Is there a "Cardio-friendly" ADT?

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Is there a "Cardio-friendly" ADT?

- Short-term increased risk of CVD (in men with pre-existing disease)
  - Most probably a class effect
- Long-term metabolic changes in everybody
Risk factors of CVD
Pre-existing cardiovascular morbidity

There were 2653 men with no comorbidity; 2168 with 1 cardiovascular risk factor including diabetes mellitus, hypercholesterolemia, or hypertension; and 256 with known coronary artery disease resulting in congestive heart failure or myocardial infarction. After applying the Bonferroni correction, *P* values <.017 are significant.

Nanda et al. JAMA 2009; 302:866-73
Lower incidence of CV events with degarelix vs LHRH agonists in patients with CV history

<table>
<thead>
<tr>
<th></th>
<th>Degarelix, n (%)</th>
<th>LHRH agonist, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=463</td>
<td>n=245</td>
</tr>
<tr>
<td>Any CV event</td>
<td>21 (4.5)</td>
<td>23 (9.4)</td>
</tr>
<tr>
<td>Death</td>
<td>9 (1.9)</td>
<td>13 (5.3)</td>
</tr>
</tbody>
</table>

CV, cardiovascular  
LHRH, luteinizing hormone-releasing hormone
Lower risk of CV event or death with degarelix in men with baseline CVD

HR adjusted by Cox regression for common CV risk factors including age, statin use, hypertension and serum cholesterol

Albertsen PC et al. 2014 Mar;65(3):565-73

CV, cardiovascular; CVD, CV disease; HR, hazard ratio
LHRH, luteinizing hormone-releasing hormone
NNT, number needed to treat
Less CV events with GnRH antagonists compared to the agonists during a median follow up period of 6.3 months

<table>
<thead>
<tr>
<th>Condition</th>
<th>GnRH agonist (n=23)</th>
<th>GnRH antagonist (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic heart disease</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Ischemic cerebrovascular accident</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>-</td>
</tr>
</tbody>
</table>

6 patients in the GnRH agonist arm developed a new CV event, none of the patients in the FIRMAGON arm experienced any new CV event.

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  - Largely a physician effect
Overall survival...
Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer.


- Median adherence to prescribed exercise was 85.5%.
- Resistance (p.010) and aerobic exercise (p.004) mitigated.
- Resistance training improved QOL (p.015), aerobic fitness (p.041), upper- (p.001) and lower-body (p.001) strength, and triglycerides (p.036), while preventing an increase in body fat (p.049).
Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer.
A prospective, randomized pilot study evaluating the effects of metformin and lifestyle intervention on patients with prostate cancer receiving androgen deprivation therapy


- 40 men with PCa due to receive ADT randomized standard care vs. 6 months of metformin, a low glycemic index diet and an exercise programme.
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  - *Can we use a drug that doesn’t induce metabolic complications*
Cardiovascular toxicity of antiandrogens

Association between androgen deprivation therapy and diabetes, coronary heart disease, myocardial infarction, sudden death, and stroke.

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Enzalutamide monotherpy in hormone-naive prostate cancer: primary analysis of an open-label, single-arm, phase 2 study

Bertrand Tombal, Michael Borre, Per Rathenborg, Patrick Werbrouck, Hendrik Van Poppel, Axel Heidenreich, Peter Iversen, Johan Braeckman, Jiri Heracek, Edwina Baskin-Bey, Taoufik Ouatas, Frank Perabo, De Phung, Mohammad Hirmand, Matthew R Smith

Long-term Efficacy and Safety of Enzalutamide Monotherapy in Hormone-naïve Prostate Cancer: 1- and 2-Year Open-label Follow-up Results

Bertrand Tombal a, Michael Borre b, Per Rathenborg c, Patrick Werbrouck d, Hendrik Van Poppel e, Axel Heidenreich f, Peter Iversen g, Johan Braeckman h, Jiri Heracek i, Edwina Baskin-Bey j, Taoufik Ouatas j, Frank Perabo k, De Phung j, Benoit Baron j, Mohammad Hirmand l, Matthew R. Smith m

### Metabolic changes under enzalutamide monotherapy

**Table 4 – Body composition and bone turnover biomarkers at weeks 49 and 97**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th></th>
<th>Week 49</th>
<th>Mean change from baseline, % (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean (SD)</td>
<td>n</td>
<td></td>
</tr>
<tr>
<td><strong>Body composition</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone mineral density (g/cm²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>1.2 (0.1)</td>
<td>36</td>
<td>-0.2 (2.1)</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>50</td>
<td>0.9 (0.2)</td>
<td>41</td>
<td>-0.4 (2.6)</td>
</tr>
<tr>
<td>Trochanter</td>
<td>50</td>
<td>0.8 (0.2)</td>
<td>41</td>
<td>-1 (3)</td>
</tr>
<tr>
<td>Spine L1–L4</td>
<td>51</td>
<td>1.2 (0.2)</td>
<td>40</td>
<td>-0.6 (3.3)</td>
</tr>
<tr>
<td>Forearm (radius 33%)</td>
<td>52</td>
<td>0.8 (0.1)</td>
<td>41</td>
<td>+0.5 (2.7)</td>
</tr>
<tr>
<td>Fat body mass (kg)</td>
<td>50</td>
<td>25 (7)</td>
<td>36</td>
<td>+9 (18)</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>50</td>
<td>57 (7)</td>
<td>36</td>
<td>-4.4 (4)</td>
</tr>
<tr>
<td><strong>Bone turnover biomarkers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone alkaline phosphatase (µg/l)</td>
<td>67</td>
<td>11 (6)</td>
<td>53</td>
<td>+12 (32)</td>
</tr>
<tr>
<td>N-telopeptide (nmol/l)</td>
<td>65</td>
<td>334 (177)</td>
<td>52</td>
<td>+62 (120)</td>
</tr>
<tr>
<td>N-telopeptide/creatinine (nmol/mol creatinine)</td>
<td>65</td>
<td>28 (13)</td>
<td>52</td>
<td>+64 (66)</td>
</tr>
</tbody>
</table>

SD = standard deviation; NA = not available.
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