Scalp Cooling to Prevent Chemotherapy-Induced Alopecia

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Baylor College of Medicine

Background

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- Chemotherapy treats micro-metastatic disease & can decrease the risk of breast cancer recurrence

- It is associated with side effects such as chemotherapy-induced alopecia. Women rate this as one of the most severe, distressing and troublesome side effects

- Many countries use scalp cooling devices to prevent chemotherapy-induced alopecia with variable success rates based on non-randomized trials (25%-100% hair retention)

Scalp Cooling Devices Worldwide 2016

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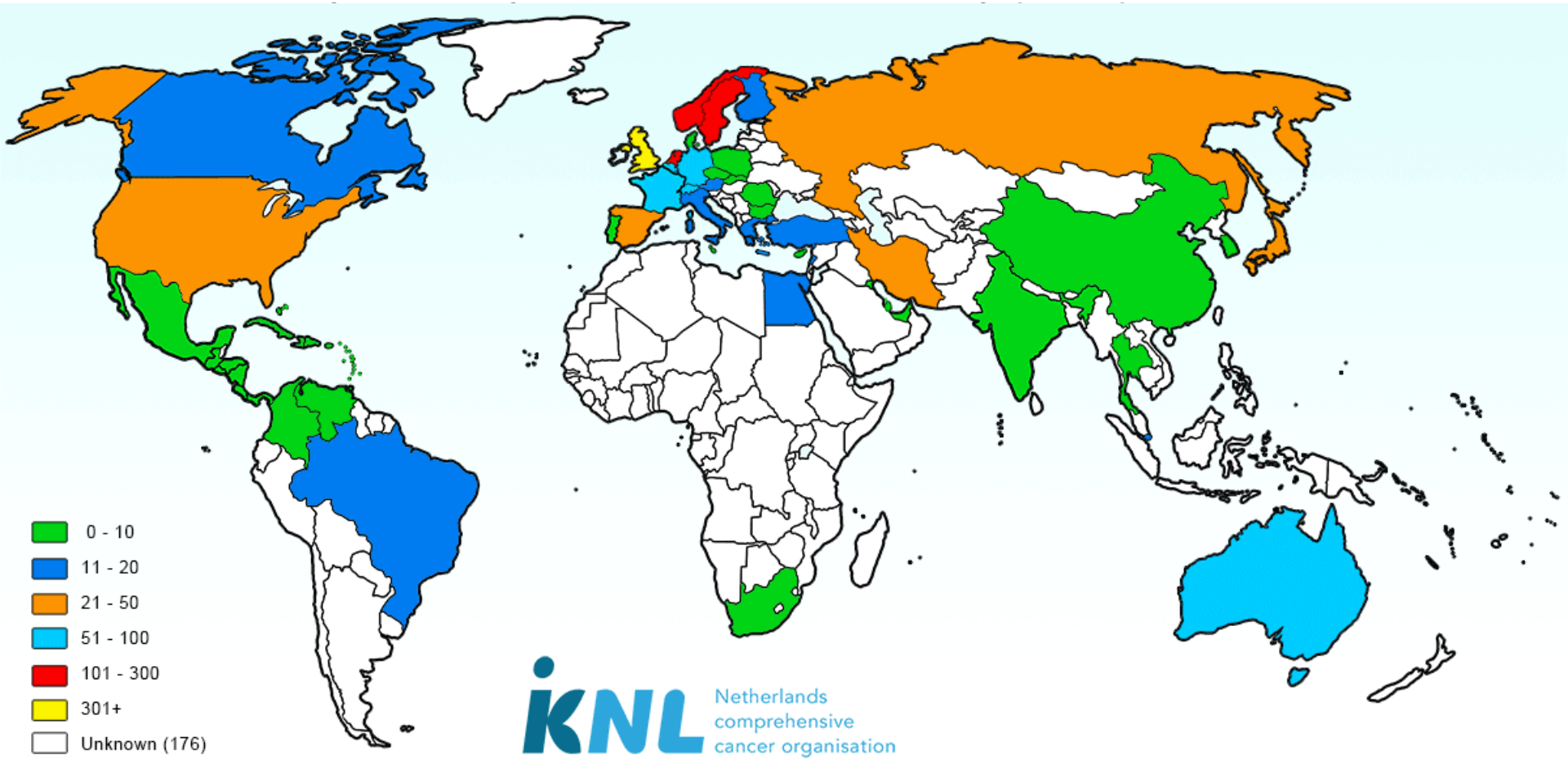

Note—this figure represents scalp cooling devices and does not include cold cap use

Borrowed/Courtesy of Corina van den Hurk
Netherlands Comprehensive Cancer Organization

History of Scalp Cooling

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- 1970s
  - Tourniquets are utilized to reduce the blood flow to hair follicles during peak chemo
  - Worked but caused headache and nerve compression so no longer utilized
- Medications
  - AS101 (immune modulator) and Minoxidil reduced the duration of alopecia but did not prevent it

History of Scalp Cooling

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- 1979
  - First US patent for Mark Barron's "Chemo Cap" which was a resizable gel-filled nylon pouches that could be frozen. Patent expired in 1998. Studies from 1995-2003 showed some success with this approach
- 1997
  - First prototype of the Paxman Scalp Cooling System was used and installed in the Huddersfield Royal Infirmary

How Scalp Cooling Works

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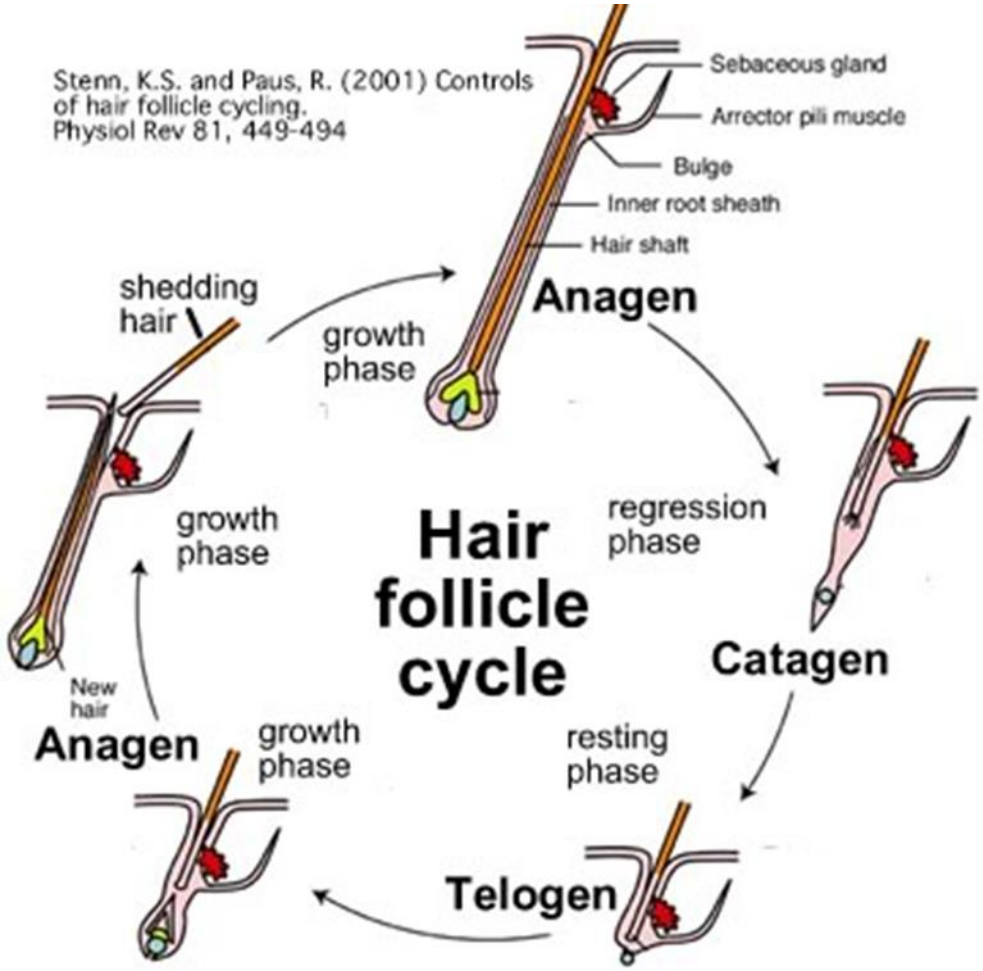

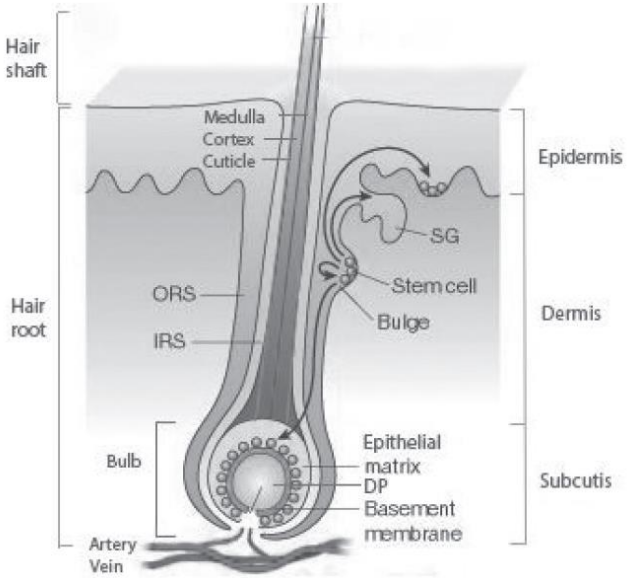

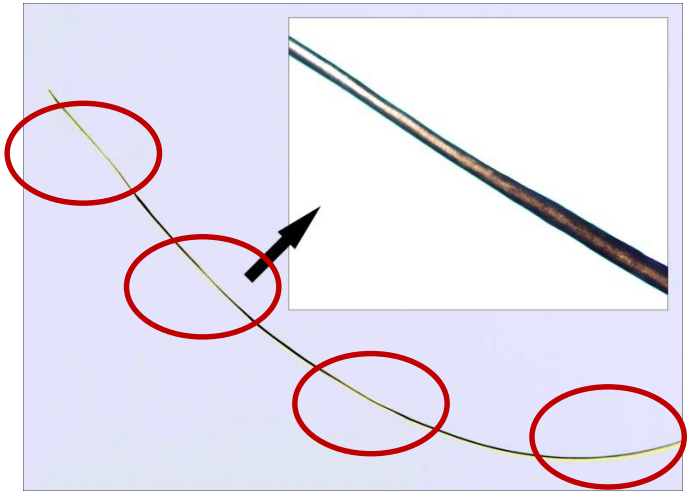

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How Scalp Cooling Works

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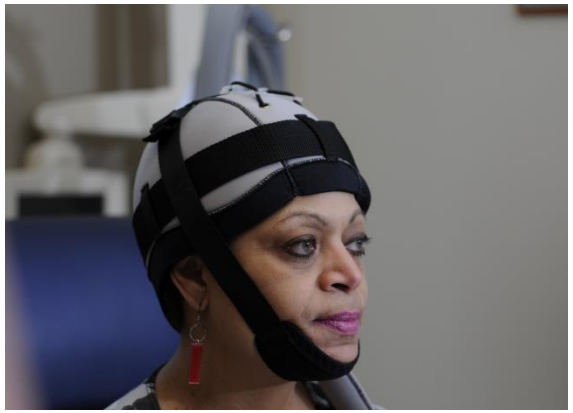

Why Not Used In the US Sooner?

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- Devices have more stringent and different approval processes which the cold caps did not have to go through

- The FDA had concerns about patient safety and the possibility of scalp metastasis. There are 2 large studies from other countries showing no increase in scalp metastasis or change in overall survival with device use.

- FDA approved the first scalp cooling device Dec 2015
  - This was a non-randomized trial and only looked at taxane-based chemotherapy.
  - Showed 66% hair retention.

Van den Hurk Breast 2013
Lemieux Breast Can Res 2015
Rugo ASCO poster 6/2015

Safety: Overall Survival

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- Retrospective study of 1370 women with stage 1-3 breast cancer from Quebec
- Median f/u 6.3 years
- No difference in Overall Survival in scalp cooled vs no scalp cooling groups

Lemieux. Breast Cancer Res Treat. 2015

Safety: Scalp Metastasis/Recurrence

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- Overview from Munich cancer registry
- >33,771 breast cancer patients
- 77% treated adjuvantly, mainly with taxanes/anthracyclines
- Incidence not higher with scalp cooling
  - Scalp cooling 0.04-1%
  - No scalp cooling 0.03-3%

Van den Hurk. Breast. Oct 2013.

Risk of Thermal Injury?

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- 4 cases from MSKCC reported with grade 1-2 thermal injury to scalp
  - Penguin:
    - Case 1: Used alternative scalp covering (paper towel)
      - Blistering at upper mid forehead
    - Case 2: used appropriate protection
      - Blistering in forehead area
    - Case 3: crusting and desquamation of scalp
  - Elastogel: used after alopecia from AC, during paclitaxel
    - Large bulla on scalp

Courtesy of Dr. Rugo
Presented at MSKCC 2016

Belum et al, BCRT 2016

Table 1 Characteristics of patients with frostbite on the scalp following the use of cold caps

Case no.	Age/ Sex	Cancer	Chemo regimen	Cold cap usage details				Onset	Follow-up[b]	Potential contributory factors
				Make	Pre-infusion	During infusion	Post-infusion			
1	49/F	Breast	TCHP	Penguin™	60′	2.5 h.	5 h.	Cycle 3	Mild persistent alopecia (at 5 months)	Lack of adequate padding between the cold cap and skin; duration of post-infusion cooling
2	55/F	Breast	AC → T	Elasto-Gel™	15′	60′	50 min.	Cycle 3	Mild persistent alopecia (at 4 months)	Pre-existing alopecia; lack of padding; duration of post-infusion cooling?
3	58/F	Breast	PH	Penguin™	50′	30′	2.5 h.	Cycle 4[a]	Alopecia resolved (at 2 months)	Pre-existing diffuse alopecia; duration of post-infusion cooling
4	50/F	Breast	CMF	Penguin™	50′	60′	4.5 h.	Cycle 1	Mild persistent alopecia, skin sensitivity (at 6 months)	Lack of adequate padding; duration of post-infusion cooling

Courtesy of Dr. Rugo
Presented at MSKCC 2016

SCALP Trial

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- Demonstrate the safety and efficacy of scalp cooling devices in reducing chemotherapy-induced alopecia

- SCALP is the first randomized trial in the world to evaluate modern scalp cooling

Clinicaltrials.gov NCT01986140
Funded by Paxman Ltd

SCALP

- December 2013 – September 2016
- Open at 7 sites across the US
  - 3 academic centers
  - 4 community oncology clinics
- 229 women signed consent

Key Eligibility

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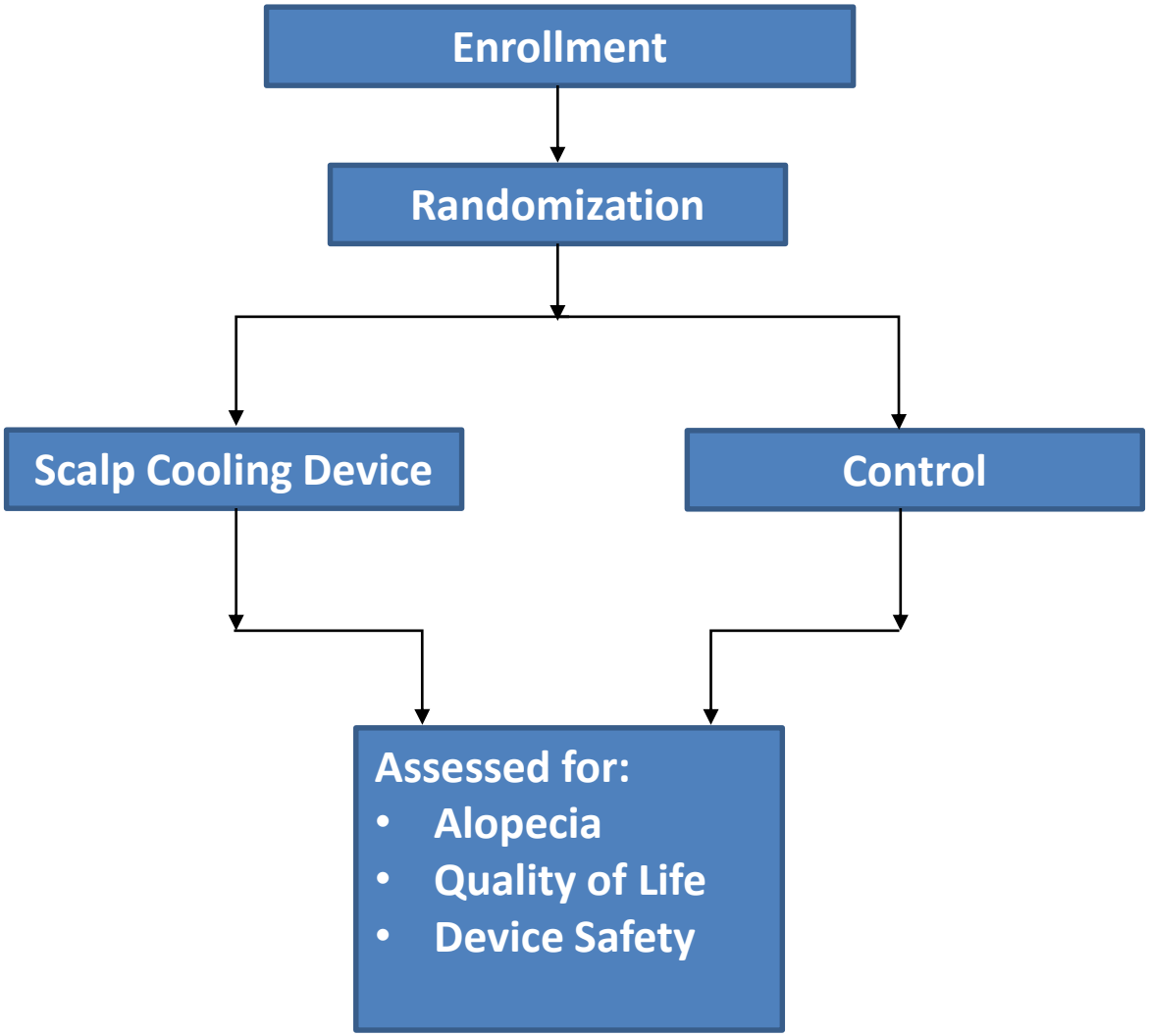
Inclusion Criteria

- Stage 1 or 2 breast cancer
- Neoadjuvant or adjuvant chemotherapy

Exclusion Criteria

- Migraines
- Anemia
- Hypothyroidism
- Other uncontrolled medical conditions

Design



Scalp Cooling Device Arm

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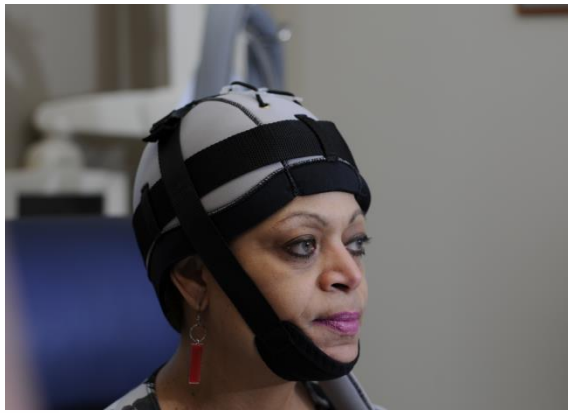

Alopecia Grading: CTCAE Version 4.0

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Grade 0

No hair loss

Grade 1

Hair loss of up to 50% of normal, no wig required

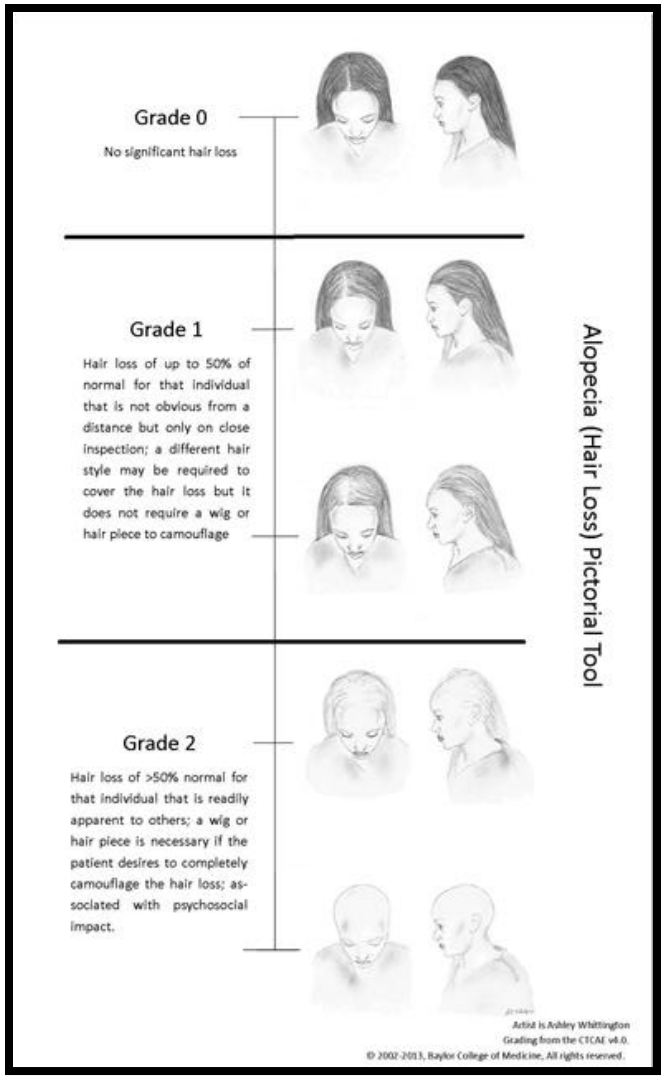
Grade 2

Hair loss of > 50% of normal, wig required

CTCAE = Common Terminology Criteria for Adverse Events Version 4.0

* CTCAE only defines alopecia through Grade 2

Pictorial Tool



Examples of Grading

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Baseline
(Grade 0 alopecia)

Grade 1 Alopecia
* 3-4 weeks after using cooling system for 4 cycles of chemo

Examples of Grading

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Baseline
(Grade 0 alopecia)

Grade 2 Alopecia

* Subject in control group; 3 weeks after 2nd cycle of chemotherapy.

* Subject in cooling group; 3 weeks after using cooling system for 2 cycles of chemotherapy

Design

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Patient Reported Comfort Scale
Very Comfortable
Reasonably Comfortable
Comfortable
Uncomfortable
Very uncomfortable

Questionnaires
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30
Hospital Anxiety Depression Scale
Body Image Scale

Comfort Scale: Massey. Europen J Onc Nur, 2004; 8: 121-130

Statistical Analysis Plan

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- 235 subjects were planned to be enrolled to provide 85% power to detect a 20% difference in hair preservation.
- The trial stopped early based on a pre-planned interim analysis for efficacy after 142 participants were evaluable for the primary endpoint with an O'Brien-Fleming spending function*

Nangia, et al. *JAMA*, 2017; 317(6):596-605.

Statistical Analysis Plan

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- Secondary endpoints included
  - Wig/scarf use
  - Quality of life
  - Hair preservation at completion of chemotherapy
- Study participants will be followed for 5 years post-study for time to first recurrence, overall survival, and site of first recurrence

Nangia, et al. *JAMA*, 2017; 317(6):596-605.

Participant Flow Chart

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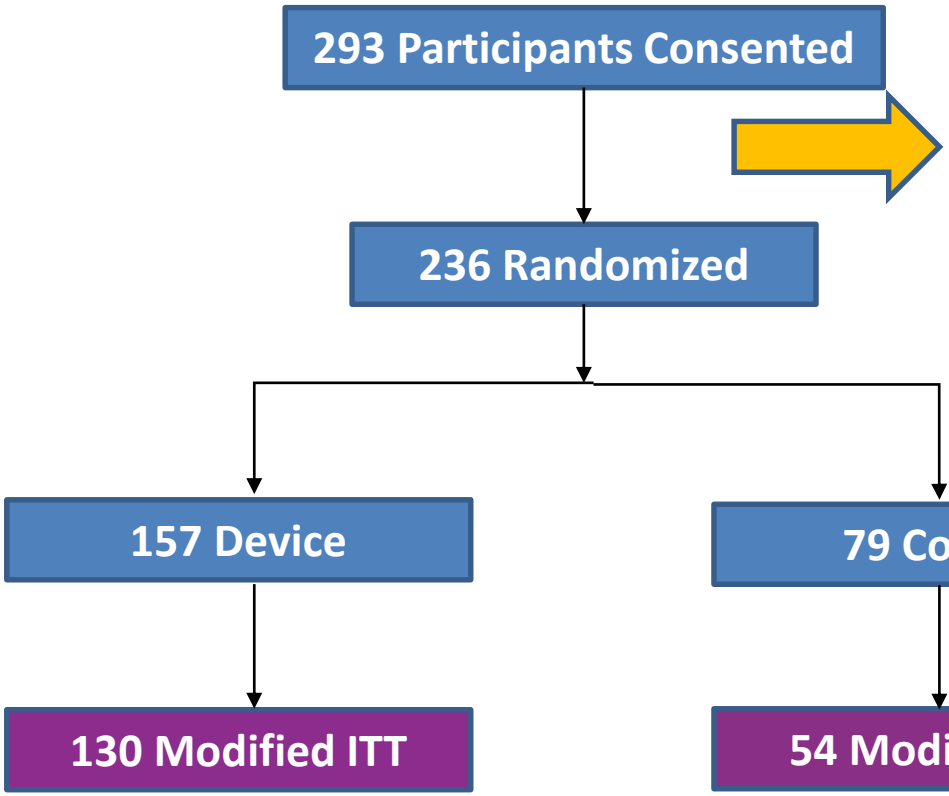

Why ineligible?

Hypothyroidism (11)
Anemia (10)
Stage 3 Breast Cancer (7)
Baseline Alopecia (5)
Migraines (4)
Age >= 70 (3)
Lichens Planus (2)
Other (6)

Why withdrew consent?

18 Randomized to Control
7 due to hair loss
6 in pre-cooling phase
- 4 Device (cold/discomfort)
- 1 Anxiety
- 1 Claustrophobia

4 during chemo (device cold)
2 alternate treatment
3 withdrew consent
1 chemo related
1 progressive disease

Demographics & Characteristics

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Parameter		Cooling	Non-Cooling	ALL
		N=130	N=54	N=184
Age (years)				
	Mean (SD)	50.4 (10.5)	51.7 (10.1)	50.8 (10.4)
Race [n (%)]				
	White	106 (81.5%)	41 (75.9%)	147 (79.9%)
	Black or African American	16 (12.3%)	8 (14.8%)	24 (13%)
	Asian	5 (3.8%)	5 (9.3%)	10 (5.4%)
Ethnicity [n (%)]				
	Hispanic or Latino	20 (15.4%)	9 (16.7%)	29 (15.8%)
	Non-Hispanic	108 (83.1%)	45 (83.3%)	153 (83.2%)
Major Chemotherapy Type [n (%)]				
	Anthracycline	45 (34.6%)	23 (42.6%)	68 (37%)
	Taxane	85 (65.4%)	31 (57.4%)	116 (63%)
Breast Cancer Stage [n (%)]				
	Stage I	50 (38.5%)	19 (35.2%)	69 (37.5%)
	Stage II	80 (61.5%)	35 (64.8%)	115 (62.5%)

Results: Primary Outcome

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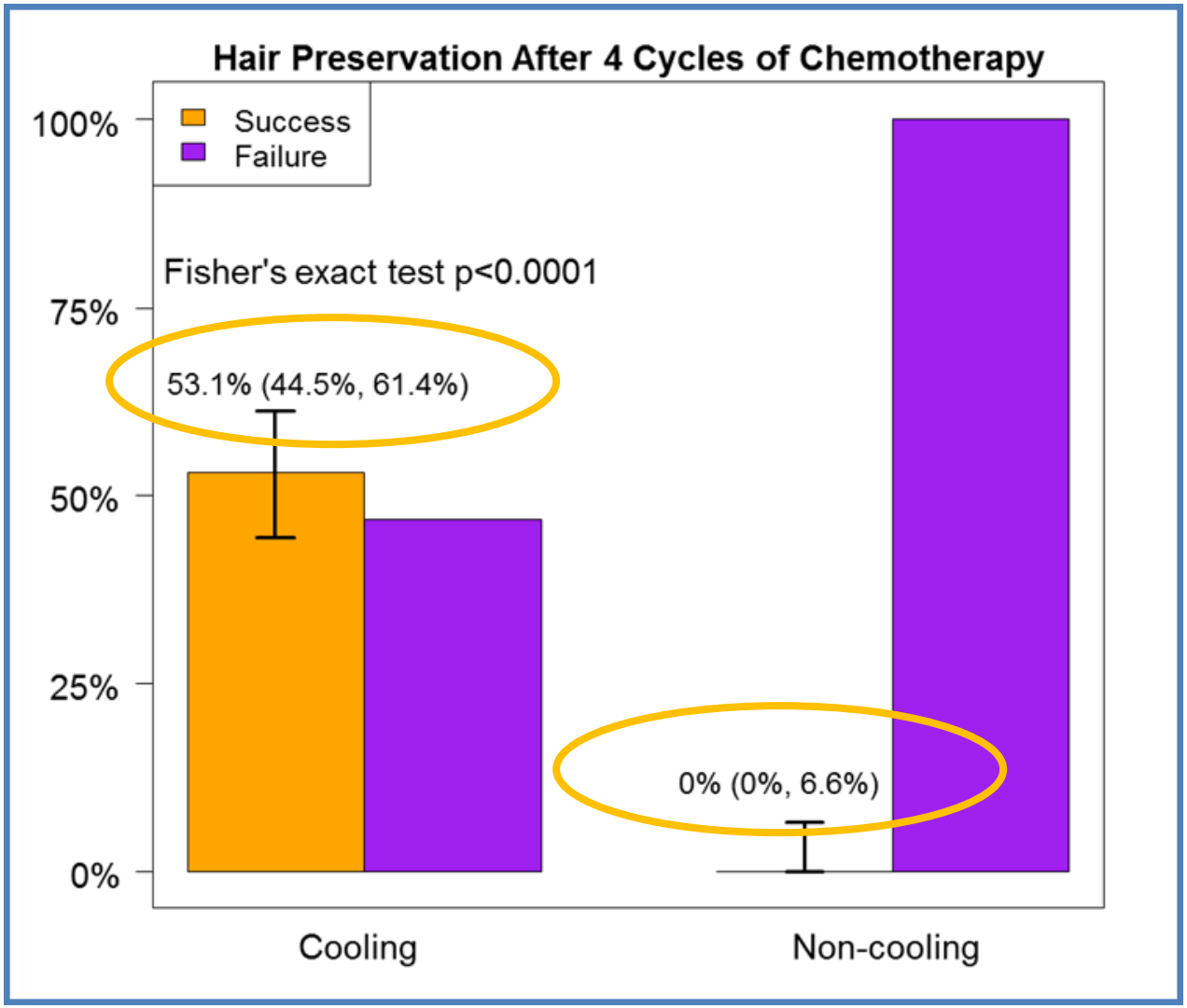

Results: Primary Outcome

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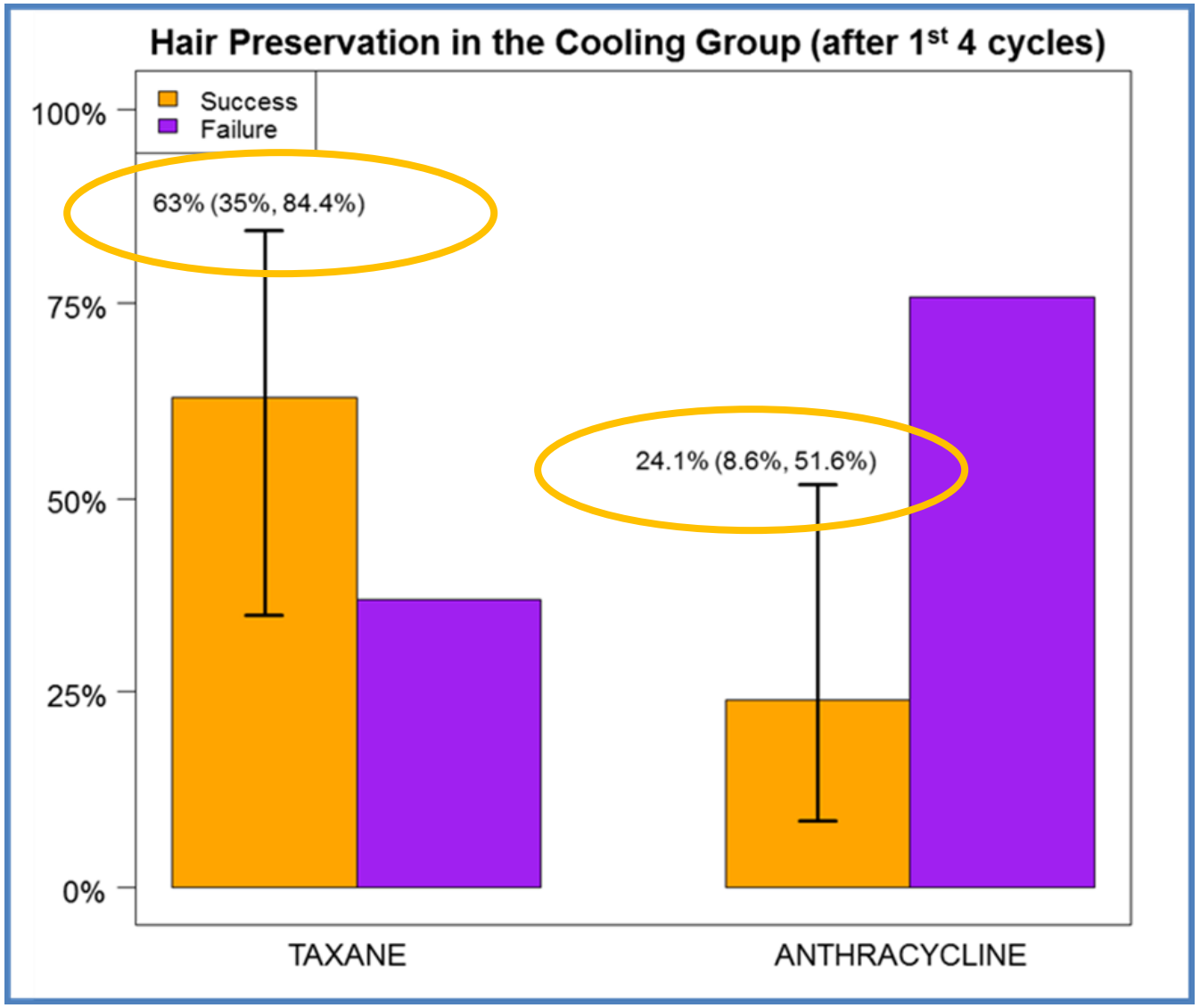

Results: Adverse Events

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Adverse Device Effects : All Grade 1 or 2						
	Cooling N = 137					
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6-8
AADEs (CTCAE V4.0)	(n=137)	n=117	n=90	n=83	n=36	n=31
Headache	11.7%	8.5%	1.1%	4.8%	5.6%	-
Nausea	4.4%	1.7%	1.1%	1.2%	-	-

<3% rate of dizziness, ear pain, scalp pain, sinus pain, pruritus, and dry skin
<1% rate of chills, jaw pain, paresthesia, skin and SC tissue disorder, and skin ulceration

Results: Quality of Life

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Patient Reported Comfort Scale

Comfort Scale	Cooling (N = 137)							
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 7	Cycle 8
	n=137	n=117	n=90	n=83	n=36	n=31	n=11	n=9
Very Comfortable	10.9%	15.4%	13.3%	15.7%	16.7%	12.9%	-	-
Reasonable Comfortable	51.8%	41.9%	50%	45.8%	50%	54.8%	45.5%	44.4%
Comfortable	27.7%	27.4%	22.2%	27.7%	22.2%	29%	36.4%	44.4%
Uncomfortable	8%	10.3%	12.2%	9.6%	8.3%	3.2%	9.1%	11.1%
Very Uncomfortable	-	3.4%	-	-	-	-	9.1%	-
Not Assessed	1.5%	1.7%	2.2%	1.2%	2.8%	-	-	-

Quality of Life Assessments showed no difference

Secondary Endpoints

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Wig or Scarf Use		
	Cooling	**Control**
No	33.9%	0%
Yes	44.6%	68.5%
Unknown (had grade 2 alopecia)	20%	31.5%

Secondary Endpoints

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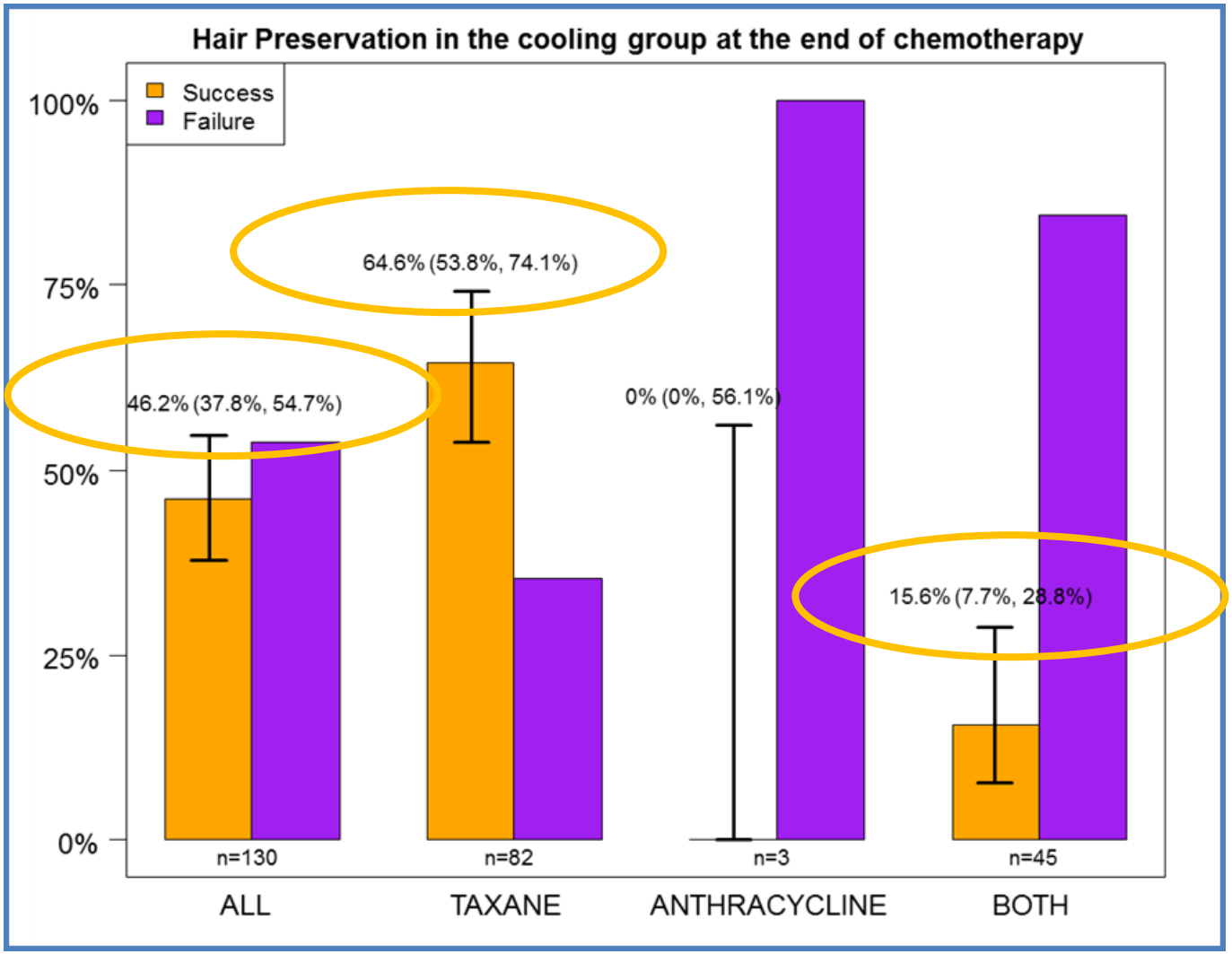

Secondary Endpoints

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Hair Retention by Regimen After Completion of Chemotherapy in Cooling Arm	
Chemotherapy Regimen	**% Successful Hair Preservation (n)**
Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2	0% (3)
Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2 + Docetaxel 100mg/m2	0% (3)
Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2 + Paclitaxel 80-90 mg/m2 weekly with carboplatin AUC of 6 every 3 weeks	66.7% (3)
Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2 + Paclitaxel 80mg-90/mg/m2 weekly	18.8% (16)
Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2 + Paclitaxel 175mg q2 weeks	40% (20)
Doxorubicin 50mg/m2 with 5-Fluorouracil 500mg/m2 and cyclophosphamide 500mg/m2 + Paclitaxel 80mg-90mg/m2 weekly	100% (1)
Doxorubicin 50mg/m2 with 5-Fluorouracil 500mg/m2 and cyclophosphamide 500mg/m2 + Paclitaxel 175mg/m2 q2 weeks	0% (1)
Paclitaxel 80mg/m2 - 90mg/m2 weekly (every 3 weeks constitute a cycle), or 175mg/m2 every 2-3 weeks as a single agent	100% (7)
Paclitaxel 80-90 mg/m2 weekly with carboplatin AUC of 6 every 3 weeks	100% (1)
Docetaxel 75mg/m2 - 100mg/m2 with pertuzumab/trastuzumab + Adriamycin 60mg/m2 with cyclophosphamide 600mg/m2	0% (1)
Docetaxel 75mg/m2 with cyclophosphamide 600mg/m2	56.5% (46)
Docetaxel 75mg/m2 with carboplatin AUC of 6 and trastuzumab at standard doses	75%(28)

Conclusion from SCALP trial

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- Scalp cooling devices are highly effective
- This device received FDA clearance in the US based on these data
- Need further studies exploring this technology for other types of tumors
- More studies for impact of chemotherapy-induced alopecia on psyche and body image
- Tailored QOL tools are needed to evaluate the impact of alopecia