Overactive Bladder

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報告日期：2022.11.17

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International Urology and Nephrology

UROLOGY - REVIEW

Vibegron 50 mg is the optimal algorithm in the pharmacologic management of overactive bladder: outcomes from a systematic review and meta-analysis

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Background

Overactive Bladder

Definition

Presence of urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence (UUI), in the **absence of urinary tract infection or other obvious pathology**

Urgency

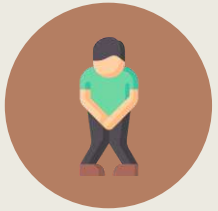
Hallmark of OAB

Frequency

> 8 micturition episodes

Nocturia

≥ 1 interruption of sleep



UUI

Involuntary leakage of urine

1. International Continence Society: Overactive Bladder

Epidemiology

Worldwide

546 million

Affected individuals

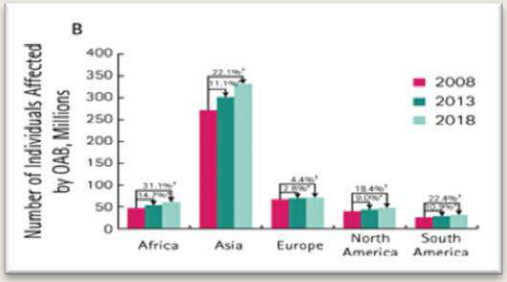
10.9%

2018

♂ < ♀

10% 11.9%

Increasing by age



Taiwan

16.9%

Prevalence

♂ < ♀

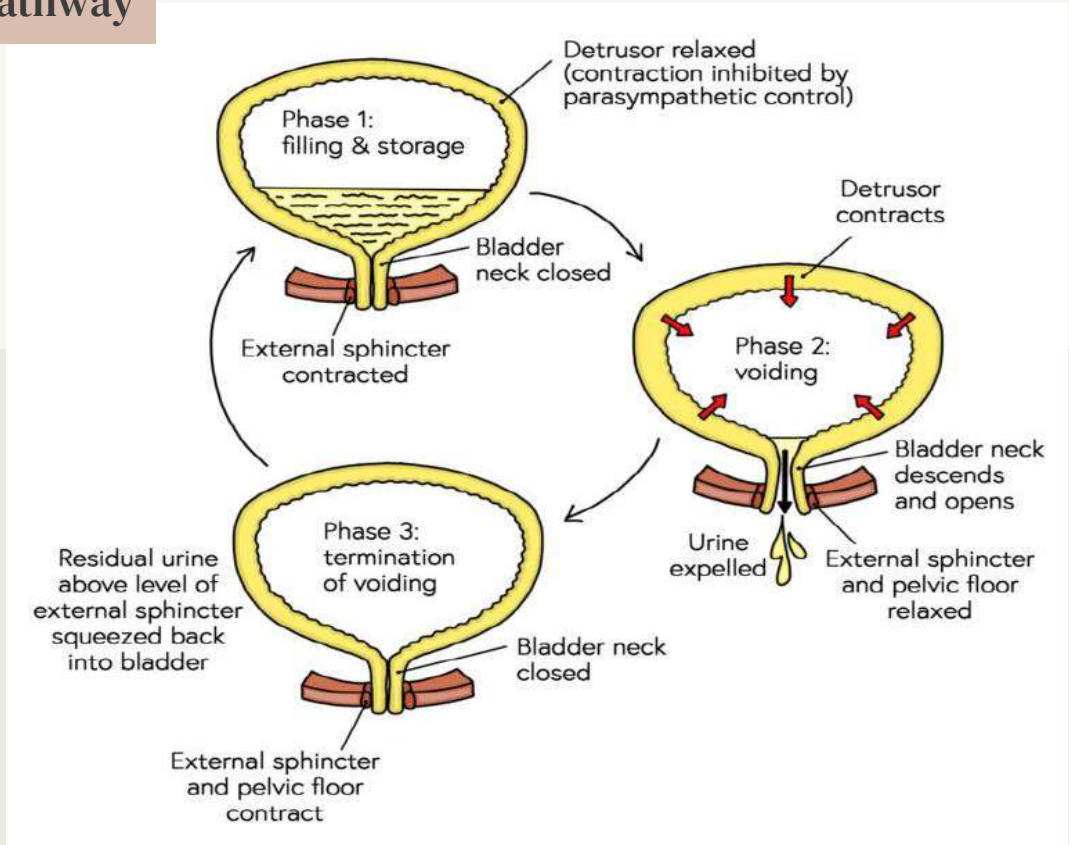
16% 18.9%

Increasing by age

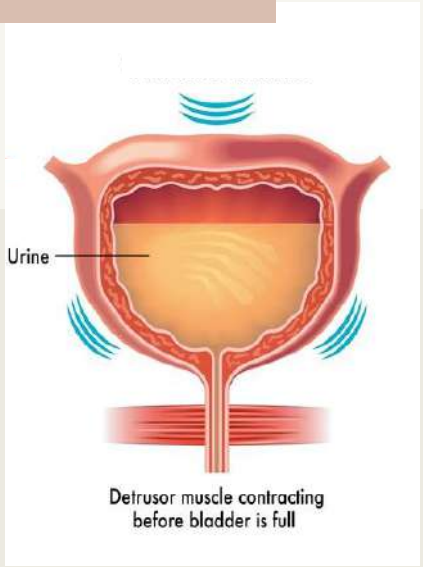
1. Irwin, D.E., Kopp, Z.S., Agatep, B., Milsom, I. and Abrams, P. (2011), Worldwide prevalence estimates of lower urinary tract symptoms, overactive bladder, urinary incontinence and bladder outlet obstruction. BJU International, 108: 1132-1138.
2. Yu HJ, Liu CY, Lee KL, Lee WC, Chen TH: Overactive bladder syndrome among community-dwelling adults in Taiwan: prevalence, correlates, perception, and treatment seeking. UrolInt2006;77:327-33.

Pathophysiology

Normal pathway



Overactive



Diagnosis

Clinical Principle

Document symptoms and signs that characterize OAB and **exclude other disorders**

Physical exam

Abdominal exam, a rectal/genitourinary exam

Urinalysis

Rule out UTI and hematuria

Others

- Urine culture
- Post-void residual
- Bladder diaries
- Symptom questionnaires

1.Report from Overactive Bladder Committee
2. Diagnosis and Treatment of Non-Neurogenic Overactive Bladder (OAB) in Adults: AUA/SUFU Guideline (2019)

Overactive Bladder Symptom Score (OABSS)

Question	Frequency	Score
1. How many times do you typically urinate from waking in the morning until sleeping at night	≤ 7 8-14 ≥ 15	0 1 2
2. How many times do you typically wake up to urinate from sleeping at night until walking in the morning?	0 1 2 ≥ 3	0 1 2 3
3. How often do you have a sudden desire to urinate, which is difficult to defer?	Not at all Less than once a week Once a week or more About once a day 2-4 times a day 5 times a day or more	0 1 2 3 4 5
4. How often do you leak urine because you cannot defer the sudden desire to urinate?	Not at all Less than once a week Once a week or more About once a day 2-4 times a day 5 times a day or more	0 1 2 3 4 5

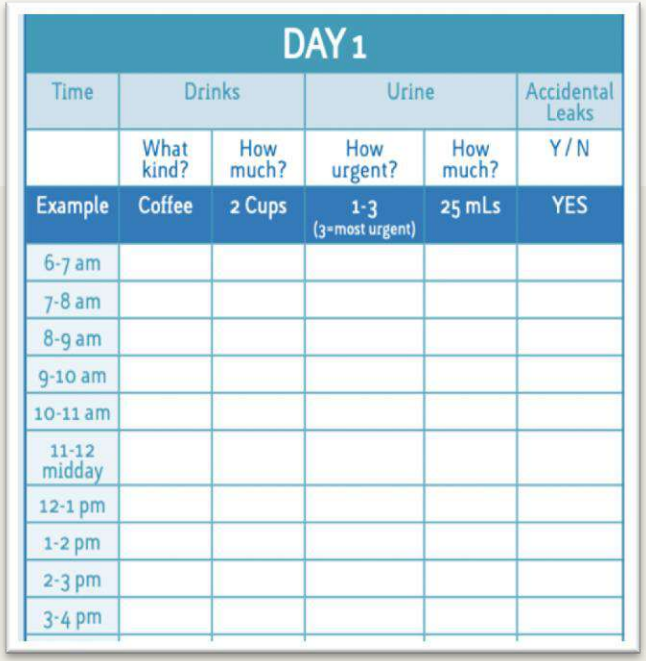
Differentiation

Nocturia Normal or large volume voids vs Small volume voids

Polydipsia Use of frequency-volume charts

Interstitial cystitis/bladder pain syndrome Pelvic pain

Others condition Atrophic vaginitis and other infections



DAY 1					
Time	Drinks		Urine		Accidental Leaks
	What kind?	How much?	How urgent?	How much?	Y / N
Example	Coffee	2 Cups	1-3 (3=most urgent)	25 mLs	YES
6-7 am					
7-8 am					
8-9 am					
9-10 am					
10-11 am					
11-12 midday					
12-1 pm					
1-2 pm					
2-3 pm					
3-4 pm					

1.Report from Overactive Bladder Committee
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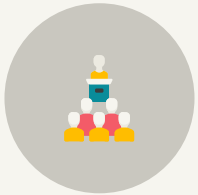
Treatment



Behavioral Treatments

- Bladder training
- Bladder control strategies
- Fluid management

Pharmacological Treatments

- Antimuscarinic
- Beta-3 adrenergic agonists

Others

- Electrical simulation therapy
- Botulinum toxin
- Surgery

Aim: Relieves symptoms and improve quality of life

Behavioral Treatment

Lifestyle interventions

Avoid drinking 2 hours before sleeping

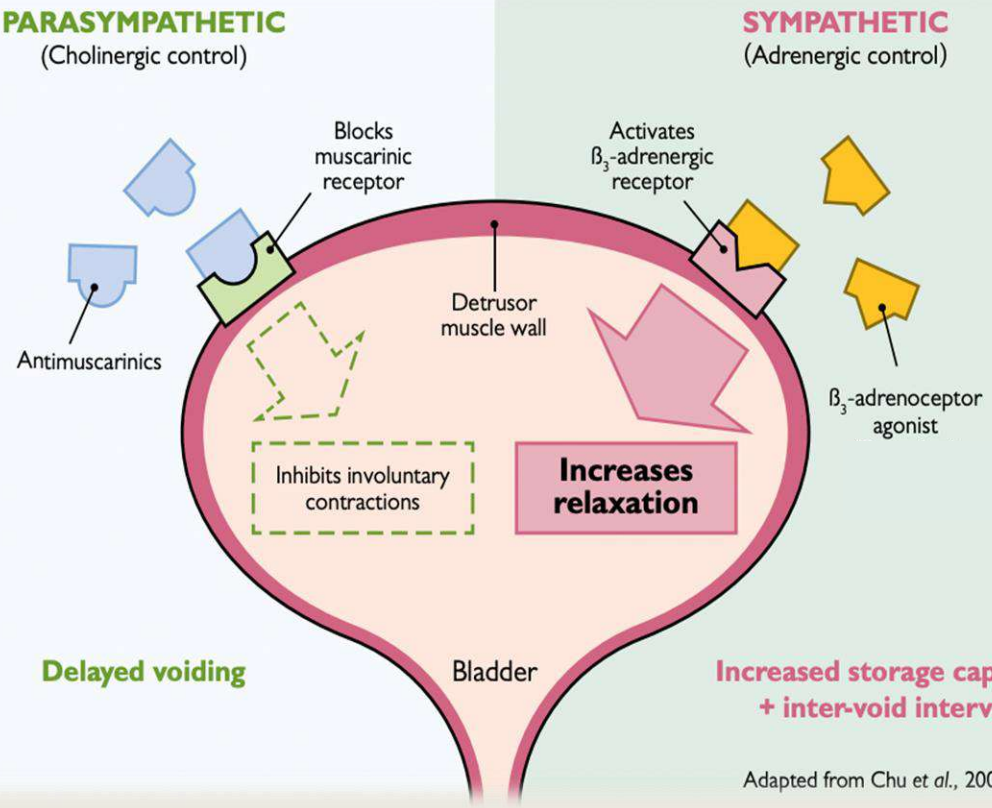
Bladder training

- Amount of time between emptying your bladder
- Amount of fluids your bladder can hold.
- Leakage and the sense of urgency

1.Report from Overactive Bladder Committee

Treatments' Mode of Action

Oxybutynin
Tolterodine
Darifenacin
Fesoterodine
Solifenacin
Trospium



Mirabegron
Vibegron

Anti-muscarinics

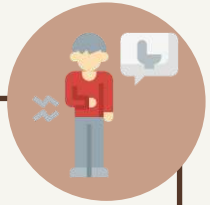
Oxybutynin (Ditropan)	Oxybutynin transdermal	Oxybutynin gel	Propiverine (Urotrol)	Imidafenacin (Uritos)
Non-selective	Non-selective	Non-selective	Non-selective +CCB	M1, M3 selective
2.5mg/tab	3.9mg/patch	10% /pack	15mg/tab	0.1mg/tab
2# BID-TID	1 patch BIW	1 packet QD	1# BID-QID	1# BID
CYP3A4	Trasndermal	Trasndermal	CYP3A4/Intestinal	CYP3A4
No dosage adjustment	-	-		CrCl<30: X Moderate /Severe hepatic: X
Dry mouth, Constipation, Dry eyes, Impaired cognitive function, Urinary retention				
6	X	X	4.63	X

Anti-muscarinics

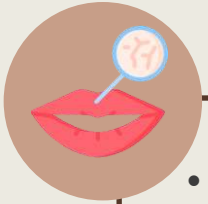
Solifenacin (Vesicare)	Tolterodine (Terodine)	Trospium (Uracare)
M3 selective	Non-selective	Non-selective
5mg/tab	2mg/tab	10mg/tab
1-2# QD	1# BID	1-2# BID AC
CYP3A4	CYP3A4	Liver via ester hydrolysis
CrCl<30: 5mg QD Moderate hepatic: 5mg QD	CrCl<30: 1mg BID Severe hepatic: 1mg BID	CrCl<30: 20mg QD
Dry mouth, Constipation, Dry eyes, Impaired cognitive function, Urinary retention		
10.7	7.6	4.29

Side Effects Management

- Manage constipation and dry mouth before abandoning effective anti-muscarinic therapy



- Adequate dietary fiber and fluid
- Psyllium-based fiber supplements
- Regular exercise
- Normal bowel habits



- Advice on oral lubricants
- Sucking on sugar-free hard candies
- Taking small sips of water
- Chewing sugar-free gum

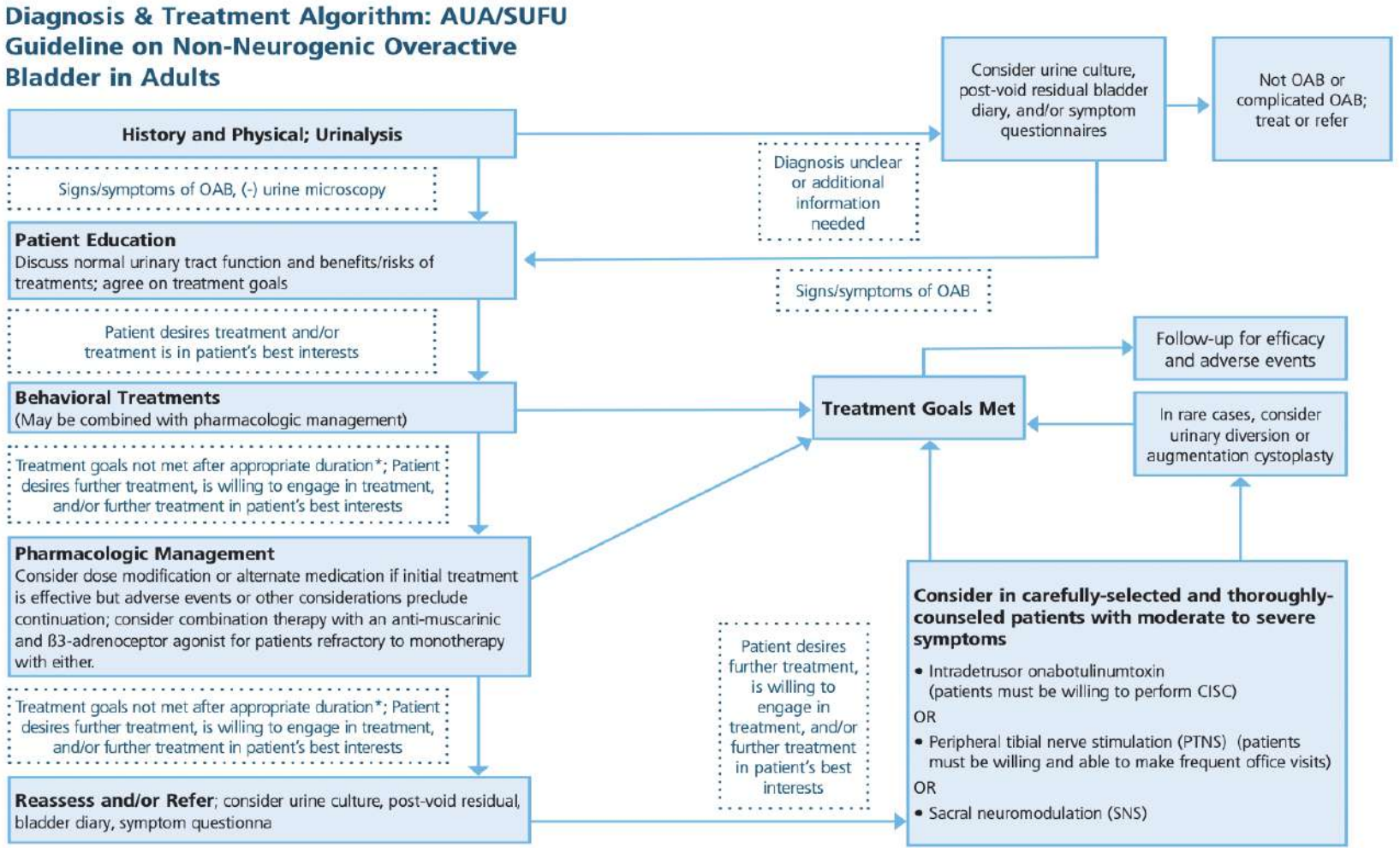
Vibegron (Gemtasa)

FDA first approval date	2020.12.27 (US)
Mechanism of Action	Beta-3 adrenergic agonist
Indications and Usage	

Overactive bladder with symptoms of urge urinary incontinence, urgency and urinary frequency

Dosage	75mg QD
Taiwan FDA approval	-

Algorithm


Diagnosis & Treatment Algorithm: AUA/SUFU Guideline on Non-Neurogenic Overactive Bladder in Adults
History and Physical; Urinalysis
Signs/symptoms of OAB, (-) urine microscopy
Consider urine culture, post-void residual bladder diary, and/or symptom questionnaires
Not OAB or complicated OAB; treat or refer
Diagnosis unclear or additional information needed
Patient Education
Discuss normal urinary tract function and benefits/risks of treatments; agree on treatment goals
Signs/symptoms of OAB
Patient desires treatment and/or treatment is in patient's best interests
Follow-up for efficacy and adverse events
Behavioral Treatments
(May be combined with pharmacologic management)
Treatment Goals Met
In rare cases, consider urinary diversion or augmentation cystoplasty
Treatment goals not met after appropriate duration*; Patient desires further treatment, is willing to engage in treatment, and/or further treatment in patient's best interests
Pharmacologic Management
Consider dose modification or alternate medication if initial treatment is effective but adverse events or other considerations preclude continuation; consider combination therapy with an anti-muscarinic and ß3-adrenoceptor agonist for patients refractory to monotherapy with either.
Consider in carefully-selected and thoroughly-counseled patients with moderate to severe symptoms
• Intradetrusor onabotulinumtoxin (patients must be willing to perform CISC)
OR
• Peripheral tibial nerve stimulation (PTNS) (patients must be willing and able to make frequent office visits)
OR
• Sacral neuromodulation (SNS)
Patient desires further treatment, is willing to engage in treatment, and/or further treatment in patient's best interests
Treatment goals not met after appropriate duration*; Patient desires further treatment, is willing to engage in treatment, and/or further treatment in patient's best interests
Reassess and/or Refer; consider urine culture, post-void residual, bladder diary, symptom questionna

02

Methods

Eligibility Criteria

P — Patients with Overactive Bladder

I — Vibegron

C — Any other drug therapy or placebo

O — Efficiency and safety

Study Design

- ✓ Comparative studies
- ✗ Case reports, reviews, meta-analysis, meeting abstracts, comments, and letters

Outcomes

Efficacy Outcomes

Primary

Micturition episodes/24 h

Secondary

Urgency urinary incontinence (UUI) episodes/24 h

Urgency episodes/24 h

Incontinence episodes/24 h

Voided volume/micturition

Safety Outcomes

Most commonly reported adverse events (AEs)

Data Analysis

Effect measures	Mean difference (Continuous) / Odds ratio (Dichotomous)
Model	Fixed model (Low heterogeneity studies) Random model (Moderate heterogeneity studies)
Subgroup analysis	Vibegron 75 mg study enrolled
Publication bias	Begg funnel plot and Egger test

03

Results

Results

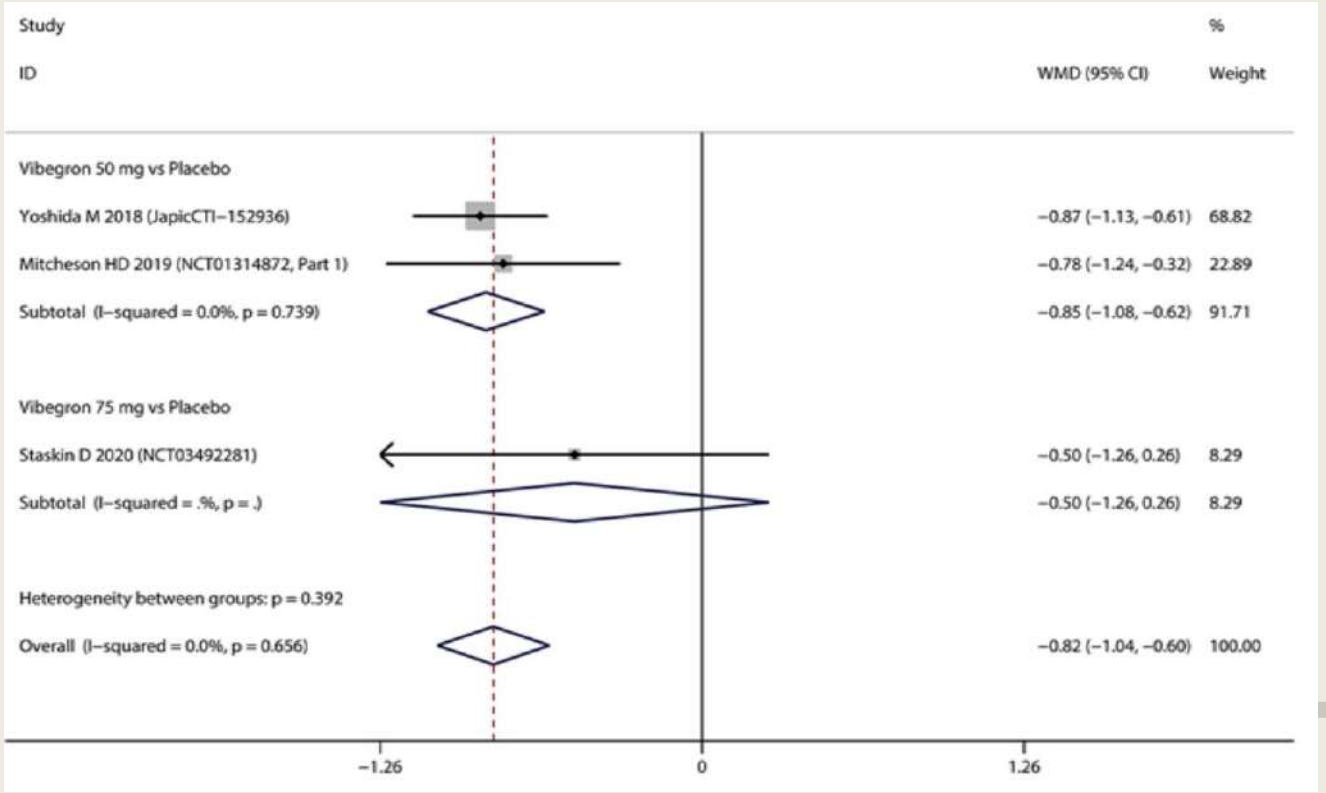
Table 1 Summary of studies included in the systematic review

Study trial number	Intervention (number of patients, *n*)	Trial design (location)	Patient population	Treatment duration (weeks)
Staskin D 2020 NCT03492281	V 75 mg (547) TER 4 mg (431) Placebo (540)	Phase III, RCT, double-blind, multicenter (US and Canada)	OAB, ≥ 18 years	12
Mitcheson HD 2019 NCT01314872	Part 1: V 3 mg (144), V 15 mg (134), V 50 mg (150), V 100 mg (149), TER 4 mg (135), V 50 mg + TER 4 mg/V 50 mg[a] (134), Placebo (141); Part 2: V 100 mg (112), TER 4 mg (122), V 100 mg + TER 4 mg (110), Placebo (64);	Phase IIb, RCT, double-blind, multicenter (18 countries)	Part 1: OAB, 40–75 years Part 2: OAB, 18–75 years	Part 1: 8 Part 2: 4
Yoshida M 2018 JapicCTI-152800	V 50 mg (118)[b] V 50 mg/V 100 mg[b] (51)	Phase III, open-label, non-controlled, multicenter (Japan)	OAB, ≥ 20 years	52
Yoshida M 2018 JapicCTI-152936	V 50 mg (372) V 100 mg (372) Placebo (371) Imidafenacin 0.1 mg twice daily (117)	Phase III, RCT, double-blind, multicenter (Japan)	OAB, ≥ 20 years	12
Yoshida M 2019 JapicCTI-152936	V 50 mg (227) V 100 mg (218) Placebo (224)	Post-hoc analysis on nocturia of the trial JapicCTI-152936	OAB, ≥ 20 years	12
Yoshida M 2020 JapicCTI-152936	V 50 mg (329) V 100 mg (327) Placebo (333)	Post-hoc analysis on severe urgency urinary incontinence of the trial JapicCTI-152936	OAB, ≥ 20 years	12

Results - Efficacy

Micturition

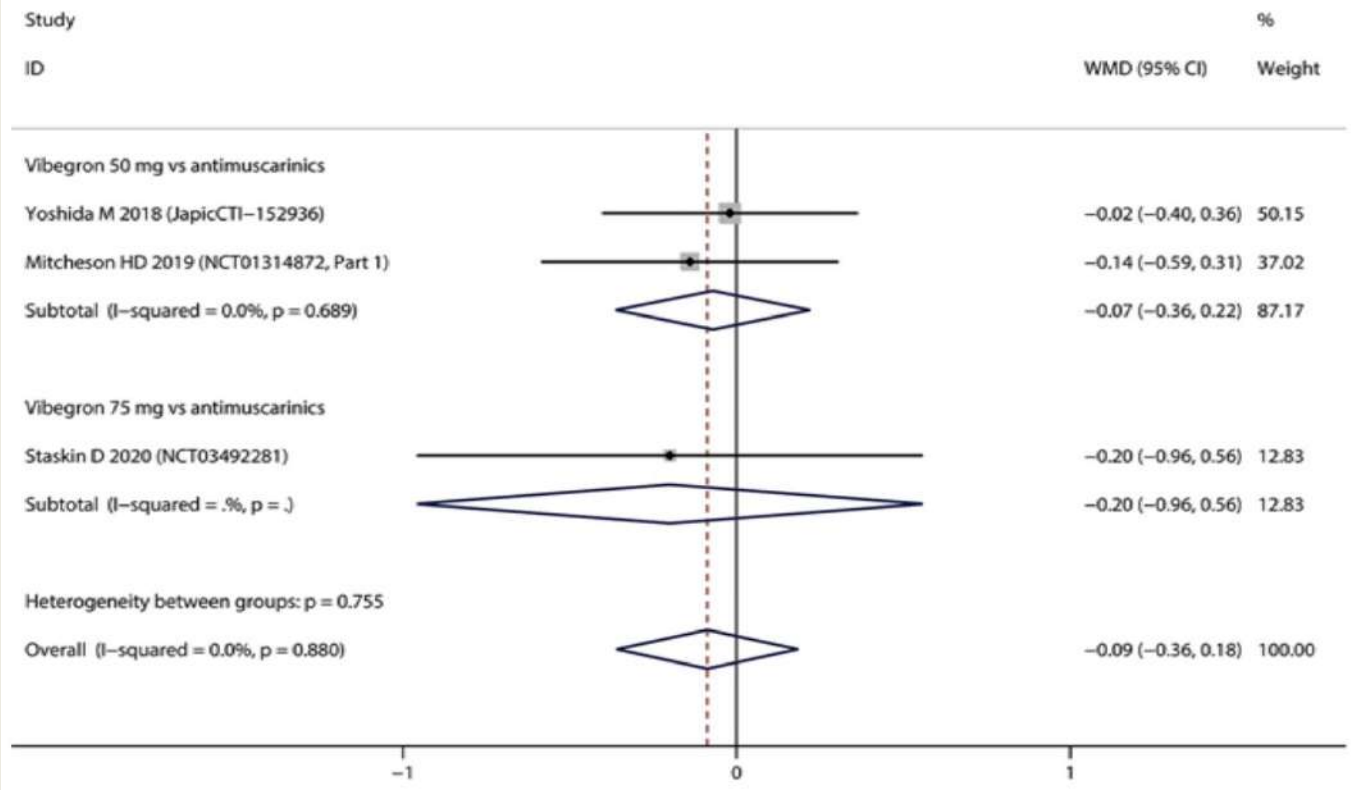
50mg vs Placebo



Results - Efficacy

Micturition

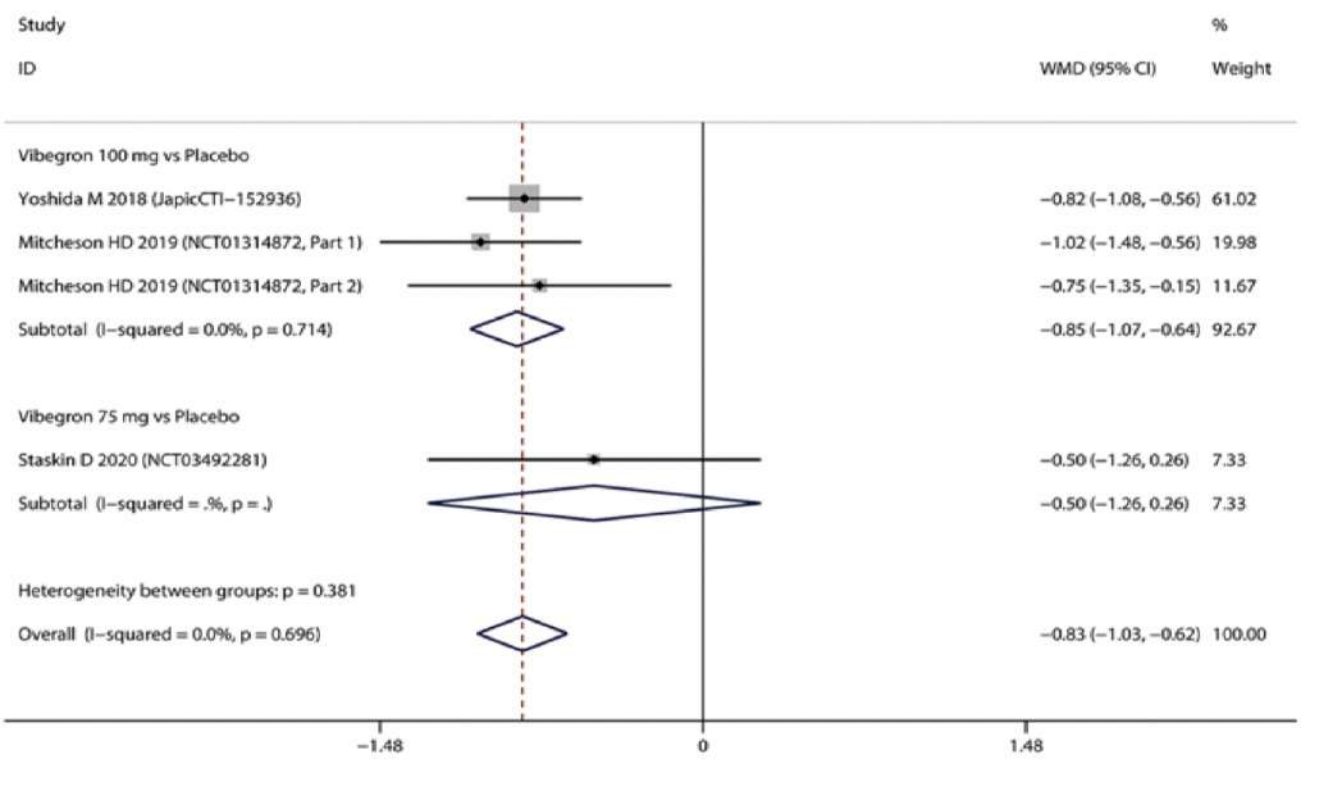
50mg vs Antimuscarinics



Results - Efficacy

Micturition

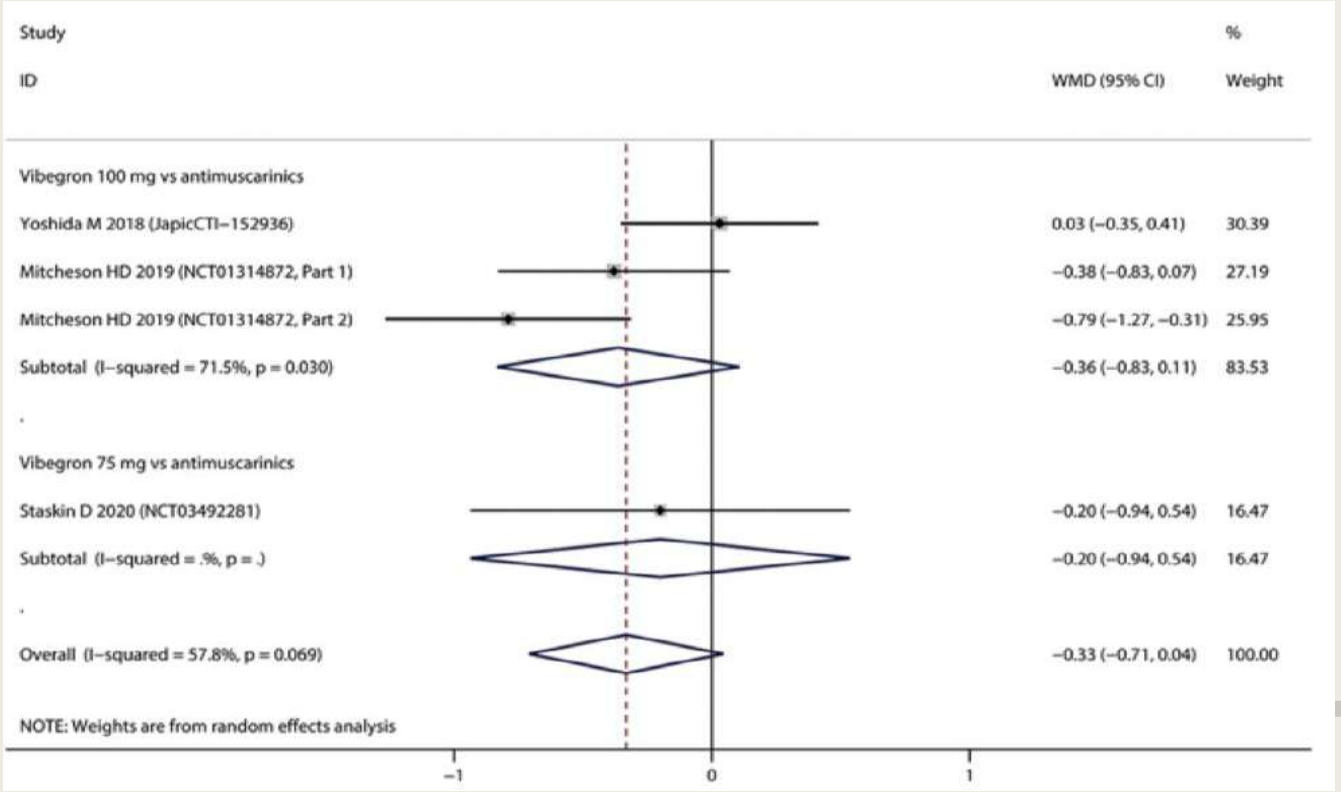
100mg vs Placebo



Results - Efficacy

Micturition

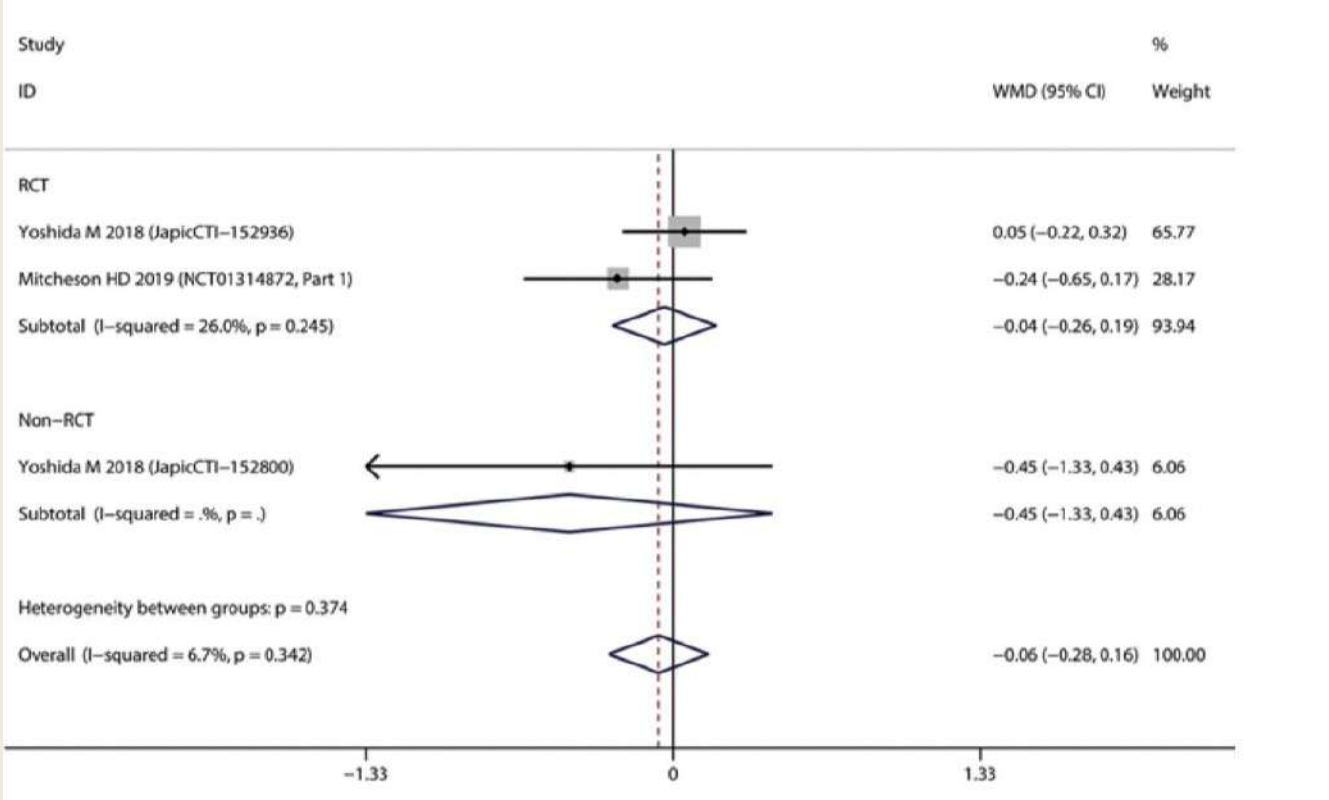
100mg vs Antimuscarinics



Results - Efficacy

Micturition

100mg vs 50mg



Results - Efficacy

Efficacy	The pooled estimates			Heterogeneity	
	Included patients, *n*	WMD (95%CI)	*P* value	I^2,%	*P* value
Urgency urinary incontinence					
V 50 mg vs Placebo	833/823	**– 0.33 (– 0.49, – 0.17)**	**< 0.001**	2.1	0.360
V 100 mg vs Placebo	918/876	**– 0.43 (– 0.58, – 0.27)**	**< 0.001**	0	0.530
V 50 mg vs Antimuscarinics	833/488	0.04 (– 0.17, 0.25)	0.721	28.8	0.246
V 100 mg vs Antimuscarinics	918/590	– 0.11 (– 0.31, 0.09)	0.278	11.7	0.334
V 100 mg vs 50 mg	494/534	– 0.26 (– 0.57, 0.06)	0.116	50.3	0.134
Urgency					
V 50 mg vs Placebo	1010/985	**– 0.53 (– 0.77, – 0.29)**	**< 0.001**	0	0.914
V 100 mg vs Placebo	1119/1049	**– 0.69 (– 0.92, – 0.45)**	**< 0.001**	24.4	0.265
V 50 mg vs Antimuscarinics	1010/629	– 0.06 (– 0.36, 0.24)	0.691	0	0.696
V 100 mg vs Antimuscarinics	1119/751	– 0.34 (– 0.62, – 0.06)	0.018	46.9	0.130
V 100 mg vs 50 mg	567/632	– 0.28 (– 0.77, 0.20)	0.257	59.9	0.083

Efficacy	The pooled estimates			Heterogeneity	
	Included patients, *n*	WMD (95%CI)	*P* value	I^2,%	*P* value
Incontinence					
V 50 mg vs Placebo	450/451	**– 0.31 (– 0.49, – 0.12)**	**0.001**	0	0.881
V 100 mg vs Placebo	535/504	**– 0.43 (– 0.61, – 0.25)**	**< 0.001**	0	0.750
V 50 mg vs Antimuscarinics	450/204	– 0.10 (– 0.52, 0.32)	0.636	57.1	0.127
V 100 mg vs Antimuscarinics	535/304	– 0.17 (– 0.40, 0.05)	0.137	31.1	0.234
V 100 mg vs 50 mg	372/422	– 0.39 (– 1.01, 0.24)	0.224	73.9	0.05
Voided volume					
V 50 mg vs Placebo	860/847	**21.8 (19.9, 23.6)**	**< 0.001**	52.4	0.147
V 100 mg vs Placebo	858/847	**21.4 (19.6, 23.2)**	**< 0.001**	0	0.780
V 50 mg vs Antimuscarinics	860/492	**8.24 (6.38, 10.11)**	**< 0.001**	17.4	0.271
V 100 mg vs Antimuscarinics	858/492	**8.06 (6.19, 9.93)**	**< 0.001**	0	0.788
V 100 mg vs 50 mg	419/485	– 4.45 (– 9.82, 0.92)	0.104	0	0.386

Results - Safety

Safety	The pooled estimates			Heterogeneity	
	Included patients, *n*	OR (95%CI)	*P* value	I^2,%	*P* value
Dry mouth					
V 50 mg vs Placebo	1063/1114	1.86 (0.92, 3.75)	0.085	0	0.915
V 100 mg vs Placebo	1175/1114	1.04 (1.47, 2.30)	0.918	4.9	0.349
V 50 mg vs Antimuscarinics	1063/804	**0.30 (0.18, 0.50)**	**<0.001**	34.6	0.217
V 100 mg vs Antimuscarinics	1175/804	**0.18 (0.09, 0.33)**	**<0.001**	10.3	0.328
V 100 mg vs 50 mg	681/634	0.66 (0.18, 2.40)	0.531	58.7	0.089
Nasopharyngitis					
	1063/1114	1.19 (0.80, 1.77)	0.397	0	0.475
	1175/1114	1.15 (0.78, 1.69)	0.492	51.9	0.125
	1063/804	**1.86 (1.07, 3.23)**	**0.027**	41.7	0.180
	1175/804	**1.83 (1.06, 3.14)**	**0.029**	28.8	0.246
	681/634	0.95 (0.64, 1.42)	0.809	0	0.615
Constipation					
	1063/1114	1.81 (0.90, 3.66)	0.096	0	0.983
	1175/1114	0.86 (0.39, 1.88)	0.703	48.5	0.144
	1063/804	0.88 (0.16, 4.72)	0.879	81.2	0.005
	1175/804	**0.26 (0.14, 0.52)**	**<0.001**	0	0.868
	681/634	0.48 (0.07, 3.54)	0.472	71.6	0.030

Safety	The pooled estimates			Heterogeneity	
	Included patients, *n*	OR (95%CI)	*P* value	I^2,%	*P* value
Diarrhea					
	1063/1114	1.21 (0.59, 2.44)	0.605	31.4	0.233
	1175/1114	1.18 (0.60, 2.33)	0.640	20.3	0.285
	1063/804	1.07 (0.59, 1.95)	0.823	5.3	0.348
	1175/804	0.69 (0.37, 1.30)	0.249	28.8	0.246
	681/634	1.30 (0.46, 3.64)	0.620	3.1	0.356
Cystitis					
	1063/1114	1.99 (0.92, 4.29)	0.079	0	0.671
	1175/1114	1.36 (0.64, 2.92)	0.426	0	0.427
	1063/804	1.36 (0.63, 2.97)	0.436	0	0.683
	1175/804	0.86 (0.40, 1.83)	0.689	0	0.488
	681/634	0.59 (0.31, 1.12)	0.108	0	0.441

04

Discussion

- Vibegron 50mg or 75mg
- Vibegron and Mirabegron comparison
- National Health Insurance Specification
- Others

Other Current Studies

	EMPOWUR 2020	EMPOWUR Extension 2021	Wever 2021
Study Type	Phase 3	Phase 3, extension	Phase I, ambulatory blood pressure monitoring
Study Duration	12 weeks	52 weeks	28 day
Experimental Group	Vibegron 75mg (N=545)	Vibegron 75mg (N=273)	Vibegron 75mg (N=106)
Control Group	Placebo (N=540) Tolterodine 4mg ER (N=430)	Tolterodine 4mg ER (N=232)	Placebo (N=108)
Outcomes Assessed	Number of micturitions UUI episode Urgency episodes Volume voided Safety	Micturitions, urgency episodes, UUI episodes,† total urinary incontinence episodes† Safety	Mean daytime and 24-hour ambulatory systolic blood pressure, diastolic blood pressure, and heart rate

Other Current Studies

EMPOWUR

	Placebo		Vibegron		Tolterodine	
No. pts	520		526		417	
Age:						
Median (IQR)	61.0	(16.0)	63.0	(18.0)	61.0	(17.0)
No. 65 or older (%)	220	(42.3)	242	(46.0)	166	(39.8)
No. 75 or older (%)	57	(11.0)	75	(14.3)	47	(11.3)
No. sex (%):						
Female	445	(85.6)	449	(85.4)	352	(84.4)
Male	75	(14.4)	77	(14.6)	65	(15.6)
No. race (%):						
White	406	(78.1)	422	(80.2)	317	(76.0)
Black/African American	79	(15.2)	74	(14.1)	69	(16.5)
Asian	29	(5.6)	27	(5.1)	26	(6.2)
American Indian or Alaska Native	3	(0.6)	1	(0.2)	0	
Other	3	(0.6)	2	(0.4)	5	(1.2)
No. region (%):						
U.S.	463	(89.0)	472	(89.7)	376	(90.2)
NonU.S.	57	(11.0)	54	(10.3)	41	(9.8)

Vibegron 75mg effect in the Taiwanese population may differ.

Beta-3 Adrenergic Agonists Comparison

Vibegron (Gemtasa)	Mirabegron (Betmiga)
75mg QD	Initial 25mg QD, titrate to 50 mg QD
99.2%	80.4%
Not measurable/Low	Measurable/Some
Headache, Diarrhea, Nasopharyngitis	**Hypertension**, Headache, UTI, Tachycardia
Child-Pugh class C or eGFR <15 mL/minute/1.73 m2: Not recommended	• Child-Pugh class B or eGFR 15 to <30 mL/minute/1.73 m2: Do not exceed 25 mg once daily • eGFR <15 mL/minute/1.73 m2: Not recommended
Minor metabolism hepatically via CYP3A4	Multiple pathways, Moderate CYP2D6 inhibitor
-	NTD 36

Hypertension Events

EMPOWUR

Adverse Events by Treatment Group in the EMPOWUR Trial (Safety Analysis Set)

	Placebo	Vibegron	Tolterodine
No. pts	540	545	430
No. summary (%)			
Any AE	180 (33.3)	211 (38.7)	166 (38.6)
Any AE of clinical interest	40 (7.4)	36 (6.6)	38 (8.8)
Any serious AE	6 (1.1)	8 (1.5)	10 (2.3)
Any AE leading to treatment discontinuation	6 (1.1)	9 (1.7)	14 (3.3)
No. by AE preferred term (%)*			
Urinary tract infection	33 (6.1)	27 (5.0)	25 (5.8)
Headache	13 (2.4)	22 (4.0)	11 (2.6)
Nasopharyngitis	9 (1.7)	15 (2.8)	11 (2.6)
Diarrhea	6 (1.1)	12 (2.2)	9 (2.1)
Nausea	6 (1.1)	12 (2.2)	5 (1.2)
Upper respiratory tract infection	4 (0.7)	11 (2.0)	2 (0.5)
Constipation	7 (1.3)	9 (1.7)	6 (1.4)
Dry mouth	5 (0.9)	9 (1.7)	28 (6.5)
Hypertension	9 (1.7)	9 (1.7)	11 (2.6)

Wever 2021

Ambulatory BP parameter	Placebo (*N* = 101)	Vibegron (*N* = 96)
SBP, mmHg		
Mean (SD) baseline	123.0 (10.0)	122.1 (11.0)
Least squares mean change at day 28 (90% CI)	0.0 (−1.2 to 1.3)	0.6 (−0.7 to 1.9)
Least squares mean difference vs. placebo (90% CI)	0.6 (−1.0 to 2.1)	
DBP, mmHg		
Mean (SD) baseline	72.6 (7.9)	72.8 (7.6)
Least squares mean change at day 28 (90% CI)	0.7 (−0.2 to 1.6)	0.5 (−0.4 to 1.4)
Least squares mean difference vs. placebo (90% CI)	−0.2 (−1.3 to 0.9)	

Studies shown that Mirabegron can increase blood pressure up to 3.5/1.5 mmHg

Direct head-to-head comparison studies of Vibegron and Mirabegron needed.

National Health Insurance Specification

Tolterodine-L-tartrate/ Solifenacin succinate / Mirabegron

限符合下列診斷標準條件之一者

頻尿 (>八次/24小時)、急尿 (突然、很強烈想解尿)、急迫性尿失禁 (24小時內有一次漏尿)

不宜使用本類藥品者

小兒夜尿、單純性應力性尿失禁、膀胱逼尿肌無反射 (detrusor areflexia) 或膀胱不收縮所引起之排尿困難或尿失禁之症狀。

Vesicare / Mirabegron 限用一顆

Discussion

Data analysis

⚠ Enrollment of Vibegron 75mg as subgroup analysis seems inappropriate

⚠ Vibegron 50mg an optimal algorithm?

- No evidence for favoring 50 mg over the higher doses

Discussion

Limitations

- Small number of studies
- One non-RCT included
- Sensitivity analysis should be treated cautiously
- Clinical factors affecting efficacy outcome

05

Conclusion

Conclusion

- Vibegron is effective and safe for treating patients with OAB
- Higher volume voided per micturition
- Lower side effects (dry mouth and constipation)
- Lesser drug-drug interactions

- Higher risk of nasopharyngitis

- Optimal dose for Taiwanese population
- Head-to-head comparison needed

06

Appraisal

此回顧是否問了一個明確的問題?

信度 Validity　重要性 Importance　可應用性 Applicability

1. Did the review address a clearly focused question?

both in vitro and in vivo [6, 7]. Since then, multiple studies have been performed to compare vibegron with placebo or antimuscarinics for patients with OAB [8–11]. Our systematic review and meta-analysis aimed to assess the efficacy and tolerability of vibegron in patients with OAB. To our knowledge, this is the first systematic review exploring the role of vibegron in the treatment of OAB.

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Primary efficacy: Micturition episodes/24 h
Safety outcomes

Yes ✓
Can't tell
No

作者是否搜尋適當的文章類型?

信度 V Validity　重要性 I Importance　可應用性 P Applicability

2. Did the authors look for the right type of papers?

Domains
1. **Study design: Comparative studies** - **3 Randomized controlled trial** - **1 Prospective study**

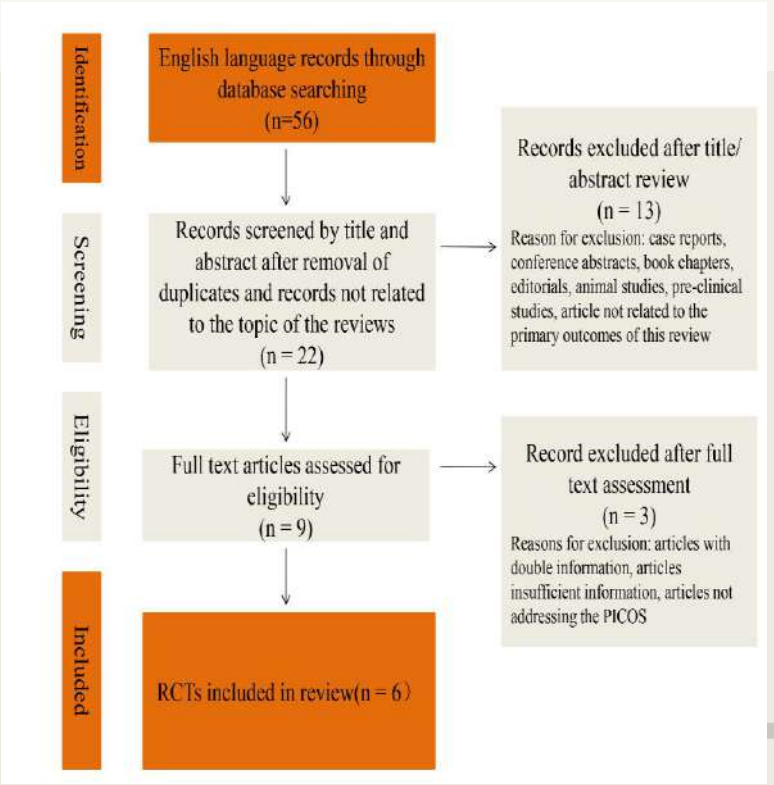
study design: comparative studies. Case reports, reviews, meta-analysis, meeting abstracts, comments, and letters were excluded.

Yes	✓
Can't tell	
No	

是否所有重要、相關的文獻皆被納入?

信度 Validity | 重要性 Importance | 可應用性 Applicability

3. Do you think all the important, relevant studies were included?



Domains
1. Search database: MEDLINE, Web of Science, and Cochrane Central Register of Controlled Trials
2. **Without** Non-English or unpublished study
3. Search date: 2020.03.15

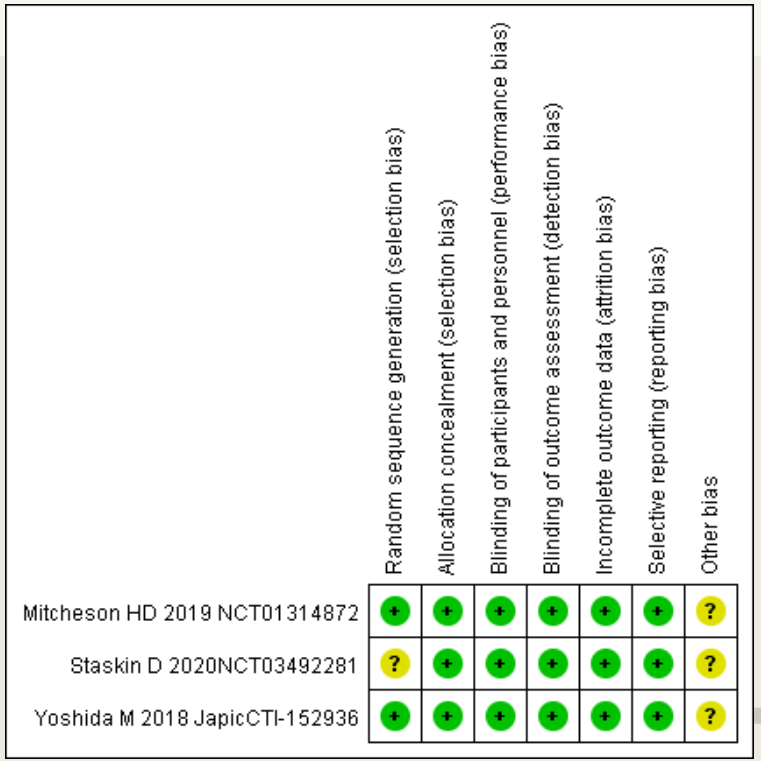
6 relevant studies

Yes ☑
Can't tell ☐
No ☐

作者是否對納入的文獻進行品質評估?

信度 V Validity　重要性 I Importance　可應用性 P Applicability

4. Did the review's authors do enough to assess quality of the included studies?



Domains	
1.	Tools: Cochrane Handbook for Systematic Reviews
3.	**Quality of non-RCT not done.**

Yes
Can't tell ✓
No

結果的合併是否合理?

5. If the results of the review have been combined, was it reasonable to do so?

Heterogeneity
Almost low to moderate heterogeneity

Micturition					
V 50 mg vs Placebo	1010/985	**– 0.82 (– 1.04, – 0.60)**	**< 0.001**	0	0.656
V 100 mg vs Placebo	1119/1049	**– 0.83 (– 1.04, – 0.62)**	**< 0.001**	0	0.696
V 50 mg vs Antimuscarinics	1010/629	– 0.09 (– 0.36, 0.18)	0.528	0	0.880
V 100 mg vs Antimuscarinics	1119/803	– 0.33 (– 0.71, 0.05)	0.084	57.8	0.069
V 100 mg vs 50 mg	567/633	– 0.06 (– 0.28, 0.16)	0.576	6.7	0.342

Yes ✓

Can't tell

No

此文章的整體結果為何?

信度 V Validity　重要性 I Importance　可應用性 P Applicability

6. What are the overall results of the review?
7. How precise are the results?

Efficacy	The pooled estimates			Heterogeneity	
	Included patients, *n*	WMD (95%CI)	*P* value	I^2,%	*P* value
Micturition					
V 50 mg vs Placebo	1010/985	**– 0.82 (– 1.04, – 0.60)**	**< 0.001**	0	0.656
V 100 mg vs Placebo	1119/1049	**– 0.83 (– 1.04, – 0.62)**	**< 0.001**	0	0.696
V 50 mg vs Antimuscarinics	1010/629	– 0.09 (– 0.36, 0.18)	0.528	0	0.880
V 100 mg vs Antimuscarinics	1119/803	– 0.33 (– 0.71, 0.05)	0.084	57.8	0.069
V 100 mg vs 50 mg	567/633	– 0.06 (– 0.28, 0.16)	0.576	6.7	0.342
Urgency urinary incontinence					
V 50 mg vs Placebo	833/823	**– 0.33 (– 0.49, – 0.17)**	**< 0.001**	2.1	0.360
V 100 mg vs Placebo	918/876	**– 0.43 (– 0.58, – 0.27)**	**< 0.001**	0	0.530
V 50 mg vs Antimuscarinics	833/488	0.04 (– 0.17, 0.25)	0.721	28.8	0.246
V 100 mg vs Antimuscarinics	918/590	– 0.11 (– 0.31, 0.09)	0.278	11.7	0.334
V 100 mg vs 50 mg	494/534	– 0.26 (– 0.57, 0.06)	0.116	50.3	0.134

Efficacy	The pooled estimates			Heterogeneity	
	Included patients, *n*	WMD (95%CI)	*P* value	I^2,%	*P* value
Urgency					
V 50 mg vs Placebo	1010/985	**– 0.53 (– 0.77, – 0.29)**	**< 0.001**	0	0.914
V 100 mg vs Placebo	1119/1049	**– 0.69 (– 0.92, – 0.45)**	**< 0.001**	24.4	0.265
V 50 mg vs Antimuscarinics	1010/629	– 0.06 (– 0.36, 0.24)	0.691	0	0.696
V 100 mg vs Antimuscarinics	1119/751	– 0.34 (– 0.62, – 0.06)	0.018	46.9	0.130
V 100 mg vs 50 mg	567/632	– 0.28 (– 0.77, 0.20)	0.257	59.9	0.083

此文章的整體結果為何?

6. What are the overall results of the review?
7. How precise are the results?

Efficacy	The pooled estimates			Heterogeneity	
	Included patients, *n*	WMD (95%CI)	*P* value	I^2,%	*P* value
Incontinence					
V 50 mg vs Placebo	450/451	**– 0.31 (– 0.49, – 0.12)**	**0.001**	0	0.881
V 100 mg vs Placebo	535/504	**– 0.43 (– 0.61, – 0.25)**	**< 0.001**	0	0.750
V 50 mg vs Antimuscarinics	450/204	– 0.10 (– 0.52, 0.32)	0.636	57.1	0.127
V 100 mg vs Antimuscarinics	535/304	– 0.17 (– 0.40, 0.05)	0.137	31.1	0.234
V 100 mg vs 50 mg	372/422	– 0.39 (– 1.01, 0.24)	0.224	73.9	0.05
Voided volume					
V 50 mg vs Placebo	860/847	**21.8 (19.9, 23.6)**	**< 0.001**	52.4	0.147
V 100 mg vs Placebo	858/847	**21.4 (19.6, 23.2)**	**< 0.001**	0	0.780
V 50 mg vs Antimuscarinics	860/492	**8.24 (6.38, 10.11)**	**< 0.001**	17.4	0.271
V 100 mg vs Antimuscarinics	858/492	**8.06 (6.19, 9.93)**	**< 0.001**	0	0.788
V 100 mg vs 50 mg	419/485	★ – 4.45 (– 9.82, 0.92)	0.104	0	0.386

Efficacy outcomes

No significant difference for 100mg vs 50mg in any outcome

A significant difference in **voided volume** when compared to antimuscarinics

此文章的整體結果為何?

信度 V Validity　重要性 I Importance　可應用性 P Applicability

6. What are the overall results of the review?
7. How precise are the results?

Safety	The pooled estimates			Heterogeneity	
	Included patients, *n*	OR (95%CI)	*P* value	I^2,%	*P* value
Dry mouth					
V 50 mg vs Placebo	1063/1114	1.86 (0.92, 3.75)	0.085	0	0.915
V 100 mg vs Placebo	1175/1114	1.04 (1.47, 2.30)	0.918	4.9	0.349
V 50 mg vs Antimuscarinics	1063/804	**0.30 (0.18, 0.50)**	**<0.001**	34.6	0.217
V 100 mg vs Antimuscarinics	1175/804	**0.18 (0.09, 0.33)**	**<0.001**	10.3	0.328
V 100 mg vs 50 mg	681/634	0.66 (0.18, 2.40)	0.531	58.7	0.089
Nasopharyngitis					
	1063/1114	1.19 (0.80, 1.77)	0.397	0	0.475
	1175/1114	1.15 (0.78, 1.69)	0.492	51.9	0.125
	1063/804	**1.86 (1.07, 3.23)**	**0.027**	41.7	0.180
	1175/804	**1.83 (1.06, 3.14)**	**0.029**	28.8	0.246
	681/634	0.95 (0.64, 1.42)	0.809	0	0.615
Constipation					
	1063/1114	1.81 (0.90, 3.66)	0.096	0	0.983
	1175/1114	0.86 (0.39, 1.88)	0.703	48.5	0.144
	1063/804	0.88 (0.16, 4.72)	0.879	81.2	0.005
	1175/804	**0.26 (0.14, 0.52)**	**<0.001**	0	0.868
	681/634	0.48 (0.07, 3.54)	0.472	71.6	0.030

Safety	The pooled estimates			Heterogeneity	
	Included patients, *n*	OR (95%CI)	*P* value	I^2,%	*P* value
Diarrhea					
	1063/1114	1.21 (0.59, 2.44)	0.605	31.4	0.233
	1175/1114	1.18 (0.60, 2.33)	0.640	20.3	0.285
	1063/804	1.07 (0.59, 1.95)	0.823	5.3	0.348
	1175/804	0.69 (0.37, 1.30)	0.249	28.8	0.246
	681/634	1.30 (0.46, 3.64)	0.620	3.1	0.356
Cystitis					
	1063/1114	1.99 (0.92, 4.29)	0.079	0	0.671
	1175/1114	1.36 (0.64, 2.92)	0.426	0	0.427
	1063/804	1.36 (0.63, 2.97)	0.436	0	0.683
	1175/804	0.86 (0.40, 1.83)	0.689	0	0.488
	681/634	0.59 (0.31, 1.12)	0.108	0	0.441

Safety outcomes
Higher risk of nasopharyngitis
Lower risk of dry mouth

此研究結果是否可應用到當地的族群?

信度 V Validity
重要性 I Importance
可應用性 P Applicability

8. Can the results be applied to the local population?

Domains	This study
Target population	Overactive bladder
Location	USA, Japan
Intervention	Vibegron vs placebo/antimuscarinics
Evaluation	Primary outcome: Micturition Safety outcomes

Yes ☑
Can't tell ☐
No ☐

所有重要的結果都有被考慮?

9. Were all important outcomes considered?

Domains	
Efficacy	• Micturition episodes/24 h • Urgency urinary incontinence (UUI) episodes/24 h • Urgency episodes/24 h • Incontinence episodes/24 h • Voided volume/micturition
Safety	• Dry mouth • Nasopharyngitis • Constipation • Diarrhea • Cystitis

Yes ☑
Can't tell ☐
No ☐

此文章的利大於弊，且符合成本效益?

10. Are the benefits worth the harms and costs?

	Vibegron	Antimuscarinics
Efficacy	Higher voided volume in vibegron	
Safety	Higher risk of nasopharyngitis	Higher risk of dry mouth, constipation
Cost	TFDA not yet approved	Solifenacin 一次一錠

Yes ☐
Can't tell ☑
No ☐

整合及評定證據品質

信度 V 5 Validity　重要性 I 2 Importance　可應用性 P 3 Applicability

V	I	P
問題明確 	結果	應用至本地 
蒐納適當 	Vibegron is **effective and safe** for treating patients with OAB	重要結果 
廣泛搜尋 	精準	利大於弊 
品質評估 	**大部分結果之信賴區間窄，分析結果之篇數稍嫌少**	
結果合併 		

References

1. International Continence Society: Overactive Bladder
2. Report from Overactive Bladder Committee
3. Diagnosis and Treatment of Non-Neurogenic Overactive Bladder (OAB) in Adults: AUA/SUFU Guideline (2019)
4. Uptodate: Urgency urinary incontinence/overactive bladder (OAB) in females: Treatment
5. Vibegron FDA Label

Thanks

Do you have any questions?