

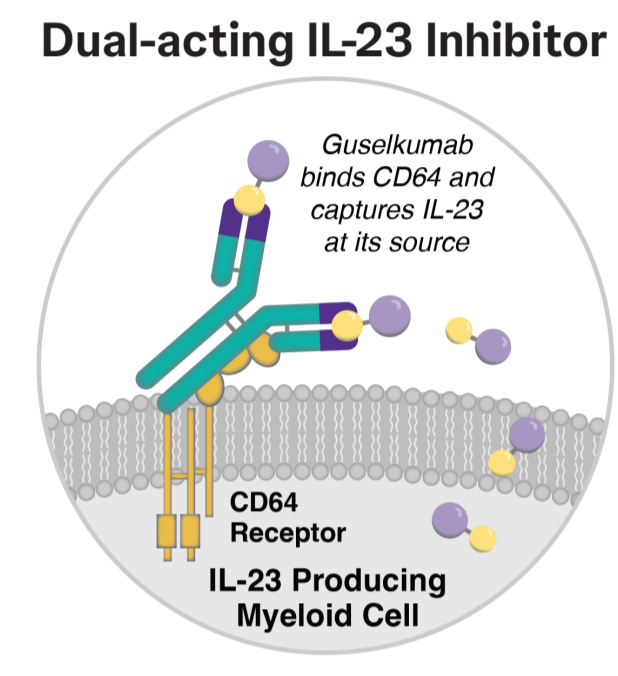
# Biological Sex-Related Differences in Radiographic Progression and Relationship with Early Clinical Response: Post Hoc Analysis of a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study in Biologic-Naïve Participants with Active Psoriatic Arthritis Treated with Guselkumab

Dafna D. Gladman<sup>1</sup>, Lihi Eder<sup>2</sup>, Carlo Selmi<sup>3,4</sup>, Philip J. Mease<sup>5,6</sup>, Alexis Ogdie<sup>7</sup>, Karissa Lozanski<sup>8</sup>, Mohamed Sharaf<sup>9</sup>, Emmanouil Rampakakis<sup>10,11</sup>, Laura Pina Vegas<sup>12,13</sup>, Laura C. Coates<sup>14</sup>

<sup>1</sup>Schroeder Arthritis Institute, Krembil Research Institute, University of Toronto, Toronto, ON, Canada; <sup>2</sup>University of Toronto and Women's College Hospital, Toronto, ON, Canada; <sup>3</sup>Rheumatology and Clinical Immunology, Humanitas Research Hospital, Rozzano Milan, Italy; <sup>4</sup>Department of Biomedical Sciences, Humanitas University, Milan, Italy; <sup>5</sup>Rheumatology Research, Providence Swedish Medical Center, Seattle, WA, USA; <sup>6</sup>University of Washington School of Medicine, Seattle, WA, USA; <sup>7</sup>University of Pennsylvania School of Medicine, Philadelphia, PA, USA; <sup>8</sup>Johnson & Johnson, Horsham, PA, USA; <sup>9</sup>Johnson & Johnson, Dubai, United Arab Emirates; <sup>10</sup>Department of Pediatrics, McGill University, Montreal, QC, Canada; <sup>11</sup>Scientific Affairs, JSS Medical Research, Inc, Montreal, QC, Canada; <sup>12</sup>Epidemiology in Dermatology and Evaluation of Therapeutics (EpiDermE), University Paris-Est Créteil Val de Marne, Créteil, France; <sup>13</sup>Rheumatology, Hospital Henri Mondor, AP-HP, Créteil, France; <sup>14</sup>Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Botnar Research Centre, Oxford, England, UK.

## Background

- Real-world studies show that women with psoriatic arthritis (PsA) have lower treatment response but less joint damage than males<sup>1-4</sup>
- Few randomized controlled trials (RCTs) in PsA report sex-disaggregated results
- Guselkumab (GUS) is a fully human, dual-acting, monoclonal antibody that selectively inhibits the interleukin (IL)-23p19 subunit<sup>5</sup> and is approved to treat moderate-to-severe plaque psoriasis (PsO), active PsA, and moderately-to-severely active Crohn's disease and ulcerative colitis<sup>6</sup>
- Pooled Phase 3 RCTs of GUS (DISCOVER-1 & -2, COSMOS) showed no sex-related differences in clinical response across PsA domains after adjusting for differences at baseline<sup>7</sup>
- GUS is the only selective IL-23i to significantly inhibit progression of structural damage in participants (pts) with active PsA
- DISCOVER-2 assessed radiographic progression in biologic-naïve pts with active PsA

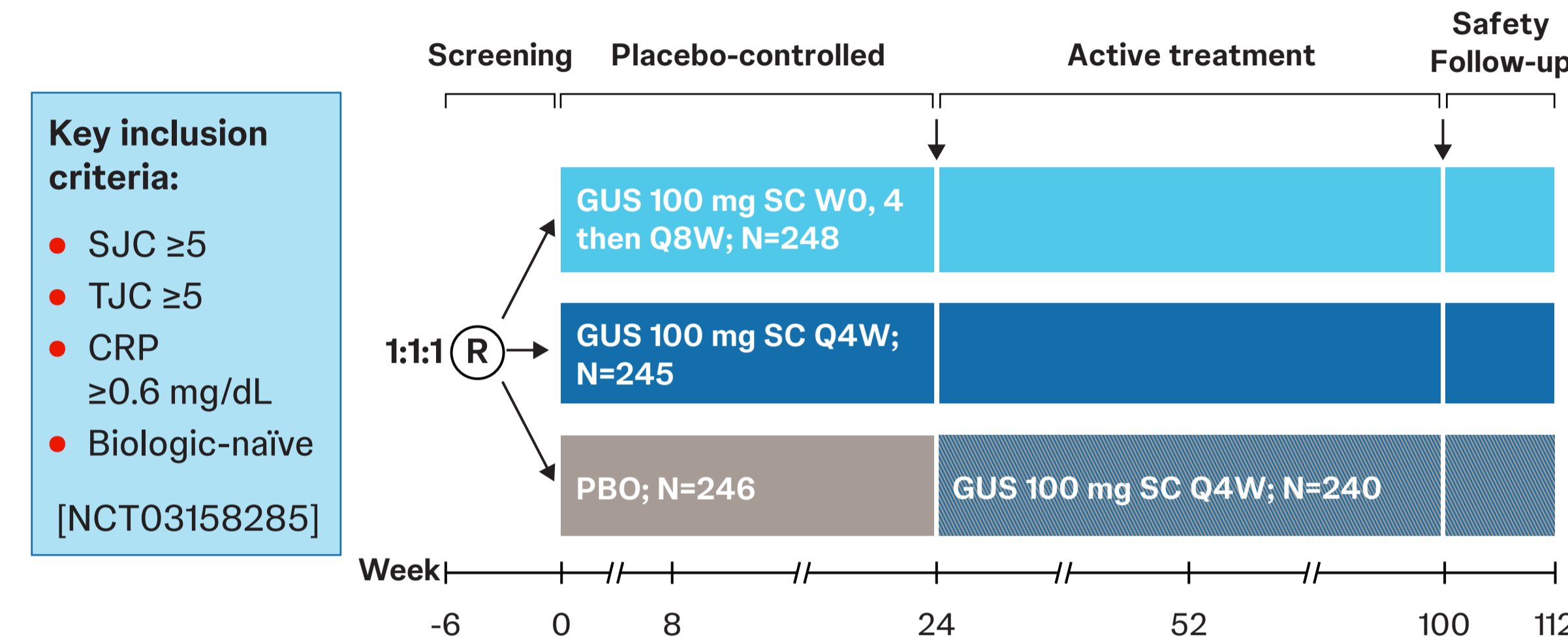


## Objective

- Conduct post-hoc analyses of DISCOVER-2 pts to determine:
- Sex-related differences in baseline characteristics
  - Relationship between sex and radiographic progression
  - Relationship between early improvement in joint manifestations and radiographic progression across sexes

## Methods

### DISCOVER-2 study design



### Key outcomes

- Total PsA-modified vdH-S score**
  - Measure of structural damage progression assessed by radiographs of hands and feet through W100
  - Sum of: Number and size of joint erosions (0-320) + Degree of joint space narrowing in the hands, wrist, and feet (0-208)
- cDAPSA score**
  - Composite measure of joint disease activity assessed at W8
  - Sum of: TJC (0-68) + SJC (0-66) + PtGA arthritis VAS (0-10 cm) + Pt pain VAS (0-10 cm)
  - cDAPSA LDA/REM: Score ≤13

cDAPSA=clinical Disease Activity Index for PsA, CRP=C-reactive protein, LDA=low disease activity, PBO=placebo, PtGA=patient global assessment, Q4W=every 4 weeks, Q8W=every 8 weeks, R=randomized, REM=remission, SC=subcutaneous, SJC=swollen joint count, TJC=tender joint count, VAS=visual analog scale, vdH-S=van der Heijde-Sharp, W=week.

### Impact of sex on radiographic progression in DISCOVER-2 pts with active PsA

Objective	Study Cohort	Analyses
<b>Baseline characteristics</b>		
1. Impact of sex	All pts	Continuous variables: 2-sample t-test Categorical variables: Chi-square test
<b>Radiographic progression via Total PsA-modified vdH-S score over W100</b>		
2. Impact of sex	GUS-treated pts	LSM change in <b>Males vs Females</b> via unadjusted and adjusted <sup>a</sup> MMRMs
3. Impact of early cDAPSA LDA/REM response <sup>b</sup> across sexes	GUS-treated pts	LSM change in <b>Males &amp; Females</b> via adjusted <sup>a</sup> MMRMs

<sup>a</sup>Adjusted for radiographic progression risk factors + baseline sex-related differences (age, PsA disease duration, BMI, CRP level, presence of dactylitis, non-biologic DMARD use, and baseline levels of outgones). <sup>b</sup>Among patients with baseline cDAPSA score >13. BMI=body mass index, DMARD=disease-modifying antirheumatic drugs, LSM=least squares mean, MMRM=multivariate mixed models for repeated measures.

## Key Takeaways

- In DISCOVER-2 biologic-naïve pts with established and active PsA:
  - Males had higher CRP and more prevalent dactylitis - both known risk factors of radiographic progression<sup>8,9</sup>
  - Males had higher rates of radiographic progression than females; impact of sex on radiographic progression was lower, but still significant, when adjusting for baseline sex disparities
  - Males exhibited a stronger relationship between early improvement in joint disease activity and lower rates of subsequent radiographic progression
- Timely and effective treatment is crucial to reduce radiographic progression sequelae
- Phase 3 APEX data provide additional support for GUS as the only selective IL-23i to significantly inhibit radiographic progression and, thus, its use in pts with active PsA at risk of structural damage progression (EULAR 2025 LB0010<sup>10</sup>)

## Results

### Baseline structural damage was similar, but CRP was higher, in male vs female pts

DISCOVER-2 Pt Characteristics at Baseline	Female (N=351)	Male (N=388)	All (N=739)
<b>Demographics</b>			
Age, yrs	46.3 (11.9)	45.1 (11.5)	45.7 (11.7)
Race, White/Asian	97%/3%*	99%/1%	98%/2%
BMI, kg/m <sup>2</sup>	29.5 (6.9)*	28.4 (5.4)	28.9 (6.2)
<b>Disease Characteristics</b>			
PsA disease duration, yrs	5.5 (5.9)	5.4 (5.5)	5.5 (5.7)
Total PsA modified vdH-S (0-528)	26.2 (43.1) <sup>b</sup>	25.5 (41.3) <sup>b</sup>	25.8 (42.1) <sup>b</sup>
CRP, mg/dL	1.6 (1.8)****	2.3 (2.8)	2.0 (2.4)

Nominal \*p<0.05, \*\*p<0.01, \*\*\*p<0.001, and \*\*\*\*p<0.0001 for males vs females. Data shown are mean (SD) unless otherwise indicated. \*N=305, \*\*N=359, \*\*\*N=664, \*\*\*\*N=664. SD=standard deviation.

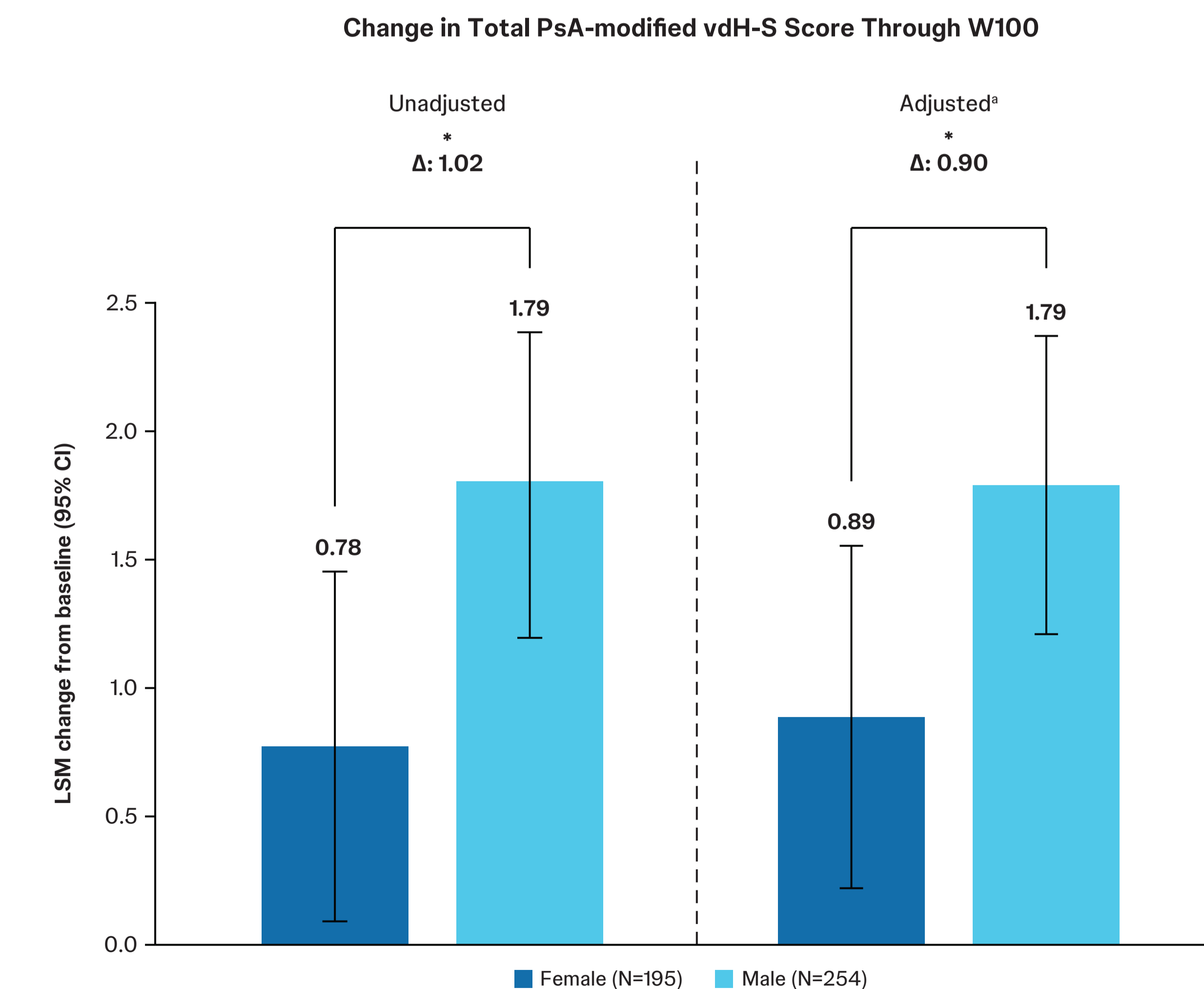
### Males had more severe PsO and more prevalent dactylitis; females reported greater fatigue and functional impairment

DISCOVER-2 Pt Characteristics at Baseline	Female (N=351)	Male (N=388)	All (N=739)
<b>Disease Characteristics</b>			
PASI (0-72)	7.5 (9.1)****	12.1 (12.3)	9.9 (11.1) <sup>b</sup>
Psoriatic BSA, %	13.7 (17.3)****	20.8 (22.4)	17.4 (20.4) <sup>d</sup>
cDAPSA (0-154)	46.1 (18.6)	46.4 (20.6)	46.3 (19.7)
Enthesitis <sup>e</sup>	71%*	66%	69% <sup>b</sup>
Dactylitis <sup>f</sup>	39%***	50%	45% <sup>b</sup>
<b>Patient-reported Outcomes</b>			
FACIT-Fatigue (0-52)	28.5 (9.6)****	30.9 (9.6)	29.7 (9.7) <sup>b</sup>
SF-36 PCS (0-100)	31.9 (7.3)***	33.6 (7.3)	32.8 (7.3) <sup>b</sup>
HAQ-DI (0-3)	1.4 (0.6)****	1.2 (0.6)	1.3 (0.6) <sup>b</sup>

Nominal \*p<0.05, \*\*p<0.01, \*\*\*p<0.001, and \*\*\*\*p<0.0001 for males vs females. Data shown are mean (SD) unless otherwise indicated. \*N=350, \*\*N=738, \*\*\*N=348, \*\*\*\*N=736. <sup>a</sup>Defined as LEI>0. <sup>b</sup>Defined by DSS>0. <sup>c</sup>BSA=body surface area, <sup>d</sup>DSS=Dactylitis Severity Score (0-60), <sup>e</sup>FACIT=Functional Assessment of Chronic Illness Therapy, <sup>f</sup>HAQ-DI=Health Assessment Questionnaire-Disability Index, <sup>g</sup>LEI=Leeds Enthesitis Index (0-6), <sup>h</sup>PASI=Psoriasis Area and Severity Index, <sup>i</sup>SF-36 PCS=36-Item Short Form Health Survey Physical Component Summary.

### Impact of sex: males showed higher rates of radiographic progression at 2 years

- Sex-related differences in radiographic progression were less prominent, but still significant, in adjusted models<sup>a</sup>

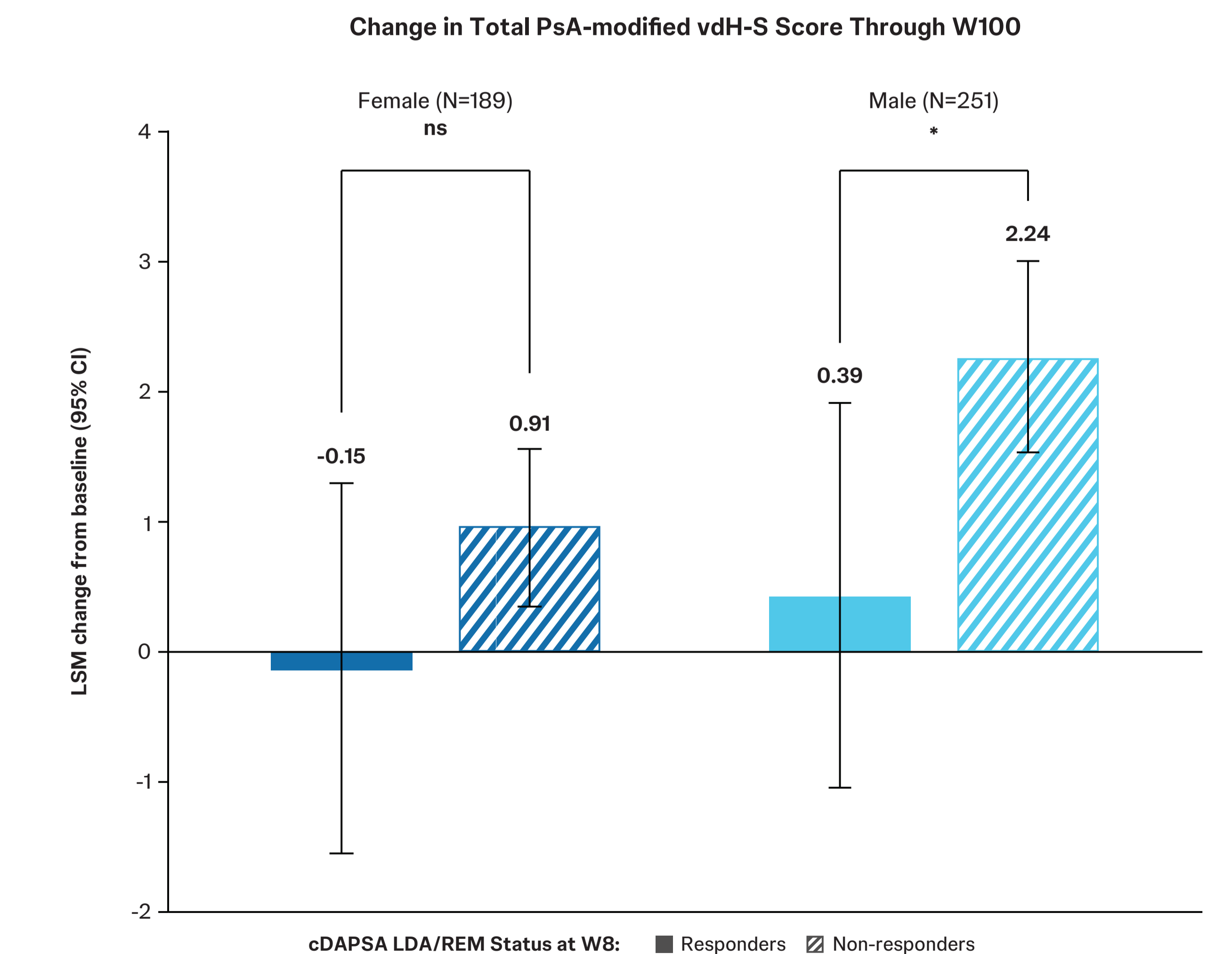


Nominal \*p<0.05 for males vs females.

<sup>a</sup>Adjusted for known radiographic progression risk factors and sex specific differences in baseline characteristics. CI=confidence interval.

### Across sexes, early (W8) cDAPSA responders had less radiographic progression through 2 years

- The relationship between early cDAPSA response and radiographic progression was stronger among males than females



Nominal \*p<0.05 for responders vs non-responders.

ns=not significant.