There are several arguments that may partially explain the discrepancies in the results of these studies: study design, technique for measuring PSAV, length of the interval of time between two measurements, stratification of the results. Beyond these technical considerations, it must be admitted that PSAV is very complicated to study because it requires a long period of time with two or more measurements. Moreover, it is also important to recognize that the relationship between PSAV and cancer risk is complex and not linear. This scenario is very similar to what happens in common clinical practice. There are so many biologic and analytic variables that may have an impact on the value of PSAV that it is very difficult to accurately evaluate the real utility of PSAV and, thus, to rely on this fascinating instrument.

Wolters et al's article has a great value because the authors have evaluated the utility of PSAV in the detection of significant versus indolent prostate cancer. This is a hot topic, but, again, it is very complex. The results are strongly associated with the definition of indolent prostate cancer, which is a controversial issue. At present, there are no reliable clinical or pathological findings to predict tumour extent and definitive Gleason score of nonpalpable prostate cancer. The distinction between significant and indolent prostate cancers, even if it is very appreciable, is questionable because it may provide unclear results on the utility of PSAV.

In conclusion, it is very difficult to evaluate PSAV in this setting, and any conclusion derived from a screening program that has not been designed to evaluate this issue might be inadequate. As correctly pointed out by the authors, PSAV was not used as a biopsy indicator and verification bias may occur because only men with a PSA ≥ 3.0 ng/ml were biopsied. For instance, the role of PSAV in patients with a PSA rising from the value of 1.0 ng/ml to 2.9 ng/ml remains to be clarified.

The article provides some evidence that PSAV is a poor biopsy indicator because it may miss a large amount of prostate cancer in general (significant or indolent) and is not an independent predictor of positive biopsy. Only a specific study will assess whether PSAV in general (and which PSAV cut-off) can identify life-threatening and still-curable prostate cancer and will clarify the utility of PSAV in the early detection of prostate cancer.

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Vincenzo Scattoni
Department of Urology, University Vita-Salute,
Scientific Institute San Raffaele,
Milan, Italy

E-mail address: scattoni.vincenzo@hsr.it

Re: The Efficacy and Safety of Udenafil, a New Selective Phosphodiesterase Type 5 Inhibitor, in Patients with Erectile Dysfunction

Paick J-S, Kim SW, Yang DY, Kim JJ, Lee SW, Ahn TY, Choi HK, Suh J-K, Kim SC

Expert's summary:

This is the first full text report on efficacy and safety of udenafil, a new phosphodiesterase type 5 inhibitor (PDE5i). It follows the typical design of multicenter, double-blind, placebo-controlled, fixed-dose, parallel-group study. A total of 167 patients with erectile dysfunction (ED) of diverse origin and severity were randomized to take placebo or udenafil at fixed doses of 100 or 200 mg as needed for 12 weeks.

Both active drug doses improved significantly the erectile function domain scores of the International Index of Erectile Dysfunction (IIEF) questionnaire as well as questions 3 and 4 of IIEF. The ability for successful vaginal penetration and the ability to maintain an erection for successful intercourse (assessed by questions 2 and 3 of the Sexual Encounter Profile–SEP, respectively) and the overall improvement of erections (assessed by the Global Assessment Question - GAQ) improved also

significantly. Success rates–based on SEP3–were 70% and 75.7% in the 100mg and 200mg udenafil group, respectively. Udenafil's safety profile is similar to other PDE5i with flushing, headache, nasal congestion and ocular hyperemia being the most common (23.2%, 8.9%, 7.1% and 7.1% in the 200mg group, respectively). There were no significant differences in terms of efficacy between the two udenafil groups. However, adverse events were almost double in the 200 mg group.

Although the study group is a typical ED group, there are no data on efficacy stratified by ED severity or normalization of erections (IIEF $\geq$26) after treatment. However, such data are to be expected in future studies.

Expert's comments:

Another PDE5i? Udenafil is a new drug in this class, 5 years after tadalafil and vardenafil. Not surprisingly, udenafil seems to offer comparable efficacy and safety to the three currently available PDE5i. Does it offer anything new or it is simply a treatment alternative? Udenafil has a different pharmacokinetic profile. Tmax is about 1–1.5 hours and T1/2 is about 11–13 hours. Therefore, udenafil has a relatively rapid onset of action (like sildenafil and vardenafil) and a long duration (but not as long as tadalafil). Furthermore, it does not inhibit PDE11 like tadalafil and it is not associated with visual disturbances or myalgia (like sildenafil–vardenafil and tadalafil, respectively).

Despite favourable efficacy and safety profile of PDE5i about 50% of patients discontinue treatment [1]. Patients' needs and expectations vary widely. The treatment approach should always be individualised according to their preference for information and involvement in the decision-making process [2]. Patient satisfaction is a complex issue that depends not only on therapeutic outcomes in terms of efficacy and adverse events or complications but also on expectations from treatment and relationship dynamics [3].

How does udenafil fit in this setting? Due to the aforementioned differences, it is not just another treatment option but it may enable better selection of treatment according to patient's sexual life profiles. Udenafil has just started its journey in the field of ED. Other PDE5i are coming (like avanafil and mirodenafil [4]). There is no doupt that new data on udenafil will be presented in the short future following the example of older PDE5i. Clinicians must not forget that a patient-centered approach is necessary for the management of ED [5]. The management strategy must be supplemented by a careful follow-up in order to identify changes in patients' expectations and possible side effects that may need treatment optimization. This is the only way to increase efficacy and safety of current and future treatments, as well as patients' adherence, with certain benefits not only for our patients, but also for the healthcare systems, especially in terms of cost-effectiveness.

Conflicts of interest: The authors have nothing to disclose.

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Konstantinos Hatzimouratidis
*2nd Department of Urology and Center
for Sexual and Reproductive Health,
Aristotle University of Thessaloniki, Greece*

E-mail address: kchatzim@med.auth.gr