The tmj Next Generation™ Device

Roger Wixtrom, Ph.D., DABT

Presentation is sponsored by TMJ Health LLC and LifeLine Sciences LLC

My Background / Disclosures

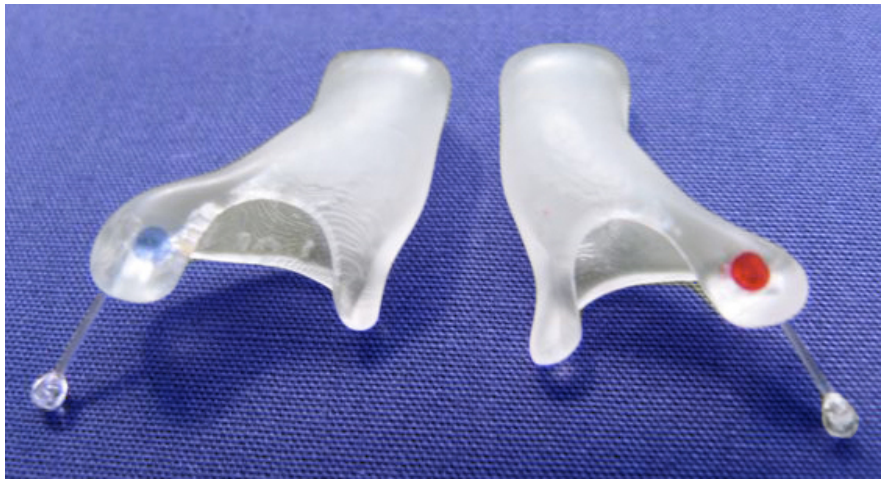
- Board-certified toxicologist
- >24 years experience evaluating the safety & clinical performance of medical devices
- Chief Scientific Officer for Ascentia Health, Inc. (developer of the device)
- Scientific Director of the Pivotal Clinical Trial for the TMJ NextGeneration™ Device
- Consultant to LifeLine Sciences LLC

Genesis of the TMJ NextGeneration™ Device

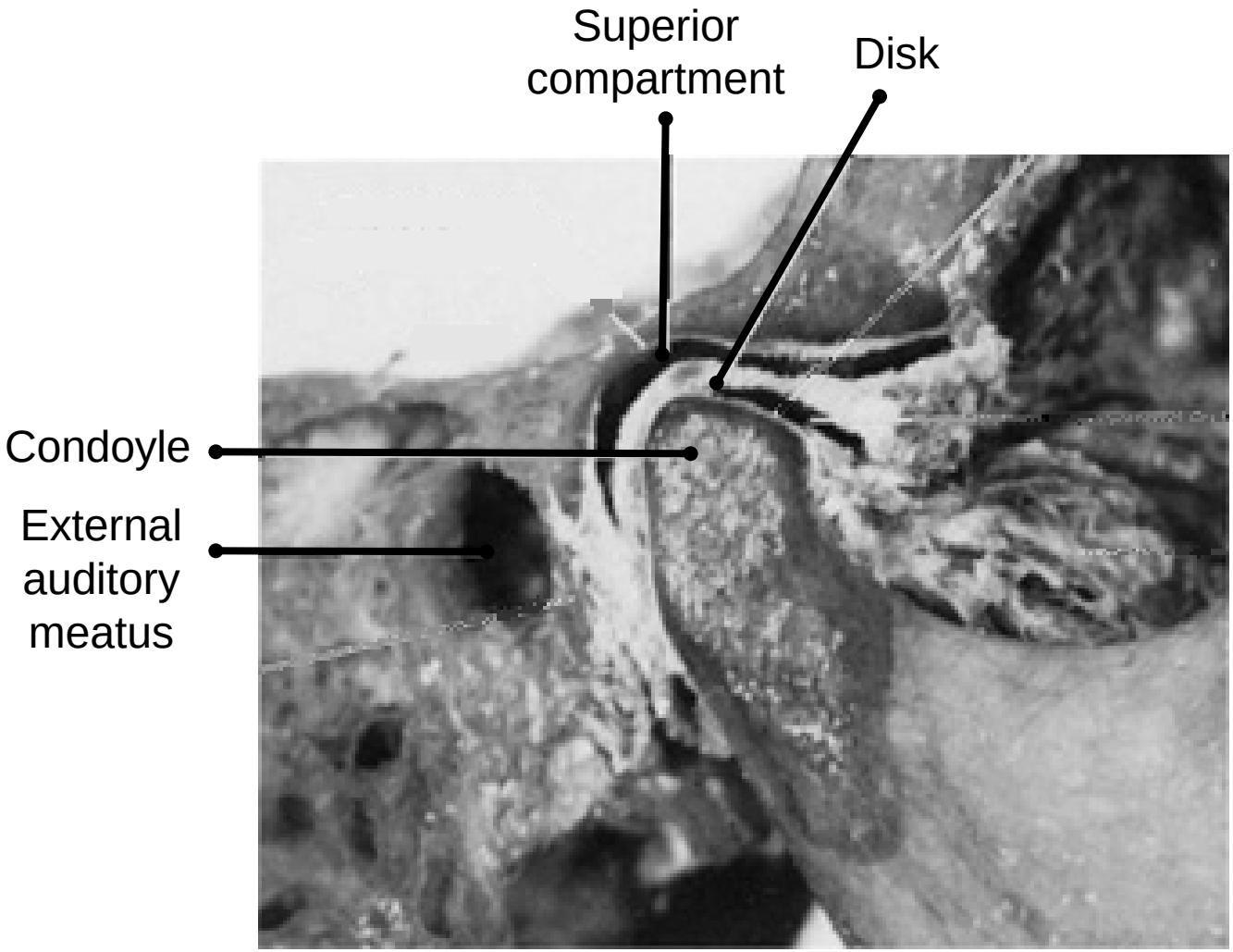
Device Description

The TMJ NextGeneration™ device provides an innovative and simple solution for TMD

- A pair of prosthetic devices, inserted in the ear canals, to reduce pain resulting from TMJ disorders
- Matches the shape of the ear canal when the jaw is in an open position
- Is hollow on the inside to permit the passage of sound
- Is made of a rigid material to retain the shape of the ear canal when inserted
- Supports the TMJ and associated secondary musculature to reduce strain in the TMJ area



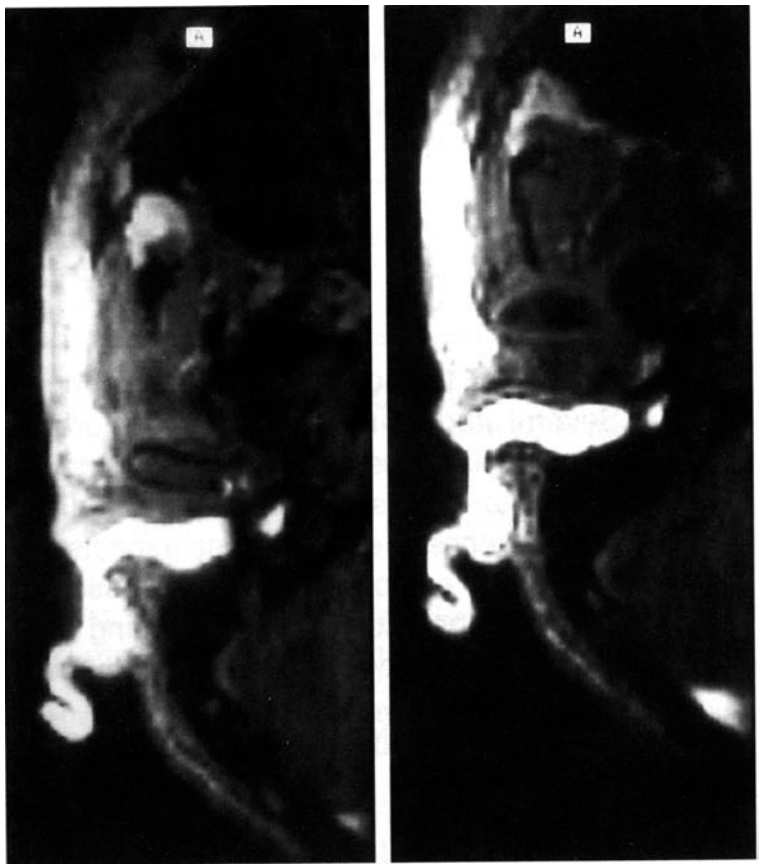
A Near Field Treatment Approach



Proximity of the ear canal to the Temperomandibular Joint

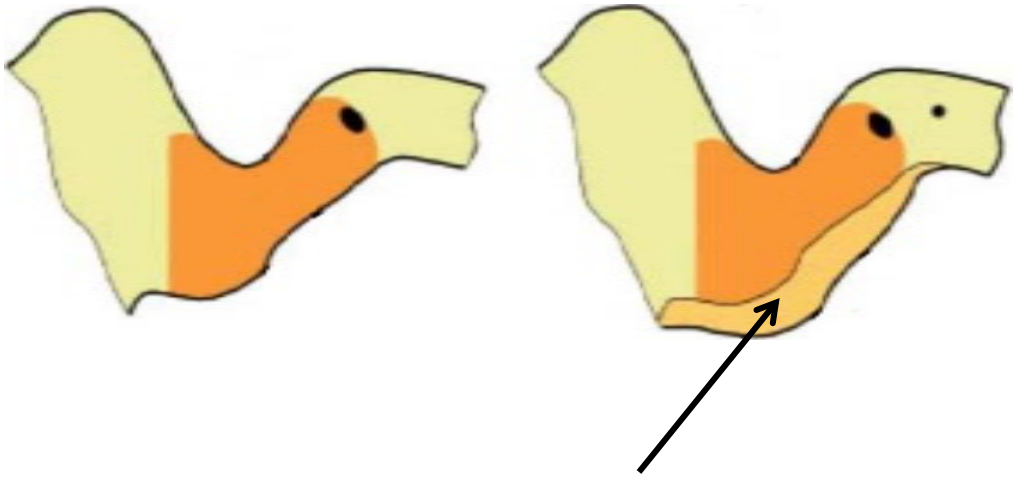
Mechanism of Action

The Dynamic Ear Canal



Jaw Closed Jaw Open

Jaw Closed Position Jaw Open Position



Ear Canal volume expansion with mouth open

Ear Canal volume changes of up to and greater than 20% can occur with jaw open [(1) (2)]

(1) Oliviera, R., Babcock, M., Venem, M., Hoeker, G., Parish, B., & Vasant, K. (2005). The dynamic ear canal and its implications: The problem may be the ear, and not the impression. The Hearing Review, 12(2),18-19, 82.

(2) Oliviera, R., Hammer, B., Stillman, A., Jons, C., Margolis, R., & Holm, J. (1992). A look at ear canal changes with jaw motion. Ear and Hearing, 13(6), 464-466

Clinical Studies Overview

TMD Prevalence & Impact

Quoted Information from OPPERA Study Publications
(Orofacial Pain Prospective Evaluation and Risk Assessment Study)

TMD Prevalence & Impact

- 5% of U.S. adults (6% women & 3% men) reported TMD-type pain in the 2002 National Health Interview Survey
- 10% of a representative sample of females in New York City had examiner-diagnosed TMD
- TMD results in an estimated 17,800,000 lost work days per year for every 100,000,000 working adults in the U.S.
- Multicenter Orofacial Pain Prospective Evaluation and Risk Assessment (OPPERA) study (NIH funded)
  - 2737 men & women (age 18-44)
  - followed for an average of 2.8 years
  - 260 (9.5%) developed TMJ disorders
  - Incidence rate of 4% per year

Maixner *et al.* 2011. Orofacial pain prospective evaluation and risk assessment study--the OPPERA study. *J. Pain* 12(11 Suppl):T4-11.

Slade *et al.* 2013. Summary of findings from the OPPERA prospective cohort study of incidence of first-onset temporomandibular disorder: Implications and future directions. *J. Pain* 14(12 Suppl 2):T116-T124.

Initial Into-Human Pilot Study

Initial Into-Human Pilot Study: Design

- Preliminary evaluation of TMJ NextGeneration™ Device safety & efficacy
- Conducted at U Penn School of Dentistry – Department of Oral Medicine
- Designed and carried out by two leading experts in the field
  - Martin S. Greenberg, DDS, FDS, RCS
    - Senior Editor and Co-author of Burket's Textbook of Oral Medicine
    - Samuel Charles Miller Award for Contributions to the Field of Oral Medicine
  - Thomas Sollecito, DMD
    - Past President of the American Academy of Oral Medicine
- Used 4 separate assessment measurement tools:
  - Visual Analog Scale (VAS)
  - Craniomandibular Index (CMI)
  - Symptom Severity Index (SSI)
  - North Carolina TMJ Scale
  - Pre-treatment screening phase (4wk), assessment at baseline, 1, 2 & 3 months

Assessment Tools for Assessing TMD (CMI & VAS)

Craniomandibular Index (CMI)

- validated method to evaluate the severity of TMD signs and symptoms
- obtained by trained study investigators
- CMI score is calculated from a dysfunction index (DI) and palpation index (PI)
  - DI calculated from the subject's mandibular movement, abnormal TMJ-related sounds, and TMJ palpation pain noted
  - PI obtained from intra-oral and extra-oral digital muscle palpation as well as digital neck palpation

Visual Analog Scale (VAS)

- a standardized, widely-used tool to measure subject perceived pain
- presented to subjects as a 100 mm scale on a continuum
- continuum of pain on the VAS ranges from "no pain" at 0 mm to "most severe pain" at 100 mm
- study subjects mark on the scale to report their pain level

Assessment Tools for Assessing TMD (SSI & TMJ Scale™)

Modified Symptom Severity Index Questionnaire (SSI)

- a method of determining the degree to which subjects perceive their TMD to be a problem
- SSI score is calculated by adding the various subjective parameters concerning the subject's symptoms and dividing by the number of symptoms queried
- encompasses questions relating to symptom intensity, affective intensity, tolerability, frequency and duration

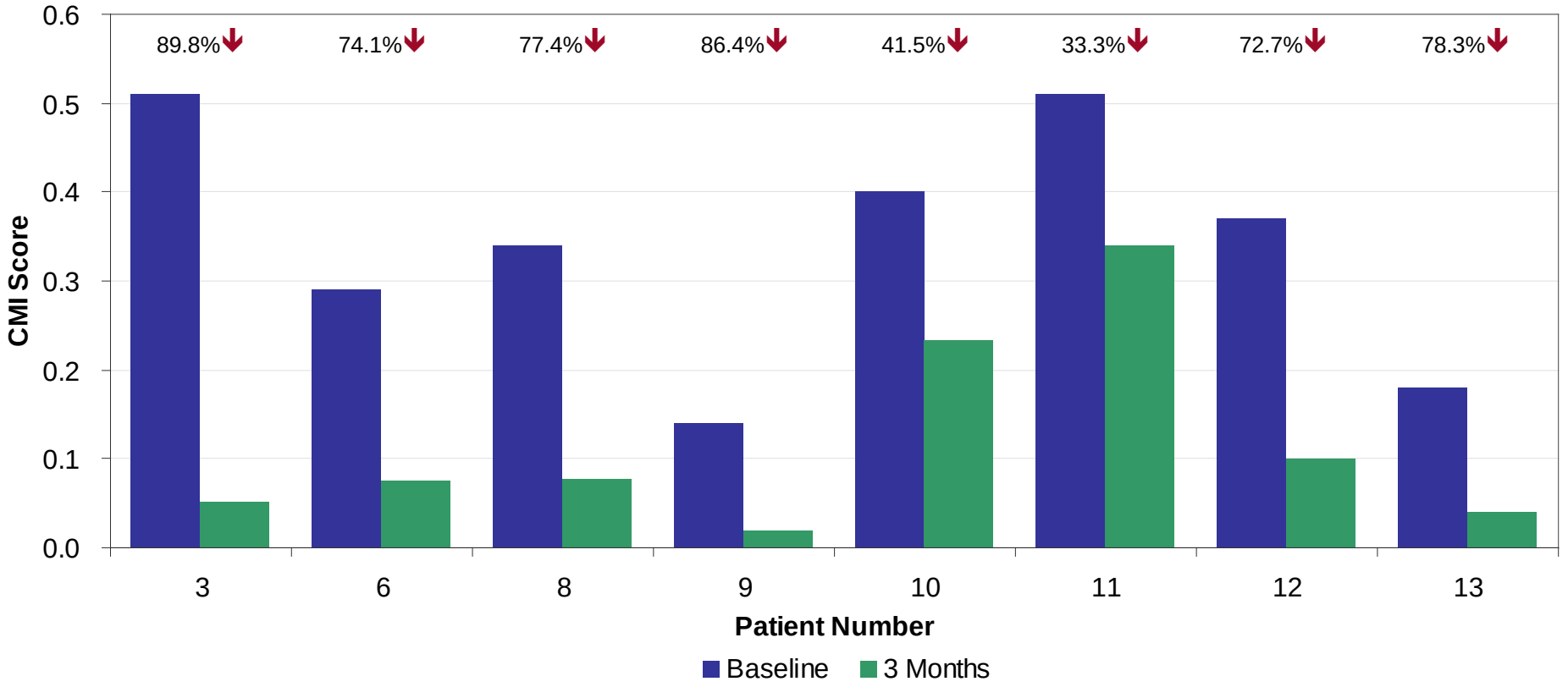
The TMJ Scale™

- a self-administered symptom inventory
- a standardized test that does not make specific diagnoses, but can assist in making diagnostic decisions
- formally accepted as an aid in diagnosing TMD by the American Dental Association
- validated and cross-validated with over 14,000 subjects across the U.S. and Canada

Initial Into-Human Pilot Study

Results

- Demonstrated TMJ NextGeneration™ *Device"led to an overall reduction of the pain and dysfunction of temporomandibular disorders"*
- Demonstrated TMJ NextGeneration™ Device had *"no significant impact on hearing sensitivity"*
- Indicated TMJ NextGeneration™ Device*"may be a safe, effective modality for the treatment of TMD"*



Definitive Clinical Trial

Definitive Clinical Trial
Design

- **Objectives**
  - Characterize the safety profile
  - Assess the effectiveness
- **Methodology**
  - Prospective, open-label, three-arm, randomized, unblinded clinical trial
  - Pre-treatment screening phase (including RDC-TMD classification), assessment at baseline visit and at 1, 2 & 3 months in treatment phase
  - Used same 4 TMD assessment measurement tools as pilot study
- **Study Center**
  - IMIC (Instituto Mexicano de Investigación Clinica)
  - Principal Investigator - Alejandro Tsuchiya Tavera, DDS
  - Certified & Approved by International Conference on Harmonization (ICH)
  - Full Implementation of Good Clinical Practice (GCP) Guidelines
  - At least seven clinical studies listed in the NIH ClinicalTrials.gov registry

Evidence-Based Medicine:

Evidence Rating Scale for Therapeutic Studies

Level 1 – *High-quality, multicenter or single-center, randomized controlled trial with adequate power; or systematic review of these studies*

Level 2 – *Lesser-quality, randomized controlled trial; prospective cohort or comparative study; or systematic review of these studies*

Level 3 – *Retrospective cohort or comparative study; case-control study; or systematic review of these studies*

Level 4 – *Case series with pre/post test or only post test*

Level 5 – *Expert opinion developed via consensus process; case report or clinical example; or evidence based on physiology, bench research, or "first principles"*

Source: Sullivan, D., K.C. Chung and F.F. Eaves III. 2011. The Level of Evidence Pyramid: Indicating Levels of Evidence in Plastic and Reconstructive Surgery Articles. *Plast. Reconstr. Surg.* 128(1):311-314.

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Definitive Clinical Trial
Design

- **Duration of Treatment**
  - 3 months

- **Comparison Treatments**

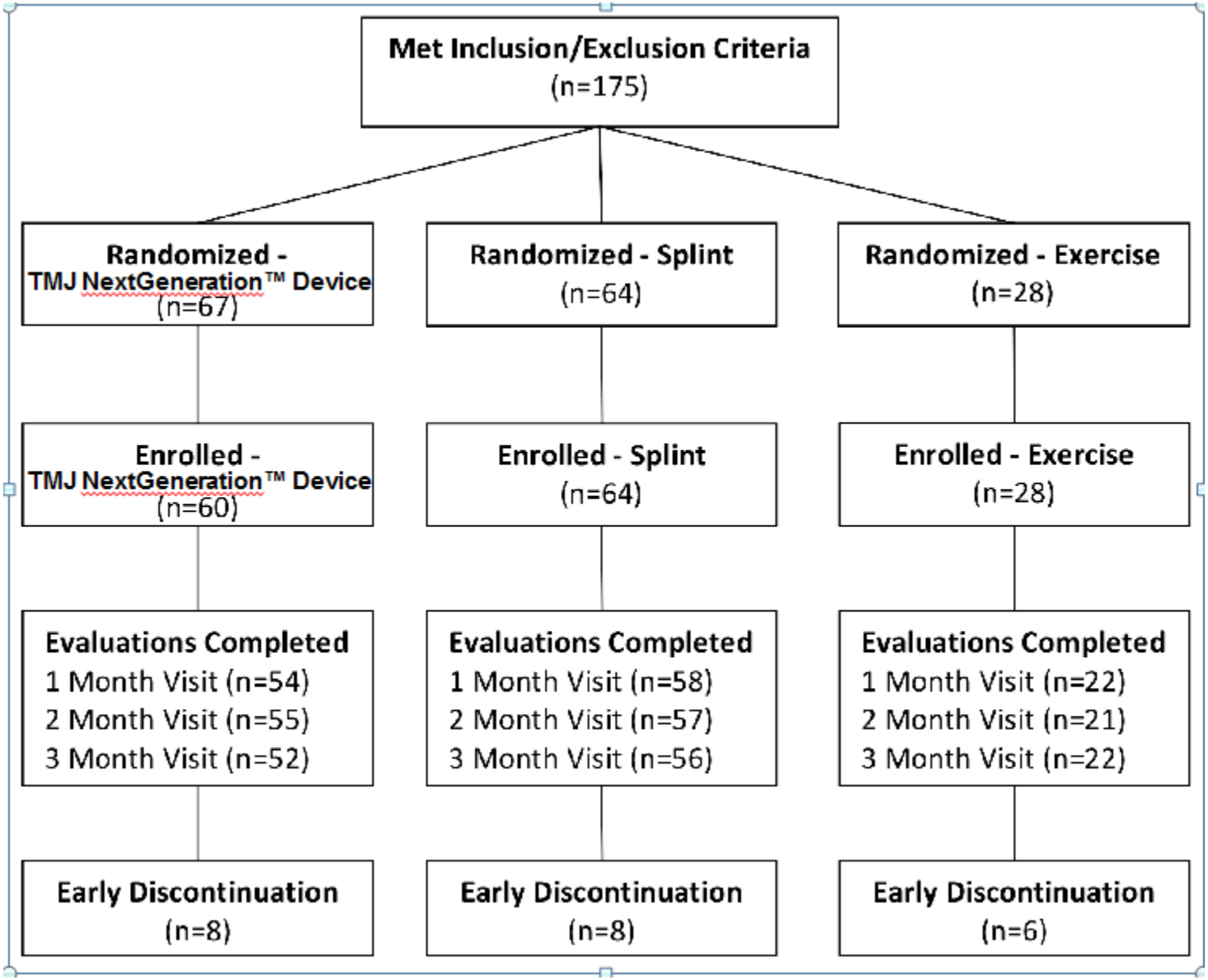
  1) Stabilization splint

  2) Jaw exercise regimen

- **Evaluation Criteria**
  - Primary Efficacy: Non-inferiority of TMJ NextGeneration™ Device to stabilization splint in the reduction of the Craniomandibular Index (CMI) score from baseline to 3 months
  - Primary Safety: Characterize the safety profile of the TMJ NextGeneration™ Device by collecting and reporting study-related adverse events

Definitive Clinical Trial

Disposition of Study Subjects



Definitive Clinical Trial Results

Non-Inferiority of TMJ NextGeneration™ Device to Splint

Non-Inferiority of TMJ NextGeneration™ Device to Splint in 3 months CMI / SSI / VAS reduction

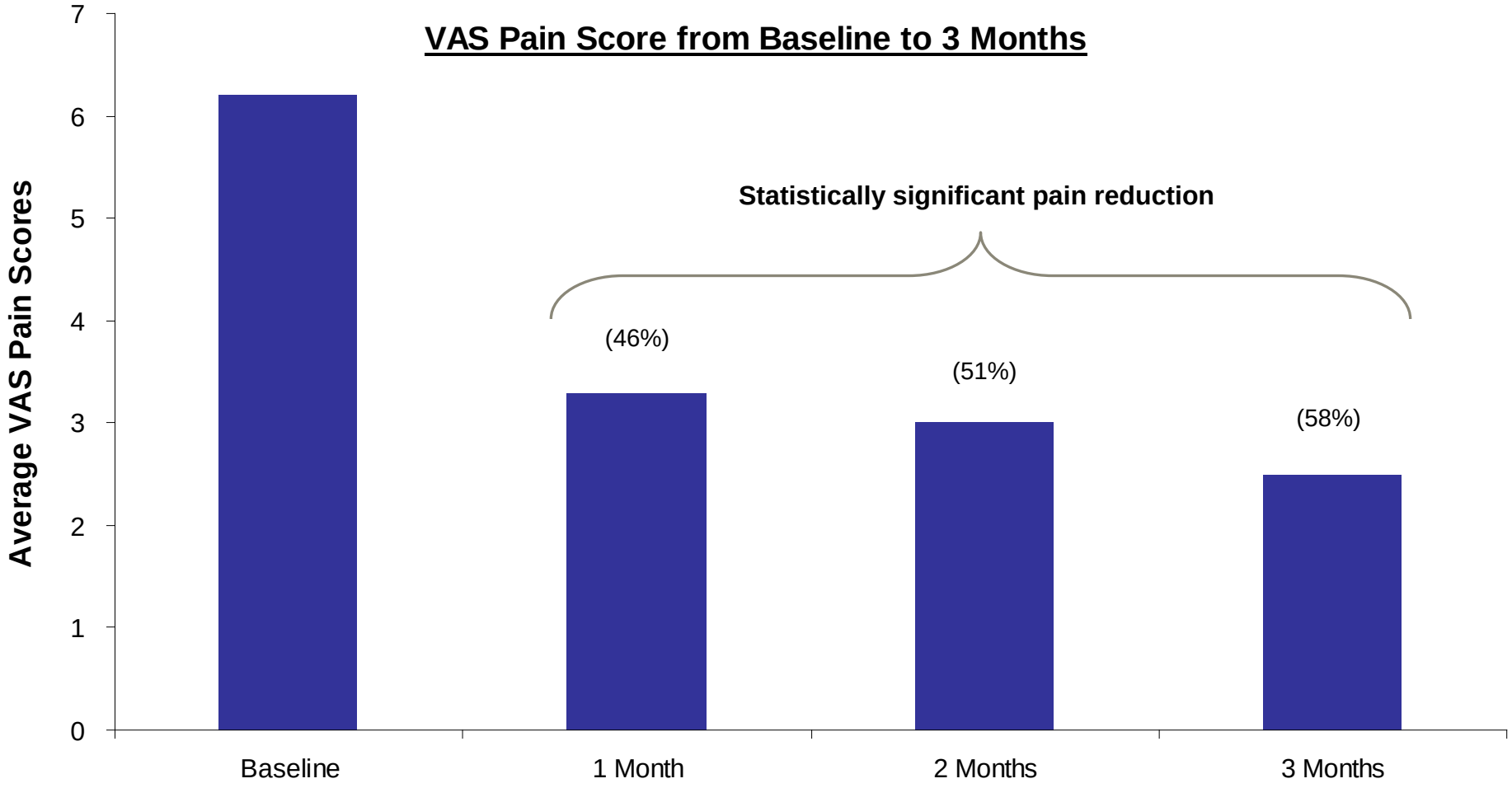
	CMI		SSI		VAS (in-office)	
	TMJ Next Generation™ Device (N = 60)	Splint (N = 64)	TMJ Next Generation™ Device (N = 60)	Splint (N = 64)	TMJ Next Generation™ Device (N = 60)	Splint (N = 64)
Unadjusted Mean Reduction	-0.227 ± 0.207 (52)	-0.196 ± 0.152 (56)	-0.383 ± 0.245 (52)	-0.278 ± 0.214 (56)	-3.60 ± 3.05 (52)	-2.90 ± 2.26 (52)
Least Square Means	-0.2392	-0.2055	-0.4058	-0.2381	-3.81	-2.44
Pain Reduction Ratio of TMJ NextGeneration™ Device to Splint (1)	1.16		1.70		1.56	
p-value	0.0096		<0.0001		<0.0001	

(1) Acceptable lower bound for TMJ Next Generation / Splint is 0.80.

Definitive Clinical Trial Results

TMJ NextGeneration™ Device Reduction in VAS Pain Score

TMJ NextGeneration™ Device produced statistically significant TMD pain reduction within the first month that lasted through the duration of the study

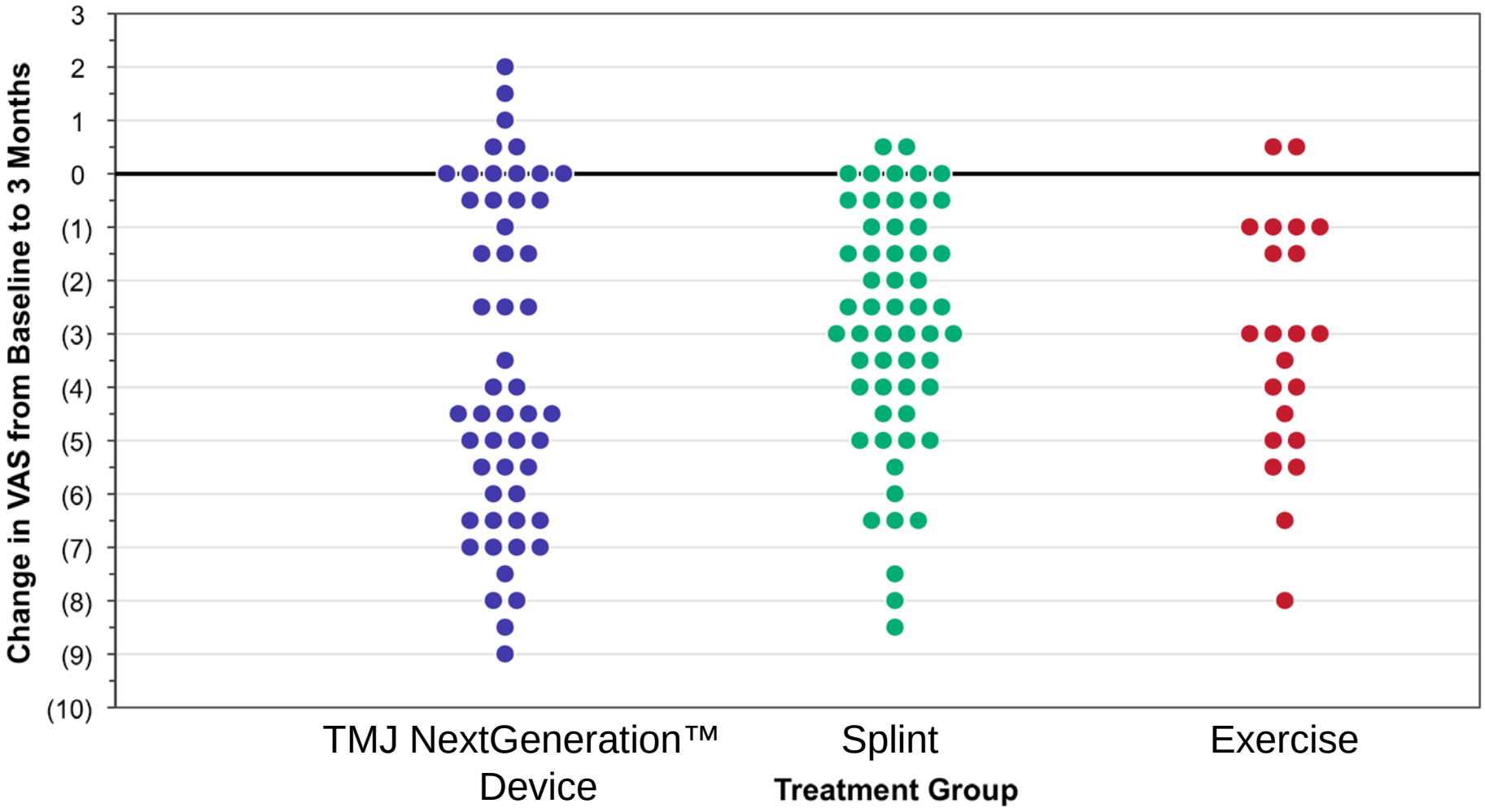


VAS scores range from 0 (no pain) to 10 (worst pain imaginable)

Definitive Clinical Trial Results

Comparative Reduction in VAS Pain Score

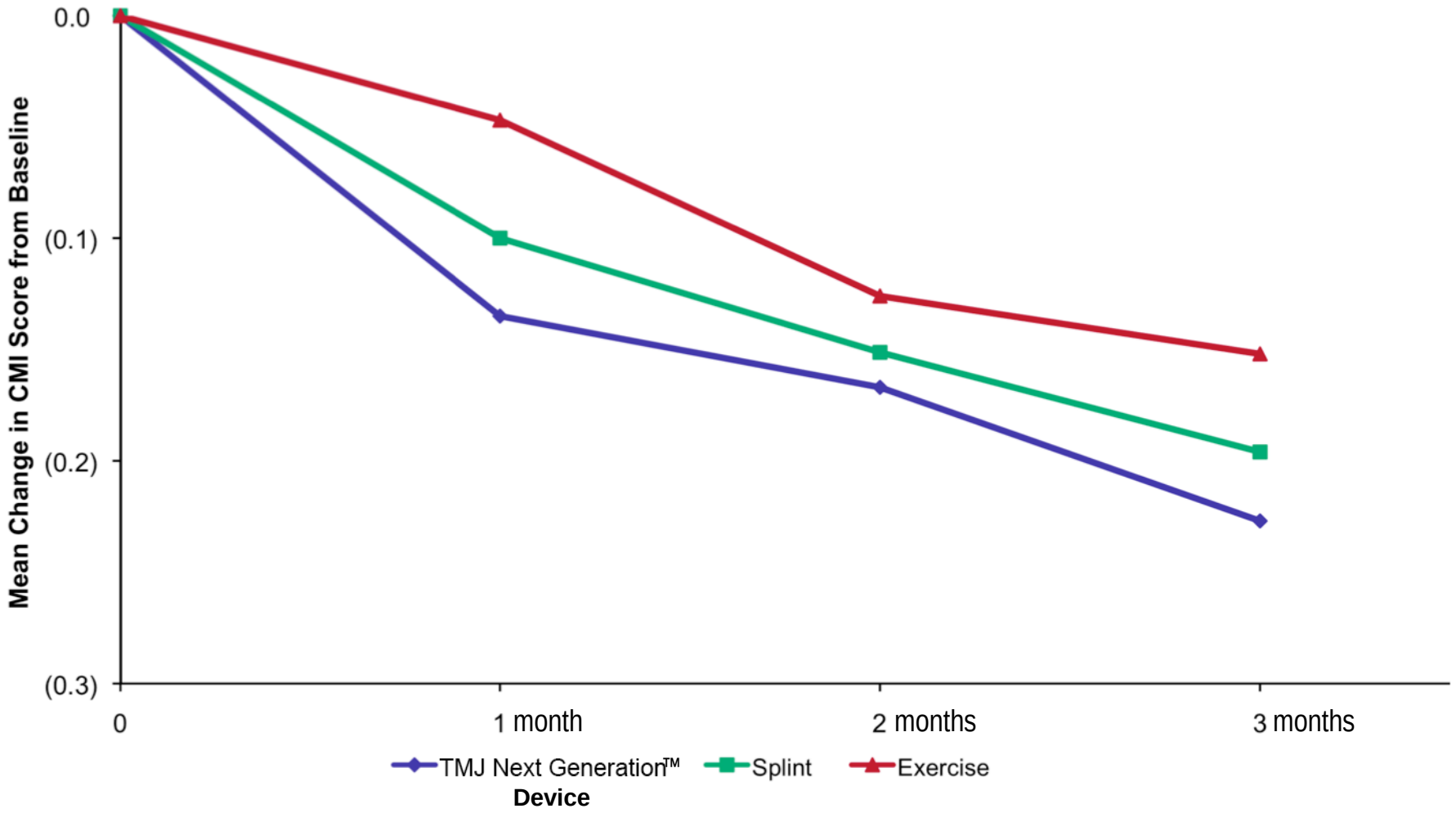
TMJ NextGeneration™ Device shows a trend towards greater magnitude of pain reduction among responders



Definitive Clinical Trial Results

Mean Change in CMI Scores From Baseline

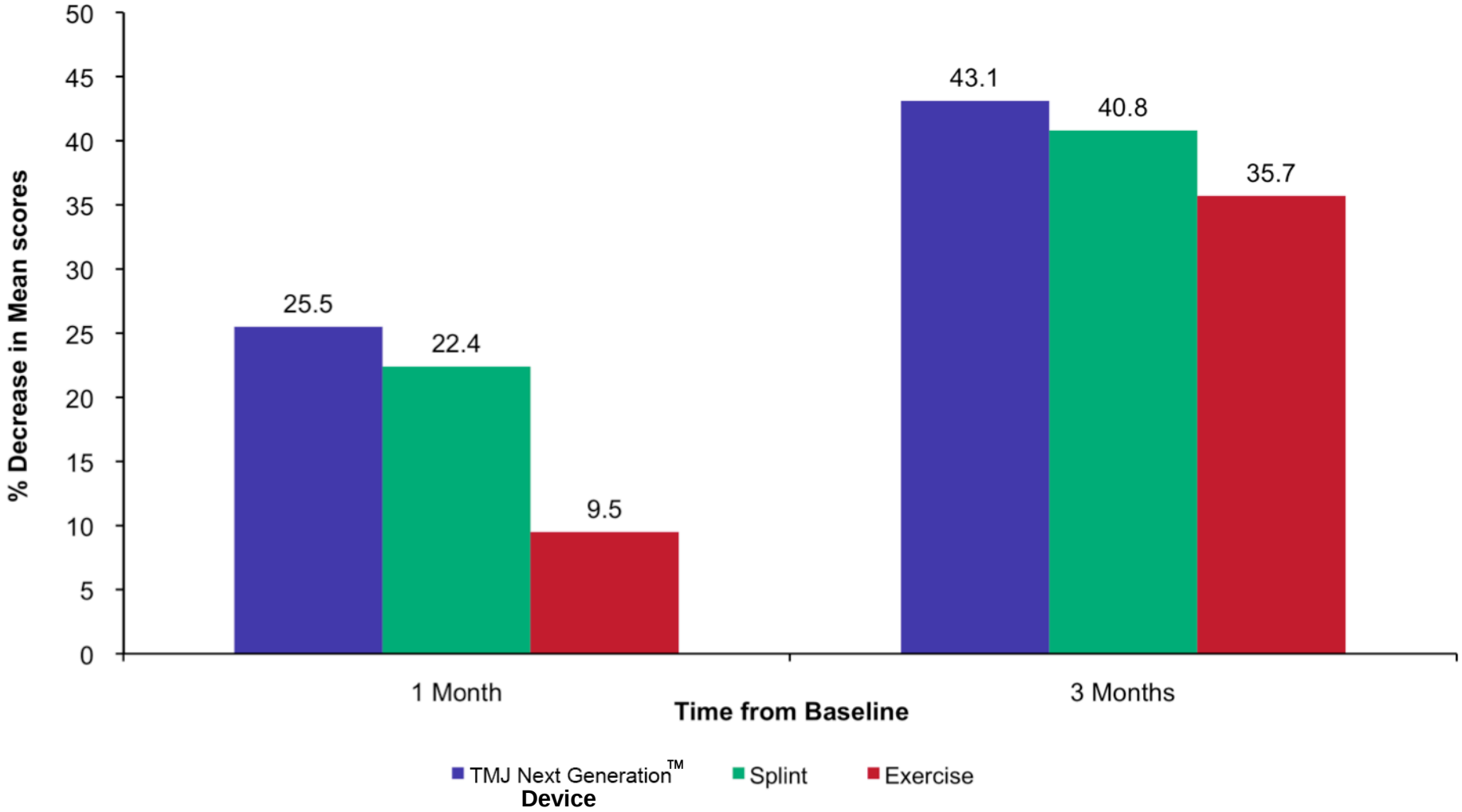
TMJ NextGeneration™ Device shows a trend towards greater magnitude of TMD relief among responders



Definitive Clinical Trial Results

CMI Percentage Decrease From Baseline

TMJ NextGeneration™ Device shows a trend towards greater magnitude of TMD relief among responders



Definitive Clinical Trial

Device Usage and Exercise Compliance

	TREATMENT GROUP		
	TMJ NextGeneration™ Device (N = 60) Hours/Day	Splint (N = 64) Hours/Day	Exercise (N = 28) Exercises/Day
Device Usage & Exercise Compliance (Month 3)			
Hour or Exercises/Day	20.56 ± 4.04 (52) 22.31 [8.02, 23.98]	8.39 ± 2.63 (56) 7.96 [4.08, 20.03]	6.97 ± 5.43 (19) 5.00 [1.89, 19.71]

Numbers are Mean ± SD (N), Median [Min, Max]

Definitive Clinical Trial

Number of Initial Fittings Required

	TREATMENT GROUP		
	TMJ NextGeneration™ Device (N = 60)	Splint (N = 64)	Exercise (N = 28)
Device Fit # Initial Fittings Required	1.03 ± 0.18 (60) 1.00 [1.00, 2.00]	1.11 ± 0.31 (64) 1.00 [1.00, 2.00]	*not applicable*

Numbers are Mean ± SD (N), Median [Min, Max]

Definitive Clinical Trial

Summary

■ Definitive clinical trial demonstrated:

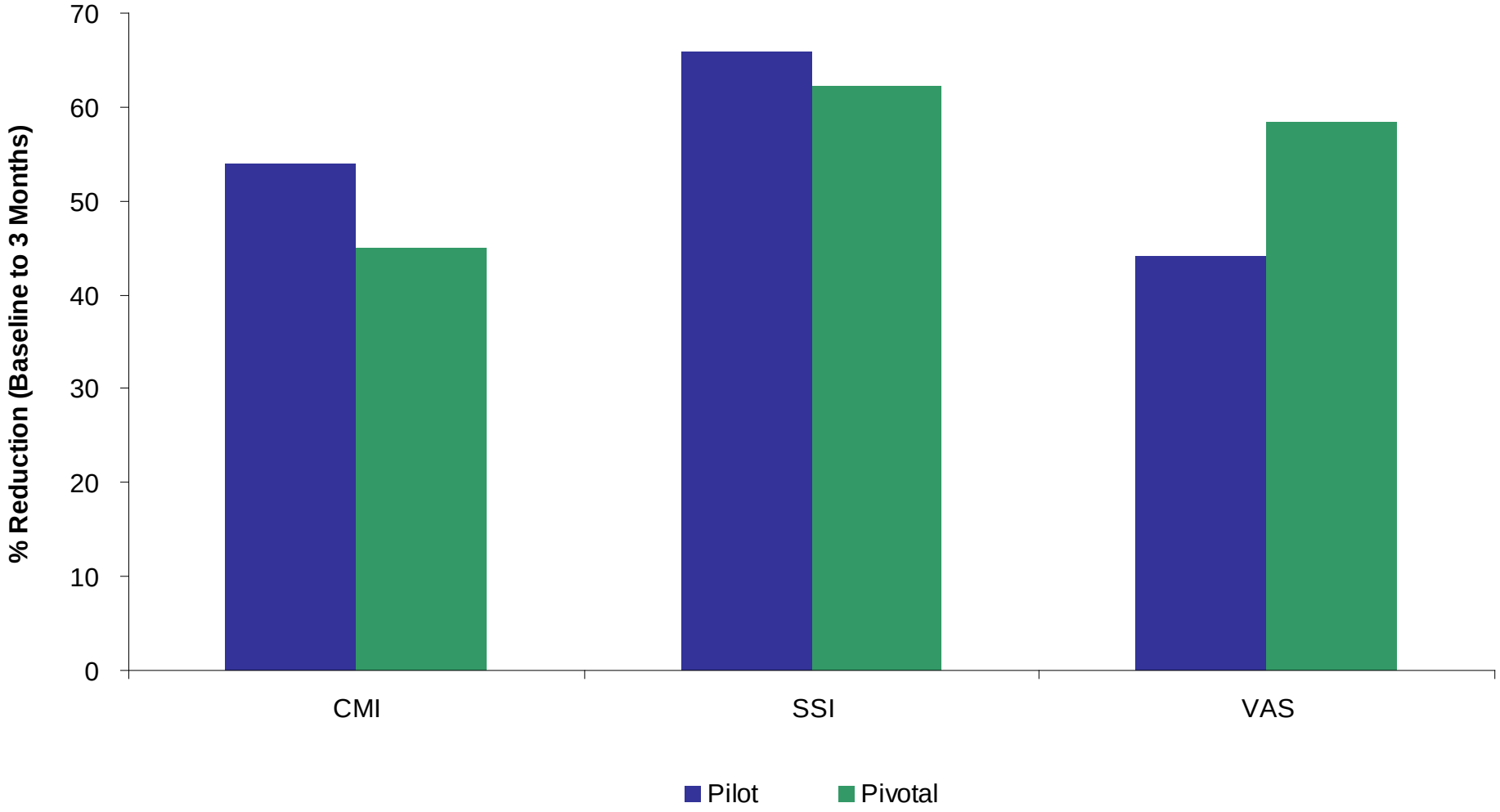
- Statistically-significant pain reduction as assessed by the VAS
- Statistically-significant non-inferiority to the most widely used current therapy – the stabilization splint
- Safety was not statistically different from the stabilization splint
- There were no serious treatment-related adverse events
- Patients showed a very high level of global satisfaction
  - 100% of subjects in TMJ NextGeneration™ group indicated excellent (71%) or good (29%) overall satisfaction with the device
- A trend towards greater and faster pain reduction

Clinical Trial Findings

Reproducibility:

Pilot Study vs. Definitive (Pivotal) Clinical Trial of TMJ NextGeneration™ Device

Consistent results seen in pilot and pivotal clinical trials



Note: Pivotal study % reduction calculated above; Pilot study % reduction from 510(k), p. 17-285

■ TMJ

Approaching Temporomandibular Disorders From a New Direction: A Randomized Controlled Clinical Trial of the TMD*es*™ Ear System

Alejandro Tsuchiya Tavera, D.D.S.; María Cecilia Perrilliat Montoya, D.D.S.; Eduardo Federico Garduño García Calderón, D.D.S.; Gina Gorodezky, M.D.; Roger N. Wixtrom, Ph.D.

ABSTRACT: TMD*es* (Registered Trademark of Ascentia Health, Inc., Rockford, Illinois), custom-fit ear inserts to aid in reducing temporomandibular disorder (TMD) pain, were evaluated in a prospective, three-month, open-label, three-arm, randomized, unblinded clinical trial, which included patients with TMD diagnoses (RDC/TMD) of myofascial pain, arthralgia, and/or disc displacement with reduction; and a screening VAS pain score of >4. The three treatment groups included: TMD*es* (n=60), stabilization splint (n=64), and jaw exercise regimen (n=28). The mean change in Craniomandibular Index (CMI) scores (reductions reflecting improvement) from baseline to one month were -27% (TMD*es*), -20% (stabilization splint), -12% (jaw exercise regimen), and from baseline to three months were -45%, -41%, -36%, reflecting statistically significant noninferiority (p=0.0096) of the TMD*es* to the stabilization splint (primary efficacy endpoint). The TMD*es* produced significant (p<0.0001) mean changes in VAS pain scores from baseline of -46% at one month and -58% at three months and demonstrated comparable efficacy and safety to the stabilization splint. (Registered at *ClinicalTrials.gov:* NCT00815776).

0886-9634/3003-172$0.25/pp, THE JOURNAL OF CRANIOMANDIBULAR PRACTICE,

Manuscript received March 24, 2011; revised manuscript received November 17, 2011; accepted November 21, 2011

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Regulatory Outcome Based on These Clinical Data

FDA 510(k) Clearance

“indicated as an aid in reducing temporomandibular disorder (TMD) pain”

Thank You