Supplementary Online Content

Rugo HS, Klein P, Melin SA, et al. Association between use of a scalp cooling device and alopecia after chemotherapy for breast cancer. *JAMA*. doi:10.1001/jama.2016.21038

Additional Information

This supplementary material has been provided by the authors to give readers additional information about their work.

Additional Information

Enrollment occurred between August of 2013 through October of 2014. Patients were enrolled at 6 institutions in the United States by their medical oncologist after a decision has been made to administer adjuvant chemotherapy. Institutions included The University of California San Francisco, Wake Forest Baptist Health Medical Center, Weill Cornell Medical College, Mount Sinai Beth Israel, St. Luke's Roosevelt Hospital Center, and The University of California Los Angeles. Enrollment ended when accrual to the trial was complete.

eBox. Allowed chemotherapy

Chemotherapy Regimen and Dose
Doxorubicin 60 mg/m^2 and cyclophosphamide 600 mg/m^2 x 4 - 6 cycles, given every 2-3 weeks
Docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 for 4 - 6 cycles, given every 3 weeks
Paclitaxel 80 mg/m^2 for at least 12 cycles, given every week
Paclitaxel weekly & carboplatin Area Under the Curve (AUC) of 2 given weekly or AUC of 6 given every 3 weeks with or without trastuzumab and with or without pertuzumab weekly or every 3 weeks for 4 - 6 cycles
Paclitaxel 175 mg/m^2 for 4 – 6 cycles, given every 2 weeks (dose dense without concurrent anthracycline)
Docetaxel 75mg/m^2, carboplatin AUC of 6 for 6 cycles, given every 3 weeks, trastuzumab weekly or every 3 weeks, and pertuzumab every 3 weeks
Pertuzumab, trastuzumab, and docetaxel 75 mg/m^2, given every 3 weeks (in the neoadjuvant setting) for 3- 6 cycles

eTable 1. Dean scale for assessment of hair loss[1]

Dean Score	Percentage of Hair Loss	Success/Failure
Grade 0	No hair loss	Treatment Success
Grade 1	>0 to ≤25% hair loss	
Grade 2	>25% to ≤50% hair loss	
Grade 3	>50% to ≤75% hair loss	Treatment Failure
Grade 4	>75% hair loss	

[1]Dean JC, Salmon SE, Griffith, KS. Prevention of doxorubicin-induced hair loss with scalp hypothermia. N Engl J Med. 1979;301(26):1427-1429.

eTable 2. Hair loss by independent panel and patient self-assessment

The independent panel evaluated only the scalp cooling patients with 1 month post-chemotherapy cycle follow-up, so the number of patients is less than in the sample analyzed for the primary endpoint

	Patient Self-Assessment N=101	**Independent Panel N=88**
Success,* No. (%)	**67 (66.3%)**	**74 (84.1%)**
Failure, No. (%)	**34 (33.7%)**	**14 (15.9%)**

*Success was determined based on patient graded hair status as Grade 0-2 on the Dean Scale 4 weeks after the last chemotherapy visit.

eTable 3. Sensitivity analysis results

eTable 3a: Alopecia Self-Report Maximum Dean Score (Evaluable)[1]

		Scalp cooling (N=101)	Control (N=16)	
	N	101	16	p-value
Success[2]	Yes	67 (66.3%)	0 (0.0%)	<0.001
	No	34 (33.7%)	16 (100.0%)	

[1]Evaluable population (EP) consists of all patients in the control group or patients who used scalp cooling at least once and completed the full prescribed chemotherapy cycles or dropped out for any reason other than toxicity of the chemotherapy, such as toxicity or intolerability of the cap or hair loss.
[2]Success: maximum Dean score of < 2 at any time during the study up to 4 weeks after the last chemotherapy treatment.
The 95% confidence interval of the success proportion for patients using scalp cooling is (56.2%, 75.4%), estimated using an exact method based on binomial distribution.

eTable 3b: Alopecia Self-Report Maximum Dean Score (Per Protocol)[1]

		Scalp cooling (N=85)	Control (N=15)	
	N	85	15	p-value
Success[2]	Yes	67 (78.8%)	0 (0.0%)	<0.001
	No	18 (21.2%)	15 (100.0%)	

[1]Per Protocol: All patients in the Evaluable population who completed the full series of measurements (i.e. Dean score available 4 weeks after the last chemotherapy treatment.
[2]Success: maximum Dean score of < 2 at any time during the study up to 4 weeks after the last chemotherapy treatment.
The 95% confidence interval of the success proportion for patients using scalp cooling is (68.6%, 86.9%), estimated using an exact method based on binomial distribution.

eTable 3c: Alopecia Self-Report Maximum Dean Score (Safety)[1]

		Scalp cooling (N=106)	Control (N=16)	
	N	104	16	p-value
Success[2]	Yes	67 (64.4%)	0 (0.0%)	<0.001
	No	37 (35.6%)	16 (100.0%)	

[1]Safety: All patients enrolled in the study. The outcome of two patients who used scalp cooling cannot be determined since they discontinued the study due to chemotherapy toxicity. These patients are not included in the safety set (104/106).
[2]Success: maximum Dean score of < 2 at any time during the study up to 4 weeks after the last chemotherapy treatment.
The 95% confidence interval of the success proportion for patients using scalp cooling is (54.4%, 73.6%), estimated using an exact method based on binomial distribution.

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eTable 4. Alopecia self-report: response rate by chemotherapy treatment (Dean score <3)

Chemotherapy Regimen & Dose	Number of scalp cooled patients N(%)	Number of controls N(%)
Docetaxel 75 mg/m^2& cyclophosphamide 600 mg/m^2 for 4 - 6 cycles every 3 weeks	46/76 (60.5%)	0/10 (0%)
Paclitaxel 80 mg/m^2 weekly for 12 cycles	10/12 (83.3%)	0/2 (0%)
Docetaxel 75mg/m^2, carboplatin AUC 6 for 6 cycles every 3 weeks, trastuzumab weekly or every 3 weeks, with or without pertuzumab every 3 weeks	10/12 (83.3%)	0/3 (0%)
Docetaxel 75 mg/m^2, trastuzumab, pertuzumab, and every 3 weeks for 6 cycles	1/1 (100%)	0

eTable 5. Alopecia self-report: maximum Dean score ≤2 at one month after the end of chemotherapy

Covariate Items at Baseline	All Scalp Cooled Patients	Untreated Control	P value
Thick Hair	68.8% (50.0%, 83.9%) (n = 32)	0% (n=5)	<0.001
Medium Hair	60.0% (45.2%, 73.6%) (n = 50)	0% (n=9)	<0.001
Thin Hair	60.0% (56.6%, 96.2%) (n = 17)	0% (n=2)	0.058
Less Than Median BMI (<25.8 kg/m^2)	66.0% (51.7%, 78.5%) (n = 53)	0% (n=5)	0.007
Greater Than Median BMI (≥25.8 kg/m^2)	66.7% (51.6%, 79.6%) (n = 48)	0% (n=11)	<0.001
Less Than Median Age (<56 years of age)	66.7% (52.1%, 79.2%) (n = 51)	0% (n=7)	0.001
Greater Than Median Age (≥56 years of age)	66.0% (51.2%, 78.8%) (n = 50)	0% (n=9)	<0.001
Chemotherapy Regimen - Docetaxel & Carboplatin	83.3% (51.6%, 97.9%) (n = 12)	0% (n=3)	0.022
Chemotherapy Regimen - Docetaxel & Cyclophosphamide	60.5% (48.6%, 71.6%) (n = 76)	0% (n=10)	<0.001
Chemotherapy Regimen - Paclitaxel	83.3% (51.6%, 97.9%) (n = 12)	0% (n=2)	0.066

Covariate Items at Baseline	All Scalp Cooled Patients	Untreated Control	P value
With Previous Hormone Therapy	52.7% (28.9%, 75.6%) (n = 19)	0% (n=2)	0.476
Without Previous Hormone Therapy	69.5% (58.4%, 79.2%) (n = 82)	0% (n=14)	<0.001

eTable 6. Quality of life measurements: baseline scores

BR23 items	**Dean Score 0 to ≤2 N=67 (95% CI)**	**Dean Score 3 to 4 N=34 (95% CI)**	**P value***
Have you lost any hair?	NA	NA	NA
Were you upset about your loss of hair?	NA	NA	NA
Have you felt physically less attractive as a result of your disease or treatment?	4.5% (0.0%, 9.4%)	8.8% (0%, 18%)	0.383
Have you been feeling less feminine as a result of your disease or treatment?	3.0% (0.0%, 7.1%)	5.9% (19.2%, 59.1%)	0.481
Did you find it difficult to look at yourself naked?	7.5% (1.2%, 13.8%)	8.8% (0.0%, 18.4%)	0.811
Have you been dissatisfied with your body?	7.6% (1.2%, 14.0%)	11.8% (0.9%, 22.6%)	0.488

*comparison of results in patients with Dean score 0 - ≤2 versus Dean score of ≥3

eTable 7. Quality of life measurements: scores of quite a bit/very much one month after the end of chemotherapy

BR23 items	Dean score 0 to ≤2 % (95% CI)	Dean score 3 to 4 % (95% CI)	P value*	All Scalp Cooled Patients	Untreated** Control	P value**	Untreated*** Control	P value***
Have you lost any hair?	27.7% (16.8%, 38.6%) (n = 65)	47.8% (27.4%, 68.2%) (n=23)	0.078	33.0% (n=88)	68.8% (n=16)	0.007	62.5% (n=8)	0.094
Were you upset about your loss of hair?	25.5% (13.9%, 37.0%) (n=55)	52.6% (30.2%, 75.1%) (n=19)	0.029	32.4% (n=74)	60.0% (n=15)	0.044	57.1% (n=7)	0.189
Have you felt physically less attractive as a result of your disease or treatment?	18.5% (9.0%, 27.9%) (n=65)	52.2% (31.8%, 72.6%) (n=23)	<0.002	27.3% (n=88)	56.3% (n=16)	0.022	55.6% (n=9)	0.078
Have you been feeling less feminine as a result of your disease or treatment?	15.4% (6.6%, 24.2%) (n=65)	29.1% (19.2%, 59.1%) (n=23)	<0.018	21.6% (n=88)	31.3% (n=16)	0.399	33.3% (n=9)	0.423
Did you find it difficult to look at yourself naked?	13.8% (5.5%, 22.2%) (n=65)	21.7% (4.9%, 38.6%) (n=23)	0.374	15.9% (n=88)	18.8% (n=16)	0.777	11.1% (n=9)	0.705
Have you been dissatisfied with your body?	12.3% (4.3%, 20.3%) (n=65)	26.1% (8.1%, 44.0%) (n=23)	0.121	15.9% (n=88)	37.5% (n=16)	0.044	33.3% (n=9)	0.190

*comparison of results in scalp cooled patients with Dean score 0 - ≤2 versus Dean score of ≥3

** comparison of results of all treated patients vs. controls. For the controls, the last observation carried forward was used.

*** comparison of results of all treated patients vs. controls one month after completion of chemotherapy (not all patients with complete alopecia returned for the one month quality of life assessment)

eTable 8. Use of head coverings one month following completion of chemotherapy in patients using scalp cooling (N=86)

Dean Score	Head Covering Never N (%)	Head Covering Sometimes N (%)	Head Covering Always N (%)	Total N
0	5 (83%)	0	1 (17%)	6
1	26 (72%)	8 (22%)	2 (6%)	36
2	6 (20%)	17 (57%)	7 (23%)	30
3	1 (10%)	5 (45%)	5 (45%)	11
4	1 (33%)	0	2 (67%)	3
Total	39 (45%)	30 (35%)	17 (20%)	86

eFigure. Patient Symptom Survey

The patient symptom survey was filled out by the patient after each cycle of chemotherapy and included questions on headaches, feeling chill, scalp pain, and use of pain medications.

SYMPTOMS SURVEY (To be filled out by the patient at the end of each chemotherapy treatment)

PATIENT STUDY NUMBER_____
SITE_____
DATE _____
CYCLE_____

1. In the past month have you experienced headache? _____yes _____no

If yes, how many headaches have you experienced in the past month?
1-2_____
3-4_____
5-6_____
> 6_____

More than usual? _____yes _____no

2. Did the scalp cooling treatment today trigger or exacerbate headache or migraine? ____yes ____no

3. If yes, please mark the location on the scale below that best describes the level of pain you experienced with headaches today.
(0= no pain 50= moderate pain 100= worst possible pain)

0 10 20 30 40 50 60 70 80 90 100

4. Please mark the point on the scale that best describes how chilled you felt during the cooling down period today.

(0=none, 100=as bad as it could be)

0 10 20 30 40 50 60 70 80 90 100

5. Please mark the point on the scale that best describes how chilled you felt with your overall cooling treatment today.

(0=none, 100=as bad as it could be)

0 10 20 30 40 50 60 70 80 90 100

6. Please mark the scale at the point that best describes any scalp pain you experienced with your treatment today.

(0= no pain 50= moderate pain 100= worst possible pain)

0 10 20 30 40 50 60 70 80 90 100

7- Did you take any pain killers today because of your scalp cooling treatment?
□ Yes □No

Comment_____