Year	Compound	Characteristics of study	Types of treatment	mechanism	Outcomes	References
2004	Docetaxel Mitoxantrone (control)	674 patients: 338 (docetaxel every 3 weeks) 336 (mitoxantrone every 3 weeks)	Docetaxel (first line of chemotherapy) Mitoxantrone (second line of chemotherapy)	Tubulin inhibition Blocking DNA synthesis and repair	Median survival than treatment with mitoxantrone and prednisone (17.5 months vs. 15.6 months) Hazard ratios (0.80 and 0.76, respectively)	(89)
2004	Docetaxel Mitoxantrone (control)	1006 patients: 335 (docetaxel every 3 weeks) 337 (mitoxantrone every 3 weeks)	Docetaxel (first line of chemotherapy) Mitoxantrone (second line of chemotherapy)		Median survival, 18.9 vs. 16.5 months; Hazard ratio [HR] = 0.76	(103)
2006, 2010	Sipuleucel-T	In 2004,127 patients 82 :sipuleucel-T or 45 placebo	Immunotherapy	Vaccine	25.9 months in the sipuleucel-T group vs. 21.4 months in the placebo group	(114,115,161)
2010	Cabazitaxel Mitoxantrone	755 men were allocated to treatment groups (377 mitoxantrone, 378 cabazitaxel)	Chemotherapy	Tubulin inhibition	median survival: 15·1 months in the cabazitaxel group and 12·7 months in the mitoxantrone group	(92)
2013	Radium-223	921 patients: 614 patients take radium 223 and 307 placebo	Radiotherapy	Targeting bone metastasis	Median survival 14.0 months vs. 11.2 months	(113)

2015	Abiraterone acetate Placebo (control)	1088 patients: 546 (abiraterone acetate 1 g daily) 542 placebo controls	Hormonotherapy	Reducing androgen production	Median overall survival was significantly longer in the abiraterone acetate group than in the placebo group (34·7 months vs 30·3 months hazard ratio 0·81	(162)
2017,2020	Enzalutamide Placebo (control)	1717 patients: 872 take Enzalutamide 845 placebo controls	Hormonotherapy	Reducing androgen production	Median OS of enzalutamide vs placebo (36 vs 31 months)	(163,164)
2019	Cabazitaxel Abiraterone or enzalutamide based on first line	255 patients: 129 patients in the cabazitaxel group 26 patients in the group that received an androgen-signaling-targeted inhibitor	Chemotherapy + Hormotherapy		The median overall survival was 13.6 months with cabazitaxel and 11.0 months with the androgen-signaling-targeted inhibitor	(165)

Table S1 : characteristics of main and second line treatment of mCRPC.

Year	Compound	Characteristics of study	Types of treatment	Outcomes	References
2012	Abiraterone Acetate after Docetaxel (phase III)	1195 patients, 797: abiraterone acetate plus prednisone (abiraterone group) and 398: placebo plus prednisone (placebo group)	Hormonotherapy + chemotherapy	The abiraterone group had a longer median overall survival (15·8 months versus 11·2 months [10·4-13·1]; hazard ratio [HR] 0·74; p<0·0001) in comparison to the placebo group.	(110)
2012	Enzalutamide after Docetaxel (phaseIII)	1199 men with castration-resistant prostate cancer after chemotherapy 800 patients: (Enzalutamide group), 399 patients (placebo group)	Hormonotherapy + chemotherapy	the enzalutamide group had a median of 18.4 months (95% CI: 17.3 to not yet reached) while the placebo group had a median of 13.6 months (95% CI: 11.3 to 15.8) (hazard ratio for death in the enzalutamide group, 0.63; 95% CI: 0.53 to 0.75; P<0.001).	(166)
2015	Abiraterone Acetate Prior to Docetaxel (phase III)	1088 patients with chemotherapy-naive prostate cancer 546 patients (abiraterone acetate group) 542 (placebo group)	Hormonotherapy + chemotherapy	OS improved at a median of 49.2 months (34.7 vs. 30.3 months,	(162)

2015	Enzalutamide Prior to Docetaxel(phaseIII)	1717 patients, 872 (Enzalutamide group) 845 (Placebo group)	Hormonotherapy + chemotherapy	Enzalutamide was associated with a higher OS compared to placebo (32.4 months versus 25.1 months; hazard ratio (HR) = 0.61 (95% CI 0.47-0.79); P = 0.0001), rPFS was higher with enzalutamide than with placebo (not reached (95% CI 12.3-not yet reached) versus 3.7 months (95% CI 3.6-5.3); HR = 0.17 (95% CI 0.12-0.24); P < 0.0001).	(167)
2020	Rucaparib	115 patients (BRCA mutated)	PARPi	ORRs per independent radiology review and investigator assessment were 43.5% (95% CI, 31.0% to 56.7%; 27 of 62 patients) and 50.8% (95% CI, 38.1% to 63.4%; 33 of 65 patients), respectively. PSA response rate 54.8%	(168)
2020	Pembrolizumab	258 patients: 133 group I (PDL-1 positive)	Immunotherapy	OS: 9.5 (group I) vs 7.9 (group	(121,122)

		66 group II (PDL1 negative) 59 group III (Bone metastasis)		II) vs 14.1 (group III)	
2017, 2020	Olaparib	2792 Patients	PARPi	In an interim analysis , the median overall survival 17.5 months in the Olaparib group and 14.3months in the control group	(118)
2021	Ipatasertib	1101 patients : 554 patients (Abiraterone + placebo 547 (abiraterone + ipatasertib)	PI3K/AKT/ mTOR inhibitors	PFS: 18.5 vs 16.5 months	(119)
2021	Talozoparib	128 patients (HRR mutations)	PARPi	objective response (OS) rate 29·8% (31 of 104 patients; 95% CI 21·2-39·6)	(169)
2021	Capivasertib	150 patients: 75 Capivasertib 75 placebo	PI3K/AKT/ mTOR inhibitors	OS: 31.1 vs 20.2 months PFS: 7.03 vs 6.7 months	(170)
2021	Lu-PSMA-617	831 patients: 551 (Lu-PSMA-617) 280 controls	Theragnostic	OS: 15.3 vs 11.3 months PFS: 8.7 vs 3.4 months	(123)
2023	Niraparib	223 patients: 142 with HRR mutations 81 with other HRR mutations	PARPi	The median survival 10.1 months 5h (HRR mutation) vs 8.6 months (other mutation)	(171)
2023	Talazoparib + Enzalutamide	805 patients 402 talazoparib + enzalutamide 403 placebo with enzalutamide	Hormonotherapy + PARPi	median rPFS was not reached (27·5 months-not reached) for	(124)

				talazoparib plus enzalutamide 21·9 months (16·6-25·1) for placebo plus enzalutamide	
2023	Niraparib + Abiraterone	423 patients 212 niraparib with abiraterone 211 placebo with abiraterone	Hormonotherapy + PARPi	rPFS in niraparib + abiraterone group compared with the placebo + Abiraterone group (16.5 *v* 13.7 months)	(125)
2023	Olaparib with abiraterone	1103 Patients : 399 patients olaparib plus abiraterone 397 patients placebo plus abiraterone	Hormonotherapy + PARPi	Median overall survival 42·1 months with Olaparib plus abiraterone and 34·7 months with placebo plus abiraterone	(126)

Table S2: Characteristics of other lines treatment of mCRPC