



Scalp Cooling to Prevent Chemotherapy-Induced Alopecia: The US Experience

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- Clinical trial funding by Paxman Ltd
(to institution)

Background

- 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)

How Scalp Cooling Works



Why Not Used In the US Sooner?

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

- 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

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

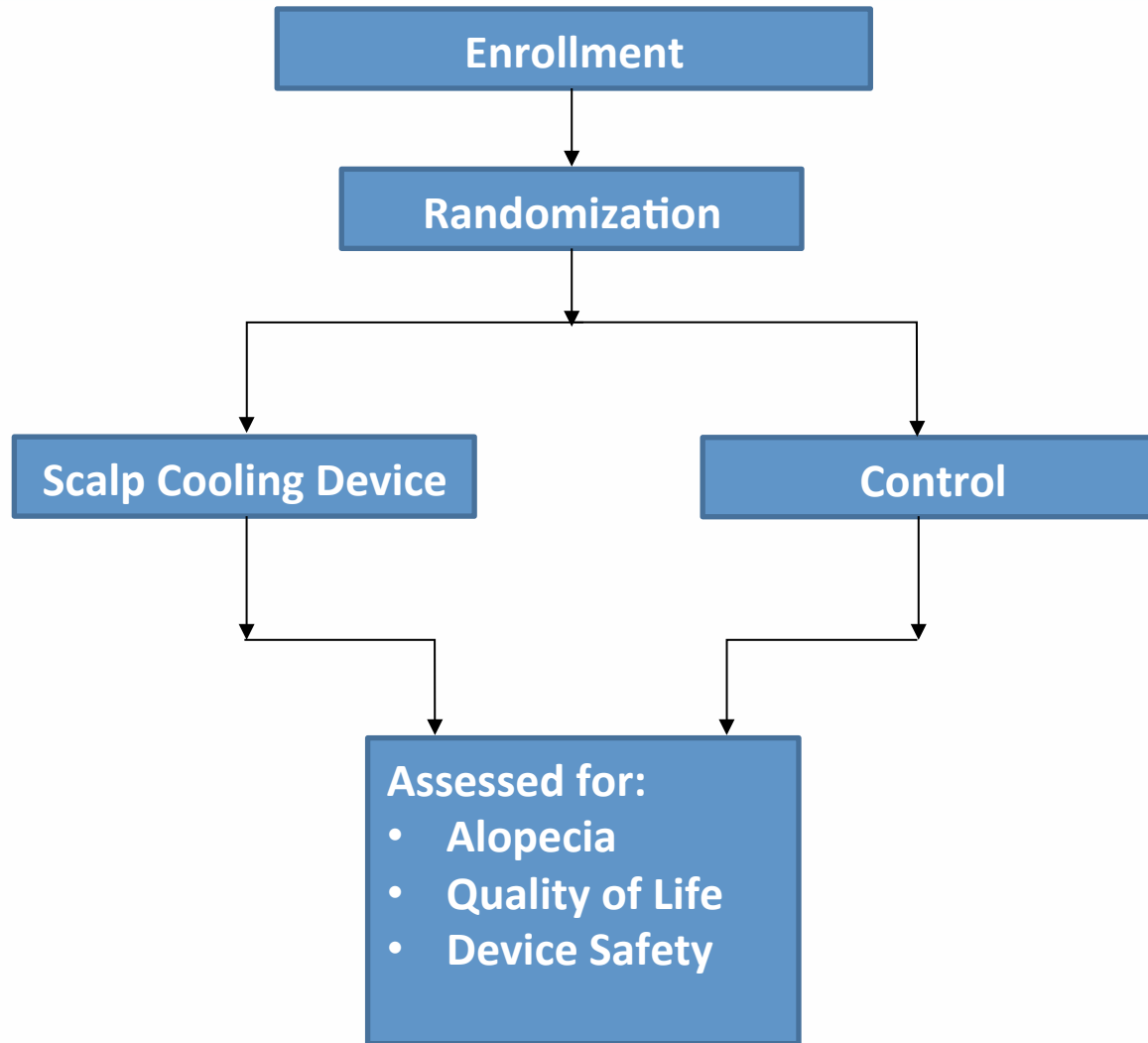
Key Eligibility

Inclusion Criteria

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

Exclusion Criteria

- Migraines
- Anemia
- Hypothyroidism
- Other uncontrolled medical conditions



Scalp Cooling Device Arm



Alopecia Grading: CTCAE Version 4.0



Grade 0
No hair loss

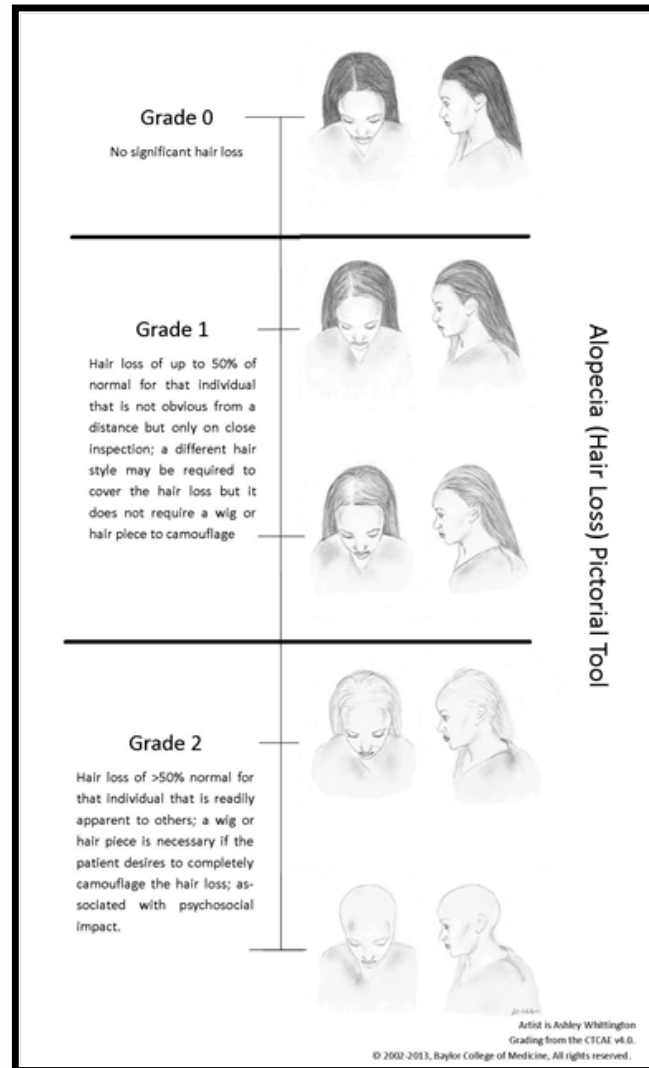


Grade 1
Hair loss of up to
50% of normal,
no wig required



Grade 2
Hair loss of > 50%
of normal, wig
required

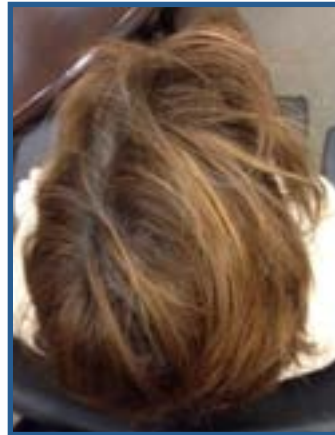
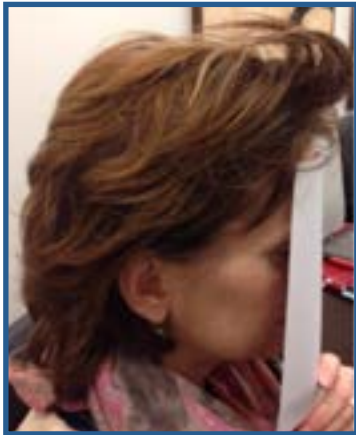
Pictorial Tool



Examples of Grading

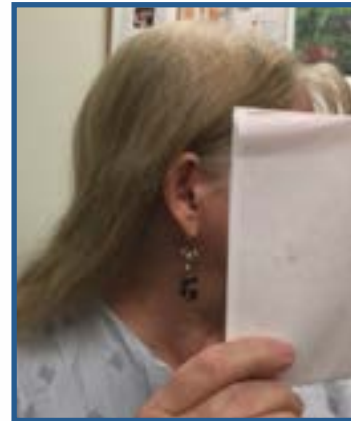
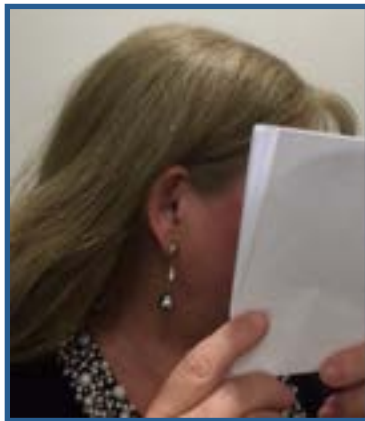
Baseline

(Grade 0 alopecia)



Grade 1 Alopecia

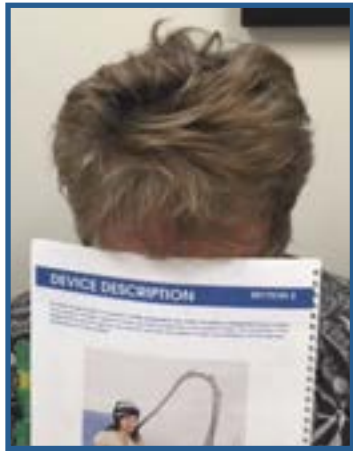
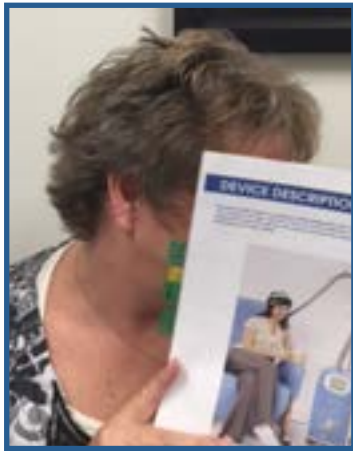
* 3-4 weeks after using cooling system for 4 cycles of chemo



Examples of Grading

Baseline

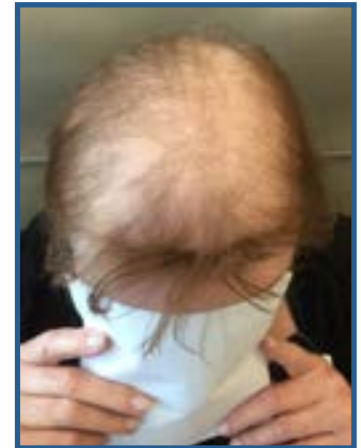
(Grade 0 alopecia)



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

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

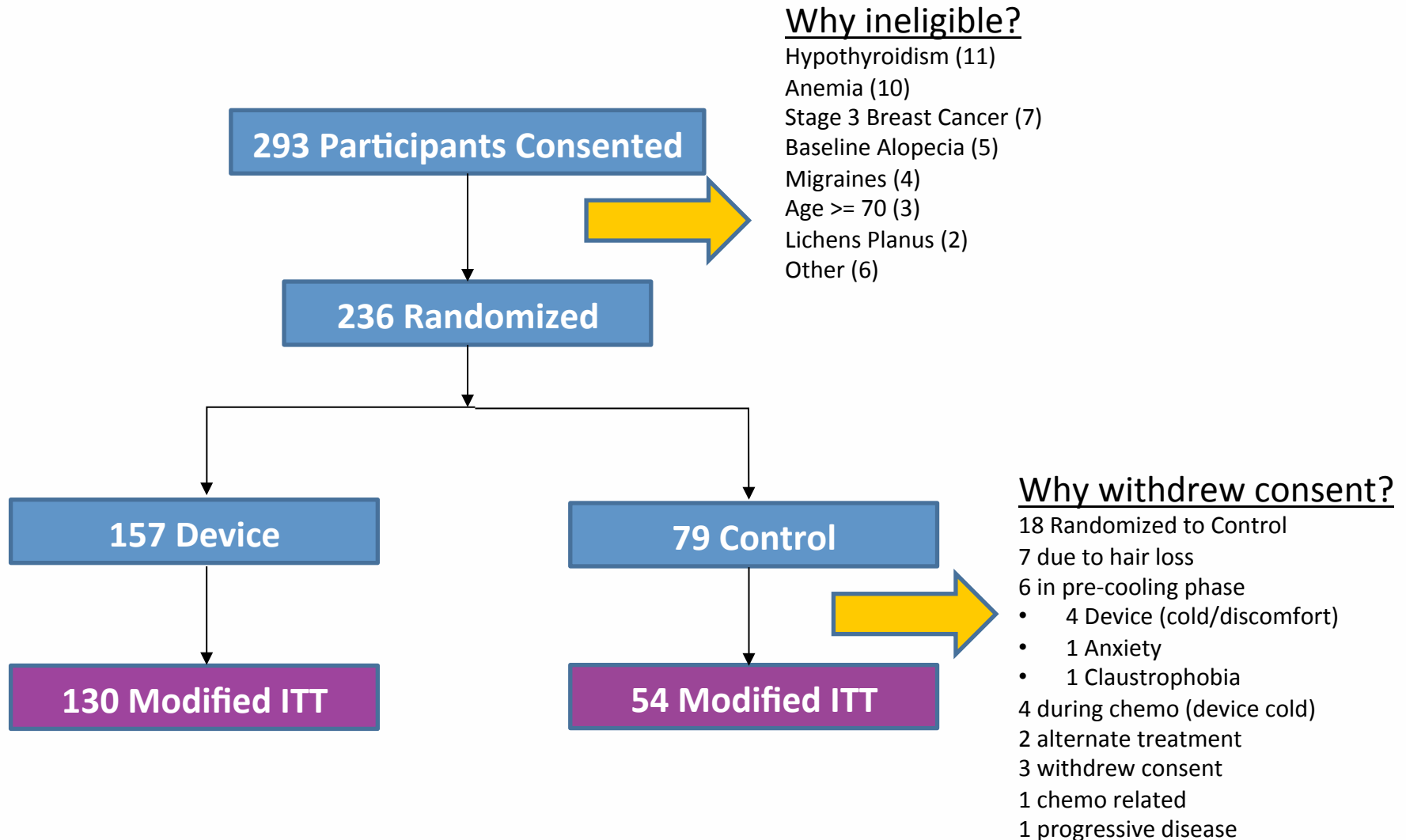
Body Image Scale

Statistical Analysis Plan

- 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*

- 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

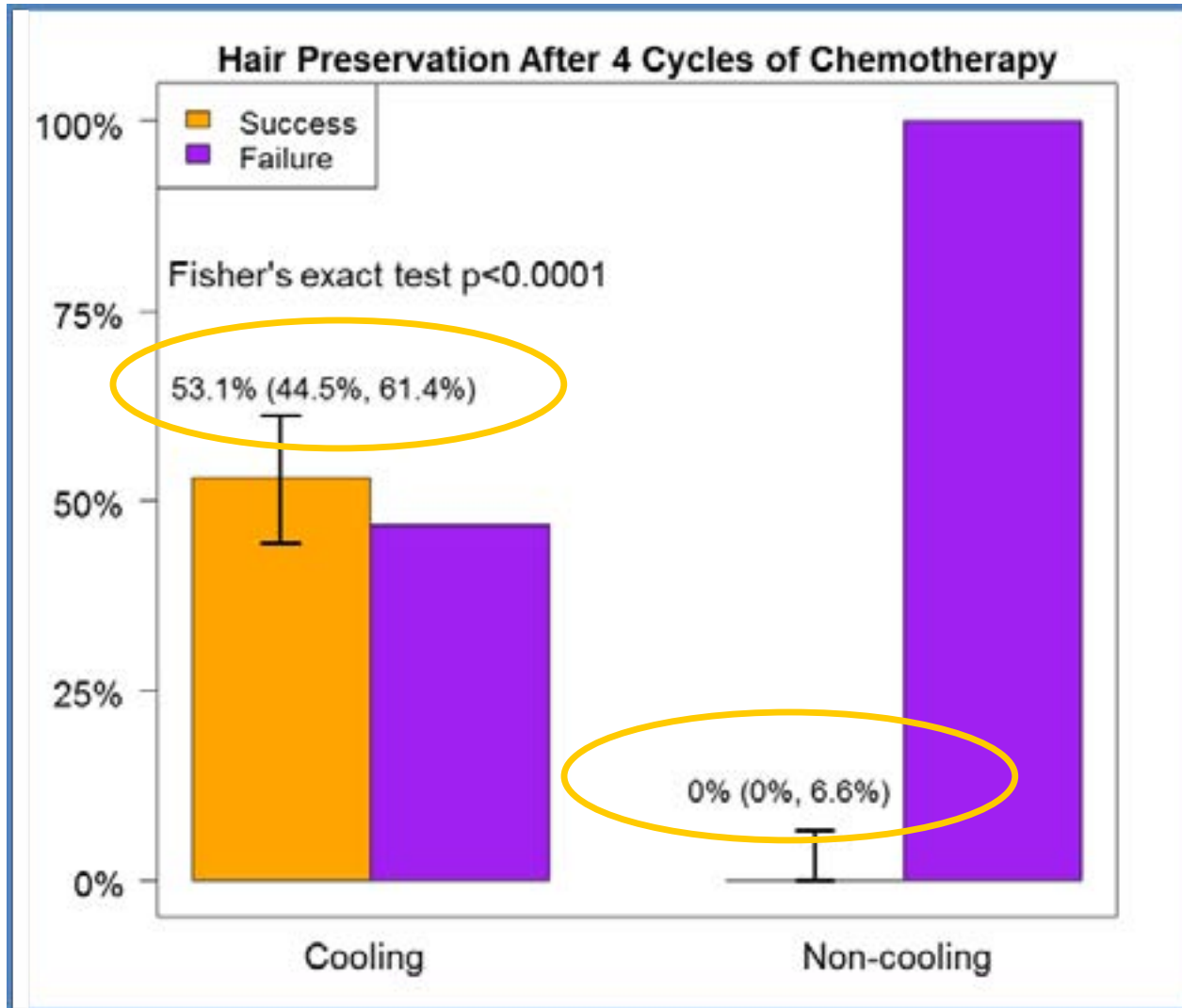
Participant Flow Chart



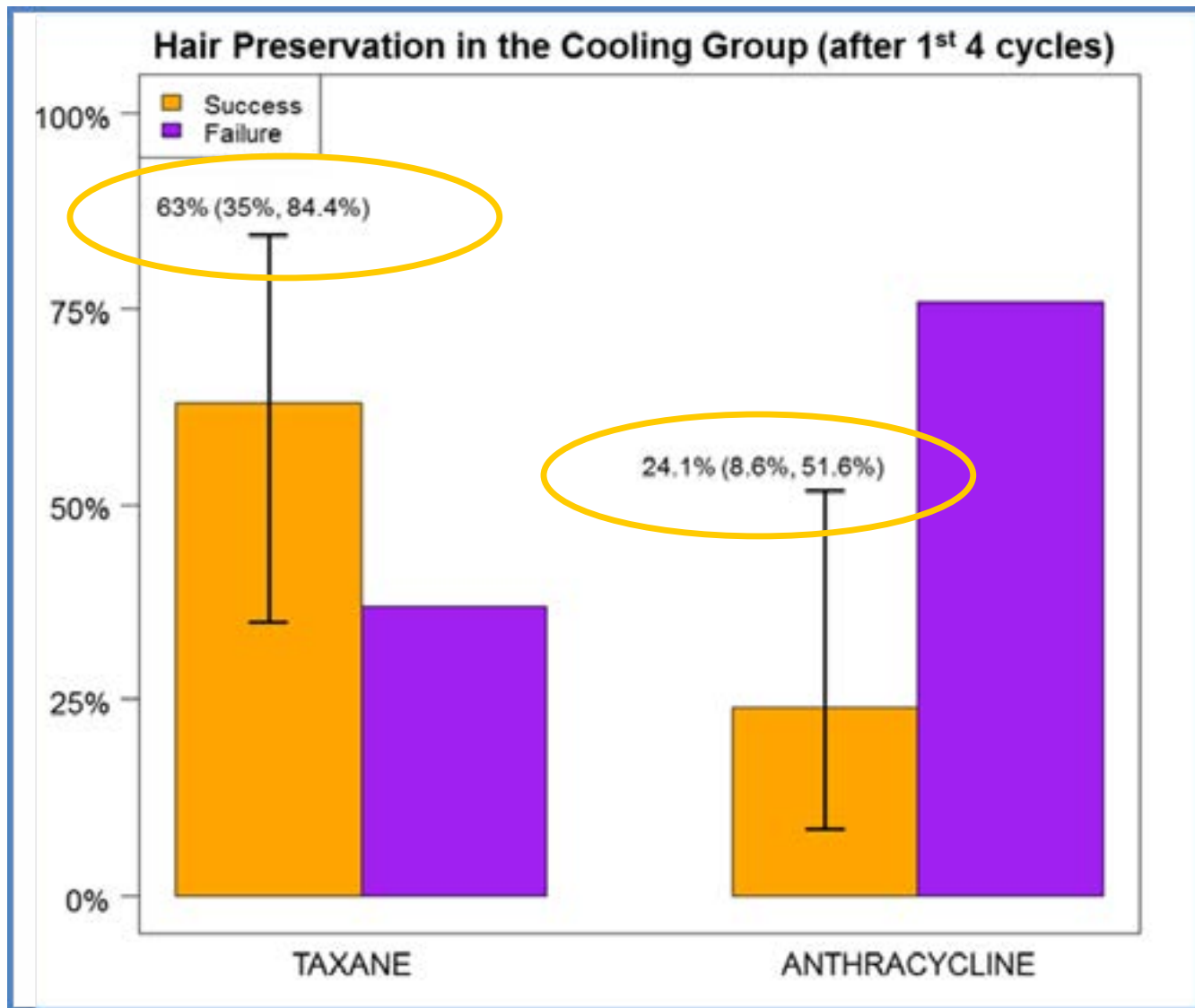
Demographics & Characteristics

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



Results: Primary Outcome



Results: Adverse Events

Adverse Device Effects : All Grade 1 or 2						
AADEs (CTCAE V4.0)	Cooling N = 137					
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6-8
	(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%	-	-
<p><3% rate of dizziness, ear pain, scalp pain, sinus pain, pruritus, and dry skin</p> <p><1% rate of chills, jaw pain, paresthesia, skin and SC tissue disorder, and skin ulceration</p>						

Results: Quality of Life

Patient Reported Comfort Scale

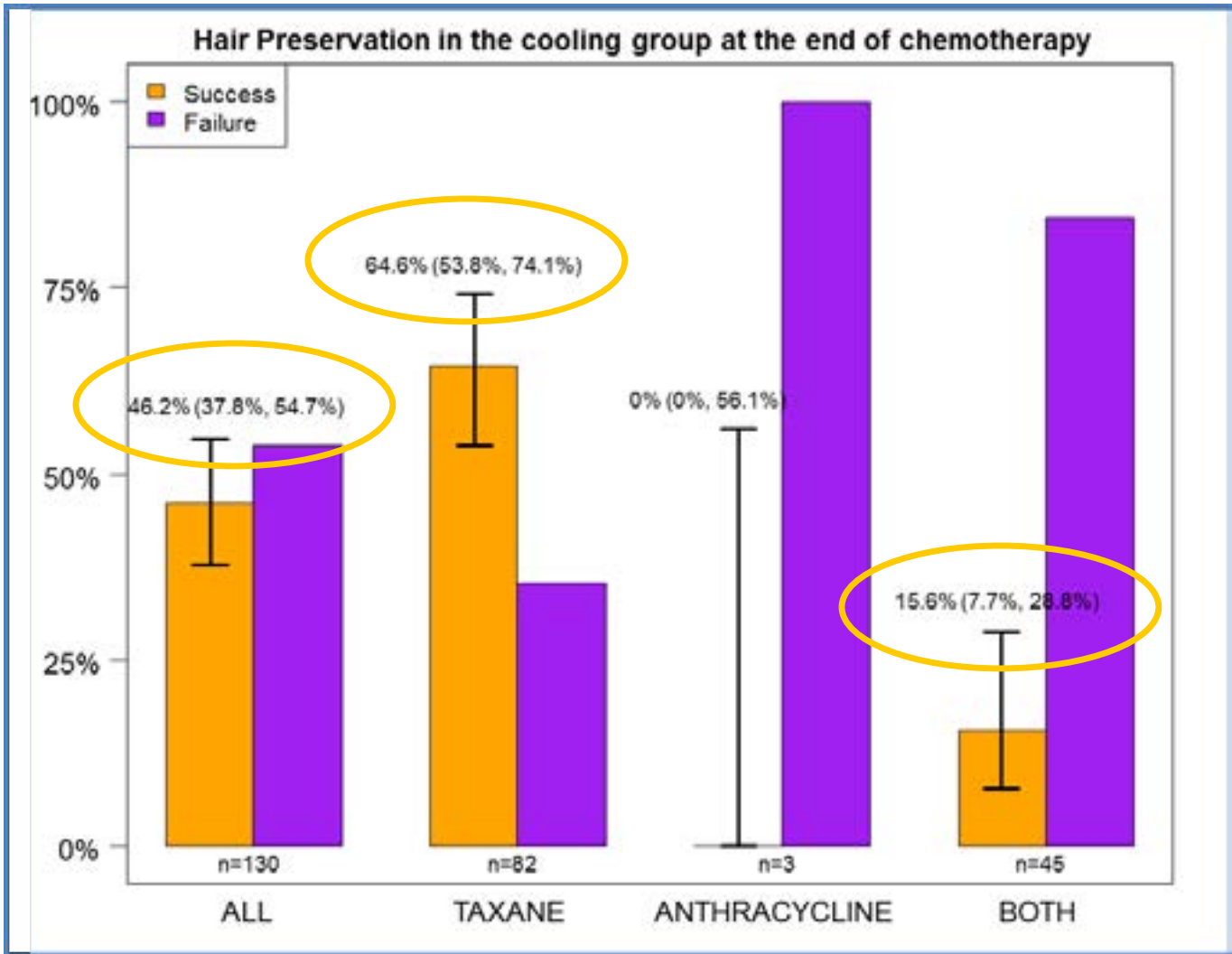
Comfort Scale	Cooling (N = 137)							
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 7	Cycle 8
	n=137	n=117	n=90	n=83	n=36	n=31	n=11	n=9
Very Comfortable	10.9%	15.4%	13.3%	15.7%	16.7%	12.9%	-	-
Reasonable Comfortable	51.8%	41.9%	50%	45.8%	50%	54.8%	45.5%	44.4%
Comfortable	27.7%	27.4%	22.2%	27.7%	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

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



Secondary Endpoints

Hair Retention by Regimen After Completion of Chemotherapy in Cooling Arm

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

Penguin Cold Cap Registry Study

Regimen	% Successful Hair Retention
TC x 4	83.8% (31/37)
TC x 4-6	50% (5/10)
Weekly P → AC	43.4% (10/23)
AC → Weekly P	20% (2/10)
Taxotere/Carbo +/- Herceptin	100% (2/2)
Other	60% (9/15)

Conclusion from SCALP trial

- 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

Limitation to Device Use In the US

- Centers having them available
- Interest in Nursing Staff and Administration
- Extra chair time
- Cost
- Insurance Coverage?

Extra Chair Time

- Can be up to 90 min
- Can move patients to a different waiting area
- For HER2+ patients you can give the herceptin/pertuzumab after the chemo during the post-cooling time
- Carboplatin doesn't cause hair loss and we also do this in the post-cooling time
- Paclitaxel use 60 min post-cooling time?
- Docetaxel use 20-40 min post-cooling time?
* Prevent permanent alopecia?

Costs for Cooling Caps in the US

- Cooling Caps
 - Rent for a monthly fee
 - Patient pay directly and is ~\$300-500 months
 - Many different companies offer these caps and anyone can rent them (not infusion center dependent)
- Cooling Devices
 - Leased by Centers
 - Patient pays per treatment (with Paxman lifetime max is \$2200, Dignitana cost is set by centers but average \$1500)

Implementation to Date

- Dignitana
 - 135 machines across 22 states
- Paxman
 - 289 machines across 23 states

- HairToStay
 - Nonprofit that offers need-based grants to help offset the expense of cooling systems for chemotherapy patients in the US
- Rapunzal Project
 - Nonprofit dedicated to helping chemotherapy patients keep their hair during treatment
 - Has a nice list of locations where scalp cooling is available
 - possible codes to help with insurance coverage and some success with BCBC, Aetana, and Horizon ranging from \$50-400 per treatment

Tips for Use

- Lay out patient expectations
 - Most patients have hair thinning and lose 30% of their hair
 - Define what a success is upfront
 - Put ownership on the patient and explain to them that the better the fit, the better the chance of success
 - Sequence chemo with agent with less hair loss first (weekly paclitaxel → AC)
 - Tell patients to avoid stress to hair
 - no dye or straighteners/curling
 - use sulfate free shampoo/conditioner
 - comb hair in shower with conditioner in
 - <https://www.paxmanusa.com/>

Who in the picture has cancer?



“Fighting Cancer on My Own Terms”

