISHRS.org

When I agreed to become co-editor of the *Forum,* Richard Shiell, whose energy and enthusiasm allowed him to single-handedly edit the *Forum,* congratulated me by saying that I had the "best job in the ISHRS." Now that I am half a year into the job, I appreciate even more both his energy as well as the wisdom of his words. But I realize that it is the best job only so long as you, my colleagues, share Richard's enthusiasm by sharing your knowledge with us through articles in the *Forum.* I appreciate your patience with Nilofer and me as we do our "editor's thing" of asking for clarifications, additional references, etc. Hopefully, these editing efforts are worthwhile.

Patients not uncommonly ask, "Isn't this boring?", referring to my job as a transplant surgeon. Being co-editor has brought into clear focus why this is not so: the breadth of medicine, biology, and business inherent to hair transplantation (an increasingly archaic term for our specialty) ranges from the many and ever changing aspects of its surgical and nonsurgical aspects to the dynamic of relationships with patients and coworkers, to the many marketing and other business considerations required to run a practice.

I suppose, hypothetically, a surgeon can get by for a while just with a business acumen to market his trade and to manage employees in combination with an "off the shelf" technique for hair transplantation. Perhaps he can stay in this restricted perspective of hair transplantation for a period of time, but, sooner or later, he will have to evolve that technique to incorporate hair transplantation's next refinement in order to remain competitive. Assisting such a progression is what the ISHRS and the *Forum* are all about and I hope we can assist such an evolution to happen, enthusiastically.

As you can see from scanning the table of contents on the cover, this issue addresses the ethical, the practical, and the technical of hair transplantation as well as the relevant cellular biology that is becoming ever more important in our field. Some articles are anecdotal or preliminary while others are more comprehensive and definitive. I appreciate the contributors' efforts because, as a result of their efforts, Nilofer and I are able to bring a glimpse of the broad breadth of knowledge and possibilities that constitute our little gem of a medical subspecialty.◆

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1. Articles should be written with the intent of sharing scientific information with the purpose of progressing the art and science of hair restoration and benefiting patient outcomes.
2. If results are presented, the medical regimen or surgical techniques that were used to obtain the results should be disclosed in detail.
3. Articles submitted with the sole purpose of promotion or marketing will not be accepted.
4. Authors should acknowledge all funding sources that supported their work as well as any relevant corporate affiliation.
5. Trademarked names should not be used to refer to devices or techniques, when possible.
6. Although we encourage submission of articles that may only contain the author's opinion for the purpose of stimulating thought, the editors may present such articles to colleagues who are experts in the particular area in question, for the purpose of obtaining rebuttal opinions to be published alongside the original article. Occasionally, a manuscript might be sent to an external reviewer, who will judge the manuscript in a blinded fashion to make recommendations about its acceptance, further revision, or rejection.
7. Once the manuscript is accepted, it will be published as soon as possible, depending on space availability.
8. All manuscripts should be submitted to editors@ISHRS.org.
9. A completed Author Authorization and Release form—sent as a Word document (not a fax)—must accompany your submission. The form can be obtained in the Members Only section of the Society website at www.ISHRS.org.
10. All photos and figures referred to in your article should be sent as separate attachments in JPEG or TIFF format. Be sure to attach your files to the email. Do NOT embed your files in the email or in the document itself (other than to show placement within the article).
11. We CANNOT accept photos taken on cell phones.
12. Please include a contact email address to be published with your article.

Submission deadlines:
October 5 for November/December 2011 issue
December 5 for January/February 2012 issue

INTERNATIONAL SOCIETY OF HAIR RESTORATION SURGERY

Vision: To establish the ISHRS as the leading unbiased authority in hair restoration surgery.

Mission: To achieve excellence in patient outcomes by promoting member education, international collegiality, research, ethics, and public awareness.

Notes from the Editor Emeritus

Russell Knudsen, MBBS *Sydney, Austrailia* drknudsen@hair-surgeon.com

The empowered patient

The past few years have seen an interesting (and irreversible) change in the interaction between hair restoration surgeons and our prospective, or existing, patients. Cosmetic surgery has always been uniquely separate from traditional, health-based medicine in that the patient is generally less accepting of the historically "paternalistic" model of health and advice delivery. They mostly came to us with little information about hair restoration surgery but wanting an explanation of what is available and what is possible. They equally auditioned us, just as we auditioned them for suitability.

The Internet has changed this forever. We are now in the era of the empowered patient. Not only are they more informed (sometimes this means "better informed"), but as I have said on other occasions, they also have higher expectations to the extent that we now often hear them express their desire for undetectable, scarless surgery in case they want to shave their head sometime in the future. A version of "wanting their cake and eating it, too."

The Internet can be a double-edged sword. In theory, freely available information about hair restoration surgery and techniques allows prospective patients to make better choices. In practice, this is somewhat limited by the preponderance of opinion and marketing spin dressed up as facts. The widespread use of blogs has reinforced the power of opinion to sometimes overwhelm facts or to harm the reputation of skilled doctors. Doctor bashing is now rampant in these blogs and sometimes the doctors have only themselves to blame.

Emphasize the importance of the service concept, because this is what differentiates you from colleagues….It is this personalized service that will help you negotiate an appropriate outcome with the modern, empowered, prospective patient.

I consulted with a patient yesterday who freely informed me he had read widely in the blogosphere, and had consulted elsewhere, but finally came to me because he couldn't find any "bad things" about me in these blogs! I didn't know whether to be entirely reassured by this, as it is a bit too "half glass empty" rather than "glass half full" for my liking. It is time we understood the obvious—ANYTHING we say to the patient in the consultation should not be regarded as confidential; rather, it should regarded as likely to be posted on a blog shortly afterwards. This is particularly important when commenting about alternative techniques or your competitor colleagues. If your comments are misinterpreted (or misreported), you now have this misinformation, attributed to you, floating in the blogosphere. It is, of course, stating the obvious that we can only control what we say to our patients, and not what they say we said.

In the consultation, sometimes the extent of the power shift to the patient can make us a little uncomfortable and we start to feel the need to be defensive about ourselves and our staff. The questions now sometimes drill down to the detail of the various component techniques and instrumentation on the patients' "checklist" as they audition the surgeon. Although his can be quite helpful because it allows a detailed discussion of the procedure, it requires a depth of understanding of the facts rather than the opinion/spin. This is clearly not always the case and sometimes an "educated" patient has to be gently "re-educated." This requires both patience and tact, and your acknowledgment that different techniques and opinions exist. I find it helpful if you also acknowledge that other good practitioners exist, as this helps diminish the most powerful factor that prevents prospective patients booking a surgery: fear.

Probably the biggest area of confusion to a prospective patient is the idea of appropriate graft numbers. Some patients tell me they know how many grafts they need from having seen photos on the Internet. Their estimate rarely conforms with mine because the subtleties of hair characteristics, what constitutes "cosmetic density," and appropriate hairline design are never considered in their calculation.

Your experience, and that of your staff, is also frequently questioned and this can be challenging to the less-experienced surgeon. Fudging the facts is not helpful as the "blogosphere" can bring you down.

I have had a couple of recent instances where the patient demands regarding every technical detail of the procedure seemed to infringe on my independence as the practitioner. We should always try to accommodate reasonable requests but should never completely surrender the decision-making process. It is always preferable not to operate on a patient who believes himself a better expert than you. Unless he is an esteemed colleague.…

How do we deal with this shift in power? We should remain calm and factual, acknowledge what is opinion, be appropriately respectful to competitors, and emphasize our care and attention to detail. Many patients confuse the Product with the Service, sometimes choosing to go with price considerations as the primary factor. Sometimes this is encouraged by advertising that seems merely price-competitive. The ultimate example of this is the significant increase in overseas medical tourism in the last couple of years. I performed a consult on a patient last year who had already booked surgery overseas, paid a deposit, could not name the surgeon or the city, had decided entirely on price, and asked me to explain the process to him before he traveled for the surgery!

Emphasize the importance of the service concept, because this is what differentiates you from colleagues. Even if you employ a consultant (I don't), make sure you spend some time with the patient early on in the consultation process so that you can gather knowledge of each other face-to-face. It is this personalized service that will help you negotiate an appropriate outcome with the modern, empowered, prospective patient.◆

Finasteride and prostate cancer

from front page

0.5mg. PCPT evaluated 18,000 men over age 55 with normal DRE and PSA, while REDUCE evaluated men at higher risk for cancer with an elevated PSA and negative prostate biopsy. Both studies showed about a 23%-25% relative reduction in diagnosed prostate cancer, which generated excitement for chemo-preventive potential. However, this reduction occurred in men with low-grade, Gleason 6 cancers, while an increased incidence of higher grade cancer, Gleason 7-10, was found in the treatment groups of both studies. These findings are the basis of a controversy in the interpretation of the data, which has been reanalyzed by numerous investigators.

Analysis of the PCPT data offered several explanations for the increase in high-grade cancer due to detection bias attributed to reduction in prostate volume and PSA by 5ARIs. Proponents point out that the sensitivity of PSA and DRE was improved with finasteride: biopsy would be more accurate with a smaller prostate volume, and there was no evidence of induction of high-grade disease. However, the FDA's analysis concluded insufficient evidence to explain the high-grade cancer to bias alone. Sixty percent of cancers were found on end-of-study biopsies, which would not have been detected in a clinical setting because of an abnormal PSA or DRE. The FDA repeated the analysis adjusting for prostate volume and modifying the Gleason score to 8-10, and concluded that increased sampling density, from prostate volume reduction, did not explain the increased diagnosis of high-grade cancer.

REDUCE was designed to evaluate dutasteride effects on prostate cancer reduction. The study included 8,231 men at risk for prostate cancer based on elevated PSA, and negative prostate biopsies were randomized and biopsied at years 2 and 4. A 23% relative reduction in biopsy-detectable cancer was reported, as was a significant reduction in pre-cancerous lesions, prostatic intraepithelial neoplasia (PIN) and atypical small acinar proliferation (ASAP). As in PCPT, the reduction was in Gleason 6 or less, and the FDA analysis was that 80% of these represented very low-risk disease that may pose little threat during one's lifetime. There was no overall increase in Gleason 7-10 cancers (220 in dutasteride arm vs. 223 in placebo). In Gleason 8-10 cancers, there were 29 with dutasteride vs. 19 placebo, but the difference was only in years 3-4 (12 dutasteride vs. 1 placebo). One explanation was ascertainment bias in that in years 1-2, 141 more patients, diagnosed with Gleason 5-7, were removed from the placebo arm, with a potential 7.6% upgrade rate as reported from other studies. If this 7.6% rate of upgrading were applied to the 141 more cancers removed during years 1-2 in the placebo arm, 11 extra cancers would have been called Gleason 8-10 in the placebo arm, which is exactly the difference between the two arms.

Product Label Change

In December 2010, the FDA Advisory Panel concluded that the risk-benefit profile of finasteride and dutasteride was insufficient to allow product label changes claiming or suggesting that they reduced the risk of prostate cancer. Proponents of the label change argued that 5ARIs reduce the risk and diagnosed number of low-grade prostate cancer, and, therefore, the number of prostate biopsies, their associated potential complications, and the costs and morbidity associated with definite therapy. They also preserve or enhance the ability to diagnose high-grade cancer, reduce the symptoms and treatment of BPH, and have an acceptable safety profile. The FDA panel was concerned about the overuse in the general population by men who do not have or may never develop prostate cancer, and their potential adverse drug-related events. In addition, no long-term studies have evaluated the effects of finasteride in younger men treated for AGA, or the biological potential of high-grade cancer in men who go off the drug.

Hair Restoration Surgery Perspective

Hair transplant surgeons diagnose and treat hair loss both medically and surgically. Since the approval of 5ARIs by the FDA, millions of men have benefited from their efficacy in the treatment of AGA. It is important to explain to patients and other physicians the risk:benefit profile of this class of drugs. Their effect on prostate cancer reduction remains controversial. Clearly there is a reduction in low-grade cancer diagnosis, while the detection of high-grade cancer was greater in the drug arms in both PCPT and REDUCE trials. Whether due to detection bias, a variation in the effect of DHT on different grades of prostate cancer, or other explanations, it remains unknown how therapy with 5ARIs might influence the progression of prostate cancer or affect high-grade prostate cancer. Patients at risk for prostate cancer should be evaluated according to American Urological Association (AUA) guidelines by their primary care physician, or urologist, and inform them that they are taking a 5ARI, as it will lower their PSA value. Other potential adverse events listed on the product label should be discussed and noted on the patient's record during the consultation and informed consent discussion.

5ARIs and Male Breast Cancer

Merck and GSK have amended product labels of Propecia, Proscar, and Avodart to reflect the reports of male breast cancer, while the relationship of long-term use of 5ARIs with breast cancer in men remains unknown. In December 2009, the Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom reviewed 53 cases of breast cancer in men using finasteride, and concluded that an increase in male breast cancer associated with finasteride could not be excluded. Four cases of female breast cancer have been reported, 3 with Propecia and 1 with Proscar. The Medicines and Healthcare products Regulatory Agency (MHRA, now the Public Health Solutions) recommended a breast cancer warning in product information.

Male Breast Cancer Facts

Less than 1% of all breast cancers occur in men. The incidence reported in 1998 was 1 per 100,000 men, with a peak age of 71. Conditions that create a relative increase in the estrogen:testosterone ratios are associated with increased risk of breast cancer in men. Breast mass is the most common clinical manifestation (75%), followed by nipple retraction (9%), and nipple discharge or ulceration (6%).

Clinical Trial Data

Placebo-controlled double blind studies in the United States involving finasteride 5mg and 1mg were reviewed. In approximately 29,000 men studied, 8 cases of breast cancer were reported: 5 in the finasteride group and 3 in the placebo. This incidence in the control groups is higher than the 1:100,000 reported in the general population, while only in the Medical Therapy of Prostate Symptoms (MTOP) study was the number of breast cancers in the finasteride groups significantly higher than control. In 22,000 men using dutasteride, 3 cases were reported; 2 in the dutasteride group and 1 in placebo.

While the incidence of reported male breast cancer in finas-

Worldwide Cases

50 finasteride 5mg + 3 finasteride 1mg

< 1 year: 8
1-2 years: 4
2-3 years: 6
3-4 years: 5
4-5 years: 3
> 5 years: 9

35 with known time to onset

Gynecomastia occurred in only 9% of breast cancer.

Source: *http://www.mhra.gov.uk/home/groups/pl-p/documents/websiteresources/con065504.pdf*

teride and dutasteride clinical trials is higher than the general population, the numbers are too small to support a cause and effect explanation. Because this association could not be excluded, the MHRA suggested changes to patient information leaflets as special warnings and precautions for use. They also recommended that patients promptly report changes in breast tissue to their physicians. Hair transplant physicians prescribing 5ARIs should include this association as part of routine risk: benefit discussions between physician and patient, and suggest routine breast examinations.

Study (years)	No. Patients	No. Breast Cancer	Finasteride	Placebo	Dutasteride
MTOP (5)	3,047	4	4	0	
PLESS (4)	3,016	2	0	2	
PCPT (7)	18,882	2	1	1	
FIN 1mg (5)	4,000	0	0	0	
	29,000	**8**	**5**	**3**	
DUT (2)	3,374	3		1	2
REDUCE (4)	14,000	0		0	0
CombAt	5,027	0		0	0
	22,401	**3**		**1**	**2**

MTOP: Medical Therapy of Prostate Symptoms: Fin, doxazosin, Fin + doxazosin, placebo (4 groups)
PLESS: Proscar Long Term Efficacy and Safety Study
CombAt: Combination with alpha blocker (tamsulosin)

Source: *http://www.mhra.gov.uk/home/groups/pl-p/documents/websiteresources/con065504.pdf*

HT Surgeon Facts and Patient Education Approach to 5ARIs

1. 5ARIs have helped millions of men in the treatment of BPH and AGA, with a relatively low side effect profile.
2. Finasteride at 1mg and 5mg have similar effects on lowering PSA, prostate gland size, and serum DHT and T levels. The 5mg dose was more effective in reducing symptoms of BPH.
3. The role of 5ARIs in prostate cancer chemoprevention remains controversial.
4. Both finasteride and dutasteride appear to reduce the lower grade prostate cancer, while dutasteride may also be effective in prostate cancer precursors.
5. While high-grade prostate cancer detection was higher in PCPT and REDUCE studies, it remains unknown how therapy with 5ARIs might influence the progression of prostate cancer or affect high-grade prostate cancer.
6. Men at age of risk, or genetically at risk for prostate cancer, should have annual PSA and DRE by a primary care physician or urologist, informing their physician that they take a 5ARI.
7. While male breast cancer has been infrequently reported, the long-term association is unknown. Patients using 5ARIs should be encouraged to perform routine self-breast examination and to report any breast changes.
8. A family or personal history of breast cancer is a contraindication to the off-label use of 5ARIs in females being treated for hair loss.
9. Informed consent discussions, including the risks, benefits, and potential adverse events, should be noted in the patient record.

Useful References

PCPT

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REDUCE

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MTOPS

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- /Drugs/OncologicDrugsAdvisoryCommittee/UCM237498.pdf
- http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/CON065479

Editor's note: This is an outstanding article by Dr. Epstein and one that can be referred to for years to come to establish a foundation for this complicated issue. I would suggest also reading the recent paper detailing the FDA's assessment of the problem (http://www.nejm.org/doi/full/10.1056/NEJMp1106783). When I did, I concluded the following: The use of 5ARIs saves the occurrence of 3-4 lower grade but clinically significant carcinomas for each additional high-grade carcinoma possibly associated with their use. This one extra case of high-grade carcinoma occurs every 150-200 high-grade carcinomas otherwise diagnosed in the general population. One must also consider the consequences of having an abnormal Gleason score below 7. Does the label "low grade but probably insignificant prostate cancer," which occurs 12-16 times for each possible extra high-grade cancer, ever leave ones mind? I'm sure the insurance companies and the frequent urological follow-ups will help remind those people of the label for years to come. In summary, it seems that total morbidity and mortality may be less with the use of the 5 ARIs and, undeniably, this "other side of the coin" has to be factored in when giving balanced counsel to our patients regarding their 5ARI use. —WR◆