Prostate International 12 (2024) 186–194

Contents lists available at ScienceDirect

Prostate International

journal homepage: https://www.journals.elsevier.com/prostate-international

Research Article

Cardiovascular risks of Asian patients on androgen-receptor-targeted agents for prostate cancer: a systematic review and meta-analysis

Lin Kyaw [a], Qi Y. Lim [a], Yu X.T. Law [a], Chloe S.H. Ong [a], Wei T. Loke [b], Edmund Chiong [a, c, *], Ho Y. Tiong [a, c]

[a] Department of Urology, National University Hospital, National University Health System, Singapore
[b] Division of Urology, Ng Teng Fong General Hospital, National University Health System, Singapore
[c] Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

ARTICLE INFO

Article history:
Received 3 June 2024
Received in revised form
22 July 2024
Accepted 29 July 2024
Available online 7 August 2024

Keywords:
Androgen receptor targeted agents
Asian
Prostate cancer

ABSTRACT

Background: Prostate cancer is now one of the most prevalent cancers in men in Asia. As the average life expectancy of Asian males with prostate cancer increases with the availability of treatment options, the possible risk of cardiac-related adverse effects arising from androgen-receptor-targeted agents (ARTAs) may be increased due to the greater exposure. We aim to perform a meta-analysis on the incidence of cardiac-related adverse events in Asian patients with prostate cancer treated with ARTAs.

Materials and methods: Databases were thoroughly searched for relevant articles. The Patient Intervention Comparison Outcome Study type model was used to frame our clinical question, and 2 independent authors went through several rounds of screening to select the final included studies. A meta-analysis was conducted using the Cochran–Mantel–Haenszel method. Quality assessment was carried out with the Cochrane risk-of-bias tool RoB 2.

Results: Seven randomized controlled trials were included for the final meta-analysis. Use of ARTA in Asian men did not show any significant increase in the total number of cardiac-related adverse events (risk ratio [RR]: 1.66 [0.84–3.26], p = 0.14). However, there was increase in incidence of hypertension (RR: 2.30 [1.41–3.73], p = 0.0008) and hypertension crises (RR: 16.87 [2.13–133.34], p = 0.007). A subgroup analysis of the type of ARTA used showed enzalutamide having the highest risk of hypertension (RR: 5.86 [2.10–16.38], p = 0.0008).

Conclusion: :Although ARTAs did not show any significant increase in incidence of cardiac-related adverse events, there is an increased risk of hypertension especially with the use of enzalutamide. With this knowledge, closer blood pressure monitoring is needed for patients started on ARTA, especially enzalutamide.

1. Introduction

Prostate cancer patients on androgen deprivation therapy inevitably progress with time, resulting in castration-resistant prostate cancer (CRPC). Multiple clinical trials have supported the use of androgen-receptor-targeted agents (ARTAs) such as abiraterone acetate, enzalutamide, darolutamide, and apalutamide in CRPC, metastatic hormone-sensitive prostate cancer, and non-metastatic CRPC, with strong evidence of improvement in oncological outcomes.[1–5] Treatment for patients with prostate cancer has improved significantly with good oncological results,[6] and metastatic prostate cancer patients who are now living longer with the addition ARTAs also have longer exposure to the therapy and its associated side-effects. Studies have examined the cause of death in prostate cancer patients, reporting that most noncancer deaths were cardiac-related.[7] Recent studies have shown ARTA increases the risk of cardiac-related adverse events, hypertension, ischemic heart disease, and arrhythmia; however, majority of the patients in the trials are non-Asian.[8] In 2020, prostate cancer was one of the top three most prevalent cancers in men in 20 of 47 Asian countries, with nearly one-third of worldwide prostate cancer deaths in 2020 occurred in Asia.[9] Therefore, in this study, we aim to assess the differences in the incidence of cardiac-related adverse events after treatment in Asian patients with prostate cancer on ADT and ARTA versus ADT and placebo.

* Corresponding author. Department of Urology, National University Hospital, National University Health System. 5 Lower Kent Ridge Road, 119074, Singapore.
E-mail address: surce@nus.edu.sg (E. Chiong).

https://doi.org/10.1016/j.prnil.2024.07.004
p2287-8882 e2287-903X/

2. Materials and methods

2.1. Search strategy

We performed a meta-analysis and systematic review following the Preferred Reporting Items for Systematic Review and Meta-analysis[10] and Cochrane Handbook of Systematic Reviews of Interventions Version 6.3.[11] This review was conducted on a prespecified protocol registered on the International Prospective Register of Systematic Reviews (CRD42022383419) prior to commencement. A thorough literature review was conducted on Medline, Embase, Cochrane CENTRAL, ClinicalTrials.gov, and International Clinical Trials Registry Platform from inception to 31st July 2023. Key search phrases used includes "Prostate cancer," "Androgen Receptor Targeted Agents," "Abiraterone," "Enzalutamide," "Apalutamide," and "Darolutamide." The full search strategy is available in the supplementary material. Additional articles were sought from the reference lists of the included articles.

2.2. Selection criteria

The Patient Intervention Comparison Outcome Study type model was used to frame and answer the clinical question. Patient: Asian patients with prostate cancer (metastatic or nonmetastatic, hormone-sensitive or hormone-resistant); Intervention: Asian patients treated with ADT and ARTA; Comparison:

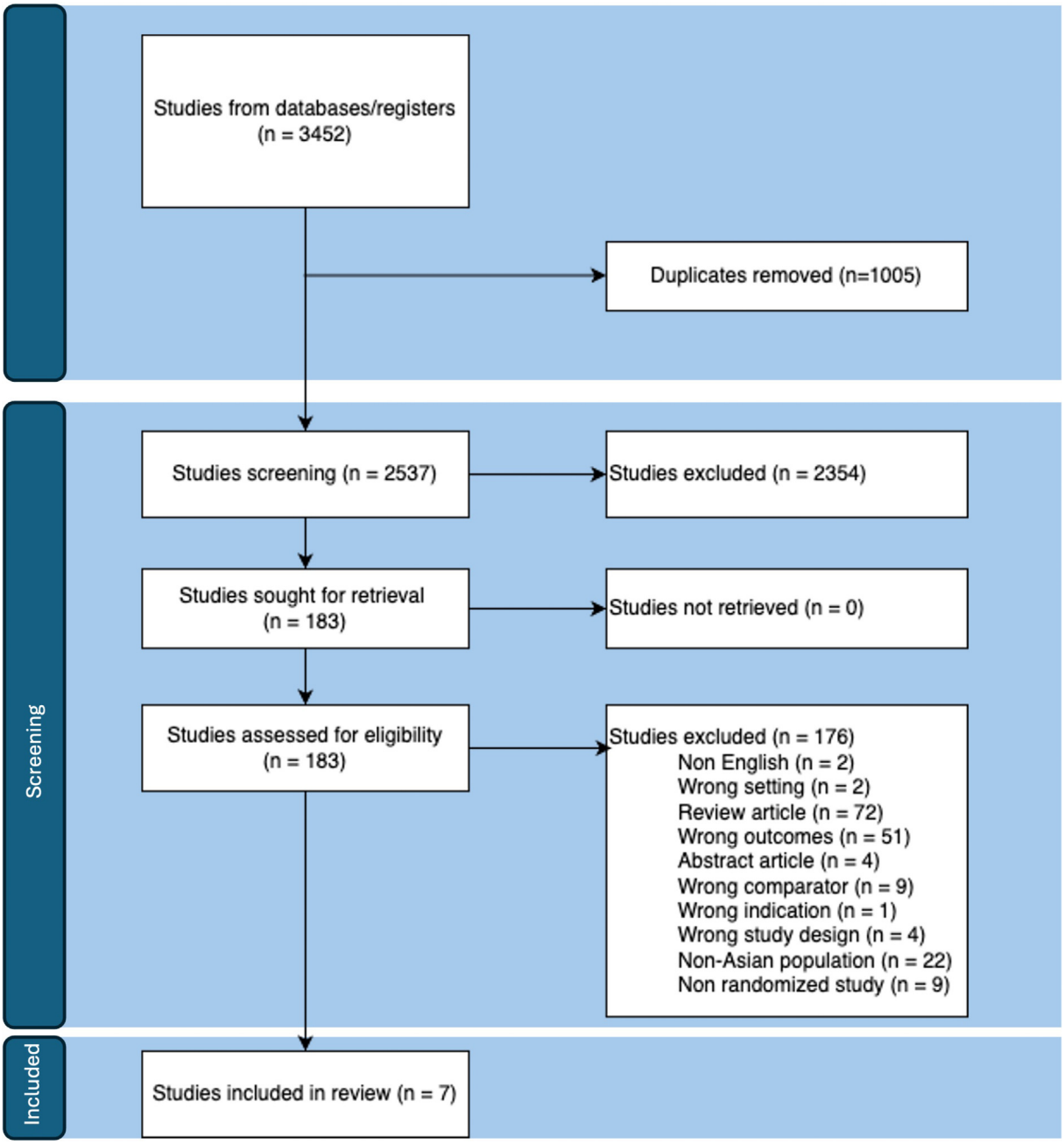


Fig. 1. PRISMA diagram. Abbreviation: PRISMA = Preferred Reporting Items for Systematic Review and Meta-analysis.

Asian patients treated with ADT and placebo; Outcome: cardiac-related adverse events; Study type: randomized clinical trials (RCTs) only.

2.3. Measured outcomes

We gathered data on the following cardiac-related adverse events: total cardiac events/disorders and cardiac arrests/deaths, hypertension, hypertension crisis, ischemic heart disease, arrhythmias, cardiac failure, valvular diseases, and pericardial diseases.

2.4. Study selection

We included only randomized controlled trials that reported results from only Asian patients, looking at ARTAs versus ADTs alone for treatment of prostate cancer, regardless of the subtype of prostate cancer (i.e., metastatic or nonmetastatic, castrate-sensitive or castrate-resistant). Studies reporting data of non-Asian patients as well as those using ARTAs for other indications were excluded if they did not contain subanalyses of Asian patients. Animal studies and studies in pediatric population were also excluded. Full manuscripts were obtained. Letters to editor, conference abstracts, and review articles were excluded. Non-English-language papers were excluded if there are no available formal translated versions available.

2.5. Data collection

After removing duplicates, two reviewers (LK, QYL) screened through titles and abstracts independently. All articles identified from the first screen then underwent another round of independent screen of full-text articles, followed by data extraction. The data to be extracted were predefined at the start of the study, and this includes first author, year of publication, country of study, study population, type of ARTA used, and cardiac-related adverse events. Any conflicts between the 2 independent reviewers were resolved by a third reviewer (CSHO). The process is facilitated through use of Covidence Systematic Review Management®. Any discrepancies were resolved with a third reviewer (YXTL).

2.6. Quality assessment and data analysis

Quality of included randomized controlled trials was assessed using the 'Risk of Bias 2.0' (RoB 2.0) tool.[12] Meta-analyses were preformed when there were two or more studies reporting the same adverse events under the same definition. The incidences of adverse events were pooled using the Cochran–Mantel–Haenszel method using the random-effect model and expressed as risk ratios (RRs), 95% confidence intervals, and p-values. RRs of >1[1] indicate increased risk of the adverse events in patients treated with ARTA. Analyses were two-tailed, with a significance set at $p < 0.05$ and a 95% confidence interval. Study heterogeneity was assessed utilizing the I^2 value. Substantial heterogeneity was defined as an I^2 value of >50% or a Chi-square p-value of <0.10. This was performed using Review Manager (RevMan) version 5.4 software by Cochrane Collaboration.

3. Results

3.1. Study selection

After removing duplicates, 2537 unique records were obtained. A total of 2354 records were excluded after review of titles and abstracts. A full-text review of the remaining 183 texts was carried

Table 1
Details of included studies.

Author	Year of publication	Name of trial, if applicable	Study population	Type of ARTA used	Median duration of treatment (months)	Median duration of follow-up (months)	Number of patients		Stage of disease	Chemo therapy	ADT	Radio therapy	Number of patients with Gleason score ≥8	
							ARTA	Placebo					ARTA	Placebo
Chung	2022	TITAN	China, Japan, Korea	Apalutamide	19.2	21.2	111	110	mHSPC	Y	Y	Y	96	95
Iguchi	2021	ARCHES	Japan	Enzalutamide	13.7	15.7	36	56	mHSPC	Y	Y	Y	33	47
Pu	2022	N/A	China, Korea, Taiwan, Hong Kong	Enzalutamide	6.6	NR	198	190	mCRPC	N	Y	Y	138	117
Sun	2016	N/A	China	Abiraterone	7.0	60.0	143	71	mCRPC	N	Y	N	72	41
Suzuki	2020	LATITUDE	Japan	Abiraterone	25.8	56.6	35	35	mHSPC	N	Y	Y	34	34
Uemura	2020	SPARTAN	Japan	Apalutamide	5.0	18.0	34	21	nmCRPC	N	Y	N	25	14
Uemura	2021	ARAMIS	Japan	Darolutamide	14.8	18.2	62	33	nmCRPC	N	Y	N	58	30

Abbreviations: ARTA, androgen-receptor-targeted agent; mHSPC, metastatic hormone-sensitive prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer.

out. Finally, a total of 7 RCT studies were identified to be included for the final meta-analysis.[13–19] More details can be found in the Preferred Reporting Items for Systematic Review and Meta-analysis diagram (Fig. 1).

3.2. Study characteristics

A total of 1135 patients were included across all studies; 619 received ARTA, whereas 516 received placebo alone. Of the 7 studies, abiraterone was used in 2 studies, enzalutamide in 2, apalutamide in 2, and darolutamide in 1 study. Five of the 7 studies are subgroup analyses of larger global trials, and the remaining 2 RCTs were held in Asian countries only. Further study characteristics are described in Table 1.

3.3. Quality assessment

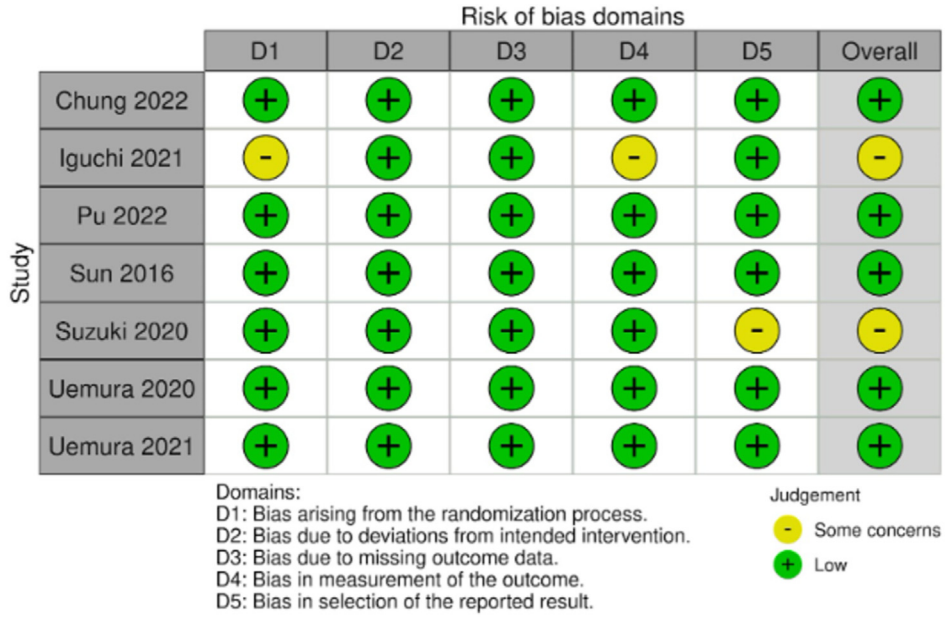
Based on the RoB 2.0 tool, 5 out of 7 studies showed a low risk of bias for all quality criteria, whereas the remaining 2 showed some concerns. Details of quality assessment are found in Fig. 2.

3.4. Cardiac events/disorders

Six out of 7 studies[14–19] reported the total number of cardiac events or disorders. The total number of patients included was 914, of which 28 events occurred in the ARTA group and 11 events in the placebo group. Analysis shows that there is no significant increase in the total number of cardiac adverse events between both groups (RR: 1.66 [0.84–3.26], p = 0.14). A subgroup analysis of the types of ARTA also did not show differences in abiraterone (RR: 1.44 [0.6–3.45], p = 0.13) and enzalutamide (RR: 1.94 [0.56–6.69]). Subgroup analyses of apalutamide and darolutamide were not possible as there was only 1 study for each (Fig. 3).

3.5. Hypertension and hypertension crisis

All studies reported total events of hypertension. The total number of patients included was 1135 (619 ARTA), of which 92 events occurred in the ARTA group and 39 events in the placebo group. Analysis shows that there is a significant increase in the total occurrence of hypertension between both groups (RR: 2.30



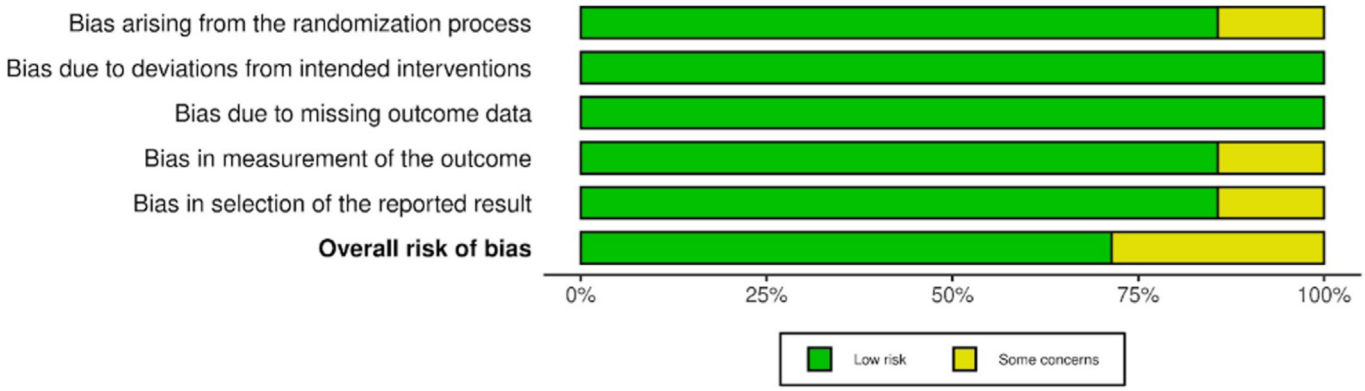


Fig. 2. Risk of bias assessment of included studies.

[1.41–3.73], p = 0.0008). A subgroup analysis of the types of ARTA also did not show differences in abiraterone (RR: 2.07 [0.78–5.46], p = 0.14) and apalutamide (RR: 1.72 [0.87–3.38], p = 0.12). There is significant difference for enzalutamide (RR: 5.86 [2.10–16.38], p = 0.0008). Subgroup analyses of darolutamide were not possible as there was only 1 study (Fig. 4).

Only 3[14,15,19] studies reported events of hypertensive crisis (2 enzalutamide, 1 apalutamide). The total number of patients included was 535 (268 ARTA), of which 12 events occurred in the ARTA group, and 0 events occurred in the placebo group. Analysis shows a significant increase in the total occurrence of hypertensive crises between both groups (RR: 16.87 [2.13–133.34], p = 0.007). Subgroup analyses were not possible as all 12 events occurred in the enzalutamide group (Fig. 5).

3.6. Cardiac arrests/deaths

Four out of 7 studies[14–16,19] reported the total number of cardiac arrests or deaths. The total number of patients included was 749 (411 ARTA), of which 2 events occurred in the ARTA group and 0 events in the placebo group. Analysis shows that there is no significant increase in the total number of cardiac arrests/deaths events between both groups (RR: 4.85 [0.23–101.63], p = 0.31). Subgroup analyses were not possible as all 2 events occurred in the enzalutamide group (Fig. 6).

3.7. Other cardiac events

We are unable to report the rest of the cardiac events of ischemic heart disease, arrhythmias, heart failure, valvular heart disease, and pericardial heart disease, which was initially part of our study protocol as there were not enough data reported amongst the included studies.

4. Discussion

This is the first study, to our knowledge, providing a meta-analysis on cardiovascular side-effects of Asian patients receiving ARTAs for prostate cancer. The result of this study is clinically important as prostate cancer is now one of the most prevalent cancers in Asian countries. With better treatment available that increases overall survival of patients with prostate cancer, side-effects of treatment are becoming more crucial. An understanding in life-threatening side-effects such as incidence of cardiac-related adverse effects in patients receiving ARTAs is important in guiding clinicians toward a judicious medical

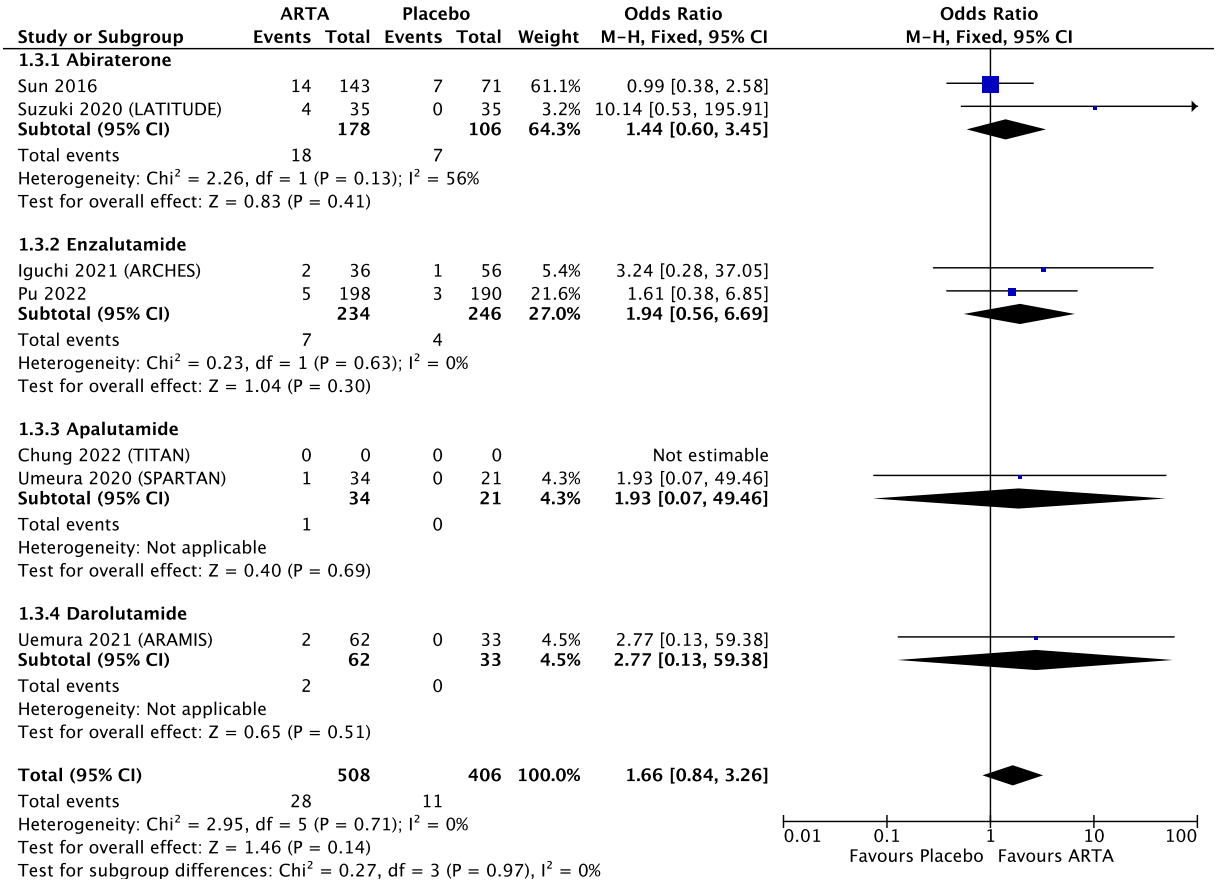


Fig. 3. Forest plot of total cardiac events/disorders.

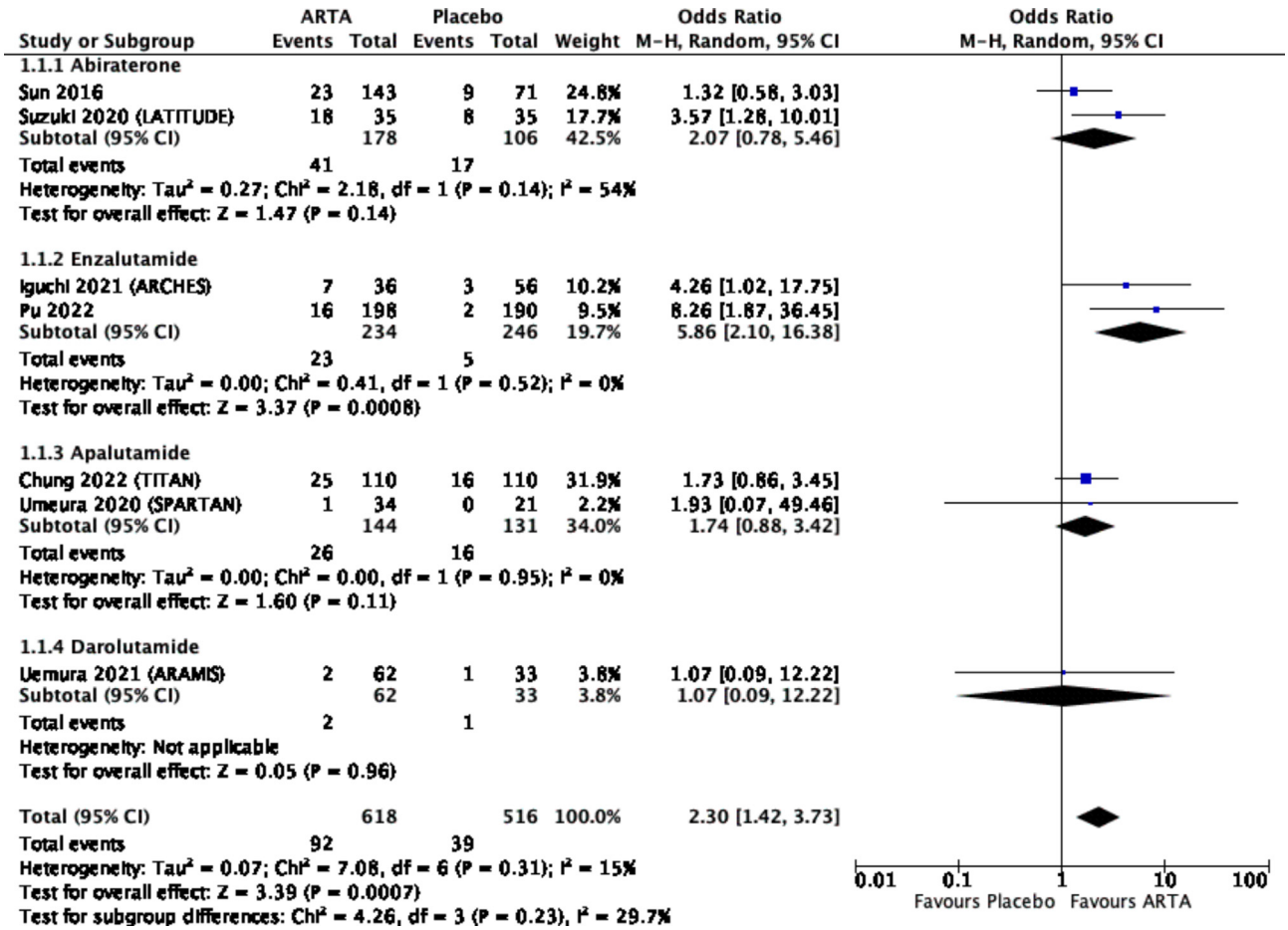


Fig. 4. Forest plot of incidence of hypertension.

intervention choice for prostate cancer patients—especially those with underlying cardiac comorbidities.

4.1. Hypertension and hypertension crisis

Our meta-analysis has shown that ARTAs increased the risk of hypertension by 130%, which was also reflected in previous studies.[20,21] In the subgroup analysis, only enzalutamide increased the risk of hypertension by 486%; the risk was not shown in abiraterone and apalutamide. This is similar to the result founf in a recent meta-analysis including both Asian and non-Asian patients that enzalutamide has the highest risk of hypertension compared with the rest of ARTAs,[8] even though enzalutamide only has the effect of antiandrogen and lacks the dual effect from androgen deprivation and increased mineralocorticoid levels resulting from CYP17 inhibition with abiraterone, suggesting a possible stronger vascular effect of hypogonadism.[22]

The mechanism by which enzalutamide causes hypertension compared to abiraterone and apalutamide may be due to multiple factors. Enzalutamide is a potent androgen-receptor inhibitor that blocks androgen signaling pathways, leading to androgen deprivation.[23] This deprivation is associated with increased vasoconstriction and smooth muscle proliferation due to endothelial dysfunction. Low testosterone levels, a consequence of androgen-receptor inhibition, are known to impair endothelial function, which can contribute to hypertension.[24] Specifically, enzalutamide's mechanism involves blocking Ca^{2+} influx through voltage-operated calcium channels and nonvoltage-operated calcium channels, leading to reduced vasodilation.[22] Furthermore, enzalutamide's antitumor effects reduce vascular endothelial growth factor production from tumors, potentially reversing cancer-induced hypotension and thereby increasing blood pressure as a part of the broader metabolic syndrome.[25] This effect is more pronounced with enzalutamide than with abiraterone, which not only inhibits CYP17, reducing testosterone synthesis, but also increases mineralocorticoid levels that contribute to hypertension.

4.2. Cardiac events/disorders, including deaths

Our meta-analysis did not show any differences in occurrence of total cardiac events, disorders, and deaths in patients taking any form of ARTAs. This is unlike what is seen in other studies

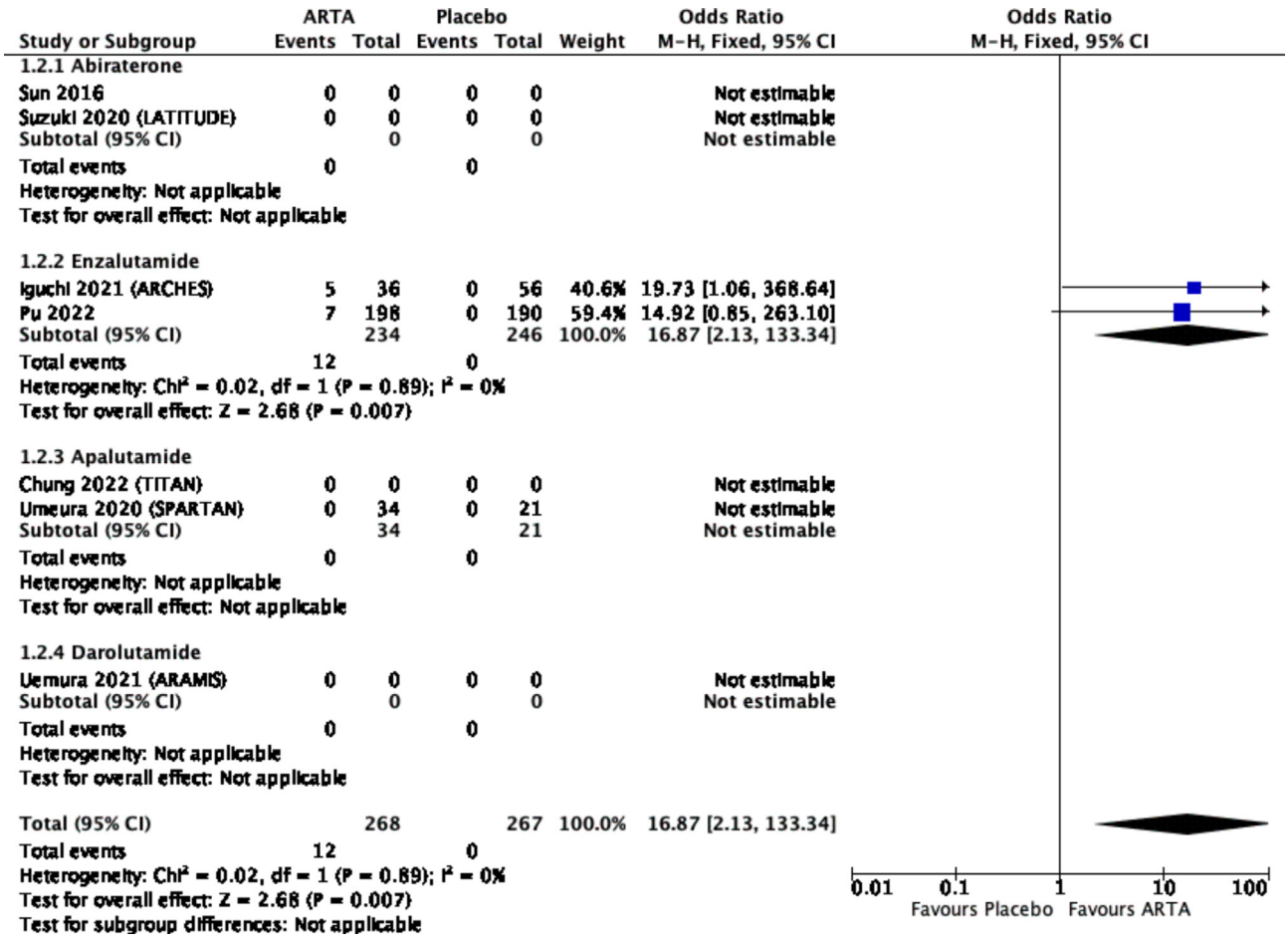


Fig. 5. Forest plot of incidence of hypertensive crisis.

comparing the wider population receiving ARTAs.[8] The likelihood of developing cardiovascular disease can vary largely based on other factors such as genetic predisposition, lifestyle, and socio-economic factors, which may account of the difference seen in our study.

However, studies looking at differences between Asian and non-Asian populations show that Asians are more prone to central obesity,[26] have higher insulin resistance,[27] and often take higher carbohydrates and sodium in their diet.[28] These factors are likely to increase the risk of cardiovascular events in the population of our study. Whether or not Asian patients on ARTAs truly have relative lower risk of developing cardiovascular events remains to be determined by further studies.

Our study did not show any difference in total cardiac events and disorders between abiraterone and enzalutamide when comparing RRs in subgroup analyses. However, in a recent head-to-head retrospective study conducted in Hong Kong by Lee et al., comparing the incidence of new-onset 4-point major adverse cardiovascular events (which is defined by occurrence of first occurrence of stroke, myocardial infarction, heart failure and all-cause mortality) between Abiraterone and Enzalutamide for patients with prostate cancer, their results show that enzalutamide was associated with lower 4-point major adverse cardiovascular events than was abiraterone.[29] This difference might be due to differences in study methodology, and further prospective studies comparing incidences of cardiovascular events while on different ARTAs should be considered.

4.3. Limitations

This meta-analysis was only able to definitively demonstrate a significant increase in hypertension and hypertensive crisis in patients treated with ARTAs but not any other cardiac-related adverse events. We do acknowledge a few limitations of our meta-analysis. Firstly, there was heterogeneity in the composite studies as the patient populations are different (nonmetastatic hormone-sensitive, nonmetastatic castration-resistant, metastatic hormone-sensitive, and metastatic castration-resistant), with different durations of treatment and different adjuvant treatment (radiotherapy, surgery, type of ADT, and chemotherapy). Secondly, this study only has 1135 patients for analysis compared to other meta-analysis studies for the non-Asian population, which has at least 10000 patients.

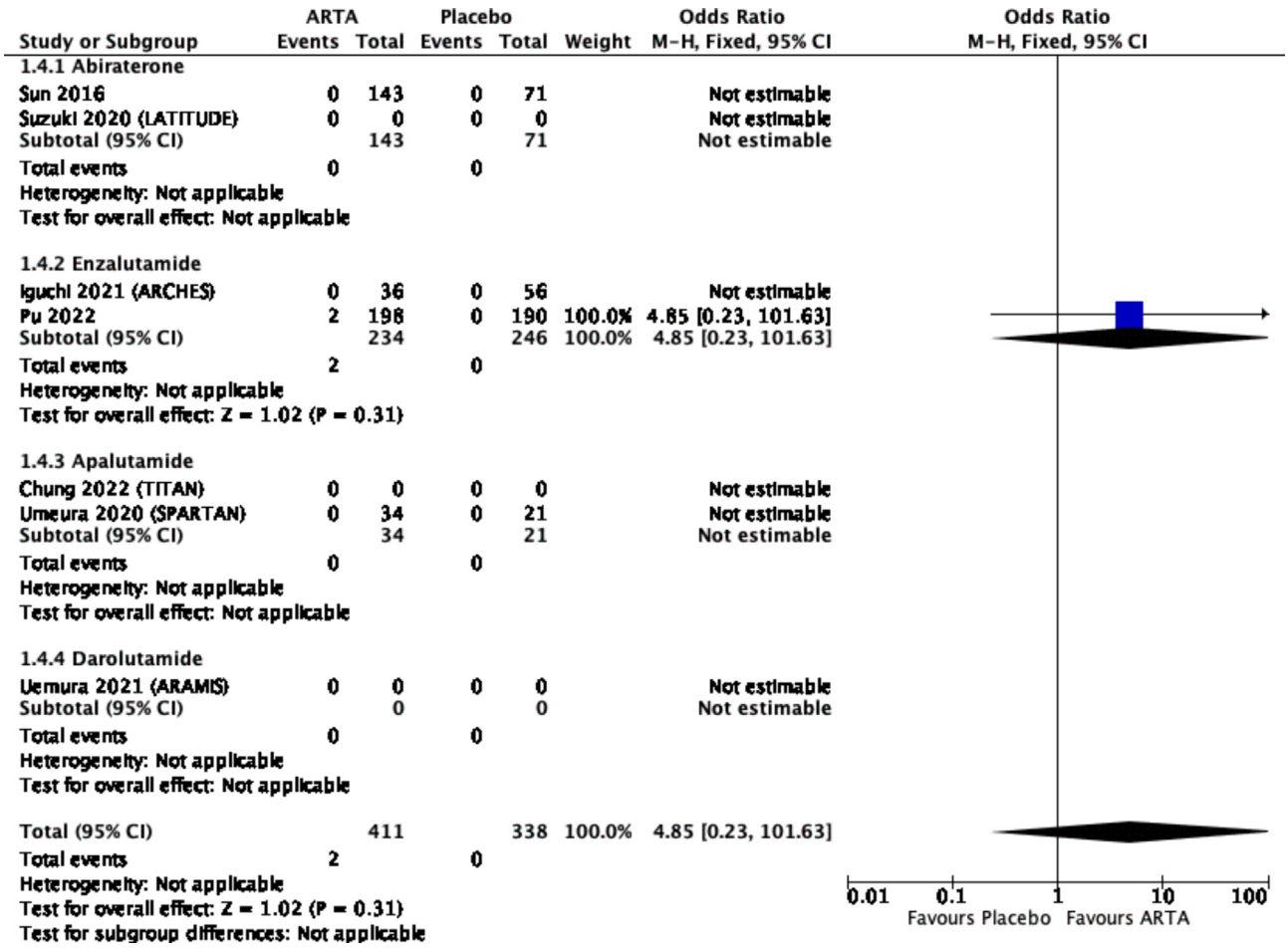


Fig. 6. Forest plot of cardiac arrest/deaths.

5. Conclusion

In conclusion, our systematic review and meta-analysis has shown that the use of ARTA in Asians with prostate cancer increases the incidence of hypertension and that this is especially apparent in enzalutamide. However, other cardiac-related adverse events and cardiac arrests/deaths are not shown to be more common in Asians with prostate cancer while on ARTAs. With this knowledge, we should monitor the blood pressure of these patients started on ARTA, especially enzalutamide, closely to catch any complications as early as possible.

Conflicts of interest

There is no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.prnil.2024.07.004.

References

1. Fizazi K, Tran N, Fein L, Matsubara N, Rodriguez-Antolin A, Alekseev BY, et al. Abiraterone acetate plus prednisone in patients with newly diagnosed high-risk metastatic castration-sensitive prostate cancer (LATITUDE): final overall survival analysis of a randomised, double-blind, phase 3 trial. Lancet Oncol 2019 May;20(5):686–700.
2. Armstrong AJ, Szmulewitz RZ, Petrylak DP, Holzbeierlein J, Villers A, Azad A, et al. ARCHES: a randomized, phase III study of androgen deprivation therapy with enzalutamide or placebo in men with metastatic hormone-sensitive prostate cancer. J Clin Oncol 2019 Nov 10;37(32):2974–86.
3. Smith MR, Shore N, Tammela TL, Ulys A, Vjaters E, Polyakov S, et al. Darolutamide and health-related quality of life in patients with non-metastatic castration-resistant prostate cancer: an analysis of the phase III ARAMIS trial. Eur J Cancer 2021 Sep;154:138–46.
4. Chi KN, Chowdhury S, Bjartell A, Chung BH, Pereira de Santana Gomes AJ, Given R, et al. Apalutamide in patients with metastatic castration-sensitive prostate cancer: final survival analysis of the randomized, double-blind, phase III TITAN study. J Clin Oncol 2021 Jul 10;39(20):2294–303.
5. Fujita N, Hatakeyama S, Tabata R, Okita K, Kido K, Hamano I, et al. Real-world effects of novel androgen receptor axis-targeted agents on oncological outcomes in non-metastatic castration-resistant prostate cancer: a multi-institutional retrospective study. Prostate Int 2024 Mar;12(1):46–51.
6. Lee J, Song J, Jung G, Song SH, Hong SK. Prognosis after radical prostatectomy in men older than 75 years: long-term results from a single tertiary center. Prostate Int 2024 Mar;12(1):15–9.
7. Guo Y, Dong X, Mao S, Yang F, Wang R, Ma W, et al. Causes of death after prostate cancer diagnosis: a population-based study. Oxid Med Cell Longev 2022 Apr 23;2022:1–12.
8. Ong CSH, Law YXT, Kyaw L, Lim QY, Loke T, Wu QH, et al. Cardiovascular risks of androgen receptor targeted agents in prostate cancer: a systematic review and meta-analysis. Prostate Cancer Prostatic Dis 2024 Jan 24;27(3):393–403.
9. Zhu Y, Mo M, Wei Y, Wu J, Pan J, Freedland SJ, et al. Epidemiology and genomics of prostate cancer in Asian men. Nat Rev Urol 2021 May 10;18(5):282–301.
10. Moher D. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009 Aug 18;151(4):264.
11. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. *Cochrane*; 2022 [cited 2023 Aug 10]. Cochrane Handbook for Systematic Reviews of Interventions version 6.3 . Available from: www.training.cochrane.org/handbook.

12. Higgins JPT, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011 Oct 18;343 (oct18 2):d5928–d5928.
13. Chung BH, Huang J, Ye ZQ, He DL, Uemura H, Arai G, et al. Apalutamide for patients with metastatic castration-sensitive prostate cancer in East Asia: a subgroup analysis of the TITAN trial. Asian J Androl [Internet] 2022 Mar 1;24(2):161–6 [cited 2024 Apr 16]. Available from: https://pubmed.ncbi.nlm.nih.gov/34259202/.
14. Iguchi T, Kimura G, Fukasawa S, Suzuki H, Uemura H, Nishimura K, et al. Enzalutamide with androgen deprivation therapy in Japanese men with metastatic hormone-sensitive prostate cancer: a subgroup analysis of the phase III ARCHES study. Int J Urol [Internet] 2021 Jul 1;28(7):765–73 [cited 2024 Apr 16]. Available from: https://pubmed.ncbi.nlm.nih.gov/33955599/.
15. Pu YS, Ahn H, Han W, Huang SP, Wu HC, Ma L, et al. Enzalutamide in chemotherapy-naïve metastatic castration-resistant prostate cancer: an Asian multiregional, randomized study. Adv Ther [Internet] 2022 Jun 1;39(6):2641–56 [cited 2024 Apr 16]. Available from: https://pubmed.ncbi.nlm.nih.gov/35397772/.
16. Sun Y, Zou Q, Sun Z, Li C, Du C, Chen Z, et al. Abiraterone acetate for metastatic castration-resistant prostate cancer after docetaxel failure: a randomized, double-blind, placebo-controlled phase 3 bridging study. Int J Urol [Internet] 2016 May 1;23(5):404–11 [cited 2024 Apr 16]. Available from: https://pubmed.ncbi.nlm.nih.gov/26879374/.
17. Suzuki H, Shin T, Fukasawa S, Hashine K, Kitani S, Ohtake N, et al. Efficacy and safety of abiraterone acetate plus prednisone in Japanese patients with newly diagnosed, metastatic hormone-naive prostate cancer: final subgroup analysis of LATITUDE, a randomized, double-blind, placebo-controlled, phase 3 study. Jpn J Clin Oncol [Internet] 2020 Jul 1;50(7):810–20 [cited 2024 Apr 16]. Available from: https://pubmed.ncbi.nlm.nih.gov/32188988/.
18. Uemura H, Matsushima H, Kobayashi K, Mizusawa H, Nishimatsu H, Fizazi K, et al. Efficacy and safety of darolutamide in Japanese patients with non-metastatic castration-resistant prostate cancer: a sub-group analysis of the phase III ARAMIS trial. Int J Clin Oncol [Internet] 2021 Mar 1;26(3):578–90 [cited 2024 Apr 16]. Available from: https://pubmed.ncbi.nlm.nih.gov/33226524/.
19. Uemura H, Satoh T, Tsumura H, Arai G, Imanaka K, Shibayama K, et al. Efficacy and safety of apalutamide in Japanese patients with nonmetastatic castration-resistant prostate cancer: a subgroup analysis of a randomized, double-blind, placebo-controlled, Phase-3 study. Prostate Int [Internet] 2020 Dec 1;8(4):190–7 [cited 2024 Apr 16]. Available from: https://pubmed.ncbi.nlm.nih.gov/33425798/.
20. Rizzo A, Merler S, Sorgentoni G, Oderda M, Mollica V, Gadaleta-Caldarola G, et al. Risk of cardiovascular toxicities and hypertension in nonmetastatic castration-resistant prostate cancer patients treated with novel hormonal agents: a systematic review and meta-analysis. Expert Opin Drug Metab Toxicol 2021 Oct;17(10):1237–43.
21. Iacovelli R, Ciccarese C, Bria E, Romano M, Fantinel E, Bimbatti D, et al. The cardiovascular toxicity of abiraterone and enzalutamide in prostate cancer. Clin Genitourin Cancer 2018 Jun;16(3):e645–53.
22. Zhu X, Wu S. Increased risk of hypertension with enzalutamide in prostate cancer: a meta-analysis. Cancer Invest 2019 Oct 21;37(9):478–88.
23. Chung C, Abboud K. Targeting the androgen receptor signaling pathway in advanced prostate cancer. Am J Health Syst Pharm 2022 Jul 22;79(15):1224–35.
24. Muniyan S, Xi L, Datta K, Das A, Teply BA, Batra SK, et al. Cardiovascular risks and toxicity - the Achilles heel of androgen deprivation therapy in prostate cancer patients. Biochim Biophys Acta Rev Cancer 2020 Aug;1874(1)188383.
25. Ali BM, El-Abhar HS, Abdallah DM, Mohamed G, Sharaky M, Shouman SA, et al. The enzalutamide and EPI-001 modulate cell proliferation and metastasis markers in T47D by targeting AR/ARV7. Indonesian J Pharm [Internet] 2023 Dec 15;34(4). Available from: https://journal.ugm.ac.id/v3/IJP/article/view/7416.
26. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004 Jan 10;363(9403):157–63.
27. Ma RCW, Chan JCN. Type 2 diabetes in East Asians: similarities and differences with populations in Europe and the United States. Ann N Y Acad Sci [Internet] 2013;1281(1):64–91 [cited 2024 Apr 16]. Available from: https://pubmed.ncbi.nlm.nih.gov/23551121/.
28. Misra A, Singhal N, Khurana L. Obesity, the metabolic syndrome, and type 2 diabetes in developing countries: role of dietary fats and oils. J Am Coll Nutr [Internet] 2010 Jun 1;29(3 Suppl):289S–301S [cited 2024 Apr 16]. Available from: https://pubmed.ncbi.nlm.nih.gov/20823489/.
29. Lee YHA, Hui JMH, Leung CH, Tsang CTW, Hui K, Tang P, et al. Major adverse cardiovascular events of enzalutamide versus abiraterone in prostate cancer: a retrospective cohort study. Prostate Cancer Prostatic Dis 2023 Dec 5. https://doi.org/10.1038/s41391-023-00757-0.