Prostate Cancer

- Sixth most common cancer in the world; \( \sim 396,000 \) new cases annually (11,191 in Australia in 2001)
- Predicted incidence in Australia rising to 15,200 in 2011
- Life time risk in ACT (to age 75 yrs) is 1:8
- Incidence ACT 186 cases, 29 deaths per year
- 85% to 100% of patients who develop advanced prostate cancer will have bone metastases (often osteoblastic)
  - Pain, fractures, and spinal cord compression are serious and morbid complications
**Risk Factors for Prostate Cancer**

- Age
- Obesity
- Alcohol and dietary factors
- Hereditary factors

*Incidence per 100,000 male population.

How to treat Prostate Cancer

- Low risk (stage T1, T2A or B, PSA < 10, GS≤7): watch and wait, prostatectomy, or radiotherapy.
- Locally advanced (T2 & GS≥8, T3 or T4, PSA <40): radiotherapy and adjuvant androgen deprivation therapy.
- Metastatic disease hormone sensitive: Androgen deprivation therapy.
- Metastatic disease castrate resistant: bisphonates (esp Zometa), and chemotherapy.

Localised Prostate Cancer

“Is cure necessary in those in whom it may possible, and is cure possible in those in whom it is necessary?”

*Whitmore, 1990*
Androgen Deprivation Therapy

► Bilateral orchidectomy: effective, cheap, safe. Also permanent.
► LHRH analogue: Simple and safe, produces a brief surge in serum testosterone at about day 10-14.
► Non-steroidal anti-androgens. Bind to competitively to the ligand-binding pocket of the AR.

Long term androgen deprivation therapy

► Loss of libido, sexual function
► Fatigue
► Osteoporosis
► Diabetes
► Hyperlipidaemia
► Reduced muscle strength
New information in 2011

► For locally advanced disease, omitting radiotherapy and relying on lifelong hormonal therapy alone is inferior.
► Second line chemotherapy with cabazitaxel associated with a small survival benefit after failure of docetaxel.
► Abiraterone is effective in castrate-resistant metastatic prostate cancer.
► Denosumab is slightly superior to zoledronate in preventing bone complications in castrate resistant prostate cancer.
Methods COU-AA-301

- 1195 pts with m castrate resistant prostate cancer previously treated with docetaxel were randomise 2:1 to abiraterone 1000mg + prednisone 5mg bd vs. placebo + prednisone 5mg bd.
- Primary endpoint was OS

Conclusions

- Abiraterone + prednisone significantly improves OS, time to PSA progression, time to radiographic progression, and PSA response rate in advanced metastatic CRPC.
- Toxicity was mechanism related and easily managed.
- A phase IV study/access program may be available in TCH in new year.
Cabazitaxel + prednisone (CBZP) versus mitoxantrone+ prednisone (MP) in the treatment of metastatic castration-resistant prostate cancer (mCRPC) previously treated with a docetaxel-based regimen

**Final Results of the Phase III TROPIC Trial**

Oliver Sartor, MD
Johann de Bono, MD, PhD

On behalf of the TROPIC Investigators

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**Primary Endpoint: Overall Survival (ITT Analysis)**

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>0 months</th>
<th>6 months</th>
<th>12 months</th>
<th>18 months</th>
<th>24 months</th>
<th>30 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MP</strong></td>
<td>377</td>
<td>300</td>
<td>188</td>
<td>67</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td><strong>CBZP</strong></td>
<td>378</td>
<td>321</td>
<td>231</td>
<td>90</td>
<td>28</td>
<td>4</td>
</tr>
</tbody>
</table>

**Proportion of OS (%)**

<table>
<thead>
<tr>
<th></th>
<th>MP</th>
<th>CBZP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median OS</strong></td>
<td>12.7</td>
<td>15.1</td>
</tr>
<tr>
<td><strong>Hazard Ratio</strong></td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td><strong>95% CI</strong></td>
<td>0.59–0.83</td>
<td></td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td>&lt;0.0001</td>
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</tr>
</tbody>
</table>
Research

► Most pressing need is a reliable biomarker of aggressiveness of an early prostate cancer to inform the decision to treat radically.

► Many clinical trials in advanced disease:
  TAK-700 in chemo naive CRMPG.
  Cabazitaxel in docetaxel resistant MPC.
  Abiraterone in docetaxel resistant MPC.

Research

► PC4 = Primary Care Collaborative Trials Group, funded by Cancer Australia.

► Proposing a trial of follow-up of post prostatectomy patients in a primary care setting.