# Methodology report RL Prostaat PICO 2

# key question

Wat is de aanbevolen 1e lijns behandeling bij patiënten met een mCRPC?

P Chemotherapie-naïeve patiënten met gemetastaseerd castratie-resistent prostaatcarcinoom (mCRPC)

 I Pre-chemotherapie (abiraterone of enzalutamide, radium 223, anti-androgeen)

C Placebo of prednison

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

# golden hits

**1.** Beer TM, Armstrong AJ, Rathkopf DE, et al. *Enzalutamide in metastatic prostate cancer before chemotherapy.* N Engl J Med 2014, 371: 424-433.

**2.** Rathkopf DE, Smith MR, de Bono JS, et al. *Updated interim efficacy analysis and long-term safety of abiraterone acetate in metastatic castration-resistant prostate cancer patients without prior chemotherapy*.Eur Urol. 2014 66(5): 815-25.

**3.** Ryan CJ, Smith MR, de Bono JS, et al.*Abiraterone in metastatic prostate cancer without previous chemotherapy.* N Engl J Med 2013 Jan 10; 368(2): 138-148;

**4.** Ryan CJ, Smith MR, Fizazi K, et al. *Abiraterone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naïve men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomized, double-blind, placebo-controlled phase 3 study.* Lancet Oncol. 2015 16(2):152-60

# Search strategy

The searches were run on 16 July 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 1199 hits, while the search in Embase yielded 739 hits, Cochrane yielded 212 hits.

After merging the search files into one file and removal of the duplicates 1951 records were screened on title and abstract. Of these 1720 were excluded. The most important reasons for exclusion was that studies were

1. Patient population
2. Intervention

Of the remaining 231 studies, the full text was retrieved. Based on the full text, an additional 216 studies were excluded. Table 4.1 provides an overview of the studies, with the reason for exclusion.

Table 1. Full text articles 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 | Post-chemotherapy patients |
| #2 | *First-line treatment of metastatic prostate cancer. Androgen suppression for symptomatic disease.* Prescrire Int, 2013. **22**(135): p. 48-51. | Excluded | Narrative review |
| #3 | *Enzalutamide before chemotherapy prolongs survival.* Cancer Discov, 2014. **4**(7): p. Of5. | Excluded | Abstract |
| #4 | 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 without pooled analysis (all studies included) |
| #5 | Agota, P., *The treatment of castration-resistant prostate cancer.* Magyar Onkologia, 2012. **56**(4): p. 219-228. | Excluded | Written in Hungarian |
| #6 | Ahmadi, H. and S. Daneshmand, *Androgen deprivation therapy: evidence-based management of side effects.* BJU Int, 2013. **111**(4): p. 543-8. | Excluded | (Narrative) review without pooled analysis and different treatments |
| #7 | Akaza, H., *Current status and prospects of androgen depletion therapy for prostate cancer.* Best Pract Res Clin Endocrinol Metab, 2008. **22**(2): p. 293-302. | Excluded | Narrative review |
| #8 | Akaza, H., et al., *Combined androgen blockade with bicalutamide for advanced prostate cancer: long-term follow-up of a phase 3, double-blind, randomized study for survival.* Cancer, 2009. **115**(15): p. 3437-45. | Included | **Design:** RCT**Patients**: untreated prostate cancer patients**Intervention:** combined androgen blockade with luteinizing hormone releasing hormone agonist plus bicalutamide**Control:** combined androgen blockade with luteinizing hormone releasing hormone agonist plus placebo |
| #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 without pooled analysis |
| #10 | Albiges, L., et al., *New drugs in metastatic castration-resistant prostate cancer.* Bulletin du Cancer, 2010. **97**(1): p. 149-159. | Excluded | Narrative review |
| #11 | 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 |
| #12 | 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. | Included | **Design:** RCT**Patients**: untreated prostate cancer patients**Intervention:** combined androgen blockade with luteinizing hormone releasing hormone agonist plus bicalutamide**Control:** combined androgen blockade with luteinizing hormone releasing hormone agonist plus placebo |
| #13 | Armstrong, A.J., et al. *Primary, secondary, and quality-of-life endpoint results from PREVAIL, a phase 3 study of enzalutamide in men with metastatic castration resistant prostate cancer (mCRPC)*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #14 | 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) |
| #15 | Basch, E., et al., *Abiraterone acetate plus prednisone versus prednisone alone in chemotherapy-naive men with metastatic castration-resistant prostate cancer: Patient-reported outcome results of a randomised phase 3 trial.* The Lancet Oncology, 2013. **14**(12): p. 1193-1199. | Included | **Design:** RCT**Patients**: chemotherapy-naive patients with metastatic castration-resistant prostate cancer**Intervention:** Abiraterone acetate plus prednisone**Control:** prednisone alone |
| #16 | Basch, E., et al., *Systemic therapy in men with metastatic castration-resistant prostate cancer:American Society of Clinical Oncology and Cancer Care Ontario clinical practice guideline.* J Clin Oncol, 2014. **32**(30): p. 3436-48. | Excluded | Clinical practice guideline without pooled analysis |
| #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 | Beer, T.M., et al. *Enzalutamide in metastatic prostate cancer before chemotherapy*. The New England journal of medicine, 2014. **371**, 424-33 DOI: 10.1056/NEJMoa1405095. | Included | **Design:** RCT**Patients**: metastatic prostate cancer who have not received chemotherapy**Intervention:** enzalutamide (at a dose of 160 mg)**Control:** placebo |
| #20 | 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) |
| #21 | 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) |
| #22 | Berruti, A., A. Pia, and M. Terzolo, *Abiraterone and increased survival in metastatic prostate cancer.* N Engl J Med, 2011. **365**(8): p. 766; author reply 767-8. | Excluded | Letter to the editor referring to an included study. |
| #23 | Bishr, M. and F. Saad, *Overview of the latest treatments for castration-resistant prostate cancer.* Nature Reviews Urology, 2013. **10**(9): p. 522-528. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #24 | Bolla, M., et al. *External irradiation with or without long-term androgen suppression for prostate cancer with high metastatic risk: 10-year results of an EORTC randomised study*. The Lancet. Oncology, 2010. **11**, 1066-73 DOI: 10.1016/S1470-2045(10)70223-0. | Excluded | Control is radiotherapy |
| #25 | 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 | Patients previously received docetaxel. |
| #26 | Borso, E., et al., *Radium 223 dichloride: A multidisciplinary approach to metastatic castration-resistant prostate cancer.* Future Oncology, 2015. **11**(2): p. 323-331. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #27 | 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 |
| #28 | 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 |
| #29 | 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 |
| #30 | 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). |
| #31 | 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). |
| #32 | Caley, A. and J. Staffurth, *Abiraterone acetate for the treatment of Castrate-Refractory prostate cancer.* Aging Health, 2013. **9**(1): p. 9-23. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #33 | Carrasquillo, J.A., et al., *Phase i pharmacokinetic and biodistribution study with escalating doses of 223Ra-dichloride in men with castration-resistant metastatic prostate cancer.* European Journal of Nuclear Medicine and Molecular Imaging, 2013. **40**(9): p. 1384-1393. | Excluded | No RCT, therefore no control group. |
| #34 | Cassinello, J., et al., *SEOM Clinical guidelines for the treatment of metastatic prostate cancer.* Clinical and Translational Oncology, 2014. **16**(12): p. 1060-1066. | Excluded | Clinical practice guideline without pooled analysis |
| #35 | Cathomas, R., et al. *Orteronel maintenance therapy in patients (pts) with metastatic castration resistant prostate cancer (mCRPC) and non-progressive disease after first-line docetaxel therapy: A multicenter randomized double-blind placebo-controlled phase III trial (SAKK 08/11)*. Onkologie, 2013. **36**, 78 DOI: 10.1159/000356365. | Excluded | Abstract |
| #36 | 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. | Excluded | Patients previously received chemotherapy. |
| #37 | 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 |
| #38 | Damber, J.E., et al., *The effect of baseline testosterone on the efficacy of degarelix and leuprolide: further insights from a 12-month, comparative, phase III study in prostate cancer patients.* Urology, 2012. **80**(1): p. 174-80. | Excluded | Control isn’t prednisone or placebo, it’s leuprolide / degarelix. |
| #39 | 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 without pooled analysis (all studies included) |
| #40 | 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. | Excluded | Patients previously received docetaxel. |
| #41 | 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 |
| #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 | Dellis, A. and A.G. Papatsoris, *The economics of abiraterone acetate for castration-resistant prostate cancer.* Expert Rev Pharmacoecon Outcomes Res, 2014. **14**(2): p. 175-9. | Excluded | No RCT (narrative review regarding costs) |
| #44 | 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 without pooled analysis (all studies included) |
| #45 | Dreicer, R., *How to approach sequencing therapy in patients with metastatic castration resistant prostate cancer.* Can J Urol, 2014. **21**(2 Supp 1): p. 93-7. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #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 | 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. | Excluded | Patients previously received docetaxel. |
| #48 | Fizazi, K., et al., *Activity and safety of ODM-201 in patients with progressive metastatic castration-resistant prostate cancer (ARADES): an open-label phase 1 dose-escalation and randomised phase 2 dose expansion trial.* Lancet Oncol, 2014. **15**(9): p. 975-85. | Excluded | No RCT (no control) |
| #49 | 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. | Excluded | Patients previously received docetaxel. |
| #50 | 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. | Excluded | Patients previously received docetaxel. |
| #51 | 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 |
| #52 | 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) |
| #53 | Fossa, S.D., et al. *Ten-and 15-year prostate cancer-specific survival in patients with nonmetastatic high-risk prostate cancer randomized to lifelong hormone treatment alone or combined with radiotherapy (SPCG VII)*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #54 | Froehner, M. and M.P. Wirth, *Enzalutamide in metastatic prostate cancer before chemotherapy.* N Engl J Med, 2014. **371**(18): p. 1755. | Excluded | Letter to the editor referring to an included study. |
| #55 | Gao, X., et al., *Neoadjuvant hormonal deprivation for patients undergoing radical prostatectomy.* Asian J Androl, 2009. **11**(1): p. 127-30. | Excluded | Control is radical prostatectomy. |
| #56 | Gleave, M., L. Klotz, and S.S. Taneja, *The continued debate: intermittent vs. continuous hormonal ablation for metastatic prostate cancer.* Urol Oncol, 2009. **27**(1): p. 81-6. | Excluded | (Narrative) review without pooled analysis |
| #57 | 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 | Patients receive docetaxel. |
| #58 | Gong, C.L. and J.W. Hay, *Cost-effectiveness analysis of abiraterone and sipuleucel-T in asymptomatic metastatic castration-resistant prostate cancer.* JNCCN Journal of the National Comprehensive Cancer Network, 2014. **12**(10): p. 1417-1425. | Excluded | No RCT (model-based cost calculation) |
| #59 | 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 or with docetaxel. |
| #60 | Hahn, N.M., et al., *Failure to suppress markers of bone turnover on first-line hormone therapy for metastatic prostate cancer is associated with shorter time to skeletal-related event.* Clin Genitourin Cancer, 2014. **12**(1): p. 33-40.e4. | Excluded | Comparison is androgen deprivation therapy (ADT) versus ADT + risedronate |
| #61 | 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 |
| #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 | Hedlund, P.O., et al., *Parenteral estrogen versus combined androgen deprivation in the treatment of metastatic prostatic cancer: Part 2. Final evaluation of the Scandinavian Prostatic Cancer Group (SPCG) Study No. 5.* Scandinavian Journal of Urology and Nephrology, 2008. **42**(3): p. 220-229. | Excluded | Comparison is polyestradiol phosphate versus combined androgen deprivation. |
| #64 | Hedlund, P.O., et al., *Significance of pretreatment cardiovascular morbidity as a risk factor during treatment with parenteral oestrogen or combined androgen deprivation of 915 patients with metastasized prostate cancer: evaluation of cardiovascular events in a randomized trial.* Scand J Urol Nephrol, 2011. **45**(5): p. 346-53. | Excluded | Comparison is polyestradiol phosphate versus combined androgen deprivation. |
| #65 | 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 |
| #66 | 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 |
| #67 | 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 |
| #68 | Hirano, D., et al., *Neoadjuvant LHRH analog plus estramustine phosphate combined with three-dimensional conformal radiotherapy for intermediate- to high-risk prostate cancer: a randomized study.* Int Urol Nephrol, 2010. **42**(1): p. 81-8. | Excluded | Comparison is ADT versus ADT + estramustine phosphate. |
| #69 | Horwitz, E.M., et al., *Ten-year follow-up of radiation therapy oncology group protocol 92-02: a phase III trial of the duration of elective androgen deprivation in locally advanced prostate cancer.* J Clin Oncol, 2008. **26**(15): p. 2497-504. | Excluded | Control is radiotherapy |
| #70 | 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 |  |
| #71 | 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 |
| #72 | 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. |
| #73 | 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  |
| #74 | Klotz, L., et al. *The efficacy and safety of degarelix: a 12-month, comparative, randomized, open-label, parallel-group phase III study in patients with prostate cancer*. BJU international, 2008. **102**, 1531-8 DOI: 10.1111/j.1464-410X.2008.08183.x. | Excluded | Comparison is degarelix versus leuprolide. |
| #75 | 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 | Review of other (included) article |
| #76 | 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 | Review of other (included) article |
| #77 | 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 |
| #78 | 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 |
| #79 | Kunath, F., et al., *Early versus deferred androgen suppression therapy for patients with lymph node-positive prostate cancer after local therapy with curative intent: a systematic review.* BMC Cancer, 2013. **13**: p. 131. | Excluded | Comparison is early versus deferred androgen suppression therapy. |
| #80 | Lam, E.T. and L.M. Glode, *Neoadjuvant and adjuvant hormonal and chemotherapy for prostate cancer.* Hematol Oncol Clin North Am, 2013. **27**(6): p. 1189-204, viii. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #81 | 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 |
| #82 | Langley, R.E., et al., *Cardiovascular outcomes in patients with locally advanced and metastatic prostate cancer treated with luteinising-hormone-releasing-hormone agonists or transdermal oestrogen: the randomised, phase 2 MRC PATCH trial (PR09).* Lancet Oncol, 2013. **14**(4): p. 306-16. | Excluded | No RCT (no control) |
| #83 | 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) |
| #84 | 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. |
| #85 | 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 |
| #86 | 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. | Excluded | Patients previously received chemotherapy. |
| #87 | 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**(12): p. 1210-1217. | Excluded | Patients previously received chemotherapy. |
| #88 | 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 |
| #89 | 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. | Included | **Design:** RCT**Patients**: asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer. **Intervention:** enzalutamide**Control:** placebo |
| #90 | 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 |
| #91 | 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 versus docetaxel in combination with estramustine. |
| #92 | 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 |
| #93 | Mainwaring, P., et al. *Association of alkaline phosphatase with clinical outcomes in chemotherapy-naive metastatic castration-resistant prostate cancer (mCRPC): Results from COU-AA-302*. BJU international, 2014. **113**, 21. | Excluded | Abstract |
| #94 | 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) |
| #95 | 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 | Comparison of Docetaxel, TotalAndrogen Blockade, and Radiotherapy |
| #96 | 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 |
| #97 | 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) |
| #98 | Merseburger, A.S., et al., *Enzalutamide in European and North American men participating in the AFFIRM trial.* BJU International, 2014. **115**(1): p. 41-49. | Excluded | Patients previously received docetaxel. |
| #99 | 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, predinose, and risedronate versus docetaxel and predinose. |
| #100 | 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) |
| #101 | 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 |
| #102 | 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 |
| #103 | 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. |
| #104 | Montgomery, B., et al., *Impact of baseline corticosteroids on survival and steroid androgens in metastatic castration-resistant prostate cancer: Exploratory analysis from COU-AA-301.* European Urology, 2015. **67**(5): p. 866-873. | Excluded | Patients previously received docetaxel. |
| #105 | Morris, M.J., et al. *A randomized, open label, multicenter, phase 3, 2-arm study of androgen deprivation with leuprolide (L), +/- docetaxel (D) for clinically asymptomatic prostate cancer (PC) subjects with a rising PSA following definitive local therapy: Safety results*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #106 | Morris, M.J., et al., *Radiographic progression-free survival as a response biomarker in metastatic castration-resistant prostate cancer: COU-AA-302 results.* Journal of Clinical Oncology, 2015. **33**(12): p. 1356-1363. | Included | **Design:** RCT**Patients**: chemotherapy-naive patients with mCRPC.**Intervention:** abiraterone acetate**Control:** placebo |
| #107 | 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 |
| #108 | 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 |
| #109 | 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 |
| #110 | 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. | Excluded | Patients previously received docetaxel. |
| #111 | 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 |
| #112 | 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) |
| #113 | 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. | Included | **Design:** RCT**Patients**: patients with castration-resistant prostate cancer and bone metastases**Intervention:** radium-223**Control:** placebo |
| #114 | 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. | Included | **Design:** RCT**Patients**: patients with castration-resistant prostate cancer and bone metastases**Intervention:** radium-223**Control:** placebo |
| #115 | 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 |
| #116 | 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 |
| #117 | 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) |
| #118 | 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 |
| #119 | 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. |
| #120 | 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. |
| #121 | 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 |
| #122 | 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 |
| #123 | Okegawa, T., et al. *Zoledronic acid improves clinical outcomes in patients with bone metastatic hormone-naive prostate cancer in a multicenter clinical trial*. Anticancer research, 2014. **34**, 4415-20. | Excluded | Comparison is combined androgen blockade versus zoledronic acid and combined androgen blockade |
| #124 | 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 |
| #125 | 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 |
| #126 | 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 |
| #127 | 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 |
| #128 | Ozguroglu, M., et al. *Impact of G-CSF prophylaxis on the occurrence of neutropenia in patients with metastatic castration-resistant prostate cancer (mCRPC) receiving cabazitaxel*. Journal of clinical oncology, 2011. **29**. | Excluded | Abstract |
| #129 | Parker, C., et al. *Updated analysis of the phase III, double-blind, randomized, multinational study of radium-223 chloride in castration-resistant prostate cancer (CRPC) patients with bone metastases (ALSYMPCA)*. Journal of clinical oncology, 2012. **30**. | Excluded | Abstract |
| #130 | Parker, C., 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 | 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 |
| #132 | 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) |
| #133 | Parker, C.C., et al., *Prostate radiotherapy for men with metastatic disease: a new comparison in the Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy (STAMPEDE) trial.* BJU Int, 2013. **111**(5): p. 697-9. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #134 | Pedley, I.D., et al. *Tolerability and efficacy of anti-androgen manipulation versus taxotere and anti-androgen manipulation in patients with hormone-naive, high-risk/metastatic prostate cancer: A phase II, open-labeled, randomized study*. Journal of clinical oncology, 2011. **29**. | Excluded | Abstract |
| #135 | 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 |
| #136 | 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) |
| #137 | 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 |
| #138 | Pisansky, T.M., et al., *Duration of androgen suppression before radiotherapy for localized prostate cancer: radiation therapy oncology group randomized clinical trial 9910.* J Clin Oncol, 2015. **33**(4): p. 332-9. | Excluded | Comparison is eight week androgen suppression versus 28 week. |
| #139 | Pond, G.R., et al., *Efficacy of docetaxel-based chemotherapy following ketoconazole in metastatic castration-resistant prostate cancer: Implications for prior therapy in clinical trials.* Urologic Oncology: Seminars and Original Investigations, 2013. **31**(8): p. 1457-1463. | Excluded | Retrospective study of an RCT regarding the variable ketoconazole use. |
| #140 | 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 |
| #141 | 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 |
| #142 | Prapotnich, D., et al., *A 16-year clinical experience with intermittent androgen deprivation for prostate cancer: oncological results.* World J Urol, 2009. **27**(5): p. 627-35. | Excluded | No RCT |
| #143 | Prezioso, D., et al., *Early versus delayed hormonal treatment in locally advanced or asymptomatic metastatic prostatic cancer patient dilemma.* World J Urol, 2014. **32**(3): p. 661-7. | Excluded | Comparison is early versus deferred androgen suppression therapy. |
| #144 | 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 |
| #145 | 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) |
| #146 | 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) |
| #147 | 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 |
| #148 | 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**, 815-25 DOI: 10.1016/j.eururo.2014.02.056. | Included | **Design:** RCT**Patients**: chemotherapy-naive mCRPC**Intervention:** abiraterone acetate + prednisone**Control:** placebo + prednisone |
| #149 | 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. | Excluded | Not metastatic CRPC |
| #150 | Ridoux, L., et al., *A phase i open-label study investigating the disposition of [<sup>14</sup>C]-cabazitaxel in patients with advanced solid tumors.* Anti-Cancer Drugs, 2015. **26**(3): p. 350-358. | Excluded | No RCT (no control, only different doses) |
| #151 | 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 |
| #152 | Roach, M., 3rd, et al., *Baseline serum testosterone in men treated with androgen deprivation therapy and radiotherapy for localized prostate cancer.* Int J Radiat Oncol Biol Phys, 2010. **78**(5): p. 1314-22. | Excluded | Comparison is androgen deprivation therapy versus radiotherapy |
| #153 | 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 |
| #154 | Ryan, C.J., et al., *A pilot dose-escalation study of the effects of nordihydroguareacetic acid on hormone and prostate specific antigen levels in patients with relapsed prostate cancer.* BJU Int, 2008. **101**(4): p. 436-9. | Excluded | No RCT (no control, only different doses) |
| #155 | Ryan, C.J., et al. *Relationship of baseline PSA and degree of PSA decline to radiographic progression-free survival (rPFS) in patients with chemotherapy-naive metastatic castration-resistant prostate cancer (mCRPC): Results from COU-AA-302*. Journal of clinical oncology, 2013. **31**. | Excluded | Abstract |
| #156 | Ryan, C.J., et al. *Serum androgens as prognostic biomarkers in castration-resistant prostate cancer: results from an analysis of a randomized phase III trial*. Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 2013. **31**, 2791-8 DOI: 10.1200/JCO.2012.45.4595. | Excluded | Patients previously received docetaxel. |
| #157 | Ryan, C.J., et al. *Androgen dynamics and serum PSA in patients treated with abiraterone acetate*. Prostate cancer and prostatic diseases, 2014. **17**, 192-8 DOI: 10.1038/pcan.2014.8. | Excluded | Patients previously received docetaxel. |
| #158 | 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.* Clin Cancer Res, 2011. **17**(14): p. 4854-61. | Excluded | No RCT (no control, single-arm) |
| #159 | Ryan, C.J., et al. *Interim analysis (IA) results of COU-AA-302, a randomized, phase III study of abiraterone acetate (AA) in chemotherapy-naive patients (pts) with metastatic castration-resistant prostate cancer (mCRPC)*. Journal of clinical oncology, 2012. **30**. | Excluded | Abstract |
| #160 | 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. | Included | **Design:** RCT**Patients**: patients with mCRPC who had not received chemotherapy**Intervention:** abiraterone acetate-prednisone**Control:** placebo-prednisone |
| #161 | 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. | Included | **Design:** RCT**Patients**: patients with mCRPC who had not received chemotherapy**Intervention:** abiraterone acetate-prednisone**Control:** placebo-prednisone |
| #162 | 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) |
| #163 | Saad, F., et al. *The prevail study: Primary and non-visceral/visceral disease subgroup results for enzalutamide-treated men with metastatic castration-resistant prostate cancer*. Urology, 2014. **84**, S98-s99 DOI: 10.1016/S0090-4295%2814%2901017-6. | Excluded | Abstract |
| #164 | Sadetsky, N., et al., *Impact of androgen deprivation on physical well-being in patients with prostate cancer: analysis from the CaPSURE (Cancer of the Prostate Strategic Urologic Research Endeavor) registry.* Cancer, 2011. **117**(19): p. 4406-13. | Excluded | No RCT (observational study) |
| #165 | 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) |
| #166 | 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 |
| #167 | 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 |
| #168 | 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 |
| #169 | Salzberg, M., et al., *An open-label, noncomparative phase II trial to evaluate the efficacy and safety of docetaxel in combination with gefitinib in patients with hormone-refractory metastatic prostate cancer.* Onkologie, 2007. **30**(7): p. 355-60. | Excluded | Comparison is gefitinib and docetaxel. |
| #170 | 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 |
| #171 | 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 |
| #172 | Sartor, A.O., et al., *Antiandrogen withdrawal in castrate-refractory prostate cancer: a Southwest Oncology Group trial (SWOG 9426).* Cancer, 2008. **112**(11): p. 2393-400. | Excluded | Single-arm post-hoc analysis |
| #173 | 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 |
| #174 | 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 and patients previously received docetaxel. |
| #175 | 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 |
| #176 | 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 |
| #177 | Scher, H.I., et al., *Increased survival with enzalutamide in prostate cancer after chemotherapy.* N Engl J Med, 2012. **367**(13): p. 1187-97. | Excluded | Patients previously received chemotherapy. |
| #178 | 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 |
| #179 | Schmidt-Hansen, M., et al., *Hormone and radiotherapy versus hormone or radiotherapy alone for non-metastatic prostate cancer: a systematic review with meta-analyses.* Clin Oncol (R Coll Radiol), 2014. **26**(10): p. e21-46. | Excluded | Hormone and Radiotherapy versus Hormone or Radiotherapy Alone |
| #180 | 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 |
| #181 | Schroder, F.H., et al., *Early versus delayed endocrine treatment of T2-T3 pN1-3 M0 prostate cancer without local treatment of the primary tumour: final results of European Organisation for the Research and Treatment of Cancer protocol 30846 after 13 years of follow-up (a randomised controlled trial).* Eur Urol, 2009. **55**(1): p. 14-22. | Excluded | Comparison is delayed endocrine treatment versus endocrine treatment |
| #182 | 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 |
| #183 | Seal, B.S., et al., *Efficacy, patient-reported outcomes (PROs), and tolerability of the changing therapeutic landscape in patients with metastatic prostate cancer (MPC): a systematic literature review.* Value Health, 2013. **16**(5): p. 872-90. | Excluded | Not a systematic review on RCTs |
| #184 | Serretta, V., et al., *Oral chemotherapy in hormone-refractory prostate carcinoma patients unwilling to be admitted to hospital.* Urol Int, 2009. **83**(4): p. 452-7. | Excluded | Comparison is estramustinephosphate (EMP) + etoposide versus EMP |
| #185 | Sfoungaristos, S., et al., *Contemporary pharmacotherapy for the prevention of skeletal complications in patients with prostate cancer.* Expert Opinion on Pharmacotherapy, 2014. **15**(17): p. 2513-2524. | Excluded | (Narrative) review without pooled analysis (all studies included) |
| #186 | Shamash, J., et al., *Whole blood stem cell reinfusion and escalated dose melphalan in castration-resistant prostate cancer: a phase 1 study.* Clin Cancer Res, 2012. **18**(8): p. 2352-9. | Excluded | No RCT (single-arm study, no control) |
| #187 | 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 |
| #188 | 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 |
| #189 | Shipley, W.U., et al. *Initial report of RTOG 9601, a phase III trial in prostate cancer: Effect of anti-androgen therapy (AAT) with bicalutamide during and after radiation therapy (RT) on freedom from progression and incidence of metastatic disease in patients following radical prostatectomy (RP) with pT2-3,N0 disease and elevated PSA levels*. Journal of clinical oncology, 2011. **29**. | Excluded | Abstract |
| #190 | 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) |
| #191 | Silva, F.C.D., 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*. European urology, 2014. **66**, 232-9 DOI: 10.1016/j.eururo.2013.03.055. | Excluded | Continuation of cyproterone acetate plus triptoreline treatment versus stop treatment |
| #192 | Small, E., et al. *A Phase 2 trial of sipuleucel-T in combination with concurrent or sequential abiraterone acetate (AA) in patients (pts) with metastatic castrate-resistant prostate cancer (mCRPC)*. European journal of cancer, 2013. **49**, S682-s683 DOI: 10.1016/S0959-8049%2813%2970064-9. | Excluded | Abstract |
| #193 | Small, E.J., et al., *A phase II trial of gefitinib in patients with non-metastatic hormone-refractory prostate cancer.* BJU Int, 2007. **100**(4): p. 765-9. | Excluded | No RCT (Single-arm study) |
| #194 | Small, E.J., et al., *Time to disease-related pain and first opioid use in patients with metastatic castration-resistant prostate cancer treated with sipuleucel-T.* Prostate Cancer Prostatic Dis, 2014. **17**(3): p. 259-64. | Excluded | Pooled analysis of three trails with comparison of sipuleucel-T versus control. |
| #195 | 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 |
| #196 | Smith, D.C., et al., *Phase II evaluation of early oral estramustine, oral etoposide, and intravenous paclitaxel combined with hormonal therapy in patients with high-risk metastatic prostate adenocarcinoma: Southwest Oncology Group S0032.* Urology, 2011. **77**(5): p. 1172-6. | Excluded | Patients receive chemotherapy during treatment with anti-androgen |
| #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 zolodronic acid versus placebo |
| #198 | Smith, M.R., et al. *Response to androgen signaling (AS)-directed therapy after treatment with abiraterone acetate (AA) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC): Post hoc analysis of study COU-AA-302*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #199 | Smith, M.R., et al., *Denosumab and bone metastasis-free survival in men with nonmetastatic castration-resistant prostate cancer: exploratory analyses by baseline prostate-specific antigen doubling time.* J Clin Oncol, 2013. **31**(30): p. 3800-6. | Excluded | Comparison is denosumab versus placebo. |
| #200 | 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 | Patients received chemotherapy + no RCT (no control) + Medicine of interest is sunitinib |
| #201 | 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 | Patients received chemotherapy + no RCT (no control) + Medicine of interest is sunitinib |
| #202 | 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) versus weekly docetaxel-prednisone versus mitoxantrone-prednisone |
| #203 | 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). |
| #204 | 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) |
| #205 | 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. | Excluded | Patients received prior chemotherapy (docetaxel) |
| #206 | 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 | Patients received prior chemotherapy (taxane chemotherapy) |
| #207 | Sternberg, C.N., et al. *Fatigue improvement/reduction with abiraterone acetate in patients with metastatic castration-resistant prostate cancer (mCRPC) post-docetaxel - Results from the COU-AA-301 phase 3 study*. European journal of cancer, 2011. **47**, S488-s489 DOI: 10.1016/S0959-8049%2811%2971966-9. | Excluded | Abstract |
| #208 | Suttmann, H., et al. *Exploratory analysis of the visceral disease patient subset in COU-AA-301, a phase III study of abiraterone acetate (AA) in metastatic castration-resistant prostate cancer (mCRPC)*. European Urology, Supplements, 2013. **12**, e105-e106. | Excluded | Patients received prior chemotherapy (docetaxel) |
| #209 | Suzman, D.L., et al., *Clinical activity of enzalutamide versus docetaxel in men with castration-resistant prostate cancer progressing after abiraterone.* Prostate, 2014. **74**(13): p. 1278-1285. | Excluded | No RCT (retrospective analysis) |
| #210 | Sweeney, C., et al. *Impact on overall survival (OS) with chemohormonal therapy versus hormonal therapy for hormone-sensitive newly metastatic prostate cancer (mPrCa): An ECOG-led phase III randomized trial*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #211 | 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) |
| #212 | 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) |
| #213 | 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) |
| #214 | 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 |
| #215 | 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 |
| #216 | 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 |
| #217 | Tomlins, S.A., et al. *Comprehensive molecular profiling of pretreatment metastatic castration resistant prostate cancer (CRPC): Secondary data from NCI 9012, a randomized ETS fusion-stratified phase II trial*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #218 | 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 |
| #219 | 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 |
| #220 | Tunn, U., G. Canepa, and E. Kienle *Intermittent androgen deprivation in patients with PSA relapse after radical prostatectomy*. Urology, 2013. **82**, S48. | Excluded | Abstract |
| #221 | 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 combined androgen blockade versus combined androgen blockade and Zoledronic acid |
| #222 | Verhagen, P., et al. *Intermittent versus continuous cyproterone acetate in bone metastatic prostate cancer: Results of a randomized trial*. European Urology, Supplements, 2013. **12**, e680. | Excluded | Abstract |
| #223 | 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. |
| #224 | 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. |
| #225 | 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 |
| #226 | 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) |
| #227 | Wirth, M., et al., *Bicalutamide (Casodex) 150 mg plus standard care in early non-metastatic prostate cancer: results from Early Prostate Cancer Trial 24 at a median 7 years' follow-up.* Prostate Cancer Prostatic Dis, 2007. **10**(1): p. 87-93. | Excluded | Not patients with metastatic CRPC |
| #228 | 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 |
| #229 | Yu, E.Y., et al. *Association of alkaline phosphatase (ALP) with clinical outcomes in chemotherapy-naive patients (pts) with metastatic castration-resistant prostate cancer (mCRPC): Results from COU-AA-302*. Journal of clinical oncology, 2014. **32**. | Excluded | Abstract |
| #230 | 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 | No control arm (only different doses of Dasatinib) |
| #231 | 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. |

**Full-text evaluation of included studies in Seal, 2013 (N = 13)**

|  |  |  |  |
| --- | --- | --- | --- |
| **#** | **Reference** | **Included / Excluded** | **Reasons** |
| #1 | NilssonS,ParkerC,BigginC,etal.Clinicalexperienceandradiationsafety ofthe first-in-class alpha-pharmaceutical,Alpharadin™(radium-223), inpatientswithcastration-resistantprostatecancer(CRPC) andbonemetastases.Posterpresentedat:AmericanSocietyforRadiation Oncology(ASTRO).SanDiego,CA,October21-November4,2010. | Excluded | Conference abstract |
| #2 | Michaelson MD,KaufmanDS,KantoffP,SmithMR. Randomized phaseII study of atrasentan alone or in combination with zoledronic acid inmen with metastatic prostate cancer.Cancer 2006;107:530–5.PMID: 16804927 | Excluded | Comparison is atrasentan with or without zoledronic acid |
| #3 | Nilsson S,FranzenL,ParkerC,etal.Bone-targetedradium-223insymptomatic, hormone-refractory prostate cancer: a randomised, multicentre, placebo-controlledphaseIIstudy.LancetOncol2007;8(7):587–94. | Excluded | Duplicate |
| #4 | Chi KN,HotteSJ,YuEY,etal.RandomizedphaseIIstudyofdocetaxeland prednisone with or without OGX-011 in patients with metastaticcastration-resistantprostatecancer.JClinOncol2010;28:4247–54.PMID: 20733135 | Excluded | Comparison is docetaxel and prednisone with or without OGX-011 |
| #5 | ParkerC,O’Bryan-Tear CG,BolstadB,etal.Alkalinephosphatase(ALP)normalization andoverallsurvivalinpatientswithbonemetastasesfrom castration-resistantprostatecancer(CRPC)treatedwithradium-223. Posterpresentedat:AmericanSocietyofClinicalOncology(ASCO)Genitourinary CancersSymposium.SanFrancisco,CA,March5–7, 2010. | Excluded | Conference abstract |
| #6 | Tannock IF,deWitR,BerryWR,etal. Docetaxel plus prednisone ormitoxantrone plus prednisone for advanced prostate cancer. N Engl JMed 2004;351:1502–12.PMID: 15470213 | Excluded | Comparison is docetaxel with or without mitoxantrone |
| #7 | Sternberg CN,PetrylakDP,SartorO,etal.Multinational,double-blind,phase III study of prednisone and either satraplatin or placebo inpatients with castrate-refractory prostate cancer progressing after priorchemotherapy: theSPARCtrial.JClinOncol2009;32:5431–8.PMID: 19805692 | Excluded | Comparison is prednisone with or without satraplatin |
| #8 | Kantoff PW,HiganoCS,ShoreND,etal. Sipuleucel- T immunotherapyfor castration-resistantprostatecancer.NEnglJMed2010;363:411–22.PMID: 20818862 | Excluded |  Not right patient population |
| #9 | KellyWK,HalabiS,CarducciMA,etal.Arandomized,double-blind,placebo-controlled phaseIIItrialcomparingdocetaxel,prednisone,andplacebo withdocetaxel,prednisone,andbevacizumabinmenwithmetastatic castration-resistantprostatecancer(mCRPC):survivalresults ofCALGB90401.Abstractpresentedat:ASCOAnnualMeeting.Chicago, IL,June4–8, 2010. | Excluded | Conference abstract |
| #10 | de BonoJS,OudardS,OzgurogluM,etal.Prednisonepluscabazitaxelormitoxantrone for metastatic castration-resistant prostate cancerprogressing afterdocetaxeltreatment:arandomizedopen-labeltrial.Lancet 2010;376:1147–54.PMID: 20888992 | Excluded | Comparison is prednisone with either cabazitaxel or mitoxantrone |
| #11 | de BonoJS,LogothetisCJ,MolinaA,etal.Abirateroneandincreasedsurvival inmetastaticprostatecancer.NEnglJMed2011;364:1995–2005. | Excluded | Patients previously received docetaxel. |
| #12 | Fizazi K,CarducciM,SmithM,etal. Denosumab versus zoledronic acidfor treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study. Lancet 2011;377:813–22.PMID: 21353695 | Excluded | Comparison is denosumab versus zoledronic acid |
| #13 | MeulenbeldHJ,vanWerkhovenED,CoenenJLLM,etal.Randomizedphase IIIstudyofdocetaxelwithorwithoutrisedronateinpatientswith bonemetastasesfromcastration-resistantprostatecancer(CRPC):the NetherlandsProstateStudy(NePro).Abstractpresentedat:ASCOAnnual Meeting.Chicago,IL,June3–7, 2011. | Excluded | Conference abstract |
| #14 | Tombal B,OudardS,OzgurogluM,etal.Clinicalbenefit of cabazitaxel plus prednisone in the TROPIC trial in men with metastatic castration resistant prostate cancer (mCRPC) who progressed after docetaxel-based treatment. Eur Urol Suppl 2011;10:335–6. | Excluded | Conference abstract |
| #15 | SternbergCN,ScherHI,MolinaA,etal.Fatigueimprovement/reductionwith abirateroneacetateinpatientswithmetastaticcastration-resistant prostatecancerpost-docetaxel:resultsfromtheCOU-AA-301phase 3study.Posterpresentedat:EuropeanMultidisciplinaryCancerCongress (EMCC).Stockholm,Sweden,September23–27, 2011. | Excluded | Conference abstract |
| #16 | Basch EM,deBonoJS,ScherHI,etal.Paincontrolanddelayintimetoskeletal-related events(SREs)inpatientswithmetastaticcastration-resistant prostatecancer(mCPRC)treatedwithabirateroneacetate(AA): long-termfollow-up.JClinOncol2012(Suppl.5):abstract183 | Excluded | Conference abstract |
| #17 | deBonoJS,FizaziK,SaadF,etal.Phase3trial(AFFIRM)ofenzalutamide (MDV3100),anandrogenreceptorsignalinginhibitor:primary, secondary,andquality-of-lifeendpointresults.Presentedat:American SocietyofClinicalOncology(ASCO).Chicago,IL,May31-June4, 2012. | Excluded | Conference abstract |
| #18 | ParkerC,NilssonS,HeinrichD,etal.UpdatedanalysisofthephaseIII,double-blind, randomized,multinationalstudyofradium-223chloridein castration-resistantprostatecancer(CPRC)patientswithbonemetastases (ALSYMPCA).Presentedat:AmericanSocietyofClinicalOncology (ASCO).Chicago,IL,May31-June4,2012. | Excluded | Conference abstract |
|  | RyanCJ,deBonoJS,MolinaA,etal.Interimanalysis(IA)resultsofCOU-AA-302, arandomized,phase3studyofabirateroneacetate(AA)inchemotherapy-naïve patients(pts)withmetastaticcastration-resistantprostate cancer(mCRPC).Presentationpresentedat:AmericanSocietyof ClinicalOncology(ASCO).Chicago,IL,May31-June4,2012. | Excluded | Conference abstract |
| #19 | Sartor AO,HeinrichD,O’Sullivan JM,etal.Radium-223chloride(Ra-223) impactonskeletalrelatedevents(SREs)andECOGperformancestatus (PS)inpatientswithcastration-resistantprostatecancer(CRPC)with bonemetastases:interimresultsofaphaseIIItrial(ALSYMPCA).J ClinOncol2012(Suppl)::abstract4551. | Excluded | Conference abstract |

# 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. #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

24. ((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]))

25. 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]

26. #24 OR #25

27. #4 AND #9 AND #23 AND #26

**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. #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

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

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

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

36. #33 OR #34 OR #35

37. #4 AND #9 AND #32 AND #36 AND [embase]/lim **739**

**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. #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

24. #4 AND #9 AND #23 **212**

**Reference list of included studies**

[[1-16](#_ENREF_1)]

1. Akaza, H., et al., *Combined androgen blockade with bicalutamide for advanced prostate cancer: long-term follow-up of a phase 3, double-blind, randomized study for survival.* Cancer, 2009. **115**(15): p. 3437-45.

2. 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.

3. Basch, E., et al., *Abiraterone acetate plus prednisone versus prednisone alone in chemotherapy-naive men with metastatic castration-resistant prostate cancer: Patient-reported outcome results of a randomised phase 3 trial.* The Lancet Oncology, 2013. **14**(12): p. 1193-1199.

4. Beer, T.M., et al. *Enzalutamide in metastatic prostate cancer before chemotherapy*. The New England journal of medicine, 2014. **371**, 424-33 DOI: 10.1056/NEJMoa1405095.

5. 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.

6. Kantoff, P.W., et al., *Sipuleucel-T immunotherapy for castration-resistant prostate cancer.* N Engl J Med, 2010. **363**(5): p. 411-22.

7. 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.

8. Morris, M.J., et al., *Radiographic progression-free survival as a response biomarker in metastatic castration-resistant prostate cancer: COU-AA-302 results.* Journal of Clinical Oncology, 2015. **33**(12): p. 1356-1363.

9. 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.

10. 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.

11. Nome, R., et al., *Changes in prostate-specific antigen, markers of bone metabolism and bone scans after treatment with radium-223.* Scand J Urol, 2015. **49**(3): p. 211-7.

12. 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.

13. 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**, 815-25 DOI: 10.1016/j.eururo.2014.02.056.

14. 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.

15. 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.

16. 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.