Treatment of metastatic castration-resistant prostate cancer

A prostate carcinoma that progresses despite an initial hormonal treatment is referred to as castration-resistant. There is only weak evidence for the efficacy of a number of hormonal therapies that can be applied as a follow-up in such cases, such as cessation of anti-androgen treatment if this was already included in the treatment (anti-androgen deprivation) or addition of an anti-androgen if this agent had not yet been included in the treatment (Gebu 2013; 47: 135-140).

One treatment option for castration-resistant prostate carcinoma (CRPC) is chemotherapy. Taxans, with docetaxel as the most thoroughly investigated member, yield a median survival gain of a few months, relative to mitoxantrone. On the other hand, taxans frequently cause haematological and non-haematological side-effects. There is insufficient evidence for a survival gain from estramustine. Recently, two new hormonal agents, abiraterone and enzalutamide, have come onto the market. Research into abiraterone (combined with prednisone/prednisolone) has found a median survival gain of a few months relative to placebo in patients who had already been treated with docetaxel, whereas patients who had not yet been treated with docetaxel only showed a longer progression-free survival. Side-effects which are inherent in the mode of action of abiraterone include hypokalemia, fluid retention and oedema, while the agent can also cause liver dysfunction or cardiac arrhythmias. One study of enzalutamide found a median survival gain of a few months relative to placebo in patients who had already been treated with docetaxel. Enzalutamide produced more side-effects, such as headache, diarrhoea and fatigue. The recently authorised hormonal agents have only been compared with placebo, not with previously available chemotherapeutics, so it is unknown how the various agents compare in terms of efficacy.

In addition, there are ancillary treatment options to alleviate pain and complications due to bone metastases, which can be administered in conjunction with the above medications. Studies comparing bisphosphonates with placebo have not conclusively shown that these agents alleviate pain, but they have been found to reduce the risk of bone complications. There is no convincing evidence that denosumab is more effective than zoledronic acid. Other pain relief options include radiotherapy or radiopharmaceuticals. Side-effects of radiotherapy include especially nausea, vomiting and skin problems. Radiopharmaceuticals particularly cause haematological side-effects. Radium223, which has recently become available, has been found to increase survival by a number of months compared to placebo, but this radiopharmaceutical can produce haematological side-effects. There have not yet been any studies comparing it with other agents, and no long-term trial outcomes are available.

The choice of treatment for each individual patient needs to be based on an assessment of whether a small gain in survival outweighs the (sometimes severe) side-effects. The recent market introduction of a number of new agents has expanded the therapeutic arsenal for the treatment of CRPC. Since many of these new medications have only been compared with placebo, and not with previously available agents, their place in the pharmaceutical repertory can as yet not be determined. The quality of research in oncology is sometimes suboptimal (Gebu 2013; 47: 117-118), and this is also true for some of the studies discussed in the present article. Many studies did not use blinding, and side-effects are not always fully described, and in some cases the efficacy is assessed using soft endpoints. Experience with these new drugs is limited, and in many cases there is insufficient information on side-effects.

References*


35. Productinformatie strontium89 (Metastron®), via: www.cbg-meb.nl, Geneesmiddeleninformatiebank.


*The literature refers to the Dutch text*