Preventing chemotherapy-induced alopecia by scalp cooling: Preliminary data from a study on the efficacy and safety of DigniCap® System in breast cancer patients

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Adjuvant Chemotherapy

• ... has been shown to delay or prevent recurrence in early stage breast cancer, and recent studies as well as ongoing work is helping to define the group of patients who are most likely to benefit from this treatment.

• Apparent freedom from disease
  ... It's supposed:
    – Possible persistence of microscopic disease
    – Same features of the primary tumor
    – Similar responsiveness
  • In case of doubt, consider the scenario ...
    – ... worst
    – ... But more convenient for the patient
Alopecia

- Few dermatological conditions bring an emotional stress such as alopecia induced by chemotherapy

- Hair loss has a negative effect on the perception of patients about appearance, body image, sexuality, and self-esteem

- The patients feel deprived of their privacy, as the hair loss is easily interpreted by others as a characteristic associated with cancer.
Alopecia induced by chemotherapy and the effects on quality of life: a literature review

- A total of 38 articles were included in the review
- Hair loss - rated among the most troublesome side effects - has been described as a stigma that affects the body image
- Further research is needed to determine the presence and the extent of the adverse effect on alopecia induced by chemotherapy on various aspects of QOL

Psycho-Oncology 17: 317–328 (2008)
Cytotoxic Agents and Hair Loss

Cytotoxic agents that usually cause hair loss (>80%):

- Adriamycin
- Daunorubicin
- Docetaxel
- Epirubicin
- Etoposide
- Ifosfamide
- Irinotecan
- Paclitaxel
- Topotecan
- Vindesine
Cytotoxic Agents and Hair Loss

Cytotoxic agents that usually cause hair loss (>70%):
- Adriamycin
- Daunorubicin
- Docetaxel
- Epirubicin
- Etoposide
- Ifosfamide
- Irinotecan
- Paclitaxel
- Topotecan
- Vindesine
Study on the efficacy and safety of DigniCap system for preventing chemotherapy-induced alopecia: Preliminary results and future developments
Knowing to have cancer causes a strong turmoil in the patient's life.

Preserving the body image is absolutely important at this stage.

The person needs help to deal with this experience to the fullest, to find the best advantages in the care and limit the disturbances.

- Hair are part of our identity and for many patients they are an important symbol for a good quality of life.

- The possibility to preserve them can be of enormous support during the course of treatment.

- The DigniLife® system was specifically developed to prevent chemotherapy-induced alopecia
The DigniCap® System has been developed to provide continuous scalp cooling with high efficacy, safety and acceptable patient comfort.

The system consists of:

- a refrigerator unit integrated into a control unit based on a computerized interface.
- a compact mobile cabinet to which a soft and tight-fitting silicon cap is connected via a tube.

Two separate cooling circuits allow coolant to flow through the front and the back of the cap autonomously.
DigniLife® System

A liquid coolant is pumped from the cooled reservoir in the cabinet to circulate through small canals within the cap. Two separate cooling circuits allow coolant to flow through the front and the back of the cap autonomously.

Scalp temperature is monitored by three separate sensors in the cap: two temperature sensors and a security sensor.

Deviations from the preset temperatures are immediately detected and automatically adjusted by the system. An outer cap made of neoprene is used to secure and insulate the inner silicon cap.
Scalp cooling and protection from alopecia

The protection from alopecia offered by scalp cooling is a consequence of:

1. Vasoconstriction resulting in reduced blood flow in the scalp: follicular cells will be less exposed to drugs.
2. Reduced metabolic rate in the hair follicles: consequent decreased exposure to the chemotherapeutic agents.

This limits the damage to dividing cells in the hair follicles, preventing alopecia.

Scalp cooling has been used in the past with limited success due to the difficulty to maintain a constant cooling.
Scalp cooling procedures: Workflow

To obtain good results, it is important to ensure an effective cooling of the scalp before (pre-cooling), during and for a certain period of time after (post-cooling) the infusion period of the drug.

The procedure for DigniCap is carried out in 3 phases:

1. **Pre-cooling phase** (20-30min): Before drug infusion, the device is positioned accurately. During the pre-cooling (30min), the pre-medication can be administered.

2. **Infusion** of chemotherapy

3. **Post-cooling** Phase: This phase can vary from 30 to 120 min, it depends on the drug treatment used.
DigniLife in IEO: Clinical Trial

The hair loss is visible **when exceeding 50%** according to the Dean-scale for the assessment of the alopecia.

- The efficacy and safety of DigniLife system is being evaluated in women with early breast cancer undergoing adjuvant chemotherapy regimens.
- The cooling system is applied to the scalp at each cycle of chemotherapy.
- Hair loss is evaluated through:
  - **Patient self-assessment** (VAS scale)
  - **by practitioner assessment** using the 5 point Dean's scale, using photographs taken from 5 angles.

### DEAN’S SCALE

- Grade 0: no hair loss
- Grade 1: less than 25% hair loss
- Grade 2: between 25 and 50% hair loss
- Grade 3: between 50 and 75% hair loss
- Grade 4: more than 75% hair loss

### VAS SCALE

- 0: No hair loss
- 100: Total hair loss
- 0: No pain
- 100: Worst possible pain
- 0: Not at all chilled
- 100: As bad as it could be
DigniLife Trial Endpoints

- **Primary endpoint:**
  reduction of hair loss in at least 55% of patients with a maximum of ≤ grade 2 hair loss (corresponding to 25-50% HL)

- **Secondary endpoints:**
  Reduction of hair loss assessed by physician by the 5 point Dean’s scale
  Secondary endpoints will include assessment of side-effects in terms of:
  - head/scalp pain, feeling chilled, rash
  - QoL and impact of hair loss will also be evaluated (EORTC BR-23 and EORTC QLQ-30 questionnaires)

**Statistical considerations:**
A two-stage design (Simon, 1989) is used in order to allow early termination of the trial:
The smallest proportion of success suggesting the device is effective is 55%.

- In the first stage, **45 patients will be accrued**. If **at least 20 patients with success** are observed, and its tolerability is judged adequate by the investigators, **59 additional patients will be enrolled**, leading to a total of **104 patients**.
- At the second stage, **if 50 or more patients obtaining a success are observed among the total of 104 patients**, the device will be considered effective.
DigniLife project: Inclusion and Exclusion criteria

Inclusion criteria:
- Women > 18 years of age
- Performance status (ECOG) 0-1
- Documented diagnosis of stage I or II breast cancer
- A planned course of chemotherapy in the adjuvant setting including one of the following regimens:
  - Doxorubicin 60 mg/m2 or Epirubicin 90 mg/m2 and cyclophosphamide 600 mg/m2 x 4 cycles IV every 3 weeks
  - Docetaxel 75 mg/m2 and cyclophosphamide 600 mg/m2 x 4 cycles IV every 3 weeks
  - Paclitaxel 80 mg/m2 weekly IV x at least 12 weeks with or without IV trastuzumab
  - Docetaxel 75-100 mg/m2 IV every 3 weeks x 4 cycles with or without trastuzumab IV weekly or every 3 weeks
  - Patients receiving a regimen including both an anthracycline and a taxane (at doses reported above) are also eligible for this trial (AC/T, EC/T, TAC, etc.)
- Plan to complete chemotherapy within 6 months
- Willing to participate in study procedures including having photographs of the

Exclusion criteria:
- Patients with female pattern baldness
- Previous chemotherapy
- Autoimmune disease affecting hair; e.g. alopecia areata, systemic lupus with associated hair loss
- Underlying clinically significant liver or renal disease
- Participation in any other clinical investigation or exposure to other investigational agents, drugs, device or procedure that may cause hair loss
Project timing: medical and nursing coordination

1. Recruitment of patients by medical staff
2. Presentation of DigniLife system in the Day Hospital
3. Assessment of patient compliance
4. Entering the treatment plan in the database
5. Organization of the Day Hospital
6. Starting treatment
7. Phases of treatment with DigniLife
8. Collection of questionnaires
Collection of questionnaires

Raffreddamento del cuoio capelluto - Valutazione del paziente

**Raffreddamento del cuoio capelluto - Valutazione da parte del personale medico ed infermieristico**

**Parte 1:** Da compilare una volta sola all'inizio del primo ciclo di trattamento

<table>
<thead>
<tr>
<th>Personale medico ed infermieristico:</th>
<th>Data:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codice identificativo del paziente:</td>
<td></td>
</tr>
</tbody>
</table>

**Data di nascita:**

**Chemioterapia:**

1. **Etnia**
   - □ Caucasica
   - □ Mediterranea
   - □ Africana
   - □ Asiatica
   - □ Altro: [ ]

2. **Stato menopausale**
   - □ Pre-menopausa
   - □ Post-menopausa

3. **Precedenti chemioterapie**
   - □ No
   - □ Sì
   - Se sì, quali: [ ] Inizio / Fine: [ ]

4. **Alopecia dovuta a precedenti terapie**
   - □ No
   - □ Sì

5. **Alopecia dovuta ad altre cause**
   - □ No
   - □ Sì
   - □ Correlata ad ormoni
   - □ Alopecia areata
   - □ Altro: [ ]

6. **Fototipo dei capelli**
   - □ Bassa
   - □ Media
   - □ Alta

7. **Struttura del capello**
   - □ Fine
   - □ Medio
   - □ Spesso
   - □ Liscio
   - □ Ondulato
   - □ Riccio

8. **Colore naturale del capello**
   - □ Biondo
   - □ Rosso
   - □ Castano
   - □ Bianco
   - □ Grigio

9. **Commenti**
   
   ___________________________________________________________

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Descriva il suo pensiero sulle seguenti questioni e barri il numero corrispondente.

**Durante il trattamento oderno:**

<table>
<thead>
<tr>
<th>Per niente</th>
<th>Poco</th>
<th>Abbastanza</th>
<th>Molto</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Si è preoccupato della perdita dei capelli?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Si sente in grado di tollerare il trattamento di raffreddamento del cuoio capelluto?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Riesce a tollerare il periodo post-raffreddamento?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Consiglierrebbe il raffreddamento del cuoio capelluto ad altri?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Quanto è soddisfatto dell'assistenza durante il trattamento?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Ha avuto effetti collaterali durante il raffreddamento del cuoio capelluto?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
| 7. Compil quanto segue solo se ha avuto effetti collaterali durante il raffreddamento del cuoio capelluto:
   a) Ha avuto mai di testa? | 1 | 2 | 3 | 4 |
   b) Ha avuto freddo? | 1 | 2 | 3 | 4 |
   c) Ha sentito la testa pesante? | 1 | 2 | 3 | 4 |
   d) Ha avuto dolori al cuoio capelluto? | 1 | 2 | 3 | 4 |
   e) Ha avuto dolori alla nuca? | 1 | 2 | 3 | 4 |
   f) Altro: [ ] | 1 | 2 | 3 | 4 |
12th patient *(E90C600 x 4 cycles every 3 weeks + PTX 12x)* 75012

- Before I Cycle (03/12/2014)

- II cycle (29/12/2014)
- III cycle (26/01/2015)
- IV cycle (16/02/2015)
12th patient \((E90C600 \times 4 \text{ cycles every 3 weeks } + T \ 12x)\) 75012

- VII cycle  Taxol (12/05/2015)

- XII cycle  Taxol (12/05/2015)

NO Follow up photos
FDA News Release

FDA allows marketing of cooling cap to reduce hair loss during chemotherapy

For Immediate Release

December 8, 2015
Dignicap System prevented alopecia in **77% of breast cancer** patients receiving planned adjuvant chemotherapy with anthracycline and/or taxanes.
Conclusion

- The greatest loss occurs in the area known as "mid-scalp", the area of the skull between the parietal and the temporal bone; delimited laterally by the temporal and parietal fringes.

- The increased hair loss in that area may be due to the rich vascularization of the scalp that has the characteristic centripetal organization with vessels running in the subcutaneous connective tissue.

- For this reason, during the positioning of the headset trying to preserve the mid-scalp by sticking where it is necessary aids (such as thickness) to adhere as much as possible the headset to the skin.

We enrolled 136 consecutive breast cancer patients. Overall, 104 patients completed planned chemotherapy with scalp cooling. According to physician’s evaluation, 84 patients (79.2%) had HL ≤ G2. According to patient self assessment, the overall success rate was of 55.6%.
Hair have always been a social symbol and over time are related to perceptions of age, social status, beliefs, and even more individuality and a sense of attractiveness.
Thank you