AUA & EAU Update on BPH & LUTS
– Medical Management –

DongGuk University
Seo Young Jin
Abstracts for BPH and Nocturia

1. Alpha blockers (3 abstracts) - Silodosin, Alfuzosin
   EAU 999, 1000, 1002

2. 5-alpha reductase inhibitors (5 abstracts)
   AUA 1781, 1783, 1784, 1786, EAU 1001

3. Combination Tx (4 abstracts) - COMBAT trial
   AUA 1782, 1785, EAU 990, 991

4. Intraprostatic injection Tx (6 abstracts)
   - Botulinum toxin, Protoxin (PRX302), Polidocanol
   AUA 1780, 1787, EAU 995-8

5. Nocturia (4 abstracts)
   - Tamsulosin vs TURP, COX-2 inhibitor, Non-peptide drug, Desmopressin (Melt)
   AUA 1528, 1529, EAU 992, 993

6. Others (4 abstracts) - Tadalafil, Behavior Tx vs Medial Tx
   AUA 498, 1516, 1791, EAU 994
Abstracts for OAB, LUTS

1. Anticholinergics (8 abstracts)
   AUA 1779, 1779, EAU 771, 772, 776-9

2. Beta-3 agonist (1 abstract) - Mirabegron (YM178)
   EAU 774

3. Alpha blocker (2 abstracts) - CaP, Female
   AUA 461, 1668

4. Botulinum toxin (11 abstracts)
   AUA 1015, 1018, 1019, 1533, 1596, 1677, EAU 91-3, 657, 780
Early efficacy of silodosin on storage and voiding function in Pts with BPH, based on pressure-flow study

95 Pts, silodosin 4 mg bid for 28 days

IPSS (13.8 - 10.1), OABSS (6.4 - 4.1), QoL score (5.1 - 3.2),
UFM (Qmax 8.6 – 11.4 ml/s) , R/U check (65 – 34 ml),
PFS
    Storage fx: FDV (113 – 141 ml) , MCC (243 – 274 ml), DO (Pts 45 - 23)
    Voiding fx: Qmax (6.8 – 9.6 ml), PdetQmax (74.5 – 53.4 cmH2O)

Improving not only subjective Sxs but also voiding and storage function and BOO
### Efficacy of silodosin as compared with tamsulosin and placebo for the treatment of the signs and Sxs of BPH. A multicentre, randomised, double-blind, controlled trial

955 Pts (≥ 50 yrs, IPSS ≥ 13, Qmax > 5 and ≤ 15 mL/sec), for 12 wks

<table>
<thead>
<tr>
<th></th>
<th>Silodosin 8 mg</th>
<th>Tamsulosin 0.4 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT population</td>
<td>N=371</td>
<td>N=376</td>
<td>N=185</td>
</tr>
<tr>
<td>Baseline IPSS (mean ± SD)</td>
<td>19 ± 4</td>
<td>19 ± 4</td>
<td>19 ± 4</td>
</tr>
<tr>
<td>Change from baseline to endpoint (adjusted means)</td>
<td>-7.0</td>
<td>-6.7</td>
<td>-4.7</td>
</tr>
<tr>
<td>Difference active-placebo (95%CI)</td>
<td>-2.3 (-3.2; -1.4)</td>
<td>-2.0 (-2.9; -1.1)</td>
<td></td>
</tr>
<tr>
<td>Difference tamsulosin-silodosin (95% CI)</td>
<td>0.3 (-0.4; 1.0)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>PP population</td>
<td>N=346</td>
<td>N=347</td>
<td>N=168</td>
</tr>
<tr>
<td>Baseline IPSS (mean ± SD)</td>
<td>19 ± 4</td>
<td>19 ± 4</td>
<td>19 ± 4</td>
</tr>
<tr>
<td>Change from baseline to endpoint (adjusted means)</td>
<td>-7.0</td>
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<td>-4.8</td>
</tr>
<tr>
<td>Difference active-placebo (95%CI)</td>
<td>-2.2 (-3.2; -1.3)</td>
<td>-1.9 (-2.8; -0.9)</td>
<td></td>
</tr>
<tr>
<td>Difference tamsulosin-silodosin (95% CI)</td>
<td>0.4 (-0.4, 1.1)</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

* p<0.001 vs placebo

Discontinuation rate due to adverse events was similar in all groups.
Alfuzosin 10mg once daily improves ejaculatory dysfunction in real life practice: Results of a 6-month study in 1681 men with LUTS/BPH

1681 sexually active men with LUTS/BPH

(age 60.7 yrs, mean IPSS 17.4, bother score 3.9)

IPSS, short form MSHQ-EjD - baseline and after 6 mons Tx

At end point, IPSS (-7.9), bother score (-1.5), nocturia ≥3 (48.1 to 16.8%)

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>No EjD</th>
<th>Partial EjD</th>
<th>Complete EjD</th>
<th>Bother due to EjD</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-point</td>
<td>54.8%</td>
<td>57.7%</td>
<td>5.8%</td>
<td>48.9%</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.72</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

3% discontinued due to adverse events.
Effect of **dutasteride** on serum testosterone and BMI in men with BPH

107 Pts, 1 yr f/u

3 groups: tamsulosin (n=37), dutasteride (n=33), combination (n=37)

Dutasteride and combination group vs Tamsulosin group

↑ s-T level (16.3 and 15%) (0.3%)

↓ BMI (0.17 and 0.20 kg/m²) (0.04 kg/m²)

**Dutasteride Tx** in men with BPH led to

significant **increase** in serum T level

significant **decrease** in BMI (esp, Pts with relatively lower baseline s-T level)
BPH – 5aRI

AUA 1786. Kaplan S et al.

A 5 YEAR STUDY OF THE USE 5A ALPHA REDUCTASE INHIBITORS IN MEN WITH BPH: FINASTERIDE HAS EQUAL EFFICACY AND PROSTATE VOLUME REDUCTION BUT HAS LESS SEXUAL SIDE EFFECTS AND BREAST ENLARGEMENT THAN DUTASTERIDE

Retrospective, 378 men with LUTS/BPH (197 on FIN, 211 on DUT)

(mean age 58.7 yrs)

Changes in IPSS, Qmax, PVR, PV, and PSA: similar for both groups at 1 and 5 yrs

Incidence of ED, EjD and decreased libido resulting in withdrawal from Tx

DUT (5.1%, 2.4%, 2.7%) vs FIN (2.1%, 1.8%, 1.4%) (p<0.01)

Self reported breast tenderness and/or enlargement

DUT (3.5%) vs FIN (1.2%) (p<0.01)
EFFICACY OF DUTASTERIDE ON BPH ENDPOINTS IN THE REDUCTION BY DUTASTERIDE OF PROSTATE CANCER EVENTS (REDUCE) STUDY ACCORDING TO BASELINE IPSS AND PROSTATE VOLUME

4 yr REDUCE study, Dutasteride vs Placebo

4 subgroups by IPSS and PV (<8, <30 cc; <8, ≥30 cc; ≥8, <30 cc; ≥8, ≥30 cc)

Nonsignificant efficacy in IPSS <8 and PV <30 cc group
CLINICAL OUTCOMES BY BASELINE PROSTATE VOLUME IN MEN WITH BPH: 4 YEAR RESULTS FROM THE COMBINATION OF AVODART AND TAMSULOSIN (COMBAT) TRIAL

4844 men aged ≥50 yrs with BPH (IPSS ≥12, PV ≥30 cc, serum PSA 1.5-10 ng/mL, Qmax 5-15 mL/s)
Divided baseline PV (<42 cc, 42-58 cc, >58 cc)

Combination Tx (vs tamsulosin monoTx)

Reduced the incidence of AUR and BPH-related surgery and clinical progression regardless of baseline PV
Evidence of greater relative risk reduction (RRR) with increasing baseline PV
Clinical outcomes after combination therapy with dutasteride and tamsulosin in men with BPH by baseline characteristics: 4 year results from the randomized, double-blind, Combat trial

<table>
<thead>
<tr>
<th>Age</th>
<th>Percent of patients with AUR or BPH-related surgery</th>
<th>RRR (%, 95% CI)</th>
<th>RRR (%, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 years</td>
<td>D+T 4.4, D 5.2, T 13.1</td>
<td>11.2 (-44.4, 46.3)</td>
<td>66.0 (48.3, 77.6)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>D+T 4.0, D 5.2, T 11.0</td>
<td>24.8 (-15.7, 51.1)</td>
<td>65.4 (49.6, 76.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IPSS</th>
<th>Percent of patients with AUR or BPH-related surgery</th>
<th>RRR (%, 95% CI)</th>
<th>RRR (%, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>D+T 3.5, D 4.8, T 10.5</td>
<td>26.7 (-10.0, 51.2)</td>
<td>67.2 (53.0, 77.0)</td>
</tr>
<tr>
<td>≥20</td>
<td>D+T 5.6, D 6.0, T 15.5</td>
<td>5.0 (-61.4, 44.1)</td>
<td>64.3 (44.2, 77.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PV</th>
<th>Percent of patients with AUR or BPH-related surgery</th>
<th>RRR (%, 95% CI)</th>
<th>RRR (%, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV &lt;40 cc</td>
<td>D+T 4.2, D 4.5, T 6.1</td>
<td>19.2 (-58.3, 58.8)</td>
<td>41.4 (-10.7, 69.0)</td>
</tr>
<tr>
<td>PV ≥40 cc</td>
<td>D+T 4.5, D 5.6, T 14.3</td>
<td>20.5 (-14.7, 44.9)</td>
<td>70.2 (59.2, 78.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PSA</th>
<th>Percent of patients with AUR or BPH-related surgery</th>
<th>RRR (%, 95% CI)</th>
<th>RRR (%, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 ng/mL</td>
<td>D+T 2.8, D 5.0, T 8.4</td>
<td>44.3 (1.0, 68.7)</td>
<td>65.8 (41.3, 80.1)</td>
</tr>
<tr>
<td>≥3 ng/mL</td>
<td>D+T 5.1, D 5.4, T 14.0</td>
<td>4.8 (-40.9, 35.7)</td>
<td>65.1 (51.7, 74.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BMI</th>
<th>Percent of patients with AUR or BPH-related surgery</th>
<th>RRR (%, 95% CI)</th>
<th>RRR (%, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;27.5 kg/m²</td>
<td>D+T 4.6, D 10.4, T 14.0</td>
<td>-5.8 (-60.8, 30.4)</td>
<td>53.4 (33.5, 67.4)</td>
</tr>
<tr>
<td>≥27.5 kg/m²</td>
<td>D+T 5.8, D 13.3, T 13.3</td>
<td>43.3 (4.3, 66.5)</td>
<td>76.9 (63.2, 85.5)</td>
</tr>
</tbody>
</table>

The **RRR for combination therapy was decreased across Pt baseline characteristics** when compared with tamsulosin or dutasteride monotherapy.
BPH – Combination Tx

AUA 1785. Siami P et al.

COMBINATION Tx WITH DUTASTERIDE AND TAMSULOSIN PROVIDED GREATER IMPROVEMENTS THAN EITHER MONOTx REGARDLESS OF PRIOR BPH OR LOWER URINARY TRACT Tx STATUS (COMBAT)

Regardless of past BPH Tx,

Combination Tx vs. tamsulosin monoTx (over 4 yrs)

provided a significantly reduced relative risk of

AUR and BPH-related surgery and clinical progression.

Significant improvements in IPSS, Qmax, and PV.

Combination vs. dutasteride : a significant RRR

in BPH clinical progression
Combination therapy with dutasteride plus tamsulosin reduces medical resource utilisation in men with BPH: 4-year data from the CombAT study

Total days of hospitalisation, or prolonged duration of hospital stay, due to AUR or BPH-related surgery was reduced in combination group (159 days),

by 74% compared with tamsulosin group (614 days)
by 33% compared with dutasteride group (238 days).
Intraprostatic injection of botulinum toxin type A causes a long-lasting improvement in LUTS and urinary flow in patients with BPE refractory to standard medical therapy

37 Pts (mean age 75.9 yrs), symptomatic BPE refractory to medication, with severe contraindications for surgery

200 U BoNT/A injected, 12 mon f/u

IPSS, QoL, Qmax, PVR – improved

PV – baseline 75.1 and 49.5, 42.6, 41.9, 42.6 ml (1, 3, 6, 12 mon)
s-PSA – no change

6 Pts developed clinical prostatitis.

Promising Tx in elderly Pts with great comorbidities or unwilling to undergo surgery.
BPH – Botulinum Toxin

AUA 1780. McVary K et al.

MIST2: BASELINE PSA AND TOTAL PROSTATE VOLUME PREDICTS CLINICAL RESPONSE TO INTRAPROSTATIC INJECTION OF BOTULINUM TOXIN FOR THE MANAGEMENT OF LUTS

MIST2: the NIDDK multi-center phase II randomized trial (BoNT/A 100 vs 300 U)

108 Pts, AUASS \( \geq 8 \) (mean 11), age \( \geq 50 \) (mean 66 yrs), mean TPV 50.1 ml,
BoNT/A 100 or 300 U, 12 mon f/u

Significant changes noted in AUASS and Qmax at 3 and 12 months
Without significant changes in TPV, TZV, or PSA
The greatest response in AUASS occurs in those with the lowest PSA and TPV.
EVALUATION OF TRANSPERINEAL PROSTATIC ADMINISTRATION OF A PSA-ACTIVATED PROTOXIN (PRX302) IN MEN WITH LUTS SECONDARY TO BPH

Mechanism of action of PRX302

- PRX302 is unique among products for BPH in that it is only activated by PSA in the prostate capsule

PRX302 binds to a receptor on cell surface

- PSA protease cleaves tail, activating toxin

PRX302 then combines with other activated PRX302 molecules

PRX302 assembles into a structure that inserts in the cell membrane, forming a pore

Cell contents leak out causing cell death

*PRX302 is a modified form of the bacterial toxin proaerolysin produced by Aeromonas hydrophila. Aerolysin is a cytolysin.
## BPH – PSA-activated Protoxin (PRX302)

**AUA 1787. Elhilali M et al.**

<table>
<thead>
<tr>
<th></th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase IIb</th>
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<tbody>
<tr>
<td><strong>Design</strong></td>
<td>Open-label Dose escalation</td>
<td>Open-label Volume escalation</td>
<td>Double-blind, placebo-controlled</td>
</tr>
<tr>
<td><strong>Patients</strong></td>
<td>15 in 5 cohorts</td>
<td>18 in 3 cohorts</td>
<td>92 enrolled 2:1 randomized</td>
</tr>
<tr>
<td><strong>PRX302 Conc.</strong></td>
<td>0.75-10.5 µg/mL</td>
<td>3 µg/mL</td>
<td>3 µg/mL</td>
</tr>
<tr>
<td><strong>PRX302 Volume</strong></td>
<td>0.25mL/deposit 1.3 mL/deposit in 1 cohort</td>
<td>10, 20 or 30% of prostate volume</td>
<td>20% of prostate volume</td>
</tr>
</tbody>
</table>
At 12 mon

**PV** (mean): Decreased **27.9%**.

**QoL** (mean): **4.6 to 1.9**
**BPH – Nocturia**

EAU 993. Simaioforidis V et al.

**Tamsulosin versus transurethral prostatectomy** in the treatment of nocturia in men with BPH as only causal factor: A prospective randomized trial

60 BPH Pts with nocturia, 30 Tamsulosin (A) vs 30 TURP (B)

3 mon, 1 yr f/u with FVC, IPSS, ICIQ-N, ICIQ-Nqol questionnaire

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>Baseline Mean(SD)</th>
<th>3 mon Mean(SD)</th>
<th>1 yr Mean(SD)</th>
<th>F-test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICIQ-N</td>
<td>A</td>
<td>3.22(1.31)</td>
<td>2(0.59)</td>
<td>1.82(0.88)</td>
<td>4.015</td>
<td>0.022</td>
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<tr>
<td></td>
<td>B</td>
<td>3.89(1.37)</td>
<td>2.14(0.94)</td>
<td>2.06(1.16)</td>
<td>25.827</td>
<td>0.000</td>
</tr>
<tr>
<td>ICIQ-Nqol</td>
<td>A</td>
<td>23.3(7.99)</td>
<td>15.88(6.31)</td>
<td>15.57(5.24)</td>
<td>2.764</td>
<td>0.070</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>25.2(6.4)</td>
<td>12.5(5.28)</td>
<td>11.66(4.4)</td>
<td>7.400</td>
<td>0.001</td>
</tr>
<tr>
<td>Awakenings per night</td>
<td>A</td>
<td>2.02(0.64)</td>
<td>1.33(0.44)</td>
<td>1.18(0.39)</td>
<td>8.324</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>2.2(0.69)</td>
<td>1.37(0.65)</td>
<td>1.35(0.61)</td>
<td>32.833</td>
<td>0.000</td>
</tr>
<tr>
<td>HUS (min)</td>
<td>A</td>
<td>152(69.8)</td>
<td>181(57.2)</td>
<td>190.8(53.4)</td>
<td>12.979</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>121(41.6)</td>
<td>128(51.6)</td>
<td>135.6(48)</td>
<td>40.615</td>
<td>0.000</td>
</tr>
</tbody>
</table>

In both groups, all parameters of nocturia improved significantly with time. The improvement of parameters between the groups: no significant difference.
Comparing the efficacy of a selective cyclooxygenase-2 inhibitor and an anticholinergic in Pts with BPH and refractory nocturia

60 BPH Pts with ≥ 2 nocturia, 32 meloxicam vs 28 propiverine for 2 wks

Mean No of nocturia: -1.7±0.8 (p=.000) and -0.9±0.9 (p=.000)
Mean nocturnal u-vol: -163.6±194.9ml (p=.000) and -9.4±45.2ml (p=.281)
Daytime frequency and u-vol; no differences in both groups (P>.05)
Nocturnal FBC was increased only in propiverine group.

Selective COX-2 inhibitor is a more effective Tx than anticholinergic for refractory nocturia in Pts with BPH.
The main Mx of COX-2 inhibitor for decreasing nocturia may be the reduction of nocturnal urine production.
BPH – Nocturia

AUA 1528. Weiss JP et al.

**FAST-DISSOLVING DESMOPRESSIN (MELT) IS WELL TOLERATED IN NOCTURIA: RESULTS OF A RANDOMIZED, PLACEBO-CONTROLLED STUDY**

Phase 3 randomized, double-blind, placebo-controlled, multicenter study

**779 Pts for 28 days**

5 groups (placebo or desmopressin Melt 10μg, 25 μg, 50 μg or 100 μg)

Hyponatremia was dose-related at doses of ≥50 μg.

more common in subjects ≥65 yrs of age (1%, <65 and 7%, ≥65 yrs)

AUA 1529. Imnadze M et al.

**NOVEL NON-PEPTIDE PHARMACOLOGIC THERAPY FOR NOCTURIA IN MEN**

(VA106483), a selective vasopressin V2-receptor agonist:

increased urine osmolality and reduced diuresis in all elderly men with nocturia
The long-term safety and efficacy of tadalafil 5mg once-daily in men with LUTS/BPH

1-year open-label extension study of 12-week double-blind dose-finding global study, men with LUTS/BPH treated with once daily placebo or tadalafil (2.5, 5, 10 or 20 mg)

57.6% of Pts reported at least 1 AE: dyspepsia (4.0%), GERD (4.0%), back pain (3.7%), headache (3.0%), sinusitis (2.8%), hypertension (2.6%), and cough (2.1%)

Discontinuation: patient decision (n=59), adverse event (n=22), patient lost to follow-up (n=16), perceived lack of efficacy (n=15)

Tadalafil 5 mg once daily provided a favourable risk/benefit profile for 1 yr.
OAB - Anticholinergics

EAU 776. Crosby RD et al.

Relationships between changes in OAB Sxs and in subjective assessments of Sx bother and health-related quality of life (HRQL) in patients taking solifenacin or placebo in the VIBRANT study

738 Pts, solifenacin (5/10 mg) or placebo for 12 wks
3-day bladder diaries, OAB-q, HRQL with 4 domains
Degree of improvement: “Major”, “Some”, “None” by bladder diaries

Sxs of urgency, incontinence, and frequency: low to moderate correlations with changes in Symptom Bother and HRQL
Both bladder diaries and the OAB-q are important for assessing efficacy in OAB clinical trials.
OAB - Anticholinergics

Effect of antimuscarinics on the linear correlation and regression between Severity of Urge Sensation (SUS) and Voided Volume (VV) in patients with OAB

Randomized, double-blind, multicenter trial

Fesoterodine 8 mg or placebo for 12 wks

5-point SUS scale (1=no urgency, 2=mild, 3=moderate, 4=severe, 5=UI)

SUS correlated linearly with VV; indicating increased bladder volume during the filling phase may trigger urgency.

Antimuscarinics may reduce urgency by increasing the urgency sensation threshold through the increase of bladder capacity.
Evaluation of fesoterodine efficacy over 24 hours following once-daily dosing in subjects with OAB

Fesoterodine 4 mg and 8 mg given once daily demonstrated efficacy over placebo for OAB symptoms across the entire 24-hour period.

How many days do patients with OAB take new anti-cholinergic agents? Results from real clinical practice

Only about 17\% of all Pts persisted with the Tx over 1 year.

The No of Pts who discontinued the Tx owing to adverse events was consistent with those of other reports.

Many Pts might discontinue the Tx owing to relief of their OAB symptoms.
THE PHARMACOLOGIC Tx OF OAB: A SYSTEMATIC EVIDENCE REVIEW

RCTs of Oxybutynin (13), Tolterodine (19), Fesoterodine (2), Solifenacin (3), Darifenacin (4), and Trospium (5)

All pharmacologic Tx were effective at improving OAB symptoms when compared to placebo. No one drug was definitively superior to others by preponderance of evidence

EAU 772. Kessler TM et al.

Adverse event assessment of antimuscarinic for treating OAB: A network meta-analytic approach

Included 69 trials enrolling 26229 Pts

Most currently used antimuscarinics seem to be equivalent 1st choice drugs to start the Tx of OAB except for oxybutynin dosages of ≥10mg/d which may have more unfavourable adverse events.
Dose-ranging study of once-daily mirabegron (YM178), a novel selective β3-adrenoceptor agonist, in Pts with OAB

The 1st report of a dose-ranging study (Phase IIb) using mirabegron
919 Pts, 12-week, multicentre, double-blind, randomized
Efficacy: micturition diaries
Safety: v/s, lab monitoring, EKG, adverse event (AE) reporting

<table>
<thead>
<tr>
<th>Variable (per 24-hour period)</th>
<th>Placebo</th>
<th>Mirabegron (mg qd)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>25</td>
</tr>
<tr>
<td>Micturitions (primary endpoint)</td>
<td>-1.4</td>
<td>-1.9</td>
</tr>
<tr>
<td>Volume voided per micturition (mL)</td>
<td>7.3</td>
<td>15.3</td>
</tr>
<tr>
<td>Incontinence episodes</td>
<td>-0.5</td>
<td>-1.4*</td>
</tr>
<tr>
<td>Urgency incontinence episodes</td>
<td>-0.4</td>
<td>-1.3*</td>
</tr>
<tr>
<td>Urgency episodes (grade ≥3)</td>
<td>-1.1</td>
<td>-1.8*</td>
</tr>
</tbody>
</table>

* p<0.05 versus placebo

AE: 45.2% of Pts ≥1 AE (placebo: 43.2%; mirabegron: 43.8–47.9%)
Discontinued: 3.2% of Pts (placebo: 3.0%; mirabegron: 2.4–5.3%).
Most common AEs: infections and infestations (14.1%), GI disorders (12.1%)
OAB – EP-1 Receptor Antagonist

EAU 777. Wilbraham D et al.

Safety, tolerability and pharmacokinetic of multiple ascending doses of the EP-1 receptor antagonist ONO-8539, a potential new and novel therapy to OAB in healthy young and elderly subjects


Randomized, double-blind, placebo-controlled design
32 young males and 10 male and 8 female elderly

The most frequent AEs: URI in 2 subjects in the young
Headache in 3 subjects in the elderly.
No evidence of a dose relationship with the occurrence of AEs
No significant changes in lab tests, v/s or ECG

ONO-8539 may be promising for the Tx of OAB without the recognized side effects seen with oral antimuscarinics.
Reduction of urgency severity is the key for long-term success of intravesical Botulinum Toxin A injection for OAB.

174 Pts, 100 U BoNT-A, 3 mon f/u (included cystometry)

- **Sensory effect:** ↓USS by > 2 scales or ↑bladder vol at urgency sensation by 50%
- **Motor effect:** ↑CBC by 50% or ↑PVR by 50% or ↓Pdet by 50%

Overall Tx effect: become dry or ↓urgency or UI episodes by 50%

Pts global satisfaction

Successful results: 138 (79.3%) Pts, Satisfactory outcome: 123 (70.7%) Pts

Both sensory & motor effects: 44.3%

Sensory effect alone: 2.9%, Motor effect alone: 47.7%

All 82 Pts who had sensory effect: successful and 95% of Pts were satisfied.

Only 60.2% of Pts with motor effect alone were successful and only 49.4% of Pts were satisfied.

The Tx effect was significantly longer in the Pts with sensory effect.

Improvement of urgency severity seems to be the key for the long-term success of BoNT-A Tx for OAB.
Effect of repeated intradetrusor injections of Botulinum-A Toxin on urodynamics and clinical parameters in Pts with refractory Idiopathic DO

45 Pts (35 women and 10 men) with relapsing Sxs of OAB
Clinical checks and standard UDS studies before and 12 wks after injections of 100 U of BoNT-A
The Tx interval: 4 to 28 mons (mean 12 mons)

MCC: 245 ml (baseline), 380 ml (1st inj), 420 ml (2nd inj) (p=0.04).
The end filling detrusor Pr: 41 cmH2O, 34 cmH2O, 23 cmH2O (p=0.003).
Bladder compliance: 22 ml/cmH2O, 45 and 52 ml/cmH2O (p=0.0001)

Improvement of Pts reported OAB Sxs after Tx, and QoL: no significant differences between a first and a consecutive injection

Repeated injections could negatively affect bladder wall structure.
OAB – Botulinum Toxin

AUA 1519. Kuo HC et al.

RISK FACTORS OF ADVERSE EVENTS AFTER INTRAVESICAL BOTULINUM TOXIN A INJECTIONS FOR REFRACTORY OAB

Risk factors

**AUR:** male, age >75, PVR >100 ml, voiding efficiency <70%

**Elevated PVR and straining to void:**

- OAB-wet, age >75, PVR >100 ml, co-morbidity, high dose (200 U) toxin

**UTI:** female, BPH Pts

Effective dose range from the benefit/risk evaluation in idiopathic OAB:

- 100-150 U of BOTOX®

Intravesical electromotive botulinum toxin type A administration: Preliminary findings for the Tx of children with myelomeningocele and refractory neurogenic DO

15 children (mean age 7.8 yrs), 9 mon f/u
10 IU/kg of BTX-A was inserted to distended bladder through a specifically designed catheter. Being connected to indwelling catheter and two dispersive pads, a pulsed current generator was set to deliver 10mA for the total of 15 minutes.

<table>
<thead>
<tr>
<th>Follow-up sessions</th>
<th>9 months</th>
<th>4 months</th>
<th>1 month</th>
<th>Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean reflex volume (mL)</td>
<td>216 ± 5 (P=0.005)</td>
<td>220 ± 38 (P&lt;0.001)</td>
<td>223 ± 36 (P&lt;0.001)</td>
<td>99 ± 35</td>
</tr>
<tr>
<td>Mean maximal bladder capacity (mL)</td>
<td>262 ± 41 (P=0.001)</td>
<td>265 ± 38 (P&lt;0.001)</td>
<td>265 ± 39 (P&lt;0.001)</td>
<td>121 ± 39</td>
</tr>
<tr>
<td>Mean maximal detrusor pressure (cm H2O)</td>
<td>39 ± 10 (P&lt;0.001)</td>
<td>38 ± 10 (P&lt;0.001)</td>
<td>36 ± 10 (P&lt;0.001)</td>
<td>75 ± 16</td>
</tr>
<tr>
<td>Mean end- filling pressure (cm H2O)</td>
<td>13 ± 2 (P=0.001)</td>
<td>12 ± 3 (P=0.001)</td>
<td>11 ± 3 (P=0.001)</td>
<td>22 ± 7</td>
</tr>
</tbody>
</table>

Electromotive BTX- A administration is a feasible, safe, and low-priced method with no need for anaesthesia or hospital admission. Delivery into the whole bladder detrusor wall
Thank you for your attention!!!