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Use of scalp cooling device to prevent alopecia for early breast cancer patients receiving chemotherapy: A prospective study

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Abstract

Chemotherapy-induced alopecia (CIA) affects the majority of patients receiving chemotherapy (CT) for early breast cancer. It is a highly distressing side effect of CT, with psychological and social impact. Primary aim of the present analysis was to assess the efficacy of scalp cooling with DigniCap® in preventing CIA. Success rate was defined as patients' self-reported hair loss <50% according to Dean scale. In this analysis, we reported success rate at 3 weeks after the first CT course and at 3 weeks after the last CT course. Secondary endpoints included self-reported tolerability and patients' judgment on scalp cooling performance. Consecutive early breast cancer patients admitted to Istituto Oncologico Veneto who were recommended to receive neoadjuvant or adjuvant CT, were eligible to undergo scalp cooling during the CT administration within this study. 135 patients were included: 74% received adjuvant CT and 26% neoadjuvant CT ($P < .001$). The type of CT was: docetaxel-cyclophosphamide (26%), paclitaxel (23%), epirubicin-cyclophosphamide followed by paclitaxel (32%), and paclitaxel followed by epirubicincyclophosphamide (19%). The rate of success in preventing alopecia was 77% (104/135) at 3 weeks from the start of CT and 60% (81/135) at 3 weeks from the end of treatment. Higher success rates were reported in non-anthracycline (71%) compared to anthracycline-containing CT regimens (54%; $P < 0.001$). Premature discontinuation of scalp cooling was reported in 29/135 patients (21.5%), including withdrawal for alopecia (16/29), for low scalp cooling tolerability (8/29) or both (5/29). Scalp cooling was generally well tolerated. These results overall suggest that the use of scalp cooling is effective in preventing alopecia in the majority of early breast cancer patients receiving neoadjuvant or adjuvant CT, especially for patients undergoing a taxane-based non-anthracycline regimen.

KEYWORDS
alopecia, dignicap, early breast cancer, scalp cooling

1 | INTRODUCTION

Chemotherapy (CT) represents one of the mainstays of therapy for early-stage breast cancer, leading to a reduction in breast cancer-related mortality of 20% in the adjuvant setting.[1] Chemotherapy-induced alopecia (CIA) is a highly distressing side effect of CT, with psychological and social impact, ultimately affecting QoL.[2] It represents an off-target CT toxic effect on the highly proliferative matrix cells and keratinocytes of the hair bulb in the scalp.[3] CIA affects the majority of patients receiving contemporary adjuvant or neo-adjuvant CT regimens for early breast cancer, particularly anthracycline (epirubicin or doxorubicin) and antimicrotubule agents (paclitaxel, docetaxel).[4,5]

CIA is dose - and schedule-dependent, usually occurs 7-28 days after first dose of CT, and is most often reversible.[2,3,6] Nevertheless, some patients may experience permanent alopecia after CT completion, especially whom received docetaxel-containing regimens.[7,8]

In this context, CIA prevention may impact on patients' QoL and may facilitate treatment acceptance.[9,10] Among all treatment options for CIA prevention, scalp cooling remains the only measure with proven efficacy in cancer patients.[10,11] Scalp cooling prevents CIA through two main mechanisms: (a) cutaneous vasoconstriction, resulting in decreased blood flow to the scalp and reduced cellular uptake of drugs by the hair follicles; (b) hypothermia, resulting in decreased follicular metabolic rate of the delivered CT drugs and lower susceptibility to CT damage.[12-14]

Two recent prospective studies (one randomized and one with a matched control group) including patients with early breast cancer receiving CT have reported success rates in hair preservation (hair loss of 50% or less) ranging from 50.5%-66.3%.[15,16] The scalp cooling systems were also well tolerated in these studies, with only grade 1 or 2 toxicities reported. However, these studies differed for the timing of hair loss prevention assessment and their design did not allow to evaluate the alopecia preventing effect of scalp cooling across the full range of available and commonly used CT regimens for early breast cancer. The primary end point of the randomized study by Nangia et al was to assess hair loss prevention after the first four courses of CT (either anthracycline or taxane).[16] The study by Rugo et al[15] evaluated hair loss prevention at the end of the full CT regimen; however, patients receiving both anthracycline and taxanes were excluded and all the patients enrolled in the scalp cooling group received taxane CT.

When discussing CT options and their implications with the patient, it is key to provide accurate and individualized information on the likelihood of preventing alopecia by using a scalp cooling system and on the potential patterns and timing of efficacy/failure throughout treatment. Therefore, there is the need to acquire data at multiple time-point from the real world setting on the activity of scalp cooling in patients receiving different regimens of CT for early breast cancer.

The present prospective study aimed to evaluate the efficacy of scalp cooling with DigniCap. Scalp Cooling System device in preventing CIA throughout CT treatment among women diagnosed with early-stage breast cancer receiving neo-adjuvant or adjuvant CT regimens and schedules.

2 | MATERIALS AND METHODS

2.1 | Study design and objectives

Consecutive early breast cancer patients admitted to the Division of Medical Oncology 2 of the Istituto Oncologico Veneto IRCCS (Padova, Italy), who were recommended to receive alopecia-inducing neo-adjuvant or adjuvant CT, were eligible to undergo scalp cooling during the CT administration within this study. The study was approved by the local Ethic Committee.

The primary objective was to assess the efficacy of scalp cooling in preventing CIA. The degree of alopecia was assessed using self-reported Dean's alopecia scale for hair loss: grade 1/excellent (<25% hair loss), grade 2/good (25%-50% hair loss), grade 3/moderate (50%-75% hair loss), and grade 4/poor (>75% hair loss).[4] Success was defined as self-reported hair loss <50% according to Dean scale (Grade 0-2); failure was defined as >50% hair loss (Grade 3-4 on Dean scale). Patients' self-assessment questionnaires were administered by an oncology nurse with the following timeline: every 3 weeks during treatment and at 3 weeks from the last CT course. In this analysis, we report success rate at 3 weeks after the first CT course and at 3 weeks after the last CT course.

Scalp cooling tolerability was also assessed. Data on self-reported device-related adverse events were collected through questionnaires administered at baseline, every 3 weeks and at 3 weeks after last CT course. Patients were asked to report the presence of predefined events such as headache, pain, heavy head, and chill. The questionnaires allowed also self-reporting of other non-predefined events. Patients were asked to grade adverse events, if present, on a scale of 1-4, with four as the worst.

Finally, patients' overall judgment on scalp cooling performance was collected through a questionnaire administered at 3 weeks after the last CT course. Patients were asked to report their judgement on a scale of 1-7, with seven as the most positive score.

2.2 | Treatments

Patients were assigned to one of the following CT regimens, routinely used at our Institution for the treatment of patients with early breast cancer: docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 for 4 three-weekly cycles (TC); paclitaxel 80 mg/m^2 weekly for 12 weeks (Txl); epirubicin 90 mg/m^2 and cyclophosphamide 600 mg/m^2 for 4 three-weekly cycles, followed by paclitaxel 80 mg/m^2 weekly for 12 weeks (EC-Txl); paclitaxel 80 mg/m^2 weekly for 12 weeks followed by epirubicin 90 mg/m^2 and cyclophosphamide 600 mg/m^2 for 4 three-weekly cycles (Txl-EC). Patients with human epidermal growth

factor receptor 2 (HER2)-positive breast cancer also received trastuzumab concomitant to the taxane component of the CT regimen. The decision to recommend a specific CT treatment was based on routine clinical evaluation, in accordance with standard national and local guidelines.

DigniCap® Scalp Cooling System (Dignitana AB, Sysmex Europe) provides a tight-fitting cap connected to a cooling machine (where liquid coolant circulates), allowing for scalp temperature control and maintenance during treatment administration. The Dignicap Scalp Cooling System device consists of a computer-controlled refrigerator unit connected by hoses to a silicon cap, covered by an insulating neoprene cap, which ensures suitability of silicon cap to patient's scalp and maintenance of optimal temperature. From the computer-controlled refrigerator unit, a glycol-based coolant fluid circulating through small channels within cap is introduced. Dignicap is provided of some sensors in the silicone cap, allowing for control and maintenance of temperature during all treatment course. Scalp cooling was initiated 30 minutes prior to each cycle (precooling 30 minutes includes 20 minutes of temperature decreasing) with a scalp temperature maintained at 3-5°C (preset treatment temperature) during the time course of CT, and for 90-120 minutes afterward (postcooling time). It is noteworthy that time and modality of scalp cooling varies according to type, dose and schedule of CT, by a scheme provided by the manufacturer. In particular, taken into account treatment schedules employed by this study, postcooling time ranged from 60 to 120 minutes.[11]

2.3 | Statistical methods

Statistical analysis was carried out using SPSS version 25. Descriptive statistics including percentages, means, medians, and ranges were performed for patients' demographics and clinical characteristics.

The association between variables was evaluated with the $\chi 2$ test or the Mann-Whitney test, as appropriate. Level of significance was set at 0.05.

TABLE 1 Clinicopathologic patients' characteristics at the time of CT starting

N (%) of patients						
	Overall (N = 135)	**TC (N = 35; 26%)**	**Txl (N = 31; 23%)**	**EC-Txl (N = 43; 32%)**	**Txl-EC (N = 26; 19%)**	***P***
Age median (range)	48 (27-76)	51 (37-76)	55 (27-76)	48 (30-68)	45 (27-64)	.026
Menopausal status						
Premenopausal	87 (64)	19 (54)	16 (52)	30 (70)	22 (85)	.030
Postmenopausal	48 (36)	16 (46)	15 (48)	13 (30)	4 (15)	
Grade 1	1 (1)	0 (0)	0 (0)	1 (2)	0 (0)	.503
Grade 2	25 (18)	6 (17)	7 (23)	10 (24)	2 (8)	
Grade 3	109 (81)	29 (83)	24 (77)	32 (74)	24(92)	
Hystotype						
Ductal	116 (86)	28 (80)	25 (81)	37 (86)	26 (100)	.343
Lobular	12 (9)	5 (14)	4 (13)	3 (7)	0 (0)	
Other	7 (5)	2 (6)	2 (6)	3 (7)	0 (0)	
N0	74 (55)	24 (69)	28 (90)	11 (26)	11 (42)	<.001
N1	61 (45)	11 (31)	3 (10)	32 (74)	15 (58)	
AJCC Stage I	52 (39)	16 (46)	20 (65)	11 (26)	5 (19)	.002
AJCC Stage II	64 (47)	18 (51)	8 (25)	22 (51)	16 (62)	
AJCC Stage III	19 (14)	1 (3)	3 (10)	10 (23)	5 (19)	
Ki67%, median (range)	34 (3-83)	30 (4-80)	35 (3-80)	35 (5-83)	37 (15-80)	.727
ER and/or PgR pos	102 (76)	32 (91)	22 (71)	35 (81)	13 (50)	.002
ER and/or PgR neg	33 (24)	3 (9)	9 (29)	8 (19)	13 (50)	
Her 2 pos	47 (35)	0 (0)	29 (93)	9 (21)	9 (35)	<.001
Her 2 neg	88 (65)	35 (100)	2 (7)	34 (79)	17 (65)	
Adjuvant CT	100 (74)	35 (100)	26 (84)	39 (91)	0 (0)	<.001
Neo-adjuvant CT	35 (26)	0 (0)	5 (16)	4 (9)	26 (100)	

Abbreviations: AJCC, American Joint Committee on Cancer; CT, chemotherapy; EC-Txl, epirubicin-cyclophosphamide-paclitaxel; ER, estrogen receptor; HER 2, human epidermal growth factor receptor 2; N, number; N0, node negative; N1, node positive; neg, negative; *P*, *P* value; PgR, progesterone receptor; pos, positive; TC, docetaxel-cyclophosphamide; Txl, paclitaxel; Txl-EC, paclitaxel-epirubicin-cyclophosphamide.

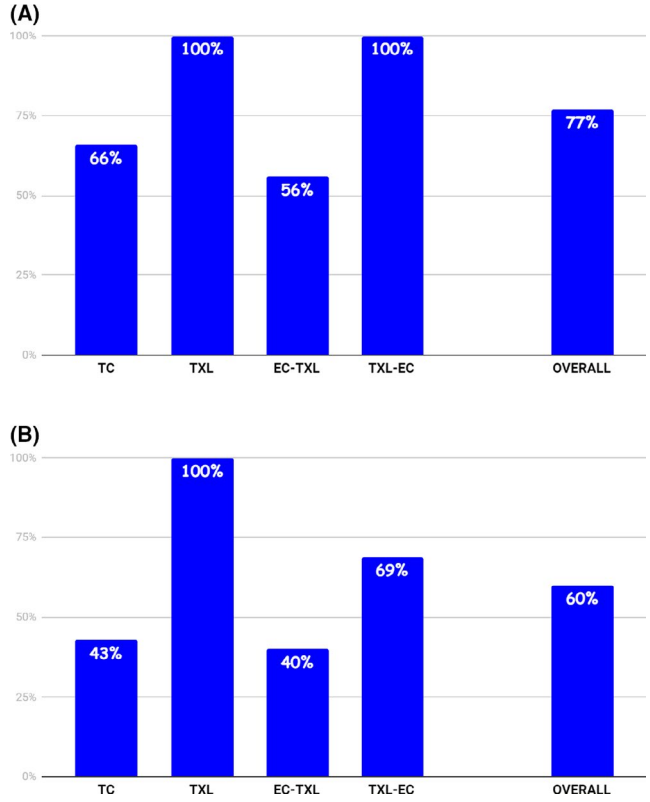

FIGURE 1 Success rate at 3 wk from treatment starting (1A) and final success rate (1B)

3 | RESULTS

3.1 | Patients' characteristics and treatment

From May 2016 to January 2018, a total of 135 patients were included in our analysis. Patients and tumor characteristics at baseline, overall and according to type of CT, are detailed in Table 1. Median age was 48 years (range 27-76); 64% of patients were premenopausal. The majority of patients showed stage I-II disease (86%), negative lymph nodes (55%), breast cancer of ductal histology (86%), grade 3 (81%), hormone receptor-positive (76%), and HER2-negative (65%). Most of the patients received CT in the adjuvant setting (74%).

The most common CT regimen was EC-Txl (32%), followed by TC (26%), Txl (23%), and Txl-EC (19%). The distribution of clinicopathological characteristics across the CT groups is consistent with the use of anthracycline-free regimens for patients with earlier stage disease, older age and in case of hormone receptor-negative tumor (TC regimen). The Txl regimen was the most commonly used for HER2-positive patients combined with trastuzumab. The Txl-EC regimen was the most frequently used in the neo-adjuvant setting.

All patients completed the neo-adjuvant/adjuvant CT treatment, except one in the TC cohort due to CT toxicity. Scalp cooling was prematurely discontinued by 29 patients (21.5%), including withdrawal for alopecia (12%, n = 16), low scalp cooling tolerability/adverse events (6%, n = 8) or both (4%, n = 5).

Across CT groups, premature discontinuation rate was 23% in TC (8/35), 0% (0/31) in Txl, 37% in EC-Txl (16/43), and 19% in Txl-EC (5/26) cohort, respectively.

3.2 | Scalp cooling efficacy

Considering the entire patients cohort, success rate in alopecia prevention by scalp cooling was 77% (104/135) at 3 weeks from the start of CT. Final success rate, assessed at 3 weeks from the end of treatment, was 60% (81/135).

The success rate was significantly different across the CT groups: in TC, Txl, EC-Txl, and Txl-EC cohorts 66% (23/35), 100% (31/31), 56% (24/43), and 100% (26/26) of the patients reported hair loss <50% at 3 weeks from start of treatment, respectively ($P < .001$; Figure 1A). Final success rate was 43% (15/35), 100% (31/31), 40% (17/43), and 69% (18/26) in TC, Txl, EC-Txl, and Txl-EC cohorts ($P < .001$; Figure 1B). The difference in terms of final success rate between EC-Txl and Txl-EC was statistically significant ($P = .017$).

3.3 | Scalp cooling tolerability and patients' perception

Most common scalp cooling-related reported AEs were as follows: chills (90%), heavy head (70%), headache (60%), and scalp pain (56%). The respective mean high scores were 2.9, 2.3, 1.9, 2 (Figure 2). The use of antalgic medication for the management of scalp pain was not necessary.

Thirteen patients (10%) discontinued scalp cooling treatment due to side effects/intolerance from cold caps, 3 (3/35) in TC cohort, 8 (8/43) in EC-Txl cohort, and 2 (2/26) in Txl-EC cohort.

Overall mean final patients' judgment score on scalp cooling performance was 5.0:4.6 in the TC cohort, 6.6 in the Txl cohort, 4.1 in the EC-Txl cohort, and 5.0 in the Txl-EC cohort ($P < .001$). More in detail, the difference in patients' judgement score between EC-Txl and Txl-EC was statistically significant ($P = .044$). The final questionnaire also asked patients how frequently they used a wig and/or a head wearing: 120 patients answered this question, among whom 58.3% reported they never used either of them (30% in the TC cohort, 92.9% in the Txl cohort, 51.2% in the EC-Txl cohort, and 66.7% in the Txl-EC cohort, $P < .001$).

4 | DISCUSSION

In the present analysis, the use of scalp cooling resulted in successful hair loss prevention for the majority of patients receiving adjuvant or neo-adjuvant CT with taxanes, anthracyclines or both agents for early breast cancer.

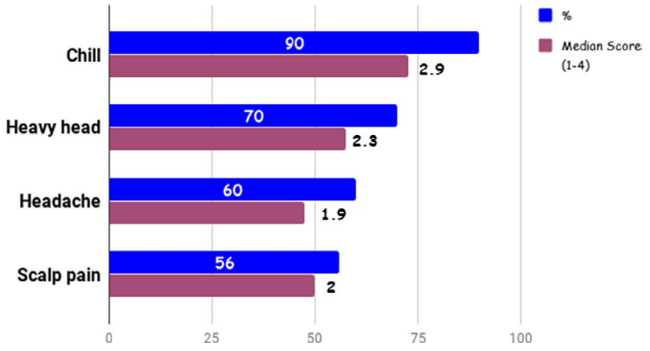

FIGURE 2 Cooling-related symptoms and the respective mean high scores

Recent meta-analyses are supportive of our efficacy results. First, in a meta-analysis by Rugo et al[13], including ten randomized clinical trials and 654 patients, mainly (66%) receiving anthracyclines, use of scalp cooling achieved successful reduction of CIA (43% reduction of relative risk of alopecia). Then, an up-to-date review of high-quality controlled and randomized clinical trials confirmed scalp cooling efficacy as preventative measure for CIA, with a reduction in the occurrence rate of CIA by 2.7-fold in the controlled clinical trials and 3.9-fold in the randomized clinical trials.[14] Finally, in a systematic review and meta-analysis by Shin et al, involving 1.098 breast cancer patients (616 interventions, 482 controls) mainly receiving anthracycline-based CT, scalp cooling use significantly reduced development of CIA, yielding 62% decrease in relative risk of alopecia (RR = 0.38, 95% CI = 0.32-0.45).[17]

In accordance with available data from studies evaluating different scalp cooling devices, our analysis highlighted higher success rates in taxane (71%) compared with anthracycline-based CT regimens (54%).[15,16,18] In our study, scalp cooling allowed a final success rate in alopecia prevention of 71% in the taxane-based therapy groups, including cohorts of three-weekly docetaxel plus cyclophosphamide (43%) and weekly paclitaxel (100%). Nevertheless, some differences in terms of CIA prevention were also found within taxane-based therapy group, in that, weekly paclitaxel showed highly better outcome than TC regimen, possibly owing to sustained scalp hypothermia permitted by weekly administration of taxane, differently from three-weekly taxane schedule. These results are consistent with those from a multicenter prospective cohort study by Rugo et al, that evaluated the Dignicap Scalp Cooling device in an early-stage breast cancer population, comprising 106 patients, among whom 101 undergoing taxane-based adjuvant or neo-adjuvant CT (not allowed sequential anthracycline-taxane schedule). The authors reported overall successful hair preservation in 67/101 patients (66%),[15] that, analyzed by chemotherapy regimen, was 60,5% in TC group versus 83% in paclitaxel alone group.

The multicenter prospective SCALP trial, by Nangia et al[16] evaluated an early-stage breast cancer population receiving Paxman® Scalp Cooling System while undergoing CT and showed success rates of 16% and 59% after anthracycline and taxane, respectively.

In our analysis, we also observed a higher final successful rate in patients who underwent anthracyclines after taxanes than in those who underwent the same CT sequence but in reverse order (69% vs 40%; P = 0,017). This may suggest a role of CT sequence on scalp cooling successful rate. A possible biological explanation could be that a prolonged hypothermia induced by the scalp cooler in the weekly administration of taxanes for 12 consecutive weeks could decrease follicular metabolism and the subsequent delivery of anthracyclines, decreasing the anthracycline-related follicular damage. This could be the same biological rationale for which Txl-EC regimen is associated with less alopecia, compared with TC regimen. Specifically, Txl-EC regimen when analyzed separately from anthracycline-based CT group, exhibited highly satisfactory success rate (69%) compared with TC regimen (43%), possibly due to prolonged scalp cooler-induced hypothermia permitted by weekly administration of paclitaxel.

In terms of adverse events and tolerability, our results are consistent with those reported in the context of available randomized clinical trials.[15,16] Only 10% patients discontinued scalp cooling before completion of CT because of scalp cooling-related AEs. Chills, heavy head, scalp pain, and headache were the most commonly self-reported AEs of scalp cooling. Furthermore, in our analysis we focused our attention also on patient's judgment on scalp cooling performance. Our results demonstrate a high degree of satisfaction. Moreover, the majority of patients in this study reported they never wore head covering during the time course of CT. Our results are in accordance with data from Dutch Scalp Cooling Registry, the largest prospective multicenter trial on scalp cooling among patients receiving CT reported in literature, where overall success rate was 50%, in terms of proportion of head cover use during the last CT session. This study showed that scalp cooling successful rates vary according to CT regimen, dose and infusion rate, especially, they decrease with polychemotherapy, higher dose and shorter infusion time of CT.[19]

Despite some limitations affecting Dignicap Scalp Cooling System either related to costs of device or to facilities for nursing time and prolonged treatment duration, our results show efficacy of scalp cooling in preventing CIA in the majority of early breast cancer patients, so its use is worthwhile.

In conclusion, among patients receiving adjuvant or neo-adjuvant CT with curative intent for early-stage breast cancer, scalp cooling proved to retain a positive effect in reducing severity of alopecia. Therefore, it should be considered as an effective strategy to be offered to women willing to reduce CIA, especially when a taxane-based regimen is indicated. Of course, further investigations are needed in order to better clarify which subgroups of patients would more likely benefit from the use of scalp cooling in terms of psychological social and aesthetic results.

CONFLICT OF INTEREST

Maria Vittoria Dieci has received fees from EliLilly for consultancy role and participation on advisory boards; fees from Genomic Health for consultancy role; fees from Celgene for participation on advisory

boards. Valentina Guarneri has received honoraria from EliLilly and Roche for participation on advisory boards, and honoraria from AstraZeneca and Novartis. The other authors do not declare any conflict of interest.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This research has been conducted in accordance with the Declaration of Helsinki. The study protocol has been approved by the Ethics Committee of Istituto Oncologico Veneto IRCCS of Padova.

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REFERENCES

1. Early Breast Cancer Trialists' collaborative group (EBCTCG). Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100 000 women in 123 randomised trials. *Lancet*. 2012;379:432-444.
2. van den Hurk CJ, Mols F, Vingerhoets AJ, Breed WP. Impact of alopecia and scalp cooling on the well-being of breast cancer patients. *Psychooncology*. 2010;19(7):701-709.
3. Chon SY, Champion RW, Geddes ER. Chemotherapy-induced alopecia. *J Am Acad Dermatol*. 2012;67:e37-e47.
4. Dean JC, Salmon SE, Griffith KS. Prevention of doxorubicin-induced hair loss with scalp hypothermia. *N Engl J Med*. 1979;301:1427.
5. Sibaud V,Lebœuf NR, Roche H, et al. Dermatological adverse events with taxane chemotherapy. *Eur J D ermatol*. 2016;26(5):427-443.
6. Batchelor D. Hair and cancer chemotherapy: consequences and nursing care a literature study. *Eur J Cancer Care (Engl)*. 2001;10:147-163.
7. Martín M, de la Torre-Montero JC, López-Tarruella S, et al. Persistent major alopecia following adjuvant docetaxel for breast cancer: incidence, characteristics, and prevention with scalp cooling. *Breast Cancer Res Treat*. 2018;171(3):627-634.
8. Kang D, Kim IR, Choi EK, et al. Permanent chemotherapy-induced alopecia in patients with breast cancer: a 3-year prospective cohort study. *Oncologist*. 2019;24(3):414-420.
9. Paus R, Haslam IS, Sharox AA. Pathobiology of chemotherapy-induced hair loss. *Lancet Oncol*. 2013;14:e50-e59.
10. Yeager CE, Olsen EA. Treatment of chemotherapy-induced alopecia. *Dermatol Ther*. 2011;24:432-442.
11. Mustoe MM, Lee CM, Melisko ME, Esserman LJ, Rugo HS. The dignicap scalp cooling system and its use in the treatment of chemotherapy-induced alopecia. *Future Oncol*. 2018;14(24):2461-2469.
12. Lemieux J, Amireault C, Provencher L, Maunsell E. Incidence of scalp metastases in breast cancer: a retrospective cohort study in women who were offered scalp cooling. *Breast Cancer Res Treat*. 2009;118(3):547-552.
13. Rugo HS, Voigt J. Scalp hypothermia for preventing alopecia during chemotherapy. A systematic review and meta-analysis of randomized controlled trials. *Clin Breast Cancer*. 2018;18(1):19-28.
14. Shah VV, Wikramanayake TC, DelCanto GM, et al. Scalp hypothermia as a preventative measure for chemotherapy-induced alopecia: a review of controlled clinical trials. *J Eur Acad Dermatol Venereol*. 2018;32(5):720-734.
15. Rugo HS, Klein P, Melin SA, et al. Association between use of a scalp cooling device and alopecia after chemotherapy for breast cancer. *JAMA*. 2017;317(6):606-614.
16. Nangia J, Wang T, Osborne C, et al. Effect of a scalp cooling device on alopecia in women undergoing chemotherapy for breast cancer: the SCALP randomized clinical trial. *JAMA*. 2017;317(6):596-605.
17. Shin H, Jin Jo S, Kim DH, Kwon O, Myung SK. Efficacy of interventions for prevention of chemotherapy-induced alopecia: a systematic review and meta-analysis. *Int J Cancer*. 2015;136(5):E442-E454.
18. Vasconcelos I, Wiesske A, Schoenegg W. Scalp cooling successfully prevents alopecia in breast cancer patients undergoing anthracycline/taxane-based chemotherapy. *Breast*. 2018;40:1-3.
19. Van Den Hurk CJ, Peerbooms M, van de Poll-Franse LV, et al. Scalp cooling for hair preservation and associated characteristics in 1411 chemotherapy patients – results of the Dutch scalp cooling registry. *Acta Oncol*. 2012;51:497-504.

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