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Real-world effectiveness of abobotulinumtoxinA (Dysport®) in adults with upper limb spasticity in routine clinical practice: an observational study

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ABSTRACT

AbobotulinumtoxinA (aboBoNT-A, Dysport®) is used in clinical practice as a well-tolerated and effective therapy for muscle spasticity. AboBoNT-A has been shown to reduce upper and lower limb spastic paresis in clinical trials, demonstrating improvements in muscle tone and limb function. This open-label, multicentre, observational, non-interventional study was the first to investigate aboBoNT-A's efficacy in adult patients with upper limb spasticity (ULS) in routine clinical practice in Poland. All enrolled patients received ≥1 aboBoNT-A injection cycles, per routine clinical practice (full analysis set, FAS), and ≥1 rehabilitation session. Patients attended a baseline visit (V1) and two follow-up visits (V2, V3) for retreatment, depending on the investigator's assessment of individual patient needs, with a mean interval (SD) between injections of 4.4 (1.4) and 4.5 (1.2) months. The primary effectiveness endpoint was patient- and physician-based evaluation using the Clinical Global Impression--Improvement Scale (CGI-I), a validated 7-point scale (1 = very much improved to 7 = very much worse) relative to baseline. CGI-I has not previously been used as a primary endpoint in studies evaluating ULS. Secondary endpoints included muscle tone in shoulder, elbow, carpal joint, and finger muscles, measured by the Modified Ashworth Scale (MAS), and muscle strength according to the Medical Research Council scale (MRC).

Of 108 enrolled patients (FAS), 92 (85.2%) completed the study and 57 (52.8%) were included in the per protocol (PP) population. AboBoNT-A improved patient conditions in 96.4% and 98.6% at V2 and V3 (investigator assessment) and 92.8% and 98.6% (as reported by patient) of patients, respectively. Significant reductions in muscle tone from baseline were observed at both visits ($p < 0.0001$–0.0077) across muscle groups. Increased muscle strength by cumulative MRC was observed at V2 ($p = 0.0566$) and V3 ($p = 0.0282$) versus baseline. Safety was consistent with the known profile of aboBoNT-A. In conclusion, aboBoNT-A treatment is beneficial in patients with post-stroke ULS in routine clinical practice, assessed by patients and investigators.

Key words: botulinum toxin type A, spasticity, upper limb, stroke, observational study

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Introduction

Spasticity is a condition of diverse aetiologies, affecting 17–38% of patients post-stroke, up to 34% and 40–78% of patients who experience traumatic brain injury (TBI) or spinal cord injury, respectively, and 17–53% of patients with multiple sclerosis [1]. Spasticity prevalence is estimated to be 20% at 6–18 months post-stroke, although higher figures have been reported [2–6]. Spasticity greatly impacts upon the activities of daily living and quality of life [7], leading to loss of independence, depression, and mood alterations in a substantial number of patients [8]. In Poland, approximately 95,000 patients are hospitalised annually because of acute stroke [6], making this condition a significant burden for patients, their relatives, and the healthcare system.

Multiple, randomised, controlled clinical trials in patients with spasticity have demonstrated that botulinum toxin type A (BoNT-A) improves muscle tone, passive function, ease of performing passive basic upper limb activities, and physician/patient global ratings of treatment response [9–15]. Coupled with rehabilitation, BoNT-A is recommended for spasticity management in clinical practice [14, 16–18].

The clinical efficacy and safety of abobotulinumtoxinA (aboBoNT-A, Dysport®, Ipsen Pharma, France) has been confirmed in randomised, double-blind clinical trials in different neurological conditions, including cervical dystonia [19–21], hemifacial paresis [22, 23], blepharospasm [22, 24], paediatric cerebral palsy [25], limb spasticity triggered by multiple sclerosis [26], and limb spasticity in adults post-stroke or post-TBI [12, 27–31].

Moreover, aboBoNT-A has been shown to be an effective focal intervention for reducing upper limb spastic paresis over single [12, 15] and repeated treatment cycles [31], with efficacy lasting up to 20 weeks [12], and exceeding 28 weeks when injected early post-stroke [32]. Funding of aboBoNT-A for post-stroke ULS treatment in Poland was approved in 2014.

The Clinical Global Impression-Improvement (CGI-I) scale is a validated instrument that assesses improvements or deteriorations in condition relative to baseline. This scale is commonly used in research and is recommended in clinical practice for quantifying the progress of patients predominantly with psychiatric and movement disorders [33]. The CGI-I has been used in published studies for spasticity and toxins [34, 35]; however, it has not previously been used as a primary endpoint for evaluating upper limb spasticity (ULS) after stroke.

Clinical rationale for the study

The present observational study was the first to evaluate the effectiveness of aboBoNT-A in post-stroke ULS based on patient and physician CGI-I ratings in real-life clinical settings in Poland. The injection regimen was tailored to patient needs regarding dose and injection frequency, enabling individualisation of therapy [12, 34]. These results may provide new evidence supporting the effectiveness of aboBoNT-A for patients with ULS in routine clinical practice (which includes rehabilitation), and will further elucidate whether the CGI-I scale is an effective and reliable method to evaluate ULS improvements. This study was initiated following the availability of funding for aboBoNT-A in Poland.

Materials and methods

Study design

The primary objective of this open, multicentre, observational, non-interventional study (NCT02444494) was to investigate the clinical effectiveness of aboBoNT-A in adults with post-stroke ULS according to patient and physician evaluation using the CGI-I scale.

The secondary objective was to assess muscle tone in muscles of the elbow, wrist, carpal joint, and fingers.

The study was carried out at seven investigational sites in Poland between March 2015 and September 2016. The planned sequence of events and assessment schedule for each visit are presented in Table S1 (see **supplementary materials**). Visits were scheduled based on investigator judgement in accordance with routine clinical practice (typically every 3–4 months), with at least one rehabilitation cycle. Study duration was approximately nine months for each patient, and 21 months overall (including the 12-month recruitment period).

Centres prescribed aboBoNT-A according to the National Health Fund (NHF) drug programme. This refers to therapies provided by hospitals free of charge for narrowly defined groups of patients.

This study was approved by the Bioethics Commission of the District Medical Chamber in Lublin (Komisja Bioetyczna przy Okregowej Izbie Lekarskiej w Lublinie); due to the non-interventional observational design, the approval of separate Commissions was not necessary for each investigational site. This study followed the recommendations from the International Epidemiological Association Guidelines for the Proper Conduct in Epidemiologic Research [36] and the International Society for Pharmacoepidemiology Good Pharmacoepidemiological Practice Guidelines [37], and was conducted in accordance with the Declaration of Helsinki. All patients provided written, informed consent to allow their medical data to be collected, analysed and shared with regulatory authorities.

Inclusion criteria

Patients were eligible to participate if they met the following criteria: age ≥ 18 years, history of ischaemic or haemorrhagic stroke ≥ 3 months prior to enrollment (documented by discharge card from the hospital), post-stroke spasticity of confirmed upper extremity (moderate or higher, Modified Ashworth Scale [MAS] score ≥ 2) in at least one muscle group, or prior inclusion in an NHF Dysport® programme. Classification of a patient into the programme occurred following a designated date of commencement of medical rehabilitation

confirmed by the providing rehabilitation services. Drug administration took place within three weeks of initiating medical rehabilitation. Patients provided written informed consent before the initiation of any study-related procedure.

Exclusion criteria

Patients were excluded from the trial if they had severe dysphagia and respiratory disorders, were pregnant, had myasthenia gravis and myasthenic syndrome (based on neurological examination, see **supplementary methods**; additional tests were only carried out in justified cases), had generalised symptoms of infection, presented with inflammation at planned sites of administration, had fixed contractures in soft tissues and joints, or had moderate or severe dementia (Mini Mental State Examination [MMSE] score ≤ 18, see **supplementary methods**).

Patient withdrawal

As this was a non-interventional study, there were no specific predetermined reasons for discontinuing. Patients could withdraw consent at any time. In such cases, data was collected up to the time of withdrawal, but no additional information was collected after this time.

Treatments

Patients who qualified for the post-stroke ULS drug programme and attended the treatment centre for routine aboBoNT-A treatment received injections, as determined by the treating physician. The decision to prescribe aboBoNT-A was made prior to and independently from the decision to enroll a patient in this study.

AboBoNT-A is a licensed medication (Dysport®) and was therefore presented and packaged according to its marketing authorisation. Investigators were free to prescribe any treatment dose according to the Polish Summary of Product Characteristics (SmPC) (38) and NHF programme rules. Investigators could alter or initiate concomitant medication or physical therapy at any time according to clinical need. To minimise needle misplacement during injections, guidance techniques were used for the majority of patients. Electrical Muscle Stimulation (EMS) was used in 51.1–63.9% of patients and ultrasonography (USG) was used in 53.3–68.5% across visits (V1, V2, and V3).

Assessments

The primary effectiveness endpoint was the patient score on the CGI-I scale at follow-up visits V2 and V3, assessed independently by the investigator and the patient. This scale measures change in clinical status from baseline (V1), using a 7-point scale, ranging from 1 (very much improved) to 7 (very much worse), with a score of 4 indicating no change.

The secondary effectiveness endpoints were global assessment of spasticity, measured on the MAS and measurement of upper limb muscle weakness by Medical Research Council (MRC) scale, evaluated at V1, V2, and V3. The MAS is a 6-point scale ranging from 0 (no increase in muscle tone) to 4 (affected parts rigid in flexion or extension) [39]. MAS was evaluated at the joints of each extremity, including shoulders, elbows, wrists, fingers, and thumbs. The MRC scale quantifies muscle weakness (range: 0 = absence of movement to 5 = muscle contracts normally against full resistance). Ten muscle groups were tested, including shoulder adductors, shoulder internal rotators, elbow flexors, elbow extensors, forearm supinators, forearm pronators, wrist flexors, wrist extensors, finger flexors, and thumb adductors.

CGI-I (patient and investigator), aboBoNT-A administration (muscle location, dose, and date of injection), neurological examination and assessments were recorded in a case report form (CRF) designed in accordance with routine practice and programme requirements. In addition to data collected during V1, V2, and V3, CGI-I results from two controlled visits between V1 and V2, and V2 and V3 (performed according to requirements of the drug programme in post-stroke ULS), were collected and reported in the CRF retrospectively using patient medical charts.

Further details of patient characteristics recorded at baseline and neurological examinations performed during qualification to the drug programme are described in the **supplementary methods**.

Safety

As this was a non-interventional study, aboBoNT-A was administered and managed within routine medical care. Investigators reported all serious and non-serious treatment-related adverse events to Ipsen's Pharmacovigilance Department, and recorded such events in the CRF.

Statistical analysis

Analysis populations were defined as enrolled population (all patients fully informed about the study who had given written informed consent to participate), full analysis set (FAS, all enrolled patients having received at least one dose of study medication), and per protocol (PP) population (all FAS patients with no major protocol violations or deviations).

A sample size of 100 patients was considered appropriate to estimate the percentage of patients with CGI-I scale improvements with a required precision of 10% (2-sided 95% CI not greater than 9.8 percentage points).

Primary efficacy analysis

CGI-I results were analysed using a 7-point scale and assessed using descriptive statistics for categorical variables as a percentage for each modality including 95% CI. CGI-I scales completed by investigators and patients at V2 and V3 were also dichotomised as either 'improvement' or 'no change or worsening'. The proportions of this binary-derived variable were analysed using descriptive statistics for qualitative variables (exact 95% CI Clopper-Pearson for binomial proportion were also presented).

Secondary efficacy analysis

The CGI-I scale completed by investigators and patients between V1 and V2, and between V2 and V3, were analysed in the same way as the primary endpoint. Bar charts were generated to view the evolution of the distribution of CGI-I scale at each time point.

MAS and MRC scores for each joint or muscle group were described as ordinal data. For both MAS and MRC, the comparison between scores for each joint or muscle group (V2 *vs.* V1, and V3 *vs.* V1) were tested using the Wilcoxon signed rank test. Cumulative MAS (0–20; total score across joints) and cumulative MRC (0–50; total score across muscle groups) were calculated and described as a quantitative variable if all joints or muscle groups were assessed at the corresponding visit. Changes from V1 (mean difference and respective 95% CI) were analysed using a paired T-test or the Wilcoxon signed rank test according to the distribution.

There were no changes to the planned conduct of the study and no protocol amendments during the study. MAS and MRC scores (for all visits and for each joint or muscle group) and respective cumulative data were not displayed for patients for whom scores at V1 were missing. If there was a significant number of missing values for a patient, a decision was made in consultation with the sponsor regarding the handling of this data in summaries, prior to a database lock. A sensitivity analysis (FAS only) of the primary criterion was performed based on the last visit performed for each patient using the last observation carried forward method.

Results

Patient disposition

Of 108 patients enrolled, 92 (85.2%) completed the study (Tab. 1). All enrolled patients received at least one aboBoNT-A injection cycle and were included in the FAS population (108 patients; 100%). Of these 108 patients, 57 (52.8%) were included in the PP population. Patients were excluded from the PP population owing to a missing MMSE score, because MMSE score is strongly dependent on language skills [40] (23 patients with aphasia; 45.1%), or because of no CGI-I assessment completed by either patient or investigator at V2 (25 patients; 49.0%) and at V3 (39 patients; 76.5%).

Table 1. Patient disposition

	Total (n = 108) n (%)
Completers	92 (85.2)
Full analysis set	108 (100)
Per protocol population	57 (52.8)
Withdrawals	16 (14.8)
Lack of efficacy	2 (1.9)
Consent withdrawn	4 (3.7)
Lost to follow-up	4 (3.7)
Other	6 (5.6)

Patient demographics and baseline characteristics

Patient demographics and baseline characteristics are shown in Table 2. More male (59.3%) than female patients were enrolled, and the mean (SD) age at inclusion was 56.9 (11.9) years. The most common type of stroke experienced by patients prior to enrollment was cerebral infarction (78.7%), and the majority of patients (63.9 %) experienced spasticity pattern III (defined in Table 2) [27, 41], with the left (58.3%) being the more affected side. Mean time (SD) between stroke diagnosis and V1 was 4.5 (5.0) years.

Previous and concomitant comorbidities were recorded in 24 patients (22.2%) and 73 patients (67.6%) respectively, with

Table 2. Patient demographics and baseline characteristics

	Total (n = 108) n
Mean age, years (SD)	56.9 (11.9)
Male, n (%)	64 (59.3)
Mean weight, kg (SD)	77.2 (14.2)
Mean BMI, kg/m^2 (SD)	26.7 (4.1)
Mean MMSE score[a] (SD)	27.5 (2.5)
Stroke type, n (%)	
Cerebral infarction	85 (78.7)
Intracerebral haemorrhage	23 (21.3)
Sequelae of CVD	3 (2.8)
Mean age at stroke, years (SD)	52.3 (12.4)
Mean time between stroke and enrollment, years (SD)	4.5 (5.0)
Mean time between stroke and spasticity, months (SD)[b]	4.5 (8.5)
Spasticity pattern, n (%)[c]	
I	16 (14.8)
II	3 (2.8)
III	69 (63.9)
IV	17 (15.7)
V	3 (2.8)
Laterality affected, n (%)	
Left	63 (58.3)
Right	45 (41.7)

[a]n = 85; [b]n = 107; [c]spasticity pattern definitions from Hefter et al. (2012) [41]
I — internal rotation and adduction of the shoulder, flexion at the elbow, supination in the forearm, and flexion at the wrist;
II — internal rotation and adduction of the shoulder, flexion at the elbow, supination in the forearm, and extension at the wrist;
III — internal rotation and adduction of the shoulder and flexion at the elbow, coupled with a neutral positioning of the forearm and wrist;
IV — internal rotation and adduction of the shoulder, flexion at the elbow, pronation in the forearm, and flexion at the wrist;
V — internal rotation and retroversion of the shoulder, extension at the elbow, pronation in the forearm, and flexion at the wrist.
BMI — body mass index; CVD — cerebrovascular disease; MMSE — mini mental state examination; SD — standard deviation

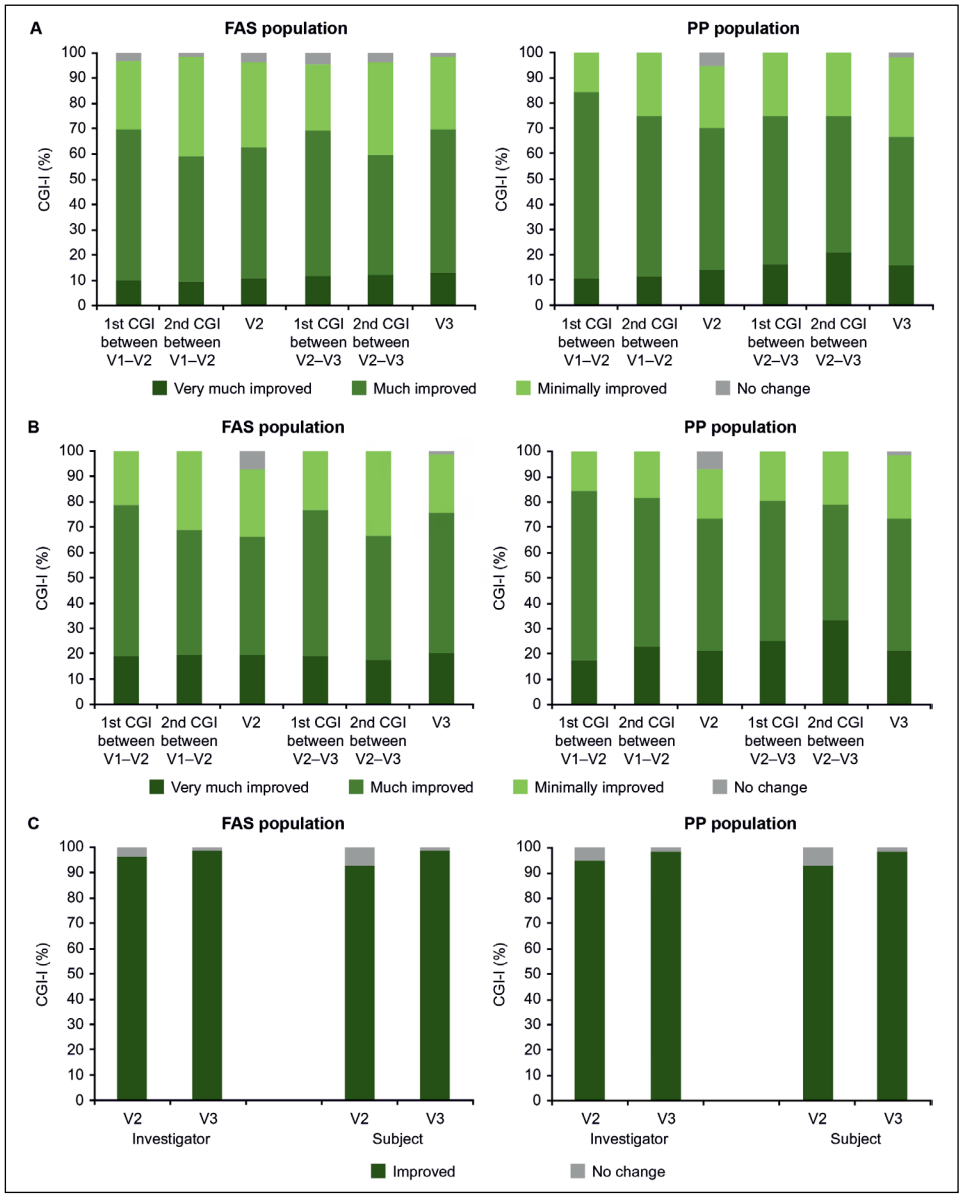

Figure 1. Primary efficacy endpoint. **A.** CGI-I by investigator assessment. **B.** CGI-I by patient assessment. **C.** CGI-I overall improvement summary. For exact values of CGI-I data at V2 and V3, see Table S3 (**supplementary materials**). CGI-I — Clinical Global Impression-Improvement Scale; FAS — full analysis set; PP — per protocol; V — visit

cerebrovascular disease (e.g. previous strokes/silent ischaemic events and/or small vascular disease confirmed by magnetic resonance imaging) the most prevalent in both cases, experienced by 17 (15.7%) and 68 (63.0%) patients respectively.

During the study, 92 (85.2%) patients received three injection cycles, six (5.6%) received two injection cycles, and 10 (9.3%) received only one injection cycle. Mean (SD) aboBoNT-A total dose administered at each visit tended to decrease, from 853.4 (231.4) U at V1 to 813.8 (264.1) U at V3. Further details of injection doses are presented in Table S2 (see **supplementary materials**). Mean (SD) injection intervals were 4.4 (1.4) and 4.5 (1.2) months between V1 and V2, and V2 and V3, respectively.

Primary efficacy endpoint

CGI-I scale measurements prior to, between, and at each follow-up visit are presented in Fig. 1A–C. According to both investigator and patient assessments, a high percentage of patients had improved conditions at V2 (96.4% and 92.8%, respectively) and V3 (98.6% and 98.6%, respectively) in the FAS population (Fig. 1A–C, left panels). Similar results were observed for the PP population (Fig. 1A–C, right panels).

Percentages of improvement by CGI-I scale were similar between the two controlled visits (i.e. first and second CGI-I between V1 and V2, and first and second CGI-I between V2 and V3). All patients in the FAS population evaluated

their medical condition as having improved between each visit (Fig. 1B), whereas the investigators did not consider the medical condition of all patients to be improved (across all visits, 95.7–98.8%; Fig. 1A). Despite a substantial number of dropouts in the PP population owing to deviations from protocol, the results from the FAS and PP populations were very similar. Detailed CGI-I score values in the FAS and PP populations are presented in Table S3 (see **supplementary materials**).

Secondary efficacy endpoint

MAS

Overall, aboBoNT-A treatment improved muscle tone as measured by MAS in the elbows, wrists, fingers, and thumbs in the FAS (Fig. 2A–E, left panels) and PP populations (Fig. 2A–E, right panels). No significant improvement was detected in the shoulders (Fig. 2A). However, shoulder muscles were not injected with aboBoNT-A, because shoulders were not included as injection sites in the Polish SmPC at the time of this study. Despite this, shoulder measurements were included as a separate (Fig. 2A) and sub-measure of the cumulative score, as the intention was to assess cumulative improvements in the whole upper limb. This reflects patient benefits in everyday life and can detect possible effects on shoulder spasticity when more distal muscles in upper limbs are injected. MAS scores for the FAS and PP populations are detailed in Table S4 (see **supplementary materials**).

There was a decrease in cumulative MAS score at V2 and V3 compared to V1 (mean [95% CI]: -1.2 [-1.7; -0.8] and -1.2 [-1.7; -0.7], respectively; $p < 0.0001$ for both; FAS), showing a statistically significant improvement in medical condition (Tab. S5, see **supplementary materials**), despite the inclusion of shoulder muscles.

MRC

The measurements of upper limb muscle weakness by MRC for elbow flexors, forearm supinators, forearm pronators, wrist flexors, wrist extensors, finger flexors, and thumb adductors for the FAS and PP populations are presented in Table S6 (see **supplementary materials**). In the FAS population, significant improvements in MRC score from V1 were observed for elbow flexors ($p = 0.0094$) and finger flexors ($p = 0.0484$) at V2. At V3, significant improvements were recorded for elbow extensors ($p = 0.0373$), wrist flexors ($p = 0.0337$), and wrist extensors ($p = 0.0075$). No significant improvements were observed in muscles of the forearm, thumb or shoulder. In the PP population, change from baseline in MRC score was only significant for elbow extensors at V3 ($p = 0.0418$).

There was a significant increase in cumulative MRC score at V3 compared to V1 (mean [95% CI]: 1.0 [0.0; 1.9]; $p = 0.0282$), showing increased muscle strength; however, results for V2 were not significant (0.8 [0.0; 1.7]; $p = 0.0566$; FAS). Cumulative MRC score for the FAS and PP populations are detailed in Table S7 (see **supplementary materials**).

Safety

One patient (a 79-year-old male; total dose received = 800 U) experienced three adverse reactions (muscle fatigue, balance disorder, and drug ineffectiveness). The investigator considered the muscle fatigue as possibly being related to aboBoNT-A. There were no serious adverse events, deaths, or other observations related to safety, in this non-interventional study.

AboBoNT-A dosing, determined by the investigator, slightly decreased across study treatments (Tab. S2, see **supplementary materials**). Dosing was in accordance with Polish SmPC and NHF drug programme rules (the maximum indicated dose for upper limb treatment is 1,100 U). Investigators injected a high dose according to patient needs in 24 patients (1,050 U in two patients and 1,100 U in 22 patients), with no subsequent adverse events observed in these patients.

Discussion

This was a non-interventional, observational study designed to investigate the effectiveness of aboBoNT-A injections for ULS in adult patients treated in Polish hospitals.

We found that treatment with aboBoNT-A within routine clinical practice, in parallel with at least one rehabilitation session, resulted in not only an overall improvement in patient condition as assessed by patients and physicians using the CGI-I scale, but also improvements in muscle tone and strength assessed using detailed, validated measures (MAS and MRC scales) frequently used for spasticity assessment.

The present study was the first to use CGI-I as a primary endpoint for ULS assessment, although it has previously been used to measure improvements in ULS [34]. CGI-I reflects the patients' overall condition, providing information about functional gains, improved limb position and cosmesis, and lack of pain [33].

In the present study, aboBoNT-A led to improvements on the CGI-I scale in almost all patients (92.8–98.6%), as reported by both investigator and patient assessment. There was no worsening of condition in any patient. These results were supported by significant reductions in muscle tone from baseline at both visits across different muscle groups. Of particular interest, finger muscle improvements may enable patients to carry out more precise finger movements. Also, muscle strength, as assessed by cumulative MRC, increased compared to baseline.

Upon being included in the study, patients received individualised, flexible injection regimens, in which dosing and injection frequency were at the investigators' discretion and aligned with routine clinical practice. Mean injection intervals (time to retreatment = 4.4 and 4.5 months) were longer than the recommended interval of 12 weeks [38], which may reduce treatment burden for both patients and physicians [42]. This long-lasting efficacy of aboBoNT-A in adult spasticity is consistent with previous upper [12, 31] and lower [28] limb

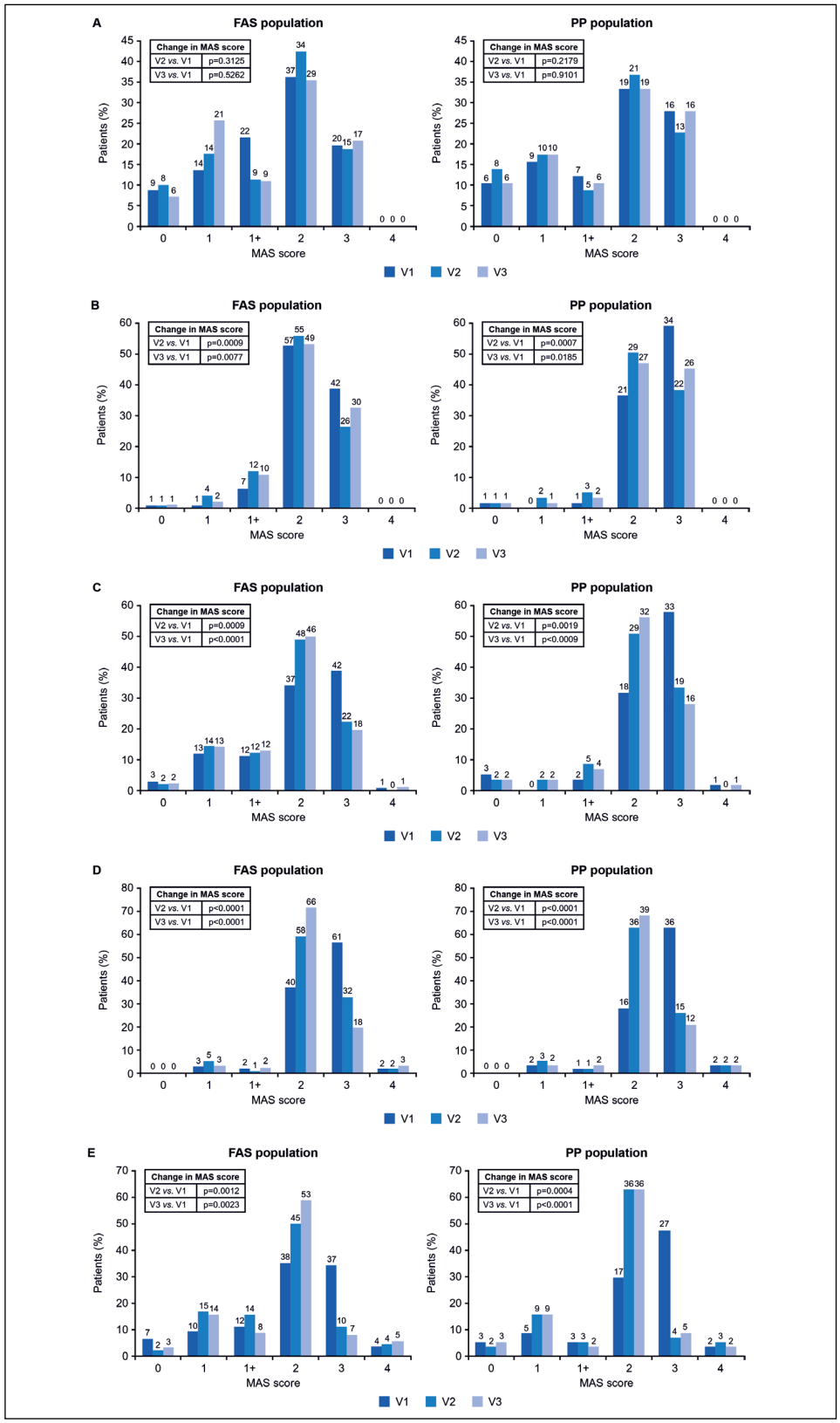

Figure 2. Global assessment of spasticity (MAS score) in FAS and PP populations. **A.** MAS score: shoulder. **B.** MAS score: elbow. **C.** MAS score: wrist. **D.** MAS score: finger. **E.** MAS score: thumb.

Clinician assessment of spasticity and resistance to passive movement. Data presented as percentage of total patients for V1 (FAS: n = 108; PP: n = 57), V2 (FAS: n = 98; PP: n = 57), and V3 (FAS: n = 92, FAS; PP: n = 57). Number of patients (n) is provided above percentage bars. For exact values in global assessment of spasticity (MAS) data, see Table S4 (**supplementary materials**).

FAS — full analysis set; MAS — Modified Ashworth Scale; PP — per protocol; V — visit

studies. However, retreatment intervals in the present study should be considered with caution, as they were not a previously determined study endpoint and visits represented both patients' needs and a typical interaction between patient and physician. The mean subsequent dose of aboBoNT-A was notably lower across treatment cycles, as, with time, smaller doses of BoNT-A are sufficient to evoke a therapeutic effect, and thus dosing was adjusted to individual patient needs.

Improvements in patients' condition observed in the present study occurred despite the relatively long time between stroke and aboBoNT-A therapy. Previous studies have shown that the time between stroke/TBI and initiation of botulinum toxin therapy can impact upon symptom severity. For instance, in patients with lower limb spasticity receiving aboBoNT-A, the greatest improvements have been observed in patients treated 0–2 years post-stroke [28]. Another study showed that aboBoNT-A administered early (2–12 weeks) post-stroke for ULS significantly delayed time to re-injection (determined by pre-defined criteria) to more than 28 weeks in 39.3% of patients [43], suggesting that patients can benefit from early intervention. Of note, concomitant neurorehabilitation aimed at improving upper limb function should be considered as a factor that could potentially enhance treatment efficacy.

In this study, separate analyses were performed for the FAS and PP populations. The rationale for this was that, firstly, the consequences of stroke such as aphasia significantly impact upon patient MMSE scores [40, 44], and secondly, that not all patients underwent CGI-I assessment by the investigator or the patient, leading to fewer patients in the PP population compared to the FAS population. Despite the substantial dropout in the PP population, CGI-I scale improvements according to investigator and patient assessments were similar between the FAS and PP populations at each recorded time point. The discrepancy in the final inclusion of patients into the FAS and PP populations reflects the observational nature of this study, and underlines that conditions determined *a priori* in clinical trials might not accurately represent those of a real-world setting.

It is important to note that the CGI-I scale is a subjective measurement that depends on the patient or investigator by whom it is performed, which could be considered a limitation of this study. However, it has been proposed that functional abilities could be better evaluated based on quality-of-life questionnaires rather than objective outcome measures [34].

Conclusion

In this non-interventional study, we evaluated the effectiveness of up to three aboBoNT-A injection cycles in adults with post-stroke ULS in routine clinical practice. This study was the first to use the CGI-I scale as a primary endpoint. AboBoNT-A led to improvements in CGI-I, by both patient and investigator assessment, as well as in muscle tone and muscle strength. No new safety information emerged from this study.

Overall, aboBoNT-A is an effective treatment option for patients with ULS, and such improvements can be measured reliably using the CGI-I scale.

Clinical implications/future directions

The results of the present study support the use of aboBoNT-A in post-stroke ULS in routine clinical practice. The effects of aboBoNT-A were shown to be long-lasting, with doses of aboBoNT-A reducing at each subsequent injection cycle, consequently easing the burden on both patient and physician. The future evaluation of aboBoNT-A in post-stroke ULS in routine clinical practice over a longer period may be beneficial. The CGI-I scale was shown to be an effective tool for measuring improvement in ULS, reliably supporting other validated measures.

Author contributions:

Conceptualisation: MJ-J, IS-D, AS-S, RR
Data curation: Ipsen Poland; ClinMed Pharma, Warsaw, Poland; ITEC, Cenon, France
Formal analysis: RR; ITEC, Cenon, France
Funding acquisition: MJ-J
Investigation: IS-D, AS-S, AD, TL, SO, AF, PS, KM, JM, EM, AN
Methodology: MJ-J, RR
Project administration: MJ-J, MMB, ClinMed Pharma, Warsaw, Poland
Resources: IS-D, AS-S, AD, TL, SO, AF, PS, KM, JM, EM, AN, RR
Software: not applicable
Supervision: MJ-J, MMB, RR
Validation: MJ-J, RR, MBB
Visualisation: Watermeadow Medical, MMB
Writing – original draft: MMB, MJ-J, IS-D, AS-S
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Data sharing: *Where patient data can be anonymised, Ipsen will share all individual participant data that underlie the results reported in this article with qualified researchers who provide a valid research question. Study documents, such as the study protocol and clinical study report, are not always available. Proposals should be submitted to DataSharing@Ipsen.com and will be assessed by a scientific review board. Data is available from six months after publication until five years after publication; after this time, only raw data may be available.*

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