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DRM04 for the Treatment of Primary Axillary Hyperhidrosis: Primary Results from the ATMOS-1 and ATMOS-2 Phase 3 Randomized Controlled Trials

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Disclosure of Relevant Relationships with Industry

- **D. Pariser:** Investigator and Consultant for Dermira, Inc.
- **A. Hebert:** Investigator and Consultant for Dermira, Inc.; Employee of the University of Texas Medical School, Houston, which received compensation from Dermira, Inc. for study participation.
- **A. Nast:** Employee of Charité – Universitätsmedizin Berlin, which received compensation from Dermira, Inc. for study participation.
- **W. P. Werschler:** Investigator and Consultant for Dermira, Inc.
- **S. Shideler:** Investigator for Dermira, Inc.
- **L. Green:** Investigator for Dermira, Inc.
- **H. Hofland:** Employee of Dermira, Inc.
- **J. Drew:** Employee of Dermira, Inc.
- **J. Quiring:** Biostatistical Consultant for Dermira, Inc.
- **D. A. Glaser:** Investigator and Consultant for Dermira, Inc.

Background and Objective

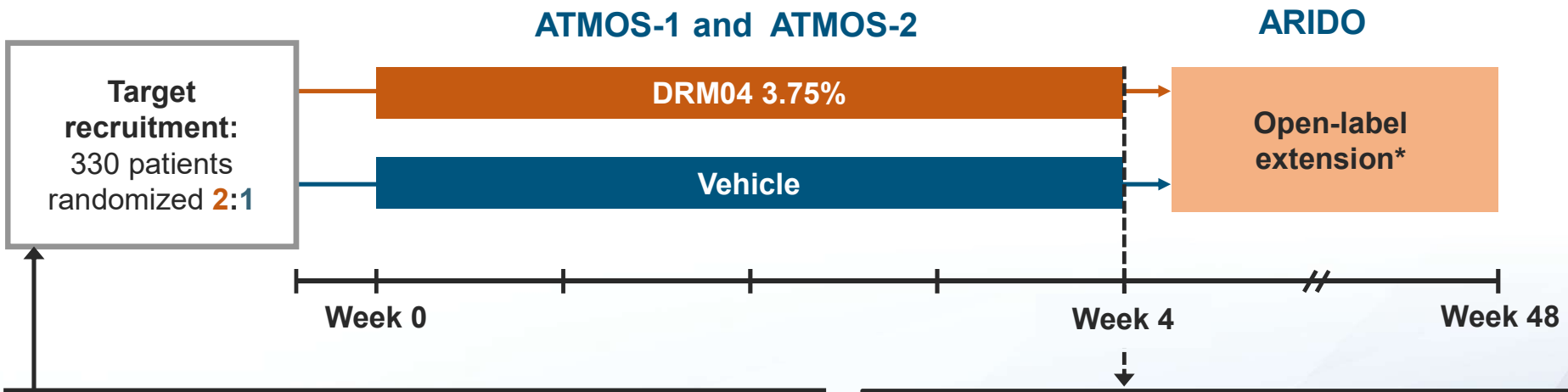
- Hyperhidrosis, which is excessive sweating beyond that physiologically required to maintain normal thermal regulation, affects an estimated 2.8% – 4.8% (7.8 – 15.3 million) of the US population.[1,2]
- The impact on quality of life is reported as comparable to, or greater than, psoriasis and eczema.[3]
- There are currently limited treatment options for patients suffering from hyperhidrosis.
- DRM04 is a cholinergic receptor antagonist developed for topical application for the treatment of primary axillary hyperhidrosis.

The **objective** of the phase 3, 4-week, double-blind, vehicle-controlled, randomized ATMOS-1 (NCT02530281) and ATMOS-2 (NCT02530294) studies was to evaluate the efficacy and safety of DRM04 in the treatment of primary axillary hyperhidrosis.

1. Strutton DR *et al.* J Am Acad Dermatol 2004;51(2):241–248; **2.** Doolittle J *et al.* Arch Dermatol Res 2016;308(10):743–749; **3.** Spalding JR *et al.* Value Health 2003;6(3):242.

ATMOS-1 and ATMOS-2 Study Design

- ATMOS-1 and ATMOS-2 were double-blind, vehicle-controlled, randomized, 4-week phase 3 trials.



Patients aged ≥9 years with primary axillary hyperhidrosis:

- ≥6 months duration
- Sweat production of ≥50 mg/5 min in each axilla
- ASDD score ≥4
- HDSS grade 3 or 4

Co-primary efficacy endpoints at Week 4:

- ASDD response (≥4-point improvement)
- Absolute change in axillary sweat production†

ASDD: Axillary Sweating Daily Diary; HDSS: Hyperhidrosis Disease Severity Scale. *Over 80% of patients completing ATMOS-1 or ATMOS-2 elected to enter the open-label extension. †Average of both axillae, measured gravimetrically.

ATMOS-1 and ATMOS-2 Study Criteria

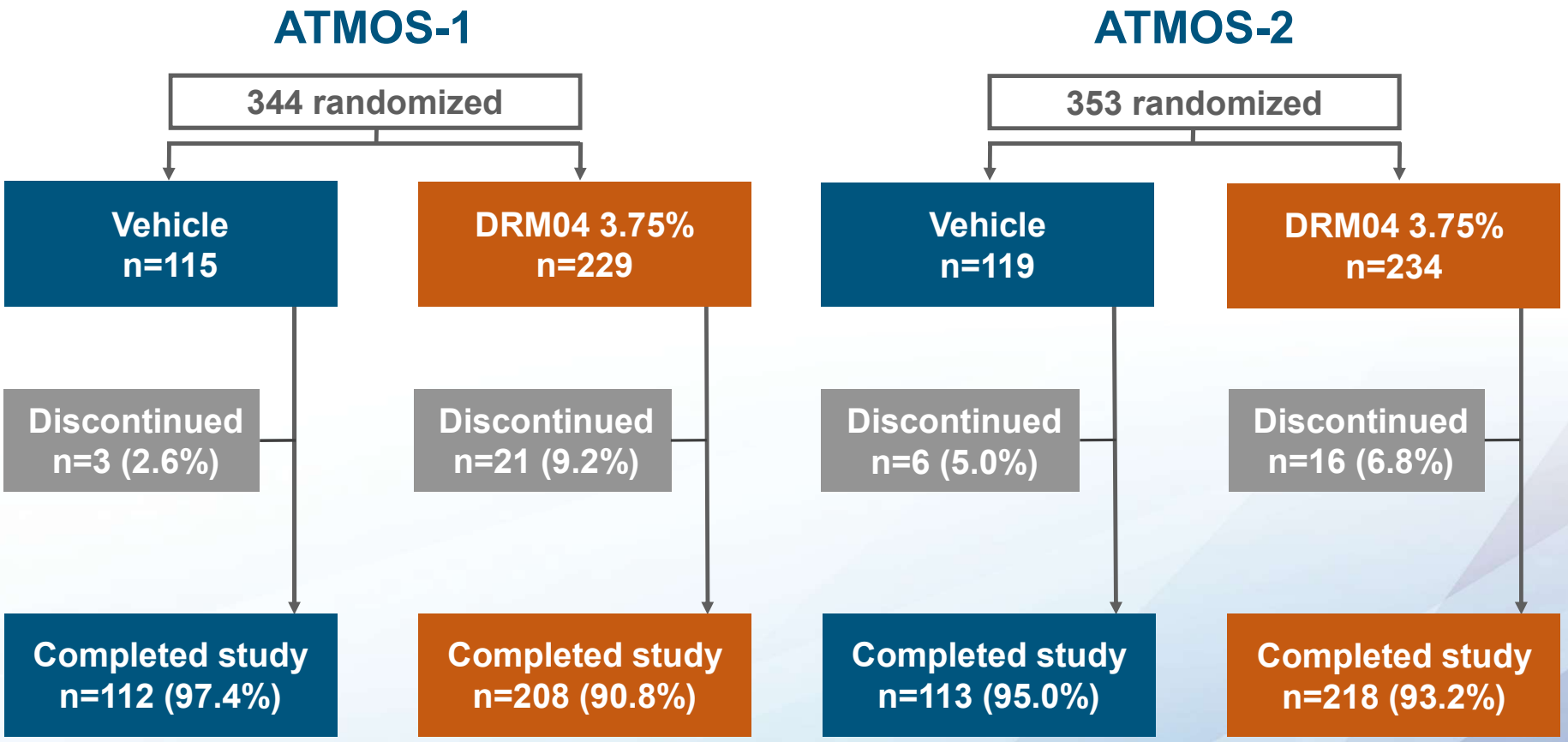
Key Inclusion Criteria

- Eligible patients, aged ≥9 years, were required to have primary axillary hyperhidrosis, defined as:
  - ≥6 months duration
  - Sweat production of ≥50 mg/5 min in each axilla, measured gravimetrically
  - Axillary Sweating Daily Diary (ASDD) score ≥4 on an 11-point scale
  - Hyperhidrosis Disease Severity Scale (HDSS) grade 3 or 4 on a 4-point scale

Key Exclusion Criteria

- Known history of a condition that could cause secondary hyperhidrosis
- Prior surgical procedure for hyperhidrosis
- Inadequate washout or discontinuation of any other hyperhidrosis product
- Other treatments having systemic anticholinergic activity or conditions which could be exacerbated by study medication

Patient Disposition



Baseline Patient Demographics and Disease Characteristics

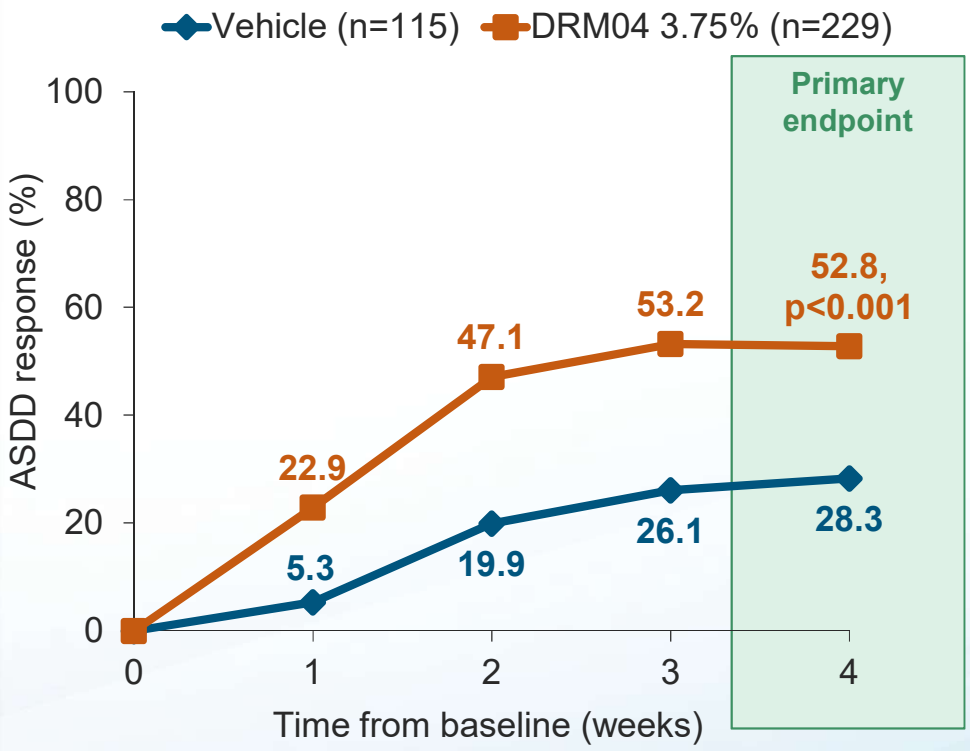
	ATMOS-1		ATMOS-2	
	Vehicle (n=115)	DRM04 (n=229)	Vehicle (n=119)	DRM04 (n=234)
Patient demographics				
Age, mean (SD) years	34.0 (13.1)	32.1 (11.2)	32.8 (11.2)	32.6 (10.9)
Gender, n (%) male	55 (47.8)	99 (43.2)	59 (49.6)	113 (48.3)
Race, n (%) white	94 (81.7)	182 (79.5)	102 (85.7)	192 (82.1)
BMI, mean (SD) kg/m^2	27.2 (4.9)	27.6 (5.8)	28.4 (5.5)	27.3 (5.0)
Disease characteristics				
Sweat production, mean (SD) mg/5 min	170.3 (164.2)	182.9 (266.9)	181.9 (160.1)	162.3 (149.5)
ASDD, mean (SD)	7.1 (1.7)	7.3 (1.6)	7.2 (1.6)	7.3 (1.6)
HDSS 3, n (%)	84 (73.0)	133 (58.1)	71 (59.7)	144 (61.5)
HDSS 4, n (%)	31 (27.0)	96 (41.9)	47 (39.5)	90 (38.5)

ASDD: Axillary Sweating Daily Diary; BMI: Body Mass Index; HDSS: Hyperhidrosis Disease Severity Scale; SD: standard deviation.

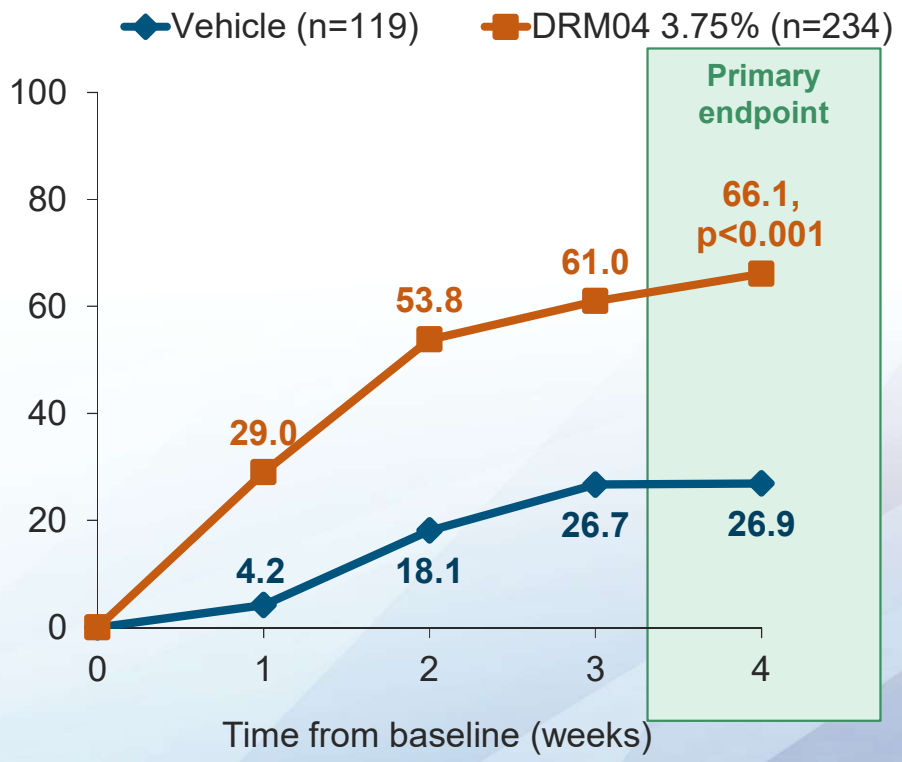
ASDD Response Rate (≥4-Point Improvement)

Co-Primary Endpoint (Week 4)

ATMOS-1



ATMOS-2



ASDD: Axillary Sweating Daily Diary. ITT population; MCMC multiple imputation; p-value calculated DRM04 vs vehicle using Cochran-Mantel-Haenszel test stratified by analysis center at Week 4.

Absolute Change in Sweat Production to Week 4

Co-Primary Endpoint (Week 4)

	ATMOS-1			ATMOS-2		
	Vehicle (n=115)	DRM04 (n=229)	p value	Vehicle (n=119)	DRM04 (n=234)	p value
Gravimetrically-Measured Sweat Production (mg/5 min)						
Week 1	-58.0	-75.5	–	-56.8	-108.0	–
Week 2	-71.5	-85.7	–	-86.0	-111.4	–
Week 3	-90.8	-88.9	–	-85.6	-110.3	–
Week 4 (co-primary endpoint)	-91.9	-104.9	p=0.065	-92.2	-110.3	p<0.001
Pre-specified sensitivity analysis excluding extreme outlier data*	-90.6 [n=110]	-96.2 [n=220]	p=0.001	–	–	–

MCMC multiple imputation; p-value calculated at primary endpoint (Week 4) DRM04 vs vehicle using ANCOVA model with treatment group and analysis center as factors and baseline sweat production as covariant.

*As outlined in the pre-specified statistical analysis plan, a sensitivity analysis was conducted that led to the exclusion of an analysis center with extreme outlier data for the gravimetric measurement of sweat. This analysis center consisted of 14 patients, of whom nine were treated with DRM04 and five received vehicle only.

Adverse Events During the 4-Week Trial

	ATMOS-1		ATMOS-2	
	Vehicle (n=114)	DRM04 (n=227)	Vehicle (n=118)	DRM04 (n=232)
Any TEAE, n (%)	33 (28.9)	123 (54.2)	42 (35.6)	134 (57.8)
Drug-related TEAE	18 (15.8)	77 (33.9)	20 (16.9)	102 (44.0)
TEAE by intensity				
Mild	22 (19.3)	79 (34.8)	31 (26.3)	91 (39.2)
Moderate	11 (9.6)	43 (18.9)	11 (9.3)	40 (17.2)
Severe	0	1 (0.4)	0	3 (1.3)
Discontinuations due to TEAE	1 (0.9)	8 (3.5)	0	9 (3.9)
Serious TEAE	0	1 (0.4)	0	1* (0.4)

* Considered not related to study drug.
Serious TEAE: ATMOS 1: Moderate unilateral mydriasis, considered related to study drug; ATMOS:2: Moderate dehydration, considered not related to study drug. TEAE: Treatment Emergent Adverse Events

Anticholinergic-Related Adverse Events During 4-Week Trial

	ATMOS-1		ATMOS-2	
	Vehicle (n=114)	DRM04 (n=227)	Vehicle (n=118)	DRM04 (n=232)
Any TEAE, n (%)	33 (28.9)	123 (54.2)	42 (35.6)	134 (57.8)
Anticholinergic-Related TEAE reported in >2% patients				
Dry mouth	4 (3.5)	43 (18.9)	9 (7.6)	68 (29.3)
Mydriasis	0	15 (6.6)	0	16 (6.9)
Urinary hesitation	0	5 (2.2)	0	11 (4.7)
Dry eye	0	2 (0.9)	1 (0.8)	9 (3.9)
Vision blurred	0	8 (3.5)	0	8 (3.4)
Nasal dryness	1 (0.9)	5 (2.2)	0	7 (3.0)
Constipation	0	4 (1.8)	0	5 (2.2)
Urinary retention	0	1 (0.4)	0	6 (2.6)

Table represents n (%) of patients experiencing one or more incidences of each TEAE (Treatment Emergent Adverse Event).

Conclusions

- Topically applied DRM04 demonstrated clinically meaningful improvements in disease severity and reductions in sweat production by Week 4, which were reported as early as Week 2.
- The majority of adverse events were related to anticholinergic activity and were mild, transitory, and rarely led to study discontinuation; daily application of DRM04 over a 4-week treatment period was well tolerated in patients with primary axillary hyperhidrosis.

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