Addition of carboplatin to chemotherapy regimens for metastatic castrate resistant prostate cancer in post-2nd generation hormone therapy setting: does it improve survival?

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Introduction and Background

- The clinical course in metastatic castrate resistant prostate cancer (mCRPC) can be complicated when patients have disease progression after failing prior treatment with 2nd generation hormone therapy (2nd HT), such as enzalutamide or abiraterone.
- We sought to investigate the survival outcomes of three common chemotherapy regimens in this setting.

Objectives

- In a retrospective study, we compared treatment response and overall survival of docetaxel-alone, combination of docetaxel and carboplatin, and cabazitaxel-alone.

Materials and Methods

- Identified 150 patients with mCRPC with disease progression on 2nd HT (i.e., enzalutamide or abiraterone) between 2014-2018.
- Of these 150 patients, 92 patients were chemo naïve while 58 patients had previously received docetaxel chemotherapy before started on 2nd HT.
- After failing 2ndHT, 90 patients were assigned for docetaxel-alone (group A), 33 patients received carboplatin plus docetaxel (group B) while 27 patients received cabazitaxel-alone (Group C).
- We reviewed patient's clinicopathological variables shown in (**Table 1**).
- Pre- chemotherapy number and site of metastases were based on reviewing radiology reports of the patient's conventional imaging (CT, MRI and Bone scan) and /or C-11 choline PET scan.
- As regards to pre- chemotherapy number of metastases, patients were categorized into two groups; high volume disease (≥ 5 metastases) or low volume disease (<5 metastases) groups.
- Favorable response was defined by ≥50% reduction in PSA from baseline level after complete course of chemotherapy.
- Survival outcomes were assessed for 30-month overall survival.

Results

- Patient's clinicopathological variables are shown in **(Table 1)**.
- Patients in group (B; combination therapy of docetaxel and carboplatin) were 2.6 times as likely to have a favorable response compared to patients in group (A; docetaxel) (OR= 2.625, 95%CI: 1.15 - 5.99) and almost 3 times compared to patients in group (C; cabazitaxel) (OR=2.975, 95%CI: 1.04 – 8.54) (p-value=0.0442).
- 30-month overall survival was 70.7%, 38.9% and 30.3% for group (B; docetaxel and carboplain), (A; docetaxel alone) and (C; cabazitaxel alone) respectively **(p-value=0.008) (Figure 1)**.
- In univariable and multivariable analyses, chemotherpay regimen was the most significant factor impacting patient's 30-month overall survival **(Table 2)**.
- We report a Hazard Ratio of 3.1 (95% CI 1.31-7.35; p=0.0037) between patients in group (A) versus those in group (B) and a Hazard Ratio of 4.18 (95% CI 1.58-11.06; p=0.0037) between patients in group (C) versus those who are in group (B).

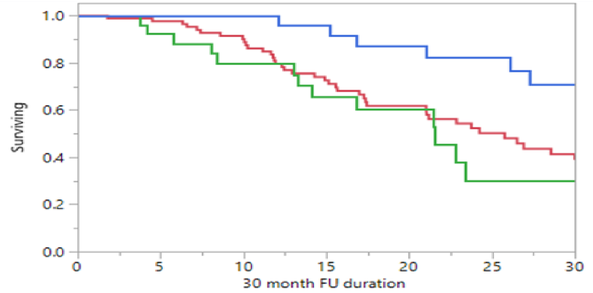
Table-1: patient's clinicopathological variables and baseline characteristics

	Group A	Group B	Group C	total	P-value
Age at chemo, mean (±SD)	71.2 (8.28)	69.5 (8.38)	67.2 (8.36)	70.1 (8.4)	0.0816
Gleason score, mean (±SD)	7.9 (1.1)	8.4 (0.88)	8.1 (1.06)	8.1 (1.06)	0.1369
Pre-treatment PSA, mean (±SD)	63.8 (138.18)	47.6 (72.48)	53.7 (88.15)	58.5 (118.15)	0.7403
History of prior chemo, N (%)	21 (23.3)	13 (39.4)	24 (88.9)	58 (38.7)	<.0001*
Number of metastases ≥5, N (%)	73 (81.1)	28 (84.9)	27 (100)	128 (85.3)	0.0293
Lymph node metastases, N (%)	48 (53.9)	16 (48.5)	16 (59.3)	80 (53.7)	0.7052
Visceral metastases, N (%)	19 (21.4)	5 (15.2)	2 (7.4)	26 (17.5)	0.2287
Bone metastases, N (%)	70 (79.6)	24 (72.7)	23 (85.2)	117 (79.1)	0.4908

Table-2: Univariable and multivariable analyses for factoring influencing patient's survival

	Univariable				Multivariable N=139		
	Risk Ratio	95% CI	p	N	Risk Ratio	95% CI	P
Type of chemo	"A" vs "B": 3.1 "C" vs "B": 4.18	1.31-7.35 1.58-11.06	0.0037*	150	"A" vs "B": 3.14 "C" vs "B": 5.88	1.27-7.78 2.08-16.65	0.0009*
Gleason score	1.19	0.93-1.56	0.1697	142	1.46	1.10-1.95	0.0083*
Age at starting chemo	1.03	1.00-1.07	0.0677	150	1.04	1.00-1.08	0.0412*
Previous chemotherapy	0.96	0.56-1.65	0.8838	150	0.68	0.33-1.41	0.2854
Pre-treatment PSA	1.002	1.000-1.003	0.0387*	148	1.002	1.000-1.004	0.0577
Number of metastases	3.56	1.29-9.88	0.0034*	150	2.18	0.71-6.70	0.1436
Lymph node metastases	1.31	0.78-2.21	0.3081	149	1.47	0.83-2.60	0.1919
Bone metastases	1.90	0.86-4.20	0.0843	148	1.50	0.58-3.84	0.3897
Visceral metastases	2.33	1.19-4.56	0.0235*	149	3.23	1.53-6.84	0.0046*

Figure-1: 30-month overall survival (KMC)



Patients at risk:

Group "A"	90	82	69	59	35	24	17
Group "B"	33	32	28	23	21	16	12
Group "C"	27	24	19	14	10	4	2

Conclusion

Adding carboplatin to chemotherapy regimens influence treatment response and survival outcomes in treatment refractory mCRPC. These results suggest providers to consider carboplatin plus docetaxel in the late mCRPC setting after failing 2nd HT.