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Efficacy of IncobotulinumtoxinA for the Treatment of Glabellar Frown Lines in Male Subjects: Post-Hoc Analyses from Randomized, Double-Blind Pivotal Studies

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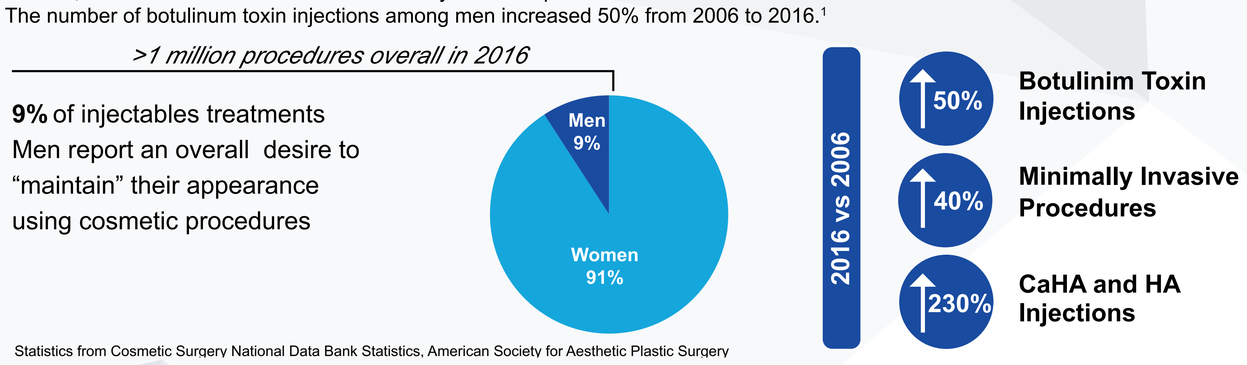
BACKGROUND

- Interest among men in minimally invasive cosmetic procedures continues to increase

Figure 1. Minimally Invasive Cosmetic Procedures in Men.
In 2016, men accounted for ~9% of all minimally cosmetic procedures.[1]
The number of botulinum toxin injections among men increased 50% from 2006 to 2016.[1]



- Despite the increasing number of men seeking aesthetic procedures, they are underrepresented in the literature on aesthetic products such as botulinum toxins
  - A previous analysis of 17 studies on botulinum toxins in aesthetic indications showed that only ~11% of subjects in these trials were male[2]
- Therefore, there remains a clinical need for studies that address how men and women respond differentially to aesthetic treatments to support individualization of treatment plans
- The objective of this analysis was to assess the efficacy of incobotulinumtoxinA (Xeomin®/Bocouture®, Merz Pharmaceuticals GmbH) for the treatment of glabellar frown lines (GFLs) in men

METHODS

Subjects and Treatment

- Previously described pooled, post-hoc analysis of incobotulinumtoxinA pivotal phase 3 GFL studies in the US[3] was extended to include a male subgroup analysis
  - N=55 males (incobotulinumtoxinA, n=34; placebo, n=21) with moderate to severe GFLs at baseline (Facial Wrinkle Scale [FWS])
- Supportive data are also provided from a post-hoc analysis of the European phase 3 study on incobotulinumtoxinA for upper facial lines (UFLs), including the glabellar area[4]
  - N=21 males (incobotulinumtoxinA, n=11; placebo, n=10) with moderate to severe GFLs at baseline (Merz Aesthetics Scales [MAS])
- 20 U of incobotulinumtoxinA (4 U in 0.1 cc in each of 5 injection sites in the GFL) were administered to each subject
  - Subjects in the UFLs study also received treatment for horizontal forehead lines and crow's feet; post-hoc analyses were not conducted for these treatment areas

Endpoints

- Pivotal Phase 3 US GFL Studies: Pooled Post-Hoc Analysis
  - % of subjects with a score of 0 or 1 on the FWS at maximum contraction at 30 days (investigator-assessed)
  - % of subjects with a ≥1-point change on the FWS at maximum contraction at 30 days (investigator-assessed)
  - % of subjects with a ≥1-point change on a separate 4-point scale at rest (subject-assessed; 0=no muscle action possible; 3=strongest muscle action possible)
- Pivotal Phase 3 EU Study on Upper Facial Lines: Post-Hoc Analysis
  - % of subjects with a score of 0 or 1 on MAS (GFLs only) at maximum contraction at 30 days (investigator-assessed)
  - % of subjects with a ≥1-point reduction on the MAS (GFLs only) at maximum contraction at 30 days (investigator-assessed)

DISCUSSION

Key Differences in Male Facial Anatomy

- Males have a greater muscle mass in the glabellar area (procerus and corrugators supercilii) compared with females[7]
- Difference in muscle mass is likely a key factor in determining males' threshold for response to botulinum toxin treatment[7]
- Male facial anatomy also varies with respect to skull shape/bony prominences and vascularization[8]

Best Practices

- Gender-specific differences in treatment response provide an opportunity to revisit best practices for botulinum toxin administration and treatment plan development
- The most important factor in achieving the best possible outcomes is the development of a customized aesthetic treatment plan
  - Careful evaluation of the patient's aesthetic concerns both at rest and during animation is particularly important for achieving natural-looking results
  - The final individualized treatment plan should be developed collaboratively with the patient and account for all variables that may affect aesthetic outcomes, including gender, age, ethnicity, skin quality, baseline wrinkle severity, muscle mass, and individual patient expectations
- Proper reconstitution technique is critical to avoid under-dosing the patient
  - In the case of incobotulinumtoxinA, gentle inversion and swirling of the vial is required to ensure the full contents of the vial are properly suspended in the diluent

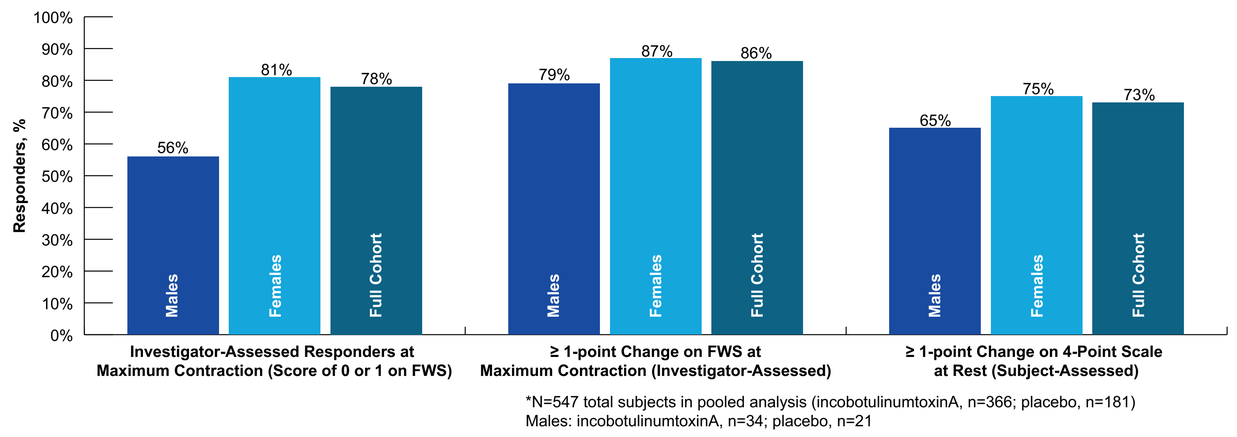
Study Limitations

- Overall, the number of male subjects available for post-hoc analyses was small
- Available active comparator studies for incobotulinumtoxinA and onabotulinumtoxinA for GFLs enrolled no male subjects,[9,10] thus preventing their inclusion in these subgroup analyses
  - However, the proportions of male responders to incobotulinumtoxinA on the FWS and MAS were consistent between studies, and similar trends have been observed individually for other botulinum toxins[5,6]

RESULTS

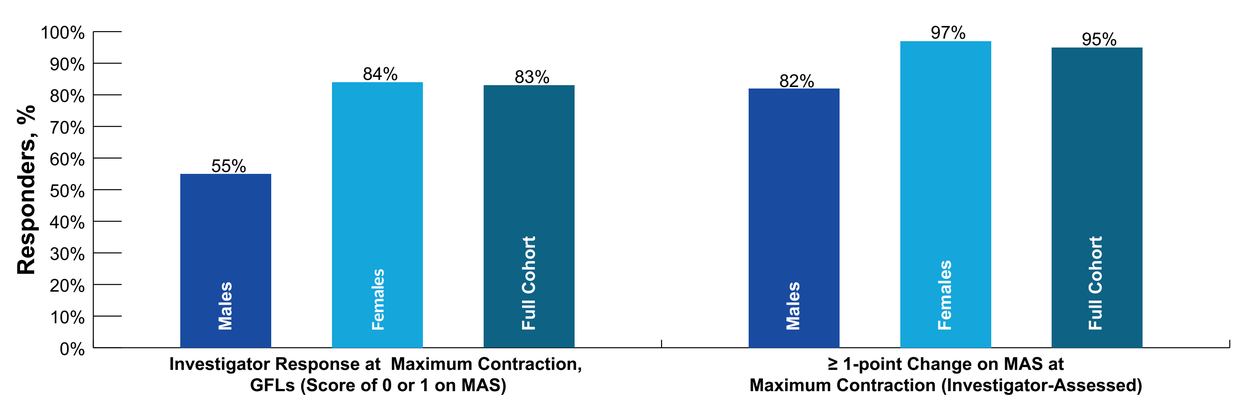
- Compared with females, males demonstrate lower response rates on GFL wrinkle severity scales (FWS, MAS) when treated with the FDA-recommended 20 U of incobotulinumtoxinA (**Figure 1 and Figure 2**)
  - Results were highly consistent between the pooled pivotal phase 3 US studies on GFLs and the European pivotal phase 3 UFL study
- A high proportion of both male and female subjects in the incobotulinumtoxinA post-hoc analyses achieved ≥1-point improvements from baseline at maximum contraction (**Figures 2 and 3**)
- Moreover, high proportions of both male and female subjects receiving incobotulinumtoxinA in the pooled phase 3 GFL studies demonstrated a ≥1-point improvement at rest (**Figures 2 and 3**)
  - A 1-point improvement at rest is an important indicator that subjects received an aesthetic benefit that is observable during typical "real-world" circumstances (ie, without having to fully contract their muscles)

Figure 2. IncobotulinumtoxinA Pooled Analysis* of Phase 3 GFL Studies: Responder Analysis at 30 Days



*N=547 total subjects in pooled analysis (incobotulinumtoxinA, n=366; placebo, n=181)
Males: incobotulinumtoxinA, n=34; placebo, n=21

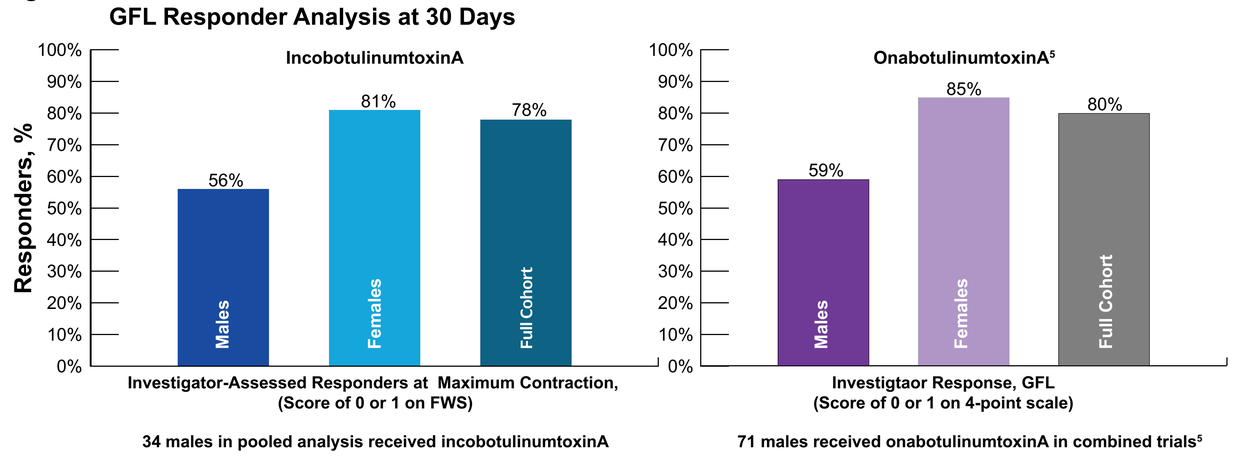
Figure 3. IncobotulinumtoxinA Phase 3 Upper Facial Lines Study*: GFL Responder Analysis at 30 Days



*N=156 total subjects in UFL study (incobotulinumtoxinA, n=105; placebo, n=51)
Males: incobotulinumtoxinA, n=11; placebo, n=10

- The proportions of males who were considered responders (ie, score of 0 or 1 on respective wrinkle severity scales) were similar between incobotulinumtoxinA and onabotulinumtoxinA (Botox®, Allergen Inc. Irvine, CA)[5] at 30 days at the same 20 U dose (**Figure 4**)
- Similar differences between male and female subjects were also observed in the pivotal phase 3 study for abobotulinumtoxinA (Dysport, Galderma) in the treatment of GFLs[6]
  - However, variations in study design and the lack of a well-defined dose conversion between abobotulinumtoxinA and other botulinum toxin formulations preclude a direct comparison of results.

Figure 4. IncobotulinumtoxinA and OnabotulinumtoxinA Pivotal Phase 3 GFL Studies: GFL Responder Analysis at 30 Days



34 males in pooled analysis received incobotulinumtoxinA

71 males received onabotulinumtoxinA in combined trials[5]

CONCLUSIONS

- **Compared with females, males demonstrate lower response rates on GFL wrinkle severity scales in studies on all 3 available botulinum toxins**
- **Variations in treatment response are potentially associated with key male anatomic differences (eg, muscle mass)**
- **Overall, results emphasize the importance of customized treatment plans**

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