PERMANENT CHEMOTHERAPY-INDUCED ALOPECIA

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Hair has been a social symbol throughout time, culminating perceptions of age, social status, beliefs, and more importantly, individuality and a sense of race/tiveness. (1)

Chemotherapy-induced alopecia (CIA) is one of the more troubling aspects of chemotherapy to patients. (2)

While hair loss may seem trivial, it can lead to poor self-esteem and ultimately unwanted psychological effects. (2)

CIA is one of the most feared side effect of chemotherapy by patients. (3)

### Impact of CIA on patients

| Table 1: Mean transformed impact scores (100 × ) and rankings (between brackets) as found with the psychophysical scaling method. |
| --- | --- | --- |
| Patients | Nurses | Physicians |
| 1 | Fear for metastases | 70 (1) | 86 (1) | 90 (1) |
| 2 | Fatigue | 56 (2) | 66 (3) | 62 (2) |
| 3 | Consciousness of one's own vulnerability | 54 (3) | 46 (7) | 48 (5) |
| 4 | Hair loss | 45 (4) | 41 (9) | 30 (12) |
| 5 | Nausea | 41 (5) | 50 (6) | 52 (4) |
| 6 | Vomiting | 38 (6) | 51 (5) | 59 (3) |
| 7 | Concentration problems | 36 (7) | 30 (13) | 23 (15) |
| 8 | Mood changes | 35 (8) | 35 (10) | 35 (10) |
| 9 | Sleeping difficulties | 34 (9) | 25 (15) | 25 (14) |
| 10 | Changes in relationship with partner | 32 (10) | 72 (2) | 48 (6) |
| 11 | Constipation | 28 (11) | 21 (17) | 17 (17) |
| 12 | Changes in relationship with children | 27 (12) | 58 (4) | 45 (7) |
| 13 | Changes in relationship with friends | 26 (13) | 45 (8) | 32 (11) |
| 14 | Mouth problems | 26 (14) | 34 (11) | 36 (9) |
| 15 | Burning eyes | 23 (15) | 14 (18) | 22 (16) |
| 16 | Skin problems | 19 (16) | 23 (16) | 15 (18) |
| 17 | Nail problems | 15 (17) | 7 (19) | 8 (19) |
| 18 | Diarrhoea | 13 (18) | 32 (12) | 29 (13) |
| 19 | Difficulties taking care of oneself | 11 (19) | 28 (14) | 36 (8) |

Chemotherapy induced alopecia (CIA) in breast cancer patients

- 40 to 100% of breast cancer patients experience complete alopecia during chemotherapy.

- A majority of breast cancer patients consider hair loss as the most traumatic aspect of chemotherapy.

- 8% reject chemotherapy because of extreme anxiety related to CIA.

- Patients with higher distress with CIA had worsen body image, more likely to have depression, lower social and role functions, problems with sexuality, and poorer quality of life.
Impact of chemotherapy-induced alopecia distress on body

<table>
<thead>
<tr>
<th>Functioning</th>
<th>Low CIA distress (%)</th>
<th>High CIA distress (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body image</td>
<td>62</td>
<td>35.2</td>
</tr>
<tr>
<td>Overall QOL</td>
<td>64.4</td>
<td>53.8</td>
</tr>
<tr>
<td>Physical</td>
<td>53.8</td>
<td>45.4</td>
</tr>
<tr>
<td>Role</td>
<td>64.4</td>
<td>58.6</td>
</tr>
<tr>
<td>Emotional</td>
<td>76.9</td>
<td>74.9</td>
</tr>
<tr>
<td>Cognitive</td>
<td>74.9</td>
<td>70.9</td>
</tr>
<tr>
<td>Social</td>
<td>51.3</td>
<td>14.8</td>
</tr>
<tr>
<td>Depression</td>
<td>19.6</td>
<td></td>
</tr>
</tbody>
</table>

* Difference greater than 10 points on the EORTC-QLQ-C30 scale to be clinically important
* Positive values indicate improvement
Permanent Chemotherapy Induced Alopecia

- CIA is often considered temporary (usually reversible within the 3–6 m) but some patients show absence of or incomplete hair growth even years after completion of chemotherapy.

- Permanent alopecia was defined as absent or incomplete hair regrowth at ≥ 6 months post chemotherapy.


• A case series of 20 women treated for breast cancer by a sequential FEC and docetaxel regimen who developed severe and permanent alopecia.

• BC patients diagnosed between 1999 to 2009 who were referred by medical oncologists to the dermatological study from 1 January 2007 to January 2011.

• Permanent alopecia was defined as absent or incomplete hair regrowth at 6 months post chemotherapy using Ludwigs classification.
• Hair loss presented with a moderate or intense androgenetic-like pattern of scalp alopecia: 1 patient (5%) a type I degree, 12 women (63%) showed a type II), and 6 (32%) a type III degree (intense)

• Biopsy specimen examinations (n=15) were normal or displayed the androgenetic like pattern.

Figure 1 58 year-old. Diffuse and severe alopecia over the parieto-occipital scalp and the vertex, with rare and marked hair thinning (type III degree according to Ludwig’s classification).

Figure 2 49 year-old. Diffuse hair loss with marked thin hairs mimicking female androgenetic-pattern hair loss (type II degree according to Ludwig’s classification).

Figure 3 Partial eyebrows alopecia of the patient in Figure 1.

PCIA characteristics

- **Physical examination**
  - Hair loss always prominent over the crown and the frontal scalp, with thinning and widening of the central parting of the scalp

- **Histology**
  - Reduced hair follicle density and/or an increased amount of vellus hair in favor of androgenetic alopecia were noted in eight cases (53%).
Women Who Say Its Chemotherapy Left Them Permanently Bald

December 2015 – The FDA approves changes to the Taxotere warning label to include information about the alleged risk of permanent hair loss from the chemotherapy drug.
PCIA among breast cancer patients

- 40% and 7% of breast cancer patients who had completed chemotherapy more than 6 months before reported still had mild and severe alopecia (1).
- Long-term survivors experienced similar levels of hair loss and poor body image than patients undergoing active chemotherapy (2).

(1) Kim et al., 2017 Chemotherapy-induced irreversible alopecia in early breast cancer patients
(2) Kang d et al., 2017
Limitations of the previous studies

• Most studies are limited by:
  • Case-series or cross-sectional designs
  • Exclusive use of patient-reported outcomes only
  • Evaluation of single agents
  • Lack of information on hair condition before chemotherapy
  • Short-term follow-up.
DERMA cohort

• **Aim**
  – To estimate the incidence of PCIA in a cohort of breast cancer patients with measurements of hair volume and density prior to chemotherapy and followed for 3 years after chemotherapy.

• **Study design**
  – A prospective cohort study at university cancer hospital Seoul, Korea

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*Kang d et al., Permanent chemotherapy-induced alopecia in breast cancer patients: A 3-year prospective cohort study, The Oncologist in press*
**Study participants**
- Stage is I, II, or III Breast cancer patients who expected to receive chemo
- Exclusion: Had history of chemotherapies or dermatologic treatment

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dose</th>
<th>Interval</th>
<th>Cycle</th>
<th>DERMA study</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAC</td>
<td></td>
<td>21 day</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>500 mg/m², day 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adriamycin</td>
<td>50 mg/m², day 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5- Fluorouracil</td>
<td>500 mg/m², day 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td></td>
<td>21 day</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>Adriamycin</td>
<td>60 mg/m², day 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>600 mg/m², day 1</td>
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<td></td>
</tr>
<tr>
<td>AC 4 → T 4</td>
<td></td>
<td>21 day</td>
<td>8</td>
<td>29</td>
</tr>
<tr>
<td>Adriamycin</td>
<td>60 mg/m², day 1 (1st-4th cycle)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>600 mg/m², day 1 (1st-4th cycle)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docetaxel</td>
<td>75 mg/m², day 1 (5th-8th cycle)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAC</td>
<td></td>
<td>21 day</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>75 mg/m², day 1</td>
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<tr>
<td>Adriamycin</td>
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<td></td>
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<tr>
<td>Cyclophosphamide</td>
<td>500 mg/m², day 1</td>
<td></td>
<td></td>
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<tr>
<td>TC</td>
<td></td>
<td>21 day</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>75 mg/m², day 1</td>
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</tr>
<tr>
<td>Cyclophosphamide</td>
<td>600 mg/m², day 1</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*Kang d et al., Permanent chemotherapy-induced alopecia in breast cancer patients: A 3-year prospective cohort study, The Oncologist in press*
Outcomes

• Outcome
  – **Permanent CIA**: an absence or an incomplete hair regrowth persisting 6 months after chemotherapy completion
  – **Incomplete hair regrowth (PCIA)** – if hair density or thickness at 6 month after post-chemotherapy were 2 standard deviations (SDs) or more below the baseline mean (before chemotherapy).

– **Hair density and thickness**: Folliscope 4.0, LeadM from vertex area region

– **Body image**: EORTC QLQ-BR23 (0-100)
– **Patient reported hair problems at 3 years post chemotherapy**

*Kluger et al., 2015
Kang d et al., Permanent chemotherapy-induced alopecia in breast cancer patients: A 3-year prospective cohort study, The Oncologist in press*
Characteristics of study participants at pre-chemotherapy

- All participants completed the baseline measurements, and 97% (T2), 93% (T3), 93% (T4), 75% (T5), and 83% (T6) of patients completed clinic visits.

- The participants’ mean age was 47.1, and 34.4% were diagnosed at stage 3.

- 52.5% patients received the taxane-based regimens

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall (N = 61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.1 (9.5)</td>
</tr>
<tr>
<td>Breast surgery type (mastectomy)</td>
<td>25 (41.0)</td>
</tr>
<tr>
<td>Disease stage at diagnosis</td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>19 (31.2)</td>
</tr>
<tr>
<td>Stage II</td>
<td>21 (34.4)</td>
</tr>
<tr>
<td>Stage III</td>
<td>21 (34.4)</td>
</tr>
<tr>
<td>Number of cycles</td>
<td></td>
</tr>
<tr>
<td>4 cycles (AC or TC)</td>
<td>16 (26.2)</td>
</tr>
<tr>
<td>6 cycles (FAC or TAC)</td>
<td>16 (26.2)</td>
</tr>
<tr>
<td>8 cycles (AC+T)</td>
<td>29 (47.5)</td>
</tr>
<tr>
<td>Taxane based chemotherapy</td>
<td>32 (52.5)</td>
</tr>
<tr>
<td>Hormone therapy (yes)</td>
<td>43 (70.5)</td>
</tr>
<tr>
<td>Targeted therapy (trastuzumab)</td>
<td>32 (52.5)</td>
</tr>
<tr>
<td>Menopause (yes)</td>
<td>22 (36.1)</td>
</tr>
<tr>
<td>Co-morbidities (yes)</td>
<td>11 (18.0)</td>
</tr>
</tbody>
</table>

Values are means (standard deviation) or number (%).
AC, doxorubicin, cyclophosphamide; FAC, fluorouracil, doxorubicin, cyclophosphamide; T, taxotere; TAC, taxotere, adriamycin, and cyclophosphamide; TC, taxotere and cyclophosphamide.
* Having hypertension, hyperlipidemia, or diabetes.
## Hair density

<table>
<thead>
<tr>
<th>Hair density (hairs/cm²)</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
<th>T5</th>
<th>T6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>138.7 (34.2)</td>
<td>12.1 (17.6)</td>
<td>15.9 (21.3)</td>
<td>96.1 (52.2)</td>
<td>134.2 (42.4)</td>
<td>115.4 (28.9)</td>
</tr>
<tr>
<td>AC</td>
<td>157.3 (38.1)</td>
<td>14.9 (30.1)</td>
<td>2.6 (7.4)</td>
<td>103.1 (40.4)</td>
<td>153.4 (42.8)</td>
<td>123.8 (23.4)</td>
</tr>
<tr>
<td>FAC</td>
<td>135.9 (29.6)</td>
<td>10.3 (12.7)</td>
<td>29.1 (22.7)</td>
<td>101.5 (39.9)</td>
<td>135.1 (36.5)</td>
<td>123.3 (34.6)</td>
</tr>
<tr>
<td>Taxane-based</td>
<td>131.1 (31.7)</td>
<td>11.6 (11.4)</td>
<td>16.5 (21.8)</td>
<td>90.2 (62.3)</td>
<td>124.2 (43.0)</td>
<td>108.4 (27.5)</td>
</tr>
<tr>
<td>P value</td>
<td>0.04</td>
<td>0.78</td>
<td>0.004</td>
<td>0.70</td>
<td>0.18</td>
<td>0.17</td>
</tr>
</tbody>
</table>

*Kang d et al., Permanent chemotherapy-induced alopecia in breast cancer patients: A 3-year prospective cohort study, The Oncologist in press*
## Hair thickness

<table>
<thead>
<tr>
<th>Hair thickness</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
<th>T5</th>
<th>T6</th>
</tr>
</thead>
<tbody>
<tr>
<td>(μm) Overall</td>
<td>71.1 (12.4)</td>
<td>19.7 (24.0)</td>
<td>12.4 (15.3)</td>
<td>39.5 (18.5)</td>
<td>49.7 (12.2)</td>
<td>52.7 (11.4)</td>
</tr>
<tr>
<td>AC</td>
<td>73.5 (11.9)</td>
<td>13.3 (21.0)</td>
<td>3.3 (10.0)</td>
<td>44.3 (13.0)</td>
<td>52.6 (11.5)</td>
<td>55.7 (9.8)</td>
</tr>
<tr>
<td>FAC</td>
<td>71.2 (12.0)</td>
<td>14.9 (19.4)</td>
<td>23.6 (15.7)</td>
<td>45.6 (15.4)</td>
<td>57.2 (13.6)</td>
<td>60.2 (11.3)</td>
</tr>
<tr>
<td>Taxane-based</td>
<td>69.9 (13.0)</td>
<td>24.8 (26.5)</td>
<td>11.7 (14.4)</td>
<td>34.3 (20.8)</td>
<td>44.8 (10.1)</td>
<td>48.3 (10.2)</td>
</tr>
<tr>
<td>P value</td>
<td>0.66</td>
<td>0.23</td>
<td>0.001</td>
<td>0.10</td>
<td>0.015</td>
<td>0.004</td>
</tr>
</tbody>
</table>

*Kang et al., Permanent chemotherapy-induced alopecia in breast cancer patients: A 3-year prospective cohort study, The Oncologist in press*
Incidence of permanent chemotherapy-induced alopecia

- Proportion of participants who had PCIA was 39·5%.
- However, 42·3% of patients still had PCIA, especially 30·8% of the patients had incompletely recovered hair thinning.

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Permanent chemotherapy-induced alopecia
Patient-reported outcomes

- Thinning hair was the most common problem (75.0%), followed by hair volume (53.9%), hair loss (34.6%), and gray hair (34.6%).
### Anti-cancer treatment associated with PCIA

- In multivariable analysis, patients who had a taxane based treatment experienced higher incidence of PCIA

<table>
<thead>
<tr>
<th></th>
<th>6 months after completion of chemotherapy</th>
<th>3 years after completion of chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Taxane</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Yes</td>
<td>6.82 (0.91, 51.06)</td>
<td>8.01 (1.20, 53.26) †</td>
</tr>
<tr>
<td><strong>Hormone therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Yes</td>
<td>8.52 (0.60, 122.08)</td>
<td>3.81 (0.35, 42.12)</td>
</tr>
<tr>
<td><strong>Targeted therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Yes</td>
<td>0.09 (0.00, 2.01)</td>
<td>0.16 (0.01, 2.33)</td>
</tr>
</tbody>
</table>

Adjusted for age, hair density and thickness at diagnosis, † Statistically significant ($P < 0.05$)
Impact of PCIA on body image

- Patient who had PCIA had lower body image compared to patient without PCIA (51.96 vs. 70.19, P = 0.014)

<table>
<thead>
<tr>
<th></th>
<th>Mean body image score (SDs)</th>
<th>Adjusted coefficient (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PCIA</td>
<td>70.19 (21.24)</td>
<td>Reference</td>
</tr>
<tr>
<td>PCIA</td>
<td>51.96 (25.09)</td>
<td>-17.96 (-32.98, -2.94)</td>
</tr>
<tr>
<td>P values</td>
<td>0.014</td>
<td>0.020</td>
</tr>
</tbody>
</table>
Aging effects?

- Average (SD) hair shaft diameter prior to chemotherapy was 71.1 (12.4) µm and the average hair thickness at 6 months after chemotherapy was 49.7 µm, corresponding to a ~30% reduction in hair thickness in less than 1 year.

- In a general population study in Korean women, the average (SD) hair thickness of women in their 5th, 6th, and 7th decades of life were 96.4 (8.8), 87.7 (9.0), and 81.6 (10.1) µm, respectively.

- It might be difficult to compare the results of this study with those of our study due to differences in setting, design, and methods, chemotherapy-induced partial alopecia seems to far exceed aging-related hair thinning.
Limitations

- A single institution, had a small sample size, and the findings may not be generalizable to patients in other settings.

- Hair parameters were measured only on the vertex area.
  - However, the vertex area is appropriate to assess alopecia in conditions with androgenic-pattern alopecia, such as breast cancer.

- Study participants may have self-selected to participate because they were interested in CIA or had prior hair problems compared to patients who did not participate.
  - Patients were recruited prior to chemotherapy and skin changes measured objectively in addition to patient-reported outcomes.
Conclusions

• Over 40% of patients had PCIA 3 years after completion of chemotherapy, primarily due to partial alopecia.
• Patients who had received taxane-based treatment regimes and additional hormone therapy were more likely to experience PCIA.
• Moreover, patients with PCIA had significantly worse body image compared to patients without PCIA.

• **PCIA is a very common problem in breast cancer patients, with important psychological consequences.**
• **Clinicians should be aware of this distressing adverse event and develop supportive care strategies to prepare patients and minimize its impact on well-being.**
• **Development of more satisfactory management strategies for PCIA remains a major research challenge in clinical oncology.**
Incidence of PCIA in cancer patients using national claim data

- Retrospective cohort study using the National Health Insurance Service-National Sample Cohort
- Study population

| Participants aged 20-79 who developed cancer between 2003 and 2013 (N = 35,879) |
| Exclusions (n = 19,574) |
| Participants who had alopecia before cancer diagnosis (n = 2,227) |
| Participants who death within a year after cancer diagnosis (n = 6,052) |
| Participants without chemotherapy (n = 22,277) |

| Participants included in this study (N = 16,305) |

- Definition of PCIA
  - PCIA was defined as patient with alopecia or any medication code after a year or more after cancer diagnosis
Incidence of PCIA in cancer patients using national claim data

- There were 719 (4.4%) patients developed PCIA after cancer diagnosis

<table>
<thead>
<tr>
<th></th>
<th>No PCIA</th>
<th>PCIA</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male (n = 7,537)</td>
<td>6,839 (90.74)</td>
<td>698 (9.26)</td>
<td></td>
</tr>
<tr>
<td>Female (n = 8,768)</td>
<td>8,747 (99.76)</td>
<td>21 (0.24)</td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>20-29 (n = 321)</td>
<td>317 (98.75)</td>
<td>4 (1.25)</td>
<td></td>
</tr>
<tr>
<td>30-39 (n = 1,253)</td>
<td>1,246 (99.44)</td>
<td>7 (0.56)</td>
<td></td>
</tr>
<tr>
<td>40-49 (n = 3,190)</td>
<td>5,562 (20.7)</td>
<td>38 (1.19)</td>
<td></td>
</tr>
<tr>
<td>50-59 (n = 4,375)</td>
<td>4,238 (96.87)</td>
<td>137 (3.13)</td>
<td></td>
</tr>
<tr>
<td>60-69 (n = 4,329)</td>
<td>4,027 (93.02)</td>
<td>302 (6.98)</td>
<td></td>
</tr>
<tr>
<td>≥70 (n = 2,837)</td>
<td>2,606 (91.86)</td>
<td>231 (8.14)</td>
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</tr>
<tr>
<td>Type of cancer</td>
<td>No PCIA</td>
<td>PCIA</td>
<td>P-value</td>
</tr>
<tr>
<td>---------------------------------------------------</td>
<td>---------------</td>
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</tr>
<tr>
<td>Thyroid (n = 1,899)</td>
<td>1,876 (98.79)</td>
<td>23 (1.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stomach (n = 2,082)</td>
<td>1,955 (93.90)</td>
<td>127 (6.10)</td>
<td></td>
</tr>
<tr>
<td>Colon and rectum (n = 2,621)</td>
<td>2,470 (94.24)</td>
<td>151 (5.76)</td>
<td></td>
</tr>
<tr>
<td>Lung (n = 1,258)</td>
<td>1,185 (94.20)</td>
<td>73 (5.80)</td>
<td></td>
</tr>
<tr>
<td>Breast (n = 2,254)</td>
<td>2,246 (99.65)</td>
<td>8 (0.35)</td>
<td></td>
</tr>
<tr>
<td>Liver (n = 1,135)</td>
<td>1,088 (95.86)</td>
<td>47 (4.14)</td>
<td></td>
</tr>
<tr>
<td>Prostate (n = 495)</td>
<td>430 (86.87)</td>
<td>65 (13.13)</td>
<td></td>
</tr>
<tr>
<td>Pancreas (n = 226)</td>
<td>220 (97.35)</td>
<td>6 (2.65)</td>
<td></td>
</tr>
<tr>
<td>Hematology (n = 661)</td>
<td>637 (96.37)</td>
<td>24 (3.63)</td>
<td></td>
</tr>
<tr>
<td>Uteri (n = 690)</td>
<td>688 (99.71)</td>
<td>2 (0.29)</td>
<td></td>
</tr>
<tr>
<td>Brain and CNS (n = 201)</td>
<td>197 (98.01)</td>
<td>4 (1.99)</td>
<td></td>
</tr>
<tr>
<td>Lip, oral cavity and pharynx (n = 431)</td>
<td>411 (95.36)</td>
<td>20 (4.64)</td>
<td></td>
</tr>
<tr>
<td>Other and unspecified (n = 741)</td>
<td>713 (96.22)</td>
<td>28 (3.78)</td>
<td></td>
</tr>
<tr>
<td>Oesophagus (n = 175)</td>
<td>169 (96.57)</td>
<td>6 (3.43)</td>
<td></td>
</tr>
<tr>
<td>Larynx (n = 129)</td>
<td>111 (86.05)</td>
<td>18 (13.95)</td>
<td></td>
</tr>
<tr>
<td>Testis (n = 31)</td>
<td>29 (93.55)</td>
<td>2 (6.45)</td>
<td></td>
</tr>
<tr>
<td>Gallbladder (n = 272)</td>
<td>259 (95.22)</td>
<td>13 (4.78)</td>
<td></td>
</tr>
<tr>
<td>Kidney (n = 228)</td>
<td>201 (88.16)</td>
<td>27 (11.84)</td>
<td></td>
</tr>
<tr>
<td>Ovary (n = 311)</td>
<td>311 (100.00)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bladder (n = 465)</td>
<td>390 (83.87)</td>
<td>75 (16.13)</td>
<td></td>
</tr>
</tbody>
</table>
# Current options against CIA

<table>
<thead>
<tr>
<th>Method</th>
<th>Proposed mechanism of action</th>
<th>How applied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalp hypothermia</td>
<td>Reduction of blood flow to hair follicle when chemotherapy serum levels highest; reduction of biochemical activity</td>
<td>Cooling cap or continuous exposure of scalp to cold air/liquid</td>
</tr>
<tr>
<td>Scalp tourniquets</td>
<td>Reduction of blood flow to hair follicle when chemotherapy serum levels highest</td>
<td>Sphygmomanometer cuff is inflated to restrict blood flow to the scalp</td>
</tr>
<tr>
<td>AS101*</td>
<td>Protection thought to be derived from up-regulation of macrophage-derived factors, such as IL-1 or possibly prostagland and in E2 secretion</td>
<td>Intravenous injections before and during chemotherapy</td>
</tr>
<tr>
<td>Minoxidil</td>
<td>Hair growth cycle modulator; induces telogen hairs to enter anagen, prolongs anagen growth phase</td>
<td>2% topical application applied to scalp during chemotherapy</td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>Thought to be related to vitamin D3’s general ability to stimulate differentiation of hair follicles and diminish DNA proliferation</td>
<td>Intraperitoneal treatments as pretreatment before chemotherapy or topical application during chemotherapy</td>
</tr>
</tbody>
</table>

Current options against CIA

• **Scalp cooling devices & caps**
  • Variable efficacy and tolerance
  • Costly to operate (Capex, staff)
  • Cost of 2’000 USD (caps)
  • Major concern = head/brain metastasis would be untreated since caps prevent chemotherapeutic agents from reaching the cells (few hospitals are willing to include caps)
Current options against CIA

Current options against CIA

Scalp Cooling to Prevent Chemotherapy-Induced Alopecia The Time Has Come
Dawn L. Hershman, MD, MS

Adjuvant chemotherapy reduces the 10-year relative risk of death from breast cancer by approximately 35%. Efforts have been made to define the subset of women who derive the most benefit from this treatment so patients who are cured without chemotherapy can avoid the toxic adverse effects, and patients who would benefit most from chemotherapy would receive it.2 Despite these efforts, a substantial number of women are still advised to undergo chemotherapy but choose not to receive treatment because of concerns about adverse effects.3,4 Therefore, an intervention that could reduce the adverse effects of chemotherapy may lead to improvements in the initiation and completion of therapy, in quality of life, and in survival outcomes. Substantial improvements in supportive care have led to significant improvements in the management of several chemotherapy-induced toxic effects such as nausea and vomiting, fever related to neutropenia, anemia, menopausal symptoms, and infertility.5 Reassuring patients that symp-

Related articles pages 596 and 606
Current options against CIA

- **Topical Treatments**
  - Minoxidil therapy requires daily application, as discontinuation can lead to loss of benefits obtained.
## Current options against CIA

<table>
<thead>
<tr>
<th>No</th>
<th>Status</th>
<th>Study</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Active, not recruiting</td>
<td>Efficacy and Safety of Dignicap System for Preventing Chemotherapy Induced Alopecia</td>
<td>Device: Dignicap System</td>
</tr>
<tr>
<td>3</td>
<td>Completed</td>
<td>START: Swiss Taxotere Alopecia Prevention Trial</td>
<td>Device: Cold Caps</td>
</tr>
<tr>
<td>4</td>
<td>Recruiting</td>
<td>Efficacy, Safety and Tolerability of CG428 Cutaneous Solution on Chemotherapy Induced Alopecia; Controlled Study (ELAN)</td>
<td>Drug: CG 428</td>
</tr>
<tr>
<td>5</td>
<td>Completed</td>
<td>EValuation of the Impact of a TOpical Lotion on Permanent Chemotherapy Induced Hair Disorders in Cancer Survivors</td>
<td>Drug: CG 428</td>
</tr>
<tr>
<td>6</td>
<td>Active, not recruiting</td>
<td>Scalp Cooling to Prevent Chemo-induced Hair Loss</td>
<td>Device: Cold Caps</td>
</tr>
<tr>
<td>9</td>
<td>Completed</td>
<td>A 6-month Post-interventional Follow-up Extension of VOLUME Study (VOLUME-2)</td>
<td>Drug: CG 428</td>
</tr>
<tr>
<td>10</td>
<td>Recruiting</td>
<td>Efficacy of the Use of Refrigerant Helmet to Prevent Alopecia in Patients Treated With Eribulin for Breast Cancer</td>
<td>Device: Cold Caps</td>
</tr>
</tbody>
</table>