prognosis compared with the scenario in which only the established clinicopathologic factors such as PSA, Gleason score, pT stage, and margin status are considered. However, some shortcomings of the current report also need to be considered in interpreting the findings. Only patients exposed to adjuvant or salvage RT were considered. Consequently, it is not clear how many patients did not experience a biochemical recurrence (BCR) despite possibly having a high GC score. Moreover, the median time of salvage RT was 5 mo after RP. As such, a high proportion of the salvage RT group had BCR very shortly after RP and thus cannot necessarily be compared with patients who experienced BCR some years after RP. Ideally, the potential of GC should be tested in future prospective trials with well-defined rules. Moreover, GC in prostate cancer awaits a formal cost-effectiveness analysis. Nonetheless, this paper is another step toward a more individualized treatment strategy for prostate cancer patients.

Conflict of interest: The authors have nothing to disclose.

Acknowledgments: Both authors are members of the Prostate Cancer Working Group of the European Association of Urology Young Academic Urologists.

Re: Drug Adherence and Clinical Outcomes for Patients Under Pharmacological Therapy for Lower Urinary Tract Symptoms Related to Benign Prostatic Hyperplasia: Population-based Cohort Study
Cindolo L, Pirozzi L, Fanizza C, et al

Expert’s summary:
Cindolo et al searched an administrative prescription database and hospital discharge codes for men aged >40 yr treated with $\alpha$-blockers and 5\alpha-reductase inhibitors alone or in combination to assess the adherence to medical treatment for lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH). Nonadherence was defined as discontinuation of any regimen for at least 2 consecutive months during the first year of treatment and at least 4 mo/yr during the follow-up period or as a regimen switch.

In this large population-based cohort study, 1-yr adherence was 29% in patients undergoing therapy for at least 6 mo. An important finding was that discontinuation of any drug treatment was an independent risk factor for hospitalization for BPH and BPH-related surgery.

Expert’s comments:
Low compliance with prescribed medications is a challenging problem for chronic diseases or conditions such as LUTS/BPH. As a result, a significant number of patients do not get the maximum benefit of medical treatment, resulting in poor health outcomes, lower quality of life, and increased health care costs [1].

Adherence has been linked to perceived efficacy, side effects, and cost of medical treatment. It is known that patients with worse LUTS tend to complain less about adverse side effects compared with those with less severe symptoms [2]. In addition, older patients are more likely to be adherent. Other risk factors for discontinuation including number of medical comorbidities, type of treatment, and polypharmacy have also been investigated [2–4].

Technical, behavioral, and educational interventions aimed at improving adherence to medications for chronic diseases have been developed [1,5]. Less frequent dosage enhances compliance, and technical adherence interventions are usually directed at simplifying the medication regimen including use of extended-release formulations or fixed-dose combination pills. Behavioral interventions are also used to provide patients with memory aids and reminders. Educational interventions focus on adequately informing patients about the disease, its management, and the potential benefits of long-term treatment with these agents.

Urologists need to interact with those patients who are observed to be noncompliant. Both understanding the needs and expectations and involving our patients in the decision-making process can play a significant role in compliance to therapy and the improvement of treatment outcomes in LUTS/BPH. Adherence to medical therapy deserves our particular attention, and further investigation into the reasons for noncompliance is still warranted.

Conflicts of interest: Stavros Gravas has received grants or research support from Pierre Fabre Medicament and GSK, and speaker honoraria from Angelini Pharma Hellas, Pierre Fabre Medicament, Lilly, and GSK. He is a consultant for Pierre Fabre Medicament and GSK.

References
Re: Disease Control Outcomes from Analysis of Pooled Individual Patient Data from Five Comparative Randomized Clinical Trials of Degarelix Versus Luteinising Hormone-releasing Hormone Agonists
Klotz L, Miller K, Crawford ED, et al

Expert’s summary:
This study has pooled the results of five randomized trials comparing luteinizing hormone-releasing hormone (LHRH) antagonists with LHRH agonists. The aim was to assess differences in efficacy and safety outcomes. The authors concluded that, compared with LHRH agonists, degarelix was associated with significant clinical benefits including improvement in prostate-specific antigen (PSA) progression-free and overall survival (hazard ratio: 0.47) and reduced incidence of joint, musculoskeletal, and urinary tract adverse events.

Expert’s comments:
The difference of magnitude in overall survival reported in this paper is astounding. Is it still ethical to advise our patients to use any chemical form of androgen deprivation therapy (ADT) except degarelix?

An intriguing issue is that the rationale behind this difference should go beyond the substantial lowering of circulating testosterone. A hypothesis: A low and steady level of testosterone seems better achieved when using antagonists. Testosterone microflares could be predictive of progression [1], although the arguments brought by the published studies cannot be considered solid evidence. Another hypothesis implies a role played by follicle-stimulating hormone (FSH); however, the clinical relevance of FSH suppression is poorly known. We remain in the realm of hypotheses that need to be validated.

What about the level of evidence of this paper? The results were based on data pooled from five randomized studies. The primary end points around which these trials were built were not survival but rather change in testosterone level, International Prostate Symptom Score, or prostate volume. The large number of patients analyzed was the advantage of this pooled study methodology at the cost of substantial heterogeneity, as trials were performed in different regions and with different inclusion criteria and study follow-up (eg, 1 yr or 3 mo). Antiandrogen use in the LHRH agonist arm, for example, was at the investigator’s discretion. The heterogeneity of Gleason score evaluation led to its exclusion from the multivariate analysis.

Klotz et al highlighted the reduced incidence of joint, musculoskeletal, and urinary tract adverse events with degarelix. This advantage is important, but it should be weighed against the significantly higher incidence of injection-site reactions and hot flushes. Eventually, a significantly higher rate of any adverse event was noted in the degarelix group.

The daunting amount of data accumulated in these five studies warrant a more thorough analysis. This was achieved by the UK National Institute for Health and Care Excellence through its appraisal committee, which concluded that there was a lack of robust evidence to support benefits with degarelix regarding overall survival, PSA progression, or difference in the rate of fractures. This is a very short summary of the 72-page document, which is available online [2].

Yes, it is still ethical to choose between analogs and antagonists when the use of ADT is appropriate to treat prostate cancer; however, the matter is not settled. It warrants an independent randomized study focused on survival and side effects.

Conflicts of interest: The author has nothing to disclose.

References

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