ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Determination of the Effects of Docetaxel Chemotherapy on Surgical Results and Survival in High-Risk Locally Advanced Prostate Cancer Before Radical Prostatectomy

Yüksek Riskli Lokal İleri Prostat Kanserlerinde Radikal Prostatektomi Öncesi Dosetaksel Kemoterapisinin Cerrahi Sonuçlar ve Sağkalım Üzerine Etkilerinin Belirlenmesi

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ABSTRACT

Aim: *Determination of the effect of neo-adjuvant docetaxel chemotherapy combined with radical prostatectomy (RP) on surgical outcome and survival.*

Material and Method: *The data of 132 non-metastatic prostate cancer (PC) patients, considered high-risk according to the D'Amico Risk Stratification System and who underwent radical prostatectomy, among those who applied to the Hacettepe University Faculty of Medicine Urology Clinic between August 1987 and August 2017, were retrospectively evaluated. Data from 28 patients selected via pair matching from the group operated without chemotherapy and 14 patients identified to have received neoadjuvant androgen deprivation therapy (NADT) preoperatively were compared regarding biochemical recurrence, survival, surgical outcomes, and some additional variables.*

Results: *The findings of our study revealed that, while NADC is usually tolerated well by patients and can be administered without severe side effects, it has no statistically significant advantage on PSA values (p=0.145), Gleason scores, and pathologic stages (p=0.273, p=0.109), biochemical recurrence risk (p=0.040) and overall survival (p=0.527). It did not affect surgical complication rates, may have benefitted malignant involvement of lymph nodes, and prolonged biochemical relapse-free survival time.*

Conclusion: *In high-risk PC patients, the ineffectiveness of neoadjuvant androgen deprivation therapy in combination with RP suggests the presence of castration-resistant cell clones that exist at the time of the diagnosis and brings up treatment options that could be effective on castration-resistant clones as systemic treatments. As a neo-adjuvant treatment, combining docetaxel chemotherapy with RP can be beneficial.*

Keywords: *neoadjuvant; docetaxel; high-risk prostate cancer*

ÖZET

Amaç: *Neo-adjuvan dosetaksel kemoterapisinin (NADC) radikal prostatektomi (RP) ile kombine edilmesinin cerrahi sonuç ve sağkalım üzerine etkisinin belirlenmesi.*

Materyal ve Metot: *Ağustos 1987 ile Ağustos 2017 tarihleri arasında Hacettepe Üniversitesi Tıp Fakültesi Üroloji Kliniğine başvuran hastalar arasından D'Amico Risk Evreleme Sistemine göre yüksek riskli kabul edilen ve RP uygulanan 132 metastatik olmayan prostat kanseri (PK) hastasının verileri geriye dönük olarak değerlendirildi. Kemoterapi almadan ameliyat edilen hasta grubundan "pair match" ile seçilen 28 hasta ile ameliyat öncesi NADC verildiği tespit edilen 14 hastanın verileri biyokimyasal nüks, sağkalım, cerrahi sonuçlar ve bazı ek değişkenler açısından karşılaştırıldı.*

Bulgular: *Çalışmamızın bulguları, NADC'nin genellikle hastalar tarafından iyi tolere edildiği ve ciddi yan etkiler olmadan uygulanabildiğini ancak PSA değerleri (p=0,145), Gleason skorları ve patolojik evre (p=0,273, p=0,109), biyokimyasal nüks riski (p=0,040) ve genel sağkalım (p=0,527) üzerine istatistiksel olarak anlamlı bir avantajının olmadığını ortaya koydu. Cerrahi komplikasyon oranları üzerinde etki saptanamadı. NADC'nin lenf nodu tutulumunun azalmasında muhtemel olumlu etkileri olduğu ve biyokimyasal nükssüz sağkalım süresini uzattığı tespit edilmiştir.*

Sonuç: *Yüksek riskli PK hastalarında RP ile birlikte neoadjuvan androjen deprivasyon tedavisinin etkisiz olması, tanı anında var olan kastrasyona dirençli hücre klonlarının varlığını düşündürmekte ve kastrasyona etkili olabilecek tedavi seçeneklerini gündeme getirmektedir. Neo-adjuvan bir tedavi olarak, dosetaksel kemoterapisinin RP ile birleştirilmesi yüksek riskli prostat kanseri taşıyan hasta grubunda faydalı olabilir.*

Anahtar kelimeler: *neo-adjuvan; dosetaksel; yüksek riskli prostat kanseri*

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Introduction

Following lung cancer, prostate cancer (PC) is the second most prevalent form of cancer. When all men with a cancer diagnosis are examined, it can lead to significant morbidity and mortality[1]. After the diagnosis, the most critical issue is predicting the disease's prognosis and selecting the most appropriate treatment based on the patient's risk. D'Amico Risk Evolution, which evaluates patients as low, moderate, and high risk according to the level of serum prostate-specific antigen (PSA) at diagnosis, the clinical stage suggested by digital rectal examination (DRE), and Gleason Score (GS) that is obtained after biopsy has been widely accepted in the risk classification of patients and has been used in studies conducted on this field[2].

Although the diagnostic and treatment guidelines developed by multinational urological associations, such as the European Association of Urology (EAU) and the American Urological Association (AUA), clearly define treatments for various risk stages, discussions on treatment protocols for patients at high-risk groups are still in progress. High-risk PC patients are at increased risk for recurrence of PSA, need for secondary treatment, risk of metastasis, and death due to PC[3]. There are several studies in this group of patients claiming that castration-resistant cancer cells may be present in the tumor at the time of diagnosis, which may lead to a relapse of the disease in a relatively short period, the use of neo-adjuvant docetaxel chemotherapy (NADC) before radical prostatectomy (RP) could reduce the likelihood of recurrence and improve survival[4–8].

This study aimed to evaluate the effects of NADC applied before RP on surgical outcomes, recurrence, and survival in high-risk prostate cancer patients.

Material and methods

Study Protocol

Ethics committee approval was obtained for the thesis study from the Hacettepe University Ethics Committee with the number GO 17/715-40 on 24.08.2017. In this study, we retrospectively evaluated non-metastatic PC patients admitted to the Hacettepe University Faculty of Medicine, Urology Clinic between 1987 and 2017 who were over 18 years of age and had high risk according to the D'Amico Risk Staging System. All patients underwent RP. It aimed to compare the patients who received preoperative NADC (combination therapy) and those who underwent surgery without chemotherapy (monotherapy) in terms of biochemical recurrence, cancer-specific and overall survival, and some additional variables.

Among 1308 cases of local or locally advanced-stage PC patients who had undergone RP surgery between 01.08.1987 and 01.08.2017, 132 cases with high risk, according to the D'Amico Risk Stage, were recruited and screened retrospectively. When the data of these 132 patients were examined, it was found that 14 patients received four cycles of NADC (combination therapy) before RP. Considering the PSA value, Gleason score, and age at the diagnosis in terms of the comparison with this group, a group of RP (monotherapy) was formed with the "pair match" technique, which consists of 28 patients with similar characteristics at the time of diagnosis.

Before the treatment, all patients were examined with computed tomography and bone scintigraphy (BS), and metastasis was investigated. The study excluded patients who had metastatic disease at the diagnosis. Patients with uncontrolled comorbidities (including oncologic diseases) who had received chemotherapy for another reason or a history of pelvic radiotherapy, which may influence the survival and the treatment process, were also left out of the study. All patients' pre– and post-treatment specimens were examined and reported by the same uropathology team at Hacettepe University, Faculty of Medicine Department of Pathology.

In a total of fourteen patients who received combined therapy, docetaxel was started at a dose of 75 mg/m^2 every three weeks, and 8 mg oral dexamethasone was given to the patient twelve hours, three hours, and one hour before the infusion of chemotherapy (CTx). Patients were given prednisolone 2×5 mg throughout CTx. The blood tests for control purposes were made in the CTx sessions immediately before each treatment cycle. "Common Terminology Criteria for Adverse Events v 4.0" was used to evaluate adverse events during treatment[9].

All patients underwent "open retropubic radical prostatectomy and bilateral pelvic lymph node dissection" (RRP-BPLND) surgery by the Urooncology Team of the Urology Clinic of the Medical Faculty of Hacettepe University. The amount of bleeding during operation, operation time, and complications were noted separately and compared between the two study groups. The duration of postoperative hospital stay was also compared between the two study groups.

Table 1. *Characteristics of the groups at the diagnosis*

		Combined Therapy Group (n=14)	Monotherapy Group (n=28)	p
Age (Years)	(Median, Min-Max)	58 (46–73)	64 (52–77)	***0.007***
PSA levels at the diagnosis (ng/mL)	(Median, Min-Max)	20.61 (3.07–170)	17 (7.44–111.33)	0.208
ISUP Scores at the diagnosis	ISUP 3	1 (7.1%)	2 (7.1%)	
	ISUP 4	4 (28.6%)	8 (28.6%)	1.000
	ISUP 5	9 (64.3%)	18 (64.3%)	
Lymph node involvement at the diagnosis	Negative	9 (64.3%)	24 (85.7%)	0.133
	Positive	5 (35.7%)	4 (14.3%)	

*PSA: Prostate Spesific Antigen, ISUP: International Society of Urological Pathology

Table 2. *PSA values during chemotherapy cycles*

PSA (ng/mL)	Cycle 1	Cycle 2	Cycle 3	Cycle 4	p
Mean	24.17	26.29	16.47	21.95	
SD	22.16	24.04	15.15	21.25	0.145
Median	16.95	18.62	13.31	17.17	
Min-Max	0.72–61.98	2.58–72.84	1.50–48.49	1.11–68.67	

* PSA: Prostate Spesific Antigen, SD – Standart Deviation

The pathologic findings of the patients and pathology results obtained after RP were compared with each other in terms of ISUP (International Society of Urological Pathology) scores, clinical stages, and presence of lymph node involvement. Post-RP PSA values of the patients were first measured after one month of surgery, every three months for the first two years afterward, and every six months for the following periods. The biochemical recurrence (BCR) criteria were a PSA limit value of 0.2ng/mL; Patients with two PSA values of 0.2 ng/mL or greater, with at least one week between them, were considered BCR. Up-to-date EAU Treatment Guidelines have been considered while adjuvant therapies were being planned. Both groups of patients were evaluated for biochemical recurrence-free survival (BRFS) and patient survival (PS).

Statistical Analysis

In numerical variables, descriptive statistics included mean, standard deviation, and median (minimum-maximum), while categorical variables included numbers and percentages. When comparing the groups receiving and not receiving chemotherapy, the "significance test of the difference between the two means" was used for the normalized numerical variables, and the Chi-square test was used for the categorical variables. The Mann-Whitney U test was utilized to compare standard non-normally distributed numerical variables between two groups. The marginal homogeneity test was used in independent groups to compare variables with more than two categories, and the Mc Nemar test in variables with two categories. Cumulative survival probabilities and mean survival times were calculated using the Kaplan-Meier method. Survival curves were drawn and compared with the log-rank or Breslow tests according to the group factor. Comparisons were considered statistically significant when $p<0.05$. Analyses were performed on IBM Statistical Package for Social Sciences (SPSS) program version 23.0 (IBM Corp., Chicago, IL, USA).

Results

The study included a total of forty-two patients. Twenty-eight (66.6%) patients had only RP monotherapy for prostate cancer treatment, and 14 (33.3%) had combined therapy with four cycles of NADC before surgery. The median age of the 14 patients receiving combined therapy was 58, whereas the median age in the monotherapy group was 64 (p=0.007). The groups did not differ significantly regarding PSA values, ISUP groups, and lymph node involvement on CT at the diagnosis (Table 1).

There was no significant change in the PSA values of the patients due to docetaxel chemotherapy (p=0.145) (Table 2). None of the patients had grade 3 or more side effects of chemotherapy. When the complications related to surgical treatment were examined, it was found that 1 (7.14%) patient in the combined therapy group experienced bleeding that necessitated a blood transfusion (p=0.233). In contrast, seven patients (25%) in the monotherapy group experienced bleeding that necessitated a blood transfusion, 2 (7.14%) had intraoperative rectal injuries (p=0.545), 1 (3.57%)

Table 3. *Comparison of ISUP scores of diagnostic biopsy and final pathologies according to groups*

	Combined Therapy Group (n=14)		p	Monotherapy Group (n=28)		p
	Diagnostic Biopsy	RP Specimen		Diagnostic Biopsy	RP Specimen	
ISUP 1	*	1 (7.1%)		*	1 (3.6%)	
ISUP 2	*	*		*	1 (3.6%)	
ISUP 3	1 (7.1%)	3 (21.4%)	0.273	2 (7.1%)	4 (14.3%)	0.109
ISUP 4	4 (28.6%)	2 (14.3%)		8 (28.6%)	3 (10.7%)	
ISUP 5	9 (64.3%)	8 (51.7%)		18 (64.3%)	19 (67.9%)	

*ISUP: International Society of Urological Pathology, RP: Radical Prostatectomy

Table 4. *Comparison of lymph node involvement by groups*

	Combined Therapy Group (n=14)		p	Monotherapy Group (n=28)		p
	CT at the Diagnosis	Final Pathology		CT at the Diagnosis	Final Pathology	
LNI Positive	5 (35.7%)	8 (57.14%)	0.375	4 (14.3%)	11 (39.29%)	**0.039**
LNI Negative	9 (64.3%)	6 (42.86%)		24 (85.7%)	17 (60.71%)	

LNI: Lymph Node Involvement, CT: Computerized Tomography

Table 5. *Data of the groups during the follow-up period*

		Combined Therapy Group (n=14)	Monotherapy Group (n=28)	p
Follow-up Periods (Months)	(Median, Min-Max)	49.50 (18-106)	34.50 (12-199)	0.759
PSA Recurrence	Yes	11 (78.6%)	25 (89.3%)	0.383
	No	3 (21.4%)	3 (10.7%)	
Biochemical Recurrence-Free Survival (Months)	(Median, Min-Max)	18 (7-95)	7 (2-162)	**0.040**

*PSA: Prostate Spesific Antigen, SD – Standart Deviation

had ureter injury and repair (p=1.000), and one patient (3.57%) who had previously undergone diagnostic laparotomy experienced intestine injury due to adhesions (p=1.000). There were no statistically significant differences between the two groups regarding complications.

There was no significant difference between the ISUP scores of the diagnostic biopsies and the ISUP scores of the surgical specimen in the combined therapy group and the monotherapy group (p=0.273, p=0.109, respectively) (Table 3).

When patients were evaluated regarding lymph node positivity, there was no statistically significant difference between the rate of lymph node involvement detected in the preoperative CT scan and the rate of lymph node involvement seen in the pathology results of the combined therapy group (p=0, 375). However, in the monotherapy group, the rate of lymph node involvement in the pathology results was statistically significantly higher than in the preoperative CT scan (p=0.039) (Table 4).

The patients' median follow-up period was 49.5 months in the combined therapy group. In comparison, the median was 34.5 months in the monotherapy group. When the patients were assessed for risk of biochemical recurrence, PSA recurrence was encountered in 11 (78.6%) patients receiving combined therapy during the study period. In contrast, when the monotherapy group was examined, PSA recurrence was seen in 25 (89.3%) patients. No statistically significant difference was found between these two groups regarding the risk of PSA relapse (p=0.383) (Table 5). When patients were examined regarding BRFS, the median time in the group receiving combined therapy was 18 months (7–95). When the data of the monotherapy group were evaluated, the median BRFS was seven months (2–162). When the two groups were compared, a significant difference was found in favor of the combined therapy group regarding BRFS (p=0.040).

When survival analyses were performed, 36 (85.7%) of the patients included in the study were alive. Two (14.29%) of 14 patients in the combined therapy group lost their lives due to prostate cancer progression. In comparison, one patient (7.14%) died due to a second primary cancer that developed within the follow-up period. In the monotherapy group, 3 (10.71%) patients died because of prostate cancer progression. No statistically significant difference was found between

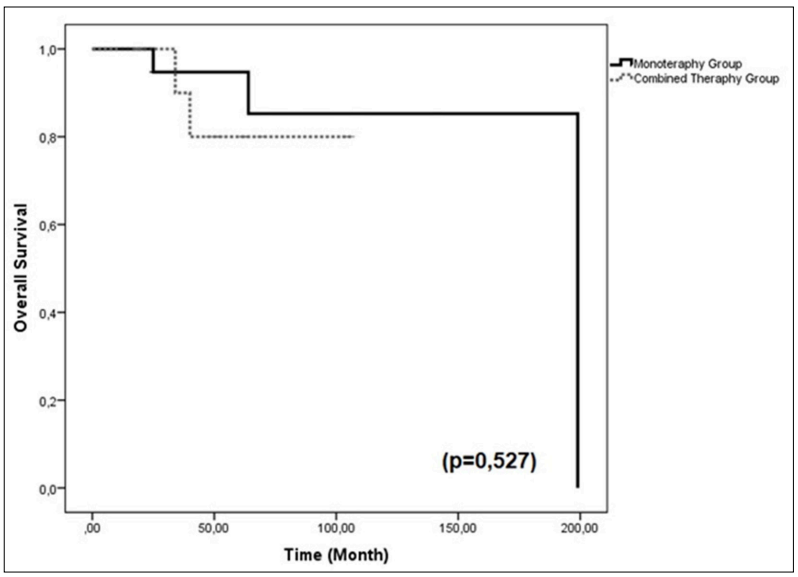

Figure 1. *Overall survival comparison of the two groups.*

the two groups when the patients in both groups were compared in terms of survival (p=0.527) (Fig. 1).

Discussion

No consensus exists on a standardized treatment currently recommended for high-risk prostate cancer patients[3,10]. In patients with high-risk PCs, local treatment alone is insufficient because of possible micrometastases that imaging methods cannot detect at diagnosis. Local therapies should be combined with systematic treatments to delay the biochemical recurrence and improve survival[11]. It can be suggested that neo-adjuvant therapies are beneficial for issues such as early treatment of micrometastatic disease compared to adjuvant treatments, less surgical margin positivity due to possible reduction in tumor size, and understanding of the molecular mechanisms of the disease by examining the effects on tumor tissue[8].

Adverse events related to NADC administration were evaluated according to the "Common Terminology Criteria for Adverse Events v4.0" criteria. Grade 3 and 4 side effects have been reported in studies in the literature; none of the patients included in our study had side effects at grade 3 and above, and no dose reduction was required in any patient[7,12,13].

In a study conducted by Nosov et al., 52.4% of patients showed a reduction of PSA by more than 50%. The median PSA value of 29.8 ng/mL before treatment was reported to be 13.4 ng/mL in the post-treatment group[12]. However, it was also noted that the serum PSA level of a patient in the same study increased from 27 ng/mL to 67 ng/mL after NADC. Similarly, Klein and colleagues reported that 21 of 28 patients had a total decrease in serum PSA levels of between 9 and 79%, and seven patients had a 2–18% increase[13]. However, our study found no statistically significant change between the median PSA values (ng/mL) monitored over four cycles. A study evaluating PSA changes during the application of a group of chemotherapeutic agents, including docetaxel, indicated that there might be significant fluctuations in the PSA value regardless of whether the tumor benefited the CT or even an increase in PSA values during the first 8-week period could occur, which should not be interpreted as 'treatment was not useful' [14].

In the Nosov et al. series, there was no difference between the combined and monotherapy groups regarding the average operation time, the average amount of bleeding, and the average length of postoperative hospital stay[12]. Similarly, there were no differences in median operative times, median bleeding volumes, blood transfusion requirements, and length of postoperative hospital stay for patients enrolled in this study.

Regarding complications, in Febbo et al.'s series, bleeding requiring blood transfusion in 3 patients and pulmonary embolism in one patient were reported[7]. Nosov and colleagues reported that the periprostatic area underwent moderate fibrosis in the NADC group, but the resectability was generally not affected; one patient in the monotherapy group had a rectal injury, and one

patient in the NADC group experienced a major vessel injury. In both groups, postoperative pelvic hematoma was reported in one patient and prolonged lymphatic drainage in two patients[12]. When the patients included in our study were examined, there were no significant differences between the two groups regarding complications. Based on these data, it can be argued that NADC did not increase the intraoperative complication rates.

In the study of Nosov et al., no pathologic response was observed in any of the patients. In contrast, one patient in the monotherapy group and three in the combined therapy group showed a reduction in Gleason score. However, the two groups' total Gleason scores were similar[12]. Likewise, there was no significant difference in the ISUP scores of patients' biopsy and operative specimens in the combined therapy and monotherapy groups. In light of these data, it was assumed that NADC had no significant effect on ISUP and Gleason scores.

Considering the computed tomography's low sensitivity of lymph node involvement (LNI) detection in the literature, a significant difference is expected between the number of LNIs detected at the time of diagnosis and the LNI detected in the surgical specimen[15,16]. Lymph node involvement in imaging studies and LNI in the pathology specimen were investigated separately at the time of diagnosis for both groups. In comparing these two, there was a significant difference in the monotherapy as expected. However, no significant statistical difference was found in the combined therapy group. Evidence may not be sufficient, but this may indicate that NADC may effectively reduce LNI.

No significant difference in PSA recurrence was found between our study's two groups during the follow-up period. However, when patients were examined regarding BRFS, a statistically significant difference was found in favor of the combination therapy group for approximately ten months. These data suggest that NADC does not reduce the risk of BCR in patients with high-risk PC but delays the onset of BCR and improves BRFS. A study by Zhao et al., published in 2015, found that BFR was 33.5%, PS was 79.7%, and cancer-specific survival was 92.2% for ten years. The authors interpreted that NADC could potentially lead to a survival advantage in potentially high-risk patients[11]. Our study found no statistically significant difference between patients in both groups when assessed for survival.

Since our research is retrospective, there are various limitations. The sample size was limited to 14 patients in the combined therapy group because the patient sample began by screening patients who accepted to receive NADC retrospectively among high-risk PC cases applied to the Hacettepe University Hospital Urology Clinic. Although performing a pair match was attempted at the beginning of the study, this difference could not be avoided because of the study's retrospective nature and because patients who were given NADC were younger than those who were not. However, the fact that the patient's age is not among the factors determining the prognosis of the PC cases minimizes the poor impact of this difference on the quality of work[10,17–21]. Some patients' information existed before the hospital system was switched entirely to the computerized electronic registration system. Because most of the patients' files were unavailable, the physical examination information noted in the patients' files during this period was unavailable, so the clinical stages of the diagnosis were unavailable during the analyses. Information on late complications, such as erectile dysfunction, incontinence, and urethral stricture, noted in the files during the patient's controls, was unavailable.

Conclusion

Although high-risk PC is a significant public health issue due to its high mortality, morbidity, and economic burden, a standardized treatment method has not yet been defined. The data obtained from these studies suggest that multimodal treatment options should be used to combine systemic treatment for local disease and possible micrometastases not detected at diagnosis. In high-risk PC patients, the ineffectiveness of neo-adjuvant androgen deprivation therapy (NADT) in combination with RP suggests the presence of castration-resistant cell clones that exist at the time of the diagnosis and brings up treatment options that could be effective on castration-resistant clones as systemic treatments. As a neo-adjuvant treatment, combining docetaxel chemotherapy with RP can be beneficial.

It has been determined that NADC, which is generally well tolerated by patients, has potential positive effects on LNI and prolongs BRFS. Extended follow-up randomized controlled trials with broad sampling on this topic will be more helpful in revealing the impact of NADC before RP in high-risk PC cases.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–49.
2. D'Amico A V., Whittington R, Bruce Malkowicz S, Schultz D, Blank K, Broderick GA, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA. 1998;280(11):969–74.
3. Mottet N, van den Bergh RCN, Briers E, Van den Broeck T, Cumberbatch MG, De Santis M, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer—2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol. 2021;79(2):243–62.
4. De Bono JS, Oudard S, Ozguroglu M, Hansen S, MacHiels JP, Kocak I, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. The Lancet. 2010;376(9747):1147–54.
5. Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN, et al. Docetaxel plus Prednisone or Mitoxantrone plus Prednisone for Advanced Prostate Cancer. N Engl J Med. 2004;351(15):1502–12.
6. Dreicer R, Magi-Galluzzi C, Zhou M, Rothaermel J, Reuther A, Ulchaker J, et al. Phase II trial of neoadjuvant docetaxel before radical prostatectomy for locally advanced prostate cancer. Urology. 2004;63(6):1138–42.
7. Febbo PG, Richie JP, George DJ, Loda M, Manola J, Shankar S, et al. Neoadjuvant Docetaxel before Radical Prostatectomy in Patients with High-Risk Localized Prostate Cancer. Clinical Cancer Research [Internet]. 2005 Jul 15 [cited 2023 Oct 18];11(14):5233–40. Available from: https://dx.doi.org/10.1158/1078-0432.CCR-05-0299
8. Cha EK, Eastham JA. Chemotherapy and novel therapeutics before radical prostatectomy for high-risk clinically localized prostate cancer. Urologic Oncology: Seminars and Original Investigations. 2015;33(5):217–25.
9. Basch E, Reeve BB, Mitchell SA, Clauser SB, Minasian LM, Dueck AC, et al. Development of the National Cancer Institute's Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). JNCI. Journal of the National Cancer Institute. 2014;106(9):244.
10. Sanda MG, Cadeddu JA, Kirkby E, Chen RC, Crispino T, Fontanarosa J, et al. Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline. Part I. Risk Stratification, Shared Decision Making, and Care Options. J Urol. 2018;199(3):683–90.
11. Zhao B, Yerram NK, Gao T, Dreicer R, Klein EA. Long-term survival of patients with locally advanced prostate cancer managed with neoadjuvant docetaxel and radical prostatectomy. Urologic Oncology: Seminars and Original Investigations. 2015;33(4):164. e19–164. e23.
12. Nosov A, Reva S, Petrov S, Mamijev E, Novikov R, Veliev E, et al. Neoadjuvant Chemotherapy Using Reduced-Dose Docetaxel Followed by Radical Prostatectomy for Patients With Intermediate and High-Risk Prostate Cancer: A Single-Center Study. Prostate. 2016;76(15):1345–52.
13. Klein EA, Dreicer R. Initial Experience with Single-Agent Docetaxel as Neoadjuvant Therapy in Men with Locally Advanced Prostate Cancer. Rev Urol 2006/09/21. 2003;5(Suppl 3):S22.
14. Thuret R, Massard C, Gross-Goupil M, Escudier B, Di Palma M, Bossi A, et al. The postchemotherapy PSA surge syndrome. Annals of Oncology. 2008;19(7):1308–11.
15. Harisinghani MG, Barentsz J, Hahn PF, Deserno WM, Tabatabaei S, van de Kaa CH, et al. Noninvasive Detection of Clinically Occult Lymph-Node Metastases in Prostate Cancer. N Engl J Med. 2003;348(25):2491–9.
16. Hövels AM, Heesakkers RAM, Adang EM, Jager GJ, Strum S, Hoogeveen YL, et al. The diagnostic accuracy of CT and MRI in the staging of pelvic lymph nodes in patients with prostate cancer: a meta-analysis. Clin Radiol. 2008;63(4):387–95.
17. Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol. 2017;71(4):618–29.
18. Mohler J, Bahnson RR, Boston B, Busby JE, D'Amico A, Eastham JA, et al. NCCN clinical practice guidelines in oncology: prostate cancer. J Natl Compr Canc Netw. 2010;8(2):162–200.
19. Graham J, Baker M, Macbeth F, Titshall V. Diagnosis and treatment of prostate cancer: summary of NICE guidance. BMJ. 2008;336(7644):610–2.
20. Horwich A, Parker C, Bangma C, Kataja V. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2010;21(SUPPL. 5):v129–33.
21. Cooperberg MR, Lubeck DP, Mehta SS, Carroll PR, Kantoff PW, Smith MR, et al. Time Trends in Clinical Risk Stratification for Prostate Cancer: Implications for Outcomes (Data From CaPSURE). J Urol. 2003;170(6 II).