# P3: PROSTATE CANCER FORUM 2025

## Perspectives, Possibilities, Progress

## POST-MEETING SUMMARY SLIDES

# At the heart of the matter: cardiovascular risk assessment and care in prostate cancer patients

**Dr Omar El-Taji**, RCS PhD Clinical Research Fellow in Urological Oncology, University of Manchester; The Christie Hospital NHS Trust
**Dr Patrick Davey**, Consultant Cardiologist, Northampton General Hospital

This promotional meeting was organised and funded by Bayer PLC. Bayer products were discussed at this meeting.
Prescribing Information for products mentioned can be found towards the end of the presentation.
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PP-NUB-GB-2461
June 2025

# Disclosures

## Dr Omar El-Taji

- Honoraria
  - Bayer
  - Accord
  - Ipsen

## Dr Patrick Davey

- Speaker fees, educational and travel support from:
  - Accord
  - Boehringer Ingelheim Ltd
  - Ferring Pharma
  - AstraZeneca
  - Daiichi Sankyo UK Ltd
  - Eli Lilly & Company Ltd
- Clinical and strategic advice for:
  - Consultant Connect, Oxford
  - iRhythm Zio

# Overview

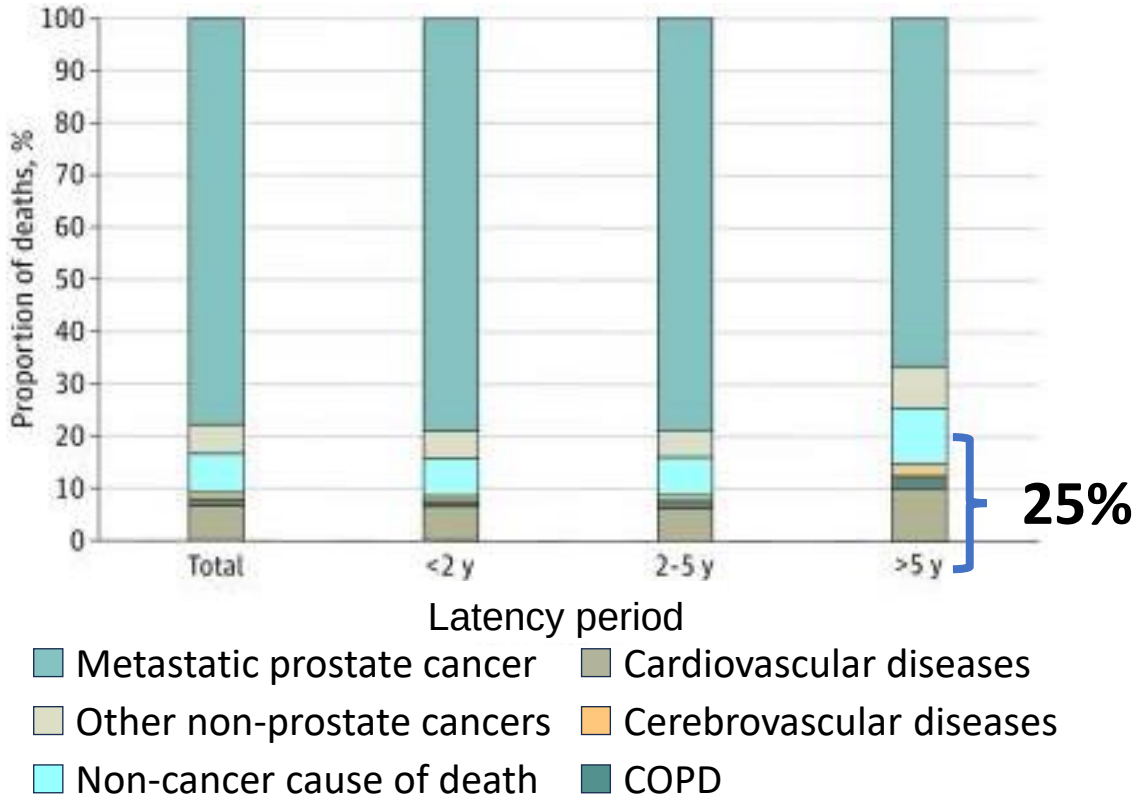
**This presentation will cover:**

- The importance of awareness of CVD in prostate cancer
- Pathophysiology of CVD in prostate cancer
- Cardiovascular risks associated with treatment for prostate cancer
- How to assess cardiovascular risk in prostate cancer patients
- Guidelines and recommendations for preventing CVD events

CVD, cardiovascular disease

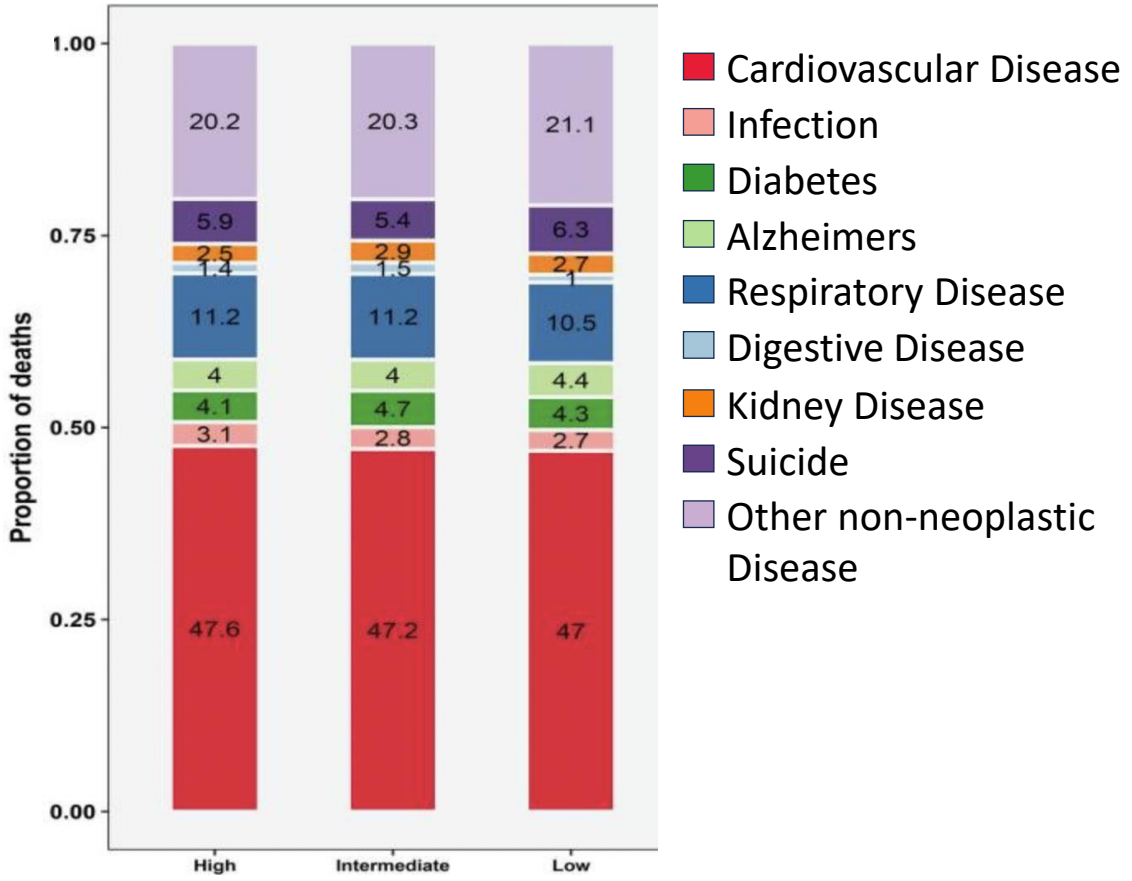
# How important is CVD in PCa?

## Non-cancer deaths amongst long-term mPCa survivors[1]




**Most common cause of NCM**

## Non-cancer deaths amongst patients with localised PCa[2]



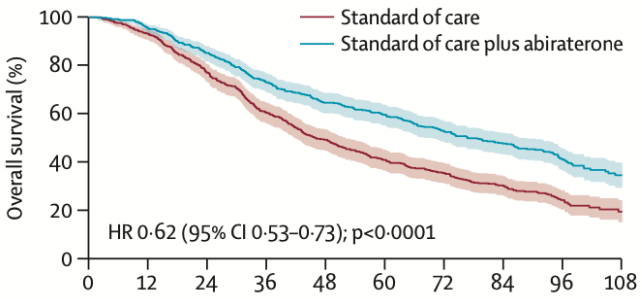

**Most common cause of death**

COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; mPCa, metastatic prostate cancer; NCM, non-cancer mortality; PCa, prostate cancer.

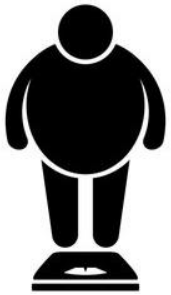
1. Elmehrath AO, et al. JAMA Netw Open. 2021;4(2):e2119568; 2. Luo Z, et al. Front Cardiovasc Med. 2023;10:1130691.

# Why do men with PCa have high CV burden?

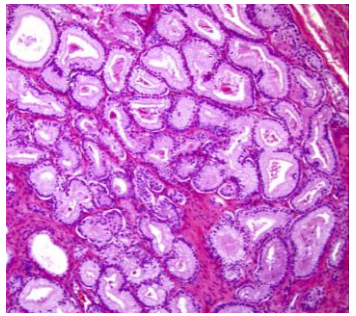
## Improving cancer-specific survival[1]




## Conventional CV risk factors[2]



## Inflammation[3]



## ADT[2]

ADT, androgen deprivation therapy; CV, cardiovascular; PCa, prostate cancer.

1. Attard G et al. Lancet Oncol 2023; 24: 443–56; 2. Ferreira VV, et al. Br J Hosp Med. 2022. https://doi.org/10.12968/hmed.2022.0334; 3. Wang Q, et al. Arterioscler Thromb Vasc Biol. 2024;44(3):698-719.

# Risk factors in men with PCa

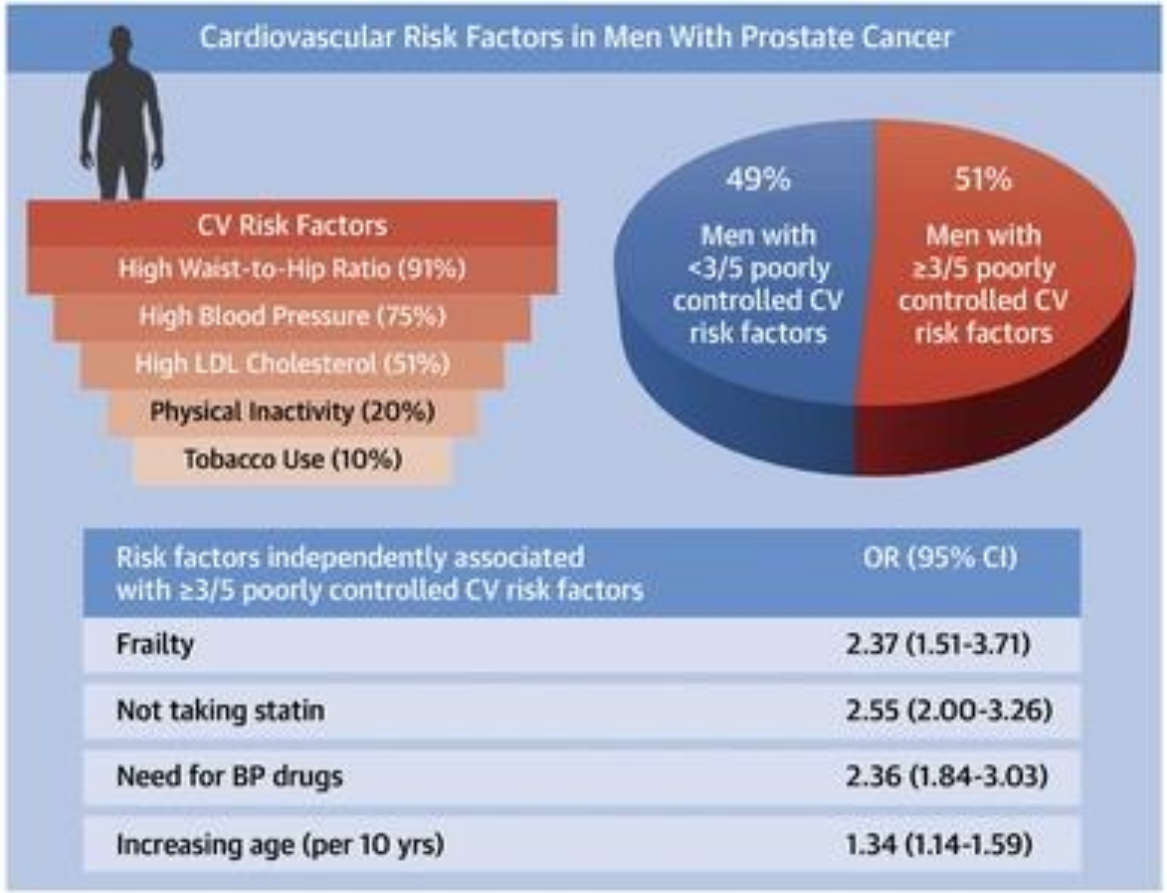
- Among men with localised/regional PCa, cardiovascular death is more frequent than death from the cancer itself.
- Among men with metastatic PCa, the risk of cardiovascular death remains higher than among otherwise similar patients without Pca
- One study investigated the rate of uncontrolled cardiovascular risk factors among men with PCa

**Almost all patients with PCa had at least 1 poorly controlled CV risk factor**

**51% had at least 3 poorly controlled CV**

- Poor control of modifiable cardiovascular risk factors is common in men with PCa
- Need for improved interventions to optimise cardiovascular risk management

## Poor control of cardiovascular risk factors in men with prostate cancer




| Risk factors independently associated with ≥3/5 poorly controlled CV risk factors | OR (95% CI) |
|---|---|
| Frailty | 2.37 (1.51-3.71) |
| Not taking statin | 2.55 (2.00-3.26) |
| Need for BP drugs | 2.36 (1.84-3.03) |
| Increasing age (per 10 yrs) | 1.34 (1.14-1.59) |

***Adapted from Klimis et al JACC CardioOncol 2023***

BP, blood pressure; CV, cardiovascular; LDL, low density lipoprotein; PCa, prostate cancer.

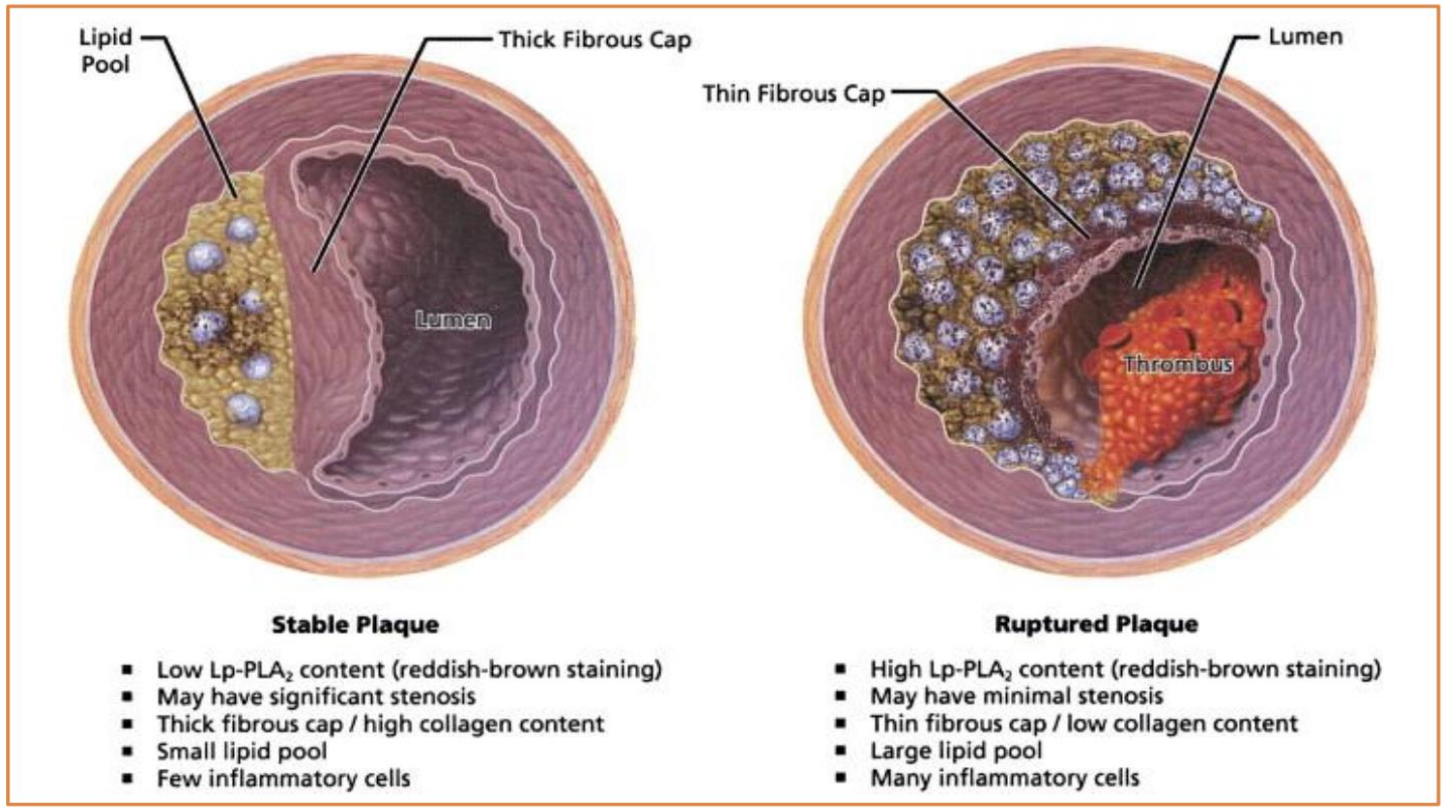
1. Klimis H, et al. JACC CardioOncol. 2023;5(1):70-81.

# Pathophysiology

Pro-inflammatory cancer state: Endothelial injury Hypercoagulability[1]

Plaque formation and possible instability: Testosterone suppression destabilises existing plaques[3]

Increased arterial stiffness[5]




FSH: Normally promotes endothelial cell inflammation and oxidative stress[2]

Metabolic syndrome: Promoting atherogenic and systemic inflammation[4]

***Image from: Corson MA, et al. The American Journal of Cardiology 2008;101(12)S41-S50***

Destabilisation of coronary plaques in patients with pre-existing coronary disease[3]
**Early acute CV events[6]**

Acceleration of de novo atherosclerosis[2]
**Delayed late CV events[6]**

FSH, follicle stimulating hormone; Lp-$PLA_2$, lipoprotein-associated phospholipase A2; CV, cardiovascular.

1. Saylor P, et al. Lancet Oncol. 2010;11(5):406-7; 2. Wang Q, et al. Arterioscler Thromb Vasc Biol. 2024;44(3):698-719; 3. Knutsson A, et al. Sci Rep. 2016;6:26220; 4. Smith MR, et al. Cancer 2008;112(10):2188-2194; 5. Hu JR, et al. Arterioscler Thromb Vasc Biol. 2020;40(3):e55-e64; 6. Ferreira VV, et al. Br J Hosp Med. 2022. https://doi.org/10.12968/hmed.2022.0334.

# GNRH agonist vs antagonist

**Systematic review: Electronic databases were searched for prospective, randomised trials comparing GnRH antagonists with agonists**

## Study selection

**1106** records identified

↓

**936** records screened

↓

**91** records assessed for eligibility

↓

**11** studies included

## Outcomes

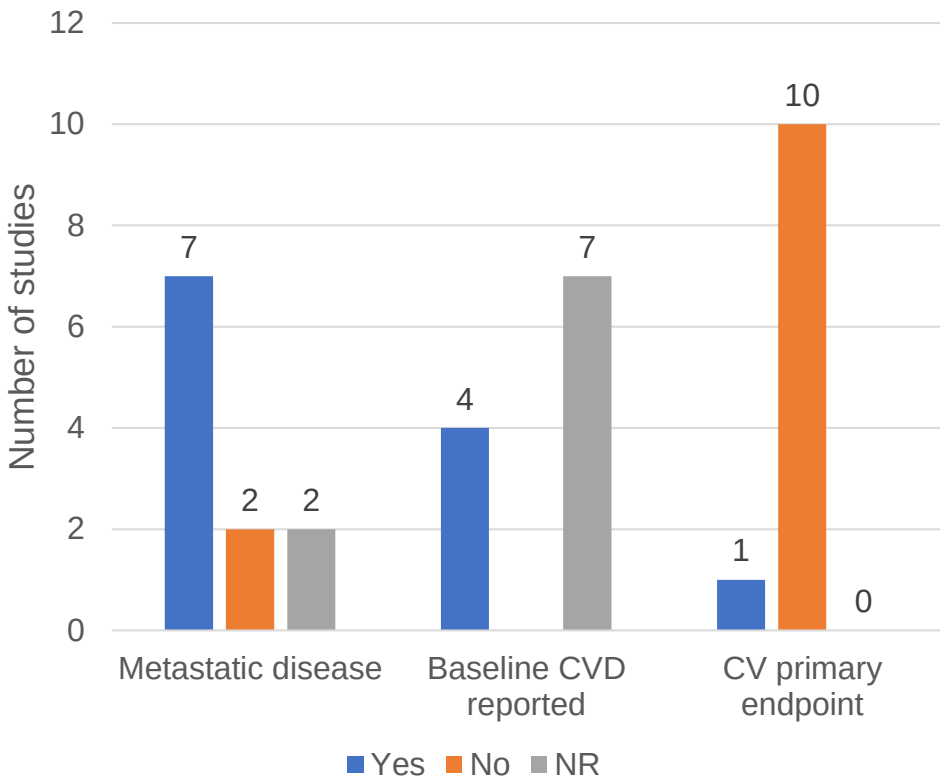
**Primary outcome:**
MACE
Defined as: myocardial infarction, central nervous system haemorrhages and cerebrosvascular conditions, and all-cause mortality

**Secondary outcome:**
All-cause mortality

## Conclusions

- Volume and quality of available data remain suboptimal
- However, data suggest that GnRH antagonists associated with fewer CV events, and possibly mortality, compared with GnRH agonists

## Study characteristics




CV, cardiovascular; CVD, cardiovascular disease; MACE, major cardiovascular event; NR, not reported.
Nelson A, et al. JACC CardioOncol. 2023;5(5):613-624.

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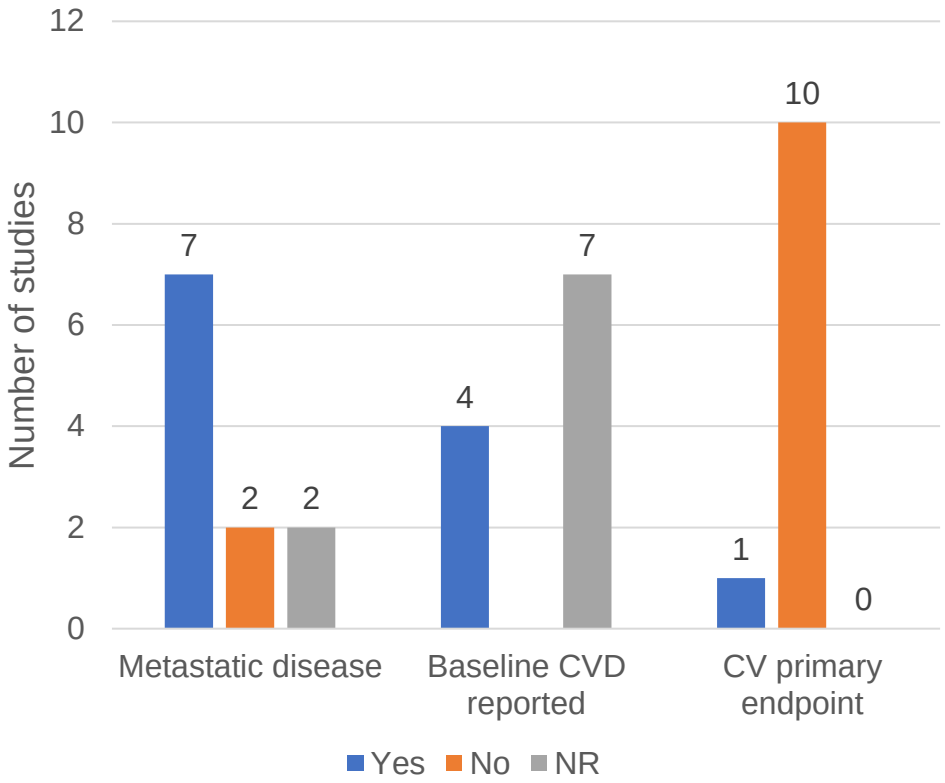


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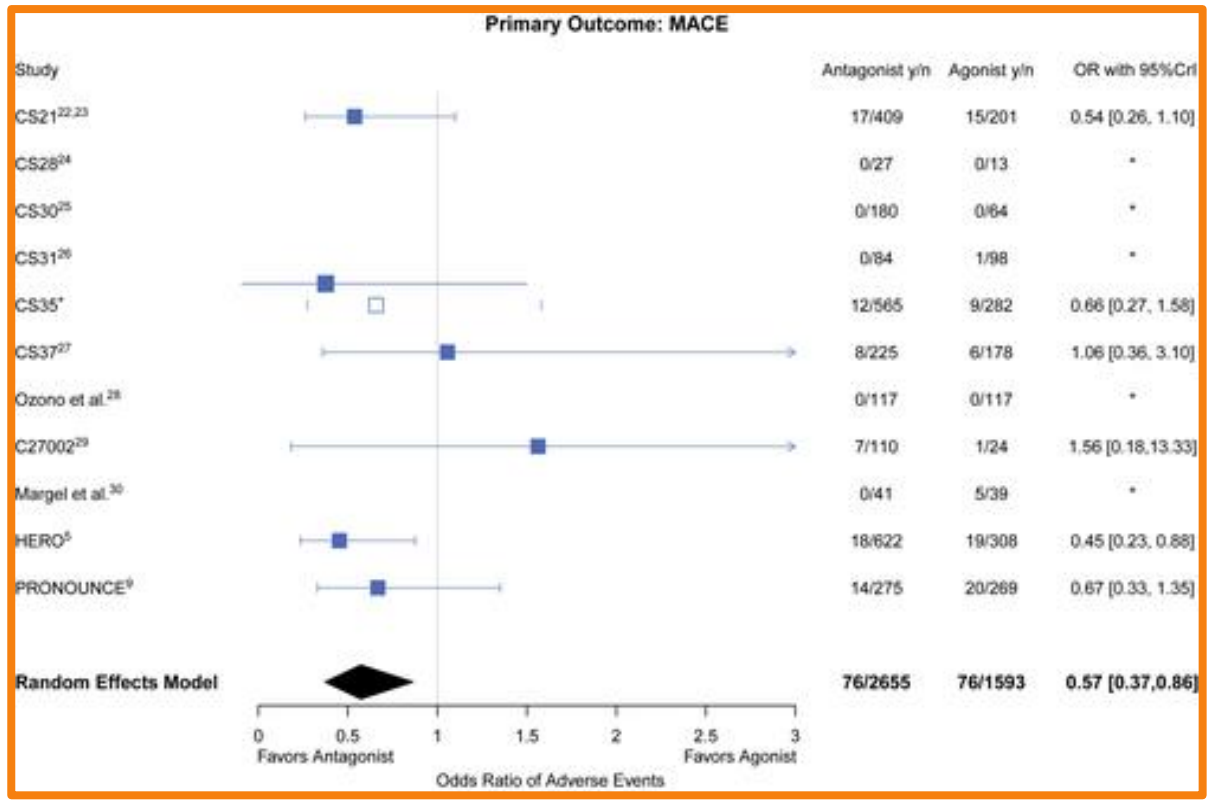
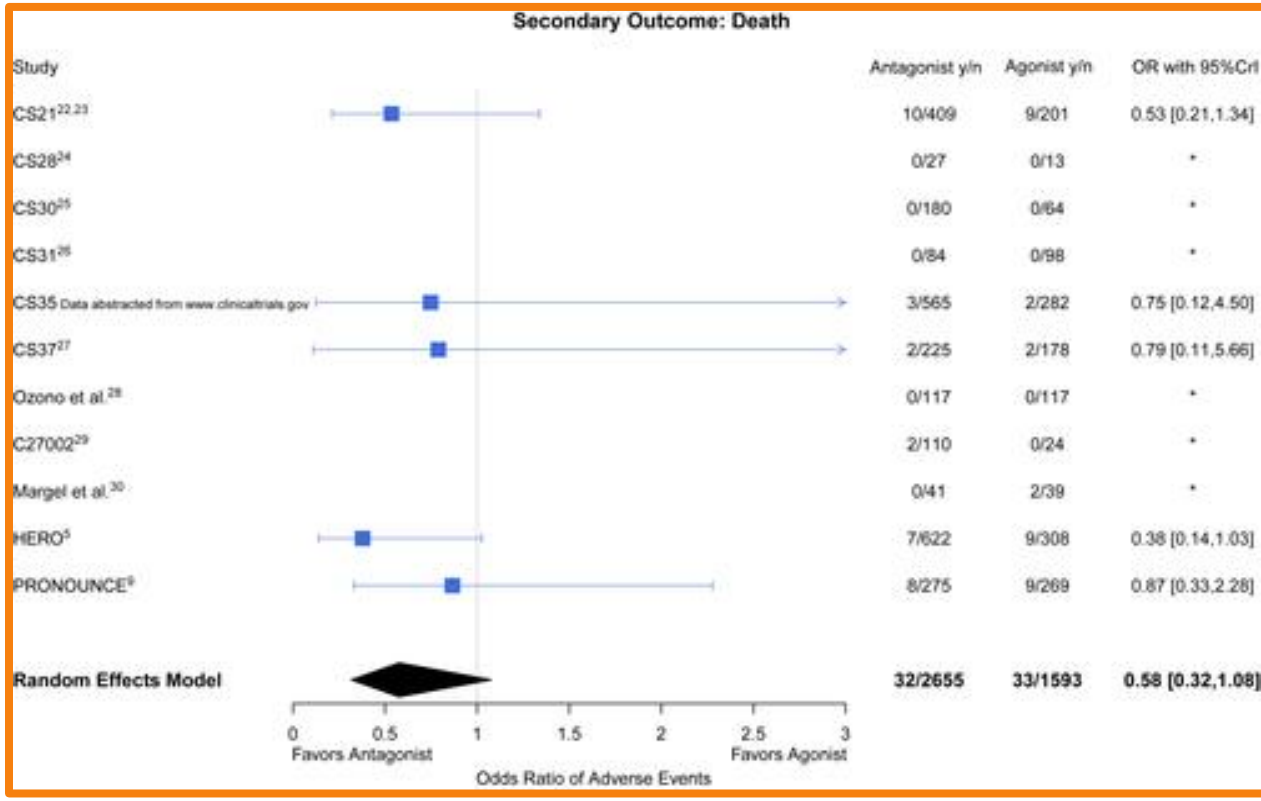
# GNRH agonist vs antagonist

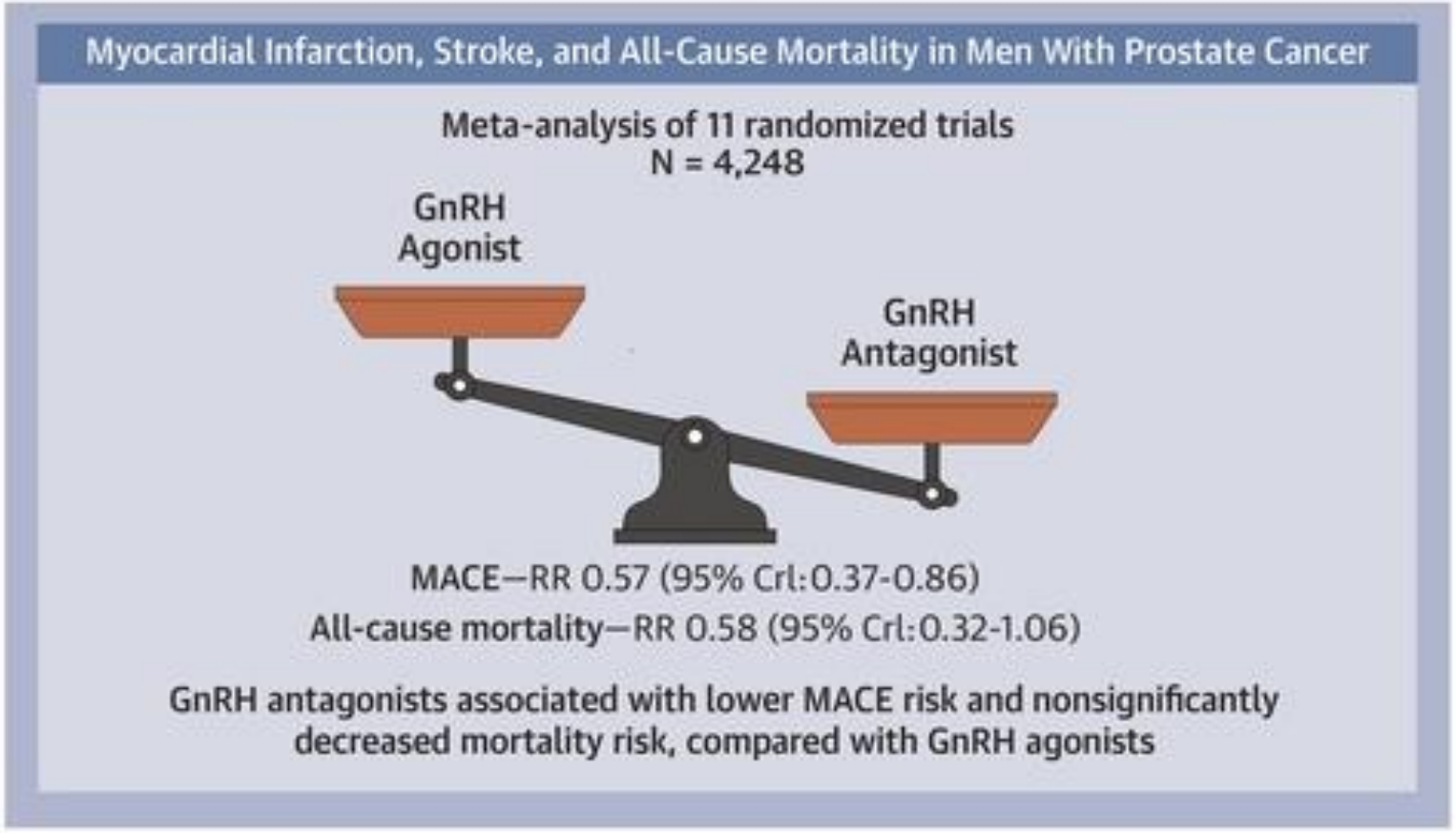



CV, cardiovascular; CVD, cardiovascular disease; MACE, major cardiovascular event.
Nelson A, et al. JACC CardioOncol. 2023;5(5):613-624.

# GNRH agonist vs antagonist

**CENTRAL ILLUSTRATION: Systematic Review of Randomized Controlled Trials Evaluating Gonadotropin-Releasing Hormone Antagonists vs Agonists**




**Key limitations:**

- Short duration of follow-up
- Unblinded study designs in some
- CV events identified through safety reporting mechanisms rather than as a pre-specified outcome

CrI, credible interval; GnRH, gonadotropin-releasing hormone; CV, cardiovascular; MACE, major cardiovascular event; RR, relative risk.
Nelson A, et al. JACC CardioOncol. 2023;5(5):613-624.

World Journal of Urology (2021) 39:307–315
https://doi.org/10.1007/s00345-020-03433-3

TOPIC PAPER

# Cardiovascular risk profiles of GnRH agonists and antagonists: real-world analysis from UK general practice

Patrick Davey[1] · Mike G. Kirby[2]

Received: 14 May 2020 / Accepted: 30 August 2020 / Published online: 26 September 2020


## Consort diagram

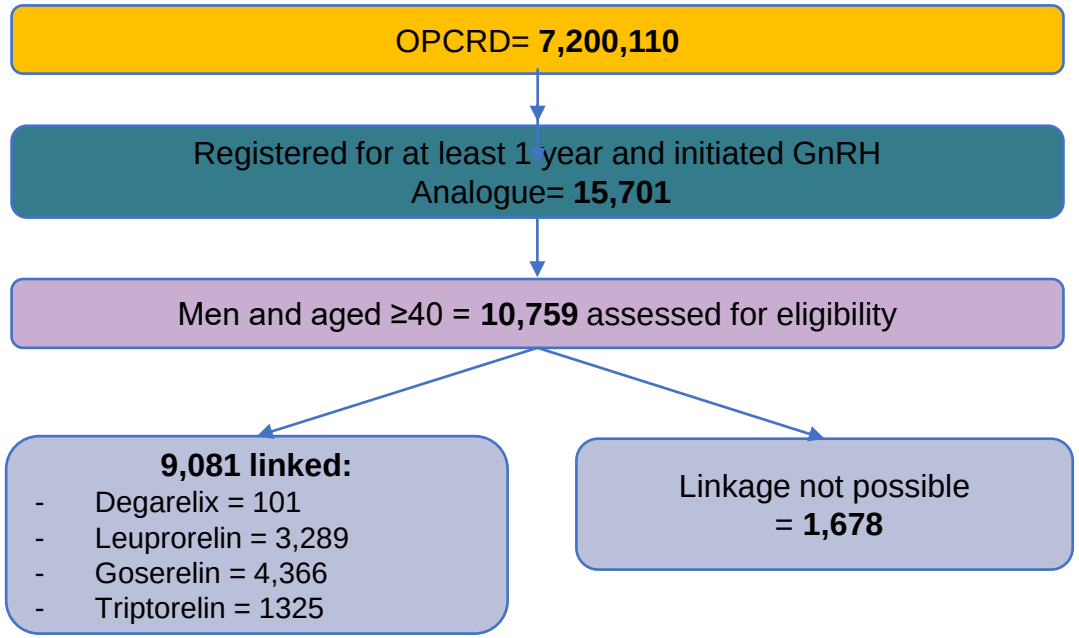



**Table 1** Baseline characteristics of prostate cancer patients prescribed degarelix, leuprorelin, goserelin, or triptorelin in a UK population-based cohort study ($n = 9081$)

| Baseline characteristics[a] | Degarelix users $n = 101$ | Leuprorelin users $n = 3289$ | Goserelin users $n = 4366$ | Triptorelin users $n = 1325$ |
|---|---|---|---|---|
| Age, year | $n = 100$ | $n = 3276$ | $n = 4366$ | $n = 1325$ |
| Mean (SD) | 74.8 (9.0) | 75.9 (8.6) | 74.0 (8.5) | 75.3 (8.3) |
| BMI, kg/m$^2$, $n$ (%) | $n = 93$ | $n = 3091$ | $n = 4012$ | $n = 1207$ |
| Mean (SD) | 26.9 (5.0) | 27.4 (4.9) | 27.5 (4.5) | 27.3 (4.5) |
| Overweight: 25–30 | 39 (41.9) | 1364 (44.1) | 1836 (45.8) | 548 (45.4) |
| Obese: > 30 | 21 (22.6) | 745 (24.1) | 993 (24.7) | 295 (24.4) |
| Smoking status, $n$ (%) | $n = 97$ | $n = 3162$ | $n = 4103$ | $n = 1258$ |
| Current smoker | 9 (9.3) | 278 (8.8) | 458 (11.2) | 146 (11.6) |
| Ex-smoker | 49 (50.5) | 1464 (46.3) | 1858 (45.3) | 567 (45.1) |
| PSA, ng/ml, closest to baseline, $n$ (%) | $n = 67$ | $n = 2663$ | $n = 3260$ | $n = 1115$ |
| Median (IQR) | 72.4 (3.7–273.0) | 10.0 (1.4–36.7) | 8.0 (0.8–24.9) | 10.6 (1.6–36.4) |
| < 20 | 27 (40.3) | 1727 (64.9) | 2312 (70.9) | 694 (62.2) |
| ≥ 20 | 40 (59.7) | 936 (35.1) | 948 (29.1) | 421 (37.8) |
| Testosterone, ng/ml | $n = 5$ | $n = 240$ | $n = 324$ | $n = 91$ |
| Mean (SD) | 14.7 (4.9) | 16.2 (18.4) | 13.8 (13.8) | 15.4 (15.1) |
| Comorbidity ever before/at baseline, $n$ (%) | | | | |
| Cardiovascular disease | 38 (37.6) | 1075 (32.7) | 1288 (29.5) | 385 (29.1) |
| IHD | 22 (21.8) | 639 (19.4) | 822 (18.8) | 213 (16.1) |
| HF | 4 (4.0) | 168 (5.1) | 154 (3.5) | 53 (4.0) |
| MI | 15 (14.8) | 324 (9.8) | 420 (9.6) | 88 (6.6) |
| Arrhythmia | 20 (19.8) | 615 (18.7) | 669 (15.3) | 222 (16.7) |
| Chronic kidney disease | 13 (12.9) | 524 (15.9) | 598 (13.7) | 208 (15.7) |
| Hepatic impairment | 2 (2.0) | 85 (2.6) | 121 (2.8) | 39 (2.9) |
| Osteoporosis | 2 (2.0) | 64 (1.9) | 94 (2.1) | 21 (1.6) |
| Urticaria | 2 (2.0) | 88 (2.7) | 152 (3.5) | 30 (2.3) |
| UTIs | | | | |
| 1 | 9 (8.9) | 169 (5.1) | 229 (5.3) | 65 (4.9) |
| 2 | 2 (2.0) | 25 (0.8) | 54 (1.2) | |
| > 2 | 0 (0) | 26 (0.8) | 19 (0.4) | 5 (0.4) |
| Diabetes mellitus | 19 (18.8) | 532 (16.2) | 704 (16.1) | 213 (16.1) |
| Drug use 6 months before/at baseline, $n$ (%) | | | | |
| Antithrombotic treatment | 50 (49.5) | 1297 (39.4) | 1676 (38.4) | 520 (39.2) |
| Anti-androgens | 10 (9.9) | 1185 (36.0) | 1521 (34.8) | 612 (46.2) |

[a]Closest to baseline for: age, sex, BMI, smoking status, PSA, testosterone; ever before baseline: comorbidity

BMI, body mass index; CV, cardiovascular; CVD, cardiovascular disease; GnRH, gonadotrophin-releasing hormone; HF, heart failure; IHD, ischaemic heart disease; MI, myocardial infarction; OPCRD, Optimum Patient Care Research Database; PSA, prostate specific antigen; UTI, urinary tract infection.

Davey P, et al. World J Urol. 2021;39(2):307-315.

World Journal of Urology (2021) 39:307–315
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TOPIC PAPER

# Cardiovascular risk profile
# real-world analysis from U

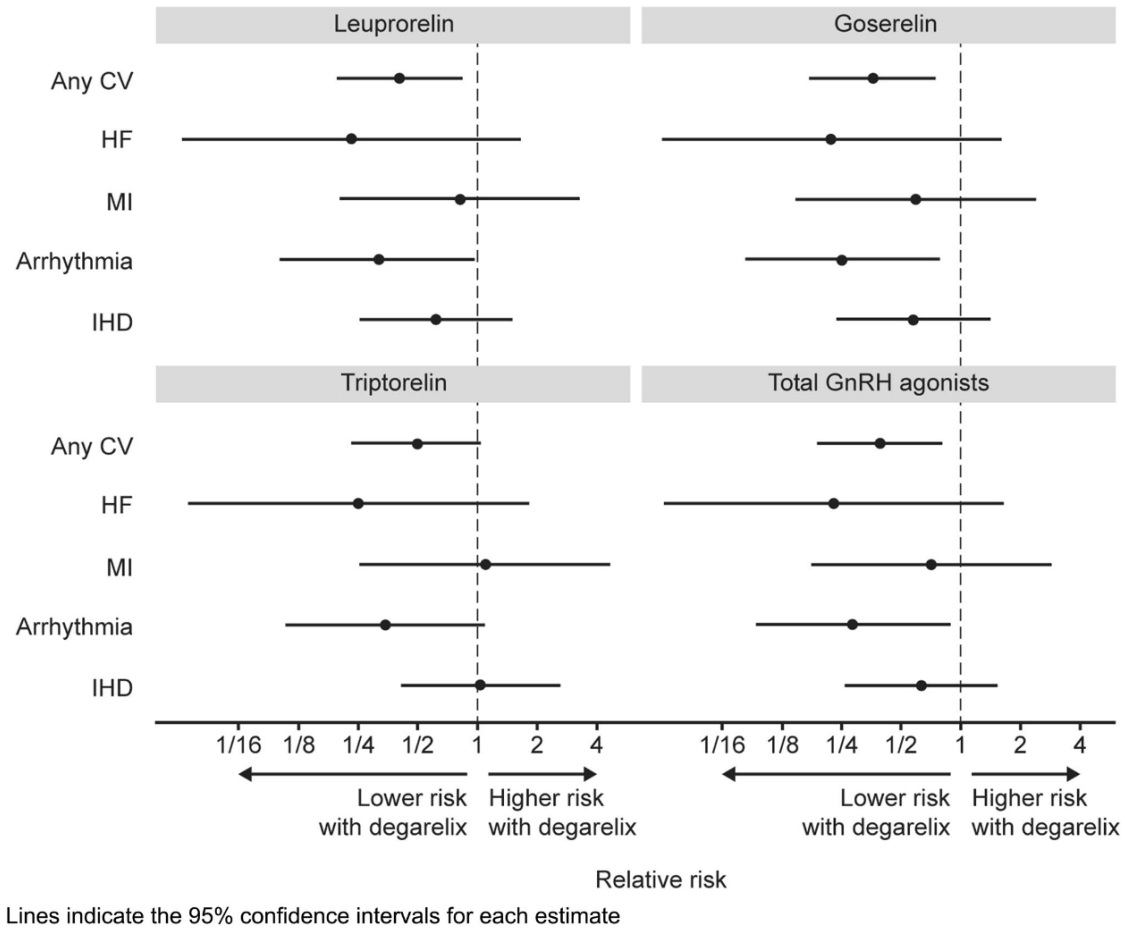
Patrick Davey[1] · Mike G. Kirby[2]

Received: 14 May 2020 / Accepted: 30 August 202


Registered f

Men and age

**9,081 linked:**
- Degarelix = 101
- Leuprorelin = 3,289
- Goserelin = 4,366
- Triptorelin = 1325

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| | Goserelin users $n=4366$ | Triptorelin users $n=1325$ |
|---|---|---|
| | $n=4366$ | $n=1325$ |
| | 74.0 (8.5) | 75.3 (8.3) |
| | $n=4012$ | $n=1207$ |
| | 27.5 (4.5) | 27.3 (4.5) |
| | 1836 (45.8) | 548 (45.4) |
| | 993 (24.7) | 295 (24.4) |
| | $n=4103$ | $n=1258$ |
| | 458 (11.2) | 146 (11.6) |
| | 1858 (45.3) | 567 (45.1) |
| | $n=3260$ | $n=1115$ |
| | 3.0 (0.8–24.9) | 10.6 (1.6–36.4) |
| | 2312 (70.9) | 694 (62.2) |
| | 948 (29.1) | 421 (37.8) |
| | $n=324$ | $n=91$ |
| | 13.8 (13.8) | 15.4 (15.1) |
| | 1288 (29.5) | 385 (29.1) |
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BMI, body mass index; CV, cardiovascular; CVD, cardiovascular disease; GnRH, gonadotrophin-releasing hormone; HF, heart failure; IHD, ischaemic heart disease; MI, myocardial infarction; OPCRD, Optimum Patient Care Research Database; PSA, prostate specific antigen; UTI, urinary tract infection.
Davey P, et al. World J Urol. 2021;39(2):307-315.

# ARSIs and CV risk

JAMA Oncology | Original Investigation

## Cardiovascular Events and Androgen Receptor Signaling Inhibitors in Advanced Prostate Cancer
### A Systematic Review and Meta-Analysis

Omar El-Taji, MBChB, MRes; Samih Taktak, MBBS; Craig Jones, MBChB, MRes; Mick Brown, PhD; Noel Clarke, MBBS, ChM; Ashwin Sachdeva, MBBS, PhD

## Study selection

**1912** records identified

↓

**1036** records screened

↓

**62** records assessed for eligibility

↓

**24** studies included

## Outcomes

**Primary outcomes:**
Any grade and grade ≥ 3 CV events

**Secondary outcomes:**
- Grade ≥ 3 Acute coronary syndrome (ACS)
- Grade ≥ 3 Cerebrovascular accident (CVA)
- Grade ≥ 3 Cardiac dysrhythmia
- Grade ≥ 3 Venous Thromboembolism (VTE)
- Cardiovascular death

**24 RCTs**
(N=22,166 participants)

- **3** RCTs **nmHSPC** (n=2,171)
- **9** RCTs **mHSPC** (n=8,994)
- **3** RCTs **nmCRPC** (n=4,256)
- **9** RCTs **mCRPC** (n=6,745)

**ARSi agents**

- **Abi** alone (N=9)
- **Abi** + **Doc** (N=1)
- **Enza** alone (N=9)
- **Abi** + **Enza** (N=2)
- **Darolutamide** alone (N=1)
- **Darolutamide** + **Doc** (N=1)
- **Apalutamide** (N=2)

**Note this is a meta-analysis not a head-to-head study**

Abi, abiraterone; ACS, acute coronary syndrome; ARSI, androgen receptor signalling inhibitors; CV, cardiovascular; CVA, cerebrovascular accident; Doc: docetaxel; Enza, enzalutamide; RCT, randomised control trial; VTE, venous thromboembolism; nmHSPC, non-metastatic hormone sensitive prostate cancer; mHSPC, metastatic hormone sensitive prostate cancer; nmCRPC, non-metastatic castrate-resistant prostate cancer; mCRPC, metastatic castrate-resistant prostate cancer

El-Taji O, et al. JAMA Oncol. 2024;10(7):874-884.

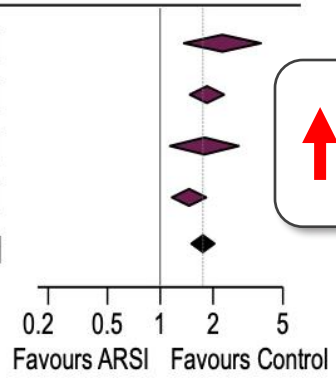
# ARSIs and CV risk

- Systematic review and meta-analysis of 24 randomised clinical trials involving 22,166 patients
- Addition of ARSI to ADT vs SOC associated with significantly increased risk of men experiencing CV events
- Increased risk of CV events observed for all ARSI agents

**Any grade CV event**

| Disease stage | RCTs | ARSI Total | Control Total | Risk Ratio MH, Random, 95% CI |
|---|---|---|---|---|
| M0 HSPC | 2 | 964 | 988 | 2.26 [1.36; 3.75] |
| M1 HSPC | 7 | 3851 | 3867 | 1.85 [1.47; 2.31] |
| M0 CRPC | 2 | 1884 | 1019 | 1.79 [1.13; 2.81] |
| M1 CRPC | 7 | 2814 | 1939 | 1.46 [1.16; 1.83] |
| **All stages** | **18** | **9513** | **7813** | **1.75 [1.50; 2.04]** |

Test for subgroup differences: $Chi^2 = 3.49$, df = 3 (P = 0.32 )




x1.8

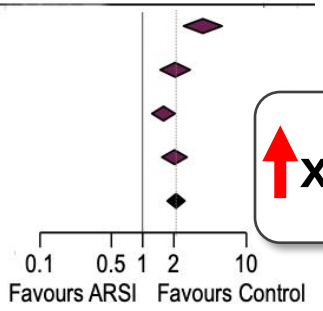
**Note this is a meta-analysis not a head-to-head study. No direct comparisons can be made.**

The incidence of all grade CV events was 22.0% (1,717 of 7,813) in patients receiving SOC and 36.6% (3,479 of 9,513) with addition of an ARSI

**Grade ≥3 CV event**

| Disease stage | RCTs | ARSI Total | Control Total | Risk Ratio MH, Random, 95% CI |
|---|---|---|---|---|
| M0 HSPC | 2 | 964 | 988 | 3.80 [2.48; 5.84] |
| M1 HSPC | 7 | 3234 | 3251 | 2.06 [1.47; 2.87] |
| M0 CRPC | 2 | 1757 | 952 | 1.59 [1.23; 2.06] |
| M1 CRPC | 5 | 2544 | 2123 | 2.03 [1.53; 2.68] |
| **All stages** | **16** | **8499** | **7314** | **2.10 [1.72; 2.55]** |

Test for subgroup differences: $Chi^2 = 11.72$, df = 3 (P < 0.01 )




x2.1

ARSI use was associated with increased risk of grade 3 or higher CV events, from 7.8% to 15.6% (16 RCTs: n = 15,813 patients; RR, 2.10; 95% CI, 1.72–2.55; P <0.001)

*Only one study available for comparison.

**Note this is a meta-analysis not a head-to-head study. No direct comparisons between agents can be made.**

ADT, androgen deprivation therapy; ARSI, androgen receptor signalling inhibitors; $Chi^2$, chi-squared test; CRPC, castrate-resistant prostate cancer; CV, cardiovascular; df, degrees of freedom; HSPC, hormone-sensitive prostate cancer; M0HSPC, nonmetastatic HSPC; M1HSPC, metastatic HSPC; MH, Mantel-Haenszel; mPCa, metastatic prostate cancer; RCT, randomised controlled trial; SOC, standard of care.

El-Taji O, et al. JAMA Oncol. 2024;10(7):874-884 (including supplementary information).

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- Addition of ARSI to ADT vs SOC associated with significantly increased risk of men experiencing CV events
- Increased risk of CV events observed for all ARSI agents

| ARSI Agent | Any grade CV Events | | Grade ≥3 CV events | |
|---|---|---|---|---|
| | **Pooled RR** | **95% CI** | **Pooled RR** | **95%CI** |
| **Abiraterone Acetate** | 1.58 | 1.31-1.90 | 2.04 | 1.63-2.55 |
| **Enzalutamide** | 1.93 | 1.47-2.54 | 1.98 | 1.46-2.69 |
| **Abiraterone Acetate + Enzalutamide** | 2.92 | 2.59-3.30 | 4.08 | 3.01-5.52 |
| **Darolutamide** | 1.30* | 1.09-1.54 | 1.91 | 1.27-2.87 |
| **Apalutamide** | 1.43 | 1.15-1.77 | 1.39 | 1.13-1.72 |

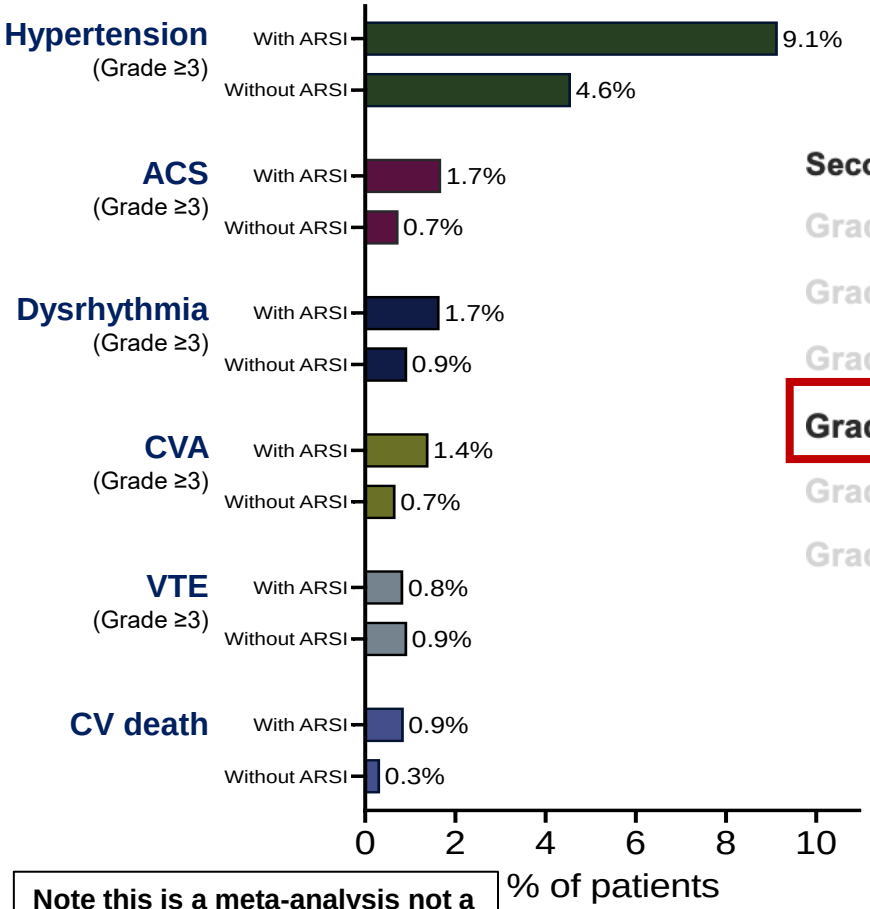
*Only one study available for comparison.

**Note this is a meta-analysis not a head-to-head study. No direct comparisons between agents can be made.**

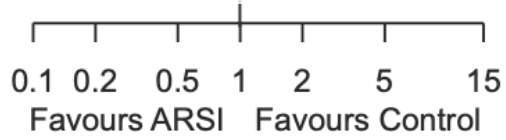
ADT, androgen deprivation therapy; ARSI, androgen receptor signalling inhibitors; $Chi^2$, chi-squared test; CRPC, castrate-resistant prostate cancer; CV, cardiovascular; df, degrees of freedom; HSPC, hormone-sensitive prostate cancer; M0HSPC, nonmetastatic HSPC; M1HSPC, metastatic HSPC; MH, Mantel-Haenszel; mPCa, metastatic prostate cancer; RCT, randomised controlled trial; SOC, standard of care.

El-Taji O, et al. JAMA Oncol. 2024;10(7):874-884 (including supplementary information).

# ARSIs and CV risk




| Secondary outcomes | ARSI Total | Control Total | Risk Ratio | RR | 95%-CI |
|---|---|---|---|---|---|
| Grade ≥3 hypertension | 11149 | 9504 | | 2.25 | [1.74; 2.90] |
| Grade ≥3 acute coronary syndrome | 11030 | 8899 | | 1.93 | [1.43; 2.60] |
| Grade ≥3 cardiac dysrhythmia | 9868 | 7807 | | 1.64 | [1.23; 2.17] |
| **Grade 5 related CV event** | 9766 | 8097 | | 2.02 | [1.32; 3.10] |
| Grade ≥3 cerebrovascular event | 9528 | 7390 | | 1.86 | [1.34; 2.59] |
| Grade ≥3 venous thromboembolism | 9776 | 8046 | | 0.84 | [0.61; 1.16] |




**Note this is a meta-analysis not a head-to-head study. No direct comparisons can be made.**

ACS, acute coronary syndrome; ARSI, androgen receptor signalling inhibitors; CV, cardiovascular; CVA, cerebrovascular accident; RR, relative risk.

El-Taji O, et al. JAMA Oncol. 2024;10(7):874-884 (including supplementary information).

# Cardiovascular risk

- **Risk** translates into **events**
- **Classification of risk**

| | |
|---|---|
| Low risk | <10% events per 10 years |
| Medium risk | 10-20% events per 10 years |
| High risk | > 20% events per 10 years |

- **Events** lead to patients becoming unwell and/or dying

- **Highest risk** patients are those with established vascular disease
- **Next highest** are those with major risk factors for vascular disease: smokers, diabetes, renal failure, hypertension, hyper-cholesterolaemia
- **Lowest** are younger people with healthy lifestyles

**It is important to identify the risk of cardiovascular disease in patients with prostate cancer**

Cardiovascular Risk Score (QRISK2) Patient Information Leaflet. Available at: Cardiovascular Risk Score (QRISK2) Patient Information Leaflet - Winchmore Hill Practice. Accessed May 2025
Yusuf S et al., Lancet 2004; 364: 937–52

# Higher risk in those with established CV disease

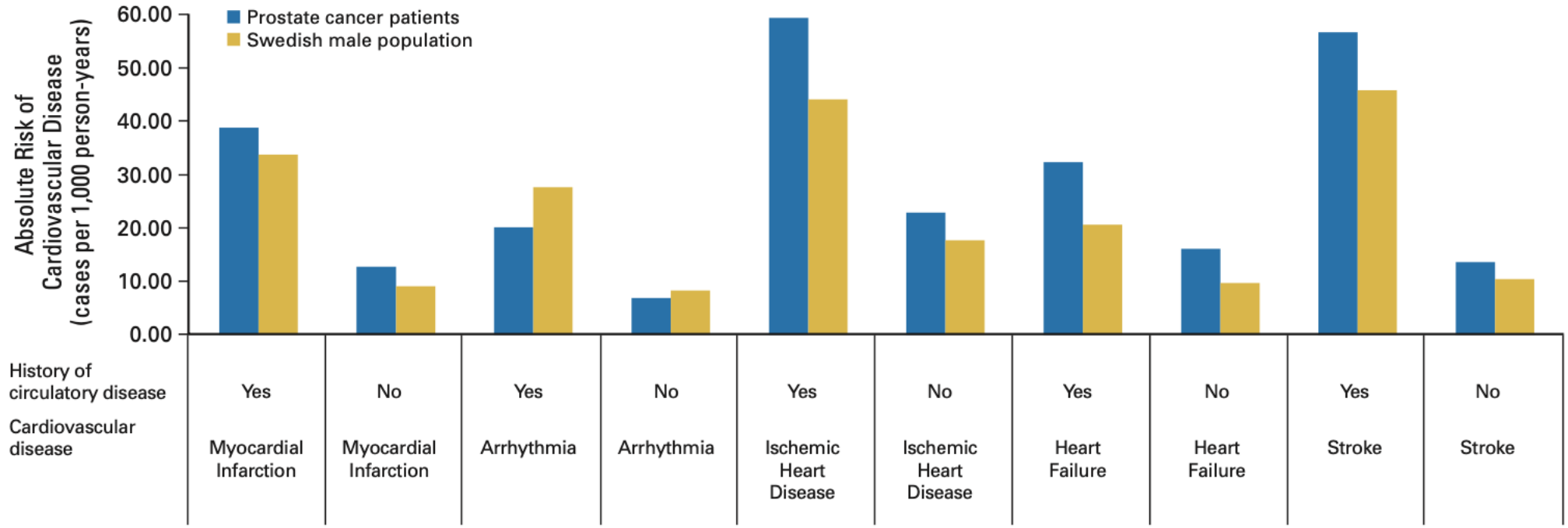



***Image adapted from: Van Hemelrijck M et al. J Clin Oncol. 2010***

CV, cardiovascular.

Van Hemelrijck M, et al. J Clin Oncol. 2010; 28(21). https://doi.org/10.1200/JCO.2010.29.1567.

# Risk and treatment benefit: Primary vs secondary prevention

- 5-year absolute benefits on particular vascular outcomes per mmol/L LDL cholesterol reduction in participants with and without previous MI or CHD
  - Many participants had more than one type of outcome

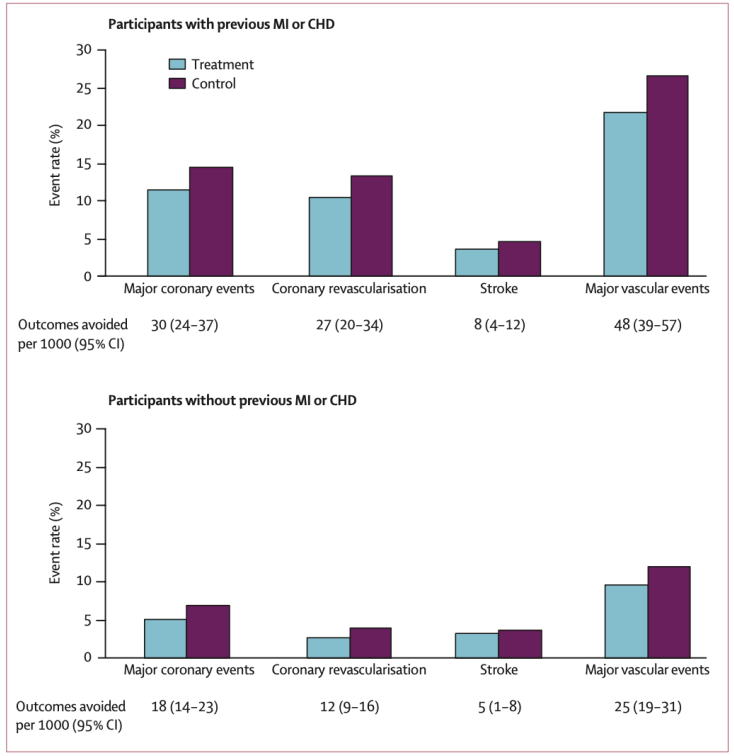
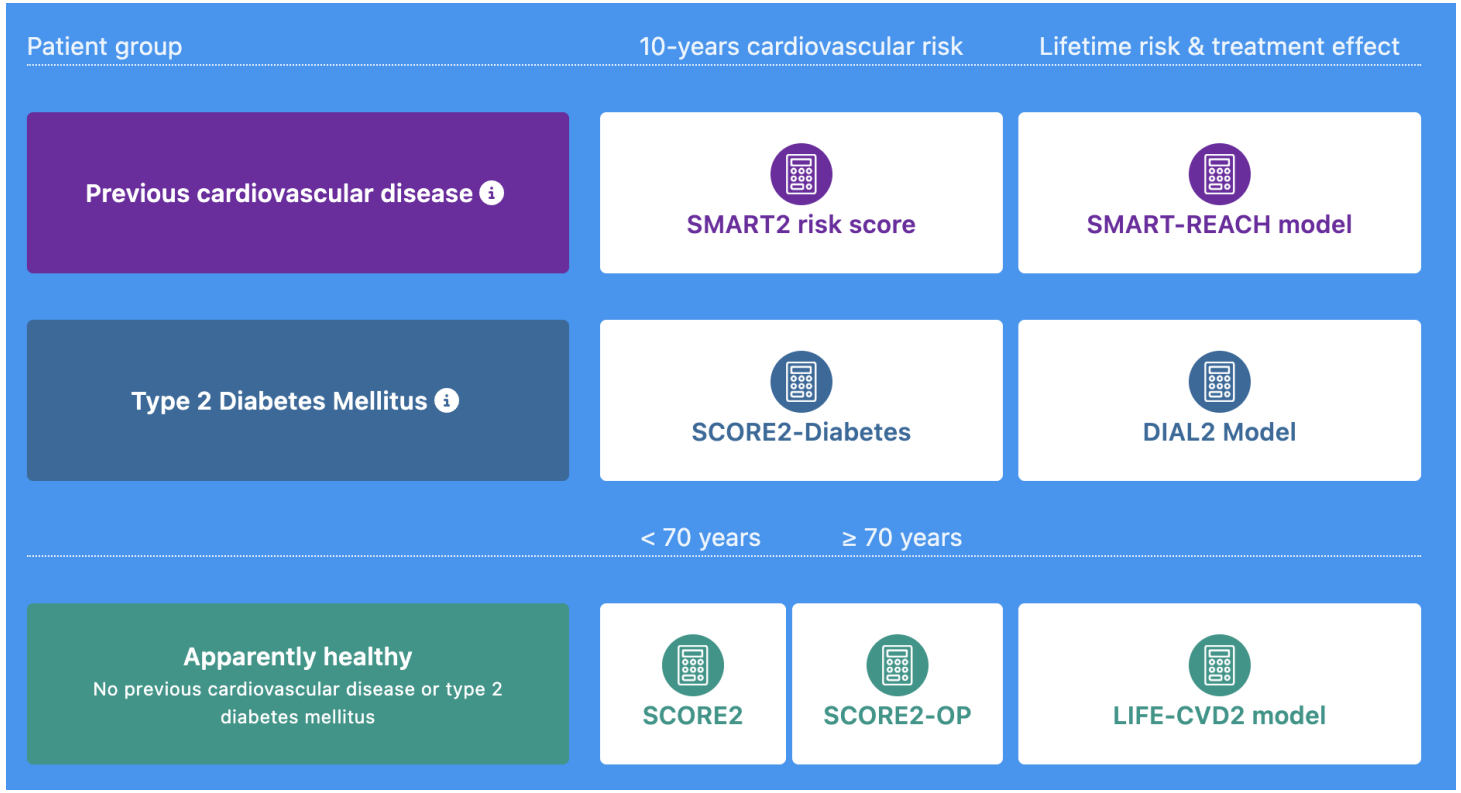



***Image adapted from: Baigent C et al. Lancet 2005.***

CHD, coronary heart disease; CI, confidence intervals; LDL, low-density lipoprotein; MI, myocardial infarction.
Baigent C, et al. Lancet 2005; 366: 1267–78.

# Cardiovascular risk (2)

- There are risk prediction models both for those with and without vascular disease https://u-prevent.com/calculators



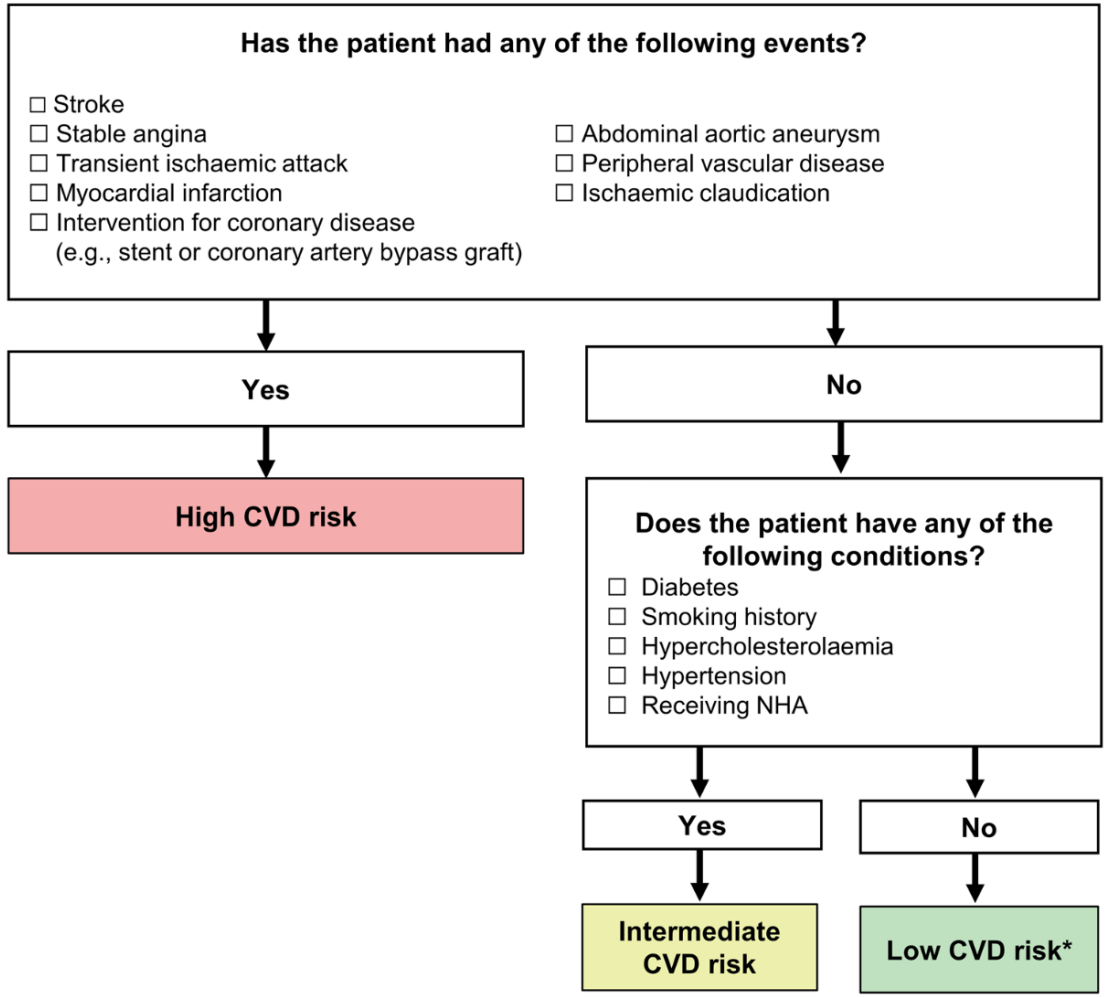

U-Prevent calculators. Available at: https://u-prevent.com/calculators. Accessed April 2025.

***Adapted from https://u-prevent.com***

# Cardiovascular risk (3)

- In practice, however, it may be better to keep it simple
- Do they have established vascular disease?
- If not, do they have major risk factors?
- If not, they are lower risk

# Checklist for CVD risk assessment and stratification



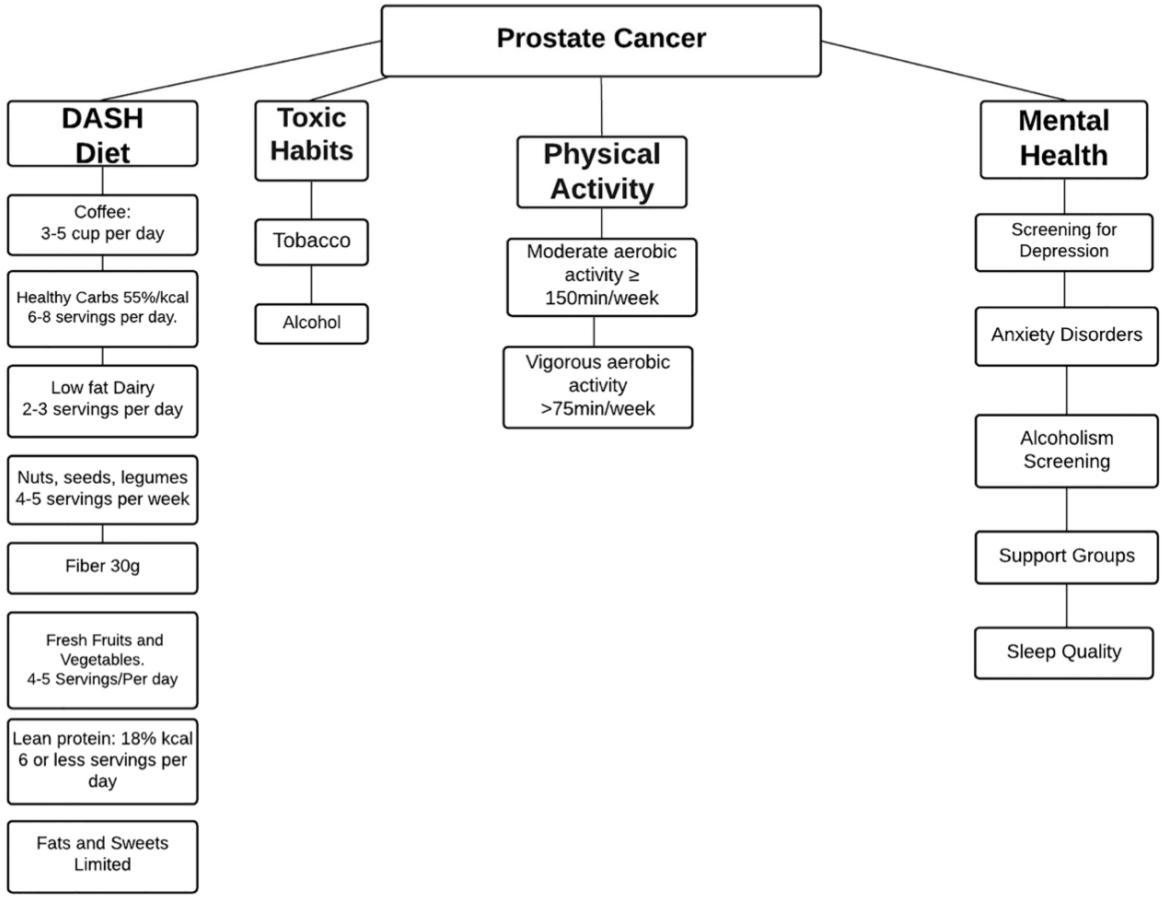

CVD, cardiovascular disease; NHA, novel hormonal agent.
*A patient's risk level may transition from "Low Risk" to "Intermediate Risk" or "High Risk" after 2 or 3 years of hormonal plus NHA treatment.
Merseburger AS, et al. World J Urol. 2024:42:156-67.

# Preventing CV events

- All men with prostate cancer are at risk of CV events, although their individual risk varies
- Management concentrates on:
  - Lifestyle, including exercise and diet
  - Reducing BP and cholesterol
  - If known CV disease, ‘aggressive’ intervention
  - If CV symptoms, see a cardiologist
- ABCDE approach

Klimis H, et al. J Am Coll Cardiol CardioOnc 2023;5:70–81.
ABCDE, risk assessment, blood pressure control, cholesterol management, diabetes care and tailored exercise prescription; BP, blood pressure; CV, cardiovascular.

# Summary outline of recommendations for a healthy lifestyle




DASH: Dietary Approaches to Stop Hypertension; AUDIT: Alcohol Use Disorders Identification Test.
Merseburger AS, et al. World J Urol. 2024:42:156-67.

# ABCDE

The “ABCDE” approach helps to guide for a consistent, comprehensive approach to managing cardiovascular risk in daily clinical practice

- A Awareness and aspirin
- B Blood pressure
- C Cholesterol and cigarettes
- D Diet and diabetes
- E Exercise

Hsu S et al. Clin Cardiol. 2013;36(7):383–393.

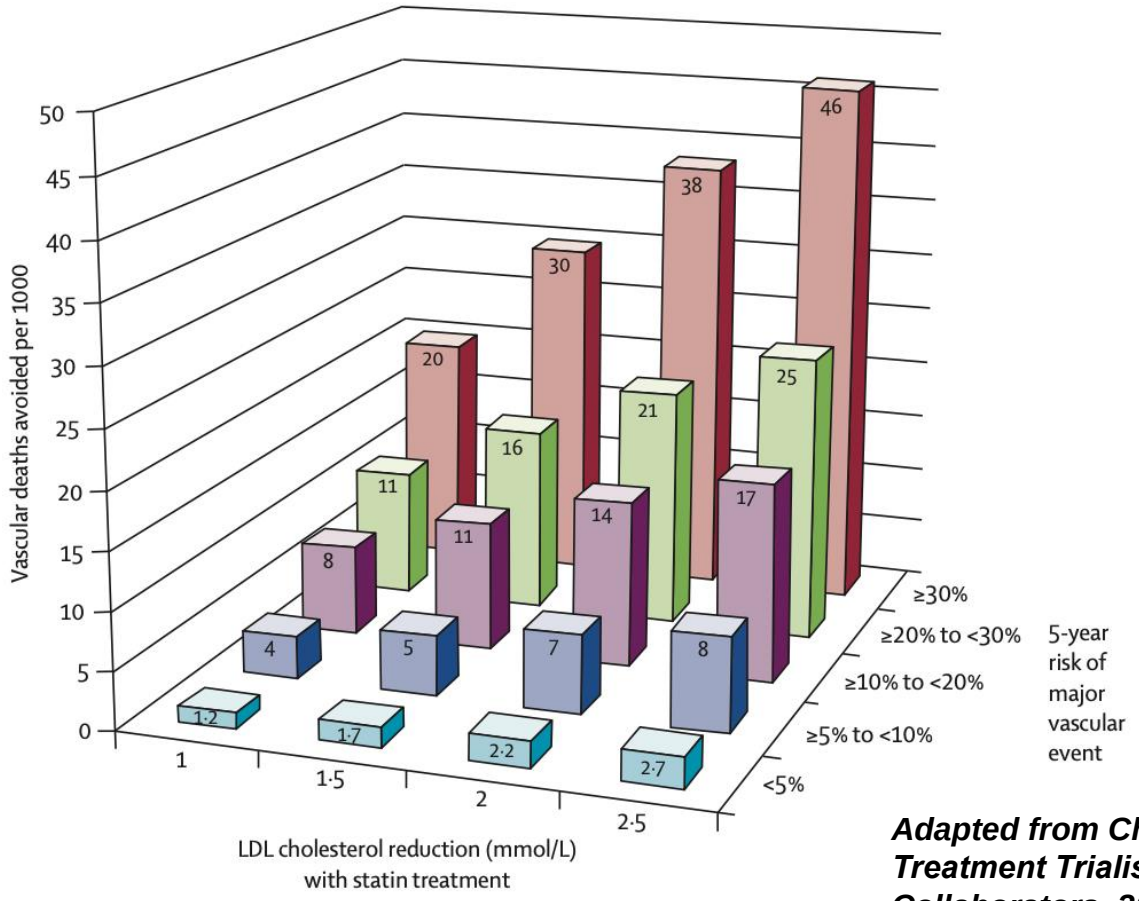
# Which drugs are suitable for patients with prostate cancer at risk of CV events?

- Statins for most patients
  - Measure cholesterol to determine treatment targets rather than to make the decision to use statins
- ACE inhibitors etc for many patients (hypertension)
- Other hypotensive drugs include amlodipine, spironolactone etc
- Modern diabetic drugs for many patients include SGLT2 inhibitors, GLP-1 receptor agonists etc

ACE, angiotension-converting enzymes; GLP-1, glucagon-like peptide 1; SGLT2, sodium-glucose co-transporter 2.

# Impact of more intensive therapy

**Predicted 5-year benefits of LDL cholesterol reductions with statin treatment at different levels of risk**




***Adapted from Cholesterol Treatment Trialists' Collaborators, 2012.***

LDL, low-density lipoprotein.

Cholerterol Treatment Trialists' Collaborators. Lancet 2012;380:581–90.

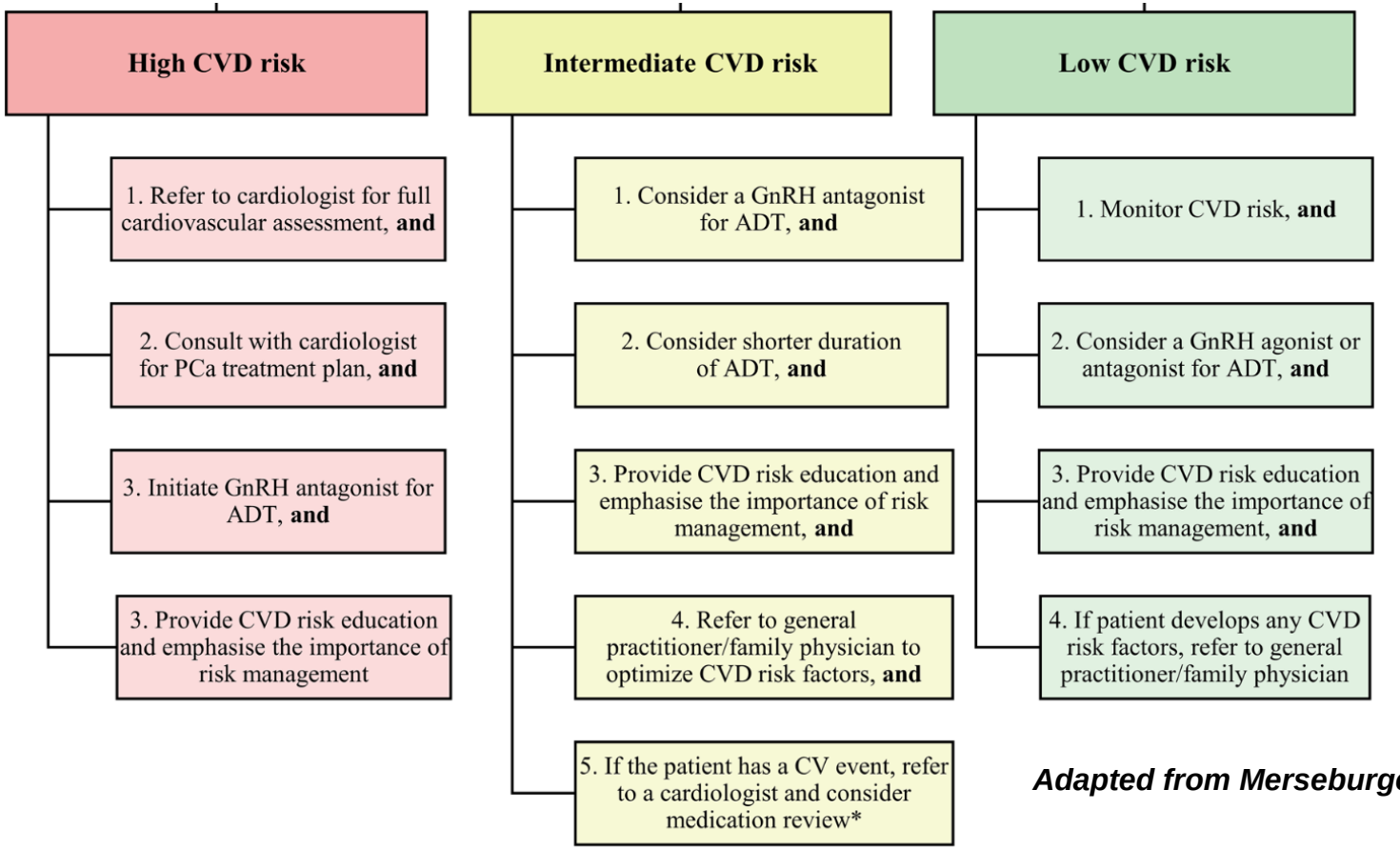
# Who benefits from advanced cardiology tests/intervention?

- Those with cardiac symptoms
- Those with left ventricular dysfunction/valve disease
- Those with electrical problems

- PCI (angioplasty/stents) does not improve prognosis in chronic stable angina
- CABG can improve prognosis in chronic stable angina
- Drugs improve prognosis
- Lifestyle changes improve prognosis

Leong DP, et al. JACC: CardioOncol. 2024;6:835–846.
CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

# Management steps for minimising cumulative CVD risk at ADT initiation




***Adapted from Merseburger AS, et al., 2024.***

ADT, androgen deprivation therapy; CV, cardiovascular; CVD, cardiovascular disease; GnRH, gonadotrophin-releasing hormone; PCa, prostate cancer.
*Referral to cardiologists is recommended but is subject to each country's healthcare system and resources.
Merseburger AS, et al. World J Urol. 2024:42:156-67.

# ESC cardio-oncology guidelines

**Recommendation Table 16 — Recommendations for baseline risk assessment and monitoring during androgen deprivation therapy for prostate cancer**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Baseline CV risk assessment[c] and estimation of 10-year fatal and non-fatal CVD risk with SCORE2 or SCORE2-OP[d] is recommended in patients treated with ADT without pre-existing CVD.[19,341,342] | I | B |
| Baseline and serial ECGs are recommended in patients at risk of QTc prolongation during ADT therapy.[e,339–342] | I | B |
| A GnRH antagonist should be considered in patients with pre-existing symptomatic CAD[f] who require ADT.[341,342] | IIa | B |
| Annual CV risk assessment[c] is recommended during ADT.[19,339,341,342] | I | B |

***Adapted from Lyon AR, et al., 2022.***

[a]Class of recommendation; [b]Level of evidence; [c]BP, lipids, fasting glucose, HbA1c, ECG, and patient education on healthy lifestyle and lifestyle risk factor control is recommended; [d]SCORE2 (,70 years) or SCORE2-OP (≥70 years) CV risk stratification: ,50 years: low risk ,2.5%, moderate risk 2.5% to ,7.5%, high risk ≥7.5%; 50–69 years: low risk ,5%; moderate risk 5% to ,10%; high risk ≥10%; ≥70 years: low risk ,7.5%, moderate risk 7.5% to,15%, high risk ≥15%; [e]See Table 9 Classification of corrected QT interval prolongation induced by cancer drug therapy in Lyon, et al. Eur Heart J 2022; [f]CCS and ACS.
ADT, androgen deprivation therapy; CAD, coronary artery disease; CV, cardiovascular; CVD, cardiovascular disease; ECG, electrocardiogram; ESC, European Society of Cardiology; GnRH, gonadotrophin-releasing hormone; QTc, corrected QT interval.
Lyon AR, et al. Eur Heart J. 2022:43:4229-4361.

# Summary

- All men with prostate cancer are at risk of CV events, although their individual risk varies[1]
  - The risk of CV events is higher in those with established CV disease versus those without established CV disease[2]
  - CV risk assessment is important to identify which men would benefit from CVD prevention[2]
  - ADT and ARPIs are associated with an increased risk of cardiovascular events[3,4]
- Approach to CV management in men with prostate cancer:[1,5,6]
  - ABCDE approach
  - Lifestyle, including exercise and diet
  - Reducing BP and cholesterol
  - If known CV disease, ‘aggressive’ intervention
  - If CV symptoms, see a cardiologist

1. Klimis H, et al. J Am Coll Cardiol CardioOnc 2023;5:70–81; 2. Van Hemelrijck M, et al. J Clin Oncol. 2010; 28(21). https://doi.org/10.1200/JCO.2010.29.1567; 3. Nelson A, et al. JACC CardioOncol. 2023;5(5):613-624; 4. El-Taji O, et al. JAMA Oncol. 2024;10(7):874-884; 5. Merseburger AS, et al. World J Urol. 2024:42:156-67; 6. Hsu S et al. Clin Cardiol. 2013;36(7):383–393.

**NUBEQA® (darolutamide) 300 mg film-coated tablets**
**Prescribing Information – United Kingdom**
(Refer to full Summary of Product Characteristics (SmPC) before prescribing)

**Presentation:** Each film-coated tablet contains 300 mg of darolutamide. **Indication(s):** NUBEQA is indicated for the treatment of adult men with non-metastatic castration resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease or with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy or with mHSPC in combination with docetaxel. **Posology & method of administration:** Treatment should be initiated and supervised by a specialist physician experienced in treatment of prostate cancer. Medical castration with a luteinising hormone-releasing hormone (LHRH) analogue should be continued during treatment of patients not surgically castrated. For oral use. The tablets should be taken whole with food. ***Adults:*** 600 mg darolutamide (two tablets of 300 mg) taken twice daily, equivalent to a total daily dose of 1200 mg. When used in combination with docetaxel in mHSPC patients, the first of 6 cycles of docetaxel should be administered within 6 weeks after the start of darolutamide treatment. Treatment with darolutamide should be continued until disease progression or unacceptable toxicity even if a cycle of docetaxel is delayed, interrupted, or discontinued. If a patient experiences a ≥ Grade 3 toxicity or an intolerable adverse reaction related to darolutamide, dosing should be withheld or reduced to 300 mg twice daily until symptoms improve. Treatment may then be resumed at a dose of 600 mg twice daily. ***Children & adolescents:*** There is no relevant use of darolutamide in the paediatric population. ***Elderly:*** No dose adjustment is necessary. ***Renal Impairment:*** No dose adjustment is necessary for patients with mild or moderate renal impairment. For patients with severe renal impairment (eGFR 15-29 mL/min/1.73 m2) not receiving haemodialysis, the recommended starting dose is 300 mg twice daily. ***Hepatic Impairment:*** No dose adjustment is necessary for patients with mild hepatic impairment. The available data on darolutamide pharmacokinetics in moderate hepatic impairment is limited. Darolutamide has not been studied in patients with severe hepatic impairment. For patients with moderate and severe hepatic impairment (Child-Pugh Classes B and C), the recommended starting dose is 300 mg twice daily. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients. Women who are or may become pregnant. **Warnings & precautions:** Monitor for signs and symptoms of ischaemic heart disease. Optimise management of cardiovascular risk factors. Discontinue darolutamide for Grade 3-4 ischaemic heart disease. Seizure occurred in patients receiving darolutamide. Advise patients of the risk of developing a seizure while receiving darolutamide. Consider discontinuation of darolutamide in patients who develop a seizure during treatment. Cases of idiosyncratic drug-induced liver injury (DILI) with increases in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) to ≥5 and ≥20 x upper limit of normal (ULN) have been reported. Idiosyncratic DILI has been reported in clinical trials and the post-marketing setting. Liver function test abnormalities were reversible upon darolutamide discontinuation. In case of liver function test abnormalities suggestive of idiosyncratic drug-induced liver injury, permanently discontinue darolutamide. The available data in patients with severe renal impairment are limited. As exposure might be increased those patients should be closely monitored for adverse reactions. The available data in patients with moderate hepatic impairment are limited, and darolutamide has not been studied in patients with severe hepatic impairment. As exposure might be increased those patients should be closely monitored for adverse reactions. Patients with clinically significant cardiovascular disease in the past 6 months including stroke, myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft, and symptomatic congestive heart failure were excluded from the clinical studies. Therefore, the safety of darolutamide in these patients has not been established. Use of strong CYP3A4 and P-gp inducers during treatment with darolutamide may decrease the plasma concentration of darolutamide and is not recommended, unless there is no therapeutic alternative. Selection of an alternate concomitant medicinal product with less potential to induce CYP3A4 or P-gp should be considered. Patients should be monitored for adverse reactions of BCRP, OATP1B1 and OATP1B3 substrates as co-administration with darolutamide may increase the plasma concentrations of these substrates. Co-administration with rosuvastatin should be avoided unless there is no therapeutic alternative. In patients with a history of risk factors for QT prolongation and in patients receiving concomitant medicinal products that might prolong the QT interval, physicians should assess the benefit-risk ratio including the potential for Torsade de pointes prior to initiating NUBEQA. NUBEQA 300mg film-coated tablets contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicinal product. **Interactions:** For the effect of other medicinal products on the action of darolutamide (e.g CYP3A4, P-gp inducers and CYP3A4, P-gp and BCRP inhibitors, UGT1A9 inhibitors and docetaxel) and the action of darolutamide on other medicinal products (BCRP, OATP1B1, OATP1B3 substrates, P-gp substrates, docetaxel, CYP3A4 substrates and other medicinal products that prolong the QT interval) refer to the relevant SmPCs. **Pregnancy & lactation:** Darolutamide is not indicated in women of childbearing potential, and it is not to be used in women who are, or may be, pregnant or breast-feeding. Unknown whether darolutamide or its metabolites are present in semen. If the patient is engaged in sexual activity with a woman of childbearing potential, a highly effective contraceptive method (<1% failure rate per year) should be used during and for 1 week after completion of treatment. Unknown whether darolutamide or its metabolites are excreted in human milk. No studies in animals have been conducted to evaluate the excretion of darolutamide or its metabolites into milk. A risk to the breast-fed child cannot be excluded. There are no human data on the effect of darolutamide on fertility. Based on animal studies, darolutamide may impair fertility in males of reproductive potential. **Effects on ability to drive and use machines:** Darolutamide has no or negligible influence on the ability to drive and use machines. **Undesirable effects:** *Adverse reactions observed in patients with nmCRPC and mHSPC* *Very common:* fatigue/asthenic conditions, neutrophil count decreased, bilirubin increased, ALT increased, AST increased, anaemia. *Common:* ischaemic heart disease, heart failure, rash, pain in extremity, fractures. *Serious adverse reactions:* cardiac arrhythmias, urinary retention, urinary tract infection, pneumonia, fractures, seizure. *Adverse reactions observed in patients with mHSPC treated with darolutamide in combination with docetaxel*. *Very common:* hypertension, rash, blood bilirubin increased, ALT increased, AST increased. *Serious adverse reactions:* fractures, ischaemic heart disease, seizure, febrile neutropenia, neutrophil count decreased, pneumonia. Prescribers should consult the SmPC in relation to other side effects (see section 4.8 of SmPC). **Overdose:** In the event of intake of a higher than recommended dose, treatment with darolutamide can be continued with the next dose as scheduled. There is no specific antidote for darolutamide and symptoms of overdose are not established. **Legal Category:** POM. **Package Quantities & Basic NHS Costs:** Pack of 112 film-coated tablets, £4,040. **MA Number(s):** PLGB 00010/0677. **Further information available from:** Bayer plc, 400 South Oak Way, Reading RG2 6AD, United Kingdom. Telephone: 0118 206 3000. **Date of preparation:** June 2025



Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in Google Play or Apple App Store.
Adverse events should also be reported to Bayer plc.
Tel: 0118 206 3500, Fax: 0118 206 3703, Email: pvuk@bayer.com