DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

July 3, 2017

Dignitana AB
% Mr. Michael Billig
Experien Group, LLC
224 Airport Parkway, Suite 250
San Jose, California 95110

Re: K170871
Trade/Device Name: DigniCap Scalp Cooling System
Regulation Number: 21 CFR 878.4360
Regulation Name: Scalp Cooling System to Reduce the Likelihood of Chemotherapy Induced Alopecia
Regulatory Class: Class II
Product Code: PMC
Dated: March 21, 2017
Received: March 23, 2017

Dear Mr. Billig:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR

Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely,

Jennifer R. Stevenson -S3

For Binita S. Ashar, M.D., M.B.A., F.A.C.S.
Director
Division of Surgical Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

K170871

Device Name
DigniCap® Scalp Cooling System

Indications for Use *(Describe)*
The DigniCap® Scalp Cooling System is indicated to reduce the likelihood of chemotherapy-induced alopecia in cancer patients with solid tumors.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary (K170871)

Applicant

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Date of Summary: June 20, 2017

Device Proprietary Name	DigniCap® Scalp Cooling System		
Common/Usual Name	Scalp Cooling System		
Classification Names / Numbers and Code	**21 CFR**	**Classification Name**	**Product Code**
	878.4360	Scalp Cooling System	PMC
Regulatory Class	II		
Prescription Status	Prescription Device		
Device / Classification Panel	General & Plastic Surgery		
Predicate Device	DigniCap® Scalp Cooling System DEN150010		
Description of Device	The DigniCap® Scalp Cooling System consists of a computer controlled system that includes a refrigerated tank containing the liquid coolant that is maintained at -7 ± 2°C. The coolant circulates from the cooling unit to and through the channels of the cap and back to the cooling unit. The scalp temperature is monitored by three separate sensors. Deviations from the treatment temperature are automatically adjusted by the system (scalp temperature can be controlled with an accuracy of ±2.0°C). The DigniCap® Scalp Cooling System components include the following:		

Description of Device (cont.)	**Digni C3** – Is a refrigerator unit with an integral control system operated via a touch screen and is capable of controlling two separate DigniCap® Cooling caps independently of each other. Scalp cooling is performed in conjunction with a silicone inner cap (DigniCap®), an outer neoprene cap (DigniTherm), and the liquid coolant (DigniCool). **DigniCap®** – A soft, tight-fitting silicone cap which has two separate cooling circuits, one for the front and one for the back of the head. Each cooling circuit is equipped with a temperature sensor, and the cap is also equipped with a third sensor for safety control. The cap is available in different sizes. **DigniCool** – The liquid coolant monopropylene glycol. **DigniTherm -** The outer neoprene cap that insulates and keeps the inner cap in place. This neoprene cover cap, called the DigniTherm, comes in different sizes and is colored coded to match the corresponding DigniCap® Cooling cap. **DigniStick**– A component used to save data from a treatment or for troubleshooting. It can also be used to update software. **DigniCard** – A key card which has to be inserted in order to start a treatment.
Indications for Use	The DigniCap® Scalp Cooling System is indicated to reduce the likelihood of chemotherapy-induced alopecia in cancer patients with solid tumors.

Limitations
The sale, distribution, and use of DigniCap™ Scalp Cooling System are restricted to prescription use in accordance with 21 CFR 801.109.
Limitations on device use are also achieved through the following statements included in the instructions for use:

Contraindications
The use of Dignicap is contraindicated in pediatric patients.

The use of Dignicap is contraindicated in adult patients with:

- cold sensitivity,
- cold agglutinin disease,
- cryoglobulinemia
- cryofibrinogenemia.
- Cold urticaria
- CNS malignancies (either primary or metastatic),
- squamous cell carcinoma of the lung,
- small cell carcinoma of the lung,
- cancers of the head and neck,
- skin cancers including melanoma, squamous cell carcinoma, and Merkel cell carcinoma.
- hematological malignancies treated with curative intent by chemotherapy

- solid tumor malignancies with a high likelihood of metastases in transit.
- patients who are scheduled for bone marrow ablation chemotherapy
- patients who are scheduled to undergo skull irradiation
- patients who have previously received skull irradiation

Warnings

Scalp and/or cutaneous metastases have been reported in patients with non-small cell lung cancer, colon cancer, renal cell carcinoma, ovarian cancer, and bladder cancer. Patients with advanced forms of these cancers may be more likely to experience scalp metastases with the scalp cooling system.

Use of Scalp Cooling in the palliative setting in patients with metastatic cancer may also increase the risk for scalp metastases.

Use of scalp cooling with taxanes plus anthracyclines when used in combination has not been shown to be successful in preventing chemotherapeutic drug induced alopecia. Dignicap® Scalp Cooling System should not be used in these patients.

Scalp radiation can cause stenosis of small cutaneous vessels decreasing device effectiveness.

The effectiveness of this device in patients who have received previous chemotherapy has not been evaluated.

The risk of scalp-cooling may outweigh the benefits in patients receiving chemotherapeutic agents with low incidence of inducing alopecia.

Long-term effects of scalp-cooling and risk of scalp metastasis have not been fully studied.

Clinical studies have demonstrated variable success rates in patient reduction of chemotherapy induced alopecia with scalp cooling since the outcome is dependent on multiple factors including chemotherapy regimen, dose, duration of drug infusion, chemotherapy drug metabolism, and concomitant comorbidities. Data have shown that women who experience hair loss in spite of using scalp cooling might have worse quality of life than women who did not have scalp cooling.

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Comparison to Predicate Devices

Aside from the change in the Indications for Use, the DigniCap® Scalp Cooling System is identical in technological characteristics, design and performance to the predicate.

Summary of Testing

Pre-clinical Testing

No additional testing was conducted for this 510(k) to support substantial equivalence. The device in this submission is identical to the previously cleared device, as the purpose of this application was for the expansion of the treatment population only. Testing of the predicate device included biocompatibility, shelf-life, shipping and packaging, electromagnetic compatibility and electrical safety, software, bench testing, and two clinical studies. All tests met the pre-determined specifications and acceptance criteria and demonstrated the DigniCap® Scalp Cooling System to be safe and effective as labeled.

Clinical Data

The efficacy of scalp cooling with the DigniCap System has been reported in 18 clinical evaluations outside of the U.S. These studies investigated the effects of scalp cooling on the incidence of alopecia in patients with various malignancies using a variety of chemotherapy regimens in both the adjuvant and palliative settings. Efficacy has best been demonstrated in chemotherapy regimens containing docetaxel, paclitaxel, cyclophosphamide, and/or carboplatin. These studies did not have long term follow up, and were single armed non-randomized prospective studies. Long-term effects of scalp-cooling and scalp metastasis have not been fully studied in the adjuvant setting outside of stage I and II breast cancer. It is not clear whether there is increased risk of recurrence, particularly scalp or skull metastases, based on the data available. Some of the studies did not list the names of the solid tumor malignancies or their frequencies.

A literature review was conducted to address the safety and effectiveness of the DigniCap device. A search in PubMed, EMBASE, Clinical Trial register and Manufacturer and User Facility Device Experience Database - (MAUDE) was performed using the following search terms: DigniCap, Digni and scalp, Digni and alopecia, Digni and hypothermia, and Dignitana. Abstracts and peer reviewed articles (Table 1) of clinical trials covering the majority of the relevance and methodology questions in the appraisal plan of the pivotal clinical trial clinical evaluation report were selected. Due to the literature review method and the design of these studies, safety and effectiveness results presented in these studies may not be accurate.

Based on the above published data there is insufficient evidence to assess long term effect. Use of DigniCap Scalp Cooling System in these patients may increase the risk of scalp metastasis, metastasis elsewhere in the body or impact the natural course of the disease

Conclusion

The DigniCap Cooling System described in this application is unchanged from the device approved in DEN150010. This application is limited to a revision of the indication for use. The clinical data described in the literature documents provided in this application do demonstrate that the DigniCap Cooling System can be used to reduce the likelihood of chemotherapy-induced alopecia in cancer patients with solid tumors.

Table 1

Clinical Data with the DigniCap® Scalp Cooling System Outside of U.S.

Publication (author, year, institution)	Type of study (RCT, retrospective, single arm prospective nonrandomized studies.)	Treatment group	Control group	Sample size	Length of Follow- up	Follow-up schedule	Completed Cooling %	% Success with <50% hair loss	List of Adverse Events	Reason for discontinuation of cooling
Hernández et al., 2016 American British Cowdray, ABC Medical Center, Mexico City	Retrospective Consecutive series of patients; December 2010 - January 2015.	Weekly TX for 12 cycles (n=4). Weekly TX for 12 cycles and AC every 3 weeks for 4-6 cycles (n=66). AC every 3 weeks for 6-8 cycles (n=28).	N/A	204 patients with **Stage I-V breast (n=120**), ovary, lung, uterus, esophagus, prostate, chest, urethra, rectum, larynx, bladder, colon, liver cancer and non-Hodgkin´s lymphoma.	Not stated	Hair loss - Photos Dean scale	72% (98/120)	84% (82/98)	At follow-up: no side effects or scalp metastasis present.	Hair loss.
Fehr et al., 2016 1. Clinic of Kempten-Oberallgäu, Germany 2. Cantonal Hospital Frauenfeld, Switzerland	Non randomized prospective	PT 175 mg/m2 and carboplatin 6 AUC (area under the curve) for 6 three-week cycles [*n* = 12 (22%)] D 60 mg/m2 and C 600 mg/m2 for 4 three-week cycles, followed by DT 100 mg/m2 for 4 three-week cycles [*n* = 11 (20%)] E 90 mg/m2 and C 600 mg/m2 for 4 three-week cycles, followed by PT 80 mg/m2 weekly for 12 weeks [*n* = 10 (18%)] PT 80 mg/m2 weekly for 16 weeks [n = 8 (15%)] DT 75 mg/m2 and C 500 mg/m2 for 4 three-week cycles [n = 6 (11%)] F 500 mg/m2, E 100 mg/m2, and C 500 mg/m2 for 3 three-week cycles, followed by DT 100 mg/m2 for 3 three-week cycles [n = 64 (7%)] DT 75 mg/m2, D 50 mg/m2, and C 500 mg/m2 for 6 three-week cycles [n = 4 (7%)	N/A	Women with breast, endometrial, or ovarian cancer (n=55) Breast cancer 35adjuvant, 5 palliative, 2 neo- adjuvant Ovarian cancer 12 (22%) Endometrial cancer 1 patient (1.8%)	Not stated	Photographs of the patient's head from 5 different views. WHO scale. Grade 0: no hair loss Grade 1: minimal hair loss (>0% to 25%). Corresponds to Dean score 0 and 1.	78% (43/55)	56% (28/50) (up to 25% hair loss)	1.8% (1/55) could not tolerate scalp cooling.	Hair loss (n=7), death (n=3), change of treatment centre (n=1), and doubts about study participation resulting in withdrawal of consent within 30 minutes of initiation of the 1st cycle (n=1).

Publication (author, year, institution)	Type of study (RCT, retrospective, single arm prospective nonrandomized studies.)	Treatment group	Control group	Sample size	Length of Follow- up	Follow-up schedule	Completed Cooling %	% Success with <50% hair loss	List of Adverse Events	Reason for discontinuation of cooling
Drinkut et al., 2016 Medizinische Hochschule Hannover, Klinik für Frauenheilkunde und Geburtshilfe, Hannover, Germany	Non randomized prospective June 2014 - February 2016	4 x E/C 90/600 mg/m2 + 12 x PT 80 mg/m2	N/A	Women with breast cancer (n=34)	Not stated	Quantification of hair loss by patients and nursing staff. Photos.	56% (19/34)	100% (Patient assessm.: all <50% hair loss, Nurses assessm.: all <25% hair loss)	Not stated (>50% of patients did not report any side effects.)	Cold sensation (n=6) Other (n=9)
Schaffrin-Nabe et al., 2016 Gemeinschaftspraxis Bochum, Germany	Non randomized prospective	Neo-adjuvant EC-PT	Neo-adjuvant EC-PT	Breast cancer patients (n=40) Scalp cooled (n=32), controls (n=8)	Not stated	Hair-mass- index (trichometer) No visible hair loss was considered treatment success.	100% (32/32)	63% (20/32) (no visible hair loss) Complete hair loss in controls.	Not stated.	N/A
Traub et al., 2016 Agaplesion Markus Krankenhaus Frankfurt am Main, Germany	Non randomized prospective October 2015 -	4 × EC → 12 × PT (n = 7) 4 × PT → 4 × EC (n = 1) 4 × EC (n = 1) 18 × PT Mono (n = 1) 4 × Nab-PT Mono (n = 1) 18 × PT plus Myocet (n = 1)	N/A	Women with breast cancer (n=12)	Not stated	Objective assessment of photographs.	75% (9/12)	75% (9/12) (<20% hair loss)	Cooling-induced side effects	Hair loss (n=1), or cooling-induced side effects (n=2)
Campennì et al., 2016 European Institute Oncology, Milan	Non randomized prospective	EC EC-TX +/- Trastuzumab TC	N/A	Patients with stage I-III breast cancer receiving adjuvant chemotherapy (n=109).	Not stated	Hair loss Patient self-assessment & assessment by treating physician Dean scale	79% (86/109)	77% (84/109)	Headaches and coldness. No serious adverse events.	Hair loss (n=12), Discomfort during the cooling period (n=4), other reasons (n=7).

Publication (author, year, institution)	Type of study (RCT, retrospective, single arm prospective nonrandomized studies.)	Treatment group	Control group	Sample size	Length of Follow- up	Follow-up schedule	Completed Cooling %	% Success with <50% hair loss	List of Adverse Events	Reason for discontinuation of cooling
Schaffrin-Nabe et al., 2015 Gemeinschafts praxis für Hämatologie und Onkologie Bochum, Germany	Non randomized prospective	E 90 mg/m² + C 3w→PT w E 90 mg/m² + C 2w→ PT w E 90 mg/m² + C 3w →DT 100 mg/m² F + E 100 mg/m² + C F + E 90 mg/m² + C DT 75 mg/m² Carboplatin AUC6 F + E 100 mg/m² + C →DT 100 mg/m² E 150 mg/m² + PT 225 mg/m² + C 2000 mg/m² DT 75 mg/m² + A50 C 500 mg/m² PT 100 mg/m² + Carboplatin AUC2 Gemcitabine 1000 mg/m² + Carboplatin AUC2 DT 75 mg/m² + C 600 mg/m²	N/A	In total 226 cancer patients with solid tumors. Breast cancer receiving (neo) adjuvant and palliative chemotherapy (n=136).	Not stated	Hair loss, common toxicity criteria (CTC German version 1.0) scale for alopecia. No or not visible hair loss, CTC 0-1.	3.1% (7/226)	65% (no or not visible hair loss, CTC 0-1.)	Slight and well tolerable sensation of cold and mild cranial pressure. No skin irritations recorded.	Cold intolerance and aversion.
Andrews et al., 2014 Patricia Ritchie Centre, the Mater Hospital Sydney, Australia	Prospective feasibility	AC or combination FEC or FEC-D TC Other	N/A	Early stage breast cancer (n=122)	Not stated	Completion rate Hair loss: Dean score	80.5% (98/122)	50% (61/122)	Not stated	Adverse events not listed specifically for patients using the DigniCap.

Publication (author, year, institution)	Type of study (RCT, retrospective, single arm prospective nonrandomized studies.)	Treatment group	Control group	Sample size	Length of Follow- up	Follow-up schedule	Completed Cooling %	% Success with <50% hair loss	List of Adverse Events	Reason for discontinuation of cooling
Friedrich and Carstensen, 2014 Mammazentrum, Jerusalem Hospital, Hamburg, Germany	Non randomized prospective June 2011-December 2012	Multiple combinations <u>(Neo-) adjuvant chemotherapy</u> E 90 mg/m² + C 600 mg/m² (q3w*4) → DT 100/175 mg/m² (q3w*4) F 500 mg/m² + E 100 mg/m² + C 500 mg/m² (q3w*6) F 500 mg/m² + E 100 mg/m² + C 500 mg/m² (q3w*6) → DT 100 mg/m² (q3w*3) E 90 mg/m² + C 600 mg/m² (q3w*4) CarboplaPt/DT (q3w*6) <u>Palliative chemotherapy</u> Taxol 135/Herceptin 8mg/kg Halaven 1.23 Taxol 90 Avastin 10mg/kg Carboplatin Gemcitabine/Cisplatin	N/A	Breast cancer (n=83) Adjuvant (n=58) Palliative (n=6) Drop outs (n=19)	Not stated	Hair loss: Photo documentation Numerical VAS (1-10)	77% (64/83 finished chemotherapy and scalp cooling.)	52.6%	Feeling of cold Headaches Heaviness of head Scalp pain Frequency differed between patients with (neo-) adjuvant and palliative CT	Out of 19 patients; hair loss (n=5), Cancer related emergency cases or disease progression (n=3), Feeling of cold/headaches (n=2), Unspecified intolerance (n=9).

Publication (author, year, institution)	Type of study (RCT, retrospective, single arm prospective nonrandomized studies.)	Treatment group	Control group	Sample size	Length of Follow- up	Follow-up schedule	Completed Cooling %	% Success with <50% hair loss	List of Adverse Events	Reason for discontinuation of cooling
Udrea et al., 2014 Medisprof Oncology day hospital, Cluj, Romania	Non randomized prospective March 2012 - November 2013	E 100mg/m² + C 600 mg/m² (n=53) DT 100 mg/m² (n=10) PT 175 mg/m² + carboplatin AUC5-6 (n=21) Irinotecan 80 mg/m² (n=4), Etoposide 100 mg/m² day 1-3 + Carboplatin AUC5 (n=3) TXT 75 mg/m² (n=2) DT 75 mg/m² + Cisplatine 75 mg/m² + Capecitabine 1000 mg/m² (n=2) Other combinations (n=13)	N/A	108 cancer patients (Treatment ongoing for 8 patients).	Not stated	Hair loss: US NCI (CTCAE) v4.0. No alopecia / crown like alopecia	96% (104/108)	57% (62/108) (No alopecia / crown like alopecia)	Not stated	Discomfort (n=4)
Meunier et al., 2013 1) Service de chimiothérapie, Clinique Charcot, Lyon, France 2) Centre Alexis Vautrin, Nancy, France 3) Jerusalem Krankenhaus Mammazentrum Hamburg, Germany	Non randomized prospective multicenter	<u>(Neo-) adjuvant chemotherapy</u> 4 E90 C600 + 4 Taxotere (n=26) 3 FEC100 + 3 Taxotere (n=10) 6 FEC 100 (n=15) 4 T75C600 +/- Trastuzumab (n=7) Taxane +/-anthracyclines (n=11) <u>Palliative chemotherapy</u> Paclitaxel, Eribuline, Carbo + cisplatin, gemcitabine (n=6)	N/A (Comparison 3 versus 8 degrees C)	Cancer patients (total n=133). Breast cancer (n=75) (Neo) adjuvant (n=69) Palliative (n=6).	Not stated	Hair loss: Patient self- assessment VAS 0-100, with 100 being total hair preservation. (success: keeping 60-100% of hair)	44.6%	(neo) adjuvant: 65% Palliative: 83%	Headaches (22%) Cold sensation or pain to the scalp (4%)	Intolerance (9%) Headaches (9%) Unknown (9%) Hair loss (22%) Stopped chemo/disease progression (9%)

Publication (author, year, institution)	Type of study (RCT, retrospective, single arm prospective nonrandomized studies.)	Treatment group	Control group	Sample size	Length of Follow- up	Follow-up schedule	Completed Cooling %	% Success with <50% hair loss	List of Adverse Events	Reason for discontinuation of cooling
Ekwall et al., 2013 Örebro University Hospital, Örebro, Sweden	Randomized prospective	PT (175 mg/m2) + carboplatin (AUC 5-6)	N/A	Gynecological cancer (total n=43); Ovarian cancer (n=22) Endometrial cancer (n=17) Cervical cancer (n=2) Tubal cancer (n=1) Peritoneal cancer (n=1)	Not stated	Hair loss: Photo documentation as assessed by two Investigators VAS (0-10) as assessed by the patients	91% (43/47)	51%	Scalp cooling was generally very well tolerated. Headaches VAS ≤ 1 Coldness VAS ≤ 3.4	Anaphylactic reactions, peripheral neuropathy and regimen modification.
Abramov et al., 2011 N.N. Blokhin Russian Center Research, Chemo- therapy and combined treatment Moscow. Russian federation	Non randomized prospective	ANR (n=5) TX (n=8) ANR+TX (n=7)	N/A	Breast cancer (n=20)	Not stated	Hair loss: CTCAE v3.0 Grade 1: (thinning or patchy)	Not stated.	100% ANR: 100% no hair loss TX: 50% no hair loss, 50% grade 1 ANR+TX: 29% no hair loss, 71% Grade 1	Not stated	N/A
Kato et al., 2011 Kato Breast Clinic, Shiga, Japan	Non randomized prospective August 2007- October 2010	PT 60 mg/m2 weekly + C 400 mg/m2 (n=252) PT+ H (n=29) E 40 mg/m2 biweekly+ C 400 mg/m2 (n=54) Other combinations (n=24) (Combination by 5FU, CPT-11, Gemcitabine and CBDCA.)	N/A	Breast cancer (n=359)	Not stated	Modified WHO scale (Grade 1-5) Success defined as <30% hair loss. Photos	Not stated	96%	No abnormal scalp sensation or headaches during or after treatment. No scalp metastasis.	N/A
Byahov et al., 2006 Semashko Central Clinical Hospital, Moscow, Russia	Non randomized prospective	ANR (n=43) Non-ANR (n=34)	N/A	Breast cancer, ovarian cancer, colorectal cancer (total n=77)	Not stated	Hair loss CTCAE v 3.0	Not stated	ANR: 79% Non-ANR: 94%	Well tolerated by all patients.	N/A

Publication (author, year, institution)	Type of study (RCT, retrospective, single arm prospective nonrandomized studies.)	Treatment group	Control group	Sample size	Length of Follow- up	Follow-up schedule	Completed Cooling %	% Success with <50% hair loss	List of Adverse Events	Reason for discontinuation of cooling
Ridderheim et al., 2003 Lund University Hospital, Sweden	Non randomized prospective pilot	PT 175 mg/m², Carboplatin AUC 5 PT 175 mg/m², E 75 mg/m2, Carboplatin AUC 5 DT 100 mg/m² PT 175 mg/m² Gemcitabine 1,000 mg/m² day 1+8, E 75 mg/m² day 1 E 60 mg/m², C 600 mg/m², 5-FU 600 mg/m² D 50 mg/m², Cisplatin 50 mg/m² E 50 mg/m², Carboplatin AUC 5 Vinorelbine 30 mg/m² D 25 mg/m² Bleomycin 10,000 E/m² Vinblastin 6 mg/m² Darcabazin 375 mg/m² Bleomycin 30,000 day 1, 5, 16 Etoposide 100 mg/m² day 1–5 Cisplatin 20 mg/m² day 1–5 Topotecan 1.0 mg/m² day 1-5 Etoposide 50 mg/day 6–12 Topotecan 1.0 mg/m²		In total 74 cancer patients Ovarian cancer (n=60) Hodgkin´s Lymphoma (n=8) Breast cancer (n=3) Endometrial cancer (n=2) Sarcoma (n=1)	15 months (range 3-44).	Hair loss: Photo documentation Numerical VAS (0-10)	97% (72/74)	Minimal to no hair loss in ANR or TX treated patients. Median hair loss was VAS 6 (range 1.5–8) in patients treated when combining ANR and TX.	Discomfort was modest (median value 1.5; range 0.5–8). No presence of scalp metastases	Discomfort

DigniCap® Scalp Cooling System

Publication (author, year, institution)	Type of study (RCT, retrospective, single arm prospective nonrandomized studies.)	Treatment group	Control group	Sample size	Length of Follow- up	Follow-up schedule	Completed Cooling %	% Success with <50% hair loss	List of Adverse Events	Reason for discontinuation of cooling
Henriksen et al., 2003 Herlev Hospital, University of Copenhagen Denmark	Non randomized prospective interim	Seven cycles of FEC (Adjuvant). Dose not stated.	N/A	Breast cancer (n=26)	Not stated	Hair loss: Patients self-assessment Clinical photos Numerical VAS, wig use Side effects: Numerical VAS Post-treatment questionnaire	Not stated	88% success rate, 23/26 patients choose not to use a wig.	Side effects and extra time accepted by the patients.	N/A
Lundgren et al., 1999 Umeå University Hospital & Lund University Hospital, Sweden	Non randomized prospective pilot	PT 135-175 mg/m² (n=3) DT 100 mg/ m² (n=3) FEC (n=2) CMF (n=1)	PT	Ovarian cancer (n=3) Breast cancer (n=6) Ovarian cancer control (n=2)	Not stated	Hair loss: Numerical VAS (1-10) assessed by independent observers. Discomfort assessed by the patients.	100%	Scalp cooled patients: 100% Controls: 0% (Minimal to no hair loss (VAS < 2.5) in all scalp cooled patients.)	Discomfort level initially low (mean VAS 3) and decreased after 10 min (mean VAS 1.5). No presence of scalp metastases	N/A

Chemotherapy and Abbreviations

ANR: anthracyclines

H: Herceptin

TCH: docetaxel + carboplatin + trastuzumab

AC: doxorubin + cyclophosphamide

M: methotrexate TC: docetaxel + cyclophosphamide

C: cyclophosphamide

D: doxorubicin

DT: docetaxel

E: epirubicin

F: 5-fluorouracil

Mi: mitoxanthrone

PT: paclitaxel

TX: taxanes

Vc: vincristine

Bibliography**:**

1. Lundgren-Eriksson,L,etal.“Totalpreventionoftacoi-induced alopecia by a new model of cold cap(dignitana).”*The European Journal of Cancer*. Vol. 35, Supp. 4. September 1999.
2. Henriksen,T,etal.“Advanced,computerizedcoldcapforpreventing chemotherapy induced alopecia.”*The European Journal of Cancer.* Vol. 1, No. 5. September 2003. S369.
3. Ridderheim,M,etal.“Scalphypothermiatopreventchemotherapy-induced alopecia is effective and safe: A pilot study oif a new difitized scalp-cooling system used in 74 patients. *Support Care Cancer*. Vol. 11. 2003. 371-377.
4. Byahov,MandOShevlev.“Alopeciapreventioninchemotherapypatients.Methodof controlledscalpcooling.”*Meditsinskaya Cartoteka*.2006.
5. Kato,M,etal.“EvaluationofDigniCap System for the Prevention of Chemotherapy-induced Hair LossinBreastCancerPatient.”*St. Gallen Oncology Conference.* 2011.
6. Abramov,MandSemenova,I.“CoolingoftheScalptoPreventAnticancerChemotherapy- induced Alopecia.”Poster.
7. Ekwall, E, et al.“Determinationofthemosteffectivecoolingtemperatureforthe prevention of chemotherapy-inducedalopecia.”*Molecular and Clinical Oncology.* Vol. 1. 2013. 1065- 1071.
8. Meunier,A,etal.“Evaluationdelatoléranceetdel’efficacitéd’uncasqueàrefrigeration continue (DIGNICAP)danslapréventiondel’alopéciechimio-induite.”(Translationfrom French). Presented at the *Society For Science-Based Medicine* , 2013.
9. Udrea,A.“Scalpcoolingsysteminpreventingchemotherapy-induced alopecia: a pilot study on 108 patients –a Romanian oncology –dayhospitalexperience.”*Medisprof Oncology. Psycho-Oncology* 23 (Suppl. 3):169-254 (2014), P1-0062.
10. Friedrichs,KandMCarstensen.“Successfulreductionofalopeciainducedbyanthracycline and taxane containing adjuvant chemotherapy in breast cancer –clinical evaluation of sensor-controlledscalpcooling.”*SPrignerPlus*. Vol. 3, No. 500 2014. 1-7.
11. Andrews,K,etal.“CrowningGlory:Isthatthewholestory?Implementingscalpcoolingin an Australian setting.” Poster presentation at *Cancer Nurses Society of Australia,* 17th winter congress, 2014.
12. Schaffrin-Nabe,D,etal.“Theinfluenceofvariousparametersonthesuccessofsensor- controlled scalp cooling in preventing chemotherapy-inducedalopecia.”*Oncology Research and Treatment*. Vol. 38. 2015. 489-495.
13. Drinkut,K,etal.“coolHAIR–scalp cooling to prevent chemotherapy-inducedalopecia.” (Translation from German). *Geburtshilfe Frauenheilkunde* 2016:76-P171.
14. Schaffrin-Nabe,D,etal.“Hair-mass-Index (HMI) as indicator for the efficacy oif scalp cooling(SC)andtheassociatedqualityoflife.”*Journal of Clinical Oncology*. 34. 2016. (suppl; abstr e21692)
15. Traub,L,etal.“EfficacyandsideeffectsoftheDigniCap®systemtopreventcytostatic- induced alopecia.”(TranslationfromGerman).*Geburtshilfe Frauenheilkunde* 2016:76-P068
16. Campenni,GM,etal.“Preventingchemotherapy-induced alopecia by scalp cooling: preliminary data from a study on the efficacy and safety of dignicap® system in breast cancer patients.”Ann Oncol. Vol. 27, Supp. 4. 2016. iv63-iv64.
17. Fehr,MK,etal.“Sensor-controlled scalp cooling to prevent chemotherapy-induced alopecia in

femalecancerpatients.”Current Oncology. Vol. 23, No. 6. December 2016. e576-e582.
18. Hernández R.E. et al., Experience at the ABC Medical Center of Mexico City, 2010-2015, using the scalp cooling system DigniCap® for the prevention of chemotherapy-induced alopecia. Poster 850794 at the San Antonio Breast Cancer Symposium, 2016.
19. Van den Hurk CJ, Mols F, Vingerhoets AJ, BreedWP(2010) Impact of alopecia and scalp c cooling on the well-being of breast cancerpatients. Psych oncol 19(7):701–709.