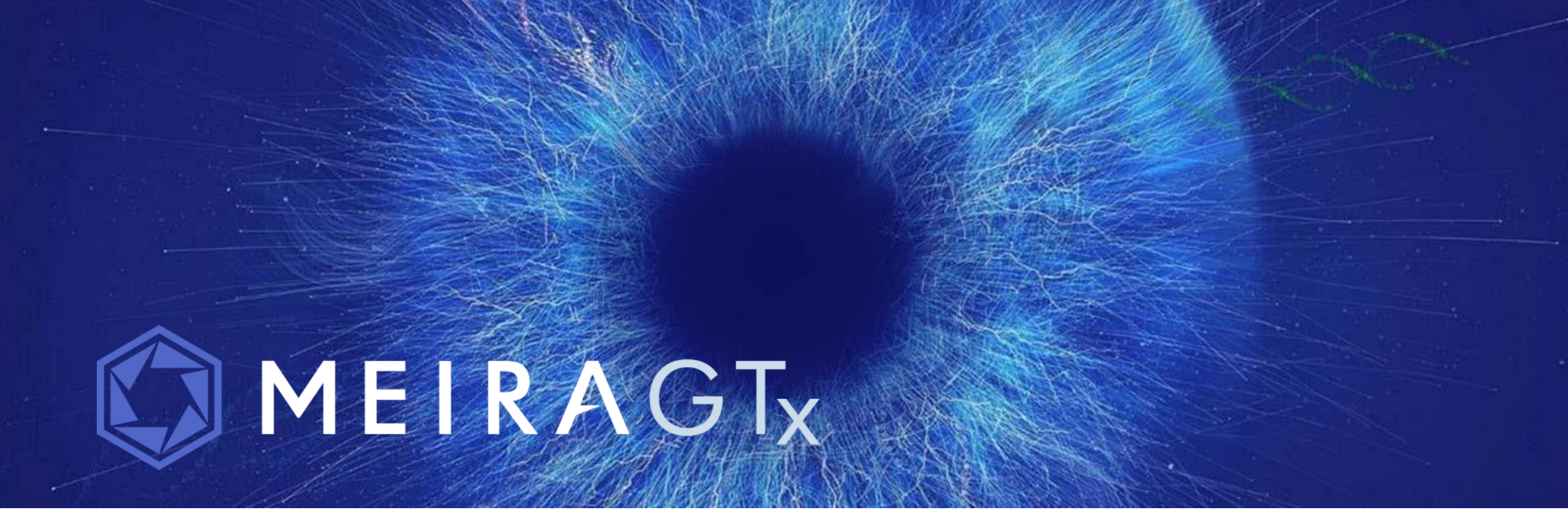


Results of a Phase 1, Open-label, Dose-escalation Study of Gene Therapy with AAV2-hAQP1 as Treatment for Grade 2 and 3 Radiation-induced Late Xerostomia and Parotid Gland Hypofunction – The AQUAx Study

Oral Abstract I

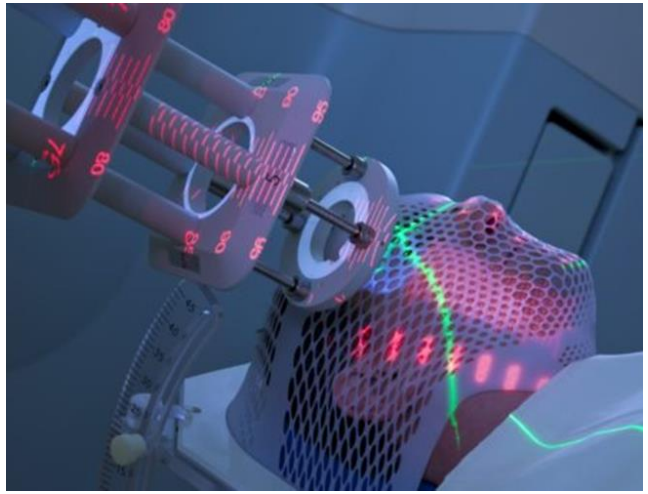
Michael T Brennan, DDS, MHS
Mike.brennan@atriumhealth.org

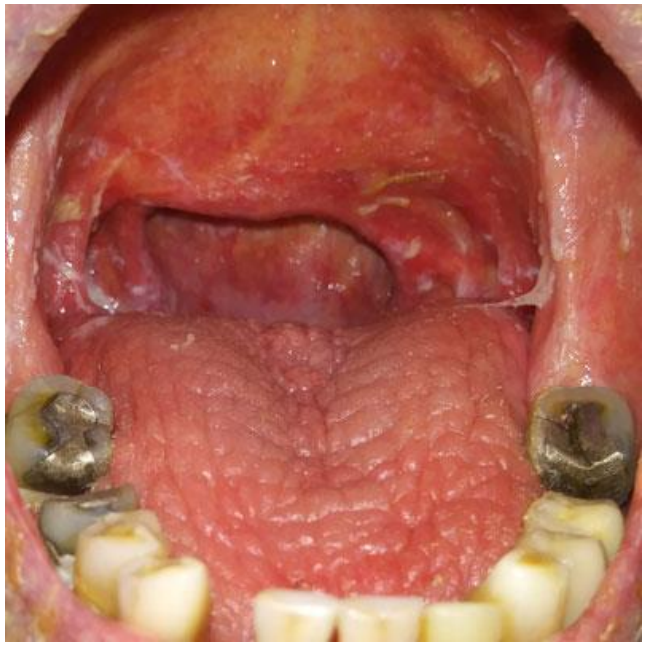
Disclosures

- I have received financial support from MeiraGTx, LLC for research studies
- I served as an investigator in the completed MGT016 (AQUAx) study, sponsored by MeiraGTx, LLC
- I currently serve as an investigator in the ongoing MGT-AQP1-201 (AQUAx2) study, sponsored by MeiraGTx, LLC

Radiation-Induced Xerostomia (RIX)

- RIX is one of the most frequent complications of radiation treatment for head and neck cancer
- IMRT has reduced the incidence of RIX, but it still affects >50% of those completing radiotherapy for head and neck cancer
- Persistent Grade 2/3 (Moderate/Severe) RIX is a common, durable, and severely debilitating condition affecting about 30% of those successfully treated for H&N cancer 2 years post-treatment
- Patients' experience
    - Difficulty eating, chewing, and swallowing; taste alterations
    - Speech difficulties and abnormalities
    - Difficulty sleeping; difficulty exercising
    - Uncontrollable dental caries with severe tooth decay/periodontal disease
    - Inability to wear dentures
    - Oral pain and throat pain
    - Burning mouth sensation in 40% of patients
    - Harmful changes in oral flora





Significant Unmet Medical Need for an Effective RIX Treatment

- >170,000 patients with long-term (i.e., at least 2 years post radiation treatment) grade 2/3 RIX in the US alone[1,2,3]
- Annually in the US, 54,000 new cases of head and neck cancer and >15,000 new patients with persistent grade 2/3 RIX[1,2,3]
- Over-the-counter agents such as lozenges, gums, and artificial saliva provide limited relief
- Pilocarpine, the only FDA-approved drug for RIX, is poorly tolerated and not effective in patients with Grade 2/3 RIX

Patients with Grade 2/3 RIX have no effective therapy available today

Prevalence (US)

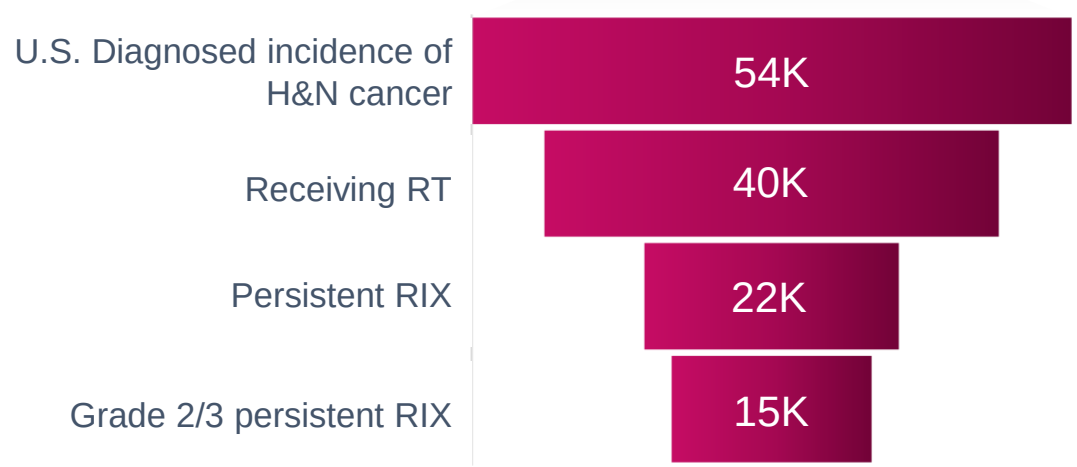
170K

Grade 2/3 RIX patients in the US

Incidence (US)

15K

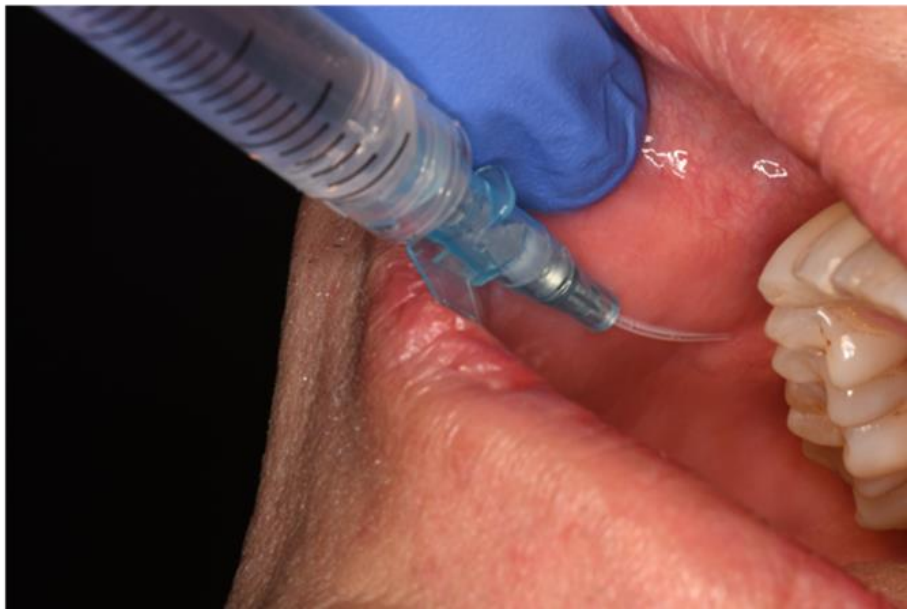
New cases of grade 2/3 RIX annually in the US



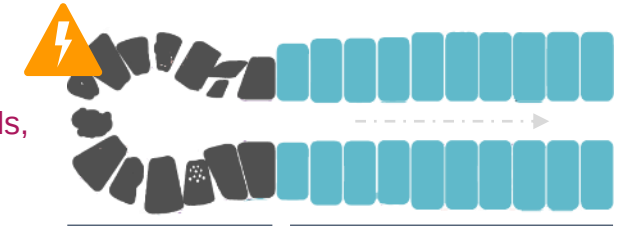
[1] SEER, Cancer.net
[2] Marta GN et al (2014). Intensity-modulated radiation therapy for head and neck cancer: systematic review and meta-analysis. Radiother Oncol. 110(1):9-15
[3] Jensen S.B., et al. (2010). A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: prevalence, severity and impact on quality of life. Support Care Cancer. 18(8):1039-1060

AAV2-hAQP1 Mechanism of Action

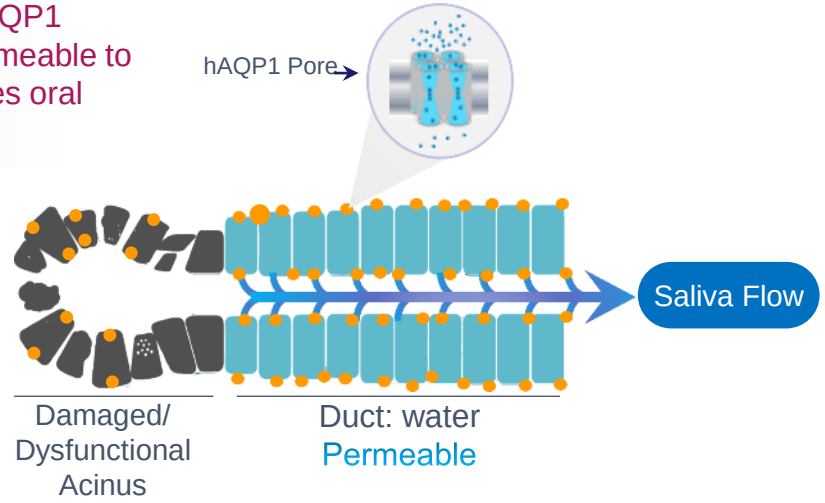
- Acinar cells are particularly vulnerable to radiation treatment
- Acinar cell death and disorganization of gland epithelium following radiation results in hyposalivation
- Expression of the water channel, Aquaporin-1 (hAQP1), via viral vector delivered locally into the salivary gland renders duct cells and surviving acinar cells permeable to water
- **hAQP1 allows water to flow through the parotid ductal system and out to the oral cavity to moisten the mouth**



Ionizing radiation causes irreversible damage to acinar cells, impairing saliva production



Expression of hAQP1 renders cells permeable to water and restores oral wetness



AQUAx: Phase 1 Clinical Study Design

- Open-label, multi-center, dose-escalation study (4 sites, US/Canada)
- One-time administration of AAV-hAQP1 to one (unilateral) or both (bilateral) parotid glands
- Four dose-escalating cohorts with 3 participants per cohort (n=12 for unilaterally treated and n=12 for bilaterally treated)
- All participants are followed for 1-year post-treatment and then invited to enroll in a long-term follow-up study for a total of 5 years

Primary Endpoint

- Safety

Secondary Endpoints

- Patient reported measures of xerostomia symptoms
  - Xerostomia Questionnaire (XQ)
  - MD Anderson Symptom Inventory – Head and Neck
  - Global Rate of Change Questionnaire (GRCQ)
- Unstimulated whole saliva flow rate

Cohort	Dose
Unilateral Treatment	
1	1×10^{11} vg/gland
2	3×10^{11} vg/gland
3	1×10^{12} vg/gland
4	3×10^{12} vg/gland
Bilateral Treatment	
1b	3×10^{10} vg/gland
2b	1×10^{11} vg/gland
3b	3×10^{11} vg/gland
4b	1×10^{12} vg/gland

AQUAx: Demographics and Baseline Characteristics

- 24 Participants
- 20 Male, 4 Female
- 23 White, 1 Black/African American
- Average Age: 63.5 years (range 48-79)
- 5+ years out from final radiotherapy treatment (2+ years for HPV+ tumors)
- Average baseline Total Xerostomia Questionnaire (XQ) Score: 46.7 (scale 0-80)
- Average baseline Dry Mouth (Question #10 of MDASI-HN) Score: 7.2 (scale 0-10)

AQUAx: Safety

- **AAV2-hAQP1 was safe and well-tolerated at all doses tested**

- No treatment-related serious adverse events
  - 2 SAEs: obstructive airways disorder and coronary artery disease
  - Assessed by the investigator as not treatment-related

- No dose-limiting toxicities

- No participant discontinued from the study

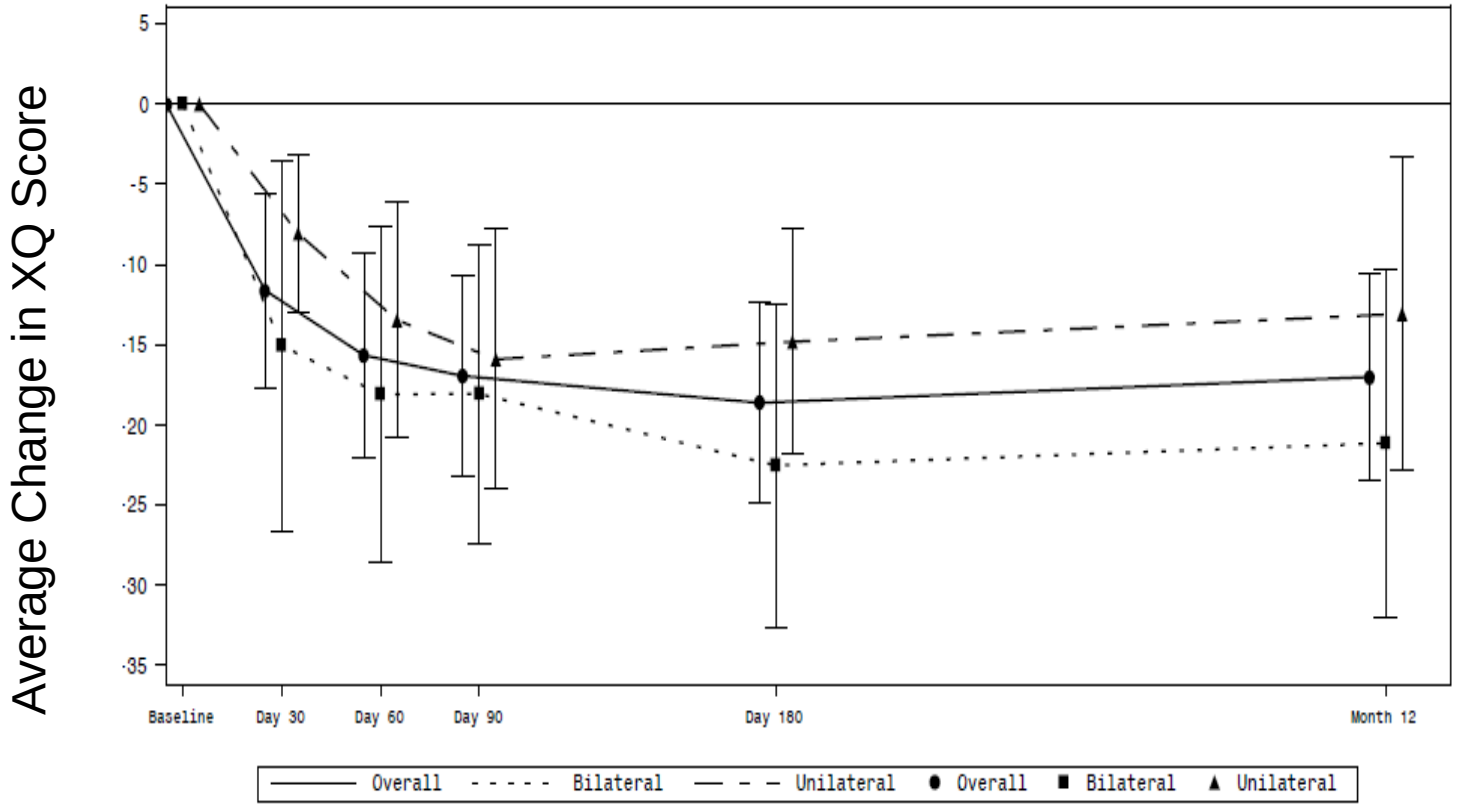
- 6 mild, treatment-related, treatment-emergent adverse events (TEAEs)
  - All resolved without sequelae

Treatment-Related Treatment-Emergent Adverse Events in the AQUAx study

System Organ Class Preferred Term	All Participant N=24 N (%)
Participants with ≥1 treatment-related TEAE	6 (25.0)
Gastrointestinal disorders Oral disorder Salivary gland pain	2 (8.3) 1 (4.2) 1 (4.2)
General disorder and administration site conditions Chills Fatigue Injection site pain	2 (8.3) 1 (4.2) 1 (4.2) 1 (4.2)
Eye disorders Eye disorder	1 (4.2) 1 (4.2)
Investigations Amylase increased	1 (4.2) 1 (4.2)
Nervous system disorders Dysgeusia	1 (4.2) 1 (4.2)

AQUAx: Xerostomia Questionnaire[1]

- 8 symptom-specific questions which the participant answers using a scale from 0 (not present) to 10 (worst possible)
- Responses to individual questions are summed to provide the Total Score (0-80), an overall measure of disease burden
- An improvement (decrease) of **8 points or more** in XQ Total Score is considered clinically meaningful[2]



Average XQ score improved by 17 points (39.5%) at Month 12, with bilaterally treated participants reporting greater improvement than those treated unilaterally

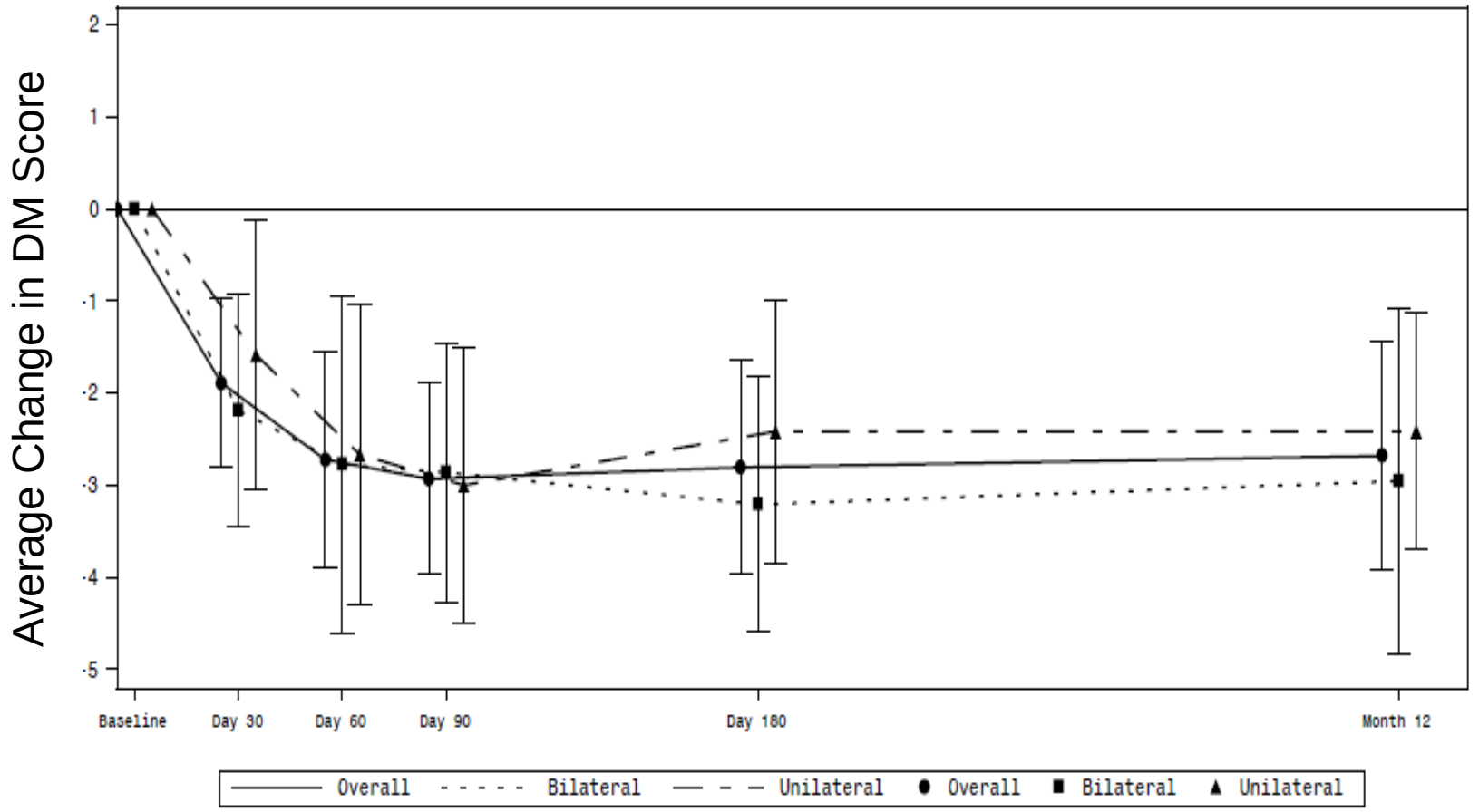
16/24 (67%) participants reported an improvement of ≥8 points in the XQ Total Score at Month 12

[1] Eisbruch A et al. Xerostomia and its predictors following parotid-sparing irradiation of head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2001 Jul 1;50(3):695-704

[2] Jabbari S et al. Matched Case–Control Study of Quality of Life and Xerostomia after Intensity-Modulated Radiotherapy or Standard Radiotherapy for Head-and-Neck Cancer: Initial Report. Int. J. Radiat. Oncol. Biol. Phys. 2005;63:725–731

AQUAx: MD Anderson Symptom Inventory Dry Mouth Question

- Question #10 from MD Anderson Symptom Inventory – Head and Neck[1]
- During the last 24 hours, please rate “Your **dry mouth** at its WORST”
- Scale from 0 (not present) to 10 (as bad as you can imagine)

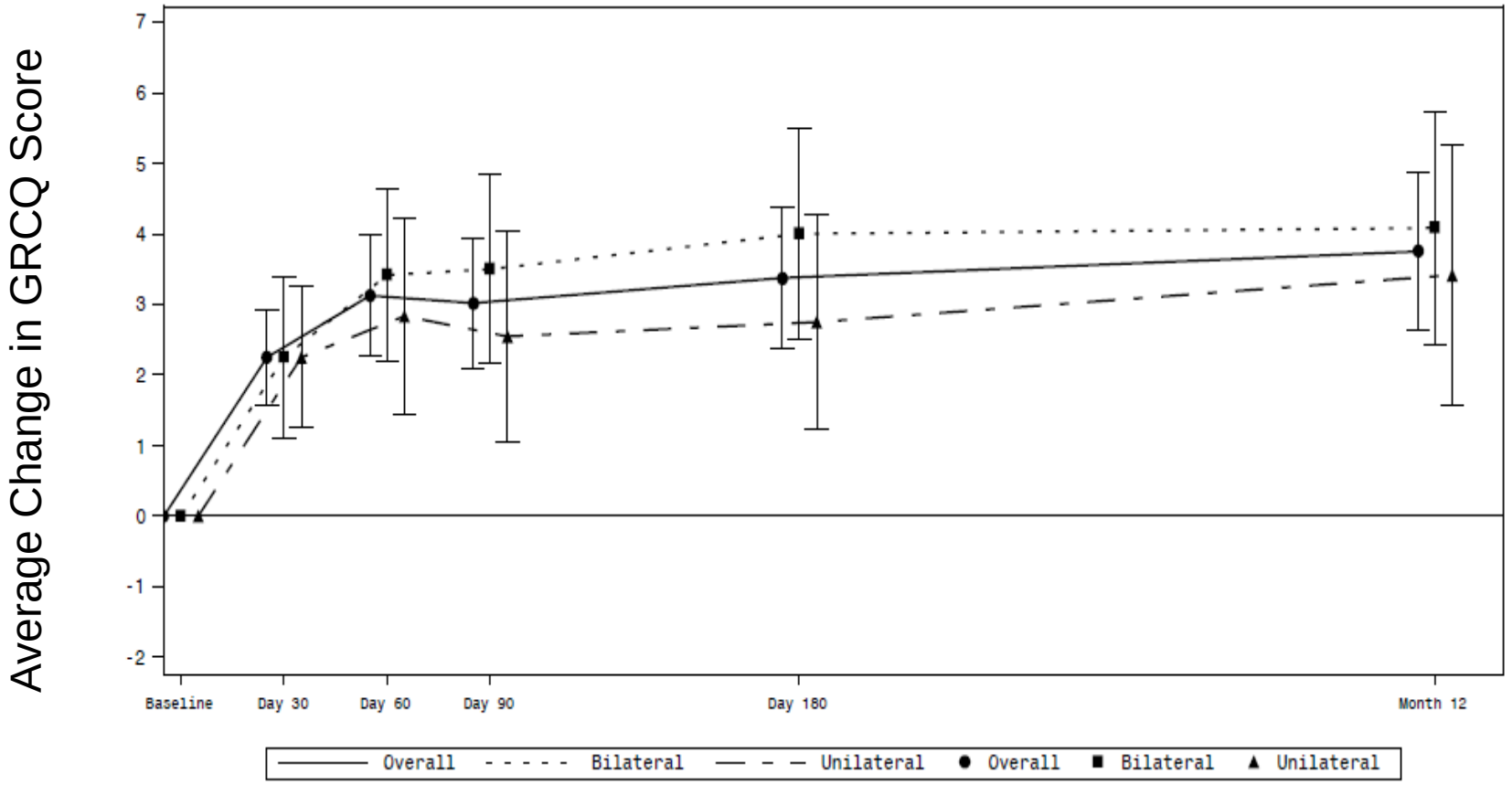


Average Dry Mouth score improved by 2.7 points (42.2%) at Month 12, with bilaterally treated participants reporting greater improvement than those treated unilaterally

[1]Rosenthal DI et al. Measuring head and neck cancer symptom burden: the development and validation of the M. D. Anderson symptom inventory, head and neck module. Head Neck. 2007 Oct;29(10):923-31

AQUAx: McMaster Global Rate of Change Questionnaire Score

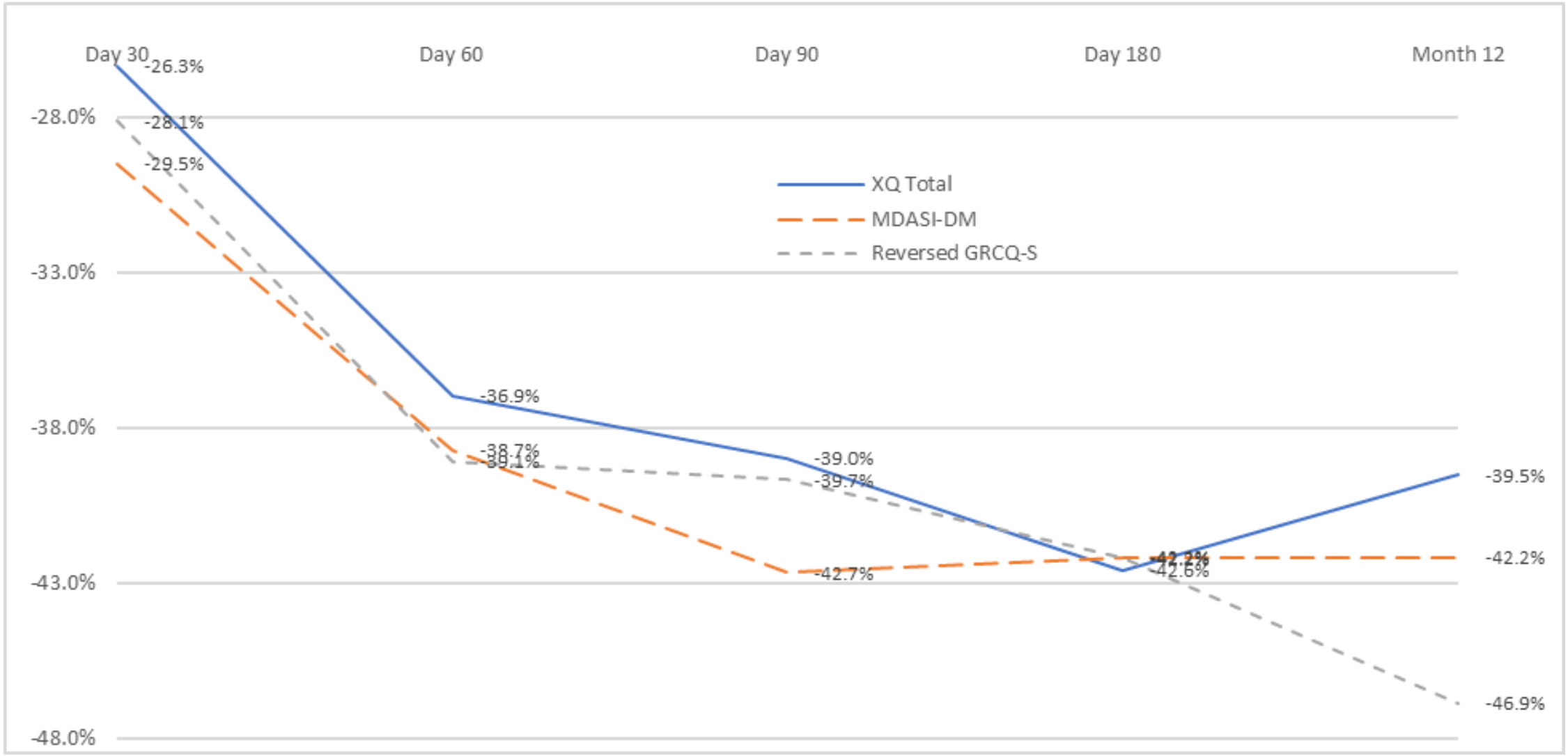
- Participants are asked, “Overall, has there been any change in your Dry Mouth since you received study treatment?”
- Potential answers are “Better”, “About the Same”, or “Worse”
- If they answer "Better" or "Worse", the participant is then asked to rate the degree of change on a 1-7 scale, with changes of 2+ being “important”



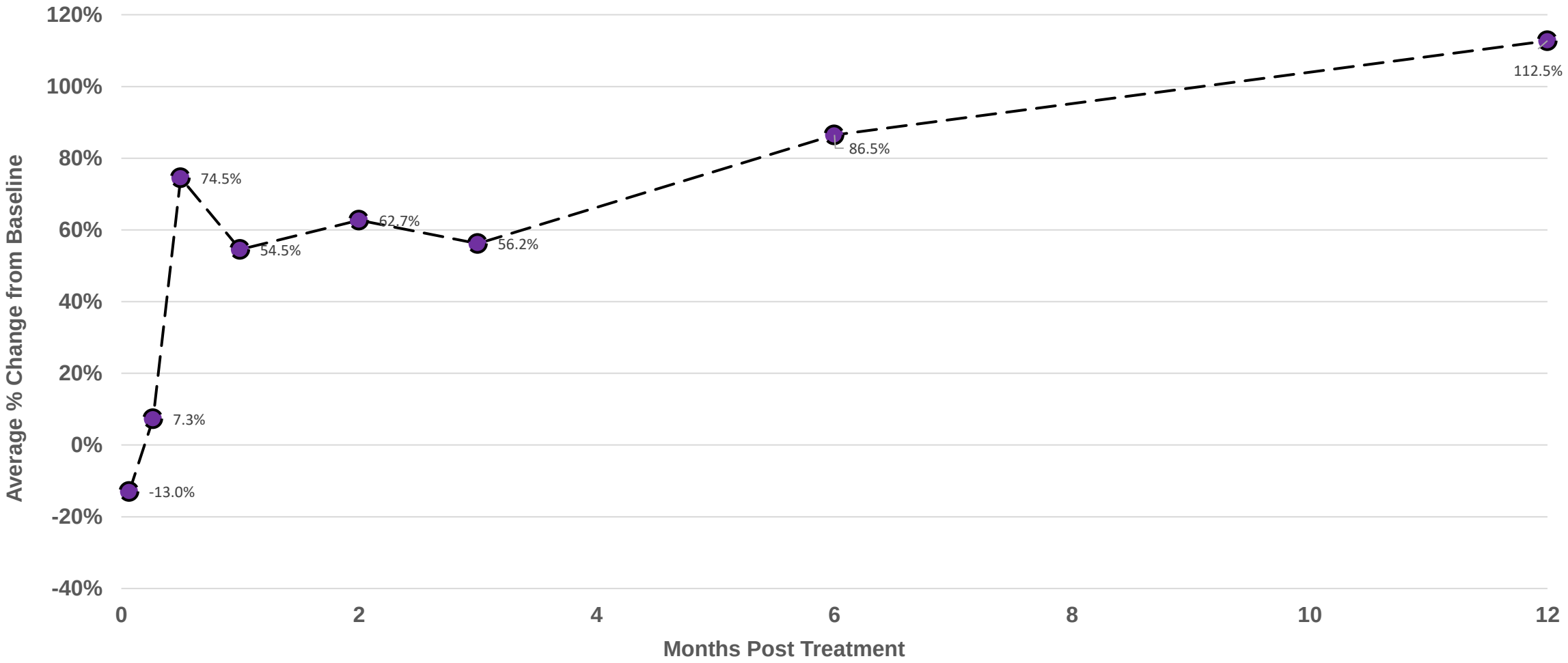
At Month 12, the average GRCQ Score was 3.8, with bilaterally-treated participants reporting higher scores than those treated unilaterally

19/24 (79%) participants reported “important” improvements in xerostomia symptoms at Month 12

AQUAx: Consistent Improvements across Patient Reported Outcome Measures



AQUAx: Unstimulated Whole Saliva Flow Rate
Average Percent Change from Baseline



At Month 12, the Unstimulated Whole Saliva Flow Rate increased from baseline by 112.5%

AQUAx - Summary of Findings

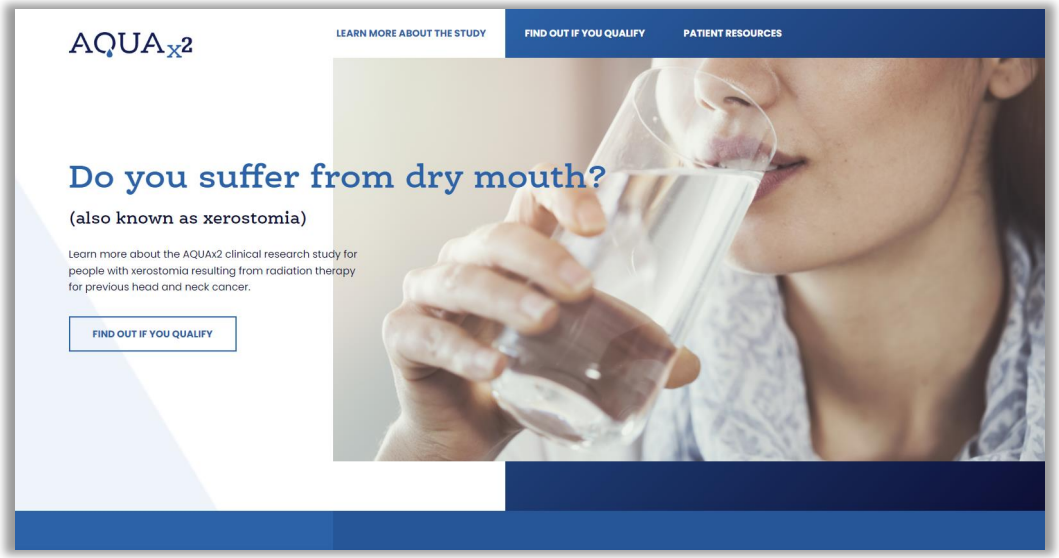
- No treatment-related serious adverse events or dose-limiting toxicities were reported, and all participants completed the study
- The 3 different PRO instruments showed statistically significant improvements by Day 30 that were maintained through Month 12
  - At Month 12, the average Total XQ Score improved by 17 points (39.5%) from baseline and 16 of 24 participants reported an improvement of ≥8 points
  - At Month 12, the MDASI-HN-DM score improved by 2.7 points (42.2%) from baseline
  - At Month 12, the average improvement in GRCQ Score was 3.8
  - Across the PROs, bilaterally-treated participants reported greater improvement than those treated unilaterally
- At Month 12, the Unstimulated Whole Saliva Flow Rate increased from baseline by 112.5%

AQUAx2: Phase 2 Study Design and Endpoints

The Phase 2 randomized, double-blind, placebo-controlled study is actively enrolling

Study Design

- Randomized, double-blind, placebo-controlled
- 120 participants: Two active doses of AAV2-hAQP1 vs Placebo, 1:1:1 randomization



Primary Efficacy Endpoint

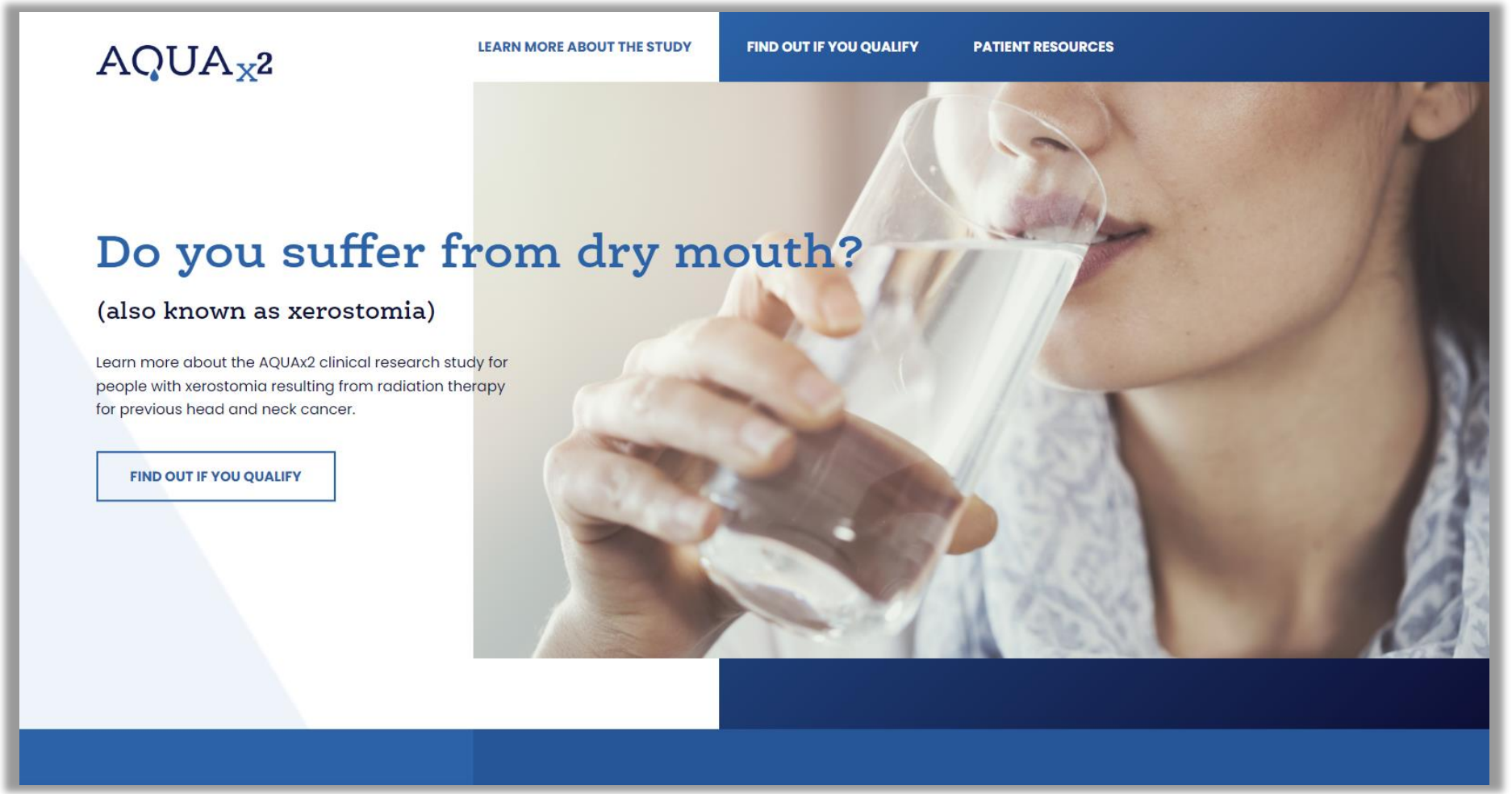
- Change from Baseline to Month 12 in Xerostomia Questionnaire (XQ) Total Score

Key Secondary Endpoints

- Change from Baseline to Month 12 in Unstimulated Whole Saliva Flow Rate
- Safety and tolerability of AAV2-hAQP1

Given the favorable safety and tolerability profile of AAV2-hAQP1 in the AQUAx study, we plan to amend the protocol to add a higher dose arm

Q & A



https://aquax2study.com/