Support Care Cancer (2013) 21:2565–2573
DOI 10.1007/s00520-013-1804-9

ORIGINAL ARTICLE

Efficacy and tolerability of two scalp cooling systems for the prevention of alopecia associated with docetaxel treatment

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Received: 5 November 2012 / Accepted: 25 March 2013 / Published online: 2 May 2013

Abstract
Purpose Chemotherapy-induced alopecia is very distressing for a patient and may have an impact on treatment decisions. On docetaxel-based therapy, alopecia occurs in a substantial proportion of patients. We aimed to investigate whether two different methods of scalp cooling can prevent hair loss.
Methods In this open-label, prospective, nonrandomized trial, patients with solid tumors receiving docetaxel in a palliative setting were allocated according to patients' preference to short-term cooling (over 45 min postinfusion) with a Paxman® PSC-2 machine (PAX), with cold cap (CC), or no cooling. The combined endpoint was alopecia World Health Organisation (WHO) III or IV or the necessity to wear a wig. Study identifier is Clinicaltrials.gov NCT01008774.
Results Two hundred thirty-eight patients were included in the trial (128 patients PAX, 71 CC, and 39 no cooling). Number of cycles (median 4) and median docetaxel doses were similar across groups (55–60 mg/day on weekly therapy, 135–140 mg/day on 3-weekly therapy). Alopecia occurred with PAX, CC, and no cooling under 3-weekly docetaxel in 23, 27, and 74 % and under weekly docetaxel in 7, 8, and 17 %, respectively. Overall, cooling (PAX and CC combined) reduced risk of alopecia by 78 % (hazard ratio 0.22; 95 % confidence interval 0.12 to 0.41). CC

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and PAX prophylaxis led to the same degree of prevention of alopecia. Adverse events (AE) were reported in 5 % (most frequently, sensation of cold), and 30 patients (13 %) discontinued cooling measures after cycle 1.
Conclusions In this first comparison published to date, both PAX and CC offer efficacious protection against hair loss, in particular when docetaxel is administered in a 3-weekly interval.

Keywords Alopecia · Hair loss · Scalp cooling · Supportive care · Patient-reported outcomes · Comparison

Introduction

In addition to bone marrow suppression and gastrointestinal disturbances, temporary hair loss or alopecia is a common side effect of chemotherapy [1]. Severe hair loss commonly starts, depending on the agent, at 1–3 weeks after the first dose and becomes clinically apparent after several treatment cycles [2]. For many patients, alopecia is emotionally extremely distressing, causing traumalike fears and anxieties, depression, reduced self-esteem, and reduced willingness to undergo cancer therapy [3, 4].

Various preventive measures have been tried to reduce chemotherapy-induced alopecia: in earlier times, the tourniquet [5], various drugs such as topical minoxidil with limited success [6, 7], and for nearly 40 years, various approaches to scalp cooling [2, 8, 9]. The latter can be achieved by procedures in which the cooling agent (ice cap, or gel cap, "Cold Cap") must be changed several times during a session [9]. Ice/gel cap systems have the benefits of unrestricted patient's mobility, low technical requirements (just a freezer is needed), and limited costs. However, such caps are heavy, and cap life expectancy is low; furthermore, caps cannot keep the temperature low throughout the application period and, thus, need changes with a high demand of nursing time [9]. A more sophisticated system is the Paxman® cooling device, a small compact mobile refrigeration system connected to lightweight silicone caps that are available in five different sizes. The patient's scalp is lowered in temperature to approximately 18 °C by circulating a special coolant throughout the cap at −4 °C [10].

There are two scientific rationales for scalp cooling. The first is vasoconstriction, which reduces blood flow to hair follicles during peak plasma concentrations of chemotherapeutic agents and so reduces cellular uptake of these agents, as demonstrated by Bülow et al. [11]. The second rationale, maybe more important than vasoconstriction, is reduced biochemical activity, which makes hair follicles less susceptible to damage by chemotherapeutic agents [11].

Docetaxel is a taxoid antineoplastic agent that has been approved for treatment of cancer of the breast, lung (nonsmall cell), prostate, gastric, and head neck tumors. In the majority of patients, docetaxel leads to hair loss [12, 13].

Rationale for the present study was that data on effectiveness and tolerability of scalp cooling measures in docetaxel-treated patients are limited. In particular, for more recent regimens using various chemotherapy schedules (3-weekly versus weekly interval), a direct comparison between cold caps and a cooling machine has not been performed to date, and the effect of reduced cooling times compared to 90-min standard cooling times on efficacy has not been established adequately, too.

Against this background, the present study allocated patients according to their preference to short-term cooling (over 45 min postinfusion) with the Paxman® PSC-2 machine (PAX) or with the cold cap (CC), or no cooling.

Methods

Design

The present study was a nonrandomized prospective controlled study between July 2009 and October 2011 (final collection of primary outcome measures) in patients at 27 sites in Switzerland. Treatment of patients was not modified by participation in the study. The study protocol conforms to ethical guidelines of the 1975 Declaration of Helsinki as reflected in the a priori approval by the 11 Swiss cantonal Ethics Committees involved and patients provided written informed consent prior to participation. Data protection of patients was closely observed. The study identifier at ClinicalTrial.gov is NCT01008774.

Patients and schedule

Adult patients were eligible if they met all of the following criteria: suffering from any solid malignancy receiving docetaxel palliative first-line chemotherapy (dose and infusion time not prespecified and, therefore, upon the decision of the treating physician), with the exception of regimens containing concomitant anthracycline (sequential anthracycline/docetaxel treatment was permitted); performance status Eastern Cooperative Oncology Group (ECOG) ≤2 [14]; and absence of alopecia at inclusion. Exclusion criteria were: Raynaud's disease or phenomenon; cold agglutinin disease; cryoglobulinemia; cryofibrinogenemia; scalp metastasis; pregnancy or lactation; and preexisting alopecia of any grade, notably androgenetic alopecia.

Patients could choose depending on local availability of alopecia prevention between the following options:

1. Alopecia prevention using Paxman® cooling machines (PAX) according to the manufacturer's instructions (Model PSC-2, Paxman Coolers Limited, Huddersfield, UK [10]), beginning 15 min before administration of chemotherapy and terminating at least 90 min (45 min according to amended protocol) after each administration of chemotherapy.
2. Alopecia prevention using CC (manufacturer not specified), beginning 15 min before administration of chemotherapy and terminating at least 90 min (45 min according to amended protocol) after each administration of chemotherapy. CC have to be exchanged after the first 25 min of treatment, after another 45 min, and every 60 minutes thereafter. The cooling temperature was not prespecified for CC.
3. No alopecia prevention (no cooling group). Patients refusing cooling treatment did not receive any alopecia prophylaxis but were also documented provided they gave informed consent.

Scalp cooling procedures could be pursued after partial, significant, or total hair loss to allow investigation of the effect of regrowth of hair during or after the end of chemotherapy. Data were collected on paper case record forms (CRF) at the screening visit, treatment visits (up to nine chemotherapy cycles), and an end-of-study visit. At baseline, physicians checked inclusion and exclusion criteria and informed consent, and allocated the patient to one of the three cooling groups. They documented demographic data (age and gender) and cancer diagnosis. During treatment visits, they documented chemotherapy regimen, assessed hair loss according to the WHO alopecia grading (I—slight and regular hair loss, II—moderate hair loss, III—complete but reversible hair loss, IV—complete and irreversible hair loss) [15]. They also documented adverse events (AE) associated with the cooling device (beginning and end, intensity, severity, and methods to treat them).

Further, patients receiving cooling measures were requested to fill out a short form after each cooling treatment with questions (How did you tolerate the cooling (visual analog scale 0–10), Did you feel cold? Did you require a blanket? Did you have side effects related to the cooling? How well did you feel during the cooling (five response categories)? Do you have hair loss? If so, limited, moderate, severe, complete hair loss? Are you wearing a wig? Did you lose your eyebrows, eyelashes, or other body hair?). At the end-of-study visit, patients were requested to provide their overall assessment about the therapy, in general, and if applicable, scalp cooling, in particular (How is your global impression of therapy? How is your global impression of the cooling method?), using the marks 1=good to 6=bad. If they had not received scalp cooling, they were requested whether they, in retrospect, would have preferred cooling measures.

During the study course, the protocol was amended as follows: In September 2009, based on the findings of a Dutch group that reduced cooling times do not compromise efficacy,[16] postinfusion cooling times in both active treatment arms were reduced from 90 to 45 min. Until the amendment was effective, 14 patients had received cooling procedures with 90-min postinfusion cooling times and nine patients were included in the arm without cooling. In September 2010, inclusion criteria were broadened in such a way that, also, patients with metastases treated in further lines with docetaxel-based regimens were eligible. In January 2011, the inclusion period was extended from March 2011 to July 2011.

Endpoints

The primary combined endpoint of the study was the incidence of the WHO grade III or IV alopecia, as assessed by the treating physician, or wearing a wig. Further endpoints comprised discontinuation of the initially chosen alopecia prevention method, received number of cycles of chemotherapy in each subgroup, patient perception of scalp cooling procedures, well-being, and tolerability/side effects of scalp cooling systems. Pre- and postinfusion cooling times were not recorded.

Sample size, data entry, and statistical analysis

The original sample size calculation was based on the following assumptions: for sample size estimation, it was assumed based on clinical expertise that no cooling would result in 60 % alopecia, CC cooling in 30 % alopecia, and PAX cooling in 15 % alopecia. To detect a statistically significant reduction ($p \leq 0.05$) of the alopecia rate from 30 % (CC) to 15 % (PAX) with an 80 % power, 121 patients were to be included in each treatment arm and 36 in the no cooling arm. Data entry was performed by a contract research organization, and plausibility checks were performed using a data validation plan [17].

Continuous variables are reported as mean with standard deviations (SD) and categorical variables as number of patients with percentages. Kaplan–Meier estimates on the time to treatment failure (WHO grade III or IV alopecia according to the WHO criteria or wearing a wig) were calculated. Hazard ratios and confidence intervals were determined by Cox regression analysis. Statistical analysis compared PAX versus CC, PAX versus no cooling, CC versus no cooling as well as PAX and CC combined versus no cooling. Censored cases were defined as cases for which grades III—IV alopecia did not occur during the period of observation. Data were analyzed with SPSS, version 15.1.

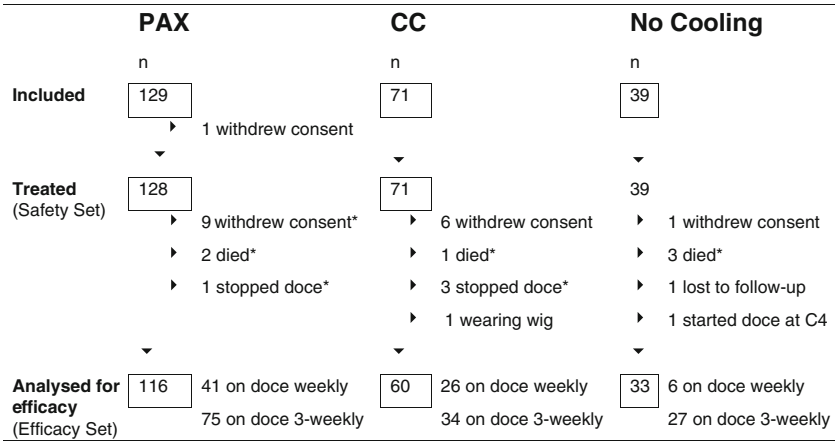

Fig. 1 Patient disposition. *C* treatment cycle, *CC* cold cap, *doce* docetaxel, *PAX* Paxman© PSC-2. *Asterisk* after cycle 1 (C1)

Results

Patient disposition and treatment

Two hundred thirty-eight patients were included in the study, 128 (53.8 %) by using PAX, 71 patients with CC (29.8 %), and 39 (16.4 %) with no cooling (Fig. 1). Patient characteristics at baseline are shown in Table 1. All patients but one in the PAX group received at least 1 cycle of docetaxel chemotherapy, alone or in combination with other agents. Compared to the 3-weekly regime, weekly docetaxel therapy was more often used in the PAX and CC groups than in the no cooling group. It is interesting to notice that patients with lung cancer were more likely not to wish a hair protection. This may explain the relatively higher

Table 1 Patient characteristics

	PAX (N=128)	CC (N=71)	No cooling (N=39)	p value[a]
Age, median (years)	67	64	67	0.56, 0.56, 0.61
Gender:				
Female	51 (39.8)	38 (53.5)	16 (41.0)	0.08, 1.00, 0.24
Male	77 (60.2)	33 (46.5)	23 (59.0)	
Cancer type				
Breast	37 (28.9)	30 (42.2)	9 (23.1)	0.06, 0.55, 0.06
Lung	18 (14.1)	6 (8.5)	14 (35.9)	0.36, 0.01, 0.001
Prostate	52 (40.6)	23 (32.4)	11 (28.2)	0.29, 0.19, 0.67
Other	21 (16.4)	12 (16.9)	5 (12.8)	1.00, 0.80, 0.78
Docetaxel schedule:				
—Weekly	44 (34.4)	31 (43.7)	7 (17.9)	0.29, 0.049, 0.007
—Every 3 weeks	82 (64.1)	40 (56.3)	32 (81.1)	
Number of cycles:				
Median (range)[b]	4 (1–9)	4 (1–9)	4 (1–6)	0.42, 0.61, 0.88
Median dose of docetaxel:				
Weekly (mg/week)	55.0	60.0	60.0	0.41, 0.40, 0.53
Every 3 weeks (mg/3 weeks)	140.0	140.0	135.0	0.48, 0.19, 0.44
Combination chemotherapy (at cycle 1)	36 (28.1)	20 (28.2)	17 (43.6)	1.00, 0.08, 0.10

Values are *n* (%) if not indicated otherwise

CC cold cap, *PAX* Paxman® PSC-2

[a] First value indicates comparison of PAX versus CC; second value, PAX versus no cooling; third value, CC versus no cooling for continuous variables: *t* test, two-sided, α=0.05; for median (age): median test, two-sided, α=0.05; for categorical variables, Fisher's exact test, two-sided, α=0.05. There was no correction for multiple testing applied. The *p* values should, therefore, be considered only in an explorative manner.

[b] Reported cycles of treatment, which were not always done with scalp cooling protection in the PAX and CC groups

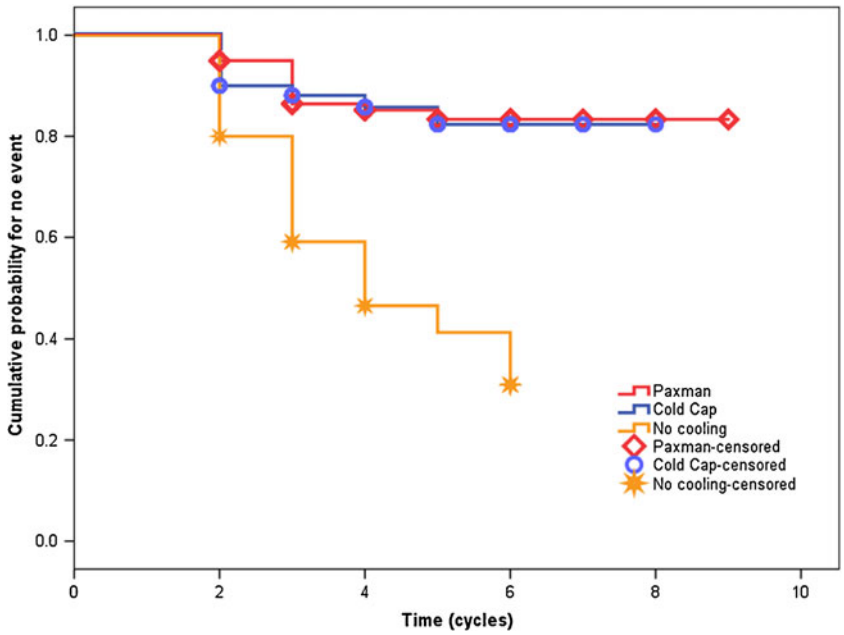

Fig. 2 Kaplan–Meier estimate of the probability to develop alopecia grade III/IV or wearing a wig (n=209). Weekly and 3-weekly docetaxel schedules are combined

number of patients receiving docetaxel every 3 weeks in the no cooling group. Patients with only 1 cycle docetaxel treatment are not included in the efficacy analyses.

The average number of cycles (median 4) was identical and median dose of docetaxel administered were similar in the three cohorts. In the PAX arm, 13 patients (10.2 %) could not be evaluated for efficacy; in the CC arm, 11 patients (15.5 %); and in the no cooling arm, six patients (15.4 %). Reasons for dropout included lost to follow-up (nine patients), early patient death (six patients), docetaxel intolerance (three patients), side effect due to the cooling system (seven patients), major protocol violations (four patients), or patient's withdrawal of informed consent (one patient).

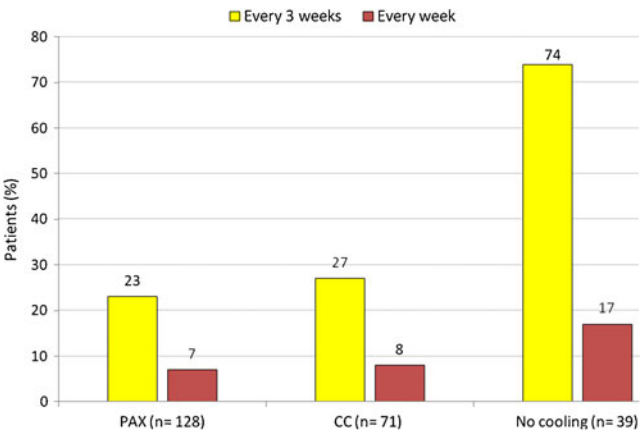

Fig. 3 Incidence of combined endpoint (alopecia WHO III/IV and/or wearing wig), by docetaxel treatment schedule

Efficacy

In the direct comparison of cooling measures versus no cooling, irrespective of the treatment regimen, use of cooling devices reduced hair loss substantially: alopecia (grades III–IV) and/or necessity to wear a wig were 17, 18, and 64 % in patients treated with PAX, CC, or no cooling, respectively. To illustrate the time pattern of alopecia occurrence, Fig. 2 displays the Kaplan–Meier estimate to reach the combined endpoint (alopecia WHO III/IV and/or wearing a wig) in the three treatment groups. While the curve of the no cooling group declined steeply, the curves of both PAX and CC overlapped

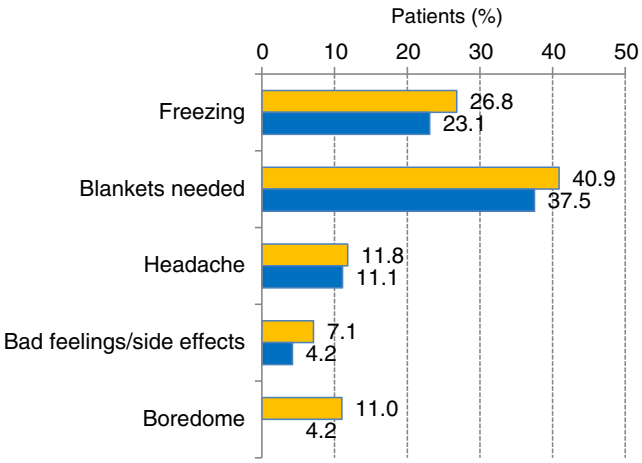

Fig. 4 Patient assessment of cooling therapy during cycle 1. Data are taken from the patient questionnaires that were completed by patients after cycle 1. Missing responses to questions were noted in five patients in the PAX group and in six patients in the CC group

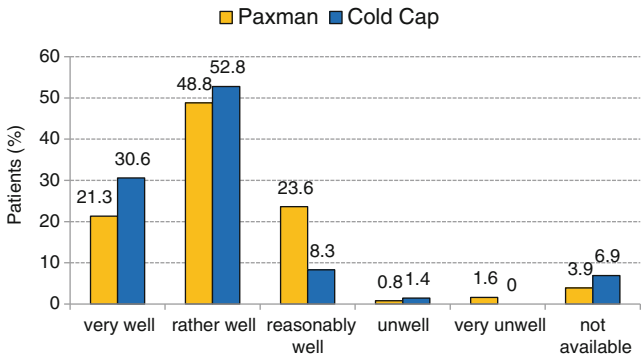

Fig. 5 Overall assessment of cooling therapy after cycle 1. Categorical response to question "How well did you feel overall during the whole cooling treatment?"

tightly during observation and remained above 80 %. PAX and CC combined significantly reduced the risk of alopecia by 78 % (hazard ratio 0.22, 95 % confidence interval 0.12 to 0.41).

Further, the risk to develop alopecia was lower if docetaxel was given weekly compared to the docetaxel regimen every 3 weeks (resulting in lower chemotherapy doses), as shown in the no cooling group (Fig. 3). For the subgroup of patients with cycles administered every 3 weeks, the risk of alopecia was significantly reduced by 70 % when protection versus no protection is compared (hazard ratio 0.30, 95 % confidence interval 0.16 to 0.55). However, comparing protection (PAX and CC combined) versus no protection for the subgroup of patients receiving docetaxel at weekly cycles, reduction of the risk for alopecia was not significant (hazard ratio 0.14, 95 % confidence interval 0.01 to 1.59). No differences in risk reduction were observed between the group of patients receiving 90-min postinfusion cooling (n=14, before protocol amendment) and those receiving 45-min postinfusion cooling (logrank test, p=0.94).

Tolerability

AE were reported by eight patients (3.3 %) for PAX and CC combined. The most frequently reported AE was the sensation of cold. Thirty patients (12.6 %) discontinued cooling measures after cycle 1.

Patient assessment and overall patient rating

On the patient questionnaire, incidence of freezing and unpleasant feelings was relatively low, as shown for the first treatment cycle (Fig. 4). As a consistent finding, only few patients reported feeling unwell during treatment (for example, during the first treatment cycle, see Fig. 5.).

On a six-point scale (1=good to 6=bad), with respect to global impression of therapy, end-of-study patients on PAX rated 4.5±1.6; on CC, 4.6±1.4; and on no cooling, 4.1±1.9. The respective grading marks (same scale) in the three groups were very similar.

Discussion

The present prospective study shows that (1) in patients receiving docetaxel therapy, both the PAX and CC devices reduced alopecia substantially, in particular when docetaxel was administered every 3 weeks; (2) no differences between devices appeared in terms of efficacy and tolerability; and (3) short-term postinfusion cooling time of 45 min is effective. Since with no protection, the great majority of patients receiving docetaxel (every 3 weeks) will temporarily lose all their hair, and the study confirms that scalp cooling is an effective measure to prevent alopecia in these patients.

The present results have to be interpreted in the context of previous studies on scalp cooling: Breed et al. in 2011 reviewed 50 studies on various methods of scalp cooling, which were mostly small, nonrandomized, and employed different chemotherapy regimens and inconsistent methods of alopecia assessment [2]. Only seven randomized trials have been reported so far [13, 18–22], and in six out of the seven randomized studies, significantly better hair preservation was seen when scalp cooling was used. Overall, the success rate varied between 50 and 92 % dependent on study and chemotherapy regimen [2].

Only few studies with small number of patients have been published on the preventive effect of cooling measures during docetaxel-based therapy in the last 10 years, with equivocal results: for a new digitized scalp-cooling system, Ridderheim et al. reported minimal to no hair loss in paclitaxel/docetaxel-treated patients, while the combination of anthracycline and taxane resulted in more hair loss [12]. Macduff et al. reported no benefit for patients on the docetaxel/epirubicin combination in a randomized study [13]. Auvinen et al. recommended cooling on the basis of a conventional cooling schedule [23], while in a very recent study, van den Hurk recommended a short-term cooling schedule in patients on docetaxel, except combined with doxorubicin and cyclophosphamide [24]. The Dutch Scalp Cooling Registry, according to an interim report, included 59 patients on docetaxel 75 mg/m^2 combinations and 42 patients on docetaxel 100 mg/m^2 combinations, of whom 80 and 60 % reported success of therapy [25].

For the PAX cooling system, a number of study results have been published in recent years. An observational multicenter study was conducted in the UK with 94 patients

aged 28–61 years treated with various chemotherapy including epirubicin, doxorubicin, and docetaxel as monotherapy. In that cohort, grade III or grade IV hair loss was observed in six patients (6.4 %),and 10 patients (11 %) required wigs; five patients (5.3 %) discontinued PAX treatment [26].

Reduced cooling times have been reported in a recent study. Based on findings in 54 patients on various chemotherapy, van den Hurk et al. recommended a 45-min postinfusion cooling time in 3-weekly docetaxel regimens with a dose of 75 or 100 mg/m^2, administered in 60 min (except if combined with doxorubicin and cyclophosphamide) [16, 24].

In the largest observational study to date, the Dutch Scalp Cooling Registry found that in 28 hospitals, 50 % of the 1,411 scalp-cooled patients (Paxman® PSC1 or PSC2 devices) did not wear a head cover during their last chemotherapy session. Use of head covering varied according to type and dose of chemotherapy from 8 to 94 % of patients. Results were best for monotherapy with low-dose taxanes: 94 % of patients on docetaxel (D75) wore no head cover. Of note, compared to the earlier studies reported above, in recent years, in general, higher doses of chemotherapy were used that may explain the lower success rates [27].

In terms of safety, both the PAX and the CC cooling procedures appeared well tolerated and were infrequently discontinued by patients. In our study, sensation of cold was sometimes reported, but the great majority of patients did not feel unwell. This is in line with earlier studies, according to which side effects were rare and, in general, not serious, and patient ratings of cooling therapy were favorable [2]. Only some trials reported discontinuation of the cooling procedure, in general, in less than 10 % of the patients.

When interpreting the results of the present study, some limitations need to be taken into account. The study was open and not randomized and, thus, prone to selection and allocation biases as patients were free to choose their preferred treatment method [28]. The number of patients in the CC arm was lower than expected due to the obvious preference of patients for PAX. The combined endpoint was assessed by physicians when determining the degree of alopecia, which is a subjective assessment. Even more, the necessity to wear a wig is largely a subjective decision made by the patient. For example, one third of patients with lung cancer (often males) in our study refused cooling, while patients with prostate cancer did not. Patients who chose not to use cooling devices may be less prone to use wigs, too. Further, the current findings are limited to docetaxel therapy (excluding concomitant anthracycline) and can only be used with caution to determine suitability of cooling when other regimens are used. However, our results are in line with positive results on cooling procedures in patients on docetaxel treatment for a variety of solid tumors in other studies.

Conclusion

This study demonstrates the feasibility and efficacy of alopecia protection in an unselected group of patients in several Swiss centers. Both scalp cooling devices, PAX and CC, were well tolerated by a large majority of patients.

Docetaxel, when administered in a 3-weekly regimen, was associated with high incidence of alopecia if no protection was used. Overall, when assessing 3-weekly and weekly regimens in combination, this risk could be reduced by 78 % by using a protection. There appears to be no difference between PAX and CC in terms of efficacy and tolerability.

Acknowledgments Christian Schmidhauser, Ph.D., (la volta statistics, Zurich, Switzerland) performed the statistical analyses. David Pittrow, MD, advised on contents of the manuscript and interpretation of data.

We appreciate the support of Frank Verholen, MD (Sanofi-Aventis (Suisse) SA) and Danièle Brack (Sanofi-Aventis (Suisse) SA) as well as the contribution of the investigators of the participating centers in Switzerland (listed in alphabetical order):

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Conflict of interest Sanofi-Aventis Suisse funded this study. Sereina Bodenmann and Vera Bühler are full-time employees of Sanofi-Aventis Suisse. The rest of the authors declare no conflict of interest related to this study. The authors had full control of all primary data. The authors agree to allow the journal to review their data if requested.

References

1. Trueb RM (2010) Chemotherapy-induced alopecia. Curr Opin Support Palliat Care 4(4):281–284
2. Breed W, van den Hurk CJG, Peerbooms M (2011) Presentation, impact and prevention of chemotherapy-induced hair loss. Expert Rev Dermatol 6(1):109–125
3. Lemieux J, Maunsell E, Provencher L (2008) Chemotherapy-induced alopecia and effects on quality of life among women with breast cancer: a literature review. Psychooncology 17(4):317–328
4. Hesketh PJ, Batchelor D, Golant M, Lyman GH, Rhodes N, Yardley D (2004) Chemotherapy-induced alopecia: psychosocial impact and therapeutic approaches. Support Care Cancer 12(8):543–549
5. Pesce A, Cassuto JP, Joyner MV, DuJardin P, Audoly P (1978) Scalp tourniquet in the prevention of chemotherapy-induced alopecia. N Engl J Med 298(21):1204–1205
6. Duvic M, Lemak NA, Valero V, Hymes SR, Farmer KL, Hortobagyi GN, Trancik RJ, Bandstra BA, Compton LD (1996) A randomized trial of minoxidil in chemotherapy-induced alopecia. J Am Acad Dermatol 35(1):74–78
7. Davis ST, Benson BG, Bramson HN, Chapman DE, Dickerson SH, Dold KM, Eberwein DJ, Edelstein M, Frye SV, Gampe RT Jr, Griffin RJ, Harris PA, Hassell AM, Holmes WD, Hunter RN, Knick VB, Lackey K, Lovejoy B, Luzzio MJ, Murray D, Parker P, Rocque WJ, Shewchuk L, Veal JM, Walker DH, Kuyper LF (2001) Prevention of chemotherapy-induced alopecia in rats by CDK inhibitors. Science 291(5501):134–137
8. Breed WP (2004) What is wrong with the 30-year-old practice of scalp cooling for the prevention of chemotherapy-induced hair loss? Support Care Cancer 12(1):3–5
9. Grevelman EG, Breed WP (2005) Prevention of chemotherapy-induced hair loss by scalp cooling. Ann Oncol 16(3):352–358
10. Paxman Coolers Ltd. Paxman PSC-2 broschure. Internet: http://ebookbrowse.com/psc2-manual-pdf-d234169346. Accessed on 9 September 2012
11. Bulow J, Friberg L, Gaardsting O, Hansen M (1985) Frontal subcutaneous blood flow, and epi- and subcutaneous temperatures during scalp cooling in normal man. Scand J Clin Lab Invest 45(6):505–508
12. Ridderheim M, Bjurberg M, Gustavsson A (2003) Scalp hypothermia to prevent chemotherapy-induced alopecia is effective and safe: a pilot study of a new digitized scalp-cooling system used in 74 patients. Support Care Cancer 11(6):371–377
13. Macduff C, Mackenzie T, Hutcheon A, Melville L, Archibald H (2003) The effectiveness of scalp cooling in preventing alopecia for patients receiving epirubicin and docetaxel. Eur J Cancer Care 12(2):154–161
14. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, Carbone PP (1982) Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 5(6):649–655
15. World Health Organisation Handbook for reporting results of cancer treatment. WHO Offset Publications, Geneva, 1979. Internet: http://whqlibdoc.who.int/offset/WHO_OFFSET_48.pdf. Accessed on 10 January 2013
16. van den Hurk C, Breed W, Nortier J (2009) Short post-infusion cooling time of scalp cooling in the prevention of docetaxel-induced hair loss.Poster presentation at the Annual Meeting of the European Cancer Organisation (ECCO), 20–24 September 2009, Berlin, Germany
17. Ottevanger PB, Therasse P, van de Velde C, Bernier J, van Krieken H, Grol R, De Mulder P (2003) Quality assurance in clinical trials. Crit Rev Oncol Hematol 47(3):213–235
18. Edelstyn GA, MacDonald M, MacRae KD (1977) Doxorubicin-induced hair loss and possible modification by scalp cooling. Lancet 2(8031):253–254
19. Giaccone G, Di Giulio F, Morandini MP, Calciati A (1988) Scalp hypothermia in the prevention of doxorubicin-induced hair loss. Cancer Nurs 11(3):170–173
20. Parker R (1987) The effectiveness of scalp hypothermia in preventing cyclophosphamide-induced alopecia. Oncol Nurs Forum 14(6):49–53
21. Ron IG, Kalmus Y, Kalmus Z, Inbar M, Chaitchik S (1997) Scalp cooling in the prevention of alopecia in patients receiving depilating chemotherapy. Support Care Cancer 5(2):136–138
22. Satterwhite B, Zimm S (1984) The use of scalp hypothermia in the prevention of doxorubicin-induced hair loss. Cancer 54(1):34–37

23. Auvinen PK, Mahonen UA, Soininen KM, Paananen PK, Ranta-Koponen PH, Saavalainen IE, Johansson RT (2010) The effectiveness of a scalp cooling cap in preventing chemotherapy-induced alopecia. Tumori 96(2):271–275
24. van den Hurk CJ, Breed WP, Nortier JW (2012) Short post-infusion scalp cooling time in the prevention of docetaxel-induced alopecia. Support Care Cancer 20(12):3255–3260
25. van den Hurk C Synoptic report in: Paxman clinical report summary of scalp cooling efficacy, page 10. Version 04–11. Internet: http://www.paxman-coolers.co.uk/index.php/professionals/professionals-downloads/. Accessed on 9. September 2012
26. Massey CS (2004) A multicentre study to determine the efficacy and patient acceptability of the Paxman Scalp Cooler to prevent hair loss in patients receiving chemotherapy. Eur J Oncol Nurs 8(2):121–130
27. van den Hurk CJ, Peerbooms M, van de Poll-Franse LV, Nortier JW, Coebergh JW, Breed WP (2012) Scalp cooling for hair preservation and associated characteristics in 1411 chemotherapy patients—results of the Dutch Scalp Cooling Registry. Acta Oncol 51(4):497–504
28. Delgado-Rodriguez M, Llorca J (2004) Bias. J Epidemiol Community Health 58(8):635–641