#131 OnabotulinumtoxinA Retreatment Not Associated With an Increased Risk of Clean Intermittent Catheterization in Patients With Idiopathic Overactive Bladder: Pooled Analysis of Randomized Controlled Trials

Eric Rovner,[1] Francisco Cruz,[2] Jennifer Sobol,[3] Kurt McCammon,[4] Rizwan Hamid,[5] Sidney Radomski,[6] Amelia Orejudos,[7] Anand Patel,[8] Gary Lemack[9]

[1]Medical University of South Carolina, Charleston, SC, USA; [2]Hospital S. João & Universidade Do Porto, Porto, Portugal; [3]Michigan Institute of Urology, West Bloomfield, MI, USA; [4]Eastern Virginia Medical School, Norfolk, VA, USA; [5]University College London Hospitals, London, UK; [6]University of Toronto, Toronto, ON, Canada; [7]Allergan plc, Irvine, CA, USA; [8]Allergan plc, Marlow, UK; [9]University of Texas Southwestern Medical Center, Dallas, TX, USA

CONCLUSIONS

In this large, pooled population of patients with OAB, the incidence of CIC was low with onabotulinumtoxinA 100U

No increased risk of CIC was seen with onabotulinumtoxinA retreatment, and a limited number of patients with CIC after the initial treatment required CIC again following retreatment

Improvements in urinary symptoms and QOL were sustained with onabotulinumtoxinA 100U between initial treatment and retreatment, and no unexpected safety signals were observed

METHODS

Study Design and Participants

- Three phase 3 trials and 1 phase 4 trial (NCT00910520, NCT00910845, NCT01767519, and NCT01945489) enrolled OAB patients who had experienced ≥3 urgency UI episodes over a 3-day period and ≥8 micturitions per day. All patients were inadequately managed by an anticholinergic. Patients with a predominance of stress UI were excluded
- CIC was initiated if post-void residual urine volume was
  - ≥200 and <350 mL and the patient had associated symptoms assessed by the investigator to require CIC
  - ≥350 mL regardless of symptoms
- In each study, patients could be retreated as needed or requested if they met the predefined criteria of ≥2 urgency UI episodes and ≤1 urgency UI–free day in a 3-day bladder diary, and ≥12 weeks had passed since the prior treatment administration
- Assessments at week 12 after treatments 1 and 2 included incidence and duration of CIC, mean and percentage change in UI episodes/day, and proportions of patients with ≥50% and 100% reduction in UI episodes/day and a positive response ("improvement" or "great improvement" in their urinary condition) on the Treatment Benefit Scale (TBS). Mean changes from baseline in King's Health Questionnaire (KHQ) Social and Role Limitations domain scores were also assessed, and adverse events (AEs) were recorded

Statistical Methods

- The incidence of AEs, including use and duration of CIC, was analyzed in the safety population (all patients who received treatment), and efficacy and QOL outcomes were analyzed in the intent-to-treat population (all randomized patients)
- Scores on the KHQ ranged from 0–100, with lower scores (and negative change over time) indicating better QOL

RESULTS

Baseline Demographics and Disease Characteristics

Table 1. Baseline Demographics and Disease Characteristics (ITT Population)

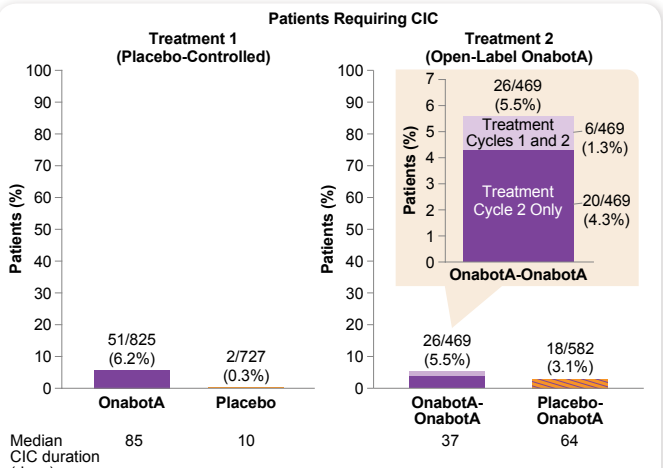
Characteristic	OnabotA 100U (n=831)	Placebo (n=733)
Age, y	60.8 ± 13.7	60.3 ± 13.2
Female, n (%)	733 (88.2)	637 (86.9)
Duration of OAB, y	6.7 ± 7.5	6.7 ± 7.8
UI episodes/day	5.4 ± 3.5	5.5 ± 3.6
Micturition episodes/day	11.5 ± 3.8	11.3 ± 3.3
Nocturia episodes/night	2.2 ± 1.4	2.0 ± 1.4
Urgency UI episodes/day	4.8 ± 3.3	4.8 ± 3.3
KHQ SL	54.1 ± 32.6	50.3 ± 32.9
KHQ RL	61.0 ± 28.8	58.7 ± 29.6
PVR urine volume, mL	22.1 ± 27.8	19.9 ± 26.6

Data are reported as mean ± standard deviation unless otherwise indicated. Demographics and baseline characteristics were not available for all patients.
ITT = intent-to-treat; KHQ = King's Health Questionnaire; OAB = idiopathic overactive bladder; onabotA = onabotulinumtoxinA; PVR = post-void residual; RL = Role Limitations; SL = Social Limitations; UI = urinary incontinence.

Incidence and Duration of CIC

- The great majority of patients did not require CIC in the 12 weeks after the initial treatment or after retreatment

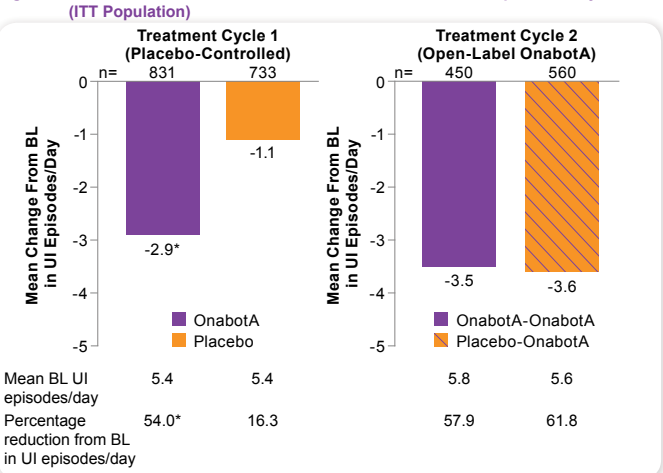
Figure 1. Low Incidence of CIC in the 12 Weeks Following the First and Second Treatments (Safety Population)



CIC = clean intermittent catheterization; onabotA = onabotulinumtoxinA.

Efficacy and QOL Outcomes

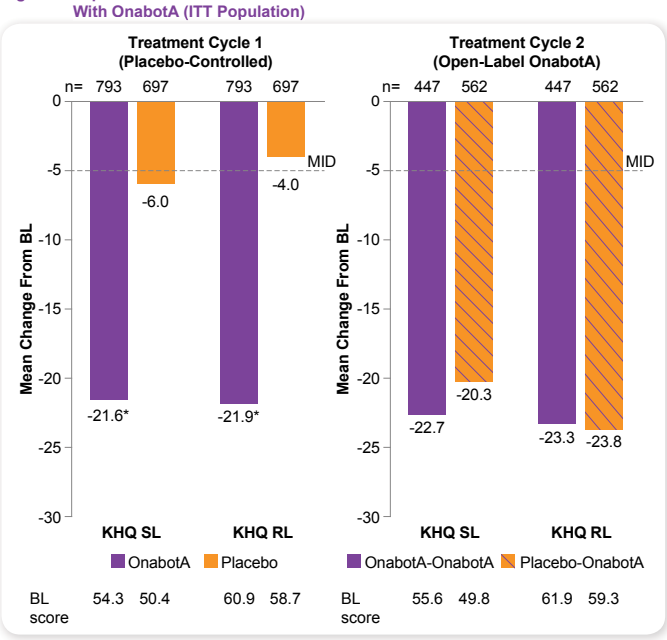
Figure 2. Substantial Reductions From Baseline to Week 12 in UI Episodes/Day (ITT Population)



*P<.001 vs placebo. n values denote the number of patients with data available at week 12.
BL = baseline; ITT = intent-to-treat; onabotA = onabotulinumtoxinA; UI = urinary incontinence.

- Following the first treatment, significantly more patients who received onabotulinumtoxinA vs placebo achieved 100% (29.0% vs 8.5%) and ≥50% (64.4% vs 32.3%) reductions in UI episodes/day at 12 weeks (*P*<.001 vs placebo for both)
  - Following the second treatment, similar proportions of patients receiving onabotulinumtoxinA retreatment or a first treatment with onabotulinumtoxinA achieved complete continence (27.1% and 32.6%, respectively) or showed ≥50% reduction in UI episodes/day (63.5% and 71.0%) at 12 weeks

Figure 3. Improvements in KHQ Domain Scores Were Greater Than 4 Times the MID With OnabotA (ITT Population)



*P<.001 vs placebo. n values denote the number of patients with data available at week 12.
BL = baseline; ITT = intent-to-treat; KHQ = King's Health Questionnaire; MID = minimally important difference (-5 points); onabotA = onabotulinumtoxinA; RL = Role Limitations; SL = Social Limitations.

- The majority of patients receiving onabotulinumtoxinA (55.2%) vs placebo (26.5%) reported improvement/great improvement in their urinary symptoms on the TBS at 12 weeks following treatment 1 (*P*<.001 vs placebo)
  - Improvements on the TBS seen at 12 weeks following the second treatment were consistent with treatment 1 in patients who were retreated with onabotulinumtoxinA (59.3%) and those receiving onabotulinumtoxinA for the first time (62.4%)

Safety and Tolerability

Table 2. AEs in the First 12 Weeks After Treatments 1 and 2 (Safety Population)

AEs, %	Treatment 1 (Placebo-Controlled)		Treatment 2 (Open-Label OnabotA)	
	OnabotA (n=825)	Placebo (n=727)	OnabotA-OnabotA (n=469)	Placebo-OnabotA (n=582)
Overall AEs	55.6	42.1	49.9	51.4
AEs ≥3%				
UTI	19.4	6.6	17.7	18.4
Dysuria	7.5	5.6	5.1	5.2
Bacteriuria	3.8	2.1	4.7	3.1
Residual urine volume[a]	3.0	0.3	2.3	3.4
Urinary retention[b]	5.9	0.3	3.4	5.3

[a]An AE of residual urine volume was recorded if, in the investigator's opinion, a raised PVR urine volume was clinically significant but did not fulfill the definition for urinary retention.
[b]Urinary retention was defined as intervention with CIC that was initiated for PVR urine volume ≥350 mL regardless of symptoms or a PVR urine volume ≥200 but <350 mL if accompanied by symptoms.
AE = adverse event; CIC = clean intermittent catheterization; onabotA = onabotulinumtoxinA; PVR = post-void residual; UTI = urinary tract infection.

INTRODUCTION

- Randomized, placebo-controlled trials with onabotulinumtoxinA have demonstrated significant improvements in urinary incontinence (UI) and quality of life (QOL) in patients with idiopathic overactive bladder (OAB) who were inadequately managed by an anticholinergic[1–3]
- Incomplete bladder emptying resulting in the need for clean intermittent catheterization (CIC) is known to occur in OAB patients who have been treated with onabotulinumtoxinA
- However, the risk of CIC in patients undergoing repeat treatment administrations requires further characterization

Objective

- This pooled post hoc analysis evaluated the risk of CIC as well as efficacy and QOL outcomes following retreatment with onabotulinumtoxinA 100U

DISCLOSURES

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ER has served as an investigator for Allergan plc. **FC** has consulted/advised and has been an investigator for Allergan plc, Astellas, Ipsen, and Recordati; and has been a lecturer for Allergan plc, Astellas, Pfizer, and Recordati. **JS** has served as a speaker for Allergan plc. **KM** has served as a consultant/advisor and meeting participant/lecturer for AMS and Solace; as study investigator for Allergan plc, AMS, Astellas, Solace, and Uroplasty; and is a board member/officer/trustee for IVUmed. **RH** has consulted/acted as an advisor for Allergan plc. **SR** has consulted/acted as an advisor for Actavis, Allergan plc, Astellas, Lilly, and Pfizer; has been an investigator for Allergan plc and Astellas; and has participated in scientific studies/trials for Allergan plc and Astellas. **AO** and **AP** are employees of Allergan plc. **GL** has served as a consultant/speaker to Allergan plc, Astellas, and Medtronic.

This formulation is not interchangeable with other botulinum toxin products and units cannot be converted using a dose ratio.

References

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