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D3T01.1: Late Breaking News

DRM04 for the treatment of 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.

These studies are funded by Dermira, Inc.

Background

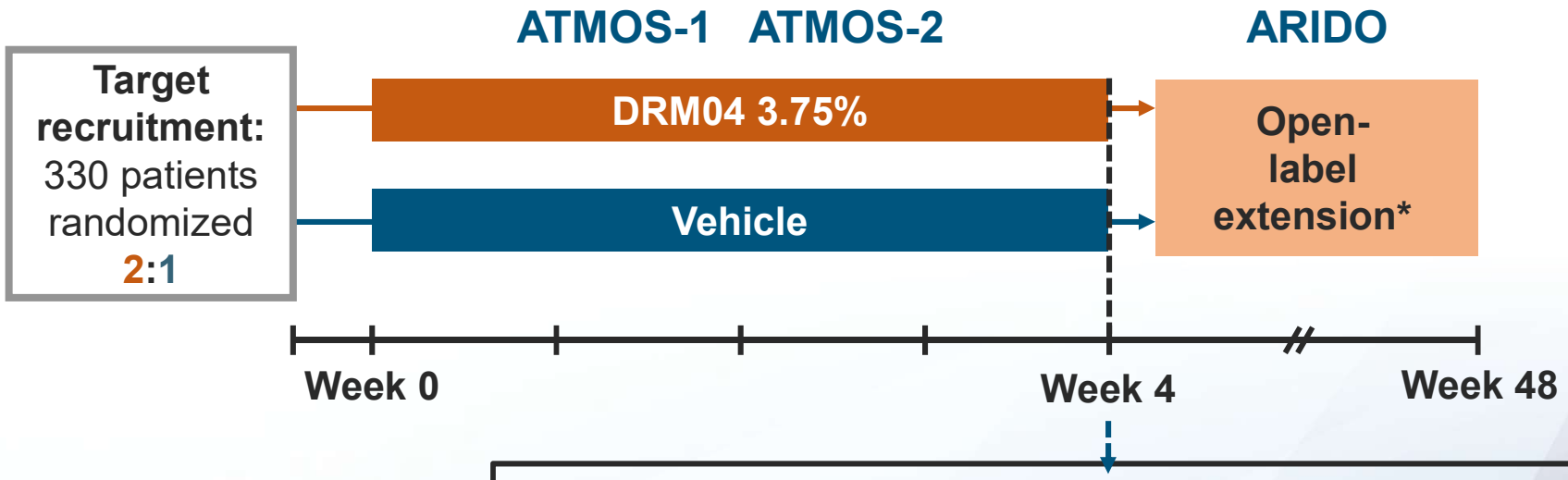
- Hyperhidrosis, which is excessive sweating beyond that physiologically required to maintain normal thermal regulation, affects an estimated 2.8% (7.8 million) of the US population.[1]
- The impact on quality of life is reported as comparable to, or greater than, psoriasis and eczema.[2]
- Currently there are 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.

Objective

[1.] Strutton DR. J Am Acad Dermatol. 2004; 51(2): 241–248; [2.] Spalding et al. Value in Health. 2003;6(3):242.

ATMOS-1 and ATMOS-2 Trial Design

OBJECTIVE: The efficacy and safety of DRM04 as a treatment of primary axillary hyperhidrosis was assessed in two parallel, randomized, double-blind, vehicle-controlled, Phase 3 trials (ATMOS-1 & ATMOS-2).



Co-primary efficacy endpoints at Week 4:

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

Other pre-specified efficacy endpoint at Week 4:

- DLQI change from baseline

ASDD: Axillary Sweating Daily Diary; DLQI: Dermatology Life Quality Index. *Over 80% of patients completing ATMOS-1 or ATMOS-2 elected to enter the open-label extension. †Average of both axillae, measured gravimetrically

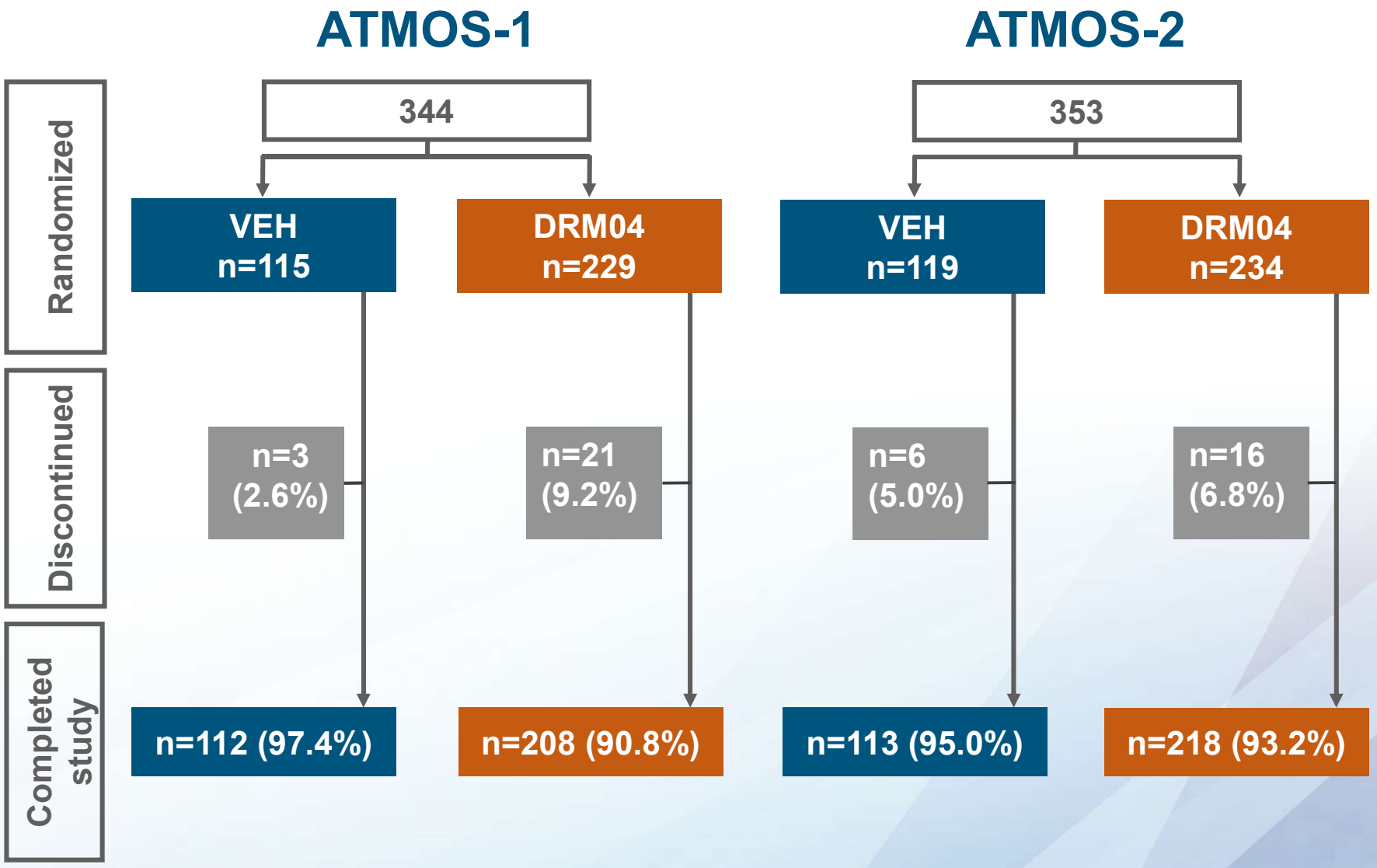
ATMOS-1 and ATMOS-2 Key Inclusion Criteria

- 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

ATMOS-1 and ATMOS-2 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

ATMOS-1 and ATMOS-2 Patient Disposition



VEH: Vehicle

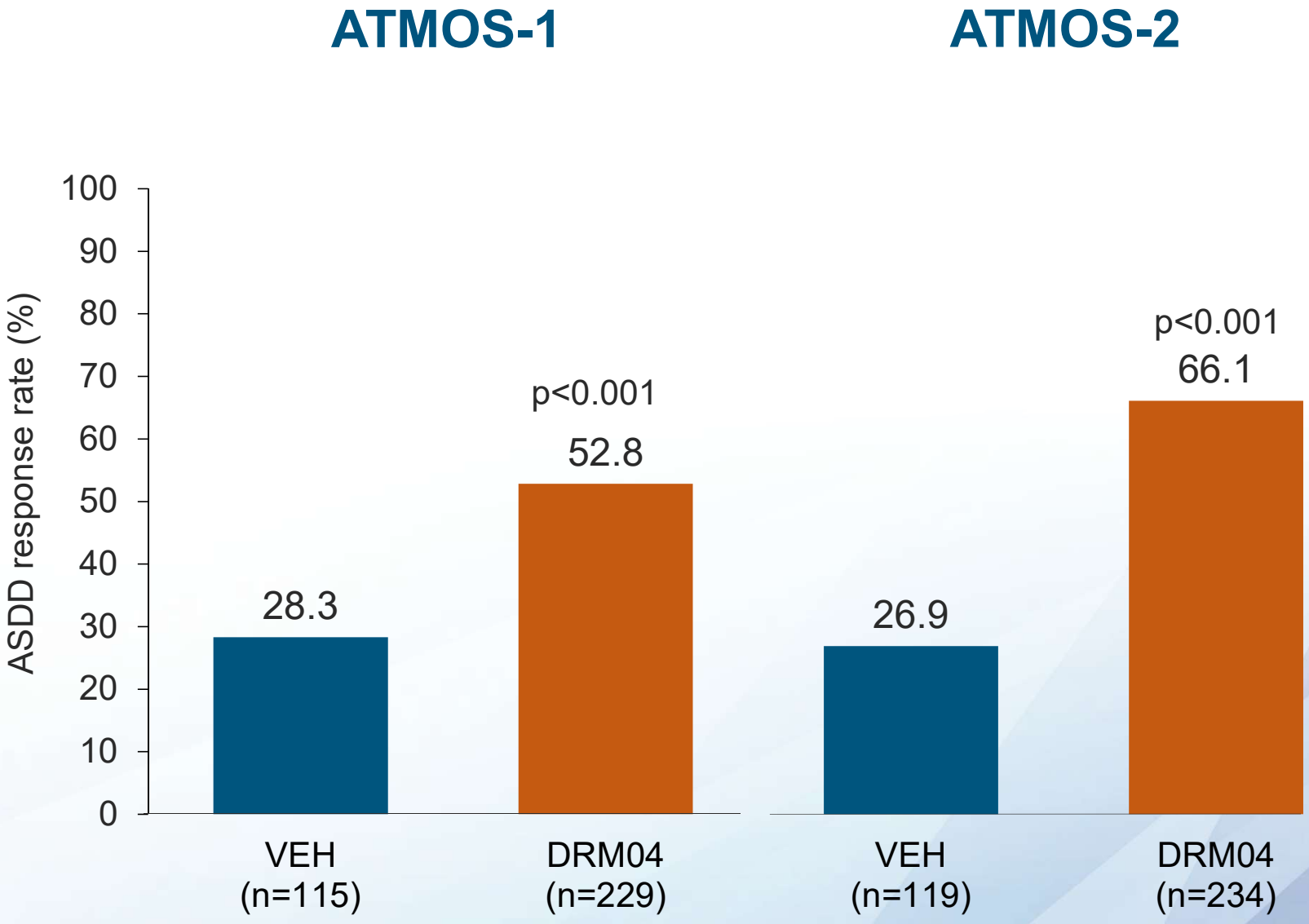
ATMOS-1 and ATMOS-2 Baseline Characteristics

	ATMOS-1		ATMOS-2	
	VEH (n=115)	DRM04 (n=229)	VEH (n=119)	DRM04 (n=234)
Patient demographics				
Age, mean (SD) years	34.0 (13.2)	32.1 (11.2)	32.8 (11.2)	32.6 (10.9)
Sex, 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; VEH: Vehicle

ASDD Response Rate (≥4-point Improvement) at Week 4

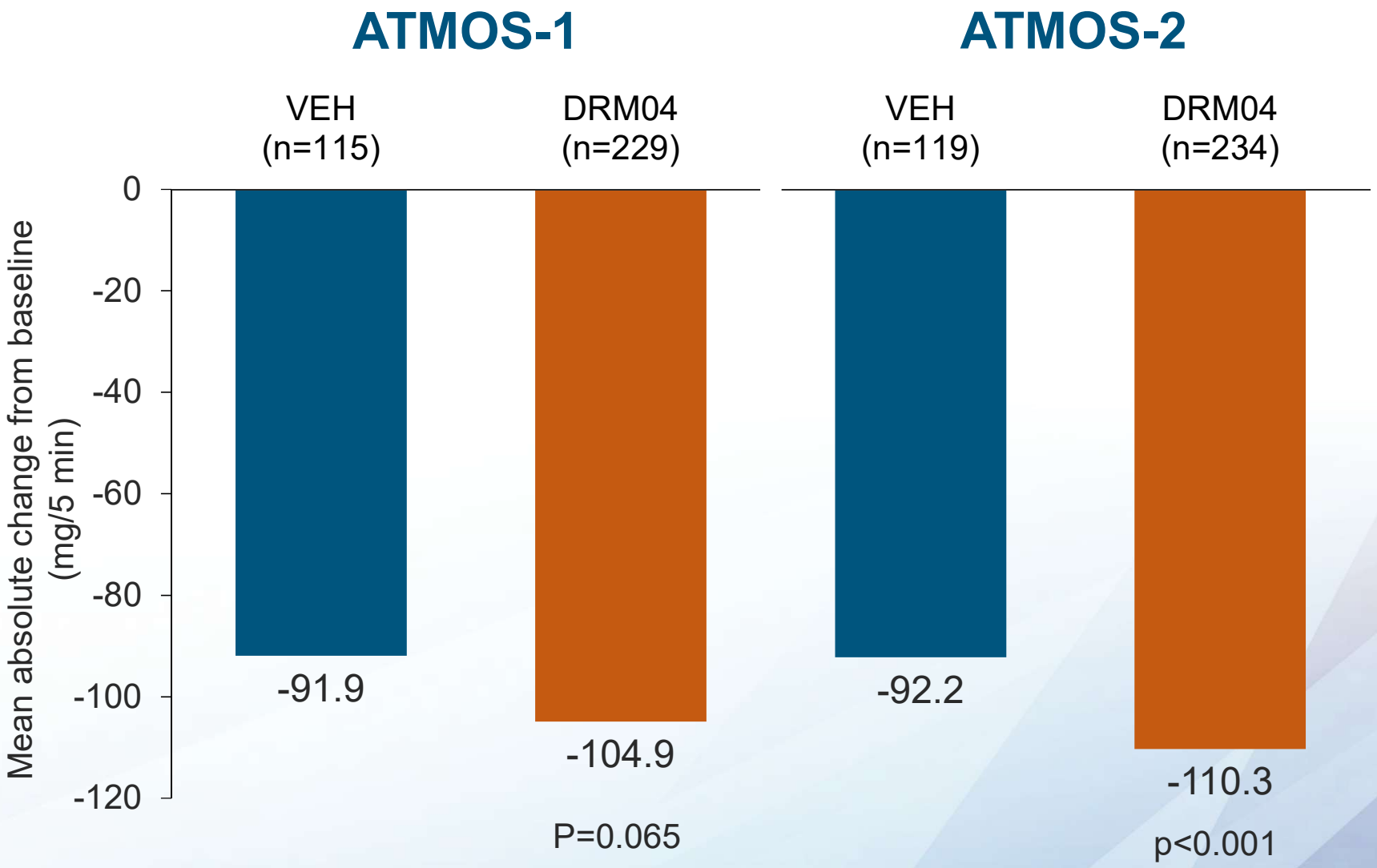
Primary Endpoint



ITT population; MCMC multiple imputation; p-value calculated DRM04 vs vehicle using Cochran-Mantel-Haenszel test stratified by analysis center; VEH: Vehicle

Absolute Change in Sweat Production at Week 4

Primary Endpoint

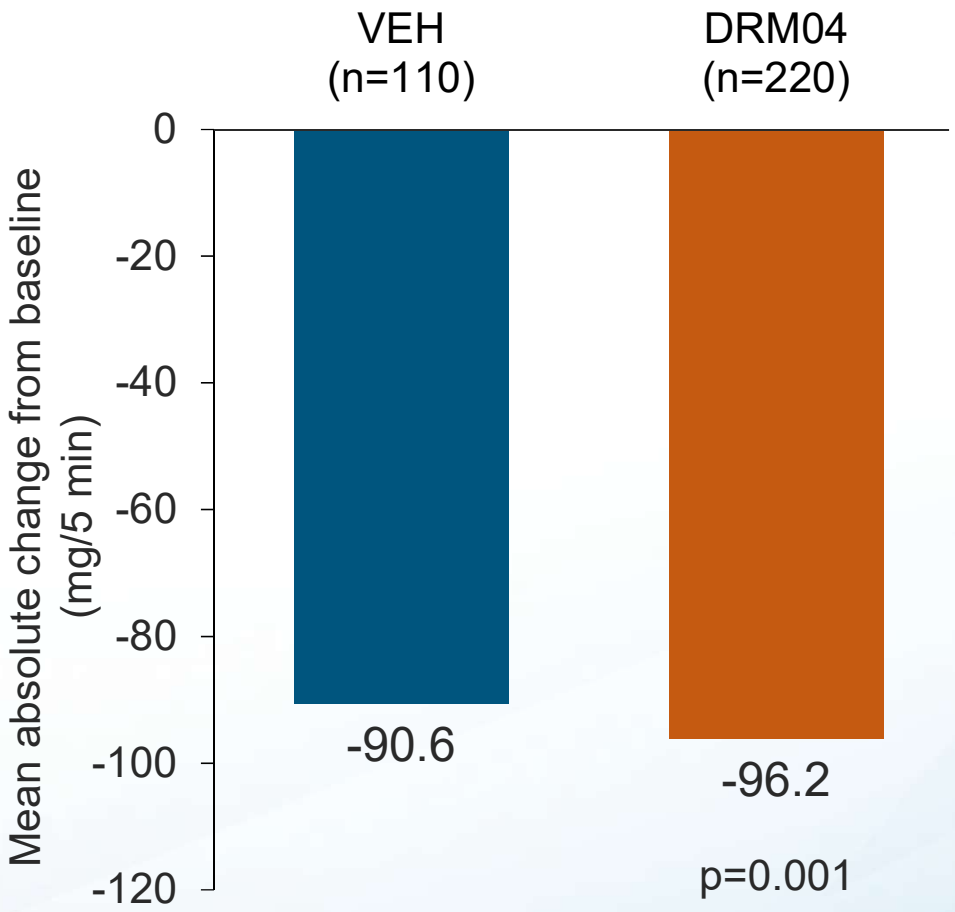


ITT population; MCMC multiple imputation; p-value calculated DRM04 vs vehicle using ANCOVA model with factors of treatment group and analysis center and a covariate of baseline gravimetrically-measured sweat production. ATMOS-1 analysis based on rank transformed data; VEH: Vehicle

Absolute Change in Sweat Production at Week 4

ATMOS-1 sensitivity analysis

ATMOS-1

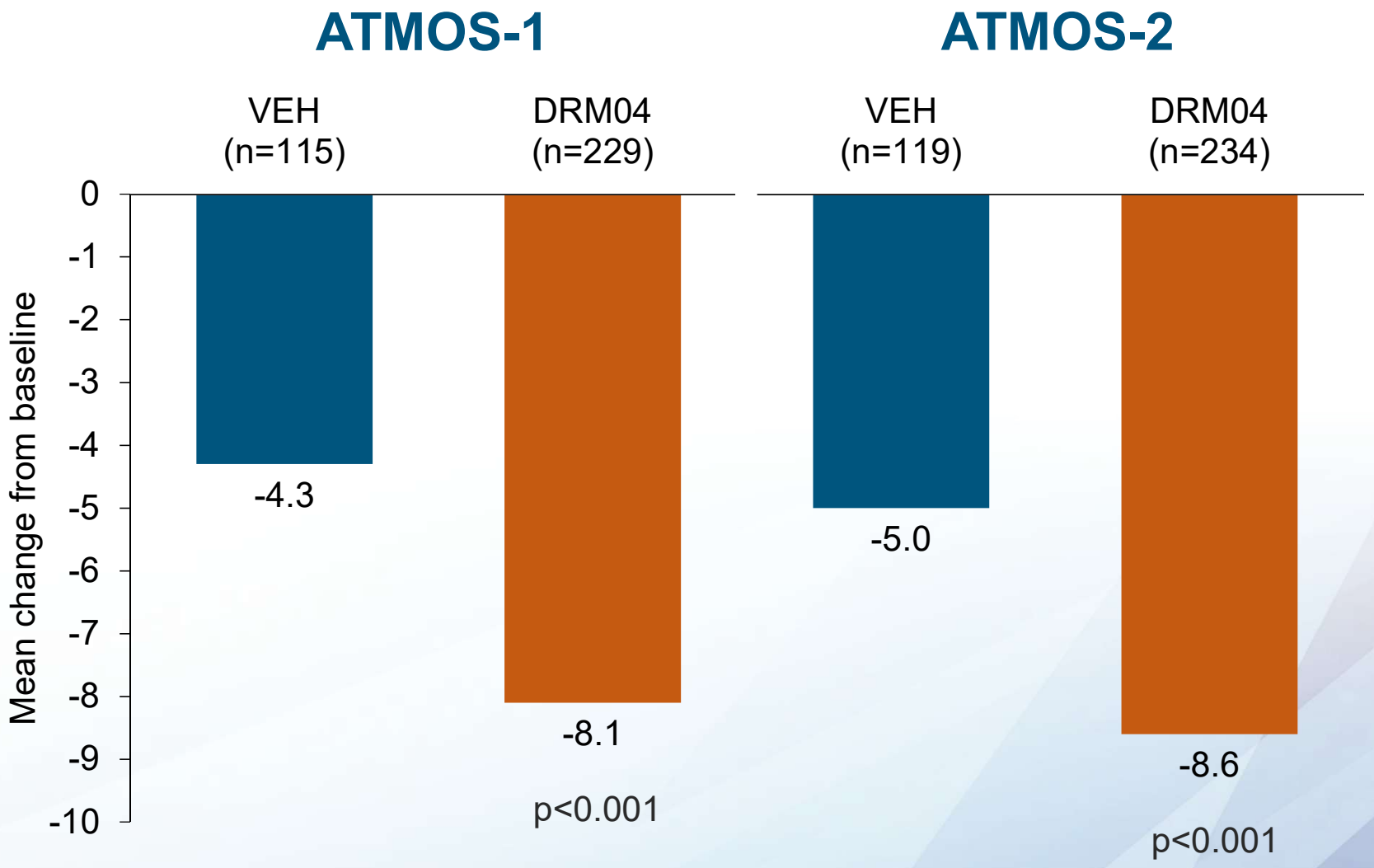


- As outlined in the pre-specified statistical analysis plan, a sensitivity analysis was conducted that led to the exclusion of an analysis center with extreme outlier data for the gravimetric measurement of sweat.
- The excluded analysis center consisted of 14 patients:
  - 9 DRM04 3.75%
  - 5 vehicle only

ITT population excluding analysis center with extreme outlier data; MCMC multiple imputation; p-value calculated DRM04 vs vehicle using ANCOVA model with factors of treatment group and analysis center and a covariate of baseline gravimetrically-measured sweat production; VEH: Vehicle

Change in DLQI from Baseline at Week 4

Other pre-specified efficacy endpoint



ITT population; no imputation for missing data; p-value calculated DRM04 vs vehicle using ANCOVA model with factors of treatment group and analysis center and a covariate of baseline DLQI score; VEH: Vehicle

ATMOS-1 and ATMOS-2 Adverse Events to Week 4
Summary

	ATMOS-1		ATMOS-2	
	VEH (n=114)	DRM04 (n=227)	VEH (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 TEAEs: 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; VEH: Vehicle

ATMOS-1 and ATMOS-2 Adverse Events to Week 4

Anticholinergic Related TEAE reported in >2% patients

	ATMOS-1		ATMOS-2	
	VEH (n=114)	DRM04 (n=227)	VEH (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

TEAE: Treatment Emergent Adverse Events; VEH: Vehicle

Conclusions

- Topically applied DRM04 demonstrated clinically meaningful improvements in disease severity and reductions in sweat production.
- A 4-week daily application of DRM04 was well-tolerated in patients with primary axillary hyperhidrosis.

Acknowledgments

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- All costs associated with the development of this presentation were funded by Dermira, Inc.

Back-up slides

ATMOS-1 and ATMOS-2 Prohibited Treatments

- The following medications and treatments were prohibited during the study:
  - Concomitant treatment for axillary hyperhidrosis (e.g. iontophoresis)
  - Non-prescription or prescription antiperspirants containing aluminum chloride or other metallic salts
  - Initiation of or change in dose of medications with topical or systemic anticholinergic effects, centrally acting alpha 2 adrenergic agonists (e.g. clonidine, guanabenz, methyldopa), or beta-blockers
  - IV, oral or topical glycopyrrolate treatment
  - Agents that promote axillary drying (e.g. powders)