Methodology report RL Prostaat PICO 3

# key question

Wat is de aanbevolen 2e lijns behandeling bij progressie tijdens/na docetaxel bij patiënten met een mCRPC?

P Patiënten met gemetastaseerd castratie-resistent prostaatcarcinoom (mCRPC) tijdens of na behandeling met chemotherapie (docetaxel)

I Cabazitaxel, Abiraterone, Enzalutamide, Radium-223, Sipuleucel-T, anti-androgenen

C Placebo of prednison

O Progressie-vrije overleving, Algehele overleving, Kwaliteit van leven, Toxiciteit

# golden hits

1. De Bono J, Oudard S, Ozguroglu M, et al. *Prednison plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomized open-label trial.* Lancet 2010; 376 (9747): 1147-1154. >>> cabazitaxel
2. Fizazi K, Scher H, Molina A, et al. *Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study.* Lancet Oncol 2012, 13: 983-992. >>> abiraterone
3. Scher H, Fizazi K, Saad F et al. *Increased survival with enzalutamide in prostate cancer after chemotherapy.* N Engl J Med 2012; 367(13): 1187-1197. >>> enzalutamide
4. Hoskin P, Sartor O, O’Sullivan JM et al. *Efficacy and safety of radium-223 dichloride in patients with castration-resistant prostate cancer and symptomatic bone metastases, with or without previous docetaxel use: a prespecified subgroup analysis from the randomized, double-blind, phase 3 ALSYMPCA trial.* Lancet Oncology 2014; 15(12): 1397-1406.

# Search strategy

The searches were run on 16 juli 2015. Pubmed Medline, Embase, Cochrane (all libraries) were searched. Detailed search strings are given below. The searches were limited to 2007-2015, English and Dutch. Study types: systematic reviews, meta-analysis and RCTs.

# Search results

The Medline search yielded 1232 hits, while the search in Embase yielded 788 hits, Cochrane yielded 212 hits.

After merging the search files into one file and removal of the duplicates 1983 records were screened on title and abstract. Of these 1755 were excluded. The most important reasons for exclusion was that studies were

1. Patient population
2. Intervention

Of the remaining 228 studies, the full text was retrieved. Based on the full text, an additional 210 studies were excluded. Table 4.1 provides an overview of the studies, with the reason for exclusion.

# Table 4.1 Full text screening and reason for in- or exclusion.

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| **#** | **Reference** | **Included / Excluded** | **Reasons** |
| #1 | *Abiraterone. After prostate cancer treatment failure: 4-month survival advantage.* Prescrire Int, 2012. **21**(128): p. 147-9. | Excluded | Narrative review |
| #2 | *Second-line treatment of metastatic prostate cancer. Prednisone and radiotherapy for symptom relief.* Prescrire Int, 2013. **22**(136): p. 74-8. | Excluded | Narrative review regarding radiotherapy |
| #3 | Acar, O., T. Esen, and N.A. Lack, *New therapeutics to treat castrate-resistant prostate cancer.* The Scientific World Journal, 2013. **2013**. | Excluded | Narrative review |
| #4 | Adesunloye, B.A. and W.L. Dahut, *Tasquinimod: Antiangiogenic agent oncolytic.* Drugs of the Future, 2012. **37**(6): p. 423-430. | Excluded | Comparison is tasquinimod vs placebo. |
| #5 | Agarwal, N., G. Sonpavde, and O. Sartor, *Cabazitaxel for the treatment of castration-resistant prostate cancer.* Future Oncology, 2011. **7**(1): p. 15-24. | Excluded | Narrative review |
| #6 | Agarwal, N., G. Sonpavde, and C.N. Sternberg, *Novel molecular targets for the therapy of castration-resistant prostate cancer.* Eur Urol, 2012. **61**(5): p. 950-60. | Excluded | Narrative review |
| #7 | Agota, P., *The treatment of castration-resistant prostate cancer.* Magyar Onkologia, 2012. **56**(4): p. 219-228. | Excluded | Written in Hungarian |
| #8 | Ahmadi, H. and S. Daneshmand, *Androgen deprivation therapy: evidence-based management of side effects.* BJU Int, 2013. **111**(4): p. 543-8. | Excluded | Review without pooled analysis |
| #9 | Al-Asaaed, S. and E. Winquist, *Secondary hormonal manipulation in castration resistant prostate cancer.* Can J Urol, 2014. **21**(2 Supp 1): p. 37-41. | Excluded | Narrative review |
| #10 | Ansari, J., et al., *Role of second-line systemic treatment post-docetaxel in metastatic castrate resistant prostate cancer- current strategies and future directions.* Anticancer Agents Med Chem, 2011. **11**(3): p. 296-306. | Excluded | Review with retrospective studies included. |
| #11 | Antonarakis, E.S., et al. *A randomized phase 2 study evaluating the optimal sequencing of sipuleucel-T and androgen deprivation therapy (ADT) in biochemically-recurrent prostate cancer (BRPC): Immune results with a focus on humoral responses*. European Urology, Supplements, 2014. **13**, e980-e980b. | Excluded | Abstract |
| #12 | Aragon-Ching, J.B., *Enzalutamide (formerly MDV3100) as a new therapeutic option for men with metastatic castration-resistant prostate cancer.* Asian Journal of Andrology, 2012. **14**(6): p. 805-806. | Excluded | Letter to editor describing other trial |
| #13 | Arai, Y., et al., *Evaluation of quality of life in patients with previously untreated advanced prostate cancer receiving maximum androgen blockade therapy or LHRHa monotherapy: a multicenter, randomized, double-blind, comparative study.* J Cancer Res Clin Oncol, 2008. **134**(12): p. 1385-96. | Excluded | Solely previously untreated advanced prostate cancer included. |
| #14 | Armstrong, A.J., et al., *Prediction of survival following first-line chemotherapy in men with castration-resistant metastatic prostate cancer.* Clin Cancer Res, 2010. **16**(1): p. 203-11. | Excluded | Comparison is docetaxel and prednisone every 3 weeks, weekly administration ofdocetaxel and prednisone, and administration of mitoxantrone and prednisone every 3 weeks |
| #15 | Auchus, R.J., et al., *Use of prednisone with abiraterone acetate in metastatic castration-resistant prostate cancer.* Oncologist, 2014. **19**(12): p. 1231-40. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #16 | Azad, A.A., et al. *A randomized phase II efficacy and safety study of vandetanib (ZD6474) in combination with bicalutamide versus bicalutamide alone in patients with chemotherapy naive castration-resistant prostate cancer*. Investigational new drugs, 2014. **32**, 746-52 DOI: 10.1007/s10637-014-0091-8. | Excluded | Comparison is vandetanib + bicalutamide versus bicalutamide |
| #17 | Basch, E.M., et al. *Pain control and delay in time to skeletal-related events (SREs) in patients with metastatic castration-resistant prostate cancer (mCRPC) treated with abiraterone acetate (AA): Long-term follow-up*. Journal of clinical oncology, 2012. **30**. | Excluded | Abstract |
| #18 | Beckett, R.D., K.M. Rodeffer, and R. Snodgrass, *Abiraterone for the treatment of metastatic castrate-resistant prostate cancer.* Annals of Pharmacotherapy, 2012. **46**(7-8): p. 1016-1024. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #19 | Beltran, H., et al., *New therapies for castration-resistant prostate cancer: efficacy and safety.* Eur Urol, 2011. **60**(2): p. 279-90. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #20 | Bennett, L.L. and A. Ingason, *Enzalutamide (Xtandi) for patients with metastatic, resistant prostate cancer.* Ann Pharmacother, 2014. **48**(4): p. 530-7. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #21 | Bono, J.S., et al. *Abiraterone and increased survival in metastatic prostate cancer*. The New England journal of medicine, 2011. **364**, 1995-2005 DOI: 10.1056/NEJMoa1014618. | Excluded | Duplicate |
| #22 | Bono, J.S., et al. *A subgroup analysis of the TROPIC trial exploring reason for discontinuation of prior docetaxel and survival outcome of cabazitaxel in metastatic castration-resistant prostate cancer (mCRPC)*. Journal of clinical oncology, 2011. **29**. | Excluded | Abstract |
| #23 | Bono, J.S., et al. *Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial*. Lancet (London, England), 2010. **376**, 1147-54 DOI: 10.1016/S0140-6736(10)61389-X. | Excluded | Duplicate |
| #24 | Bono, J.S., et al. *Cabazitaxel shows a consistently greater survival benefit compared to mitoxantrone in patients with mCRPC*. Nowotwory, 2014. **64**, 1-6 DOI: 10.5603/NJO.2014.0001. | Excluded | Non-English |
| #25 | Botrel, T.E., et al., *Intermittent versus continuous androgen deprivation for locally advanced, recurrent or metastatic prostate cancer: a systematic review and meta-analysis.* BMC Urol, 2014. **14**: p. 9. | Excluded | **Design:** SR with meta-analysis**Patients**: locally advanced, recurrent ormetastatic hormone-sensitive prostate cancer**Intervention:** Intermittent androgendeprivation**Control:** continuous androgendeprivation |
| #26 | Brodszky, V., et al. *Clinical efficacy and safety of enzalutamide in metastatic castration-resistant prostate cancer: systematic review and meta-analysis (Provisional abstract)*. Database of Abstracts of Reviews of Effects, 2014. 189-197. | Excluded | Written in Hungarian |
| #27 | Brungs, D., et al., *Intermittent androgen deprivation is a rational standard-of-care treatment for all stages of progressive prostate cancer: results from a systematic review and meta-analysis.* Prostate Cancer Prostatic Dis, 2014. **17**(2): p. 105-11. | Excluded | **Design:** SR with meta-analysis**Patients**: patients diagnosed with any stage of prostate cancer**Intervention:** Intermittent androgendeprivation**Control:** continuous androgendeprivation |
| #28 | Calais da Silva, F., et al., *Locally advanced and metastatic prostate cancer treated with intermittent androgen monotherapy or maximal androgen blockade: results from a randomised phase 3 study by the South European Uroncological Group.* Eur Urol, 2014. **66**(2): p. 232-9. | Excluded | RCT in which the randomisation was based on a variable (PSA level). |
| #29 | Calais da Silva, F.E., et al., *Intermittent androgen deprivation for locally advanced and metastatic prostate cancer: results from a randomised phase 3 study of the South European Uroncological Group.* Eur Urol, 2009. **55**(6): p. 1269-77. | Excluded | RCT in which the randomisation was based on a variable (PSA level). |
| #30 | Cella, D., et al., *Impact of enzalutamide on quality of life in men with metastatic castration-resistant prostate cancer after chemotherapy: Additional analyses from the AFFIRM randomized clinical trial.* Annals of Oncology, 2015. **26**(1): p. 179-185. | Included | **Design:** RCT**Patients**: histologically or cytologically confirmed adenocarcinoma of the prostate and castrate levels of serum testosterone after chemotherapy.**Intervention:** oral enzalutamide 160mg**Control:** placebo |
| #31 | Chakravarti, A., et al., *Prognostic value of p16 in locally advanced prostate cancer: a study based on Radiation Therapy Oncology Group Protocol 9202.* J Clin Oncol, 2007. **25**(21): p. 3082-9. | Excluded | Comparison is long-term (LT) versus short-term (ST) androgen-deprivation therapy (AD). |
| #32 | Climent, M.A., et al. *Randomized phase II study of abiraterone acetate maintenance in combination with docetaxel after disease progression to abiraterone acetate in metastatic castration-resistant prostate cancer (mCRPC): ABIDO SOGUG trial*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #33 | Conti, P.D., et al., *Intermittent versus continuous androgen suppression for prostatic cancer.* Cochrane Database Syst Rev, 2007(4): p. Cd005009. | Excluded | **Design:** SR with meta-analysis**Patients**: prostatic cancer patients**Intervention:** Intermittent androgendeprivation**Control:** continuous androgendeprivation |
| #34 | Corona, G., et al., *Androgen deprivation therapy in prostate cancer: focusing on sexual side effects.* J Sex Med, 2012. **9**(3): p. 887-902. | Excluded | Narrative review |
| #35 | Crook, J., *The role of intermittent androgen suppression in biochemically recurrent or newly diagnosed metastatic prostate cancer.* Curr Opin Support Palliat Care, 2013. **7**(3): p. 258-64. | Excluded | Comparison is: continuous combined androgen blockade or intermittent. |
| #36 | Danila, D.C., et al., *Phase II multicenter study of abiraterone acetate plus prednisone therapy in patients with docetaxel-treated castration-resistant prostate cancer.* J Clin Oncol, 2010. **28**(9): p. 1496-501. | Excluded | Single-arm study. |
| #37 | Dason, S., et al., *Intermittent androgen deprivation therapy for prostate cancer: translating randomized controlled trials into clinical practice.* Can J Urol, 2014. **21**(2 Supp 1): p. 28-36.  | Excluded | Narrative review |
| #38 | De Bono, J.S., et al., *Abiraterone and increased survival in metastatic prostate cancer.* New England Journal of Medicine, 2011. **364**(21): p. 1995-2005. | Included | **Design:** RCT**Patients**: histologically or cytologicallyconfirmed prostate cancer that had previously been treated with docetaxel,**Intervention:** abiraterone acetate and prednisone **Control:** placebo and prednisone |
| #39 | De Bono, J.S., et al., *Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: A randomised open-label trial.* The Lancet, 2010. **376**(9747): p. 1147-1154. | Included | **Design:** RCT**Patients**: pathologically proven prostate cancer with documented disease progression during or after completion of docetaxel treatment.**Intervention:** prednisolone and cabazitaxel**Control:** prednisolone and mitoxantrone |
| #40 | De Conti, P., et al. *Intermittent versus continuous androgen suppression for prostatic cancer*. Cochrane Database of Systematic Reviews, 2007. DOI: 10.1002/14651858.CD005009.pub2. | Excluded | **Design:** SR with meta-analysis**Patients**: prostatic cancer patients**Intervention:** Intermittent androgendeprivation**Control:** continuous androgendeprivation |
| #41 | de Giorgi, U., et al., *Early outcome prediction on 18F-fluorocholine PET/CT in metastatic castration-resistant prostate cancer patients treated with abiraterone.* Oncotarget, 2014. **5**(23): p. 12448-12458. | Excluded | Single-arm study. |
| #42 | Dearden, L., et al. *Comparison of mean overall surviva l (OS) and radiographic progression free survival (RPFS) based on matching adjusted indirect comparison of abiraterone acetate and enzalutamide for the treatment of castration-resistant prostate cancer in chemotherapy naive patients*. Value in health, 2014. **17**, A616 DOI: 10.1016/j.jval.2014.08.2170. | Excluded | Abstract |
| #43 | Den, R.B., L.A. Doyle, and K.E. Knudsen, *Practical guide to the use of radium 223 dichloride.* Can J Urol, 2014. **21**(2 Supp 1): p. 70-6. | Excluded | Narrative review |
| #44 | Dreicer, R., et al., *A randomized, double-blind, placebo-controlled, Phase II study with and without enzastaurin in combination with docetaxel-based chemotherapy in patients with castration-resistant metastatic prostate cancer.* Invest New Drugs, 2013. **31**(4): p. 1044-50. | Excluded | Comparison is docetaxel + prednisone + enzastaurin versus docetaxel + prednisone. |
| #45 | Dreicer, R., et al. *Results from a phase 3, randomized, double-blind, multicenter, placebo-controlled trial of orteronel (TAK-700) plus prednisone in patients with metastatic castration-resistant prostate cancer (mCRPC) that has progressed during or following docetaxel-based therapy (ELM-PC 5 trial)*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #46 | Dreicer, R., et al., *Phase I/II trial of orteronel (TAK-700)-an investigational 17,20-lyase inhibitor-in patients with metastatic castration-resistant prostate cancer.* Clinical Cancer Research, 2014. **20**(5): p. 1335-1344. | Excluded | No RCT (no control) |
| #47 | Dyer, M., et al., *NICE guidance on abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen.* Lancet Oncol, 2012. **13**(8): p. 762-3. | Excluded | Letter to the editor about RCT that is already included. |
| #48 | Fizazi, K., et al. *Phase III, randomized, double-blind, multicenter trial comparing orteronel (TAK-700) plus prednisone with placebo plus prednisone in patients with metastatic castration-resistant prostate cancer that has progressed during or after docetaxel-based therapy: ELM-PC 5*. Journal of clinical oncology, 2015. **33**, 723-31 DOI: 10.1200/JCO.2014.56.5119. | Included | **Design:** RCT**Patients**: confirmed adenocarcinoma of the prostate and radiographically documented metastatic disease after receiving docetaxel.**Intervention:** orteronel 400 mg plus prednisone**Control:** placebo plus prednisone |
| #49 | Fizazi, K., et al. *Regional differences observed in the phase 3 trial (ELM-PC 5) with orteronel (TAK-700) plus prednisone in patients with metastatic castration-resistant prostate cancer (mCRPC) that has progressed during or following docetaxel*. Journal of clinical oncology, 2014. **32.** | Excluded | Abstract |
| #50 | Fizazi, K., et al. *Effect of enzalutamide on time to first skeletal-related event, pain, and quality of life in men with castration-resistant prostate cancer: results from the randomised, phase 3 AFFIRM trial*. The Lancet. Oncology, 2014. **15**, 1147-56 DOI: 10.1016/S1470-2045(14)70303-1. | Included | **Design:** RCT**Patients**: progressive metastatic castration-resistant prostate cancer that had been previously treated with docetaxel.**Intervention:** enzalutamide**Control:** placebo |
| #51 | Fizazi, K., et al. *Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study*. The Lancet. Oncology, 2012. **13**, 983-92 DOI: 10.1016/S1470-2045(12)70379-0. | Included | **Design:** RCT**Patients**: histologically or cytologically confirmed metastatic castration-resistant prostate cancer were eligible if they had had previous treatment with docetaxel**Intervention:** abiraterone acetate plus prednisone**Control:** placebo plus prednisone |
| #52 | Fizazi, K., et al. *Final overall survival (OS) analysis of COU-AA-301, a phase 3 study of abiraterone acetate plus prednisone in patients with metastatic castration-resistant prostate cancer (mCRPC) pretreated with docetaxel*. European journal of cancer, 2011. **47**, S483-s484 DOI: 10.1016/S0959-8049%2811%2971951-7. | Excluded | Abstract |
| #53 | Fossa, S.D., et al., *Circulating tumor cells in patients with metastatic castration resistant prostate cancer: Exploratory findings at a tertiary referral hospital.* Research and Reports in Urology, 2014. **6**: p. 121-126. | Excluded | No RCT (prospective cohort study) |
| #54 | Francini, E., et al., *Abiraterone in heavily pretreated patients with metastatic castrate-resistant prostate cancer.* Anti-Cancer Drugs, 2014. **25**(4): p. 472-477. | Excluded | Single-arm study. |
| #55 | Goldkorn, A., et al., *Circulating tumor cell counts are prognostic of overall survival in SWOG S0421: a phase III trial of docetaxel with or without atrasentan for metastatic castration-resistant prostate cancer.* J Clin Oncol, 2014. **32**(11): p. 1136-42. | Excluded | Comparison is atrasentan versus placebo. |
| #56 | Goodman, O.B., Jr., et al., *Exploratory analysis of the visceral disease subgroup in a phase III study of abiraterone acetate in metastatic castration-resistant prostate cancer.* Prostate Cancer Prostatic Dis, 2014. **17**(1): p. 34-9. | Included | **Design:** RCT**Patients**: post-docetaxel mCRPC patients**Intervention:** abiraterone acetate**Control:** placebo |
| #57 | Graff, J.N., M.J. Gordon, and T.M. Beer, *Safety and effectiveness of enzalutamide in men with metastatic, castration-resistant prostate cancer.* Expert Opinion on Pharmacotherapy, 2014. **16**(5): p. 749-754. | Excluded | Narrative review |
| #58 | Gravis, G., et al., *Androgen-deprivation therapy alone or with docetaxel in non-castrate metastatic prostate cancer (GETUG-AFU 15): a randomised, open-label, phase 3 trial.* Lancet Oncol, 2013. **14**(2): p. 149-58. | Excluded | Comparison is androgen deprivation therapy alone versus docetaxel + androgen deprivation therapy |
| #59 | Hamilton, R.J., et al. *Effect of concomitant medication use on outcomes of treatment and placebo arms of the COU-AA-301 and COU-AA-302 studies of abiraterone acetate (AA) in metastatic castration-resistant prostate cancer (mCRPC)*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #60 | Hao, Y., et al. *Effect of abiraterone acetate (AA) on patient-reported pain in metastatic castration-resistant prostate cancer (mCRPC) post-docetaxel: Results of longitudinal sensitivity analyses*. Journal of clinical oncology, 2013. **31**. | Excluded | Abstract |
| #61 | Harland, S., et al. *Effect of abiraterone acetate treatment on the quality of life of patients with metastatic castration-resistant prostate cancer after failure of docetaxel chemotherapy*. European journal of cancer (Oxford, England : 1990), 2013. **49**, 3648-57 DOI: 10.1016/j.ejca.2013.07.144. | Included | **Design:** RCT**Patients**: mCRPC post-docetaxel**Intervention:** abiraterone acetate(1 g daily) plus prednisone (5 mg twice daily)**Control:** placebo plus prednisone (5 mg twice daily) |
| #62 | Harrison, M.R., et al., *Radium-223 chloride: a potential new treatment for castration-resistant prostate cancer patients with metastatic bone disease.* Cancer Manag Res, 2013. **5**: p. 1-14. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #63 | Heidenreich, A., et al., *Cabazitaxel plus prednisone for metastatic castration-resistant prostate cancer progressing after docetaxel: Results from the German compassionate-use programme.* European Urology, 2013. **63**(6): p. 977-982. | Excluded | Single-arm study |
| #64 | Heinrich, D., et al. *Updated analysis of radium-223 dichloride (Ra-223) impact on pain, skeletal-related events (SRE), and survival from the phase 3 randomized trial (ALSYMPCA) in patients with castration-resistant prostate cancer (CRPC) and bone metastases*. European Urology, Supplements, 2013. **12**, e101-e102. | Excluded | Abstract |
| #65 | Heinrich, D., et al. *Effects of radium-223 dichloride (Ra-223) on total alkaline phosphatase (ALP) and prostate-specific antigen (PSA) in patients with castration-resistant prostate cancer (CRPC) and symptomatic bone metastases from the phase 3 ALSYMPCA trial*. European Urology, Supplements, 2014. **13**, e865. | Excluded | Abstract |
| #66 | Higano, C.S., *Intermittent versus continuous androgen deprivation therapy.* J Natl Compr Canc Netw, 2014. **12**(5): p. 727-33. | Excluded | Comparison is intermittent versus continuous androgen deprivation therapy |
| #67 | Hoskin, P., et al., *Efficacy and safety of radium-223 dichloride in patients with castration-resistant prostate cancer and symptomatic bone metastases, with or without previous docetaxel use: A prespecified subgroup analysis from the randomised, double-blind, phase 3 ALSYMPCA trial.* The Lancet Oncology, 2014. **15**(12): p. 1397-1406. | Included | **Design:** RCT**Patients**: progressive, symptomatic castration-resistant prostate cancer, at least two bone metastases.**Intervention:** six intravenous injections of radium-223**Control:** or matching placebo |
| #68 | Hoy, S.M., *Abiraterone acetate: a review of its use in patients with metastatic castration-resistant prostate cancer.* Drugs, 2013. **73**(18): p. 2077-91. | Excluded | Narrative review |
| #69 | Hussain, M., et al., *Intermittent versus continuous androgen deprivation in prostate cancer.* N Engl J Med, 2013. **368**(14): p. 1314-25. | Excluded | Comparison is intermittent versus continuous androgen deprivation therapy |
| #70 | James, N.D., et al., *Final safety and efficacy analysis of the specific endothelin A receptor antagonist zibotentan (ZD4054) in patients with metastatic castration-resistant prostate cancer and bone metastases who were pain-free or mildly symptomatic for pain: A double-blind, placebo-controlled, randomized Phase II trial.* BJU International, 2010. **106**(7): p. 966-973. | Excluded | Comparison is zibotentan versus placebo. |
| #71 | Jana, B.R.P., *Cabazitaxel and prednisone as second-line therapy of metastatic, castration-resistant prostate cancer.* Community Oncology, 2010. **7**(12): p. 540-542. | Excluded | Letter to the editor. |
| #72 | Jha, G.G. and J.S. Miller *A randomized, double-blind phase 2 study of sipuleucel-T followed by indoximod or placebo in the treatment of patients with asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #73 | Joshua, A.M., et al., *Safety of enzalutamide in patients with metastatic castration-resistant prostate cancer previously treated with docetaxel: expanded access in North America.* Prostate, 2015. **75**(8): p. 836-44. | Excluded | Single-arm study |
| #74 | Kantoff, P.W., et al. *Sipuleucel-T immunotherapy for castration-resistant prostate cancer*. The New England journal of medicine, 2010. **363**, 411-22 DOI: 10.1056/NEJMoa1001294. | Excluded | Results not stratified among patients that received chemo and those that did not. |
| #75 | Kindlova, E., *Radium-223 dichloride (Xofigo) - management of the treatment of castration-resistant prostate cancer.* Onkologie (Czech Republic), 2014. **8**(1): p. 24-26. | Excluded | Narrative review |
| #76 | Kirby, M., C. Hirst, and E.D. Crawford, *Characterising the castration-resistant prostate cancer population: A systematic review.* International Journal of Clinical Practice, 2011. **65**(11): p. 1180-1192. | Excluded | Systematic review that includes retrospective studies |
| #77 | Klotz, L., *Intermittent versus continuous androgen deprivation therapy in advanced prostate cancer.* Curr Urol Rep, 2013. **14**(3): p. 159-67. | Excluded | (Narrative) review without pooled analysis  |
| #78 | Kluetz, P.G., et al., *Abiraterone acetate in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer: U.S. food and drug administration drug approval summary.* Clinical Cancer Research, 2013. **19**(24): p. 6650-6656. | Excluded | Patients included were chemotherapy-naïve mCRPC. |
| #79 | Kluetz, P.G., et al., *Radium Ra 223 dichloride injection: U.S. food and drug administration drug approval summary.* Clinical Cancer Research, 2014. **20**(1): p. 9-14. | Excluded | No original treatment data |
| #80 | Koenig, F., et al. *Efficacy and safety of radium-223 dichloride (Ra-223) in castration-resistant prostate cancer (CRPC) patients with bone metastases who had prior or no-prior docetaxel (D) therapy in the phase 3 ALSYMPCA trial*. Onkologie, 2013. **36**, 77-8 DOI: 10.1159/000356365. | Excluded | Abstract |
| #81 | Kratiras, Z., C. Konstantinidis, and K. Skriapas, *A review of continuous vs intermittent androgen deprivation therapy: redefining the gold standard in the treatment of advanced prostate cancer. Myths, facts and new data on a ''perpetual dispute''.* Int Braz J Urol, 2014. **40**(1): p. 3-15; discussion 15. | Excluded | (Narrative) review without pooled analysis |
| #82 | Kuczyk, M.A., et al. *Overall survival benefit and safety profile of radium-223 chloride, a first-in-class alpha-pharmaceutical: Results from a phase III randomized trial (ALSYMPCA) in patients with castration-resistant prostate cancer (CRPC) with bone metastases*. Onkologie, 2012. **35**, 182 DOI: 10.1159/000178474. | Excluded | Abstract |
| #83 | Langenhuijsen, J.F., et al., *Continuous vs. intermittent androgen deprivation therapy for metastatic prostate cancer.* Urol Oncol, 2013. **31**(5): p. 549-56. | Excluded | Comparison is intermittent versus continuous androgen deprivation therapy |
| #84 | Lee, J.L., et al., *Effectiveness and safety of cabazitaxel plus prednisolone chemotherapy for metastatic castration-resistant prostatic carcinoma: data on Korean patients obtained by the cabazitaxel compassionate-use program.* Cancer Chemother Pharmacol, 2014. **74**(5): p. 1005-13. | Excluded | Single-arm study |
| #85 | Lin, T.H., et al., *Anti-androgen receptor ASC-J9 versus anti-androgens MDV3100 (Enzalutamide) or Casodex (Bicalutamide) leads to opposite effects on prostate cancer metastasis via differential modulation of macrophage infiltration and STAT3-CCL2 signaling.* Cell Death Dis, 2013. **4**: p. e764. | Excluded | Animal study |
| #86 | Lin, T.H., et al., *Differential androgen deprivation therapies with anti-androgens casodex/bicalutamide or MDV3100/Enzalutamide versus anti-androgen receptor ASC-J9(R) Lead to promotion versus suppression of prostate cancer metastasis.* J Biol Chem, 2013. **288**(27): p. 19359-69. | Excluded | Animal study |
| #87 | Liu, G., et al., *Phase II trial of weekly ixabepilone in men with metastatic castrate-resistant prostate cancer (E3803): a trial of the Eastern Cooperative Oncology Group.* Clin Genitourin Cancer, 2012. **10**(2): p. 99-105. | Excluded | No RCT (no control) |
| #88 | Loblaw, D.A., et al., *Initial hormonal management of androgen-sensitive metastatic, recurrent, or progressive prostate cancer: 2006 update of an American Society of Clinical Oncology practice guideline.* J Clin Oncol, 2007. **25**(12): p. 1596-605. | Excluded | Systematic review without pooled analysis on the outcomes that are of interest. |
| #89 | Loblaw, D.A., et al., *Systemic therapy in men with metastatic castration-resistant prostate cancer: a systematic review.* Clin Oncol (R Coll Radiol), 2013. **25**(7): p. 406-30. | Excluded | Meta-analysis includes solely therapies not of interest. |
| #90 | Lodde, M., L. Lacombe, and Y. Fradet, *Salvage therapy with bicalutamide 150 mg in nonmetastatic castration-resistant prostate cancer.* Urology, 2010. **76**(5): p. 1189-93. | Excluded | Single-arm study |
| #91 | Logothetis, C., et al. *Effect of abiraterone acetate (AA) on pain control and skeletal-related events (SRE) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) post docetaxel (D): Results from the COU-AA-301 phase III study*. Journal of clinical oncology, 2011. **29**. | Excluded | Abstract |
| #92 | Logothetis, C.J., et al. *Effect of abiraterone acetate and prednisone compared with placebo and prednisone on pain control and skeletal-related events in patients with metastatic castration-resistant prostate cancer: exploratory analysis of data from the COU-AA-301 randomised trial*. The Lancet. Oncology, 2012. **13**, 1210-7 DOI: 10.1016/S1470-2045(12)70473-4. | Included | **Design:** RCT**Patients**: metastatic castration-resistant prostate cancer after one or two lines of chemotherapy (one docetaxel based)**Intervention:** abiraterone acetate**Control:** matching placebo |
| #93 | Loriot, Y., et al., *Antitumour activity of abiraterone acetate against metastatic castration-resistant prostate cancer progressing after docetaxel and enzalutamide (MDV3100).* Annals of Oncology, 2013. **24**(7): p. 1807-1812. | Excluded | Retrospective study |
| #94 | Loriot, Y., et al. *Bicalutamide in combination with vandetanib or placebo in patients with castration-refractory metastatic prostate cancer without any clinical symptom related to disease progression - A randomized, double-blind phase II trial*. European journal of cancer, 2011. **47**, S500 DOI: 10.1016/S0959-8049%2811%2972002-0. | Excluded | Abstract |
| #95 | Loriot, Y., et al., *Effect of enzalutamide on health-related quality of life, pain, and skeletal-related events in asymptomatic and minimally symptomatic, chemotherapy-naive patients with metastatic castration-resistant prostate cancer (PREVAIL): results from a randomised, phase 3 trial.* Lancet Oncol, 2015. **16**(5): p. 509-21. | Excluded | Chemotherapy-naïve patients included. |
| #96 | Loriot, Y., et al. *Efficacy outcomes by baseline prostate-specific antigen (PSA): Results from the Phase III AFFIRM trial*. European Urology, Supplements, 2013. **12**, 173 DOI: 10.1016/S1569-9056%2813%2962434-3. | Excluded | Abstract |
| #97 | Loriot, Y., A. Zoubeidi, and M.E. Gleave, *Targeted Therapies in Metastatic Castration-Resistant Prostate Cancer. Beyond the Androgen Receptor.* Urologic Clinics of North America, 2012. **39**(4): p. 517-531. | Excluded | Narrative review |
| #98 | Lovett, R., E. George, and A. Adler, *NICE guidance on sipuleucel-T for asymptomatic or minimally symptomatic metastatic hormone-relapsed prostate cancer.* Lancet Oncol, 2015. **16**(4): p. 369-70. | Excluded | Letter to the editor regarding different medication. |
| #99 | Lundstrom, E.A., et al., *Triptorelin 6-month formulation in the management of patients with locally advanced and metastatic prostate cancer: an open-label, non-comparative, multicentre, phase III study.* Clin Drug Investig, 2009. **29**(12): p. 757-65. | Excluded | Single-arm study |
| #100 | Machiels, J.P., et al., *Prospective randomized study comparing docetaxel, estramustine, and prednisone with docetaxel and prednisone in metastatic hormone-refractory prostate cancer.* J Clin Oncol, 2008. **26**(32): p. 5261-8. | Excluded | Comparison is docetaxel alone versus docetaxel and estramustine. |
| #101 | Madan, R.A., et al., *Analysis of overall survival in patients with nonmetastatic castration-resistant prostate cancer treated with vaccine, nilutamide, and combination therapy.* Clin Cancer Res, 2008. **14**(14): p. 4526-31. | Excluded | Comparison is poxvirus-based prostate-specific antigen (PSA) vaccine or nilutamide |
| #102 | Malone, S., et al., *Mature results of the Ottawa phase II study of intermittent androgen-suppression therapy in prostate cancer: clinical predictors of outcome.* Int J Radiat Oncol Biol Phys, 2007. **68**(3): p. 699-706. | Excluded | No RCT (no control) |
| #103 | Marshall, D.T., et al., *Phase I trial of weekly docetaxel, total androgen blockade, and image-guided intensity-modulated radiotherapy for localized high-risk prostate adenocarcinoma.* Clin Genitourin Cancer, 2014. **12**(2): p. 80-6. | Excluded | Single-arm study |
| #104 | Mason, M.D., et al., *Oral sodium clodronate for nonmetastatic prostate cancer--results of a randomized double-blind placebo-controlled trial: Medical Research Council PR04 (ISRCTN61384873).* J Natl Cancer Inst, 2007. **99**(10): p. 765-76. | Excluded | Comparison of clodronate versus or placebo |
| #105 | McGann, S. and E.R. Horton, *Radium-223 dichloride: a novel treatment option for castration-resistant prostate cancer patients with symptomatic bone metastases.* Ann Pharmacother, 2015. **49**(4): p. 469-76. | Excluded | Review without pooled analysis |
| #106 | McNeel, D.G., et al., *Phase I trial of tremelimumab in combination with short-term androgen deprivation in patients with PSA-recurrent prostate cancer.* Cancer Immunol Immunother, 2012. **61**(7): p. 1137-47. | Excluded | No RCT (no control) |
| #107 | Merseburger, A.S., et al., *Enzalutamide in European and North American men participating in the AFFIRM trial.* BJU Int, 2015. **115**(1): p. 41-9. | Included | **Design:** RCT**Patients**: confirmed diagnosis of metastatic prostate cancer and previous treatment with docetaxel**Intervention:** enzalutamide**Control:** placebo |
| #108 | Meulenbeld, H.J., et al., *Randomised phase II/III study of docetaxel with or without risedronate in patients with metastatic Castration Resistant Prostate Cancer (CRPC), the Netherlands Prostate Study (NePro).* Eur J Cancer, 2012. **48**(16): p. 2993-3000. | Excluded | Comparison is docetaxel with risedronate versus docetaxel. |
| #109 | Michaelson, M.D., et al., *Multicenter phase II study of trabectedin in patients with metastatic castration-resistant prostate cancer.* Ann Oncol, 2012. **23**(5): p. 1234-40. | Excluded | No RCT (no control) |
| #110 | Michalski, J., et al. *Radium-223 dichloride (Ra-223) impact on skeletal-related events, external beam radiation therapy (EBRT), and pain in patients with castration-resistant prostate cancer (CRPC) with bone metastases: Updated results from the phase 3 alsympca trial*. International Journal of Radiation Oncology Biology Physics, 2013. **87**, S108-s109 DOI: 10.1016/j.ijrobp.2013.06.280. | Excluded | Abstract |
| #111 | Miller, K., et al. *Radium-223 chloride impact on skeletal-related events in patients with castration-resistant prostate cancer (CRPC) with bone metastases: A phase III randomized trial (ALSYMPCA)*. Onkologie, 2012. **35**, 238-9 DOI: 10.1159/000178474. | Excluded | Abstract |
| #112 | Miller, K., et al. *Enzalutamide improves health-related quality of life in men with metastatic castration-resistant prostate cancer following docetaxel-based therapy: Results from the affirm study*. Urology, 2013. **82**, S52. | Excluded | Abstract |
| #113 | Miller, K., et al. *Effect of enzalutamide on health-related quality of life (HRQoL) in men with metastatic castration-resistant prostate cancer (mCRPC) following docetaxel-based therapy: Results from the AFFIRM study*. Journal of clinical oncology, 2013. **31**. | Excluded | Abstract |
| #114 | Millikan, R.E., et al., *Phase III trial of androgen ablation with or without three cycles of systemic chemotherapy for advanced prostate cancer.* J Clin Oncol, 2008. **26**(36): p. 5936-42. | Excluded | Comparison is hormone therapy only versus chemohormonal therapy. |
| #115 | Morrissey, C., et al., *Effects of androgen deprivation therapy and bisphosphonate treatment on bone in patients with metastatic castration-resistant prostate cancer: results from the University of Washington Rapid Autopsy Series.* J Bone Miner Res, 2013. **28**(2): p. 333-40. | Excluded | Post-mortem study |
| #116 | Mottet, N., et al., *Addition of radiotherapy to long-term androgen deprivation in locally advanced prostate cancer: an open randomised phase 3 trial.* Eur Urol, 2012. **62**(2): p. 213-9. | Excluded | Comparison is ADT plus radiotherapy with ADT alone |
| #117 | Mottet, N., et al., *Intermittent hormonal therapy in the treatment of metastatic prostate cancer: a randomized trial.* BJU Int, 2012. **110**(9): p. 1262-9. | Excluded | Comparison is intermittent versus continuous androgen deprivation therapy |
| #118 | Mulders, P., et al. *MDV3100, an androgen receptor signaling inhibitor, improves overall survival in patients with prostate cancer post docetaxel: Results from the Phase 3 AFFIRM study*. Urology, 2012. **80**, S30 DOI: 10.1016/S0090-4295%2812%2900879-5. | Excluded | Abstract |
| #119 | Mulders, P.F., et al. *Efficacy and safety of abiraterone acetate in an elderly patient subgroup (aged 75 and older) with metastatic castration-resistant prostate cancer after docetaxel-based chemotherapy*. European urology, 2014. **65**, 875-83 DOI: 10.1016/j.eururo.2013.09.005. | Included | **Design:** RCT**Patients**: Metastatic Castration resistant Prostate Cancer After Docetaxel-based Chemotherapy**Intervention:** Abiraterone acetate plus prednisone**Control:** prednisone |
| #120 | Mulders, P.F.A., et al. *Improved survival in elderly (>75 yr) metastatic castration-resistant prostate cancer (mCRPC) patients upon treatment with abiraterone acetate (AA) plus prednisone (P) progressing after docetaxel-based chemotherapy: Results from COU-AA-301, a randomized, double-blind, placebo-controlled, phase III study*. European Urology, Supplements, 2012. **11**, e127-e127a. | Excluded | Abstract |
| #121 | Munger-Beyeler, C., et al., *Quality of analgesic treatment in patients with advanced prostate cancer: do we do a better job now? The Swiss Group for Clinical Cancer Research (SAKK) experience.* Support Care Cancer, 2008. **16**(5): p. 461-7. | Excluded | Comparison of different chemotherapies |
| #122 | Musende, A.G., et al., *Rh2 or its aglycone aPPD in combination with docetaxel for treatment of prostate cancer.* Prostate, 2010. **70**(13): p. 1437-47. | Excluded | In vitro study |
| #123 | Nadal, R., et al., *Clinical activity of enzalutamide in Docetaxel-naive and Docetaxel-pretreated patients with metastatic castration-resistant prostate cancer.* Prostate, 2014. **74**(15): p. 1560-8. | Excluded | Retrospective study |
| #124 | Nakabayashi, M., et al., *Phase II trial of RAD001 and bicalutamide for castration-resistant prostate cancer.* BJU Int, 2012. **110**(11): p. 1729-35. | Excluded | No RCT (no control) |
| #125 | Nakabayashi, M., et al., *Secondary hormonal therapy in men with castration-resistant prostate cancer.* Clin Genitourin Cancer, 2011. **9**(2): p. 95-103. | Excluded | Retrospective study |
| #126 | Nayyar, R., N. Sharma, and N.P. Gupta, *Docetaxel-based chemotherapy with zoledronic acid and prednisone in hormone refractory prostate cancer: Factors predicting response and survival.* International Journal of Urology, 2009. **16**(9): p. 726-731. | Excluded | Single-arm study |
| #127 | Nilsson, S., *Radium-223 dichloride for the treatment of bone metastatic castration-resistant prostate cancer: An evaluation of its safety.* Expert Opinion on Drug Safety, 2015. **14**(7): p. 1127-1136. | Excluded | Narrative review |
| #128 | Nilsson, S., et al., *Two-year survival follow-up of the randomized, double-blind, placebo-controlled phase II study of radium-223 chloride in patients with castration-resistant prostate cancer and bone metastases.* Clinical Genitourinary Cancer, 2013. **11**(1): p. 20-26. | Excluded | Patients were excluded when they received chemotherapy. |
| #129 | Nilsson, S., et al., *Bone-targeted radium-223 in symptomatic, hormone-refractory prostate cancer: a randomised, multicentre, placebo-controlled phase II study.* Lancet Oncol, 2007. **8**(7): p. 587-94. | Excluded | Patients were excluded when they received chemotherapy. |
| #130 | Nilsson, S., et al. *Alkaline phosphatase (ALP) normalization and overall survival in patients with bone metastases from castration-resistant prostate cancer (CRPC) treated with radium-223*. Journal of clinical oncology, 2011. **29**. | Excluded | Abstract |
| #131 | Nilsson, S., et al. *Long-termsafety of radium-223 dichloride (Ra-223) in patients with castration-resistant prostate cancer (CRPC) and bonemetastases from the phase 3 ALSYMPCA study*. European Urology, Supplements, 2013. **12**, 178 DOI: 10.1016/S1569-9056%2813%2962445-8. | Excluded | Abstract |
| #132 | Nilsson, S., et al., *A randomized, dose-response, multicenter phase II study of radium-223 chloride for the palliation of painful bone metastases in patients with castration-resistant prostate cancer.* European Journal of Cancer, 2012. **48**(5): p. 678-686. | Excluded | No RCT (no control, only different doses) |
| #133 | Nilsson, S., et al. *1.5-year post-treatment follow-up of radium-223 dichloride (Ra-223) in patients with castration-resistant prostate cancer (CRPC) and bone metastases from the phase 3 ALSYMPCA study*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #134 | Ning, Y.M., et al., *Enzalutamide for treatment of patients with metastatic castration-resistant prostate cancer who have previously received docetaxel: U.S. foodand drugadministrationdrug approval summary.* Clinical Cancer Research, 2013. **19**(22): p. 6067-6073. | Excluded | No original treatment data |
| #135 | Niraula, S., L.W. Le, and I.F. Tannock, *Treatment of prostate cancer with intermittent versus continuous androgen deprivation: a systematic review of randomized trials.* J Clin Oncol, 2013. **31**(16): p. 2029-36. | Excluded | Comparison is early versus deferred androgen suppression therapy. |
| #136 | Nishiyama, T., *Serum testosterone levels after medical or surgical androgen deprivation: a comprehensive review of the literature.* Urol Oncol, 2014. **32**(1): p. 38.e17-28. | Excluded | Comparison is intermittent versus continuous androgen deprivation therapy |
| #137 | Noguchi, M., et al., *A randomized phase II trial of personalized peptide vaccine plus low dose estramustine phosphate (EMP) versus standard dose EMP in patients with castration resistant prostate cancer.* Cancer Immunology, Immunotherapy, 2010. **59**(7): p. 1001-1009. | Excluded | Comparison is personalized peptide vaccination plus low-dose estramustine phosphate or standard-dose estramustine phosphate. |
| #138 | Nome, R., et al., *Changes in prostate-specific antigen, markers of bone metabolism and bone scans after treatment with radium-223.* Scandinavian Journal of Urology, 2014. **49**(3): p. 211-217. | Included | **Design:** RCT**Patients**: patients with metastatic castration-resistant prostate cancer (mCRPC) with bone metastases after treatment with docetaxel**Intervention:** Ra-223**Control:** placebo |
| #139 | Noonan, K.L., et al., *Clinical activity of abiraterone acetate in patients with metastatic castration-resistant prostate cancer progressing after enzalutamide.* Annals of Oncology, 2013. **24**(7): p. 1802-1807. | Excluded | Single-arm study |
| #140 | Nozawa, M., et al., *Phase II trial of zoledronic acid combined with androgen-deprivation therapy for treatment-naive prostate cancer with bone metastasis.* Int J Clin Oncol, 2014. **19**(4): p. 693-701. | Excluded | Single-arm study |
| #141 | Nuhn, P., et al., *Association of pretreatment neutrophil-to-lymphocyte ratio (NLR) and overall survival (OS) in patients with metastatic castration-resistant prostate cancer (mCRPC) treated with first-line docetaxel.* BJU Int, 2014. **114**(6b): p. E11-7. | Excluded | Single-arm study |
| #142 | Oh, W.K., et al., *Does oral antiandrogen use before leuteinizing hormone-releasing hormone therapy in patients with metastatic prostate cancer prevent clinical consequences of a testosterone flare?* Urology, 2010. **75**(3): p. 642-7. | Excluded | Single-arm study |
| #143 | Ohlmann, C.H., et al. *Improved Overall Survival (OS) in patients with metastatic Castration Resistant Prostate Cancer (mCRPC) progressing after docetaxel-based chemotherapy: Results from the phase III study COU-AA-301 with abiraterone acetate*. Onkologie, 2011. **34**, 9-10 DOI: 10.1159/000333299. | Excluded | Abstract |
| #144 | Okihara, K., et al., *Assessment of permanent brachytherapy combined with androgen deprivation therapy in an intermediate-risk prostate cancer group without a Gleason score of 4 + 3: a single Japanese institutional experience.* Int J Urol, 2014. **21**(3): p. 271-6. | Excluded | No RCT |
| #145 | Oliver Sartor, A., et al. *Radium-223 chloride (Ra-223) impact on skeletal-related events (SREs) and ECOG performance status (PS) in patients with castration-resistant prostate cancer (CRPC) with bone metastases: Interim results of a phase III trial (ALSYMPCA)*. Journal of clinical oncology, 2012. **30**. | Excluded | Abstract |
| #146 | O'Sullivan, J., et al. *Hematologic safety of radium-223 dichloride (Ra-223) in the phase 3 ALSYMPCA trial in castration-resistant prostate cancer (CRPC) patients with bone metastases: Baseline prognostic factor subgroup analysis*. European journal of cancer, 2013. **49**, S688 DOI: 10.1016/S0959-8049%2813%2970064-9. | Excluded | Abstract |
| #147 | O'Sullivan, J.M., et al. *Results from a phase III randomized trial (ALSYMPCA) of radium-223 chloride, a first-in-class alpha-emitter, in patients with castration-resistant prostate cancer (CRPC) and bone metastases: Overall survival benefit and safety profile*. European journal of nuclear medicine and molecular imaging, 2012. **39**, S294 DOI: 10.1007/s00259-012-2221-x. | Excluded | Abstract |
| #148 | Oudard, S., *TROPIC: Phase III trial of cabazitaxel for the treatment of metastatic castration-resistant prostate cancer.* Future Oncol, 2011. **7**(4): p. 497-506. | Excluded | Narrative review regarding cabazitaxel |
| #149 | Parker, C., et al. *Overall survival benefit and impact on skeletal-related events for radium- 223 chloride (Alpharadin) in the treatment of castration-resistant prostate cancer (CRPC) patients with bone metastases: A phase III randomized trial (ALSYMPCA)*. European Urology, Supplements, 2012. **11**, e130-e130a. | Excluded | Abstract |
| #150 | Parker, C., et al. *Overall survival benefit of radium-223 chloride (Alpharadin) in the treatment of patients with symptomatic bone metastases in Castration-resistant Prostate Cancer (CRPC): A phase III randomized trial (ALSYMPCA)*. European journal of cancer, 2011. **47**, 3 DOI: 10.1016/S0959-8049%2811%2970100-9. | Excluded | Abstract |
| #151 | Parker, C., et al. *Overall survival benefit and safety profile of radium-223 chloride, a first-in-class alpha-pharmaceutical: Results from a phase III randomized trial (ALSYMPCA) in patients with castration-resistant prostate cancer (CRPC) with bone metastases*. Journal of clinical oncology, 2012. **30**. | Excluded | Abstract |
| #152 | Parker, C., et al., *Alpha emitter radium-223 and survival in metastatic prostate cancer.* New England Journal of Medicine, 2013. **369**(3): p. 213-223. | Included | **Design:** RCT**Patients**: histologically confirmed, progressive castration-resistant prostate cancer with two or more bone metastases and had received docetaxel**Intervention:** radium-223**Control:** placebo |
| #153 | Parker, C.C., et al., *A randomized, double-blind, dose-finding, multicenter, phase 2 study of radium chloride (Ra 223) in patients with bone metastases and castration-resistant prostate cancer.* European Urology, 2013. **63**(2): p. 189-197. | Excluded | No RCT (no control, only different doses) |
| #154 | Petrylak, D.P., et al. *A randomized open-label phase 2a study evaluating the efficacy and safety of radium-223 dichloride (Ra-223) in combination with abiraterone acetate or enzalutamide in patients with castration-resistant prostate cancer (CRPC) and bone metastases*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #155 | Pienta, K.J., et al., *Phase 2 study of carlumab (CNTO 888), a human monoclonal antibody against CC-chemokine ligand 2 (CCL2), in metastatic castration-resistant prostate cancer.* Invest New Drugs, 2013. **31**(3): p. 760-8. | Excluded | No RCT (no control) |
| #156 | Pili, R., et al., *Phase II randomized, double-blind, placebo-controlled study of tasquinimod in men with minimally symptomatic metastatic castrate-resistant prostate cancer.* J Clin Oncol, 2011. **29**(30): p. 4022-8. | Excluded | Comparison is tasquinimod versus placebo |
| #157 | Poppel, H., et al. *Updated interim analysis (IA): Results of randomized phase 3 study COUAA-302 of abiraterone acetate (AA) in metastatic castration-resistant prostate cancer (mCRPC) patients (pts) without prior chemotherapy*. European Urology, Supplements, 2013. **12**, e97-e98. | Excluded | Abstract |
| #158 | Pouessel, D., et al., *Cabazitaxel for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: The TROPIC study in France.* Bulletin du Cancer, 2012. **99**(7-8): p. 731-741. | Excluded | Comparison of mitxantrone versus cabazitaxe |
| #159 | Quinn, D.I., et al. *A randomized phase II, open-label study of sipuleucel-T with concurrent or sequential enzalutamide in metastatic castration-resistant prostate cancer (mCRPC)*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #160 | Rajdev, L., et al., *Phase I trial of metronomic oral vinorelbine in patients with advanced cancer.* Cancer Chemother Pharmacol, 2011. **68**(5): p. 1119-24. | Excluded | No RCT (no control, only different doses) |
| #161 | Rathkopf, D.E., et al., *Phase I study of ARN-509, a novel antiandrogen, in the treatment of castration-resistant prostate cancer.* J Clin Oncol, 2013. **31**(28): p. 3525-30. | Excluded | No RCT (no control, only different doses) |
| #162 | Rathkopf, D.E., et al. *Long-term safety and efficacy analysis of abiraterone acetate (AA) plus prednisone (P) in metastatic castration-resistant prostate cancer (mCRPC) without prior chemotherapy (COU-AA-302)*. Journal of clinical oncology, 2013. **31**. | Excluded | Abstract |
| #163 | Rathkopf, D.E., et al., *Updated interim efficacy analysis and long-term safety of abiraterone acetate in metastatic castration-resistant prostate cancer patients without prior chemotherapy (COU-AA-302).* European Urology, 2014. **66**(5): p. 815-825. | Excluded | Chemotherapy-naïve patients |
| #164 | Ray, M.E., et al., *Potential surrogate endpoints for prostate cancer survival: analysis of a phase III randomized trial.* J Natl Cancer Inst, 2009. **101**(4): p. 228-36. | Included  | **Design:** RCT**Patients**: Locally advanced prostatecancer had been treated with 4 months of neoadjuvant and concurrent androgen deprivation therapy.**Intervention:** Androgen deprivation therapy**Control:** No additional therapy |
| #165 | Roach, M., 3rd, *Dose escalated external beam radiotherapy versus neoadjuvant androgen deprivation therapy and conventional dose external beam radiotherapy for clinically localized prostate cancer: do we need both?* Strahlenther Onkol, 2007. **183 Spec No 2**: p. 26-8. | Excluded | (Narrative) review without pooled analysis |
| #166 | Roach, M., 3rd, et al., *Short-term neoadjuvant androgen deprivation therapy and external-beam radiotherapy for locally advanced prostate cancer: long-term results of RTOG 8610.* J Clin Oncol, 2008. **26**(4): p. 585-91. | Excluded | Comparison is androgen deprivation therapy versus radiotherapy |
| #167 | Ryan, C.J., et al. *Phase II study of abiraterone acetate in chemotherapy-naive metastatic castration-resistant prostate cancer displaying bone flare discordant with serologic response*. Clinical cancer research, 2011. **17**, 4854-61 DOI: 10.1158/1078-0432.CCR-11-0815. | Excluded | No RCT (no control, single-arm) |
| #168 | Ryan, C.J., et al. *Abiraterone in metastatic prostate cancer without previous chemotherapy*. The New England journal of medicine, 2013. **368**, 138-48 DOI: 10.1056/NEJMoa1209096. | Excluded | Chemotherapy-naïve patients |
| #169 | Ryan, C.J., et al. *Abiraterone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naive men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomised, double-blind, placebo-controlled phase 3 study*. The Lancet. Oncology, 2015. **16**, 152-60 DOI: 10.1016/S1470-2045(14)71205-7. | Excluded | Chemotherapy-naïve patients |
| #170 | Ryan, C.J., et al., *Phase I clinical trial of the CYP17 inhibitor abiraterone acetate demonstrating clinical activity in patients with castration-resistant prostate cancer who received prior ketoconazole therapy.* Journal of Clinical Oncology, 2010. **28**(9): p. 1481-1488. | Excluded | No RCT (no control, only different doses) |
| #171 | Safarinejad, M.R., *Safety and efficacy of sorafenib in patients with castrate resistant prostate cancer: a Phase II study.* Urol Oncol, 2010. **28**(1): p. 21-7.  | Excluded | No RCT (no control) |
| #172 | Saigal, C.S., et al., *Androgen deprivation therapy increases cardiovascular morbidity in men with prostate cancer.* Cancer, 2007. **110**(7): p. 1493-500. | Excluded | No RCT (no control) |
| #173 | Salonen, A.J., et al., *Comparison of intermittent and continuous androgen deprivation and quality of life between patients with locally advanced and patients with metastatic prostate cancer: a post hoc analysis of the randomized FinnProstate Study VII.* Scand J Urol, 2014. **48**(6): p. 513-22. | Excluded | Comparison is intermittent versus continuous androgen deprivation therapy |
| #174 | Salonen, A.J., et al., *The FinnProstate Study VII: intermittent versus continuous androgen deprivation in patients with advanced prostate cancer.* J Urol, 2012. **187**(6): p. 2074-81. | Excluded | Comparison is intermittent versus continuous androgen deprivation therapy |
| #175 | Salonen, A.J., et al., *Finnish multicenter study comparing intermittent to continuous androgen deprivation for advanced prostate cancer: interim analysis of prognostic markers affecting initial response to androgen deprivation.* J Urol, 2008. **180**(3): p. 915-9; discussion 919-20. | Excluded | Comparison is intermittent versus continuous androgen deprivation therapy |
| #176 | Sartor, A.O., et al. *Radium-223 chloride impact on skeletal-related events in patients with castration-resistant prostate cancer (CRPC) with bone metastases: A phase III randomized trial (ALSYMPCA)*. Journal of clinical oncology, 2012. **30**. | Excluded | Abstract |
| #177 | Sartor, A.O., et al. *Survival benefit from first docetaxel treatment for cabazitaxel plus prednisone compared with mitoxantrone plus prednisone in patients with metastatic castration-resistant prostate cancer (mCRPC) enrolled in the TROPIC trial*. Journal of clinical oncology, 2011. **29**. | Excluded | Abstract |
| #178 | Sartor, O., et al., *Effect of radium-223 dichloride on symptomatic skeletal events in patients with castration-resistant prostate cancer and bone metastases: Results from a phase 3, double-blind, randomised trial.* The Lancet Oncology, 2014. **15**(7): p. 738-746. | Included | **Design:** RCT**Patients**: progressive, symptomatic castration-resistant prostate cancer with two or more bone metastases**Intervention:** radium-223**Control:** placebo |
| #179 | Sartor, O., M. Halstead, and L. Katz, *Improving outcomes with recent advances in chemotherapy for castrate-resistant prostate cancer.* Clin Genitourin Cancer, 2010. **8**(1): p. 23-8. | Excluded | Narrative review |
| #180 | Satoh, T., et al., *A phase 2 study of abiraterone acetate in Japanese men with metastatic castration-resistant prostate cancer who had received docetaxel-based chemotherapy.* Jpn J Clin Oncol, 2014. **44**(12): p. 1206-15. | Excluded | Single-arm study |
| #181 | Schellhammer, P.F., et al. *Lower baseline prostate-specific antigen is associated with a greater overall survival benefit from sipuleucel-T in the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) trial*. Urology, 2013. **81**, 1297-302 DOI: 10.1016/j.urology.2013.01.061. | Excluded | Comparison is sipuleucel-T versus PBMCs without PA2024. |
| #182 | Schelman, W.R., et al., *A phase I study of zibotentan (ZD4054) in patients with metastatic, castrate-resistant prostate cancer.* Invest New Drugs, 2011. **29**(1): p. 118-25. | Excluded | No RCT |
| #183 | Scher, H.I., et al., *Antitumour activity of MDV3100 in castration-resistant prostate cancer: A phase 1-2 study.* The Lancet, 2010. **375**(9724): p. 1437-1446. | Excluded | No RCT |
| #184 | Scher, H.I., et al. *Impact of on-study corticosteroid use on efficacy and safety in the phase III AFFIRM study of enzalutamide (ENZA), an androgen receptor inhibitor*. Journal of clinical oncology, 2013. **31**. | Excluded | Abstract |
| #185 | Scher, H.I., et al., *Increased survival with enzalutamide in prostate cancer after chemotherapy.* N Engl J Med, 2012. **367**(13): p. 1187-97. | Included | **Design:** RCT**Patients**: castration-resistant prostate cancer after chemotherapy**Intervention:** enzalutamide**Control:** placebo |
| #186 | Scher, H.I., et al. *Evaluation of circulating tumor cell (CTC) enumeration as an efficacy response biomarker of overall survival (OS) in metastatic castration-resistant prostate cancer (mCRPC): Planned final analysis (FA) of COU-AA-301, a randomized, double-blind, placebo-controlled, phase III study of abiraterone acetate (AA) plus low-dose prednisone (P) post docetaxel*. Journal of clinical oncology, 2011. **29**. | Excluded | Abstract |
| #187 | Schroder, F., et al., *Dutasteride treatment over 2 years delays prostate-specific antigen progression in patients with biochemical failure after radical therapy for prostate cancer: results from the randomised, placebo-controlled Avodart After Radical Therapy for Prostate Cancer Study (ARTS).* Eur Urol, 2013. **63**(5): p. 779-87. | Excluded | **Design:** RCT**Patients**: localised prostate cancer patients**Intervention:** dutasteride 0.5 mg**Control:** placebo |
| #188 | Schroder, F.H., et al., *Changes in alkaline phosphatase levels in patients with prostate cancer receiving degarelix or leuprolide: results from a 12-month, comparative, phase III study.* BJU Int, 2010. **106**(2): p. 182-7. | Excluded | Comparison is leuprolide versus degarelix |
| #189 | Schweizer, M.T., et al., *Effect of bipolar androgen therapy for asymptomatic men with castration-resistant prostate cancer: Results from a pilot clinical study.* Science Translational Medicine, 2015. **7**(269). | Excluded | Narrative review |
| #190 | Shamash, J., et al., *A multi-centre randomised phase III trial of Dexamethasone vs Dexamethasone and diethylstilbestrol in castration-resistant prostate cancer: immediate vs deferred Diethylstilbestrol.* Br J Cancer, 2011. **104**(4): p. 620-8. | Excluded | Comparison is Diethylstilbestrol versus Dexamethasone and Aspirin |
| #191 | Shaw, G.L., et al., *International study into the use of intermittent hormone therapy in the treatment of carcinoma of the prostate: a meta-analysis of 1446 patients.* BJU Int, 2007. **99**(5): p. 1056-65. | Excluded | Systematic review with individual patient data from non-RCTs |
| #192 | Sheikh, N.A., et al. *Sipuleucel-T generates robust and persistent cellular and humoral immune responses-Results from the IMPACT trial*. Cancer research, 2010. **70**, DOI: 10.1158/1538-7445.AM10-2932. | Excluded | Abstract |
| #193 | Sheikh, N.A., et al. *Evaluation of immune activation following neoadjuvant sipuleucel-T in subjects with localized prostate cancer*. Journal of clinical oncology, 2012. **30**. | Excluded | Abstract |
| #194 | Shirakawa, T., et al., *Long-term outcome of phase I/II clinical trial of Ad-OC-TK/VAL gene therapy for hormone-refractory metastatic prostate cancer.* Hum Gene Ther, 2007. **18**(12): p. 1225-32. | Excluded  | No RCT (no control) |
| #195 | Slovin, S.F., et al., *Ipilimumab alone or in combination with radiotherapy in metastatic castration-resistant prostate cancer: Results from an open-label, multicenter phase i/ii study.* Annals of Oncology, 2013. **24**(7): p. 1813-1821. | Excluded | Comparison is ipilimumab versus ipilimumab + radiotherapy |
| #196 | Smith, D.C., et al., *Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial.* J Clin Oncol, 2013. **31**(4): p. 412-9. | Excluded | Comparison is cabozantinib versus placebo |
| #197 | Smith, M.R., et al., *Randomized controlled trial of early zoledronic acid in men with castration-sensitive prostate cancer and bone metastases: results of CALGB 90202 (alliance).* J Clin Oncol, 2014. **32**(11): p. 1143-50. | Excluded | Comparison is zoledronic acid versus placebo |
| #198 | Sonpavde, G., et al., *Phase II trial of sunitinib for the therapy of progressive metastatic castration-refractory prostate cancer after previous docetaxel chemotherapy.* Clin Genitourin Cancer, 2008. **6**(2): p. 134-7. | Excluded | Protocol |
| #199 | Sonpavde, G., et al., *Sunitinib malate for metastatic castration-resistant prostate cancer following docetaxel-based chemotherapy.* Ann Oncol, 2010. **21**(2): p. 319-24. | Excluded | Single-arm study regarding sunitinib |
| #200 | Sonpavde, G., et al., *The association between radiographic response and overall survival in men with metastatic castration-resistant prostate cancer receiving chemotherapy.* Cancer, 2011. **117**(17): p. 3963-71. | Excluded | Comparison is docetaxel-prednisone every 3 weeks (D3W), weekly docetaxel-prednisone (DW), or mitoxantrone-prednisone (MP |
| #201 | Souhami, L., et al., *Impact of the duration of adjuvant hormonal therapy in patients with locally advanced prostate cancer treated with radiotherapy: a secondary analysis of RTOG 85-31.* J Clin Oncol, 2009. **27**(13): p. 2137-43. | Excluded | Comparison is RT and adjuvant goserelin(3.6 mg) monthly (arm 1) or RT alone followed by goserelin at time of relapse(arm 2). |
| #202 | Sridhar, S.S., et al., *Castration-resistant prostate cancer: From new pathophysiology to new treatment.* European Urology, 2014. **65**(2): p. 289-299. | Excluded | Review without pooled analysis |
| #203 | Sridhar, S.S., et al., *A multicenter phase II clinical trial of lapatinib (GW572016) in hormonally untreated advanced prostate cancer.* Am J Clin Oncol, 2010. **33**(6): p. 609-13. | Excluded | No RCT (single-arm study) |
| #204 | Sternberg, C.N., et al. *Improved outcomes in elderly patients with metastatic castration-resistant prostate cancer treated with the androgen receptor inhibitor enzalutamide: Results from the phase III AFFIRM trial*. Annals of Oncology, 2014. **25**, 429-434 DOI: 10.1093/annonc/mdt571. | Included | **Design:** RCT**Patients**: progressive mCRPC who had received prior docetaxel-based chemotherapy**Intervention:** enzalutamide**Control:** placebo |
| #205 | Sternberg, C.N., et al. *Abiraterone acetate for patients with metastatic castration-resistant prostate cancer progressing after chemotherapy: final analysis of a multicentre, open-label, early-access protocol trial*. The Lancet. Oncology, 2014. **15**, 1263-8 DOI: 10.1016/S1470-2045(14)70417-6. | Excluded | Single-arm study. |
| #206 | Sydes, M.R., et al. *Flexible trial design in practice - stopping arms for lack-of-benefit and adding research arms mid-trial in STAMPEDE: a multi-arm multi-stage randomized controlled trial*. Trials, 2012. **13**, 168 DOI: 10.1186/1745-6215-13-168. | Excluded | No RCT (protocol) |
| #207 | Szmulewitz, R., et al., *A Randomized Phase 1 Study of Testosterone Replacement for Patients with Low-Risk Castration-Resistant Prostate Cancer.* European Urology, 2009. **56**(1): p. 97-104. | Excluded | No control arm, only different doses (Androderm® transdermal testosterone) |
| #208 | Taplin, M.E., et al., *A phase II study of mifepristone (RU-486) in castration-resistant prostate cancer, with a correlative assessment of androgen-related hormones.* BJU Int, 2008. **101**(9): p. 1084-9. | Excluded | No control arm (only different doses of Mifepristone) |
| #209 | Taplin, M.E., et al. *Intense androgen-deprivation therapy with abiraterone acetate plus leuprolide acetate in patients with localized high-risk prostate cancer: results of a randomized phase II neoadjuvant study*. Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 2014. **32**, 3705-15 DOI: 10.1200/JCO.2013.53.4578. | Excluded | Not about patients with metastatic CRPC  |
| #210 | Tombal, B., et al., *Long-term Efficacy and Safety of Enzalutamide Monotherapy in Hormone-naive Prostate Cancer: 1- and 2-Year Open-label Follow-up Results.* European Urology, 2015. | Excluded | Single-arm study |
| #211 | Tombal, B., et al. *Enzalutamide in men with chemotherapy-naive metastatic castration resistant prostate cancer (MCRPC): Primary and European regional results of the phase 3 prevail study*. European Urology, Supplements, 2014. **13**, Lba3. | Excluded | Abstract |
| #212 | Tombal, B., et al., *Additional analysis of the secondary end point of biochemical recurrence rate in a phase 3 trial (CS21) comparing degarelix 80 mg versus leuprolide in prostate cancer patients segmented by baseline characteristics.* Eur Urol, 2010. **57**(5): p. 836-42. | Excluded | Control is not placebo or prednisone. Comparison is degarelix versus leuprolide |
| #213 | Tsai, H.T., et al., *Efficacy of intermittent androgen deprivation therapy vs conventional continuous androgen deprivation therapy for advanced prostate cancer: a meta-analysis.* Urology, 2013. **82**(2): p. 327-33. | Excluded | Comparison is intermittent Androgen Deprivation Therapy vsConventional Continuous Androgen Deprivation Therapy |
| #214 | Tu, S.M. and S.H. Lin, *Current trials using bone-targeting agents in prostate cancer.* Cancer J, 2008. **14**(1): p. 35-9. | Excluded | Comparison is docetaxel versus Samarium-153 Lexidronam |
| #215 | Tu, S.M., et al., *Phase I study of concurrent weekly docetaxel and repeated samarium-153 lexidronam in patients with castration-resistant metastatic prostate cancer.* J Clin Oncol, 2009. **27**(20): p. 3319-24. | Excluded | Comparison is docetaxel versus Samarium-153 Lexidronam |
| #216 | Uemura, H., et al., *Possible anti-tumor activity of initial treatment with zoledronic acid with hormonal therapy for bone-metastatic prostate cancer in multicenter clinical trial.* Int J Clin Oncol, 2013. **18**(3): p. 472-7. | Excluded | Comparison is zoledronic acid versus maximal androgen blockade |
| #217 | Ueno, S., et al., *Efficacy of combined androgen blockade with zoledronic acid treatment in prostate cancer with bone metastasis: the ZABTON-PC (zoledronic acid/androgen blockade trial on prostate cancer) study.* Anticancer Res, 2013. **33**(9): p. 3837-44. | Excluded | Comparison is androgen blockade versus androgen blockade + zoledronic acid. |
| #218 | Vogelzang, N.J., et al. *Efficacy and safety of radium-223 dichloride (Ra-223) in castration-resistant prostate cancer (CRPC) patients with bone metastases who did or did not receive prior docetaxel (D) in the phase III ALSYMPCA trial*. Journal of clinical oncology, 2013. **31**. | Excluded | Abstract |
| #219 | Vogelzang, N.J., et al. *Updated analysis of radium-223 dichloride (Ra-223) impact on skeletal-related events (SRE) in patients with castration-resistant prostate cancer (CRPC) and bone metastases from the phase III randomized trial (ALSYMPCA)*. Journal of clinical oncology, 2013. **31**. | Excluded | Abstract |
| #220 | Walsh, P.C. *Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: A randomised open-label trial*. Journal of urology, 2011. **185**, 2156-7 DOI: 10.1016/j.juro.2011.02.2681. | Excluded | Letter to the editor about an included study. |
| #221 | Wang, J., et al., *Lenalidomide and cyclophosphamide immunoregulation in patients with metastatic, castration-resistant prostate cancer.* Clin Exp Metastasis, 2015. **32**(2): p. 111-24. | Excluded | Narrative review |
| #222 | Wedel, S., et al. *Updated analysis of radium-223 dichloride (Ra-223) impact on survival, safety, and skeletal-related events in castration-resistant prostate cancer (CRPC) patients with bone metastases from the phase 3 ALSYMPCA trial*. European journal of nuclear medicine and molecular imaging, 2013. **40**, S190 DOI: 10.1007/s00259-013-2535-3. | Excluded | Abstract |
| #223 | West, T.A., B.E. Kiely, and M.R. Stockler, *Estimating scenarios for survival time in men starting systemic therapies for castration-resistant prostate cancer: A systematic review of randomised trials.* European Journal of Cancer, 2014. **50**(11): p. 1916-1924. | Excluded | Systematic review without pooled analysis regarding the outcomes of interest. Identified trials are included here as well. |
| #224 | Wiechno, P., et al. *Radium-223 dichloride (Ra-223) efficacy and safety in patients with castration-resistant prostate cancer (CRPC) with bone metastases: Phase 3 ALSYMPCA study findings stratified by age group*. European journal of cancer, 2013. **49**, S690-s691 DOI: 10.1016/S0959-8049%2813%2970064-9. | Excluded | Abstract |
| #225 | Wirth, M., et al., *A multicenter phase 1 study of EMD 525797 (DI17E6), a novel humanized monoclonal antibody targeting alphav integrins, in progressive castration-resistant prostate cancer with bone metastases after chemotherapy.* Eur Urol, 2014. **65**(5): p. 897-904. | Excluded | No control arm (only different doses of EMD 525797) |
| #226 | Wit, R., et al. *Phase 3, randomized, placebo-controlled trial of orteronel (TAK-700) plus prednisone in patients (pts) with chemotherapy-naive metastatic castration-resistant prostate cancer (mCRPC) (ELM-PC 4 trial)*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #227 | Yu, E.Y., et al., *Phase II study of dasatinib in patients with metastatic castration-resistant prostate cancer.* Clin Cancer Res, 2009. **15**(23): p. 7421-8. | Excluded | Abstract |
| #228 | Zapatero, A., et al., *High-dose radiotherapy with short-term or long-term androgen deprivation in localised prostate cancer (DART01/05 GICOR): a randomised, controlled, phase 3 trial.* Lancet Oncol, 2015. **16**(3): p. 320-7. | Excluded | Comparison is RT + short-term androgen deprivation versus RT + long-term androgen deprivation. |

# Appendix

# Search strategies

**Medline via Pubmed**

1. "prostatic neoplasms"[MeSH Terms]

2. "prostate cancer"[Title/Abstract]

3. "prostatic cancer"[Title/Abstract]

4. #1 OR #2 OR #3

5. "neoplasm metastasis"[MeSH Terms]

6. metastasi\*[Title/Abstract]

7. "metastatic disease"[Title/Abstract]

8. "metastatic prostate"[Title/Abstract]

9. #5 OR #6 OR #7 OR #8

10. "antineoplastic agents"[MeSH Terms]

11. "antineoplastic agents"[Title/Abstract]

12. "androstadienes"[MeSH Terms]

13. "abiraterone"[Supplementary Concept]

14. "MDV 3100"[Supplementary Concept]

15. Cabazitaxel [Supplementary Concept]

16. Cabazitaxel[Title/Abstract]

17. Enzalutamide[Title/Abstract]

18. Radium-223[Title/Abstract]

19. "androgen antagonists"[MeSH Terms]

20. "bicalutamide"[Supplementary Concept]

21. "nilutamide"[Supplementary Concept]

22. "cyproterone"[MeSH Terms]

23. "cabazitaxel"[Supplementary Concept]

24. "cabazitaxel"[Title/Abstract]

25. "sipuleucel-T"[Supplementary Concept]

26. "sipuleucel-T"[Title/Abstract]

27. #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26

28. ((review[tiab] OR "Review"[Publication Type] OR "Meta-Analysis as Topic"[Mesh] OR meta-analysis[tiab] OR "Meta-Analysis "[Publication Type]) NOT ("Letter"[Publication Type] OR "Editorial"[Publication Type] OR "Comment"[Publication Type])) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))

29. randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]

30. #28 OR #29

31. #4 AND #9 AND #27 AND #30 **1232**

**Embase**

1. 'castration resistant prostate cancer'/exp

2. 'castration resistant prostate cancer':ab,ti

3. 'prostatic cancer':ab,ti

4. #1 OR #2 OR #3

5. 'metastasis'/exp

6. 'metastasis':ab,ti

7. 'metastatic disease':ab,ti

8. 'metastatic prostate':ab,ti

9. #5 OR #6 OR #7 OR #8

10. 'androstane derivative'/exp

11. 'abiraterone acetate'/exp

12. 'abiraterone'/exp

13. 'enzalutamide'/exp

14. 'cabazitaxel'/exp

15. 'radium chloride ra 223'/exp

16. 'antiandrogen'/exp

17. 'bicalutamide'/exp

18. 'nilutamide'/exp

19. 'cyproterone'/exp

20. 'cyproterone acetate'/exp

21. 'androstane derivative':ab,ti

22. 'abiraterone acetate':ab,ti

23. 'abiraterone':ab,ti

24. 'enzalutamide':ab,ti

25. 'cabazitaxel':ab,ti

26. 'Radium-223':ab,ti

27. 'antiandrogen':ab,ti

28. 'bicalutamide':ab,ti

29. 'nilutamide':ab,ti

30. 'cyproterone':ab,ti

31. 'cyproterone acetate':ab,ti

32. 'cabazitaxel'/exp

33. 'cabazitaxel':ab,ti

34. 'sipuleucel T'/exp

35. 'sipuleucel T':ab,ti

36. #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35

37. ([cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

38. ([article]/lim OR [article in press]/lim OR [review]/lim)

39. ([controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND ([article]/lim OR [article in press]/lim)

40. #37 OR #38 OR #39

41. #4 AND #9 AND #36 AND #40 AND [embase]/lim **788**

**Cochrane**

1. MeSH descriptor: [Prostatic Neoplasms, Castration-Resistant] explode all trees

2. castration resistant prostate cancer

3. prostatic cancer

4. #1 OR #2 OR #3

5. MeSH descriptor: [Neoplasm Metastasis] explode all trees

6. metastasis

7. metastatic disease

8. metastatic prostate

9. #5 OR #6 OR #7 OR #8

10. MeSH descriptor: [Cyproterone] explode all trees

11. MeSH descriptor: [Cyproterone Acetate] explode all trees

12.androstane derivative

13. abiraterone acetate

14. abiraterone

15. enzalutamide

16. cabazitaxel

17. Radium-223

18. antiandrogen

19. bicalutamide

20. nilutamide

21. cyproterone

22. cyproterone acetate

23. cabazitaxel

24. sipuleucel T

25. #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24

26. #4 AND #9 AND #25 **212**