Patient ranking of late symptoms after breast and prostate cancer and their influence on self initiated nutritional therapies

The Bedford Real World Study

MASCC/IS00
Annual Meeting on Supportive Care in Cancer
Adelaide, Australia | 23-25 June, 2016
Background and aims

To explore whether asking patients from a real world population to rank their troublesome late toxicities would give a difference profile than expected from RCT data who to be:

- Older
- Ethnically more diverse
- More co-morbidities
- Be in other trials
- Have had previous malignancies

Precise knowledge of toxicities are important to:

- Counsel patients on the risks and benefits of adjuvant therapies
- Advise appropriate exercise / lifestyle strategies
- Educate physicians on what to expect in the follow up period
- Help priorities clinical trials to patient needs
Funding: The Primrose Oncology Research Fund. No commercial input

<table>
<thead>
<tr>
<th>Company Name</th>
<th>Honoraria/Expenses</th>
<th>Consulting/Advisory Board</th>
<th>Funded Research</th>
<th>Royalties/Patent</th>
<th>Stock Options</th>
<th>Ownership / Equity Position</th>
<th>Employee</th>
<th>Other (please specify)</th>
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<tr>
<td>Astrazeneca</td>
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<td>Prostate Cancer</td>
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<td>Nature-medical Ltd</td>
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Aims

Studies have reported 50-65% cancer patients take OTCS\(^1,2\)

This study aimed to establish whether:
- Treatment pathways and the level of side effects influence OTC supplement intake.
- Which supplements are taken and for what reason

Methods

Every patients with Ca prostate & breast, >6months post sx, rxt or chemo - Primrose unit

Data recorded during their routine consultation by one of 5 oncologist or 2 specialist nurses.

Sept 15 to Feb 16.
830 (97%) filled questionnaire

480 men (Prostate) and 350 women (Breast Cancer)

Average age 63 years (Range 36-87 years)

437 (53%) on hormone therapies:
- LHRH agonists
- Tamoxifen
- Anastrozole
- Exemestane
- Letrozole
Level of self reported troublesome toxicities

(>1):

- Overall: 393 of 830 (47%)
- Hormones: 305 of 437 (70%)
- No hormones: 88 of 393 (22%)
  Diff 48% (Chi$^2$ P = 0.002)

(>2):

- Overall: 370 of 830 (45%)
- Hormones: 300 of 437 (69%)
- No hormones: 70 of 393 (18%)
  Diff 51% (Chi$^2$ P = 0.001)

(>3):

- Overall: 319 of 830 (38%)
- Hormones: 284 of 437 (65%)
- No hormones: 35 of 393 (9%)
  Diff 56% (Chi$^2$ P = 0.001)
## Ranking of distress

<table>
<thead>
<tr>
<th>Women:</th>
<th>Men:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hot flushes</td>
<td>1. Hot flushes</td>
</tr>
<tr>
<td>62%</td>
<td>61%</td>
</tr>
<tr>
<td>2. Arthralgia</td>
<td>2. Fatigue</td>
</tr>
<tr>
<td>55%</td>
<td>42%</td>
</tr>
<tr>
<td>3. Fatigue</td>
<td>3. Arthralgia</td>
</tr>
<tr>
<td>42%</td>
<td>39%</td>
</tr>
<tr>
<td>4. Mood</td>
<td>4. ED / Libido*</td>
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<tr>
<td>29%</td>
<td>25%</td>
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<tr>
<td>5. Weight gain</td>
<td>5. Mood</td>
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<tr>
<td>28%</td>
<td>15%</td>
</tr>
<tr>
<td>6. Vag dryness</td>
<td>6. Weight gain</td>
</tr>
<tr>
<td>10%</td>
<td>15%</td>
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</tbody>
</table>

* Afro-Caribbean men ranked erectile dysfunction over hot flushes.
Established Arthritis incidence

<table>
<thead>
<tr>
<th>Muscle &amp; Skeletal</th>
<th>Anastrozole</th>
<th>Tamoxifen</th>
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</thead>
<tbody>
<tr>
<td>Arthritis</td>
<td>512 (17)</td>
<td>445 (14)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>467 (15)</td>
<td>344 (11)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>325 (11)</td>
<td>226 (7)</td>
</tr>
<tr>
<td>Fracture</td>
<td>315 (10)</td>
<td>209 (7)</td>
</tr>
<tr>
<td>Bone pain</td>
<td>201 (7)</td>
<td>185 (6)</td>
</tr>
<tr>
<td>Arthrosis</td>
<td>207 (7)</td>
<td>156 (5)</td>
</tr>
<tr>
<td>Joint Disorder</td>
<td>184 (6)</td>
<td>160 (5)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>179 (6)</td>
<td>160 (5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Men LHRH analogues (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot Flashes</td>
</tr>
<tr>
<td>Sexual Dysfunction</td>
</tr>
<tr>
<td>Decreased Erections</td>
</tr>
<tr>
<td>Lower Urinary Tract Symptoms</td>
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<tr>
<td>Lethargy</td>
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<tr>
<td>Pain (worsened in the first 30 days)</td>
</tr>
<tr>
<td>Edema</td>
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<tr>
<td>Upper Respiratory Infection</td>
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<tr>
<td>Rash</td>
</tr>
<tr>
<td>Sweating</td>
</tr>
<tr>
<td>Anorexia</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
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<tr>
<td>Dizziness</td>
</tr>
<tr>
<td>Insomnia</td>
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<tr>
<td>Nausea</td>
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</table>
Arthralgia & cancer treatments

- Osteoarthritis
- Chemotherapy (Taxotere)
- Tamoxifen
- Aromatase inhibitors
- Herceptin
- Tyrosine kinase inhibitors
Arimidex (anastrozole)

Your doctor has recommended a medication call Arimidex. It summarises possible side effects and methods to manage them. It can cause the cancer cells to stop growing and it does this by stopping the production of oestrogen.

How do they work? Some tumours such as breast cancers can cause the cancer cells to stop growing and it does this by stopping the production of oestrogen.

How are they taken? Arimidex is prescribed by your doctor. Some women prefer to take it with food as it may cause nausea. It is easier to remember to take the tablets in the long term.

If you forget to take your tablet don’t panic – levels of the drug in your body will drop gradually over a couple of weeks before you run out of the tablets and make sure you have your next dose covered.

What are they taken for? There are 6 main reasons why post menopausal women are prescribed Arimidex.

- To control or shrink an established breast cancer (palliation), e.g. if your cancer has spread.
- To shrink a tumour in the breast before surgery (neo-adjuvant therapy).
- Given in a frail or elderly women to control a tumour in the breast.
- In the adjuvant setting (given after the main therapies such as surgery and chemotherapy).
- There is also evidence that some women may be better off taking it than not.
- Finally, they have been shown to be slightly more effective in some patients than were initially aggressive (grade 3) or had spread to the nodes, were
Exercise after Cancer

Current exercise levels
GPPAQ

<table>
<thead>
<tr>
<th>Status</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive</td>
<td>62%</td>
</tr>
<tr>
<td>Moderately Inactive</td>
<td>14%</td>
</tr>
<tr>
<td>Moderately Active</td>
<td>13%</td>
</tr>
<tr>
<td>Active</td>
<td>11%</td>
</tr>
</tbody>
</table>

Barriers to exercise

- Arthritis
- Other health issues
- No time
- Not enjoyable
- Already exercising

Thomas et al Clinical Oncology (2013) 25 (4) 246-51
Benefits of physical activity after cancer

Meta-analysis of 33 RCT

Significant benefits for Fatigue, Mood, QoL.

Fong, Bourke et al  *BMJ* 2012; 344:

Evidence review of international studies

Hot flushes, peripheral neuropathy, weight gain

2-4 hrs PA a week linked to 30-40% reduction in relapse

Thomas et al *BJMP* 2015; 7 (1) 2-9.
Exercise for arthritis

HOPE study New York 2014

121 patients

Usual post treatment care

30 mins 4 times/wk aerobic exercise

30% better pain, stiffness and qol at 12 weeks

Irwin et al JCO 2015,(33),10.
Barrier to exercise is arthralgia
OTC supplementation - men

Total group  498 of 830 (60%) took OTCS

Men (prostate cancer) -

- Overall 309 of 480 (64%) took OTCS
- >1 symptoms  107 of 191 (56%)
- No symptoms 202 of 289 (69%)*
  Diff 13% (Chi² p=0.15).

*78% of men managed on active surveillance took Pomi-T or other polyphenol rich OTCS.
What OTCS are men taking?

- Pomi-T 78%
- Saw palmetto 18%
- Lycopene 15%
- Selenium or/plus Zinc 14%
- Multivitamins 10%
- Apricot kernels 8%
- Turmeric 8%
- Other 12%
Median percentage rise in PSA between the two randomised groups

Difference 63.8% ANCOVA p=0.0008

- Median rise 78% 95% CI 48-115%
- Median rise 14.7% 95% CI 3-36%

Thomas et al. The Pomi-T study Prostate cancer & Prostate diseases 2014, (17)
Thomas et al. J Lifestyle Med. 2015 (1) 01
HPF: Men taking Zn 100mg/day - prostate ca worse [Leitzmann]
SELECT: Vit E & selenium - prostate ca worse [Klein].
CV247: RCT - no benefit of Cu, Mg, Vit C over lifestyle [Thomas]
VITAL cohort: Lycopene, Saw Palmetto, Genistein – no effect [Brasky]
VITAL cohort: prostate cancer lower with grape seed extract [Brasky]
RCT of saw palmetto: – No effect on BPH or cancer [Brent]
Phase II: genistein no psa effect, increased IFGF [Spentzos]
RCT (x2): lycopene – no effect on psa [Barber, Clark]
Women (breast cancer)

- Overall 189 of 350 (54%) took PTCS
- >1 symptoms 159 of 202 (79%)
- No symptoms 30 of 148 (20%)
  Diff 59% (Chi² p=0.003).
### OTCS among women with symptoms

<table>
<thead>
<tr>
<th>Supplement</th>
<th>% Taking*</th>
<th>Helpful</th>
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</thead>
<tbody>
<tr>
<td>Evening primrose / Starflower oil</td>
<td>45%</td>
<td>45%</td>
</tr>
<tr>
<td>Glucosamine or/+ Chondroitin</td>
<td>41%</td>
<td>30%</td>
</tr>
<tr>
<td>Fish oils</td>
<td>21%</td>
<td>48%</td>
</tr>
<tr>
<td>Multivitamins</td>
<td>12%</td>
<td>50%</td>
</tr>
<tr>
<td>Pomi-T</td>
<td>8%</td>
<td>85%</td>
</tr>
<tr>
<td>St Johns wart</td>
<td>5%</td>
<td>74%</td>
</tr>
<tr>
<td>Grape seed</td>
<td>10%</td>
<td>70%</td>
</tr>
<tr>
<td>Other</td>
<td>12%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>54%</strong></td>
<td><strong>63%</strong></td>
</tr>
</tbody>
</table>

*at time of survey
Supplements for arthritis

**Glucosamine** – 13 RCT - Two Meta-analysis - Doubtful benefit

**Chondroitin** - 22 RCT - Two meta-analysis - Doubtful benefit

**Fish oils** - 17 RCT Rheumatoid arthritis benefits but not OA

Reichenbach et al Anns of Int Med 2007; 146(8):580
Cleland 2006, Fortin 1995
Polyphenol rich foods

Populations who eat these foods have a lower incidence of arthritis and laboratory studies show they have cartilage protecting properties:

1. Anti-inflammatory properties, which reduce the discomfort and stiffness [Mitchel].

2. Anti-oxidant properties, which protect the joint from oxidative damage [Giovannucci, Stivala].

3. Anti-apoptopic effects on chondrocytes reducing cartilage degeneration [Shen].

4. Modulation metalloproteinases – remodels cartilage in arthritic joints [Dahlberg, Brinckerhoff].
A double blind RCT of phytochemical rich food for arthralgia post hormonal treatments

(EudraCT 2015-002018-66)

220 Breast and Prostate patients Taking hormonal therapies)

110 randomised placebo

- Arthralgia scores
- QoL
- Exercise levels
- Hot flushes
- Breast pain

110 randomised to interventional supplement

- Arthralgia scores
- QoL
- Exercise levels
- Hot flushes
- Breast Pain
Conclusion

Asking a large real world group of patients to rank their most trouble symptoms reveals:

- Hormone therapies in men and women have a considerable burden of late effects
- Patients rank arthritis at considerable higher level than expected from previous RCT’s

  - Counsel patients on the risks and benefits of adjuvant therapies
  - Improve accuracy and specificity of information tools
  - Educate physicians and patients – what to expect.
  - Preventative advice:
    - Weight control
    - Exercise and stretching
    - Polyphenol rich foods

- OTCS similar to previous studies but
  - In women >3 times more likely if troubled with symptoms - unmet needs?
  - In men common in AS – some of which appropriate

- Highlight the need for a National RCT evaluating whether polyphenol supplements and exercise will reduce arthritis incidence and improve wellbeing
Our ongoing research programme