Impact of Cancer Therapies on Hair and Management Strategies

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- Research funding
  - Berg, BMS, Genentech/Roche, RJR Fund, Galderma, Paxman, Novartis

- Consulting/Advisory
  - Legacy, Novartis, Janssen, BMS, Genentech/Roche, Galderma, Debio, Pfizer, Helsinn, Silk Therapeutics, Foamix, Boehringer Ingelheim, Medische Voet
Targeting Cancer

1.7 million in US; 14.1 million worldwide

65% - systemic therapy

Holzel et al, Nat Rev Cancer 2013
And Targeting Hair

Cytotoxic /Endocrine Metabolites/ER/AR

Targeted EGFR/MEK/RAF

Immune Checkpoint Inhibitors CTLA-4/PD1/L1
Chemotherapy-Induced Alopecia (CIA): Impact

- Incidence
  - Chemotherapy: 60-100%
  - Targeted therapies: 30-50%
  - Immunotherapies: 5%

- Psychosocial impact
  - 17% most traumatic AE (n=91)
  - 30% severely limited by alopecia
  - Discordance between patient, PRO and clinician

- Detrimental Treatment Choices
  - 14% would consider refusing curative therapy (n=217)

CIA Prevention: Scalp Cooling Methods

Static
- Penguin™
- Elasto-Gel

Dynamic
- Dignitana®
- Paxman®

Shah et al, JEADV 2018
### Association Between Use of a Scalp Cooling Device and Alopecia After Chemotherapy for Breast Cancer

<table>
<thead>
<tr>
<th>Maximum Dean Score(^{a})</th>
<th>Hair Loss, %</th>
<th>Scalp Cooling Group (n = 101)(^{b})</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>5</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>&gt;0-≤25</td>
<td>31</td>
<td>67%</td>
</tr>
<tr>
<td>2</td>
<td>&gt;25-≤50</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>&gt;50-≤75</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>&gt;75</td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>

**67% hair retention**

### Effect of a Scalp Cooling Device on Alopecia in Women Undergoing Chemotherapy for Breast Cancer

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cooling (n = 95)</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hair preservation(^{b})</td>
<td>No.</td>
<td></td>
</tr>
<tr>
<td>Success(^{c})</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Alopecia grade 0</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Alopecia grade 1</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Failure</td>
<td>47</td>
<td></td>
</tr>
</tbody>
</table>

**51% hair retention**

Rugo et al, JAMA 2017; Nangia et al, JAMA 2017
Scalp Cooling to Prevent CIA

Baseline

AC→Paclitaxel
Permanent Chemotherapy-Induced Alopecia...

Did You Suffer Permanent Hair Loss After Chemotherapy?

Popular chemo drug Taxotere® has been linked to alopecia (permanent hair loss)...

Taxotere® (Docetaxel) is a "taxane" chemotherapy drug that is given intravenously for patients of...

- Breast cancer
- Non-small cell lung cancer
- Advanced stomach cancers
- Head and neck cancers
- ...and other serious cancers

FAILED TO WARN PATIENTS: Sanofi-Aventis™, the drug company behind Taxotere® is under allegations of negligence for having FAILED TO WARN patients and physicians of the known risk of permanent hair loss (alopecia)
Persistent Chemotherapy-Induced Alopecia

- Alopecia lasting >6 mos post completion (n=98)
  - Paclitaxel: 39.5% (n=61)
  - Docetaxel: 6.3-15.8% (n=112-134)

Kang et al, MASCC 2017; Freites-Martinez et al, MASCC 2017, JAAD 2018
Persistent Chemotherapy-Induced Alopecia

Impact on QoL (n=94)

Hair Shaft Density/Diameter (n=82)

Docetaxel pCIA

Control

Minoxidil ± Spironolactone
n=54

No Improvement
Moderate Improvement
Significant Improvement

Freites-Martinez et al, MASCC 2017
pCIA Management-Clinical Outcome

Docetaxel, 56 y/o

Tamoxifen + Minoxidil + PRP
Tamoxifen-Induced Total Alopecia

Aromatase inhibitors induce ‘male pattern hair loss’ in women?

Estrogen (not Testosterone) is Good for Hair

Estradiol + Spironolactone

Adenuga et al, JAAD 2012
**CHANCE: A Prospective, Longitudinal Study of Chemotherapy-Induced Hair, Skin And Nail Changes in Women with Breast Cancer**

- That I will permanently lose my hair from chemotherapy or with hormones?
  - Primary endpoint: Incidence/severity of permanent CIA or HTIA

### Therapy Init | Eval | Eval | Eval | Eval | Study end
---|---|---|---|---|---
Yr 0 | Yr 1 | Yr 2 | Yr 3

<table>
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<th>Cohorts</th>
<th>Treatment Regimen</th>
<th>Individual Drugs</th>
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<td>CYTOTOXIC CHEMOTHERAPY</td>
<td>I (n=100)</td>
<td>ddAC-T</td>
<td>Doxorubicin + Cyclophosphamide + Paclitaxel</td>
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<td>II (n=100)</td>
<td>CMF</td>
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<td>III (n=100)</td>
<td>Newer Combination Regimens</td>
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<td>ENDOCRINE THERAPY</td>
<td>IV (n=100)</td>
<td>Tamoxifen</td>
<td>Tamoxifen</td>
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<td>V (n=100)</td>
<td>Aromatase Inhibitor</td>
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<tr>
<td>COMPARATOR (menopausal women)</td>
<td>VI (n=100)</td>
<td>NA</td>
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ClinicalTrials.gov Identifier: [NCT02530177](https://clinicaltrials.gov/ct2/show/NCT02530177)
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Memorial Sloan Kettering Cancer Center.

ClinicalTrials.gov Identifier: NCT02530177
### Alopecia

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<thead>
<tr>
<th>Alopecia</th>
<th>Tamoxifen cohort N=21 (%)</th>
<th>Aromatase inhibitor cohort N= 20 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CTCAE v4.03</strong></td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td>Grade 0 (no alopecia)</td>
<td>14 (66.7)</td>
<td>6 (28.6)</td>
</tr>
<tr>
<td>Grade 1 (&lt;50% of hair loss)</td>
<td>7 (33.3)</td>
<td>15 (71.4)</td>
</tr>
<tr>
<td>Grade 2 (&gt;50% of hair loss)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Trichoscopy data</strong></td>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td>Hair shaft N per cm²</td>
<td>199 (36.51)</td>
<td><strong>190.4 (33.49)</strong></td>
</tr>
<tr>
<td>Hair thickness (microns)</td>
<td>70 (10)</td>
<td>70 (10)</td>
</tr>
</tbody>
</table>

**CHANCE study** (Data cutoff December 2017)

Lacouture et al, ASCO Annual Meeting 2018
### CHANCE study (Data cutoff December 2017)

<table>
<thead>
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<th>Skin disorders a year after follow-up</th>
<th>Tamoxifen cohort N=21 (%)</th>
<th>Aromatase inhibitor cohort N= 20 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyelash alopecia (any grade)</td>
<td>3 (14.3)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Eyebrow alopecia (any grade)</td>
<td>2 (9.5)</td>
<td>2 (10)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nail disorders*</th>
<th>Tamoxifen cohort N=17 (%)</th>
<th>Aromatase inhibitor cohort N= 16 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nail discoloration (Grade 1)</td>
<td>6 (35.3)</td>
<td>7 (43.8)</td>
</tr>
<tr>
<td>Nail ridging</td>
<td>8 (47)</td>
<td>10 (62.5)</td>
</tr>
<tr>
<td>Nail loss</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Paronychia</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Lacouture et al, ASCO Annual Meeting 2018
Quality of Life  
\( n=52 \)

Hair Shaft Diameter  
\( n=82 \)
Tamoxifen, 39 y/o

Tamoxifen + Minoxidil

Freites-Martinez et al, JAMA Dermatol 2018
Anastrozole, 72 y/o

Freites-Martinez et al, JAMA Dermatol 2018
Endocrine Therapy-Induced Alopecia in Patients With Breast Cancer

Minoxidil 5% (n=46)

- No Improvement: 26%
- Moderate Improvement: 50%
- Significant Improvement: 24%

Freites-Martinez et al, *JAMA Dermatol* 2018
Increasing Therapies ➔ Increased Survival

14.7 million in US; 32 million worldwide

DeSantis et al, CA Cancer J Clin 2014
<table>
<thead>
<tr>
<th>Target</th>
<th>Agent</th>
<th>Incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAF Inhibitor(s)</td>
<td>Vemurafenib</td>
<td>23.7%</td>
</tr>
<tr>
<td></td>
<td>Dabrafenib</td>
<td>18.9%</td>
</tr>
<tr>
<td>MEK Inhibitor</td>
<td>Trametinib</td>
<td>13.3%</td>
</tr>
<tr>
<td>BRAF/MEK Inhibitors</td>
<td>Vemurafenib/Cobimetinib*</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>Dabrafenib/Trametinib</td>
<td>6%</td>
</tr>
</tbody>
</table>

Alopecia Areata to Immune Checkpoint Inhibitors

- Alopecia reported in 1-1.6% (n=855)
  - Biopsy: CD4+ T cells, scant CD8+ T cells

- Areata (totalis, universalis)

- PD-L1 is expressed on the hair follicle dermal sheath cup cell

- Melanocyte-specific cytotoxic T cells in melanoma patients treated with ICI

Zarbo et al, Br J Dermatol 2016
Late Event: Radiation Induced Alopecia

• Childhood survivors (n=14,358)
  • Incidence: 14%
  • Anxiety: RR 1.38 (95% CI 1.12-1.70)
  • Depression: RR 1.42 (95% CI 1.18-1.71)

Therapy-Induced Alopecia: Conclusions

- Therapies frequently result in alopecia
- Impact on QoL significant
- Severity usually is grade 1 (mild) and responds to minoxidil and spironolactone
- Alopecia will increase in importance
  - Longer adjuvant therapy and increased survival
  - Decreased incidence of CIA with novel therapies
  - Clinical trials
Thank you

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