



Perbandingan efikasi dan keamanan *Imidafenacin* dan *Solifenacin*

Dipresentasikan pada:

Rapat Komite Farmasi dan Terapi RSK. St. Vincentius a Paulo.

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Oleh: Steven Victoria H., M.Farm., Apt.



Imidafenacin dan Solifenacin

- Golongan antikolinergik/antimuskarinik
- Salah satu indikasinya adalah untuk terapi ***overactive bladder (OAB)***
 - *Urinary urgency*
 - *Frequency and nocturia*
 - *Incontinence*



Terapi untuk OAB berdasarkan panduan terapi *Canadian Urological Association, 2017*

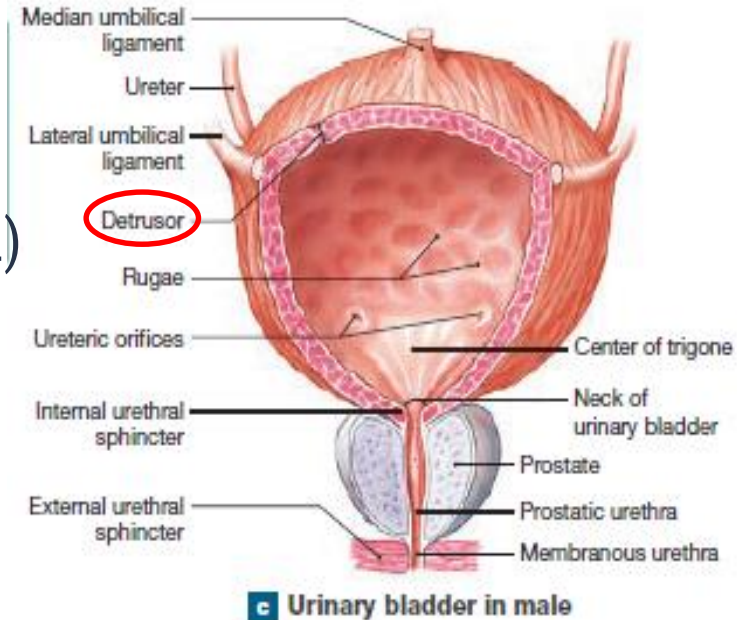
- Lini pertama: perubahan perilaku dan gaya hidup, serta pemberian edukasi
- Lini kedua: antimuskarinik (*oxybutynin, tolterodine, darifenacin, trospium, solifenacin, propiverine*, dan *fesoterodine*)

Lokasi Reseptor Muskarinik



Reseptor muskarinik berada di beberapa lokasi:

1. Sistem saraf pusat (M1-M5)
2. Otot jantung dan nodus *atrioventricular* (M2)
3. Saluran pernafasan (M2 dan M3)
4. Saluran cerna (M2 dan M3)
5. **Saluran kemih (M2 dan M3)**
6. Mata (M3)



Perbandingan Profil Farmakokinetik dan Farmakodinamik



Parameter	<i>Imidafenacin</i>	<i>Solifenacin</i>
Farmakokinetik		
Bioavailabilitas	57,8%	90%
<i>Onset of action</i>	1-3 jam	NI
Volume distribusi	43,9 L	600 L
Ikatan obat-protein	88% (albumin dan $\alpha 1$ acid glycoprotein)	98% ($\alpha 1$ acid glycoprotein)
Waktu paruh	2,9 jam	38 jam
Eliminasi di urin	65,6%	69,2%

Perbandingan Profil Farmakokinetik dan Farmakodinamik



Parameter	<i>Imidafenacin</i>	<i>Solifenacin</i>
Farmakodinamik		
Enzim metabolisme	CYP3A4/UGT1A2	CYP3A4/CYP2C19
Aktivitas farmakologis dari metabolit	None	Ya
Efek anti kolinergik	M3≥M1>M2	M3>M1>M2

Efficacy and safety of imidafenacin for overactive bladder in adult: a systematic review and meta-analysis

Wei Huang · Huantao Zong · Xin Zhou · Yong Zhang

Jumlah artikel: 5 *randomized control trials* (RCTs)

Imidafenacin vs plasebo (1), *Imidafenacin* vs *propiverine* (2), dan *Imidafenacin vs solifenacin* (2)

Efikasi (OABSS)

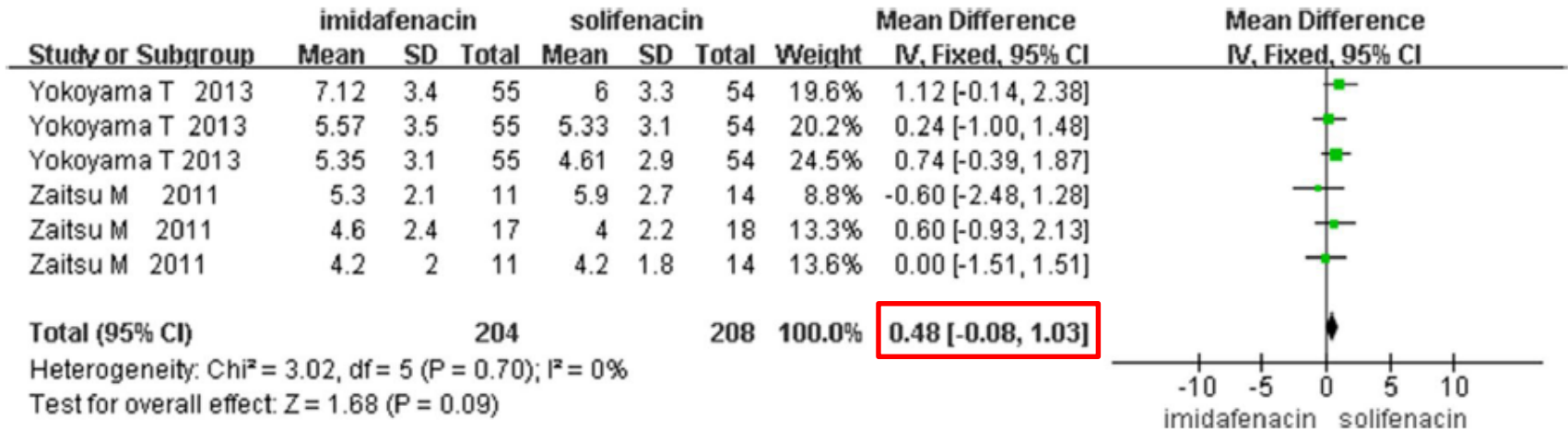


Fig. 5 OABSS in imidafenacin versus solifenacin

OABSS : *overactive bladder symptom score*

Keamanan (konstipasi dan keseluruhan *adverse event*)

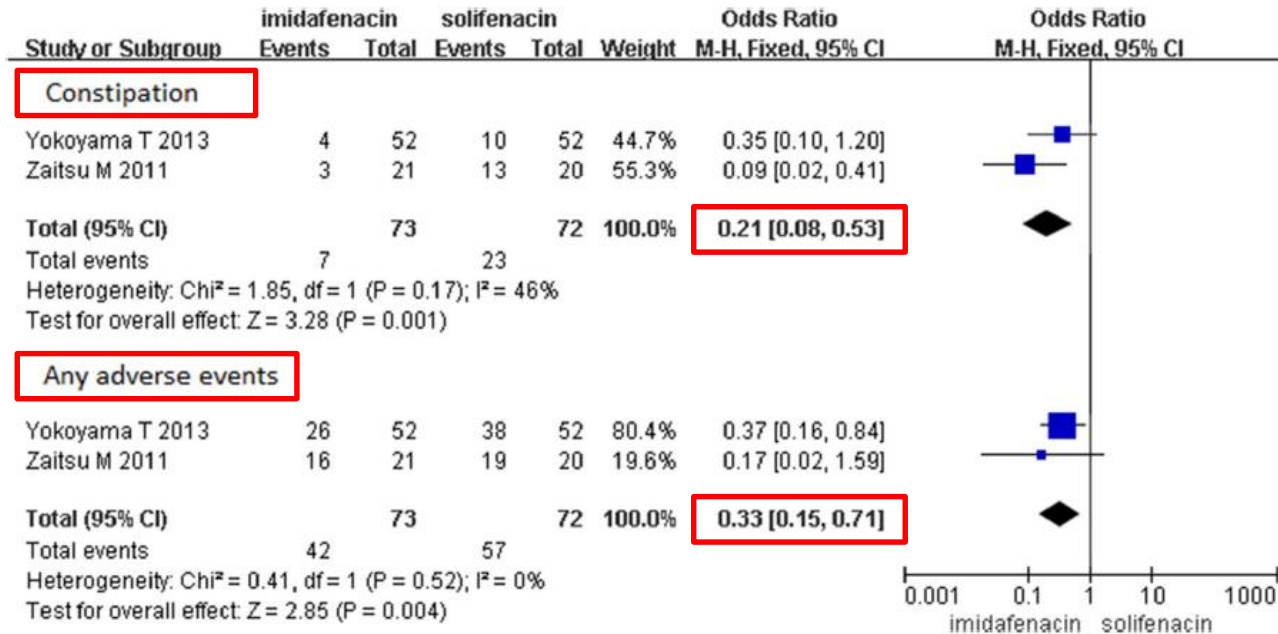


Fig. 7 The incidence of constipation and any adverse events in imidafenacin versus solifenacin

Clinical Study

Comparative Evaluation of the Safety and Efficacy of Long-Term Use of Imidafenacin and Solifenacin in Patients with Overactive Bladder: A Prospective, Open, Randomized, Parallel-Group Trial (the LIST Study)

Masayoshi Zaitso,¹ Koji Mikami,¹ Noriko Ishida,² and Takumi Takeuchi¹

Imidafenacin 0,1 mg 2x sehari **vs**

Solifenacin 5 mg sehari

Jumlah subyek: 41 pasien OAB

Lama penelitian: 52 minggu

Efikasi (perubahan nilai OABSS)

	Imidafenacin (n = 17)	P value versus 0W	Solifenacin (n = 18)	P value versus 0W	P value versus intergroup
0W	8 ± 2		8.7 ± 2.4		0.2989
4W	4.9 ± 2.2	***	5.7 ± 2.6	***	0.2789
12W	4.1 ± 2.4	***	3.9 ± 2.1	***	0.8535

Short term

*** p value <0,001

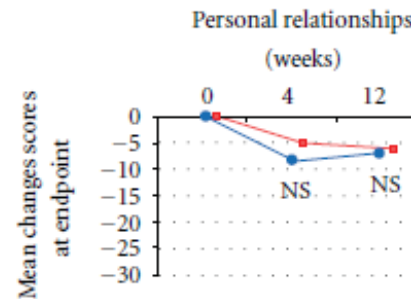
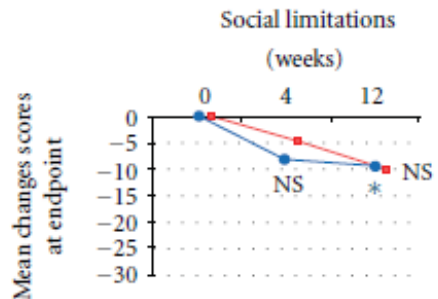
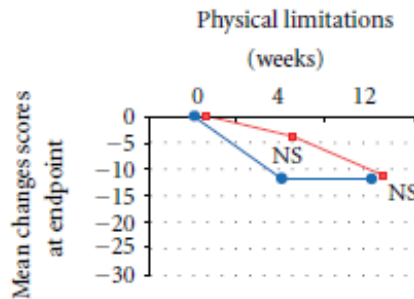
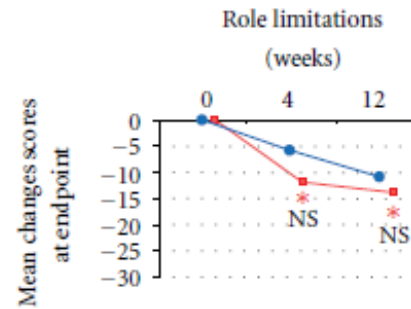
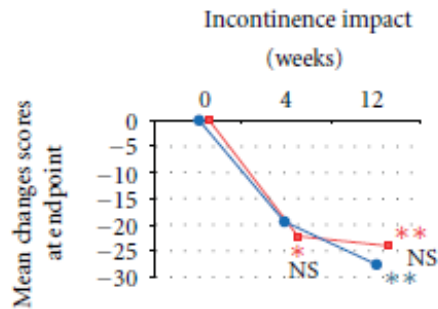
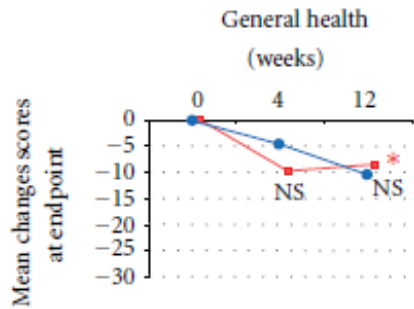
	Imidafenacin (n = 11)	P value versus 0W	Solifenacin (n = 14)	P value versus 0W	P value versus intergroup
0W	9.0 ± 1.3		8.9 ± 2.6		0.8543
4W	5.3 ± 2.1	***	5.9 ± 2.7	***	0.3910
12W	4.6 ± 2.4	***	4.0 ± 2.2	***	0.5599
28W	4.2 ± 2.0	***	4.2 ± 1.8	***	0.8459
40W	4.2 ± 2.5	***	5.3 ± 1.7	***	0.2870
52W	4.3 ± 2.8	**	5.1 ± 2.1	***	0.6384

Long term

** p value <0,01

*** p value <0,001

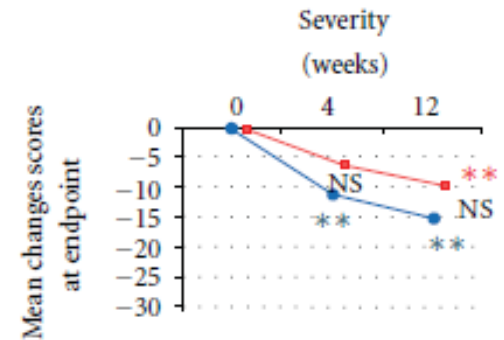
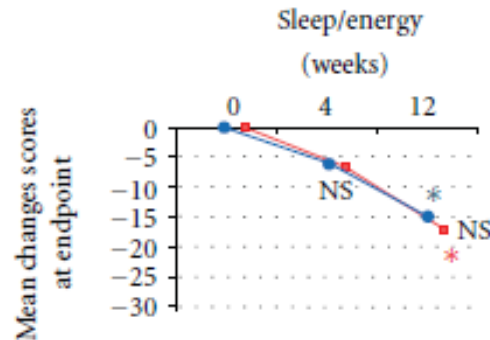
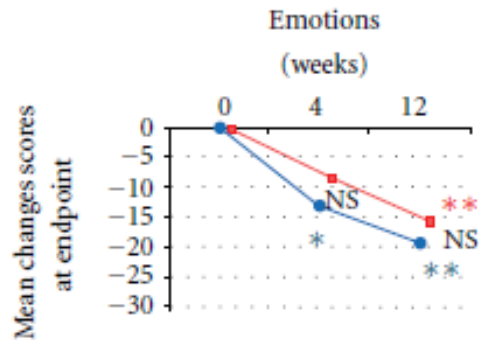
Efikasi (QoL) – *short term*



● Imidafenacin (n = 17)
■ Solifenacin (n = 18)

Zaitu et al. (2011)

Efikasi (QoL) – *short term*



* p value <0,05

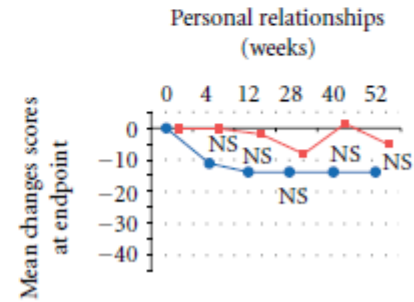
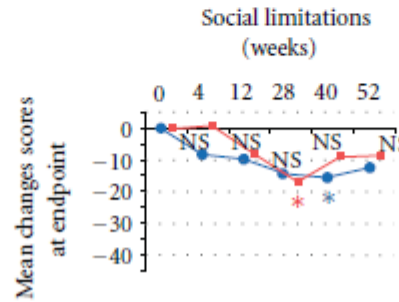
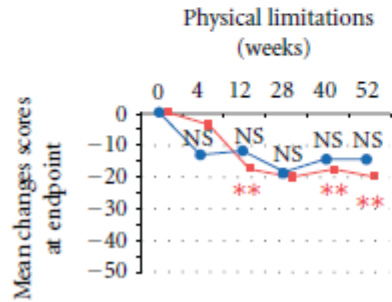
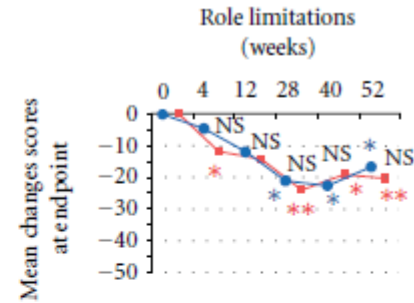
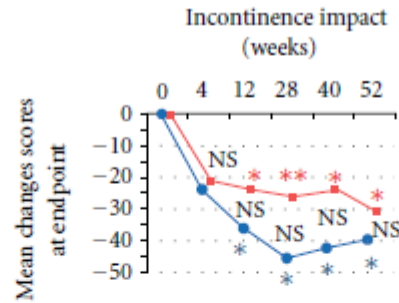
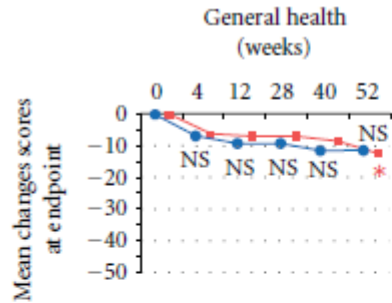
** p value <0,01

NS: *not significant*

—●— Imidafenacin (n = 17)

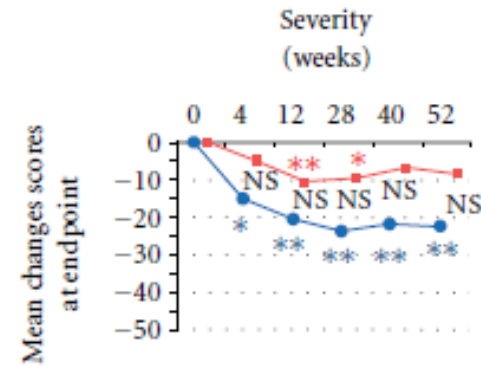
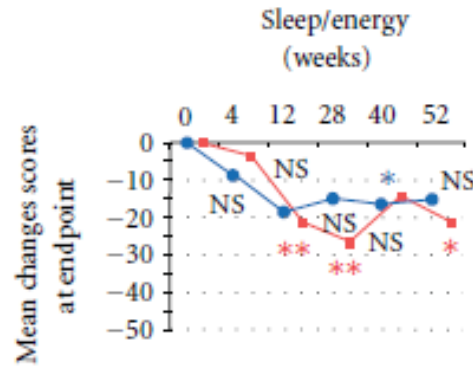
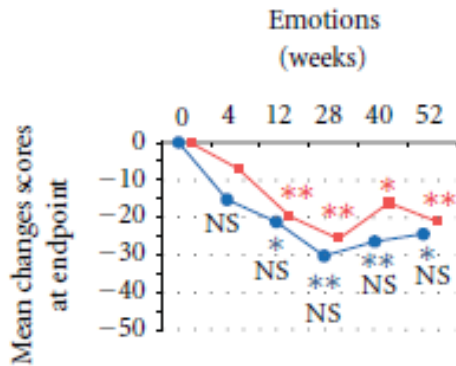
—■— Solifenacin (n = 18)

Efikasi (QoL) – *long term*



● Imidafenacin (n = 17)
 ■ Solifenacin (n = 18)

Efikasi (QoL) – *long term*



* p value < 0,05

** p value < 0,01

NS: *not significant*

—●— Imidafenacin (n = 17)

—■— Solifenacin (n = 18)

Keamanan – *short term* (NI)

Keamanan – *long term*

Variable, n (%)	Imidafenacin	Solifenacin	P-value
N (safety population)	21	20	
Dry mouth	15 (71.4%)	18 (90.0%)	0.2379 ^b
Mild	8 (38.1%)	4 (20.0%)	
Moderate	7 (33.3%)	10 (50.0%)	0.0092 ^a
Severe	0 (0%)	4 (20.0%)	
Constipation	3 (14.3%)	13 (65.0%)	0.0013 ^b
Blurred vision	2 (9.5 %)	7 (35.0%)	0.0670 ^b

Keamanan (*residual urine volume* dan interval QT) – *short term*

Variable	Imidafenacin	Solifenacin	
Number of subjects	17	18	
Residual urine volume (mL)			
0 week (Mean ± SD)	14.2 ± 15.1	13.5 ± 11.4	
4 week (Mean ± SD)	29.3 ± 26.2**	40.8 ± 33.2**	NS
12 week (Mean ± SD)	37.7 ± 32.7**	29.4 ± 28.1*	NS
QT interval (ms)			
0 week (Mean ± SD)	414.8 ± 20.7	423.2 ± 21.8	
4 week (Mean ± SD)	415.5 ± 16.5	423.5 ± 19.0	NS
12 week (Mean ± SD)	415.0 ± 16.4	423.6 ± 23.5	NS

* p value <0,05; ** p value <0,01; NS: *not significant*



Keamanan (*residual urine volume* dan interval QT) – *long term*

Variable	Imidafenacin	Solifenacin	
Number of subjects	11	14	
Residual urine volume (mL)			
0 week (Mean ± SD)	15.1 ± 14.7	13.4 ± 11.0	
4 week (Mean ± SD)	30.9 ± 20.4*	38.6 ± 32.1**	NS
12 week (Mean ± SD)	30.7 ± 28.0	30.6 ± 27.7*	NS
52 week (Mean ± SD)	20.6 ± 25.4	31.1 ± 23.4**	NS
QT interval (ms)			
0 week (Mean ± SD)	413.6 ± 24.6	426.9 ± 22.4	
4 week (Mean ± SD)	415.8 ± 18.9	426.2 ± 20.1	NS
12 week (Mean ± SD)	416.4 ± 18.4	427.2 ± 23.0	NS
52 week (Mean ± SD)	417.0 ± 20.3	424.4 ± 22.5	NS

* p value <0,05; ** p value <0,01; NS: *not significant*

Long-Term Safety and Efficacy of Two Different Antimuscarinics, Imidafenacin and Solifenacin, for Treatment of Overactive Bladder: A Prospective Randomized Controlled Study

Teruhiko Yokoyama Takao Koide Ryoei Hara Kazuhiko Fukumoto
Yoshiyuki Miyaji Atsushi Nagai

Imidafenacin 0,1 mg 2x sehari **vs**

Solifenacin 5 mg sehari

Jumlah subyek: 55 pasien OAB

Lama penelitian: 12 bulan

Efikasi (total IPSS dan QoL)

		Baseline	1 month after	3 months after	6 months after	12 months after
Total IPSS	Imidafenacin	15.3 ± 5.6	13.5 ± 5.5	9.70 ± 7.3	9.65 ± 6.5	8.71 ± 5.8
	Intragroup		0.0060	0.0010	0.0007	0.0074
	Solifenacin	13.7 ± 4.7	9.20 ± 5.1	8.63 ± 5.4	8.17 ± 5.3	8.50 ± 6.0
	Intragroup		<0.0001	<0.0001	0.0001	0.0009
	Intergroup	0.108	0.0029*	0.481	0.418	0.922
IPSS QoL index	Imidafenacin	4.80 ± 0.8	3.65 ± 1.5	3.03 ± 1.4	3.10 ± 1.3	2.57 ± 0.76
	Intragroup		<0.0001	<0.0001	0.0008	<0.0001
	Solifenacin	4.81 ± 0.8	3.06 ± 1.4	2.76 ± 1.4	2.57 ± 1.1	2.56 ± 1.5
	Intragroup		<0.0001	<0.0001	<0.0001	0.0010
	Intergroup	0.943	0.0472*	0.408	0.161	0.984

IPSS : *International Prostate Symptom Score*

* p value <0,05



Efikasi (OABSS)

		Baseline	1 month after	3 months after	6 months after	12 months after
OABSS	Imidafenacin	9.89 ± 2.6	7.12 ± 3.4	5.57 ± 3.5	5.35 ± 3.1	4.57 ± 2.9
	Intragroup		<0.0001	<0.0001	<0.0001	<0.0001
	Solifenacin	10.0 ± 2.9	6.00 ± 3.3	5.33 ± 3.1	4.61 ± 2.9	4.75 ± 3.2
	Intragroup		<0.0001	<0.0001	<0.0001	<0.0001
	Intergroup	0.810	0.101	0.746	0.426	0.875

OABSS : *overactive bladder symptom score*

* p value <0,05



Keamanan

		Baseline	1 month after	3 months after	6 months after	12 months after
VAS of dry mouth	Imidafenacin	0.57 ± 1.4	2.11 ± 2.6	1.67 ± 1.8	1.05 ± 1.7	1.50 ± 1.7
	Intragroup		0.0001*	0.0002*	0.0583	0.0654
	Solifenacin	0.65 ± 1.4	2.26 ± 2.2	2.57 ± 2.1	2.17 ± 1.9	1.63 ± 1.8
	Intragroup		0.0001*	0.0001*	0.0002*	0.0058*
	Intergroup	0.714	0.758	0.0647	0.0487*	0.848 
VAS of constipation	Imidafenacin	0.82 ± 1.6	1.06 ± 1.9	0.93 ± 1.8	0.25 ± 0.79	0.43 ± 1.1
	Intragroup		0.207	0.766	0.0352*	0.0366*
	Solifenacin	0.74 ± 1.8	1.22 ± 1.9	1.00 ± 1.7	0.52 ± 1.2	0.56 ± 1.2
	Intragroup		0.0412*	0.356	0.6803	0.999
	Intergroup	0.855	0.685	0.876	0.382	0.754 

VAS : visual analog scale

* p value <0,05

Keamanan

		Baseline	1 month after	3 months after	6 months after	12 months after
Duration of dry mouth (h)	Imidafenacin	1.42 ± 4.8	2.16 ± 5.0	1.52 ± 2.5	1.15 ± 2.3	1.36 ± 1.8
	Intragroup		0.412	0.660	0.731	0.5745
	Solifenacin	1.09 ± 3.6	3.44 ± 5.9	4.07 ± 6.9	3.09 ± 5.2	2.88 ± 6.0
	Intragroup		0.0001*	0.0003*	0.0374*	0.149
	Intergroup	0.711	0.042*	0.0596	0.0892	0.373 
Residual urine volume	Imidafenacin	12.3 ± 19.8	16.3 ± 19.9	25.8 ± 32.5	23.2 ± 37.6	21.1 ± 31.5
	Intragroup		0.274	0.0424*	0.192	0.5288
	Solifenacin	11.2 ± 17.0	16.5 ± 18.3	21.9 ± 22.3	19.6 ± 23.6	28.7 ± 62.9
	Intragroup		0.0046*	0.0002*	0.0096*	0.260
	Intergroup	0.751	0.956	0.547	0.712	0.688 

VAS : *visual analog scale*

* p value <0,05



Keamanan

	Group I	Group S	p value
n (safety population)	52	52	
Dry mouth	20 (38.5)	21 (40.4)	0.999
Mild	11 (21.1)	14 (26.9)	0.659
Moderate	7 (13.5)	5 (9.6)	0.762
Severe	2 (3.8)	2 (3.8)	0.999
Constipation	4 (7.7)	10 (19.2)	0.161
Blurred vision	2 (3.8)	5 (9.6)	0.439
Difficulty	0 (0)	2 (3.8)	0.495
Dropout due to adverse events	3 (5.8)	7 (13.5)	0.324

Values are n (%). Fisher's exact test was used for comparisons between the two groups.

Harga



Solifenacin

Vesicare[®] 5 mg (Rp. 22.750/tablet)

Vesicare[®] 10 mg (Rp. 25.300/tablet)

Imidafenacin

Uritos[®] 0,1mg (Rp. 7.200/tablet)

Kesimpulan



Imidafenacin dan *solifenacin* memiliki profil efikasi dan keamanan yang relatif sebanding. Namun kejadian efek samping konstipasi pada *imidafenacin* lebih sedikit dibandingkan dengan *solifenacin*.

Bila ditinjau dari segi harga, *imidafenacin* relatif lebih mahal dibandingkan *solifenacin*.

Daftar pustaka



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Thank You



Tolterodine I-tartrate (2x sehari)

Detrusitol[®] 2 mg (Rp. 273.758/28 tablet selaput ~ Rp. 9.777/tablet selaput)

Propiverine HCl (2-3x sehari)

Mictonorm[®] 15 mg (Rp. 271.040/28 tablet ~ Rp. 9.680/tablet)

(MIMS, 2017)



Aksi Asetilkolin pada M1

The muscarinic acetylcholine receptor mediates various cellular responses, including inhibition of adenylate cyclase, breakdown of phosphoinositides and modulation of potassium channels through the action of G proteins. Primary transducing effect is P_i turnover



Aksi Asetilkolin pada M2

The muscarinic acetylcholine receptor mediates various cellular responses, including inhibition of adenylate cyclase, breakdown of phosphoinositides and modulation of potassium channels through the action of G proteins. Primary transducing effect is adenylate cyclase inhibition. Signaling promotes phospholipase C activity, leading to the release of inositol trisphosphate (IP₃); this then triggers calcium ion release into the cytosol.



Aksi Asetilkolin pada M3

The muscarinic acetylcholine receptor mediates various cellular responses, including inhibition of adenylate cyclase, breakdown of phosphoinositides and modulation of potassium channels through the action of G proteins. Primary transducing effect is P_i turnover.