EDITORIAL

Treatment of prostate and renal cancer with oral drugs (abiraterone and antiangiogenic agents): Positioning statement from the Spanish Association of Urology☆

Tratamiento del cáncer de próstata y cáncer renal con fármacos orales (abiraterona y antiangiogénicos): posicionamiento de la Asociación Española de Urología

On December 10, 2012, the FDA approved the use of abiraterone acetate in patients with asymptomatic or minimally symptomatic castration-resistant prostate cancer (CRPC) prior to the use of chemotherapy (CT). The EMA, after a positive preliminary comment, approved on December 21, 2012, the use of abiraterone in the same case. This molecule has approved indication in CRPC, both post-CT and pre-CT, the latter being where the urologist has a very important role in its prescription.

This compound blocks the complex 17 of the p450 cytochrome, inhibiting androgen production at all levels: testis, adrenal gland, and even intracrine production by prostate tumor cells themselves. The clinical benefits of abiraterone along with prednisone (PDN) have been studied in a phase III, multinational, multicenter, randomized, double-blind, placebo-controlled trial in patients with metastatic CRPC and asymptomatic or mildly symptomatic chemo-naïve ones. 1088 patients were randomized 1:1, having as primary objectives progression-free recurrence (pRFS) and overall survival (OS). The secondary objectives were time to opiate use, time to onset of chemotherapy, and time to deterioration of the ECOG-PS. In a first interim analysis, we could demonstrate a significant impact of the use of abiraterone + PDN in pRFS, and a significant trend, although not significant, to improve OS. Likewise, it was possible to demonstrate an improvement in pain scores, analgesic requirements, PSA control, and improved functional status of patients. These data promoted break of the blinding, FDA approval, and immediate approval by the EMA. It is an oral drug of excellent safety profile in relation to its adverse effects: mild symptoms related to increased mineral-corticoids (edema, fluid retention, hypertension, hypokalemia), which are greatly reduced with the concomitant use of PDN. This drug will probably replace the second hormonal maneuvers, so far performed by urologists. Its efficacy and safety, with easily manageable side effects and oral administration, make it an excellent alternative to be prescribed by specialist urologists.

We witnessed with concern the attempts by the Spanish Society of Medical Oncology (SEOM) to restrict the use of oral drugs, including abiraterone, to their specialty. In our opinion, this fact does not respond to medical reasons, but to the hope to restrict the use of antineoplastic drugs to their specialty, including oral ones with a good safety profile, trying to set borders where there should not be. No criteria are established from the evidence, but from the mercantilism.

The incongruity of the arguments suggested in the editorial of Annals of Oncology by the SEOM 2 years ago, in terms of the use of oral drugs in the different oncology specialties, is the attempt to monopolize a drug that says no to an exercise of responsibility, but a spurious attempt of irrational expansion of the specialty of medical oncology at the cost of limiting other specialties, in addition to other possible interests difficult to confess. To monopolize the oral treatments, that editorial appeals to the greater experience of oncologists, and therefore less trained specialists should be excluded. However, it does not take into account that the experience in hormonal treatments in humans began in 1945, or that these treatments have been...

managed since then by urologists, many years before the specialty of medical oncology was established.\textsuperscript{4,5} The urologist knows perfectly the efficacy and morbidity of these therapies, both first and second line. However, in complicity with the administration, the urologist is excluded from the management of a drug of evident hormonal action in humans. Where is the consistency of action and argument, when do we appeal to the greatest experience in some cases and it is avoided in others? There is no choice but to deduce that it is due to different interests of the patient’s benefit, as it is the attempt of expansion of the specialty of medical oncology at the expense of other specialties with greater experience in treating these patients and in the management of hormone treatment, but this time, as on other preceding occasions, it is an easy-to-use new drug with known side effects, more by urologists than by oncologists.

But where is the consistency of the SEOM when a multidisciplinary committee is encouraged and in the therapeutic decision the most experienced specialty in drug management of hormone action is excluded, or … could it be that the purpose of the committee is the increased incorporation of patients to clinical trials that involve the scientific and economic modus vivendi of the specialty of medical oncology?

The consensus among specialists, which stems from the uro-oncological joint sessions with the participation of urologists, oncologists, radiotherapists, and pathologists is essential for the decision-making to be the most correct in each case. This mutual partnership attitude affects all the urological cancers. When systemic chemotherapy is necessary, whether it is muscle-invasive bladder cancer or testicular cancer or castration-resistant prostate cancer, the patient is transferred from urology to medical oncology due to the complexity of handling cytotoxic drugs. It is not the case of intravesical chemotherapy in non-muscle-invasive bladder cancer which is applied by the urologist, without any involvement of Oncology. It would not be logical that immunologists claimed the treatment, nor it is, to our knowledge, that medical oncologists claim exclusivity to prescribe second-line hormonal therapy or antiangiogenic drugs.

Urologists have always taken responsibility for the hormonal treatment of locally advanced or metastatic prostate cancer, medical oncologists and radiotherapists having assimilated to it in recent decades, with no reason for conflict. Any attempt to monopolize the therapies, in this case by medical oncology, is a misconception and failed strategy that will particularly affect patients. Regarding prostate hormone therapy, urologists have been the forerunners of the treatment, have extensive experience in its management, and are responsible for the patient from the onset of the disease, regardless of being directly involved in the investigation and scientific advances in this area.\textsuperscript{4,7} There is no objective justification supporting the incomprehensible initiative of excluding urologists from the use of abiraterone in prostate cancer. For our part, we remain open to join multidisciplinary teams of uro-oncology, as we have always promoted and that has resulted so well so far, not only among specialists but also in comfort and patient care, but we will never support an exclusionary and exclusivist attitude like the SEOM intends.

In connection with advanced kidney cancer, we urologists have been trying this entity for over a century, both surgically, performing cava thrombus resection and/or metastasectomies, and by systemic medical treatment. Because it is a tumor intrinsically resistant to radiotherapy and chemotherapy, since the decade of the 1970s, we have been the specialists most involved in immune therapies in these patients. The oral antiangiogenics arise in the current decade as a new cellular target therapy, which administered orally, on an outpatient basis, and with perfectly controllable side effects by the well trained physician, have been moving to immunotherapy as standard treatment for advanced or metastatic kidney cancer. Many urologists have been trained in courses, congresses, and seminars on this type of therapy, accepting that other specialists have come to treat it, where urologists have declined its use. But we do not accept or will ever accept limiting its use to a single specialty, medical oncology, as the SEOM has been surprisingly defending explicitly in its congresses and opinion articles. Antiangiogenics, as their name indicates, are inhibitors of tumor angiogenesis and have nothing to do with chemotherapy, systemic form of treatment under whose light and intravenous form of administration, Medical Oncology emerged in the mid-1980s as a specialized branch of internal medicine, allowing for better and specific management of such chemotherapeutic agents.

Therefore, we demand from the AEU and the National Speciality Committee that the diagnosis and treatment of kidney cancer at all stages is the responsibility of the urologist, as well as the use of medical and surgical treatments that are required for healing. Such knowledge is an area of knowledge that is included in the subject Urology at the faculties of Medicine of Spain, and in the syllabus of the ‘Médico Interno Residente’ (MIR) of Urology, prepared by the National Specialty Committee, endorsed by the Ministries of Education and Science and Health respectively.

Thus, the Plenary Board of the Spanish Association of Urology wants to make clear its position regarding the use of these new oral therapies for the citizen, the main beneficiary of the quality of care we provide, and the health authorities of our country, guarantors that citizens receive adequate attention, to know that we assume medical responsibility for our actions, arising from the decision that every urologist, voluntarily and freely, makes before the use of their freedoms as a professional and specialist of using such drugs. Finally, this paper serves for other medical scientific societies to know our strong position, as well as the concepts and arguments that we will defend in as many scientific forums we consider appropriate.

References


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