

Hormonal Therapy in Prostate Cancer, - Overview and Recent Trend in Japan -.

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Background.

Hormonal therapy has been one of the standard treatment modalities in prostate cancer, although it has been regarded as a palliative treatment. Today, it is still selected as the initial treatment for advanced metastatic prostate cancer.

Purpose.

Hormonal therapy including modality and mechanism in prostate cancer is reviewed and recent trend of hormonal therapy in Japan is introduced.

Results.

There are many drugs in hormonal therapy at the point of action mechanism. Luteinizing hormone-releasing hormone (LHRH) agonist, medical castration, inhibits LH activity at pituitary gland. Surgical castration inhibits testosterone at testis. Non-steroidal antiandrogen inhibits a binding of dihydrotestosterone and androgen receptor at prostate. Steroidal antiandrogen inhibits LHRH release at hypothalamus as well as a binding of dihydrotestosterone and androgen receptor at prostate. Finally, estrogen inhibits LHRH release at hypothalamus. Maximum androgen blockade is a combination therapy of either LHRH agonist or castration with an antiandrogen, mainly non-steroidal antiandrogen.

Many clinical trials have been conducted to elucidate the survival benefit of hormone therapy in localized or locally advanced prostate cancer. Adjuvant hormonal therapy following radical prostatectomy or radiotherapy reveals survival benefit for selected patients. But, there is still no evidence that neoadjuvant hormonal therapy in combination with either radical prostatectomy or radiotherapy has a survival benefit. In case of maximum androgen blockade, superiority of MAB to hormonal monotherapy is still controversial.

Recently Japanese prostate cancer group (JCaP) has been established. The aim of this study group is; survey of patients who receive initial hormonal therapy, development of data base of hormonal therapy for prostate cancer in Japan, evaluation of treatment

response, and establishment of standard treatment method concerning hormonal therapy in prostate cancer. From January 2001 to October 2003, more than 17,000 patients were registered. Hormonal therapy was selected as a hormonal monotherapy in most patients with localized prostate cancer as well as advanced prostate cancer and this incidence was far higher than that of neoadjuvant or adjuvant hormonal therapy. Of the modalities of hormonal therapy, MAB was frequently selected and most of MAB was LHRH agonist in combination with non-steroidal antiandrogen. This study is ongoing and further analysis will be made.

In order to evaluate the efficacy of MAB in Japanese patients, LHRH agonist plus bicalutamide versus LHRH agonist alone, double blind randomized controlled trial was conducted. A patient with newly diagnosed, untreated advanced prostate cancer (stage C, D) was eligible. Enrolled patients were randomized to receive LHRH agonist in combination with bicalutamide or placebo. From December 1999 to September 2002, 205 patients were enrolled and 203 were randomized. PSA normalization rate of MAB group at 12 weeks was significantly higher than that of LHRH agonist monotherapy group. Time to progression (TTP) of MAB group was longer than that of the monotherapy group, but this study is now ongoing and further analysis is needed.

Conclusion,

Hormonal therapy including modality and mechanism for prostate cancer was reviewed. Japanese prostate cancer group was introduced and characteristics of hormonal therapy in Japan were presented. Most of hormone therapy was selected as the main treatment even for localized prostate cancer and the incidence of MAB was the highest of the modalities of hormonal therapy. Interim analysis of MAB versus LHRH agonist double blind randomized controlled trial was presented. PSA normalization rate of MAB group at 12 weeks was significantly higher than that of LHRH agonist monotherapy group. TTP of MAB group was longer than that of the monotherapy group, but further analysis is needed.