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Letter: Shared Decision-Making in Prostate Cancer Management: Easy to Say, Hard to Measure

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To the Editor: Joyce and Siemens' recent editorial on shared decision-making (SDM) is timely and insightful.¹ They describe a number of obstacles that may account for low adherence to SDM interactions. I propose a situation that will soon challenge physicians committed to SDM; that is, an androgen deprivation therapy (ADT) that has great merit but is not currently standard of care (SOC).

With all approved ADT agents—whether used as monotherapy or as part of doublet/triplet therapy—the loss of estrogen as a consequence of testosterone deprivation leads to significant decline in prostate cancer (PCa) patients' quality of life (QoL). Hot flashes interfere with daytime activities and interrupt sleep for the patient and his partner. The lack of sleep can lead to daytime fatigue/energy deficit. Depression and cognitive impairment (ie, “brain fog”) are common. There is increased risk of metabolic syndrome. The absence of estradiol leads to osteoporosis. Rates of fractures requiring hospital admission after traditional ADT

have been reported as high as 25% at 10-year follow-up, with only 5% reduction when bone protective agents are concurrently administered.²

For decades, these adverse effects of ADT have been accepted as the price for prolonging life. In this era, where patients on ADT typically survive for many years, QoL assumes greater importance.

This evidence-based challenge is presented by the PATCH/STAMPEDE randomized controlled trial (NCT00303784), which tested transdermal estradiol (tE2) for ADT against luteinizing hormone-releasing hormone (leuprolide) ADT.^{3,4} The results of the randomized controlled trial show that tE2 is as effective in disease control as leuprolide, with no increase in cardiovascular events and elimination/attenuation of the associated harms from loss of estrogen. ADT with tE2 improves bone mineral density.⁵ ADT with tE2 costs significantly less than standard luteinizing hormone-releasing hormone agonists and antagonists.

The most common side effect of estrogen is gynecomastia. In a survey of over 800 PCa patients, for which men were asked about their ADT-related concerns (see <https://estradiolinitiative.org/>), none of the 23 participants who reported using tE2 for ADT expressed undue concern about gynecomastia. Furthermore, over 90% of all participants felt that PCa patients should have the option of access to tE2.

I am a prostate cancer patient and have been using tE2 for my own ADT since I entered the castration resistant state in 2008. The improvement in my QoL was dramatic. My good fortune includes life with energy, a relatively sound mind, and strong bones. I can thus testify to the benefit of tE2 for ADT. The major obstacle is that tE2 is not an approved SOC. To gain that status, it will need to come before a guideline committee, without a Food and Drug Administration–approved product for men. However, pharma has little financial incentive to produce such a product. Physicians caring for patients with advanced PCa have prescribed abiraterone, enzalutamide, and PARP inhibitors before SOC guideline statements. How should the well-being of the PCa patient in need of androgen suppression enter the SDM discussion when the treatment option with arguably the most significant power to improve the QoL of such a patient is not SOC?

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To the Editor: I thank Drs Joyce and Siemens¹ for their editorial on shared decision-making, which can be time efficient and genuinely rewarding, or protracted failures for both the patient and the urologist. As such, I want to emphasize how important common understandings are at the outset of consults.

The authors suggest that artificial intelligence (AI) may help improve urological consults. AI is taking over the lead from health care providers as the first place patients with cancer go for information on treatments. As a result, more and more patients can come to a consult well aware of the standard of care (SOC) options they are likely to be offered.

At the same time, many patients are on chat lists daily where they can get variously reliable, although admittedly often biased, information from other patients. That can lead to the patients pushing for treatments that are outside of SOC, leading, in turn, to prolonged and contentious consults.

What has not been appreciated is that the internet now makes it possible for the patients to be aware of

credible treatments well before they become SOC or even known to most physicians. A case in point is using transdermal estradiol (tE2) for androgen deprivation therapy (ADT). In the last year, the results of the 14-year PATCH/STAMPEDE trial (NCT00303784) have been presented at 3 major oncological meetings.²⁻⁴ Although full-length, peer-reviewed papers have yet to be published, the 3 abstracts show that tE2 provides equally good survival as the standard ADT drugs, but with a significantly better quality of life for the patients.

Those 3 meeting abstracts appeared on chat lists within a day of their publication. They were soon followed by testimonials from patients, who were aware of the PATCH protocol and were already using tE2 for ADT outside of the PATCH/STAMPEDE trial.

The PATCH/STAMPEDE data endorsing tE2 for ADT have led to patients increasingly asking about tE2 as an option for ADT.⁵ Situations like this can create a major dilemma for the physician, who is trapped between relying on SOC protocols and patients knowledgeable about new research findings and seeking novel therapies in advance of any guidelines for administration.

How can the physicians get out of this bind? One suggestion is that physicians let patients know in advance of any consults what information they are expecting patients to present, if the patient is going to propose any treatments outside of SOC. They can let their patients know that they ideally want to see the abstracts from the peer-reviewed literature (not necessarily the full papers) for the treatment that the patients prefer.

If the patients got their information from AI, they should be told to be ready to identify the AI source and the peer-reviewed citations they got from AI. The patients can be told—again in advance of the consult—that, as a physician, they are not committed to going off-label. Consults can best fit the shared decision-making model if the patients are primed in advance about how to clearly state what treatments they prefer and why.

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