Case SIGNOUT:

29 yo AA male inmate with known pulmonary sarcoid presented to CPMC from an outside hospital with ventricular tachycardia and a reduced EF of 15%. Initial attempts to pharmacologically control his rhythm as well as an attempt at ablation failed. Ventricular arrhythmias felt to be secondary to cardiac involvement of sarcoidosis and pt started on prednisone 1 mg/kg/day with near complete resolution of arrhythmia after 3 days. Pt advised to maintain on oral prednisone for at least 1 year. After reading the risks of the medications pt wants to do everything to avoid the complications of osteoporosis.

Clinical Question: Is there any evidence that bisphosphonates prevent osteoporosis in patient taking long term steroids?

Search Strategy

Database: Pubmed search


### Group Criteria or definition n

<table>
<thead>
<tr>
<th>Population screened.</th>
<th>15 center in the US and 22 centers in 15 other countries</th>
<th>Not clear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria</td>
<td>Male and female 17-83 with underlying derm, GI, pulm requiring ≥1 yr of at least 7.5 mg prednisone or equivalent</td>
<td>560</td>
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<tr>
<td>Exclusion criteria</td>
<td>Metabolic bone disease, low serum 25 vit D, currently taking calcitonin or bisphosphonate, preg, creat clear &lt;35, severe cardiac or upper GI disease</td>
<td>D</td>
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<tr>
<td>Treatment group</td>
<td>2.5, 5, or 10 mg of alendronate qd</td>
<td>83, 161 and 157</td>
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<tr>
<td>No treatment group</td>
<td>Placebo</td>
<td>159</td>
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Primary endpoints: Difference in the % change in lumbar spine bone density from baseline to 48 wks.

Secondary endpoints: Changes in bone density of the hip, biochemical markers of bone turnover and new vertebral markers.

- Are the Results of the Trial Valid?
  - Randomized? Yes
  - All patients accounted for at end? No. For primary endpoint 12 pts missing in the 10 mg group, 15 pts in the 5 mg group and 17 pts in the placebo group
  - Intention to treat? Yes-Data used from last BMD measurement if pt not available for 48 wk
  - Blinding? Yes
  - Groups similar at start of trial? Yes
  - Equal treatment of groups? Yes
  - Did randomization work? Yes

- Are the Results of the Trial important?
  - Size of treatment effect? -0.4 % in placebo, 2.1% in 5 mg, 2.9% in 10 mg
  - Precision of the estimate of the effect? Study only provides SE of the mean. If we calculate the SD based on our knowledge of the # of pts in the study group SD would be ~3.6 % in the treatment groups. Not a very precise measurement of effect.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Result</th>
<th>Significance</th>
<th>ARR</th>
<th>NNT</th>
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</thead>
<tbody>
<tr>
<td>Bone mineral density</td>
<td>+2.1 and +2.9 % inc</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>Vertebral fractures</td>
<td>RR 0.6 (0.1-4.4)</td>
<td>0.18</td>
<td>-1.3</td>
<td>77</td>
</tr>
</tbody>
</table>

- Can I apply these results to my patient?
  - Comparison of my patient to trial patients. My patient would potentially be excluded from this trail due to underlying “severe cardiac disease” though this is not defined. Otherwise our patient would be included.
- All clinically important outcomes considered. Bone density in the past has been shown to be a good surrogate for risk of fractures. Would like to have seen clinically (as opposed to radiographically) noted fractures sited. Study to brief and too small to show a difference in even radiographically noted fractures.

- Likely benefits outweigh potential harms and cost? Would like to see longer follow up to this study particularly seeing what happens to patients who stop steroids & bisphosphonates at 1 year. Are they protected against fractures in the long run? Other studies have shown a precipitous drop in bone mineral density once bisphosphonates are d/ced. I think I would like to see longer follow particularly since our patient is so young. Nevertheless a well validated surrogate marker (change in bone density) clearly is improved in this study and the potential harms of this therapy are few. Of note though in this study with the placebo group taking >1000 mg of calcium + vit D there is very little bone density (-0.4%) over the course of 1 yr.