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

**Abstract:**

**Background:** Prostate cancer remains the most common cancer in men worldwide and in Sudanese people. The initial treatment of choice for prostate cancer is androgen deprivation. If resistant to treatment, this leads to a state 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 docetaxel

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

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

To determine the optimal number of cycles of docetaxel for mCRPC, we retrospectively collected data from 60 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 we found that docetaxel has an effective role in the treatment of mCRPC patients with an optimal number of 6–8 cycles every 3 weeks and with a dose of 75 mg

**Conclusion:** the benefits for using Docetaxel for mCRPC, Sudanese patients, declined of PSA serum level, improve performance status and pain improvement 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**

33 Prostate cancer still the most common cancer among men with global health concern, almost 1.6  
34 million cases were diagnosed prostate cancer worldwide in 2015 [1]. In Sudan, it is considered  
35 the second among cancers with a high mortality rate [2]. Approximately twenty to thirty percent  
36 of patients with localized prostate cancer who cured with surgery or radiation therapy, disease  
37 recurrent may occur [3]. Many patients present with potentially curable localized prostate  
38 cancer, unfortunately, large number of deaths result from development of metastatic disease  
39 [4]. Prostate-specific antigen PSA is used for mentoring prostate cancer, elevates serum of PSA  
40 indicates disease progression in addition to Gleason's score patient with metastatic prostate  
41 cancer used to predict survival rate [5]. Androgen deprivation known to be the initial treatment  
42 of choice for prostate cancer is if resistant, progress to castration-resistant prostate cancer may  
43 result in most patients (CRPC) [6]. Combined docetaxel (a taxane drug that induces  
44 polymerization of microtubules and phosphorylation of the Bcl-2 protein) and prednisone is  
45 currently considered the standard of care for men with CRPC and detectable metastatic disease,  
46 based largely on the simultaneous publication of two large randomized controlled trials  
47 comparing this combination with the previously established standard of mitoxantrone and  
48 prednisone [7,8]. For patients with metastatic castration-resistant prostate cancer (mCRPC),  
49 docetaxel was first cytotoxic agent to approve a survival advantage; such as pain relieve and  
50 improved quality of life [9]. Docetaxel approved dose is 75 mg/m<sup>2</sup>, rote of administration  
51 intravenously as a one-hour infusion every 21 days on day 1 with 5 mg oral prednisone twice  
52 daily for 10 cycles.[10]. Study done among mCRPC Indian Patients with aged ≥80 year and  
53 Prostate-specific antigen was elevated, they received docetaxel , as a result serum PSA decline  
54 was seen in 34.3%of patients [9] to determined optimal number of cycle ,study carried in Taiwan  
55 concluded that; at least four cycle and less than ten cycle should be administrated and  
56 administration of more than ten cycle had no effect on survival and leded to unfavorable effects  
57 [11]. (55.6%) of Japanese mCRPC patients, showed decreased PSA level after treatment with  
58 docetaxel as weekly (70-75 mg/m<sup>2</sup>) regimen [12]. The over survival became longer in patients  
59 treated with ≥ 9 cycles of docetaxel among Denmark patients [13] Korean castration-resistant  
60 prostate cancer patients who received at least 6 cycles of docetaxel (75 mg/m<sup>2</sup>) , result showed  
61 that (48.9%)of patients reduction in PSA , good performance status and first-line setting predicts  
62 longer survival[14].

63 USA patients who were received docetaxel at a dose of 36 mg/m<sup>2</sup> intravenously over 15-30  
64 minutes weekly for six consecutive weeks ,the cycle was repeated every eight weeks showed,  
65 Palliative and PSA response rate was (48%), (46% )respectively [15].

66 **1.2. Objective:** To determine the benefits of docetaxel in patients with metastatic castrated  
67 resistant prostate cancer after initial good response to first line hormonal therapy and determine  
68 the effective number of cycles and doses of doectaxel.

## 69 **2. METHODS**

### 70 **2.1 Study Design**

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

### 72 **2.2 Data collection methods &tools:**

73 Data were collected by reviewing medical records of a total number 60 of patients men  
74 clinically-confirmed Metastatic Castration-Resistant Prostate Cancer (mCRPC) in the period  
75 from 2013 to 2017. All patients were stage: IV had testosterone level less than 50ng/ml and bone  
76 scan showed 100% bone metastases. Information collected include: Age of the patient, residence  
77 and occupation of the patient, the Gleason scores, Testosterone and PSA level Performance  
78 status before and after treatment, type of treatment and, Dose of Docetaxel and number of cycle  
79 and pain response.

### 80 **2.3 Study Area:**

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

### 84 **2.4 Study Population**

85 Medical records of Sudanese men clinically-confirmed Metastatic Castration-Resistant Prostate  
86 Cancer (mCRPC) after initial good response to first line hormonal therapy in Khartoum Center  
87 for Radiation & Isotopes RICK(213-2017)

88 **2.4.1Inclusion criteria:** any prostatic cancer patient become castrated resistant and now on  
89 docetaxel therapy.

90 **2.4.2Exclusion criteria:** prostatic cancer patient not castrated resistant and not on docetaxel  
91 therapy

### 92 **2.5 Sample Size**

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

### 95 **2.6 Ethical Issue**

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

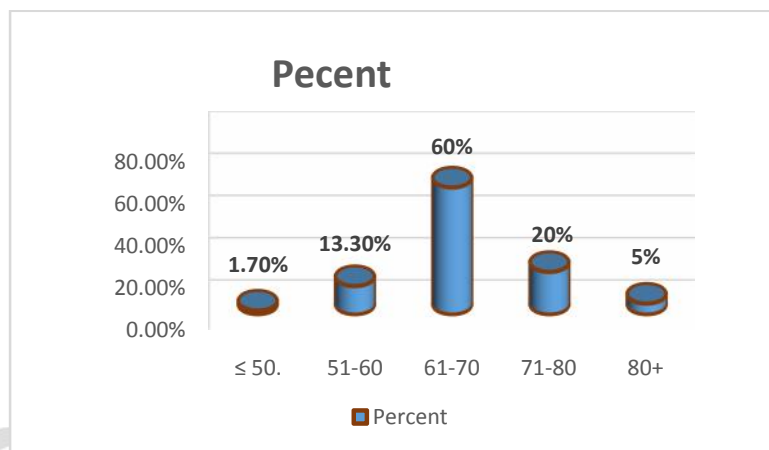
### 100 **3. RESULTS:**

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100 To determine the optimal number of cycles of docetaxel for mCRPC, we retrospectively  
101 collected data from 60 patients receiving varying numbers of docetaxel plus Prednisone and  
102 analyzed the clinical outcomes

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

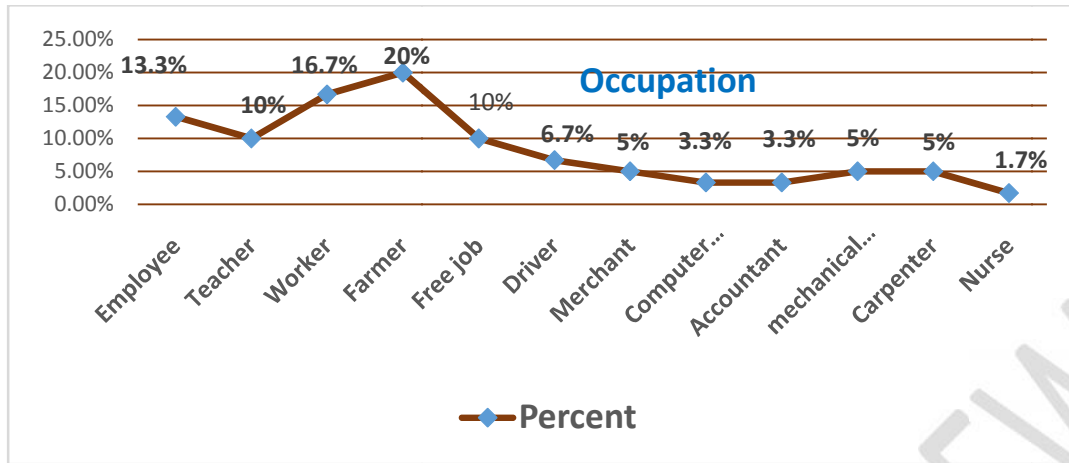
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107 Fig.1: shows the frequency distribution of the age group involved with (mCRPC) in (RICK)  
108 Sudan, (2013-2017), Sudan, (n=60).

109 For occupation of patients high percentage was found among farmer (20%) followed by workers  
110 (16.7%) (Fig2).



111  
112 Fig. 2: Distribution of (mCRPC ) patients according to occupation , in (RICK), (2013-  
113 2017),Sudan ,(n=60)

114 Type of treatment patients was received, higher percentage was registered by hormonal :(  
115 98.3%) followed by surgical :( 56.7%) and radiotherapy: (46.7) (table 1)

116 Table (1): Distribution of Metastatic castration-resistant prostate cancer (mCRPC) patients  
117 according to type of treatment received for, Khartoum Center for Radiation & Isotopes (RICK),  
118 (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%

119  
120 All patients had testosterone level less than 50ng/ml (table2) Gleason score <8 (53.3%) and <8  
121 were (46.7%) (table3)

122 Table :( 2) Distribution of (mCRPC) patients according to testosterone level before start  
123 Docetaxel treatment, in (RICK), (2013-2017), Sudan, (n=60)

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

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130 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%

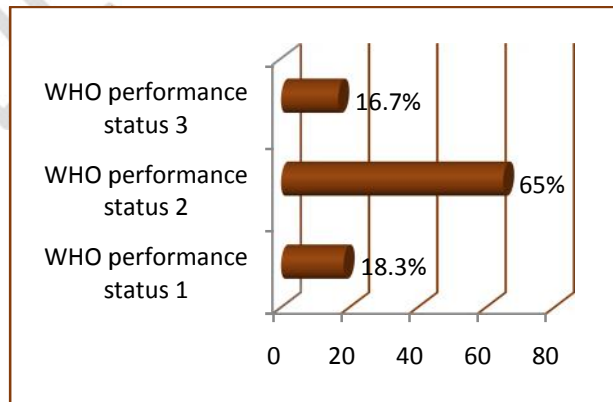
137 Performance status before treatment 1,2 and3 was 1.7%,46.6% and51.7% respectively while  
138 (table4),after treatment was 1,2,and 3 was18.3%,65%,16.7% respectively (fig.3).

139

140 Table 4: Distribution of (mCRPC) patients according performance status before starting  
141 Docetaxe treatment.

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

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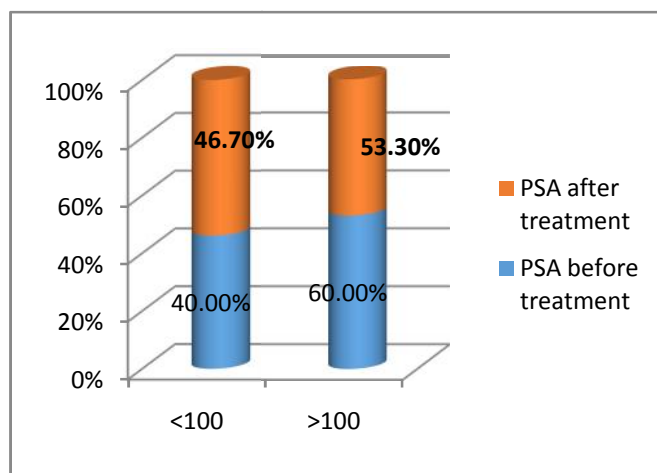


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150 Fig. 3: Distribution (mCRPC ) patients according performance status after Docetaxel treatment

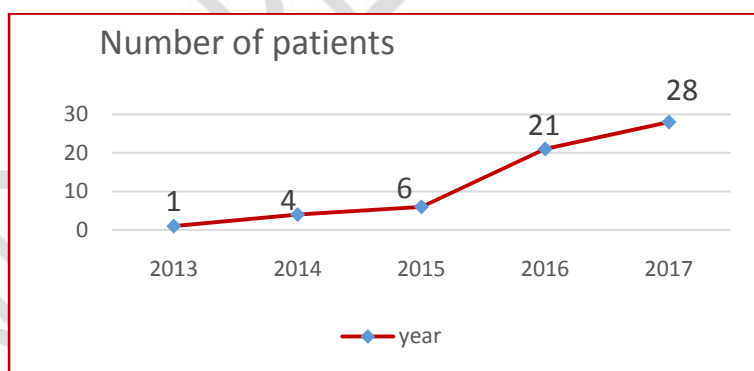
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152 It was shoed that: 60% of patients before treatment had PSA level >100 and 40% of them had  
 153 PSA level <100, while after treatment 53.3 %had PSA level > 100 and 46.7% their PSA level  
 154 was <100 (Fig. 4).



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

165  
 166 70% of patients started treatment with Docetaxel in 2016 and 2017(fig.5).



167  
 168 Fig .5: Distribution of ( mCRPC )patients according Docetaxel received per year, (RICK), (2013-  
 169 2017), Sudan, (n=60)

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

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 173  
 174

175 Table .5: Distribution (mCRPC ) patients according to PSA start to increase, , in (RICK), (2013-  
 176 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

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

190 Table: 6 Distribution of (mCRPC) patients according Dose of Docetaxel, in (RICK), (2013-  
 191 2017), Sudan, (n=60)  
 192

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

199 Regarding umber of Docetaxel cycles: 6cycles, & 8 cycles (16.7%) followed by 10cycles  
 200 (15%):( table7).  
 201  
 202  
 203



204 Table (7): Distribution (mCRPC) patients according number of Docetaxel cycle in (RICK),  
205 (2013-2017), Sudan, (n=60).

206

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

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208 73.3% of patients showed pain improvement while 26.7% was not (fig. 6).

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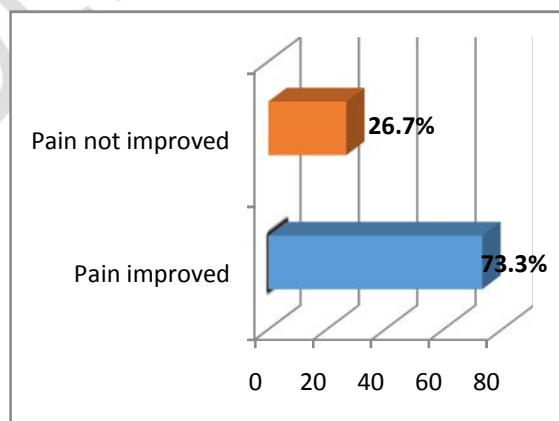
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216 Fig. 6: Distribution of (mCRPC) patients according pain improvement after Docetaxel, in (RICK),  
217 (2013-2017), Sudan (n=60)

218 4. DISCUSSION

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

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

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

233 On follow up the pain get improved by 73.3% response different finding was reported by another  
234 study, which revealed only 48% Palliative response rate[15] .It was suggested that, Prednisone  
235 had a role in pain improvement. According to WHO, the performance status get better from 3 to  
236 2 also good performance status , A similar pattern of result was obtained in Korean patients  
237 after receiving dose 75 mg Docetaxel [14].It was found that optimal number of Docetaxel cycles  
238 are between 6-8 cycles every 3 weeks in dose of 75mg, our finding was slightly comparable  
239 value to the finding among Taiwan patients [11] and to some extent similar to what was  
240 reported by Denmark patients treated with  $\geq 9$  cycles of docetaxel [13]

241 **5. CONCLUSION AND RECOMMENDATION:**

242 According to this study we found that taxotere has effective role in the treatment of mCRPC  
243 patients with optimal number of cycles 6 to 8 every 3weeks and dose of 75mg.

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

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UNDER PEER REVIEW