Original Research Article

Benefits ofDocetaxelfor Metastatic Castration-Resistant Prostate Cancer Sudanese Patients and the Effective Number of Cycle and Dose (2013–2017)

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Abstract:

Background: Prostate cancer remains the most common cancer in men worldwide and in Sudanese people. The initialtreatment of choice for prostate cancer is androgen deprivation. If resistant to treatment, this leads to astate termed metastatic castration-resistant prostate cancer (mCRPC) which leads to the use of docetaxel(Taxotere) which has been a mainstay of therapy for patients with mCRPC.The aim of this study was to determine the benefits of docetaxel in patients with metastatic castrated resistant prostate cancer after initial good response to first line hormonal therapy and determine the effective number of cycles and doses of doectaxel

Study design; retrospective study (duration, 2013–2017).

Area; The Radiation and Isotopes Centre of Khartoum (RICK).Studypopulation; mCRPC in RICK.Data collected by reviewing medical of records of patients confirmed (mCRPC).

To determine the optimal number of cycles of docetaxel for mCRPC, we retrospectively collected data from60 patients receiving varying numbers of docetaxel plus prednisone and analyzed the clinical findings.

Outcomes: Including: performance status, prostate-specific antigen (PSA) response and pain. According to this study wefound that docetaxel has an effective role in the treatment of mCRPC patients with an optimal number of6–8 cycles every 3 weeks and with a dose of 75 mg

Conclusion: the benefits for using Docetaxelfor mCRPC~~,~~ Sudanese patients~~,~~ decline~~d~~ of PSA serum level, ~~improve~~improvement of performance status and pain ~~improvement~~ decrease (?),effective optimal number of cycles 6 to 8 every 3 weeks and dose of 75 mg

Key words:**Benefits, Docetaxel, mCRPC, Sudanese, Men**

1. INTRODUCTION

Prostate cancer is still the most common cancer among men with global health concern, almost 1.6 million cases were diagnosed prostate cancer worldwide in 2015 [1]. In Sudan, it is considered the second among cancers with a high mortality rate [2].Approximately in twenty to thirty percent of patients with localized prostate cancer who were cured with surgery or radiation therapy, disease recurrent may occur [3].Many patients present with potentially curable localized prostate cancer, but unfortunately, a large number of deaths result from development of metastatic disease [4].Prostate-specific antigen PSA is used for mentoring prostate cancer, thus serum PSA elevated~~serum of PSA~~levels indicate~~s~~ disease progression in addition to Gleason's score of patients with metastatic prostate cancer, which is used to predict survival rate [5]. Androgen deprivation, known to be the initial treatment of choice for prostate cancer ~~is~~ if resistant, progress to castration-resistant prostate cancer may result in most patients (CRPC) [6].Combined docetaxel (a taxane drug that induces polymerization of microtubules and phosphorylation of the Bcl-2 protein) and prednisone is currently considered the standard of care for men with CRPC and detectable metastatic disease, based largely on the simultaneous publication of two large randomized controlled trials comparing this combination with the previously established standard of mitoxantrone and prednisone [7,8]. For patients with metastatic castration-resistant prostate cancer (mCRPC), docetaxel was the first cytotoxic agent to be approve~~da survival advantage; such as~~for pain relieve and improved quality of life [9].Docetaxel approved dose is 75 mg/m2, rote of administration intravenously as a one-hour infusion every 21 days on day 1 with 5 mg oral prednisone twice daily for 10 cycles.[10].~~Study done~~A study reported that~~among~~ mCRPCIndian Patients with aged ≥80 year and elevated Prostate-specific antigen ~~was elevated~~ who ~~, they~~ received docetaxel ~~, as a result~~showed a decline ofserum PSA ~~decline was seen~~ in 34.3%of patients [9] to determined optimal number of cycle ,study carried in Taiwan concluded that; at least four cycle and less than ten cycle should be administrated and administration of more than ten cycle had no effect on survival and leaded to unfavorable effects [11].In another research, ~~(~~55.6%~~)~~of Japanese mCRPCpatients, showeddecreasedPSA level after treatment with docetaxel as weekly (70-75 mg/m2) regimen [12]. The over survival became longer in patients treated with ≥ 9 cycles of docetaxel among Denmark patients [13] Korean castration-resistant prostate cancer patients who received at least 6 cycles of docetaxel (75 mg/m2) , result showed that (48.9%)of patients reduction in PSA , good performance status and first-line setting predicts longer survival[14].

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USA patients who were received docetaxel at a dose of 36 mg/m2 intravenously over 15-30 minutes weekly for six consecutive weeks ,the cycle was repeated every eight weeks showed, Palliative and PSA response rate was (48%), (46%)respectively [15].

1.2. Objective: To determine the benefits of docetaxel in patients with metastatic castrated resistant prostate cancer after initial good response to first line hormonal therapy and determine the effective number of cycles and doses of docetaxel.

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2. METHODS

2.1 Study Design

This is a retrospective hospital-Based study conducted in Khartoum Center for Radiation

2.2 Data collection methods &tools:

Data were collected by reviewing medical records of a total number 60 of male patients menclinically-confirmed Metastatic Castration-Resistant Prostate Cancer (mCRPC) in the period from 2013 to 2017. All patients were atstage IVwith hadtestosterone level less than 50ng/ml and bone scan showinged 100% bone metastases.Information collected include: Age of the patients, residence and occupation of the patient, the Gleason scores, Testosterone and PSAlevel Performance status before and aftertreatment, type of treatment and, Dose of Docetaxel and number of cycle and pain response.

2.3 Study Area:

Khartoum center for Radiation & Isotopes (RICK), the center located in central of Khartoum city, it is the first specialize center for cancer treatment in Sudan, providing chemotherapy and radiotherapy services, and the center receives referrals from all over the country.

2.4 Study Population

Medical records of Sudanese menclinically-confirmed Metastatic Castration-Resistant Prostate Cancer (mCRPC) after initial good response to first line hormonal therapy in KhartoumCenter for Radiation & Isotopes RICK(213-2017)

2.4.1Inclusion criteria: any prostatic cancer patient become castrated resistant and now on docetaxel therapy.

2.4.2Exclusion criteria:prostatic cancer patient not castrated resistant and not on docetaxel therapy

2.5 **Sample Size**

All medical records of patients diagnosed as Metastatic castration-resistant prostate cancer (mCRPC), (60 patients)

2.6Ethical Issue

Ethical approval was obtained from Institutional review board of Omdurman Islamic university-Faculty of Medicine. Data were collected after taking the necessary agreement from Khartoum State Ministry of Healthas well as fromKhartoum center for Radiation & Isotopes (RICK).

3. RESULTS:

To determine the optimal number of cycles of docetaxel for mCRPC, we retrospectively collected data from60 patients receiving varying numbers of docetaxel plus Prednisone and analyzed the clinical outcomes

Regarding age groups, higher percentage(60%) was among Metastatic Castration-Resistant Prostate Cancer the age group (61-70) ~~years was (60%)~~, followed by age group (17-80) :(Fig1)

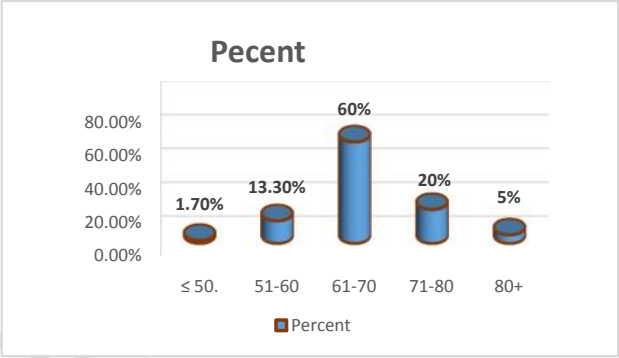

Fig.1: shows the frequency distribution of the age group involved with (mCRPC)in (RICK) Sudan, (2013-2017), Sudan, (n=60).

For occupation of patients higher percentage was found among farmer (20%) followed by workers (16.7%) (Fig2).

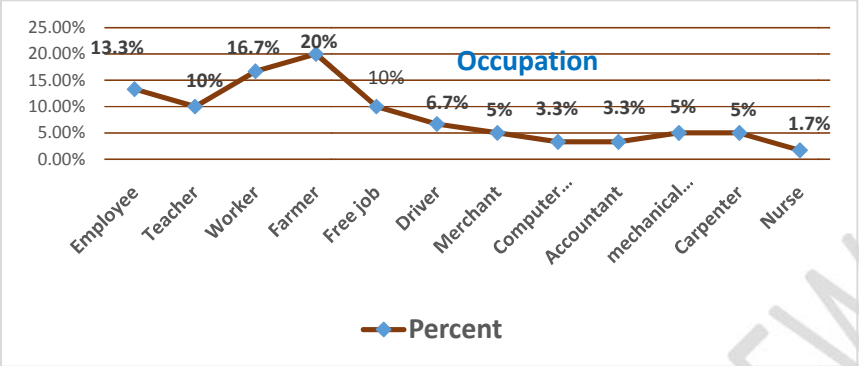

Fig. 2: Distribution of (mCRPC) patients according to occupation , in (RICK), (2013-2017),Sudan ,(n=60)

Type of treatment that patients ~~was~~ received~~,~~ higher percentage was registered by hormonal :(98.3%)followed by surgical :(56.7%)and radiotherapy: (46.7) (table 1)

Table (1): Distribution of Metastatic castration-resistant prostate cancer (mCRPC) patients according to type of treatment received for, Khartoum Center for Radiation & Isotopes (RICK), (2013-2017), Sudan, (n=60).

Type of treatment	Yes		No	
	Frequency	Percent	Frequency	Percent
Surgery	34	56.7%	26	43.3%
Hormonal therapy	59	98.3%	1	1.7%
radiotherapy	28	46.7%	32	53.3%

All patients had testosterone levels less than 50ng/ml (table2)Gleason score <8 (53.3%) and <8 were (46.7%) (table3)

Table :(2) Distributionof (mCRPC) patients according to testosterone level before startDocetaxel treatment, in (RICK), (2013-2017), Sudan, (n=60)

Testosterone level	Frequency	Percent
<50	60	100%
>50	00	00
Total	60	100.0

Table: (3) Distribution of (mCRPC) patients according Gleason score in (RICK)

Gleason score	Frequency	Percent
<8	28	53.3%
>8	32	46.7
Total	60	100.0

Performance status before treatment 1,2 and3 was 1.7%,46.6% and51.7% respectively while (table4),after treatment was 1,2,and 3 was18.3%,65%,16.7% respectively (fig.3).

Table 4:Distribution of (mCRPC) patients according performance status before startingDocetaxetreatment.

WHO performance status	Frequency	Percent
1	1	1.7
2	28	46.6
3	31	51.7
Total	60	100.0

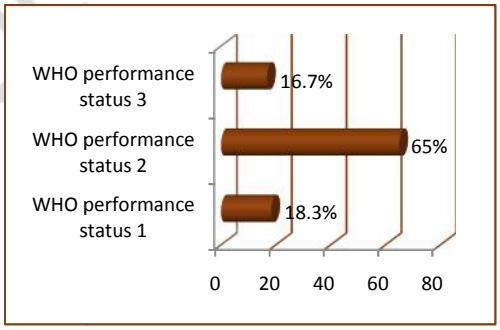

Fig. 3:Distribution (mCRPC) patients according performance status after Docetaxel treatment

It was showed that:60% of patientsbefore treatmenthad PSA level >100 and40% of them had PSA level<100,while after treatment 53.3 %had PSA level > 100 and 46.7% their PSA level was<100(Fig. 4).

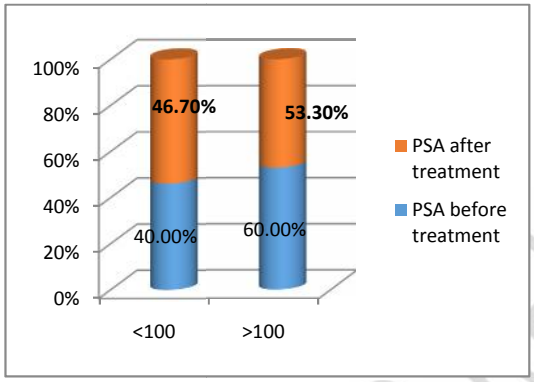

Fig 4: Distribution of (mCRPC) patients according to PSA after Docetaxeltreatment, in (RICK), (2013-2017), Sudan, (n=60)

70% of patients started treatment with Docetaxel in 2016 and 2017(fig.5).

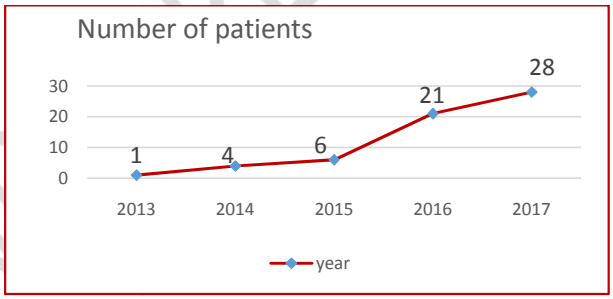

Fig .5: Distribution of (mCRPC)patients accordingDocetaxelreceived per year, (RICK), (2013-2017), Sudan, (n=60)

High percentage was showed for PSA start to increase in the first year and second year :(48.4%) and (23.3%) respectively. (table5)

Table .5:Distribution (mCRPC) patients according to PSA start to increase, , in (RICK), (2013-2017)), Sudan, (n=60)

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		frequency	percent
	0-1	9	15
	1yrs	29	48.4
	2yrs	14	23.3
	3yrs	5	8.3
	4yrs	0	0
	5yrs	2	3.3
	6yrs	1	1.7
	Total	60	100.0

For the dose of Docetaxel (35%) received low dose 75 mg,(31.7%) received high dose 100mg, the rest received both high and low dose (table 6).

Table: 6 Distribution of (mCRPC) patients according Dose of Docetaxel, in (RICK), (2013-2017), Sudan, (n=60)

Dose of Docetaxel	Frequency	Percent
Low dose 75 mg	21	35.0
High dose 100 mg	19	31.7
Both High and low dose	20	33.3
Total	60	100.0
Prednisone used	17	28.3

Regarding umber of Docetaxel cycles: 6cycles, & 8 cycles (16.7%) followed by 10cycles (15%):(table7).

Table (7): Distribution (mCRPC) patients according number of Docetaxel cycle in (RICK), (2013-2017), Sudan, (n=60).

Number of Docetaxel cycle	Frequency	Percent
1Cycle	4	6.7
2Cycle	7	11.7
3Cycle	4	6.7
4Cycle	5	8.3
5Cycle	3	5.0
6Cycle	10	16.7
7Cycle	2	3.3
8Cycle	10	16.7
9Cycle	1	1.7
10Cycle	9	15.0
<10Cycle	5	8.39
Total	60	100.0

73.3% of patients showed pain improvementwhile 26.7% was not (fig. 6).

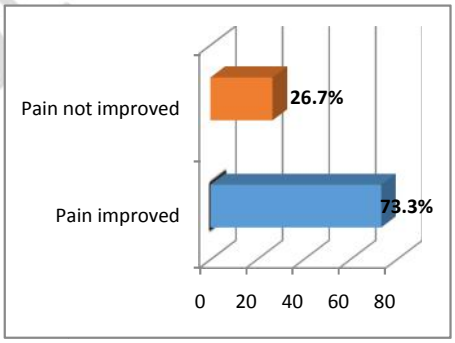

Fig. 6: Distributionof (mCRPC) patients according pain improvement after Docetaxel, in (RICK), (2013-2017), Sudan (n=60)

4. DISCUTION

In this retrospective study (2013-2017) of 60Sudanese MCRPC patients, done at Radiation and isotope center of Khartoum,aimed to study the optimal number of cycles and effective dose of docetacexel therapy in(mCRPC).According to our data collection and analysis we found out the prevalence ofMCRPC is higher among the age group of60-70years old(about60%)was Mainly higher in Khartoum state(31.7%).that may be attributed to lack of awareness about regular follow up.).After one year most of patient's PSA restart to increase on about 48.4% of despite of castration which indicate castration resistant,60%of them thePSA>100.

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After starting different modality of treatment including hormonal, surgical and radiotherapy treatment, the hormonal therapy accounted the higher percent by 98.3%, those patient achieve castration and the level of testosterone become less than 50ng\dl. (Achieve the castration level).

With regard PSA level, 46.7.3% of patients had serum of PSA< 100 after receiving Docetaxel treatmentcompare to the level before treatment the level was obviously declined, A similar conclusion was suggested by a study done in India [9],Japan [12],Korea [14]and USA [15].Docetaxel treatment taken by dose of 75mg represent as frequent dose in 35%,accompanied~~y~~ with Prednisone.

On follow up the pain get improved by 73.3% response different finding was reported by another study, which revealed only 48% Palliative response rate[15].It was suggested that,Prednisone had arole in pain improvement. According to WHO, the performance status get better from 3 to 2 also good performance status , A similar pattern of result was obtained in Korean patients after receiving dose 75 mg Docetaxel [14].It was found that optimal number of Docetaxel cycles are between 6-8 cycles every 3 weeks in dose of 75mg, our finding wasslightly comparable value to the finding among Taiwan patients[11]and to some extentsimilar to what was reported by Denmark patients treated with ≥ 9 cycles of docetaxel [13]

5. CONCLUSION AND RECOMMENDATION:

According to this study we found that taxotere has effective role in the treatment of mCRPC patients with optimal number of cycles 6 to 8 every3weeks and dose of 75mg.

Further study to address survival improvement after Docetaxel treatment is highly recommended.

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