Walking improvements after repeated abobotulinumtoxinA injections and correlation with time since stroke or TBI in adults with lower limb spastic hemiparesis

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Disclosures

Author	Disclosure
Ian Baguley	Consulting and teaching for Ipsen, Allergan and Merz; investigator on Ipsen trial
Steven Faux	Investigator on Ipsen trial
Senen Gonzalez	Hospitality from Allergan; research grants from Ipsen; consultancy fees from Merz; investigator on Ipsen trial
Katya Kotschet	Investigator on Ipsen trial
John Estell	Hospitality, research funding and consultancy fees from Allergan, Ipsen and Merz; investigator on Ipsen trial
John Olver	Consultant, conduct and/or involvement in educational activities for Ipsen, Allergan and Merz; investigator on Ipsen trial
Claire Villain	Employee of Ipsen
Phillippe Picaut	Employee of Ipsen
Jean-Michel Gracies	Research grants from Allergan, Ipsen and Merz; investigator on Ipsen trial

Introduction

Background

- Patients with chronic hemiparesis following stroke or TBI often have reduced mobility[1,2]
- Our previous double-blind trial demonstrated that a single aboBoNT-A (Dysport®) injection improves muscle tone in adults with lower limb spasticity[3]
- Published studies have demonstrated that there is an optimal time for post-stroke spasticity management, suggesting potential benefits of earlier intervention (within 3 months)[4,5]

Objectives

- This descriptive sub-analysis of the open-label extension assesses:
  - Walking speed, step length and cadence after repeat administration
  - Whether time since event (stroke or TBI) affects outcomes

1. Eng J. *Expert Rev Neurother* 2007; 2. Ochi F. *J Head Trauma Rehabil* 1999; 3. Gracies JM. *Neurology* 2017; 4. Rosales RL. *Toxins* 2018; 5. Rosales RL. *J Neurol Sci* 2016. aboBoNT-A, abobotulinumtoxinA; TBI, traumatic brain injury.

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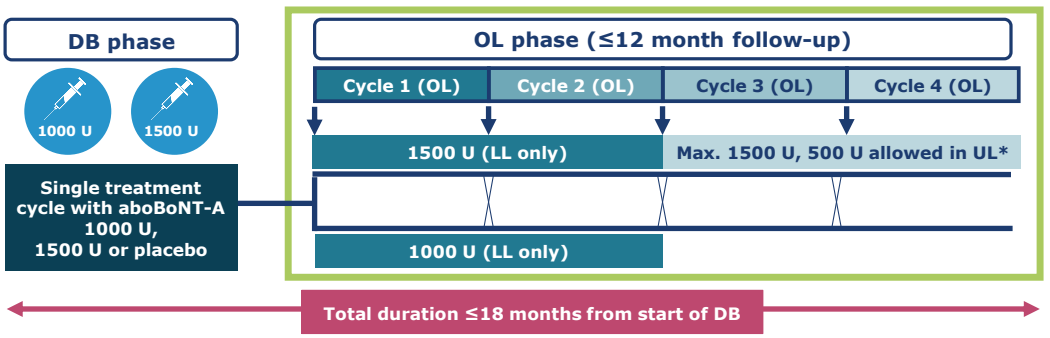
Study design

- Phase 3, prospective, multicentre, randomised, double-blind study (NCT01249404), followed by an open-label extension (NCT01251367)



*UL injection allowed at investigator's discretion. aboBoNT-A, abobotulinumtoxinA; DB, double-blind; LL, lower limb; max., maximum; OL, open-label; U, units; UL, upper limb.

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Methods

Study participants

- Ambulatory adults with hemiparetic lower limb spasticity causing gait dysfunction
- ≥6 months post stroke

Outcome measures

- Changes assessed relative to double-blind baseline for mean walking speed, step length and cadence across 4 categories:
  - Barefoot: comfortable vs maximal
  - With shoes: comfortable vs maximal
- *Post-hoc* Pearson correlation coefficients by treatment group (aboBoNT-A doses combined) estimated relationships between time since events and walking speed improvements

aboBoNT-A, abobotulinumtoxinA.

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Results: patients

Of 388 patients enrolled in the double-blind study, 352 (91%) were eligible for the open-label extension

- **Mean age (SD):** 53.2 years (12.7)
- **Gender:** majority of patients were male (68%)
- **Etiology:** 88% (n=309) had stroke and 12% (n=43) had TBI
- **Affected limbs:** left limbs affected slightly more than right (55% [n=194] vs 45% [n=158], respectively)
- **Mean time (SD):** post stroke = 4.5 (4.8) years; post TBI = 9.2 (10.1) years

n, number; SD, standard deviation; TBI, traumatic brain injury.

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Results: improvement in walking performance

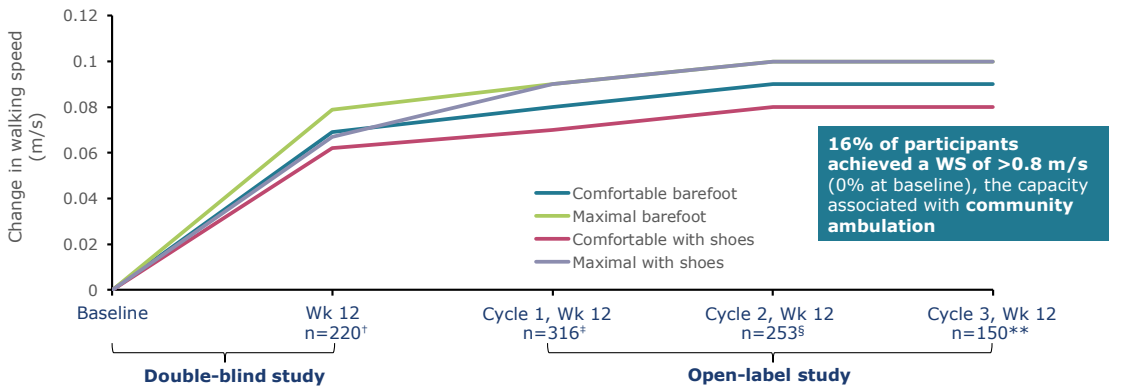
- At Cycle 3, Week 12*, improvements in walking speed, step length and cadence were observed in all 4 categories

WS test category	Mean Δ – BL to Cycle 3 (m/s [SD])			Improvement from BL to Cycle 3 (%)		
	WS	SL	Cadence	WS	SL	Cadence
Barefoot comfortable	+0.09 (0.14)	+0.04 (0.08)	+0.08 (0.20)	23.6	13.8	8.4
Barefoot maximal	+0.10 (0.19)	+0.04 (0.09)	+0.10 (0.25)	22.9	11.2	9.7
With shoes comfortable	+0.08 (0.15)	+0.04 (0.09)	+0.06 (0.21)	22.6	13.2	7.2
With shoes maximal	+0.10 (0.20)	+0.03 (0.10)	+0.10 (0.26)	19.7	9.5	8.6

- At an observational level, all parameters were improved post intervention to a similar degree

*Data are last treatment cycle with available data (Cycle 3) at Week 12. Δ, change in; BL, baseline; SD, standard deviation; SL, step length; WS, walking speed. Results are presented as all doses of aboBoNT-A combined.

Results: improvement in walking speed

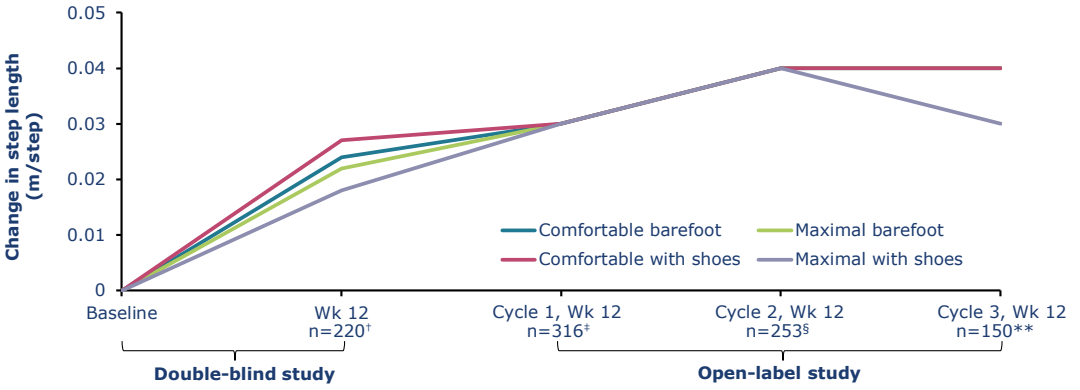


Walking speed improved to the greatest extent following the first aboBoNT-A injections

Small continuous improvements in walking speed with subsequent aboBoNT-A injections

Patients received either 1000 U or 1500 U of aboBoNT-A. *222 for comfortable WS with shoes, 221 for maximal WS with shoes; †219 for maximal WS with shoes; ‡317 for maximal WS barefoot, 319 for comfortable WS with shoes, 318 for maximal WS with shoes; §254 for comfortable WS with shoes and maximal WS with shoes; **151 for comfortable WS with shoes and maximal WS with shoes. aboBoNT-A, abobotulinumtoxinA; n, number of patients; WS, walking speed; Wk, week. Results are presented as all doses of aboBoNT-A combined.

Results: improvement in step length



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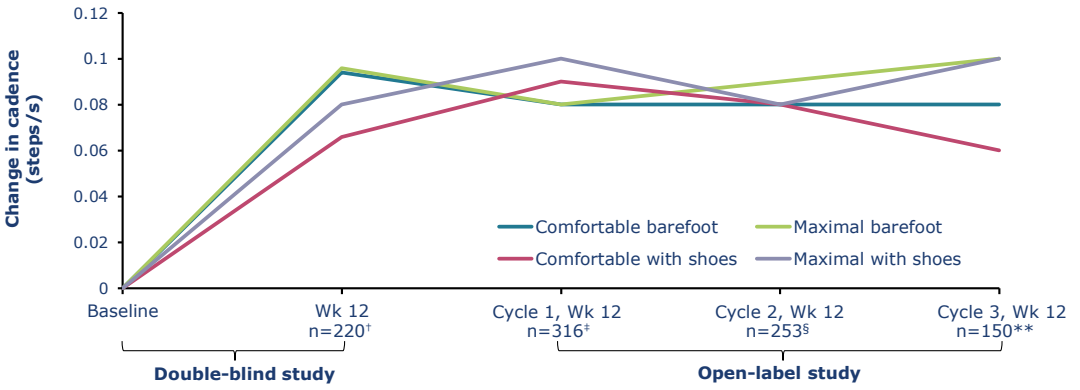
Results: improvement in cadence



Cadence improved to the greatest extent following the first aboBoNT-A injections

Cadence performance plateaued with subsequent aboBoNT-A injections

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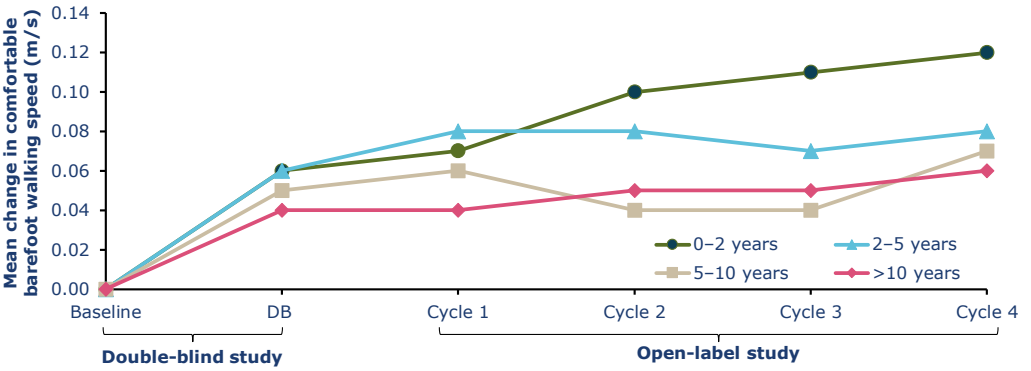
Results: mean change in comfortable barefoot walking speed evaluated by time since event



- At Cycle 4, Week 4, mean (SD) change* was 0.12 m/s (0.17) for events within 0–2 years vs 0.06 m/s (0.15) for events >10 years prior to study
- Mean change* and time since event were significantly correlated during Cycle 2:
  - Week 4, r=-0.124 (p=0.037); and Week 12, r=-0.151 (p=0.016)

*In comfortable barefoot walking speed, from baseline. DB, double-blind; SD, standard deviation; WS, walking speed. Results are presented as all doses of aboBoNT-A combined.

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Conclusions

- Walking speed, step length and cadence all improved with repeated administration of aboBoNT-A in hemiparetic adults with lower limb spasticity
- Inverse correlations were observed between time since event (years) and walking speed improvements
- This suggests that spasticity treatment may result in better functional outcomes when commenced earlier post event
- Improvements in walking ability may increase community participation and independence, and improve quality of life for patients with lower limb spasticity

aboBoNT-A, abobotulinumtoxinA.

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Thank you!