Supporting Information

Efficacy of Vibegron and Mirabegron for Overactive Bladder:
A Systematic Literature Review and Indirect Treatment Comparison

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Supplementary Table 1. Systematic Literature Review Eligibility Criteria

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| --- | --- |
| **Study Characteristic** | **Criteria** |
| Population | Adults, ≥18 years, with a prior diagnosis of OAB; no restrictions on sex, race, or other demographic characteristics |
| Interventions | β3-adrenergic receptor agonist (vibegron 75 mg, mirabegron 25/50 mg) |
| Comparators | Placebo or active controls |
| Outcomes | Daily number of total urinary incontinence episodes, daily number of micturitions, volume voided per micturition |
| Timing | ≥12 weeks of exposure |
| Study design | Phase 3, randomized, double-blind, controlled trials |
| Language | English |

OAB, overactive bladder.

Supplementary Table 2. Data Extraction

|  |  |
| --- | --- |
| **Data Item** | **Description** |
| Source | Authors, citation, corresponding author contact details |
| Study design | Randomized, double-blind, controlled phase 3 clinical trial with placebo or active controls; time points: baseline and weeks 4, 12, and 52 |
| Population | Total number of participants, inclusion and exclusion criteria, OAB type (ie, wet vs dry at baseline), age, sex, ethnicity, country |
| Analysis  | Measures assessed (eg, change from baseline, missing data methods) |
| Confounding factors | If applicable since studies are randomized |
| Drug interventions | Drug name(s), dosage, frequency, duration of treatment |
| Outcome assessment | Manner of assessment; outcomes of interest: mean daily number of total urinary incontinence episodes, mean daily number of micturitions, volume voided per micturition |
| Control interventions | Placebo or active control  |
| Results | Number of participants in each intervention group; for each documented outcome of interest: sample size, missing participants, study measures of association, CIs, *P* values, statistical test used  |
| Limitations | Limitations reported  |
| Quality and bias assessments | Cochrane Risk of Bias Tool for randomized controlled trials |

OAB, overactive bladder.

Supplementary Table 3. Baseline Characteristics for Total Incontinence Episodes, Micturitions, and Volume Voided

| **Study** | **Treatment** | **Total Incontinence Episodes,\* No.** | **Micturitions,† No.** | **Volume Voided,† mL** |
| --- | --- | --- | --- | --- |
| Chapple et al 2013 [1], mean (SE) | Mirabegron 50 mg | 2.66 (0.12) | 11.13 (0.10) | 160.1 (2.09) |
| Tolterodine 4 mg ER | 2.42 (0.11) | 10.94 (0.09) | 160.1 (2.01) |
| Herschorn et al 2013 [2], mean (SE) | Placebo | NR | NR | NR |
| Mirabegron 25 mg | 2.65 (0.16) | 11.68 (0.15) | 165.2 (2.8) |
| Mirabegron 50 mg | 2.51 (0.15) | 11.66 (0.16) | 159.3 (2.5) |
| Khullar et al 2013 [3], mean (SE) | Placebo | 2.67 (0.14) | 11.71 (0.14) | NR |
| Mirabegron 50 mg | 2.83 (0.17) | 11.65 (0.14) | NR |
| Tolterodine 4 mg ER | 2.63 (0.15) | 11.55 (0.13) | NR |
| Nitti et al 2013 [4], mean (SD) | Placebo | 3.0 (3.1) | 11.5 (3.3) | 157.5 (58.7) |
| Mirabegron 50 mg | 2.8 (2.7) | 11.8 (3.5) | 156.0 (58.7) |
| Yamaguchi et al 2014 [5], mean (SD) | Placebo | 1.91 (1.76) | 11.29 (2.75) | 146.8 (44.2) |
| Mirabegron 50 mg | 1.99 (2.05) | 11.15 (2.65) | 149.6 (46.4) |
| Tolterodine 4 mg ER | 1.89 (1.83) | 11.10 (2.57) | 145.9 (46.9) |
| Kuo et al 2015 [6], mean (SD) | Placebo | 2.35 (2.70) | 12.59 (4.91) | 152.6 (55.0) |
| Mirabegron 50 mg | 2.37 (2.54) | 12.09 (4.11) | 147.8 (52.7) |
| Tolterodine 4 mg ER | 2.25 (2.78) | 12.13 (3.67) | 150.2 (57.2) |
| Herschorn et al 2017 [7], mean (SD) | Placebo | 3.41 (3.37) | 10.97 (2.86) | 157.9 (58.8) |
| Mirabegron 25 mg | 3.42 (3.40) | 10.81 (2.63) | 152.5 (61.0) |
| Mirabegron 50 mg | 3.18 (3.47) | 11.19 (3.27) | 155.3 (60.8) |
| Staskin et al 2020 [8], mean (SD)‡ | Placebo | 4.17 (3.82) | 11.75 (4.01) | 148.3 (60.7) |
| Vibegron 75 mg | 4.14 (3.63) | 11.31 (3.42) | 155.4 (63.1) |
| Tolterodine 4 mg ER | 4.06 (3.07) | 11.48 (3.15) | 147.0 (60.8) |

ER, extended release; FAS, full analysis set; FAS-I, FAS for incontinence; NR, not reported.

\*Analyzed in the FAS-I, broadly defined as all patients receiving ≥1 dose of double-blind study drug who had a baseline and ≥1 postbaseline assessment and ≥1 incontinence episode at baseline.

†Analyzed in the FAS, broadly defined as all patients receiving ≥1 dose of double-blind study drug who had a baseline and ≥1 postbaseline assessment.

‡Baseline values reported for the 12-week EMPOWUR trial. Baseline definitions for the extension trial differed for patients continuing active treatment vs patients who received placebo during the 12-week trial.

Supplementary Table 4. Differences in Effect Size of Change From Baseline for Vibegron, Mirabegron, and Tolterodine

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Efficacy Endpoint | Week | Vibegron vs Mirabegron 25 mg | Vibegron vs Mirabegron 50 mg | Vibegron vs Tolterodine 4 mg ER |
| Effect Size (95% CI)\* | *P* Value | Effect Size (95% CI)\* | *P* Value | Effect Size (95% CI)\* | *P* Value |
| Total incontinence episodes | 4 | ‒0.46 (‒0.89, ‒0.03) | 0.037 | ‒0.35 (‒0.67, ‒0.02) | 0.038 | ‒0.39 (‒0.73, ‒0.06) | 0.023 |
| 12 | ‒0.32 (‒0.70, 0.06) | 0.1 | ‒0.31 (‒0.65, 0.03) | 0.074 | ‒0.44 (‒0.80, ‒0.07) | 0.02 |
| 52 | N/A | ‒ | ‒0.85 (‒1.40, ‒0.30) | 0.003 | N/A | ‒ |
| Micturitions | 4 | ‒0.42 (‒0.86, 0.02) | 0.059 | ‒0.17 (‒0.47, 0.14) | 0.279 | ‒0.28 (‒0.59, 0.03) | 0.076 |
| 12 | ‒0.09 (‒0.47, 0.29) | 0.634 | 0.06 (‒0.26, 0.39) | 0.709 | ‒0.20 (‒0.56, 0.15) | 0.265 |
| 52 | N/A | ‒ | ‒0.52 (‒1.25, 0.21) | 0.163 | N/A | ‒ |
| Volume voided | 4 | N/A | ‒ | 8.34 (‒0.37, 17.05) | 0.06 | 8.94 (0.20, 17.69) | 0.045 |
| 12 | 16.48 (8.13, 24.83) | 0 | 8.69 (1.37, 16.01) | 0.02 | 7.94 (‒0.77, 16.65) | 0.074 |
| 52 | N/A | ‒ | 18.30 (1.16, 35.44) | 0.036 | N/A | ‒ |

ER, extended release; N/A, not available.

\*Effect sizes are calculated using placebo-subtracted changes from baseline for weeks 4 and 12 and tolterodine-subtracted changes from baseline for week 52.

Supplementary Table 5. Summary of AEs Occurring in ≥5% of Patients and Reported in Each Short-Term Trial (Safety Analysis Sets)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **AE, %** | **Herschorn et al 2013 [2]** | **Khullar et al2013 [3]** | **Nitti et al 2013 [4]** | **Yamaguchi et al 2014 [5]** | **Kuo et al2015 [6]** | **Staskin et al 2020 [8]** |
| **M25** | **M50** | **PBO** | **M50** | **PBO** | **T4ER** | **M50** | **PBO** | **M50** | **PBO** | **T4ER** | **M50** | **PBO** | **T4ER** | **V75** | **PBO** | **T4ER** |
| N | 432 | 440 | 433 | 493 | 494 | 495 | 442 | 453 | 379 | 379 | 375 | 366 | 366 | 371 | 545 | 540 | 430 |
| Hypertension | 11.3 | 10.7 | 8.5 | 5.9 | 7.7 | 8.1 | 6.1 | 6.6 | \* | \* | \* | \* | \* | \* | \* | \* | \* |
| UTI | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | 5.0 | 6.1 | 5.8 |
| Dry mouth | \* | \* | \* | \* | \* | 10.1 | \* | \* | \* | \* | 13.3 | \* | \* | 8.1 | \* | \* | 6.5 |
| Nasopharyngitis | \* | 5.7 | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* | \* |

AE, adverse event; M25, mirabegron 25 mg; M50, mirabegron 50 mg; PBO, placebo; T4ER, tolterodine 4 mg extended release; UTI, urinary tract infection; V75, vibegron 75 mg.

\*AE present in <5% of patients in treatment group.

Supplementary Table 6. Summary of AEs Occurring in ≥5% of Patients and Reported in Each Long-Term Trial (Safety Analysis Sets)

|  |  |  |
| --- | --- | --- |
| **AE, %** | **Chapple et al 2013 [1]** | **Staskin et al2021 [9]** |
| **Mirabegron 50 mg** | **Tolterodine 4 mg ER** | **Vibegron 75 mg** | **Tolterodine 4 mg ER** |
| N | 812 | 812 | 273 | 232 |
| Hypertension | 9.2 | 9.6 | 8.8 | 8.6 |
| UTI | 5.9 | 6.4 | 6.6 | 7.3 |
| Dry mouth | \* | 8.6 | \* | 5.2 |
| Nasopharyngitis | \* | \* | \* | 5.2 |
| Headache | \* | \* | 5.5 | \* |

AE, adverse event; UTI, urinary tract infection.

\*AE present in <5% of patients in both treatment groups.

Supplementary Figure 1. Network map of treatments for overactive bladder. Solid lines indicate a direct comparison between treatments; dashed line indicates an indirect comparison between treatments that can be made using the adjusted indirect treatment comparison method by Bucher et al [10]. Solid lines between vibegron and tolterodine and between mirabegron and tolterodine indicate a comparison at week 52. ER, extended release.



Supplementary Figure 2. Weighted average of change from baseline in total incontinence episodes for active treatment groups; n indicates the number of trials included in each assessment. Effect sizes at weeks 4 and 12 were calculated using placebo-subtracted changes from baseline; effect size at week 52 was calculated using tolterodine-subtracted changes from baseline. ER, extended release.



Supplementary Figure 3. Weighted average of change from baseline in mean daily micturitions for active treatment groups; n indicates the number of trials included in each assessment. Effect sizes at weeks 4 and 12 were calculated using placebo-subtracted changes from baseline; effect size at week 52 was calculated using tolterodine-subtracted changes from baseline. ER, extended release.



Supplementary Figure 4. Weighted average of change from baseline in volume voided per micturition (mL) for active treatment groups; n indicates the number of trials included in each assessment. Effect sizes at weeks 4 and 12 were calculated using placebo-subtracted changes from baseline; effect size at week 52 was calculated using tolterodine-subtracted changes from baseline. ER, extended release.



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