# XEOMIN (INCOBOTULINUMTOXIN A) INJECTION FOR TEMPOROMANDIBULAR DISORDER: A DOUBLE BLINDED RANDOMIZED CONTROLLED STUDY

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## ABSTRACT

Objectives: Temporomandibular Disorder (TMD) involves dysfunction of the temporomandibular joint and associated muscles of mastication causing pain with chewing, limitation of jaw movement, and chronic orofacial pain. While the exact pathophysiology of TMD is not completely understood, it is thought that hyperfunction of the muscles of mastication place undue stress on the temporomandibular joint, which leads to degeneration of the joint and associated symptoms. We hypothesize that chemodenervation of the muscles of mastication with Xeomin (Incobotulinumtoxina) will decrease the stress on the temporomandibular joint and thus improve pain associated with TMJD.

Methods: 20 patients were randomized to either Xeomin (170 units) or saline injection of the masseters and pterygoid muscles. Patient reported pain scale (0-10) was recorded at 4-week intervals following injection for 16 weeks. Patients who received saline injection initially were assessed for reduction in pain at the first four week interval and if still had significant pain, were rolled over into the Xeomin arm.

Results: Results were available for 19/20 patients. Preinjection average pain scores were similar between patients. While there was a statistically significant reduction in pain score in the placebo group after one month, there was an overall larger drop in average pain scores in those patients injected with Xeomin initially. All patients injected with placebo initially crossed over into the Xeomin group. Similar results were seen when examining the composite masticatory muscle tenderness scores. There was no significant change in usage of pain medication.

Conclusions: We demonstrate utility of Xeomin (incobotulinumtoxinA) in treating patients with TMD with persistent pain despite pain medication usage and other conventional treatments

## METHODS AND MATERIALS

- Inclusion Criteria:

Subjects with painful TMD characterized by the following: 1)TMD pain assessment > 3 on a 0-10 ordinal scale 2) Pain occurring at least 10 days per month 3) Signs/symptoms of TMD present for at least 3 months prior to first visit 4) Signs/symptoms of TMD refractory to conventional therapy for at least six weeks prior to baseline, including analgesia and/or devices

- 20 patients enrolled
- Preinjection pain scales include overall pain (0-10) and composite masticatory muscle pain scale (0-4 for each muscle, total maximum pain score of 20).
- Patients randomized to be injected in bilateral masseters and external pterygoids with Xeomin or saline
- Patients assessed for response at 4 week intervals out to 16 weeks.
- Patients initially receiving saline were crossed over into Xeomin arm if still had significant pain at 4 weeks.
- Primary endpoint was reduction in overall pain scale at 4 weeks
- Secondary endpoints included duration of response and to assess for change in pain medication usage.
- Statistical analysis performed with Microsoft Excel using paired and unpaired student's t-tests where applicable.

## RESULTS

| Months post-injection | PLACEBO n = 9 | | XEOMIN n = 10 | |
|---|---|---|---|---|
| | Δ pain score | *p-value* | Δ pain score | *p-value* |
| 1 | **1.7** *** | *0.01* | **4.5** | *0.0002* |
| 2 | **4.43** | *0.0003* | **4.1** | *0.0014* |
| 3 | **3.54** | *0.004* | **4.4** | *0.004* |
| 4 | **1.54** | *0.2* | **2.9** | *0.009* |

**Average Pain Scores: Xeomin vs. Placebo**

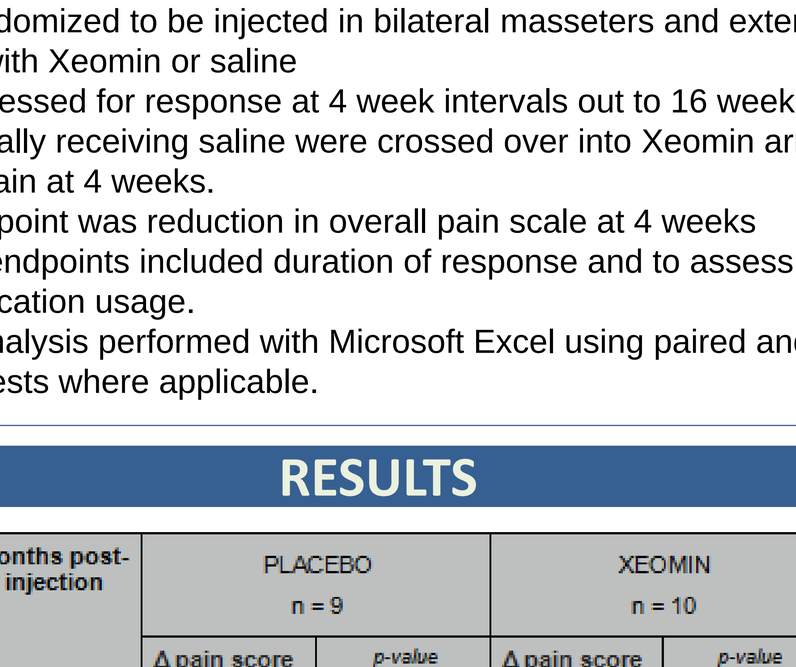


**Figure 1: Average reduction in pain score – Data and Graphical Representation**

Note significant drop in pain scores in placebo and Xeomin groups. All patients in placebo crossed over into Xeomin group.

| Months post-injection | PLACEBO n = 9 | *p-value* | XEOMIN n = 10 | *p-value* |
|---|---|---|---|---|
| Pre-injection | 15.9 ±3.3 | *0.566* | 14.9 ±3.9 | |
| 1 | 13.8 ±3.7 *** | ***0.003*** | 8.6 ±2.8 | |
| 2 | 9.4 ±2.7 | *0.333* | 8.3 ±2.3 | |
| 3 | 9.7 ±4.3 | *0.716* | 9.0 ±3.5 | |
| 4 | 12.7 ±3.8 | *0.909* | 12.5 ±5.1 | |

**Average Composite Muscle Tenderness Scores: Xeomin vs. Placebo**

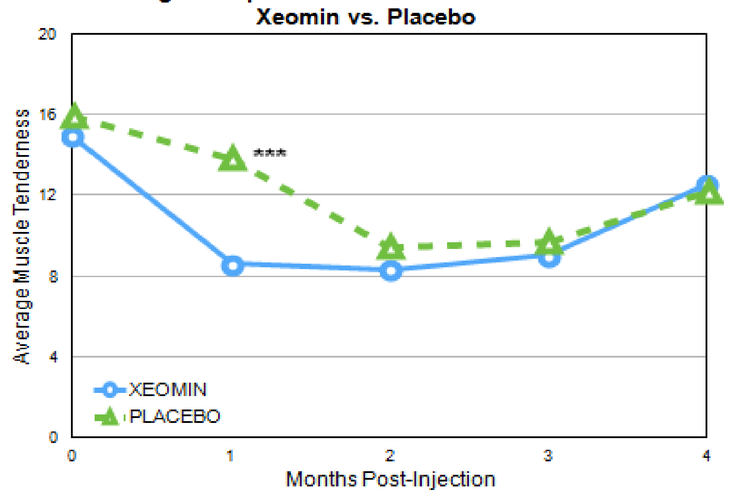


**Figure 2: Average Composite Muscle Tenderness Scores**

**No change in average tenderness scores was noted in the placebo group, while the group injected with Xeomin had a statistically significant drop in pain**

| Months post-injection | PLACEBO n = 9 | *p-value* | XEOMIN n = 10 | *p-value* |
|---|---|---|---|---|
| Pre-injection | 15.9 ±3.3 | *0.566* | 14.9 ±3.9 | |
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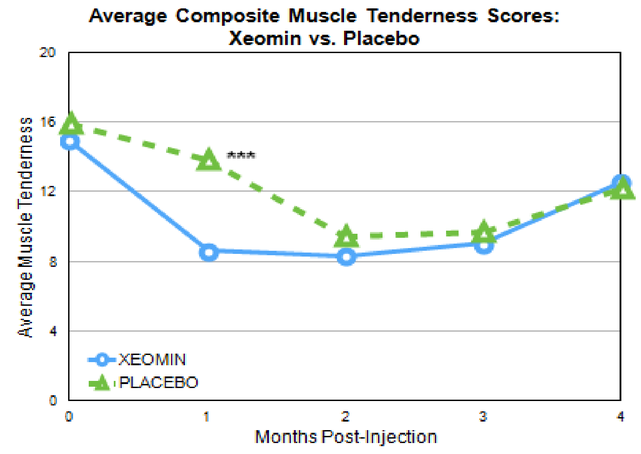


**Graph 2: Average Composite Muscle Tenderness Scores**

**No change in average tenderness scores was noted in the placebo group, while the group injected with Xeomin had a statistically significant drop in pain**

## DISCUSSION/CONCLUSIONS

- Temporomandibular Disorder (TMD) is thought to result from hyperfunction of the muscles of mastication
- We demonstrate in this trial benefit of weakening the muscles of mastication with Xeomin (incobolutulinumtoxinA) in treating patients with TMD
- While there was no statistically significant change between the placebo and Xeomin groups at 4 weeks of injection we noted a larger drop in pain scores between the groups from initial equivalency
- When comparing the groups at 4 weeks in terms of composite masticatory muscle tenderness score, patients receiving placebo initially did NOT receive benefit while there was a statistically significant difference in the group injected with Xeomin.
- No statistically significant difference in days of pain medication usage was noted between the groups.
- Limitations of the study include subjective nature of pain scale used, as well as small study
- We demonstrate utility of Xeomin (incobotulinumtoxinA) in treating patients with TMD with persistent pain despite pain medication usage and other conventional treatments
- While further study is needed, we feel that Xeomin injection can serve as a tool in the armamentarium in treating refractory TMD.

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