Original Research Article

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.

This study aimed to determine the optimal number of cycles of docetaxel plus prednisone in patients with metastatic castration-resistant prostate cancer, through the evaluation of a number of parameters, such as performance status, prostate-specific antigen response and pain

Methods: Retrospective study of (60) metastatic castration-resistant prostate cancer (mCRPC) Sudanese patients who received docetaxel plus prednisone (duration, 2013–2017). Area; The Radiation and Isotopes Centre of Khartoum (RICK).Data collected by reviewing medical of records of patients confirmed (mCRPC).

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 of6–8 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, improvement of performance status and pain reduction. 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 to observe prostate cancer, thus serum PSA elevated levels indicate 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), the first cytotoxic agent to be approved 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]. A study reported that mCRPC Indian Patients with aged ≥80 year and elevated Prostate-specific antigen who received docetaxel showed a decline of serum PSA in 34.3% of patients [11]and (54.6%) of Japanese mCRPC patients, also showed decreased PSA level after treatment with docetaxel as weekly (70-75 mg/m2) regimen [12]. Regarding docetaxel optimal and impact of number of cycles for metastatic castration -resistant prostate cancer, study carried in Taiwan to determine the optimal number of cycles ,concluded that; at least four cycles and less than ten cycles should be administrated and administration of more than ten cycles had no effect on survival and leaded to unfavorable effects [13]. In another research, improve survival rate among Denmark patients treated with ≥ 9 cycles of docetaxel-based chemotherapy (75 mg/m,^{2} every 3 weeks) [14].It was observed that :Docetaxel-based systemic chemotherapy effective treatment modality in elderly patients with good performance status among Korean

castration-resistant prostate cancer patients who received at least 6 cycles of docetaxel (75 mg/m2) [15].

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 [16]. According to landmark studies; TAX-327 and SWOG-9916, Docetaxel based chemotherapy could prolong overall survival and improve response rate of pain, serum prostate specific antigen (PSA) [17, 18].

1.2. Objective: To determine the optimal number of cycles of docetaxel plus prednisone in patients with metastatic castration-resistant prostate cancer, through the evaluation of a number of parameters, such as performance status, prostate-specific antigen response and pain.

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:

An information sheet has been used for data collection, data were collected by reviewing medical records of a total number 60 of male patients clinically-confirmed Metastatic Castration-Resistant Prostate Cancer (mCRPC) in the period from 2013 to 2017. All patients were at stage: IV with testosterone level less than 50ng/ml and bone scan showing 100% bone metastases. Information collected include: Age of patients, residence and occupation of the patient, the Gleason scores, Testosterone and PSA level Performance status before and after treatment, 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 men clinically-confirmed Metastatic Castration-Resistant Prostate Cancer (mCRPC) after initial good response to first line hormonal therapy in Khartoum Center 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)

2.6 Ethical 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 Health as well as from Khartoum 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 Cancer the age group (61-70) years was (60%), followed by age group (17-80) :(Fig1)

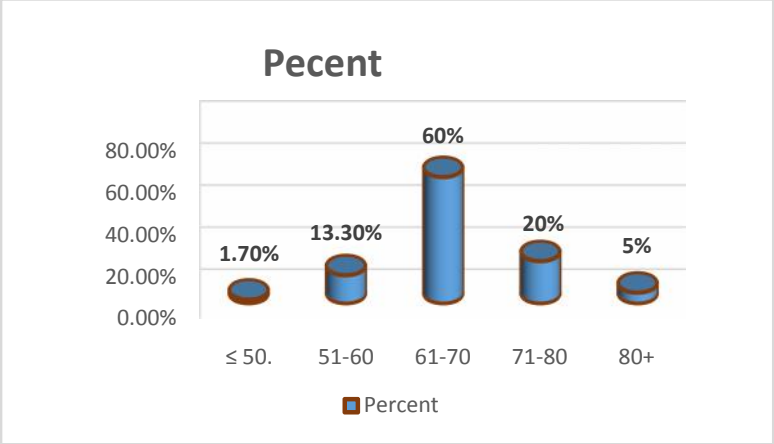

Fig.1: shows the frequency distribution of the age group involved with (mCRPC) in (RICK) Sudan, (2013-2017), Sudan, (n=60).

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

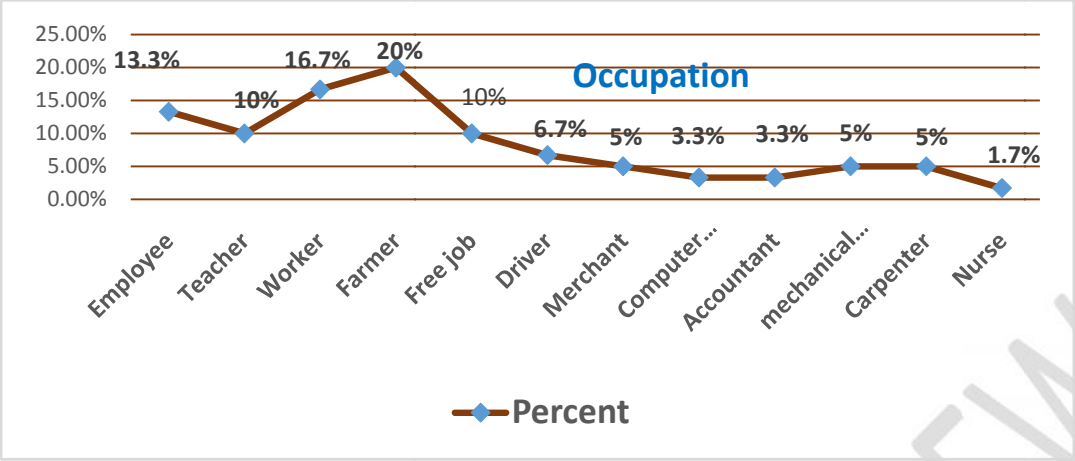

Fig. 2: Distribution of (mCRPC) patients according to occupation , in (RICK), (2013-2017),Sudan ,(n=60)

Type of treatment that patients 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 level less than 50ng/ml (table2) Gleason score <8 (53.3%) and <8 were (46.7%) (table3)

Table :(2) Distribution of (mCRPC) patients according to testosterone level before start Docetaxel 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 starting Docetaxe treatment.

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

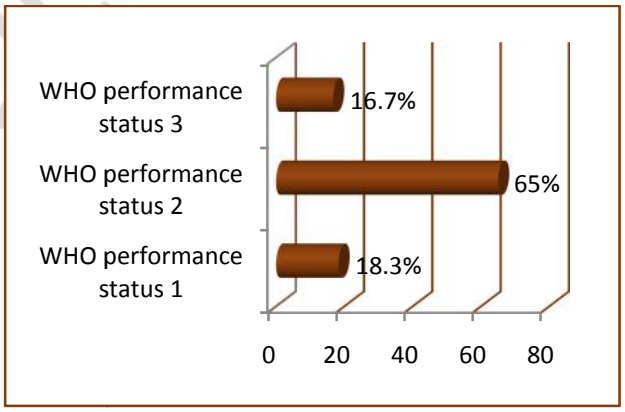

Fig. 3: Distribution (mCRPC) patients according performance status after Docetaxel treatment

It was 6showed: 60% of patients before treatment had PSA level >100 and 40% 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).

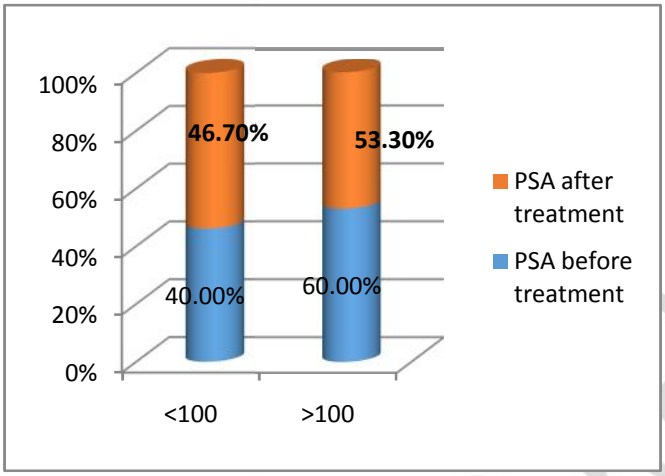

Fig 4: Distribution of (mCRPC) patients according to PSA after Docetaxel treatment, in (RICK), (2013-2017), Sudan, (n=60)

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

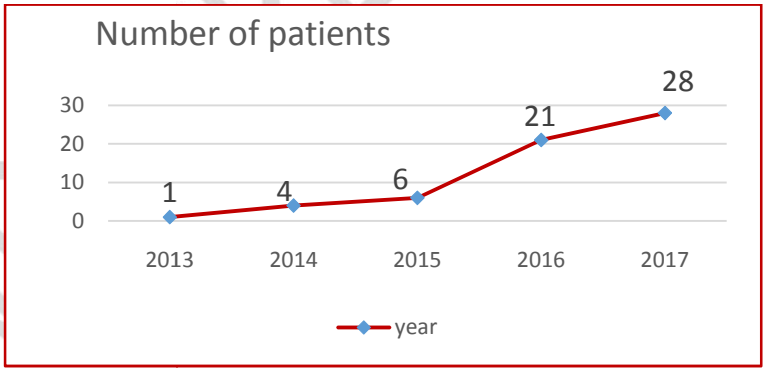

Fig .5: Distribution of (mCRPC)patients according Docetaxel received per year, (RICK), (2013-2017), Sudan, (n=60)

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: 5 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%):(table 6).

Table (6): 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 improvement while 26.7% was not (fig. 6).

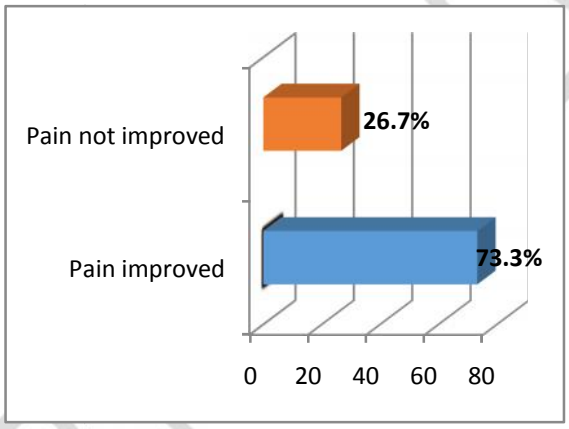

Fig. 6: Distribution of (mCRPC) patients according pain improvement after Docetaxel, in (RICK), (2013-2017), Sudan (n=60)

4. DISCUTION

In this retrospective study (2013-2017) of 60 Sudanese 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), the majority of patients were diagnosed (mCRPC), between the age of 61 and 70, which indicates that: The combination of docetaxel with prednisone, treatment was in general well-tolerated in elderly patients, It correlates with the findings in the literature: Docetaxel-based systemic chemotherapy effective treatment modality in elderly patients with good performance status among Korean castration-resistant prostate cancer patients [15]most of patients were from Khartoum state(31.7%).31.7% of mCRPC patients

from Khartoum State, in comparison to other states, this is the heavily populated, and there is availability of facilities for investigations ,so the higher percentage is may due to lack of awareness about regular follow up.

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 treatment compare to the level before treatment the level was obviously declined, a similar conclusion was suggested by a study done in India [11], Japan [12] and USA [16]. Also TAX 327 (docetaxel arm 75mg/m2 given every third week = B-arm) they found response rates of PSA reduction ≥ 50% at 45% of the patients [17] PSA declines of at least 50 % in SWOG-9916 study This implies that, high rate of PSA response we found in our study.

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 [15]. We found that optimal number of Docetaxel cycles are between 6-8 cycles every 3 weeks in dose of 75mg optimal number of taxotere cycles arebetween6-8 cycles every3 weeks in dose of 75mg.it is agreed with study conducted in Taiwan, concluded that there was no survival benefit in men with mCRP who received >10 cycles of docetaxel [13] and to some extent similar to what was reported by Denmark patients treated with ≥ 9 cycles of docetaxel lead improvement of survival rate [14] This is supported by The original design of the TAX-327 and SWOG 99-16 studies ,which showed that, the optimal number of taxotere cycles are10 To 12 with dose of 75mg/m2[17,18].

Our study showed reduction in pain for mCRPC patients when treated with Docetaxel every 3 weeks in dose of 75mg. Pain reduction after treatment with docetaxel was demonstrated in USA [16], Tax 327 [17] and SWOG-9916 study [18]

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 every 3weeks and dose of 75mg.

Further studies to clarify the relationship between PSA response and overall survival in patients with mCRPC patients treated with a combination of docetaxel and prednisone.

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