Y a-t-il encore de vraies limitations à l'utilisation de la toxine en intradetrusorien

Pr Pierre Denys

Hopital Raymond Poincaré

Garches

Liens d'intérêt

- Ipsen
- Allergan
- Wellspect
- Coloplast

Les indications validées et enregistrées

- Actuellement en deuxieme ligne de traitement après échec des traitements médicamenteux
- Botox 200 U pour l'hyperactivité du detrusor neurologique chez le BM ou la SEP sous autosondages
- Botox 50/100 pour le syndrome d'hyperactivité vésicale non neurologique
- Botox 100 pour le syndrome d'hyperactivité vésicale chez la SEP sans autosondages

En pratique

- Peu de limitations
- Sous anesthésie locale
- Fibro ou cysto rigide
- En France du fait de l'AMM sous antibiothérapie prophylactique ou curative d'une colonisation
- CI si myasthénie ou Lambert Eaton, association à la gentamycine

Les possibles limitations

- Le geste
- Le patient
  - Neurologique sous autosondage
  - Neurologique sans autosondage
  - OAB
  - Enfant
- La préparation du patient
- La durée totale d'efficacité
- Les effets secondaires

Original Article - Lower Urinary Tract Dysfunction

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INVESTIGATIVE AND CLINICAL UROLOGY
ICUROLOGY

Transvaginal ultrasound guided trigone and bladder injection: A cadaveric feasibility study for a novel route of intradetrusor chemodenervation

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Cystoscopie

Huit cadavres féminins
5 point d'injection (2 trigone, 3 paroi postérieure)
Bleu de méthylene
65% de succès histologique
Pas d'étude de diffusion

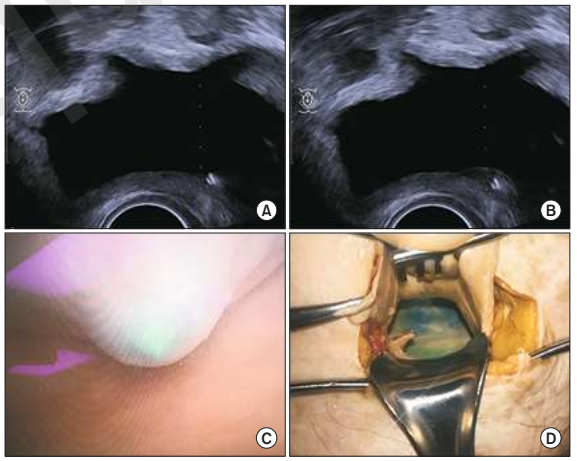

Fig. 1. Ultrasound, cystoscopic and gross visualization of the bladder trigone. (A) Ultrasound pre-injection. (B) Ultrasound post-injection. (C) Cystoscopy pre-injection. (D) Cystotomy post-injection.

Low-dose onabotulinumtoxinA improves urinary symptoms in noncatheterizing patients with MS

Mark Tullman, MD, Emmanuel Chartier-Kastler, MD, PhD, Alfred Kohan, MD, Veronique Keppenne, MD, Benjamin M. Brucker, MD, Blair Egerdie, MD, Meryl Mandle, BS, Jean Paul Nicandro, PharmD, Brenda Jenkins, BS, and Pierre Denys, MD

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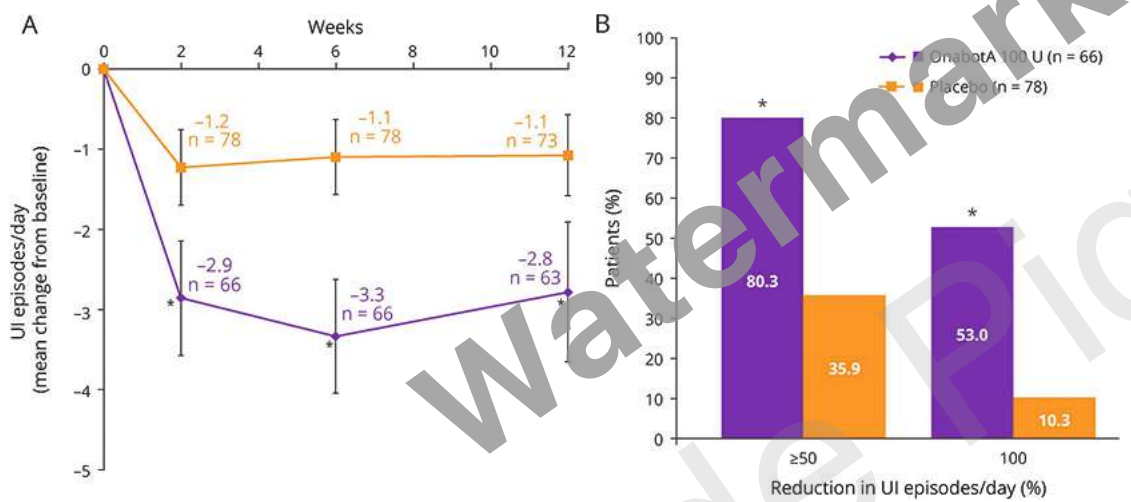
Figure 1 Effects of onabotulinumtoxinA 100 U vs placebo on UI



(A) Mean change from baseline in urinary incontinence (UI) episodes at weeks 2, 6, and 12. (B) Proportion of patients achieving ≥50% and 100% UI episode reduction at week 6. Error bars represent 95% confidence intervals; n values denote the numbers of patients with data available at the evaluated time point after OnabotA (onabotulinumtoxinA) 100 U treatment. *$p < 0.001$ vs placebo.

Table 3 TEAEs ≥3% within the first 12 weeks of treatment cycle 1 (safety population)

Events	Placebo (n = 78), n (%)	OnabotA 100 U (n = 66), n (%)
Overall	38 (48.7)	45 (68.2)
UTI[a]	5 (6.4)	17 (25.8)[b]
Symptomatic	1 (1.3)	9 (13.6)
Asymptomatic	4 (5.1)	8 (12.1)
Residual urine volume[c]	1 (1.3)	11 (16.7)[d]
Urinary retention[e]	1 (1.3)	10 (15.2)[f]
Bacteriuria	4 (5.1)	6 (9.1)
Dysuria	1 (1.3)	3 (4.5)
Diarrhea	3 (3.8)	1 (1.5)
Arthralgia	1 (1.3)	2 (3.0)
Bladder discomfort	0 (0)	2 (3.0)
Ear infection	0 (0)	2 (3.0)
Fall	1 (1.3)	2 (3.0)
Hematuria	5 (6.4)	2 (3.0)
Renal cyst	1 (1.3)	2 (3.0)
Leukocyturia	4 (5.1)	2 (3.0)
Vulvovaginal mycotic infection[g]	0 (0)	2 (3.5)
Patients initiating CIC at any time during treatment cycle 1, %	2 (2.6)	10 (15.2)

SCIENTIFIC REPORTS

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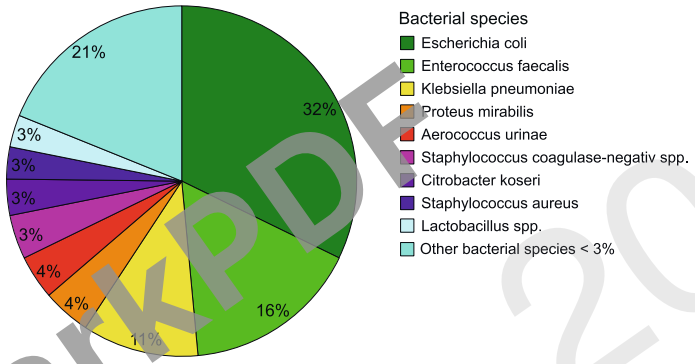
Antibiotic prophylaxis may not be necessary in patients with asymptomatic bacteriuria undergoing intradetrusor onabotulinumtoxinA injections for neurogenic detrusor overactivity

Lorenz Leitner[1,2,*], Ulla Sammer[1,*], Matthias Walter[1], Stephanie C. Knüpfer[1], Marc P. Schneider[1,3], Burkhardt Seifert[4], Jure Tornic[1], Ulrich Mehnert[1] & Thomas M. Kessler[1]



	Asymptomatic bacteriuria (n = 200)	No bacteriuria (n = 73)
No adverse event	188	68
Gross haematuria	1	0
Urinary tract infection	9	5
Bladder pain	1	0
Autonomic dysreflexia	1	0

Discussion

Main findings. Investigating a consecutive series of 154 patients with refractory NDO undergoing 273 intradetrusor onabotulinumtoxinA injections without antibiotic prophylaxis, safety and efficacy of the therapy could be ensured, even if asymptomatic bacteriuria was present. Within 6 weeks after treatment, UTI occurred in 5% (9/200) of the patients with asymptomatic bacteriuria pre-treatment and in 7% (5/73) of those with a sterile urine culture. The efficacy rate of 70%, i.e. appropriate clinical and urodynamic effect, was without any association between asymptomatic bacteriuria and therapy failure. In addition, there was sustained onabotulinumtoxinA effect duration of a mean of 10 months showing no significant differences between patients with and without bacteriuria before treatment.

Manque une étude randomisée sur le risque infectieux à 1 mois versus placebo dans une population homogène

A review of prospective Clinical Trials for neurogenic bladder: Pharmaceuticals

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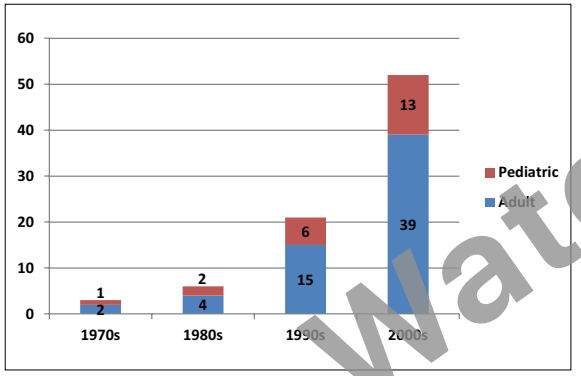

Figure 1. *Number of trials for each ten year period.*

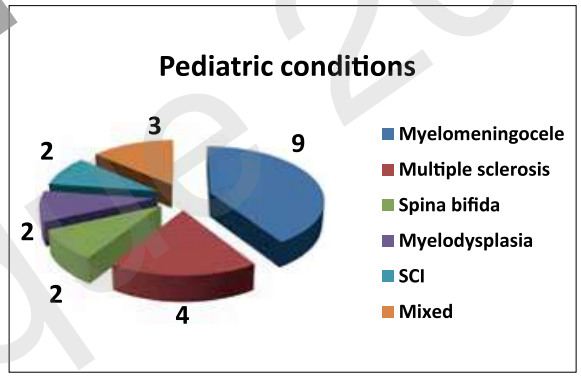

Figure 3. *Pediatric conditions behind the neurogenic bladder.*

Outcomes of Intra-Detrusor Injections of Botulinum Toxin in Patients With Spina Bifida: A Systematic Review

Juliette Hascoet,[1]* Andrea Manunta,[2,3] Charlène Brochard,[3,4,5] Alexis Arnaud,[1] Mireille Damphousse,[3,6] Hélène Menard,[3] Jacques Kerdraon,[3,7] Hubert Journel,[3] Isabelle Bonan,[3,6] Sylvie Odent,[3,8] Benjamin Fremond,[1,3] Laurent Siproudhis,[3,4,5] Xavier Gamé,[9] Benoit Peyronnet,[2,3,5] and For the French Referral Network of Spina Bifida

Pas d'études randomisées
Problème de sélection des patients
Association de l'hyperactivité au trouble de compliance
Insuffisance sphinctérienne qui peut dégrader le résultat

TABLE II. Clinical Outcomes

Author	Delay before clinical evaluation (months)	Incontinence resolution rate after injection	Mean interval between injections (months)	Total number of injections	Adverse events
Tiryaki[10]	1, 3, and 6	If detrusor overactivity: 55.5% (5/9) If no detrusor overactivity: 0%	12–16	1 (81%) 2 (9%)	NR
Tarcan[11]	1	96% (30/31)	7–8	1 (68%) 2 (29%) 3 (3 %)	UTI: 29% (9/31)
Marte[12]	2	100%	6–9	1 (15%) 2 (47%) 3 (38%)	UTI: 4% (2/47)
Zeino[13]	3, 9, and 12	32% (9/28)	13.7	1–6 (mean = 2.5)	0
Horst[14]	3 and 12	NR	12	1 (45%) 2 (27%) 3 (18%) 4 (10%)	0
Safari[15]	3 6	63% (19/30) 23% (7/30)	NR	1	NR
Neel[16]	6	87% (7/8)	6	2	0
Deshpande[17]	1, 3–6, and 9	NR	NR	1	UTI: 14% (1/7)
Kajbafzadeh[18]	4	73% (19/26)	NR	1	0
Altaweel [19]	3	65% (13/20)	NR	NR	NR
Riccabona[20]	3	87% (13/15)	12	2	0
Schulte-Baukloh[21]	1	NR	NR	1	0

NR, not reported; UTI, urinary tract infection.

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ORIGINAL CLINICAL ARTICLE

WILEY Neurourology Urodynamics ICS SUFU

Outcomes of intradetrusor onabotulinum toxin A injection in patients with Parkinson's disease

Gregory Vurture[1] | Benoit Peyronnet[1,2] | Andrew Feigin[3] | Milton C. Biagioni[3] | Rebecca Gilbert[3] | Nirit Rosenblum[3] | Steven Frucht[3] | Alessandro Di Rocco[3] | Victor W. Nitti[1] | Benjamin M. Brucker[1]

24 PD 17 hommes
100 U Botox évalués à 4 semaines
Augmentation Résidu
12,5% de sondages intermittents
résidu pré injection prédictif du risque de sondage

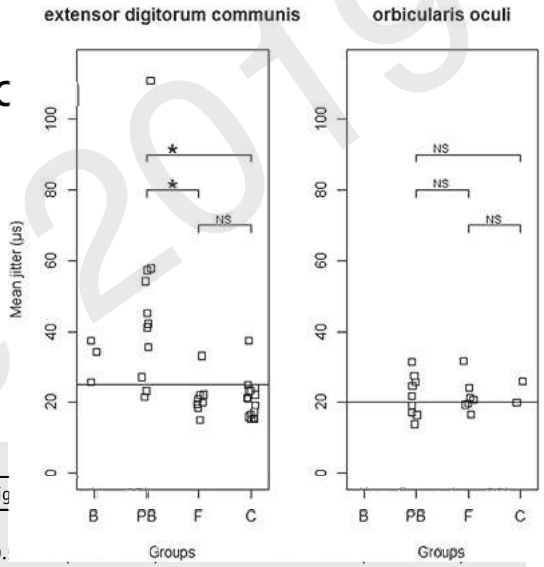
TABLE 2 Clinical and VUD correlates before and after BoNT-A injection

	Before onabotulinum toxin injections	4 weeks after onabotulinum toxin injections	*P*-value
Mean maximum urinary flow rate	11.3 ± 5.4	NA	NA
Median number of pads per day [IQR]	3 [1–5]	0 [0–4]	0.016*
Urinary incontinence			
Yes	24 (100%)	17 (70.8%)	<0.001*
No	0	7 (29.1%)	
OAB symptoms—subjective			
Self-assessment			
Improved		19 (79.2%)	
Unchanged	NA	3 (12.5%)	NA
Worsened		2 (8.3%)	
Post void residual volume (mL)	17.6 ± 30.3	125.3 ± 161.5	<0.001*
Clean-intermittent catheterization			
Yes	0	3 (12.5%)	<0.001*
No	24 (100%)	21 (87.5%)	
Detrusor overactivity			
Yes	24 (100%)	NA	NA
No	0		

NA, not applicable.
*Statistically significant.

Que faire si une diffusion générale a été constatée suite à une injection ?

- Comment faire le diagnostique d'une diffusion générale de la to
- Contre-indiquer toute nouvelle injection de toxine
- Diminuer les doses
- Refaire puisque les précédentes se sont bien passées ?



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Archives of Physical Medicine and Rehabilitation

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Archives of Physical Medicine and Rehabilitation 2015;96:1103-9

ORIGINAL RESEARCH

Single-Fiber Electromyography Analysis of Botulinum Toxin Diffusion in Patients With Fatigue and Pseudobotulism

Alexis Ruet, MD,[a] Marie Christine Durand, MD,[b] Pierre Denys, MD, PhD,[a] Frederic Lofaso, MD, PhD,[b] François Genet, MD, PhD,[a] Alexis Schnitzler, MD[a]

Table 2 SFEMG results for each group

SFEMG Parameters	Control Group (n=17)	Fatig	
Mean jitter (µs)			
EDC muscle	20.9±7.2 (15.2–37.5)	20.	
OO muscle	22.9±2.9 (20–25.9)	20.8±3.17 (16.6–31.6)	21.7±8.7 (13.8–31.3)
Pathologic fibers (%)			
EDC muscle	4.8±7.9 (0–27.7)	5.0±2.4 (0–28.5)	31.5±28.8 (0–83.3)
OO muscle	23.0±2.0 (21–25)	11.1±10.6 (5–31.5)	19.0±17.7 (0–36.8)
Blocked fibers (%)	0±0 (0–0)	0±0 (0–10.5)	5.35±15 (0–58.3)
Abnormal SFEMG*			
EDC muscle	1 (7)	1 (12.5)	9 (82)
OO muscle	2 (100)	6 (86)	5 (56)

NOTE. Values are median ± interquartile range (minimum–maximum) or n (%).
* SFEMG was considered abnormal if mean jitter, percentage of pathologic fibers, or percentage of blocked fibers was abnormal.

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ORIGINAL CLINICAL ARTICLE

Long-term outcomes and risks factors for failure of intradetrusor onabotulinumtoxin A injections for the treatment of refractory neurogenic detrusor overactivity

Charles Joussain[1] | Mélanie Popoff[2] | Véronique Phé[3] | Alexia Even[2] | Pierre-Olivier Bosset[4] | Sandra Pottier[5] | Laetitia Falcou[2] | Jonathan Levy[2] | Isabelle Vaugier[5] | Emmanuel Chartier Kastler[3] | Brigitte Schurch[6] | Pierre Denys[1,2]

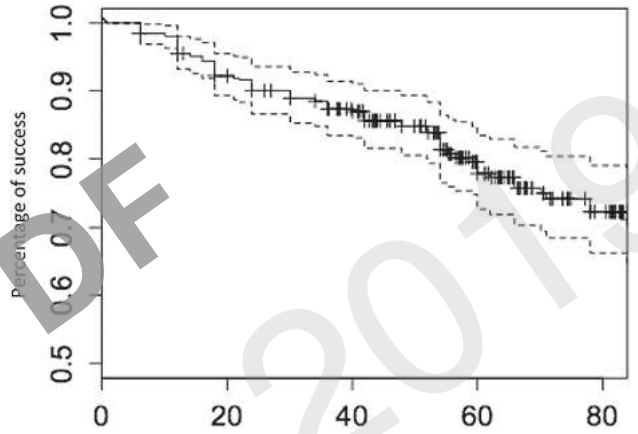
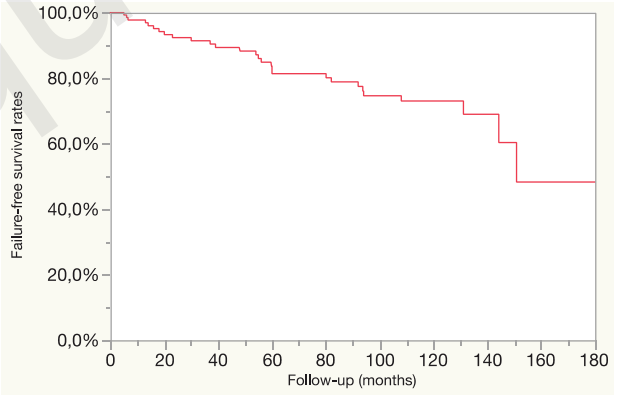


FIGURE 2 Long term failure survival curve

Long-Term Discontinuation of Botulinum Toxin A Intradetrusor Injections for Neurogenic Detrusor Overactivity: A Multicenter Study

Maximilien Baron,* Benoit Peyronnet,[†,‡,*] Annabelle Aublé, Juliette Hascoet, Evelyne Castel-Lacanal, Gabriel Miget, Sabine Le Doze, Thomas Prudhomme, Andrea Manunta,[‡] Jean-Nicolas Cornu[‡] and Xavier Gamé[§]

From the Departments of Urology (MB, AA, JNC) and Physical Medicine and Rehabilitation (GM), University of Rouen, Rouen, Department of Urology, University of Rennes (BP, JH, AM), Rennes, Departments of Urology (TP, XG) and Physical Medicine and Rehabilitation (ECL), University of Toulouse, Toulouse and Department of Physical Medicine and Rehabilitation, Functional Re-Education and Rehabilitation Center Le Normandy (SLD), Granville, France



		20 months	40 months	60 months	80 months	100 months	120 months	140 months	160 months	180 months
Whole cohort N= 140	Number at risk	102	87	72	65	53	34	11	3	2
	Number of failure	8	12	19	20	24	25	26	28	28
	Failure-free survival	93.3%	89.4%	81.4%	80.1%	74.6%	73%	69%	48.3%	48.3%

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ARTICLE

High prevalence of neutralizing antibodies after long-term botulinum neurotoxin therapy

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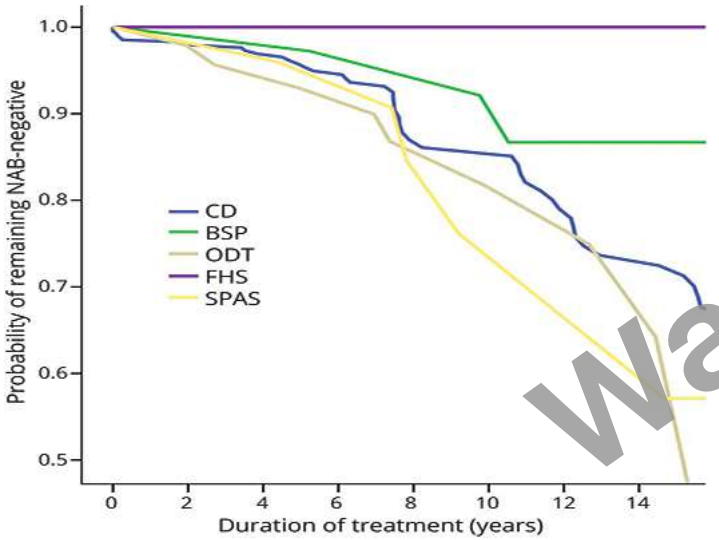
Figure 2 Kaplan-Meier curves of probability to remain NAB negative by diagnosis



Kaplan-Meier analysis of the probability of remaining neutralizing antibody (NAB) negative in all 5 patient subgroups. With duration of treatment, the decline of the Kaplan-Meier curves becomes steeper and steeper. In the other dystonia (ODT), cervical dystonia (CD), and spasticity (SPAS) subgroups, up to 40% of the patients had become NAB positive after a duration of treatment of 15 years. BSP = blepharospasm; FHS = facial hemispasm.

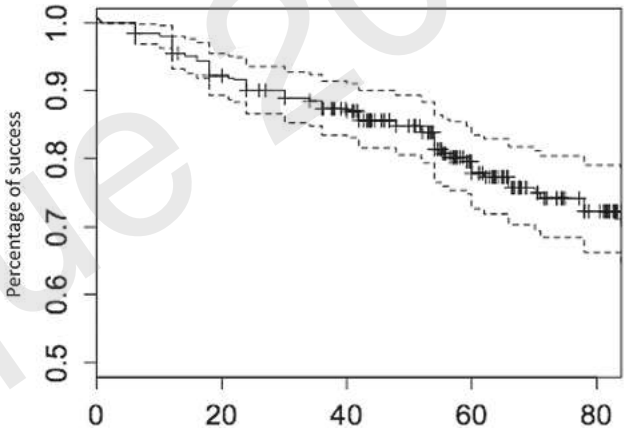


FIGURE 2 Long term failure survival curve

La réelle limitation est la durée de maintien sous traitement

- Patients à espérance de vie comparable à la population générale
- Pas de données sur la durée d'effet des différentes lignes thérapeutiques
- Anticholinergiques et toxine restent des traitements réversibles
- Mécanisme de résistance inconnu
- Acquisition d'anticorps antitoxine ou bien mécanismes neuropharmacologiques d'échappement

En conclusion

L'autosondage, sa faisabilité et sa compliance

L'épuisement de l'effet thérapeutique avec le temps

La diffusion générale de la toxine