Scalp Cooling to Prevent Chemotherapy-Induced Alopecia: The US Experience

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Baylor College of Medicine
• Clinical trial funding by Paxman Ltd (to institution)
Background

- Chemotherapy treats micro-metastatic disease & can decrease the risk of breast cancer recurrence

- It is associated with side effects such as chemotherapy-induced alopecia. Women rate this as one of the most severe, distressing and troublesome side effects

- Many countries use scalp cooling devices to prevent chemotherapy-induced alopecia with variable success rates based on non-randomized trials (25%-100% hair retention)
How Scalp Cooling Works
Why Not Used In the US Sooner?

• Devices have more stringent and different approval processes which the cold caps did not have to go through

• The FDA had concerns about patient safety and the possibility of scalp metastasis. There are 2 large studies from other countries showing no increase in scalp metastasis or change in overall survival with device use.

• FDA cleared the first scalp cooling device Dec 2015
  – This was a non-randomized trial and only looked at taxane-based chemotherapy.
  – Showed 66% hair retention.
SCALP Trial

• Demonstrate the safety and efficacy of scalp cooling devices in reducing chemotherapy-induced alopecia

• SCALP is the first randomized trial in the world to evaluate modern scalp cooling
SCALP Trial

- December 2013 – September 2016
- Open at 7 sites across the US
  - 3 academic centers
  - 4 community oncology clinics
- 229 women signed consent
Key Eligibility

**Inclusion Criteria**
- Stage 1 or 2 breast cancer
- Neoadjuvant or adjuvant chemotherapy

**Exclusion Criteria**
- Migraines
- Anemia
- Hypothyroidism
- Other uncontrolled medical conditions
Design

Enrollment → Randomization

Scalp Cooling Device → Assessed for:
- Alopecia
- Quality of Life
- Device Safety

Control → Assessed for:
- Alopecia
- Quality of Life
- Device Safety
Scalp Cooling Device Arm
Alopecia Grading: CTCAE Version 4.0

**Grade 0**
No hair loss

**Grade 1**
Hair loss of up to 50% of normal, no wig required

**Grade 2**
Hair loss of > 50% of normal, wig required

CTCAE = Common Terminology Criteria for Adverse Events Version 4.0
* CTCAE only defines alopecia through Grade 2
Pictorial Tool

Grade 0
No significant hair loss

Grade 1
Hair loss of up to 50% of normal for that individual that is not obvious from a distance but only on close inspection. A different hairstyle may be required to cover the hair loss but it does not require a wig or hair piece or camouflage.

Grade 2
Hair loss of >50% normal for that individual that is readily apparent to others. A wig or hair piece is necessary if the patient desires to completely camouflage the hair loss associated with psychosocial impact.
Examples of Grading

**Baseline**
(Grade 0 alopecia)

**Grade 1 Alopecia**
* 3-4 weeks after using cooling system for 4 cycles of chemo
Examples of Grading

Baseline
(Grade 0 alopecia)

Grade 2 Alopecia

* Subject in control group; 3 weeks after 2nd cycle of chemotherapy.

* Subject in cooling group; 3 weeks after using cooling system for 2 cycles of chemotherapy.
### Patient Reported Comfort Scale

<table>
<thead>
<tr>
<th>Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Comfortable</td>
</tr>
<tr>
<td>Reasonably Comfortable</td>
</tr>
<tr>
<td>Comfortable</td>
</tr>
<tr>
<td>Uncomfortable</td>
</tr>
<tr>
<td>Very uncomfortable</td>
</tr>
</tbody>
</table>

### Questionnaires

<table>
<thead>
<tr>
<th>Questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30</td>
</tr>
<tr>
<td>Hospital Anxiety Depression Scale</td>
</tr>
<tr>
<td>Body Image Scale</td>
</tr>
</tbody>
</table>
• 235 subjects were planned to be enrolled to provide 85% power to detect a 20% difference in hair preservation.

• The trial stopped early based on a pre-planned interim analysis for efficacy after 142 participants were evaluable for the primary endpoint with an O’Brien-Fleming spending function*
Statistical Analysis Plan

• Secondary endpoints included
  – Wig/scarf use
  – Quality of life
  – Hair preservation at completion of chemotherapy

• Study participants will be followed for 5 years post-study for time to first recurrence, overall survival, and site of first recurrence
Participant Flow Chart

293 Participants Consented

236 Randomized

157 Device

293 Participants Consented

236 Randomized

157 Device

130 Modified ITT

79 Control

54 Modified ITT

Why ineligible?
Hypothyroidism (11)
Anemia (10)
Stage 3 Breast Cancer (7)
Baseline Alopecia (5)
Migraines (4)
Age >= 70 (3)
Lichens Planus (2)
Other (6)

Why withdrew consent?
18 Randomized to Control
7 due to hair loss
6 in pre-cooling phase
• 4 Device (cold/discomfort)
• 1 Anxiety
• 1 Claustrophobia
4 during chemo (device cold)
2 alternate treatment
3 withdrew consent
1 chemo related
1 progressive disease
## Demographics & Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cooling</th>
<th>Non-Cooling</th>
<th>ALL</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=130</td>
<td>N=54</td>
<td>N=184</td>
<td></td>
</tr>
<tr>
<td>Age (years) Mean (SD)</td>
<td>50.4 (10.5)</td>
<td>51.7 (10.1)</td>
<td>50.8 (10.4)</td>
</tr>
<tr>
<td>Race [n (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>106 (81.5%)</td>
<td>41 (75.9%)</td>
<td>147 (79.9%)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>16 (12.3%)</td>
<td>8 (14.8%)</td>
<td>24 (13%)</td>
</tr>
<tr>
<td>Asian</td>
<td>5 (3.8%)</td>
<td>5 (9.3%)</td>
<td>10 (5.4%)</td>
</tr>
<tr>
<td>Ethnicity [n (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>20 (15.4%)</td>
<td>9 (16.7%)</td>
<td>29 (15.8%)</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>108 (83.1%)</td>
<td>45 (83.3%)</td>
<td>153 (83.2%)</td>
</tr>
<tr>
<td>Major Chemotherapy Type [n (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anthracycline</td>
<td>45 (34.6%)</td>
<td>23 (42.6%)</td>
<td>68 (37%)</td>
</tr>
<tr>
<td>Taxane</td>
<td>85 (65.4%)</td>
<td>31 (57.4%)</td>
<td>116 (63%)</td>
</tr>
<tr>
<td>Breast Cancer Stage [n (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>50 (38.5%)</td>
<td>19 (35.2%)</td>
<td>69 (37.5%)</td>
</tr>
<tr>
<td>Stage II</td>
<td>80 (61.5%)</td>
<td>35 (64.8%)</td>
<td>115 (62.5%)</td>
</tr>
</tbody>
</table>
Results: Primary Outcome

Hair Preservation After 4 Cycles of Chemotherapy

- Success
  - Cooling: 53.1% (44.5%, 61.4%)
  - Non-cooling: 0% (0%, 6.6%)

Fisher's exact test p<0.0001
Results: Primary Outcome

Hair Preservation in the Cooling Group (after 1st 4 cycles)

- **Taxane**: 63% (35%, 84.4%)
- **Anthracycline**: 24.1% (8.6%, 51.6%)
## Results: Adverse Events

<table>
<thead>
<tr>
<th>Adverse Device Effects: All Grade 1 or 2</th>
<th>Cooling N = 137</th>
</tr>
</thead>
<tbody>
<tr>
<td>AADEs (CTCAE V4.0)</td>
<td>Cycle 1</td>
</tr>
<tr>
<td></td>
<td>(n=137)</td>
</tr>
<tr>
<td>Headache</td>
<td>11.7%</td>
</tr>
<tr>
<td>Nausea</td>
<td>4.4%</td>
</tr>
</tbody>
</table>

<3% rate of dizziness, ear pain, scalp pain, sinus pain, pruritus, and dry skin
<1% rate of chills, jaw pain, paresthesia, skin and SC tissue disorder, and skin ulceration
## Results: Quality of Life

### Patient Reported Comfort Scale

<table>
<thead>
<tr>
<th>Comfort Scale</th>
<th>Cooling (N = 137)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cycle 1</td>
<td>Cycle 2</td>
<td>Cycle 3</td>
<td>Cycle 4</td>
<td>Cycle 5</td>
<td>Cycle 6</td>
<td>Cycle 7</td>
<td>Cycle 8</td>
</tr>
<tr>
<td>Very Comfortable</td>
<td>n=137</td>
<td>n=117</td>
<td>n=90</td>
<td>n=83</td>
<td>n=36</td>
<td>n=31</td>
<td>n=11</td>
<td>n=9</td>
</tr>
<tr>
<td>Very Uncomfortable</td>
<td>10.9%</td>
<td>15.4%</td>
<td>13.3%</td>
<td>15.7%</td>
<td>16.7%</td>
<td>12.9%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Reasonable Comfortable</td>
<td>51.8%</td>
<td>41.9%</td>
<td>50%</td>
<td>45.8%</td>
<td>50%</td>
<td>54.8%</td>
<td>45.5%</td>
<td>44.4%</td>
</tr>
<tr>
<td>Very Uncomfortable</td>
<td>-</td>
<td>3.4%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9.1%</td>
<td>-</td>
</tr>
<tr>
<td>Not Assessed</td>
<td>1.5%</td>
<td>1.7%</td>
<td>2.2%</td>
<td>1.2%</td>
<td>2.8%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Quality of Life Assessments showed no difference
### Secondary Endpoints

<table>
<thead>
<tr>
<th>Wig or Scarf Use</th>
<th>Cooling (%)</th>
<th>Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>33.9%</td>
<td>0%</td>
</tr>
<tr>
<td>Yes</td>
<td>44.6%</td>
<td>68.5%</td>
</tr>
<tr>
<td>Unknown (had grade 2 alopecia)</td>
<td>20%</td>
<td>31.5%</td>
</tr>
</tbody>
</table>
## Secondary Endpoints

### Hair Preservation in the Cooling Group at the End of Chemotherapy

<table>
<thead>
<tr>
<th>Category</th>
<th>Success (%)</th>
<th>Failure (%)</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>64.6% (53.8%, 74.1%)</td>
<td>-</td>
<td>n=130</td>
</tr>
<tr>
<td>TAXANE</td>
<td>46.2% (37.8%, 54.7%)</td>
<td>-</td>
<td>n=82</td>
</tr>
<tr>
<td>ANTHRACYCLINE</td>
<td>0% (0%, 56.1%)</td>
<td>-</td>
<td>n=3</td>
</tr>
<tr>
<td>BOTH</td>
<td>15.6% (7.7%, 28.8%)</td>
<td>-</td>
<td>n=45</td>
</tr>
</tbody>
</table>

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## Secondary Endpoints

<table>
<thead>
<tr>
<th>Chemotherapy Regimen</th>
<th>% Successful Hair Preservation (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2</td>
<td>0% (3)</td>
</tr>
<tr>
<td>Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2 + Docetaxel 100mg/m2</td>
<td>0% (3)</td>
</tr>
<tr>
<td>Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2 + Paclitaxel 80-90 mg/m2 weekly with carboplatin AUC of 6 every 3 weeks</td>
<td>66.7% (3)</td>
</tr>
<tr>
<td>Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2 + Paclitaxel 80mg-90/mg/m2 weekly</td>
<td>18.8% (16)</td>
</tr>
<tr>
<td>Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2 + Paclitaxel 175mg q2 weeks</td>
<td>40% (20)</td>
</tr>
<tr>
<td>Doxorubicin 50mg/m2 with 5-Fluorouracil 500mg/m2 and cyclophosphamide 500mg/m2 + Paclitaxel 80mg-90mg/m2 weekly</td>
<td>100% (1)</td>
</tr>
<tr>
<td>Doxorubicin 50mg/m2 with 5-Fluorouracil 500mg/m2 and cyclophosphamide 500mg/m2 + Paclitaxel 175mg/m2 q2 weeks</td>
<td>0% (1)</td>
</tr>
<tr>
<td>Paclitaxel 80mg/m2 - 90mg/m2 weekly (every 3 weeks constitute a cycle), or 175mg/m2 every 2-3 weeks as a single agent</td>
<td>100% (7)</td>
</tr>
<tr>
<td>Paclitaxel 80-90 mg/m2 weekly with carboplatin AUC of 6 every 3 weeks</td>
<td>100% (1)</td>
</tr>
<tr>
<td>Docetaxel 75mg/m2 - 100mg/m2 with pertuzumab/trastuzumab + Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2</td>
<td>0% (1)</td>
</tr>
<tr>
<td>Docetaxel 75mg/m2 with cyclophosphamide 600mg/m2</td>
<td>56.5% (46)</td>
</tr>
<tr>
<td>Docetaxel 75mg/m2 with carboplatin AUC of 6 and trastuzumab at standard doses</td>
<td>75% (28)</td>
</tr>
</tbody>
</table>
# Penguin Cold Cap Registry Study

<table>
<thead>
<tr>
<th>Regimen</th>
<th>% Successful Hair Retention</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC x 4</td>
<td>83.8% (31/37)</td>
</tr>
<tr>
<td>TC x 4-6</td>
<td>50% (5/10)</td>
</tr>
<tr>
<td>Weekly P → AC</td>
<td>43.4% (10/23)</td>
</tr>
<tr>
<td>AC → Weekly P</td>
<td>20% (2/10)</td>
</tr>
<tr>
<td>Taxotere/Carbo +/- Herceptin</td>
<td>100% (2/2)</td>
</tr>
<tr>
<td>Other</td>
<td>60% (9/15)</td>
</tr>
</tbody>
</table>
Conclusion from SCALP trial

• Scalp cooling devices are highly effective
• This device received FDA clearance in the US based on these data
• Need further studies exploring this technology for other types of tumors
• More studies for impact of chemotherapy-induced alopecia on psyche and body image
• Tailored QOL tools are needed to evaluate the impact of alopecia
Limitation to Device Use In the US

- Centers having them available
- Interest in Nursing Staff and Administration
- Extra chair time
- Cost
- Insurance Coverage?
Extra Chair Time

• Can be up to 90 min
• Can move patients to a different waiting area
• For HER2+ patients you can give the herceptin/pertuzumab after the chemo during the post-cooling time
• Carboplatin doesn’t cause hair loss and we also do this in the post-cooling time
• Paclitaxel use 60 min post-cooling time?
• Docetaxel use 20-40 min post-cooling time?
  * Prevent permanent alopecia?
Costs for Cooling Caps in the US

• Cooling Caps
  – Rent for a monthly fee
  – Patient pay directly and is ~$300-500 months
  – Many different companies offer these caps and anyone can rent them (not infusion center dependent)

• Cooling Devices
  – Leased by Centers
  – Patient pays per treatment (with Paxman lifetime max is $2200, Dignitana cost is set by centers but average $1500)
Implementation to Date

• Dignitana
  – 135 machines across 22 states

• Paxman
  – 289 machines across 23 states
Assistance for patients in the US

- HairToStay
  - Nonprofit that offers need-based grants to help offset the expense of cooling systems for chemotherapy patients in the US

- Rapunzal Project
  - Nonprofit dedicated to helping chemotherapy patients keep their hair during treatment
  - Has a nice list of locations where scalp cooling is available
  - Possible codes to help with insurance coverage and some success with BCBC, Aetana, and Horizon ranging from $50-400 per treatment
Tips for Use

• Lay out patient expectations
  – Most patients have hair thinning and lose 30% of their hair
  – Define what a success is upfront
  – Put ownership on the patient and explain to them that the better the fit, the better the chance of success
  – Sequence chemo with agent with less hair loss first (weekly paclitaxel → AC)
  – Tell patients to avoid stress to hair
    • no dye or straighteners/curling
    • use sulfate free shampoo/conditioner
    • comb hair in shower with conditioner in

– [https://www.paxmanusa.com/](https://www.paxmanusa.com/)
Who in the picture has cancer?
“Fighting Cancer on My Own Terms”