Hope S. Rugo, MD
Professor of Medicine
Director, Breast Oncology and Clinical Trials Education
University of California San Francisco Comprehensive Cancer Cente

Cooling for the Prevention of Chemotherapy induced Alopecia: The Evidence

MASCC/ISOO
Annual Meeting on Suppportive Care in Cancer
www.mascc.org/meeting
Follow us on Twitter: @CancerCareMASCC

MASCC Multinational Association of Supportive Care in Cancer
ISOO International Society of Oral Oncology
#MASCC19

Conflict of Interest Disclosure

Hope S. Rugo, MD

- Institutional research funding from:
  - Pfizer, Novartis, Eli Lilly, Roche/Genentech, MacroGenics, Odonate, Merck, OBI, Eisai, Immunomedics, Daichi
- Travel support from:
  - Lilly, Pfizer, Mylan, Puma, Amgen, Astra Zeneca

2019
21-23 JUNE
SAN FRANCISCO
SUPPORTIVE CARE MAKES EXCELLENT CANCER CARE POSSIBLE

Chemotherapy Induced Hair Loss

- Temporary hair loss is one of the most distressing and traumatic side effects of chemotherapy
- Women with chemotherapy induced alopecia compared to those without report:
  - Lower self-esteem
  - Poorer body image
  - Lower quality of life
- May impact patients' decision to accept or decline chemotherapy
- Delayed recovery or permanent alopecia has been reported with docetaxel
  - Incidence related to dose, duration of therapy
    - Variable reports of 8-10%
    - Less frequent at 75 mg/m2 than 100 mg/m2

Munstedt K et al. Support Care Cancer, 1997; McGarvey EL et al. Clinical Prac, 2001

Scalp Cooling: Potential Mechanisms of Action

- Vasoconstriction
  - Reduces the blood flow to hair follicles during peak plasma concentrations of chemotherapy
  - Reduces cellular uptake of chemotherapy
- Reduced biochemical activity
  - Makes hair follicles less susceptible to damage from chemotherapeutic agents

Available Scalp Cooling Devices for the Prevention of Chemotherapy Induced Alopecia

Device	Details
Free-standing with circulating coolant (automated)	
Dignicap	US FDA cleared
Paxman caps	
Frozen cold caps (manual)	
Penguin caps	Cap must be frozen and changed every 30 minutes as it begins to thaw. The Penguin cap can be molded to the shape of the head
Elastogel caps	
Polar cold caps	
Artic cold caps	
Chemo cold caps	

2019
21-23 JUNE
SAN FRANCISCO
SUPPORTIVE CARE MAKES EXCELLENT CANCER CARE POSSIBLE

Two Prospective Multi-Center Trials in the US

- Dignicap
  - Prospective, stage I-II breast cancer pts
  - TAC and AC/T excluded
  - Non-randomized concurrent matched controls
  - Dean Scale assessed by patients compared to baseline
- Paxman SCALP trial
  - Prospective, randomized, stage I-II breast cancer pts
  - Control vs scalp cooling; any chemotherapy allowed
  - Used NCI CTCAE scale assessed by providers
- Results
  - Both treatments demonstrated markedly reduced hair loss with scalp cooling
  - Improved measures of quality of life
  - Paxman: improved outcome with experience

Rugo et al, JAMA 2017; Nangia et al, JAMA 2017

Success (keeping >50% of hair) by Chemotherapy Regimen in Treatment and Control Groups

Chemotherapy regimen	DigniCap	Control
	Treatment success[4]	Treatment success[4]
TC[1]	46/76 (60.5%)	0/10
TCarbo[2]	10/12 (83.3%)	0/3
Paclitaxel[3]	10/12 (83.3%)	0/2

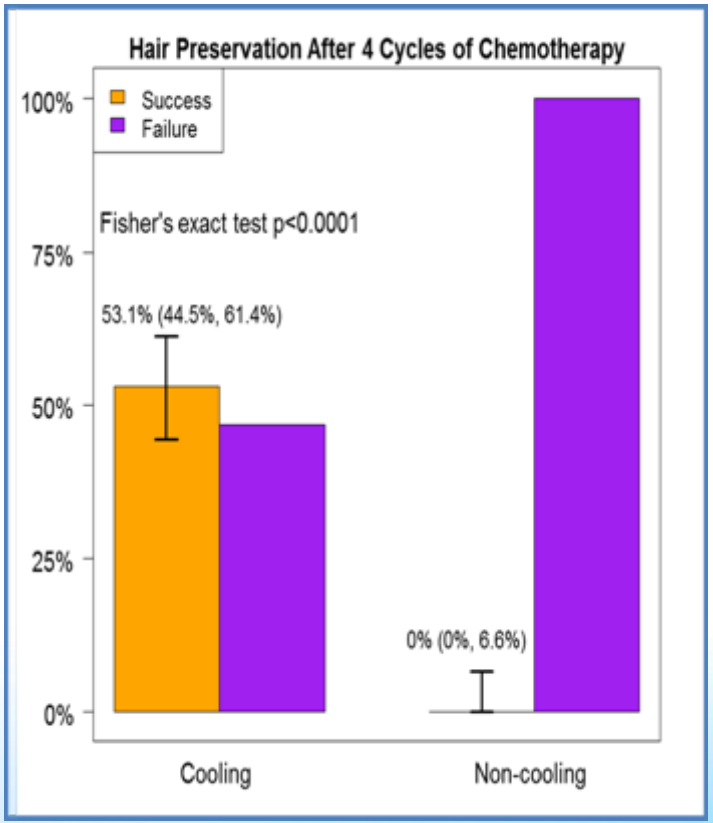
1. TC: Docetaxel/cyclophosphamide x 4-6 cycle 2. TCarbo: Docetaxel/carboplatin + HER2 targeted therapy x 4-6 cycles 3. Paclitaxel: Paclitaxel weekly x 12 4.Treatment success: Dean score < 3

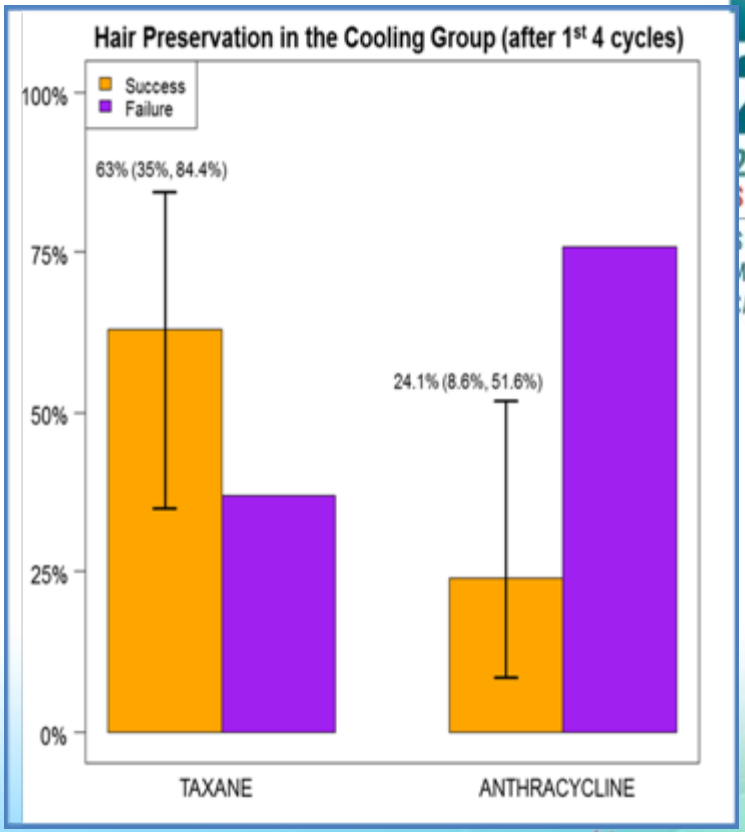
Overall Treatment Success: 66.3%

Rugo et al, JAMA 2017

Results: Success Overall and by Regimen

Assessed after 4 cycles of chemotherapy



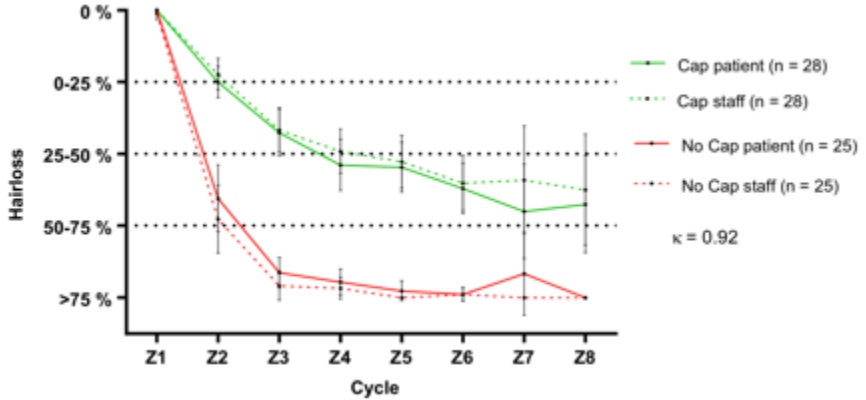


Nangia et al, JAMA 2017

CoolHair

- Small prospective randomized trial using Dignicap
  - All received anthracycline based regimens
  - Patient assessment by modified Dean scale
  - 54% received anthracycline/taxane based therapy

Parameter	CAP $n=28$ (100%)	NoCAP $n=25$ (100%)	p value
Patient-reported hair loss by Dean Scale (Primary endpoint)			
Success	11 (39.3)	0 (0)	<0.001
Failure	17 (60.7)	25 (100.0)	



Smetanay et al, BCRT 2019

Penguin Cold Cap: UCSF Registry Study

Chemotherapy regimen	Pts enrolled in registry	Discontinued scalp cooling			Lost to follow-up (%)
		Due to device-related side effects (%)	Due to hair loss (%)	Discontinued chemotherapy for toxicity unrelated to scalp cooling (%)	
TC × 4	40	0	2 (5)	3 (7.5)	0
TC × 5–6	10	1 (10)	0	0	0
P/AC	23	1 (4.3)	2 (8.7)	0	0
AC/P	10	2 (20)	2 (20)	0	0
T/Carboplatin × 4–6 (±Herceptin)	4	0	0	0	2 (50)
Other	16	2 (12.5)	3 (18.75)	0	1 (6.25)
Overall	103	6 (5.8)	9 (8.7)	3 (2.9)	3 (2.9)

TC docetaxel/cyclophosphamide, *P* paclitaxel, *AC* doxorubicin/cyclophosphamide

Chemotherapy regimen	Evaluable pts	Successful alopecia prevention		Mean maximum VAS by pt report
		% success by patient self-assessment (≤50% hair loss)	% success by physician report (Dean's score ≤2)	
TC × 4	37	83.8% (31)	80% (28/35[a])	38.6
TC × 5–6	10	50% (5)	75% (6/8[a])	44.4
P/AC	23	43.4% (10)	55.5% (10/18[a])	58.9
AC/P	10	20% (2)	20% (2/10)	62.5
T/Carboplatin × 4–6 (±Herceptin)	2	100% (2/2)	100 (1/1[a])	20
Other	15	60% (9)	61.5% (8/13[a])	46.9
Overall	97	60.8% (59)	64.7% (55/85[a])	47

[a]Data unavailable for remaining patients

Rice et al, BCRT 2018

Beware of risk of thermal injury from inadequate scalp protection.
Belum et al, BCRT 2016

Meta-Analysis:
Risk of Scalp Metastases with Scalp Cooling

- 23 full text articles
  - 10 quantified quantified the incidence of scalp metastasis with scalp cooling over time
- Results
  - Scalp cooling: 1,959 pts evaluated over ~ 43.1 mo.
    - Incidence rate of scalp mets
      - 0.61% (95% CI: 0.32% to 1.1%)
  - Non-scalp cooling: 1,238 pts evaluated over ~ 87.4 mo.
    - Incidence rate of scalp mets
      - 0.41% (95% CI: 0.13% to 0.94%)
    - P = 0.43 for the comparison

2019
21-23 JUNE
SAN FRANCISCO
SUPPORTIVE CARE MAKES EXCELLENT CANCER CARE POSSIBLE

Rugo et al, BCRT 2017

Long-term Safety Follow-up of Patients Treated with Scalp Cooling on the Dignitana Trial (1)

- 106 patients enrolled, 16 concurrent controls
- 91 patients have FU out to 3 years
  - 73 with ER+ disease
  - 18 with ER- disease
- No scalp metastases report in either arm to date
- Of 12 control patients
  - 1 developed liver metastases in year, and died of metastatic disease

Rugo et al, SABCS 2018

Long-term Safety Follow-up of Patients Treated with Scalp Cooling on the Dignitana Trial (2)

Treated Subjects - Summary of Annual Follow-up					
# in Primary Analysis 101	# Evaluable 91	# Annual Follow-up Assessments Completed			
		Year 1	Year 2	Year 3	Year 4
Evaluated		91	80	77	63
Disease Free		85	79	71	57
Recurrence					
Site of recurrence/ metastases		• Breast (2) • Liver	• Breast • Breast and bone	• Bone • Breast, bladder, GI, bone • Chest wall and supraclavicular lymph nodes	• Breast and nodes • Bone and liver • Breast, bladder, GI, bone • Thoracic and lumbar spine • Bone, liver, lungs, nodes
Scalp Metastases		0	0	0	0
New Cancers		0	0	Non-Primary Breast (1)	Thyroid (1)
Deaths		1	0	0	0
Lost to Follow-up		6	1	6	2

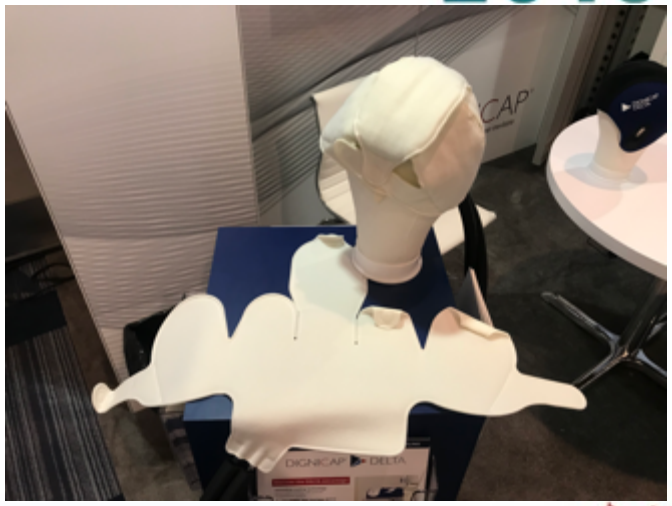
Rugo et al, SABCS 2018

Follow-up is ongoing

Scalp Cooling Prevents CIA

Success is Regimen and Experience Dependent

- Considerations for practices and patients
  - 'Chair time' and post-cooling time
    - Both automated devices have or will have a single patient use machine
  - Cost to patient and infusion center
    - Hair to stay: philanthropic funds to offset costs
  - Cap fitting: precise fit is critical to success
    - New cap design from Dignitana allowing customized fit
  - For manual devices
    - Space considerations for center; need for assistance for patients to change caps
- Other issues
  - Failure rate with anthracyclines, individual patients
    - Better fitting caps?
    - Optimal post-cooling time?



HairToStay