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OnabotulinumtoxinA vs Sacral Neuromodulation for Urgency Incontinence-Reply

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We are happy to respond to the letters to the editor. Our responses will follow the order of comments from each letter.

1. Our decision to study a one- time 200 U injection over 6 months was that we desired the highest durability of effect for the continence outcome and to have equipoise with the comparator arm of sacral neuromodulation where the effect, once optimized will continue greater than 6 months. The recent prospective study reporting 3.5 yr outcomes using 100U had less stringent baseline urgency urinary incontinence (UUI) for enrollment and 34% of subjects required a second injection by 6 months.[1] The findings in our study suggest that 200U does provide long term efficacy with lower rates of retention then reported by other studies[2] and with lower or similar urinary tract infection (UTI) rates to those studies using 100U.[2,3] The FDA approved 100U dosage for treatment of refractory idiopathic OAB, which is broadly defined as urinary urgency, frequency, with or without UUI. Given the efficacy and durability of 200U onabotuliumtoxinA in women with UUI, with its similar or lower risk of retention and UTIs, flexible dosing of onabotulinumtoxinA seems logical.

2. This study is comparing longer-term outcomes over 24 months. In addition, there will be a comparison of utilization of medical resources for cost effectiveness analysis and cost utility at 24 months. (clinicaltrials.gov NCT01502956)

3. Our study population was severely incontinent community dwelling women and half were under 65 yrs. of age. Whether the patients in our study represent a majority or minority of your UUI patients depends on your particular practice referral pattern.

1. The application of design bias (defined as incorrect design architecture to answer the research question[4,5]) to hypothesis selection in this RCT is questionable. We concluded that for this comparative effectiveness trial with no assumed direction of relative effectiveness of the two comparators, a superiority design with a two-sided hypothesis test is preferred over a non-inferiority design, which is inherently one-sided. The former design allows either treatment to demonstrate superiority, while the latter allows only a one-way comparison. Furthermore, the study conduct and results would be identical under either hypothesis choice, so we disagree that this choice affected study clinical conclusions.

2. A small set of participants provided no post-randomization outcome data. Our primary analysis recognized this possibility and planned to treat those missing

data as missing at random in a likelihood-based analysis, which excluded participants with no follow-up data from the primary analysis. Because the sensitivity analyses reported in the manuscript imputed data for those individuals (and hence includes all randomized participants) and yielded the same results, the manuscript results are robust to our missing at random assumption (i.e. using a modified ITT population) and hence are valid.

3. Prior placebo (or sham) controlled trials demonstrated each of the active treatment regimens to be superior to placebo (referenced in manuscript). Including a placebo arm in this trial was not necessary and doing so could be considered unethical.

References

1. Nitti VW, Ginsberg D, Sievert KD, Sussman D, Radomski S. Durable Efficacy and Safety of Long Term OnabotulinumtoxinA treatment in Patients with OAB Syndrome: Final Results of a 3.5 yr study. J Urol. 2016; 196:791–800. [PubMed: 27038769]
2. Dmochowski R, Chaple C, Nitti VW, et al. Efficacy and safety of onabotulinumtoxinA for idiopathic overactive bladder: a double-blind, placebo controlled, randomized dose ranging trial. J Urol. 2010; 184(6):2416–2422. [PubMed: 20952013]
3. Visco AG, Brubaker L, Richter HE, et al. Pelvic Floor Disorders Network. Anticholinergic therapy vs. onabotulinumtoxinA for urgency urinary incontinence. N Engl J Med. 2012; 367(19):1803–1813. [PubMed: 23036134]
4. Jadad, AR., Enkin, MW. Bias in Randomized Controlled Trials, in Randomized 60 Controlled Trials: Questions, Answers, and Musings. 2. Vol. 61. Blackwell Publishing Ltd; Oxford, UK: 2007.
5. Sackett DL. Choosing the best research design for each question: It's time to stop squabbling for the "best" method. British Medical Journal. 1997; 315:1626.