

# *Hyperactivité vésicale et Toxine Botulique*

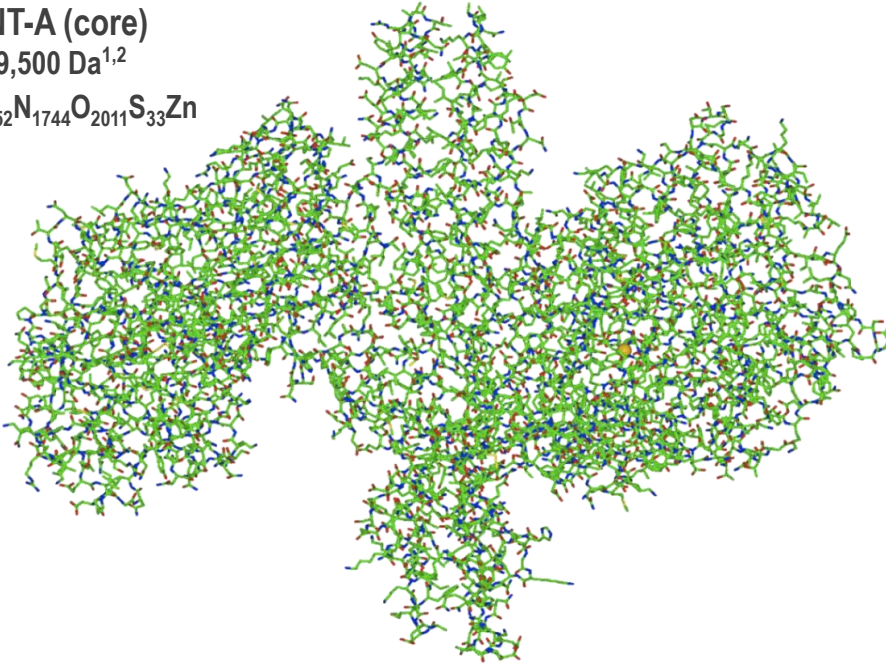
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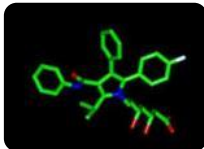


# Botulinum toxin type A

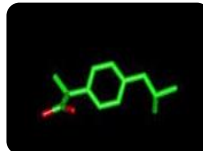
BoNT-A (core)  
149,500 Da<sup>1,2</sup>  
 $C_{6763}H_{10452}N_{1744}O_{2011}S_{33}Zn$



Lipitor® (atorvastatin)<sup>3</sup>  
559 Da  
 $C_{33}H_{35}FN_2O_5$



Ibuprofen<sup>3</sup>  
206 Da  
 $C_{13}H_{18}O_2$

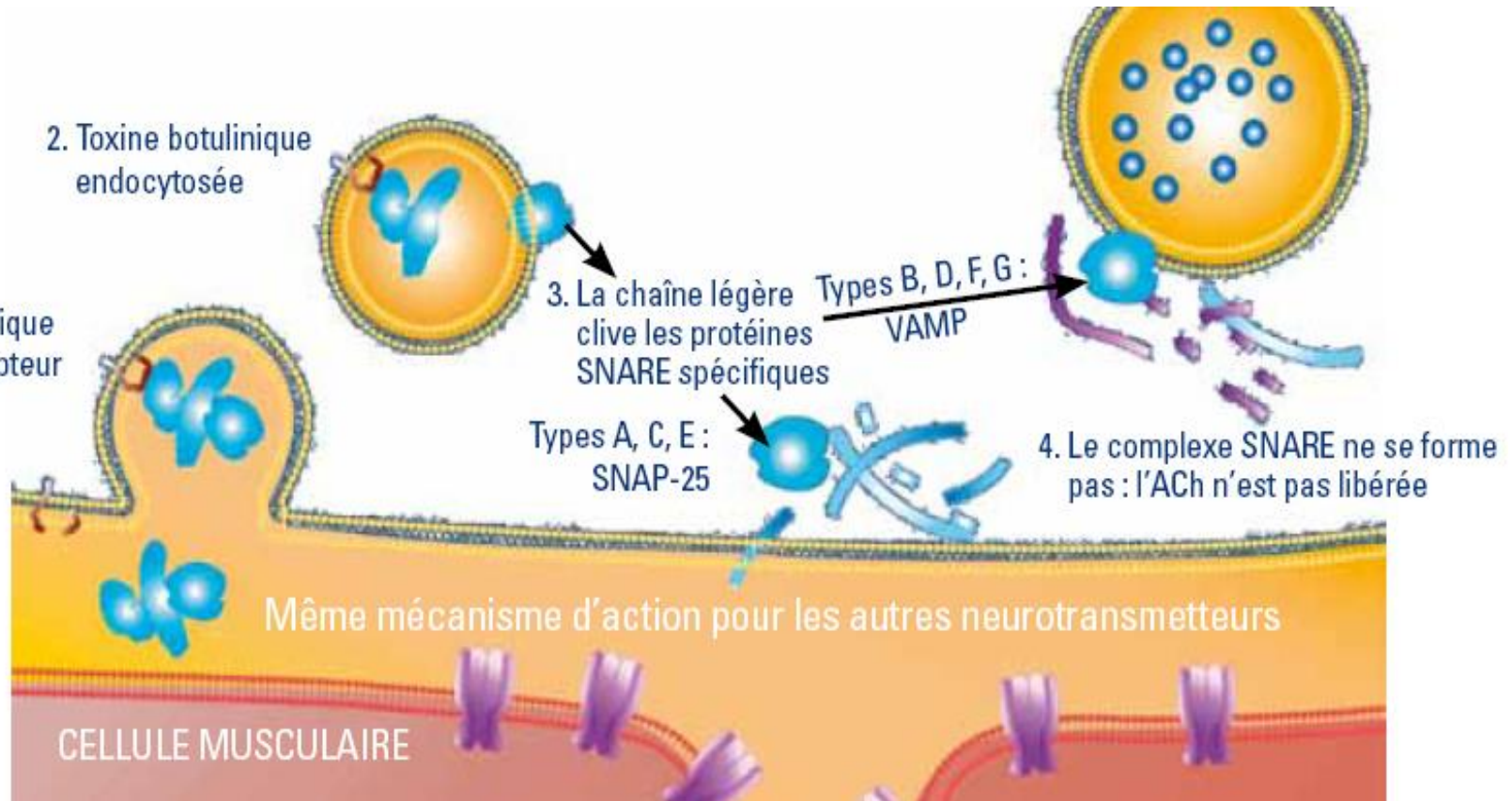


Compound	MW
Aspirin (acetylsalicylic acid)	180 Da <sup>3</sup>
Sanctura® (trospium chloride)	430 Da <sup>3</sup>
Flomax® (tamsulosin)	445 Da <sup>3</sup>
Viagra® (sildenafil citrate)	667 Da <sup>3</sup>
BOTOX® complex (botulinum toxin type A)	~900,000 Da <sup>4</sup>

BoNT-A, botulinum toxin type A; MW, molecular weight.

1. Lacy DB, et al. *Nat Struct Biol* 1998;5:898–902.
2. Lacy DB, Stevens RC. *J Mol Biol* 1999;291:1091–104.
3. DrugBank. Available from <http://www.drugbank.ca/drugs/DB01076>. Last accessed February 2013.
4. Schantz EJ, Johnson EA. *Perspect Biol Med* 1997;40:317–27.

# BOTOX : mode d'action



Reproduit avec l'autorisation de Arnon SS, et al. JAMA.

Arnon SS, Schechter R, Inglesby TV et al. Botulinum toxin as a biological weapon: medical and public health management. JAMA 2001; 285(8): 1059–70

# Neuromodulation : mode d'action

E Chartier Kastler et col, Pit. J Neurrol 2015

?

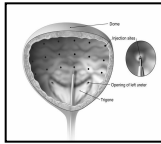




1988 1994 1997 1998 2002 2003 2010 2011 2013/2011



Approval of BOTOX® for the treatment of wrist and hand disability due to upper limb spasticity associated with stroke in adults

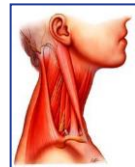


Approval of BOTOX® for the treatment of urinary incontinence caused by idiopathic detrusor overactivity in patients who are refractory to anticholinergics<sup>4†</sup>

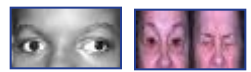
Allergan acquires *Oculinum* and changes product name to BOTOX®<sup>1</sup>



Approval of BOTOX® for the symptomatic relief of cervical dystonia



Approval of BOTOX® for the symptomatic relief of blepharospasm, hemifacial spasm



Approval of BOTOX® for management of dynamic equinus foot deformity caused by spasticity in ambulant children ≥2 years old with cerebral palsy



Approval for the management of axillary hyperhidrosis<sup>3</sup>



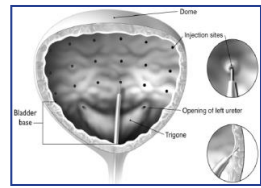
First approval for the cosmetic indication of BOTOX® in Switzerland<sup>2</sup>



Approval of BOTOX® for the prophylaxis of headaches in adult patients with chronic migraine<sup>3†</sup>



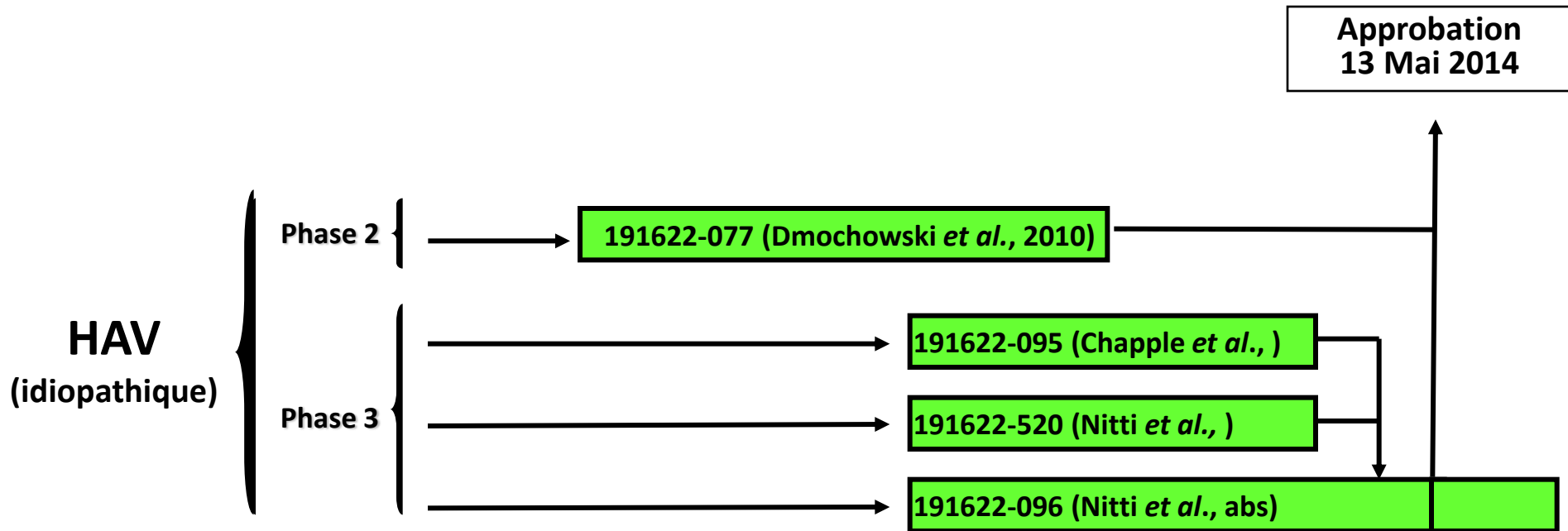
Approval of BOTOX® for the treatment of urinary incontinence caused by neurogenic detrusor overactivity in patients who have not been adequately managed with anticholinergic therapy<sup>4</sup>



\*Licenses may vary between countries †Only licensed in the UK; ‡only licensed in some EU countries (e.g. Germany, the Nordics)

1. Allergan website: [http://www.allergan.com/assets/pdf/botox\\_history\\_and\\_development.pdf](http://www.allergan.com/assets/pdf/botox_history_and_development.pdf). Last accessed February 2013.
2. <http://agn.client.shareholder.com/earningsreleasedetail.cfm?ReleaseID=93322>. Last accessed February 2013.
3. [http://www.emea.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Botox/human\\_referral\\_000088.jsp](http://www.emea.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Botox/human_referral_000088.jsp). Last accessed February 2013.
4. BOTOX® Summary of Product Characteristics.

# - Programme de Développement Clinique: Hyperactivité Vésicale Idiopathique -



# Pour quels patients ?

- Syndrome clinique d'hyperactivité vésicale
- Refractaire aux anticholinergiques
  - Intolérance
  - Inefficacité
  - Deux anticholinergiques

# Quelles contre indications ?

- Infection
- Refus ou impossibilité autosondages
- Anticoagulants
- Grossesse allaitement
- Injection dans les 12 semaines

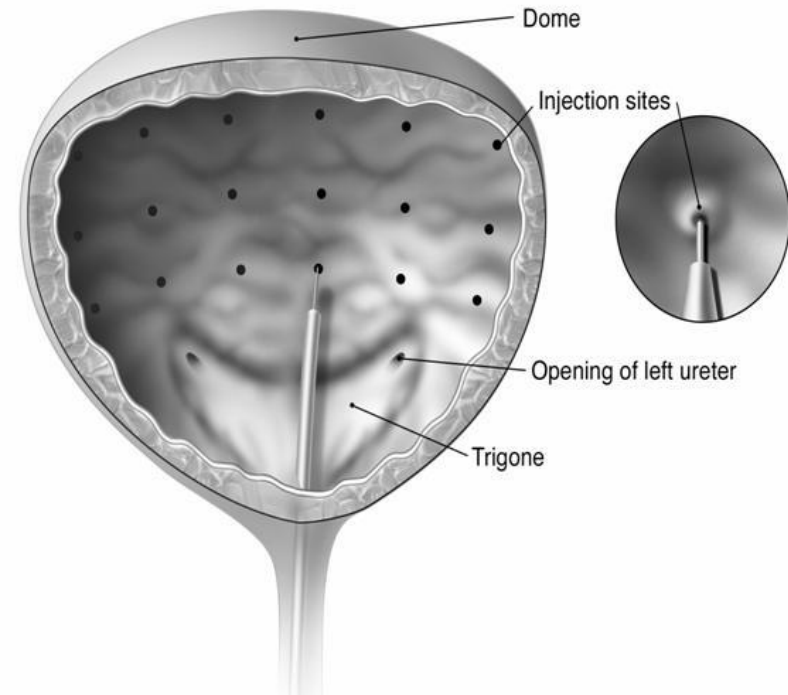


# Quel bilan ?

- Clinique
- Calendrier mictionnel
- ECBU
- Cystoscopie
- Discuter Urodynamique

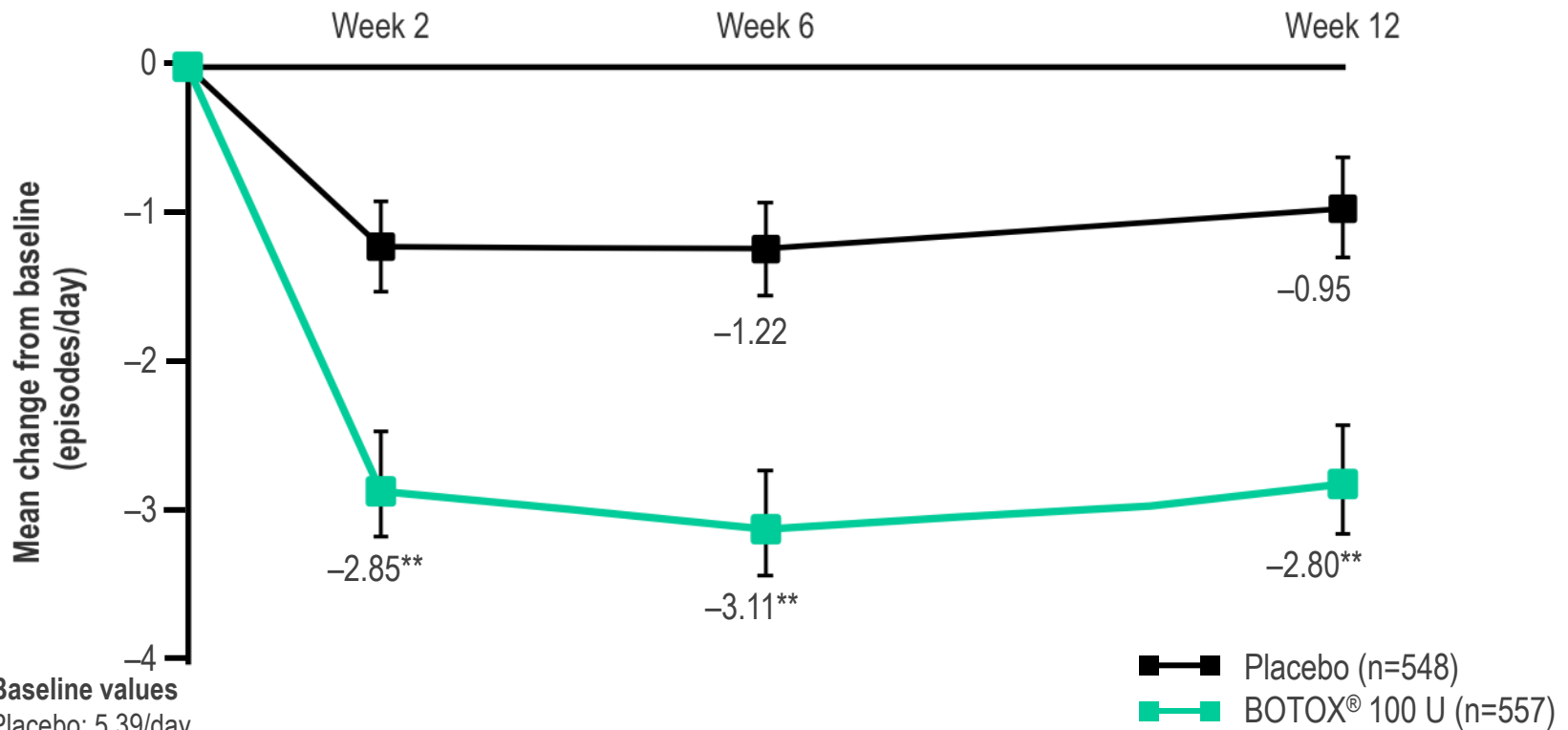
# Comment?

- Hopital de jour
- Anesthesie locale
- Endoscopie
- Dose test 50 UI
- Dose habituelle : 100 UI



# EFFICACITE

A 12 SEMAINES, réduction de 51% des épisodes de fuites



## Baseline values

Placebo: 5.39/day

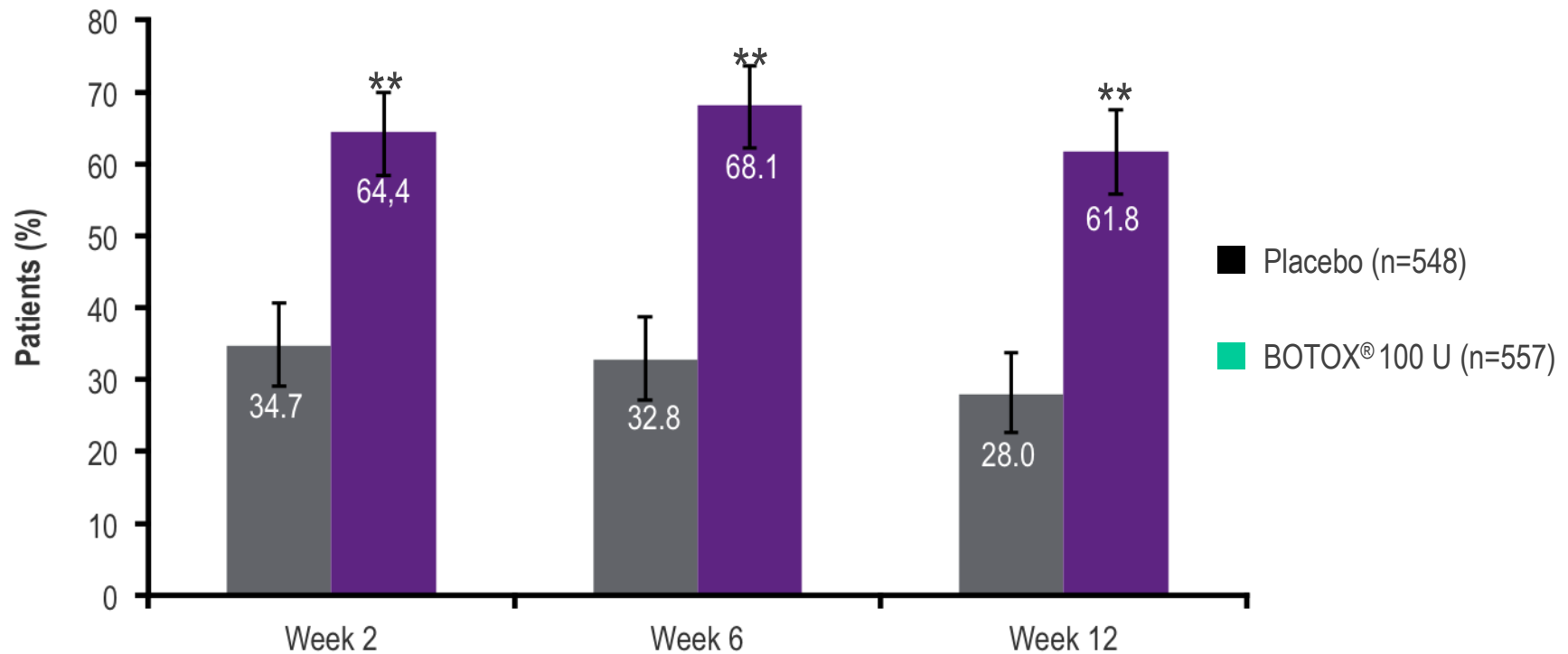
BOTOX® 100 U: 5.49/day

\*\*p<0.001 vs. placebo.

UI, urinary incontinence.

Adapted from: BOTOX® Summary of Product Characteristics, Ireland, Allergan Ltd, 2013.

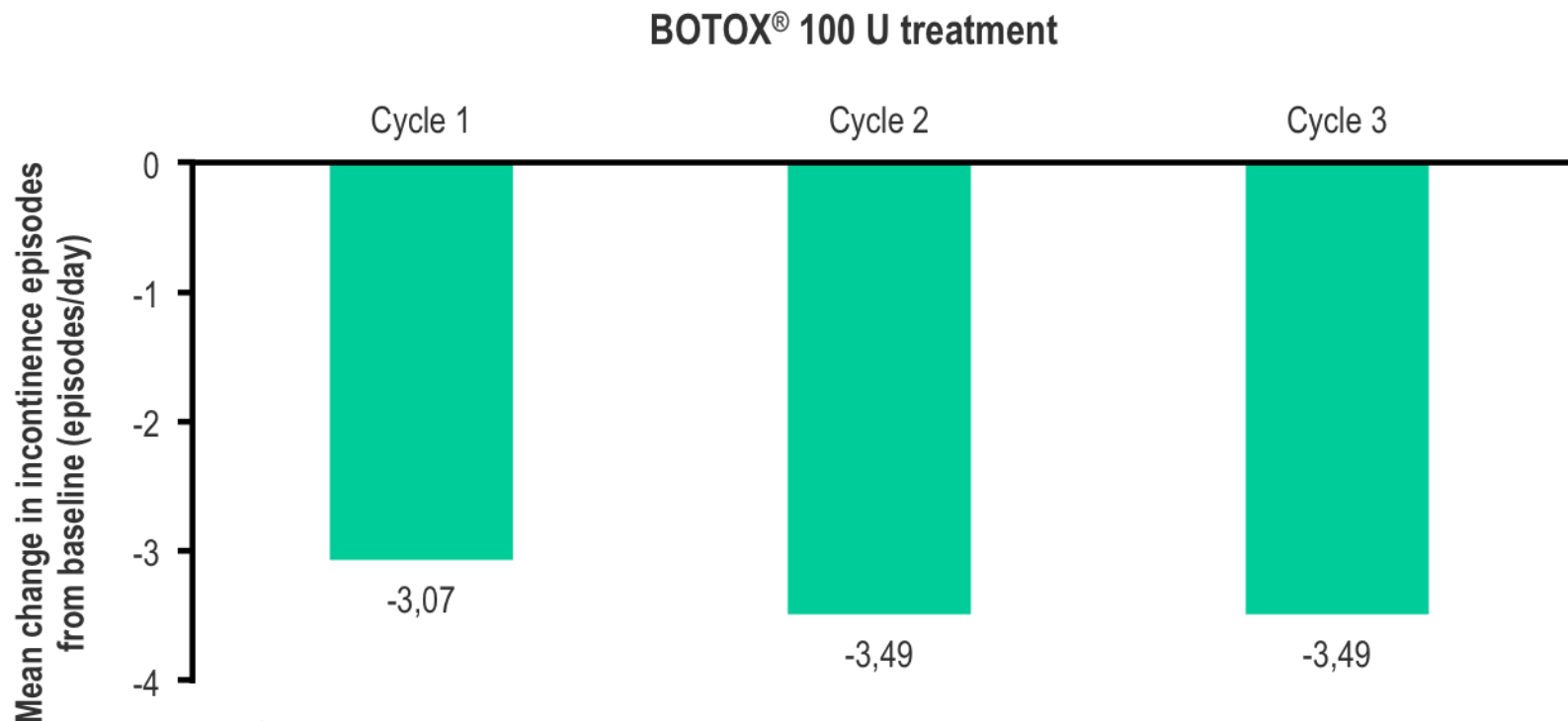
# Plus de 60% de patients améliorés ou très améliorés



\*\*p<0.001 vs. placebo.

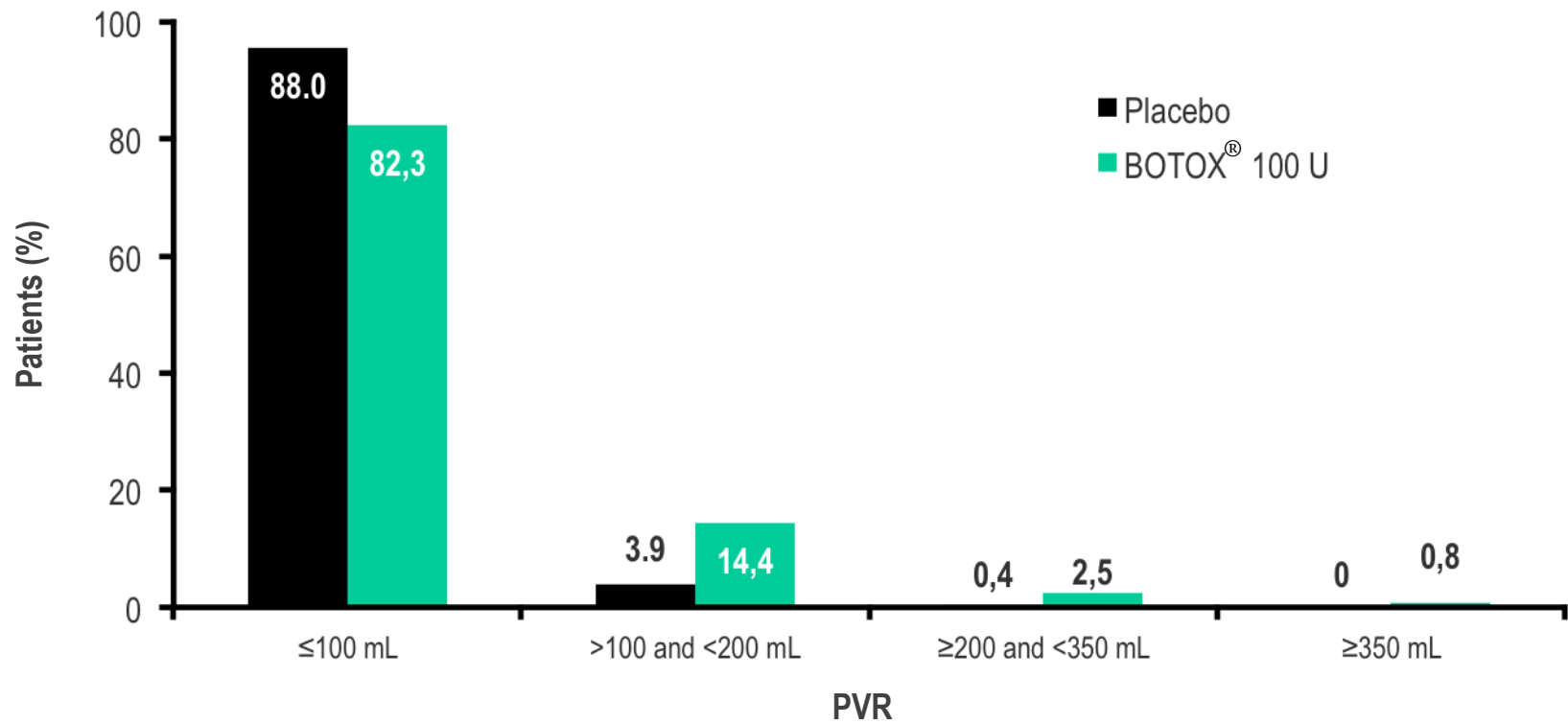
Adapted from: BOTOX® Summary of Product Characteristics, Ireland, Allergan Ltd, 2013.

# Durée d'efficacité moyenne : 6 mois



Adapted from: BOTOX® Summary of Product Characteristics, Ireland, Allergan Ltd, 2013.  
Adapted from Allergan Data on File.

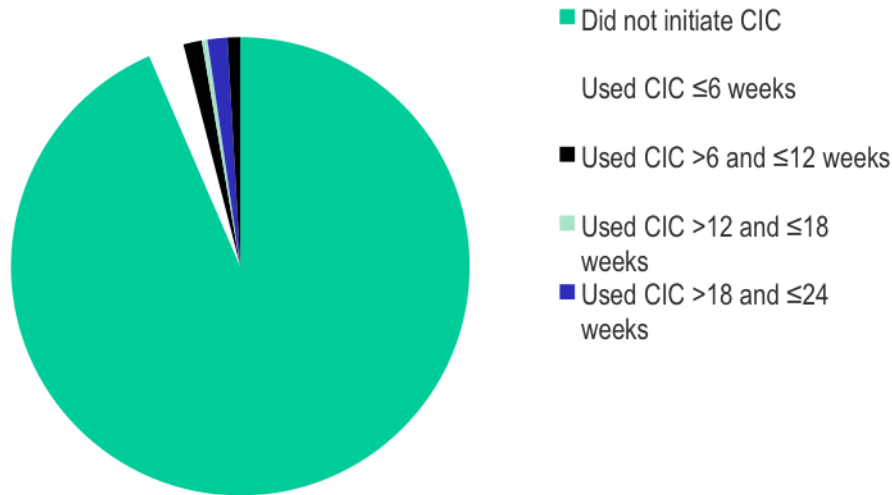
# Evaluation du résidu post mictionnel



PVR, post-void residual.

Adapted from Allergan Data on File.  
ISS Table 3-14.1.

# Recours à l'autosondage : 36/552

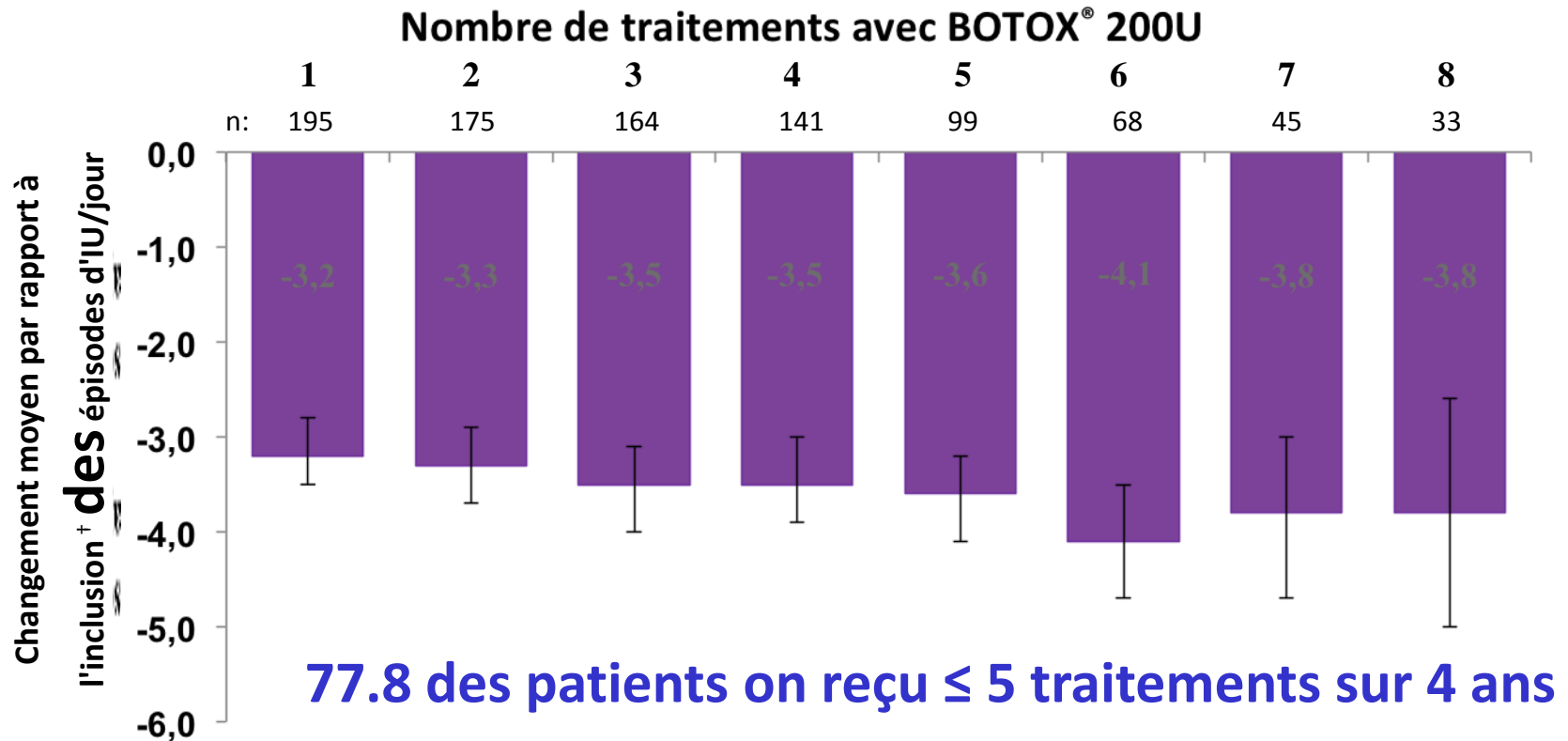


- Transitoire
- Spontanément réversible
- Information
- Facteurs de risque
  - Age
  - Hypertonie uréthrale
  - Bandelette sous urethrale

\*Patients requiring CIC at any point during treatment cycle 1.  
CIC, clean intermittent catheterisation.

Adapted from: BOTOX® Summary of Product Characteristics, Ireland, Allergan Ltd, 2013 and Allergan Data on File.

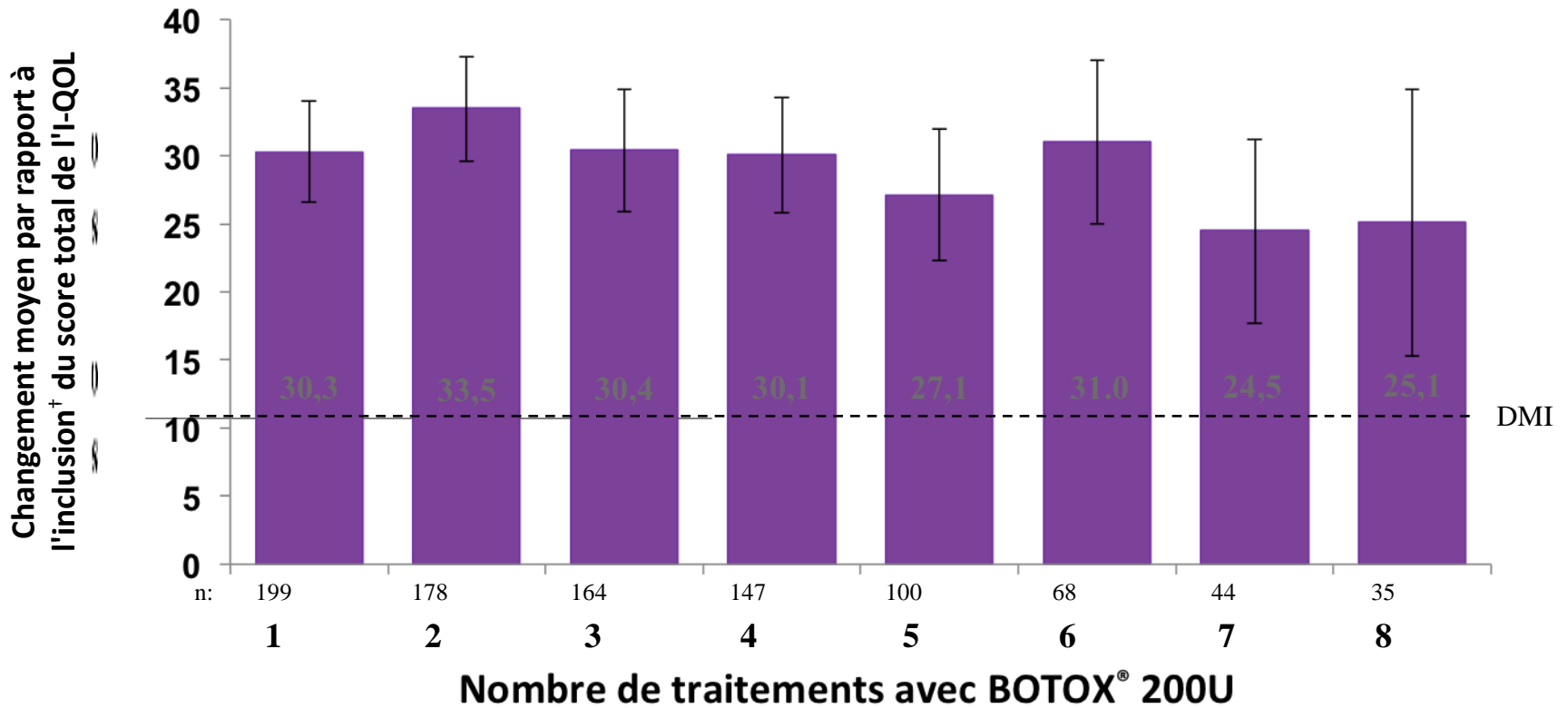
# - Diminution Significative des Episodes Quotidiens d'IU suite aux Traitements Répétés de BOTOX® -



Semaine 6 après chaque traitement. † La ligne de base est avant la 1ère dose de BOTOX® dans les études de phase 3 initiales pour tous les patients entrant dans l'étude de prolongation les valeurs de n sont basées sur les patients avec des données disponibles à la semaine 6. Les barres d'erreur représentent des intervalles de confiance de 95 %.



# - Augmentation Significative de la QdV suite aux Traitements Répétés de BOTOX® -



\*Semaine 6 après chaque traitement. † La ligne de base est avant la 1ère dose de BOTOX® dans les études de phase 3 initiales pour tous les patients entrant dans l'étude de suivi à long-terme. Les valeurs de n sont basées sur les patients avec les données disponibles à la semaine 6. Les barres d'erreur représentent des intervalles de confiance de 95%. I-QOL = incontinence Quality Of Life questionnaire; DMI = différence minimale importante

## - Recommendations de l'EAU: BOTOX® et HAV

Evidence summary	LE
A single treatment session of intravesical onabotulinumtoxinA (100-300 U) is more effective than placebo at curing UUI and improving UUI and QoL for up to 12 months.	1a
Doses of onabotulinumtoxinA above 100 U are associated with an increased risk of de novo CIC.	1a
Doses of onabotulinumtoxinA above 100 U do not add additional improvement in QoL.	1b
There is no evidence that repeated injections of botulinumtoxinA have reduced efficacy.	3
There is a high risk of increased PVR when injecting elderly frail patients.	3
There is a high risk of UTI in those who require CIC.	1b
There is no evidence that one technique of injecting botulinumtoxinA is more efficacious or harmful than another.	1b

Recommendations	GR
Offer botulinum toxin A intravesical injections to patients with urge urinary incontinence refractory to antimuscarinic therapy.	A
Always check the botulinum toxin brand before injection, as units among the available brands are not interchangeable.	A
Offer onabotulinumtoxinA 100 U as initial dose to minimise the risk of urinary retention and urinary tract infection.	A
Warn patients of the limited duration of response, the possible prolonged need to self-catheterise (ensure that they are willing and able to do so) and the associated risk of urinary tract infection.	A
Patients should also be informed of the licensing status of botulinumtoxinA, and that long-term adverse effects, although improbable, remain uncertain.	A

# - Recommandations Pratiques Françaises -

Progrès en urologie (2014) 24, e1–e7



ELSEVIER  
MASSON

RECOMMANDATION

Guidelines for the use of botulinum toxin type A in idiopathic overactive bladder: Translation

Recommandation pour l'utilisation de la toxine botulique de type A (Botox®) dans l'hyperactivité vésicale idiopathique

Prog Urol. 2015 Jun;25(8):461-73



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REVUE DE LA LITTÉRATURE

## Hyperactivité vésicale idiopathique et BOTOX® : revue de la littérature

*Idiopathic overactive bladder and BOTOX®: Literature review*

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J.-F. Hermieu<sup>l</sup>, L. Le Normand<sup>m</sup>, C. Saussine<sup>n</sup>,  
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# CONCLUSION

- Traitement efficace
- Simple d'administration
- Effets secondaires connus et maîtrisé





SANTÉ  
INCONTINENCE URINAIRE, UNE AVANCÉE  
AVEC LA TOXINE BOTULIQUE

PARIS  
**MATCH**