



FOUR NEWER HORIZONS FOR THE TREATMENT OF METASTATIC RESISTANT PROSTATE CANCER

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ABSTRACT

Prostate cancer is the second most common tumor affecting the men, ranking next to non melanoma skin cancers. It is also the second most cause of cancer mortality among men , next to neoplasm's of the lung. Significant earlier detection, improved surveillance increases the number of cancer prostate men detection at an earlier stage and various treatment options are being tried to improve prognosis . The objective of our article is to provide a comprehensive review of newer molecules of prostate cancer management.

KEY WORDS: PROSTATE CANCER, SIPULEUCEL, CABAZITAXEL



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INTRODUCTION

Cancer prostate: Summary

It is predominant cancer affecting the elderly men , having a peak incidence between 65 and 75 years , however 5-10 % of prostate cancer with defined hereditary origin can be of early onset disease .Age adjusted incidence rate of prostate cancer varies in different geographical region , in the United States with incidence of 124 cases per 100,000 men . Majority of cancer originates from the outer region of prostate , spread to local nodes and blood borne metastasis is also common. Digital rectal examination , measure of serum prostate specific antigen are the common screening procedures employed in the diagnosis , transrectal ultrasound and transrectal biopsy are some of the most useful and specific investigations to diagnose the prostate cancer and to evaluate its local invasion . Apart from watchful waiting , surgery , radiotherapy and chemotherapy are used cancer over decades in the treatment of prostate cancer. Prognosis of prostate cancer with significant spread remains poor, with 10-year survival rates in this group ranging from 10% to 40%.It has been estimated 1 man in 30 with prostate cancer will die of his disease. Need of newer approaches in the non surgical way of treating cancer is still an unmet need , however there are few molecules showed a significant cure rate against prostate cancer and various approaches like targeted therapy , immunotherapy are being employed currently . This review article will give us a overview of multimodality approach of prostate cancer.

CABAZITAXEL

It is a microtubule inhibitor , a synthetic derivative of a 10-deacetylbaccatin III. It possesses potent anti neoplastic activity against prostate cancer , including refractory and/or resistant prostate cancer. Being a poor substrate for p-glycoprotein drug resistance is less than other taxane compounds . In a study conducted on prostate cancer patients after initial treatment with prostate cancer, cabazitaxel was to be effective in reducing progression of the disease . In an another open, randomized trial with 755 participants who were all

received prednisone 10 mg oral prednisone daily and either mitoxantrone intravenously over 15—30 min or cabazitaxel 25 mg/m² cabazitaxel intravenously over 1 h every 3 weeks , treatment with cabazitaxel increased median survival of 15.1 months than the comparator group. Dose limiting toxicity includes severe diarrhoea , asthenia ,leukopenia , thrombocytopenia , hematuria and rarely renal failure [1]. FDA approved cabazitaxel in combination with prednisone for prostate cancer on June 17 , 2010 .

ABIRATERONE

A newer hormonal analogue found to be highly effective in resistant prostate tumours . prostate cancer is androgen dependent tumor and many androgen depletors and androgen antagonist are used with various success in the treatment . Extra gonadal synthesis of androgen is blocked by abiraterone and have been found highly effective in achieving remission of treatment failure prostate cancer . In a multinational , double blind , placebo controlled trial conducted between April 28, 2009, and June 23, 2010 in patients with progressive metastatic castration-resistant prostate cancer , 1088 patients were randomly divided into two group, 546 were assigned to abiraterone plus prednisone and 542 patients to placebo plus prednisone. Study results showed that Abiraterone plus prednisone delays patient-reported pain progression and deterioration in patients with metastatic castration-resistant prostate cancer. Liver toxicity is the significant side effect seen with abiraterone[3] . October 10 , 2012 abiraterone was approved by FDA for the treatment of resistant prostate cancers

SIPULEUCEL-T

This is the first vaccine approved for cancer in the history of cancer therapeutics which is remarkable , it is approved by FDA for resistant , metastatic prostate cancer . it is an autologous dendritic cellular product consists of antigen-presenting cells (APCs) pulsed *ex vivo* and activated *in vitro* with a recombinant fusion protein (PA2024). In a double blind , placebo controlled phase 3 trial with 512 patients , sipuleucel is significant in achieving 22 % risk of death due to prostate cancer [4].

ENZALUTAMIDE

This is an androgen receptor blocker , newer hormonal analogue based treatment of metastatic resistant prostate cancer . Unlike other treatment options for metastatic resistant prostate cancer , enzalutamide does not require concurrent administration of steroids . enzalutamide increases all the primary and second end points in the treatment of prostate cancer like enzalutamide also resulted in significant

improvement in all secondary endpoints, with increase in median survival of 4.8 months[5] .

CONCLUSION

Being said and predicted, prostate cancer is the second cancer related cause of death in men . A complete Treatment regimen of prostate cancer is still a goal unachieved , with the arrival of these newer agents we are much ahead towards the complete cure of metastatic prostate cancer .

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