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Hands-free Atalante exoskeleton in post-stroke gait and balance rehabilitation: a safety study

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Abstract

Background Stroke often results in gait dysfunction, impairing daily activities and quality of life. Overground robotic exoskeletons hold promise for post-stroke rehabilitation. This study primarily aimed to assess the safety of hands-free Atalante exoskeleton training in post-stroke subjects, with a secondary aim to assess gait and balance.

Methods Forty subjects (10.2 ± 12.1 months post-stroke) with gait dysfunction (Functional Ambulation Category [FAC] score ≤ 3) underwent five training sessions over three weeks with a hands-free exoskeleton (Atalante, Wandercraft, France). Safety, the primary outcome, was evaluated by the number and severity of adverse events (AEs), judged by an independent clinical evaluation committee (CEC). A usability test was performed during the fifth training session followed by the exoskeleton use questionnaire. Gait and balance were assessed pre/post-training via walking capacity score (FAC), gait speed by 10-meter walk test (10MWT), walked distance by 6-minute walk test (6MWT), and balance by Berg Balance Scale (BBS). Spasticity was assessed with the Modified Ashworth scale. Anxiety and depression were quantified using the Hospital Anxiety and Depression Scale. Safety outcomes were analyzed using the Wilson, Lee and Dubin methods for proportions, and occurrence rates were computed. Within-group differences were compared using Wilcoxon, McNemar, and Friedman tests, with significance set at $P < 0.05$.

Results Thirty-one subjects completed the training sessions, while nine discontinued. The study reported two serious adverse events (SAE) (vertigo, dysarthria) and six AEs, with the CEC concluding that no SAE was linked to the device/study procedure. The average AE rate per session was 2.5 ± 1.4%, including four events possibly linked to the device/study procedure (knee pain [$n = 1$], skin lacerations [$n = 3$]), classified as negligible or minor by the CEC. A high proportion (82.6%) successfully completed the usability test and reported satisfaction (90%) on the exoskeleton use questionnaire. For gait and balance, favorable changes were observed in FAC, 10MWT, 6MWT, and BBS scores Post-training ($p < 0.05$, respectively). Spasticity, anxiety, and depression remained unchanged.

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Conclusions This study indicates that the hands-free Atalante exoskeleton is safe, feasible, and well-tolerated for gait and balance rehabilitation in post-stroke subjects, warranting larger randomized controlled trials to assess its efficacy.

Trial registration Evaluation of the Use of the Atalante Exoskeleton in Patients Presenting an Hemiplegia Due to Cerebrovascular Accident (INSPIRE) trial was registered at ClinicalTrials.gov (NCT04694001, registered on 20201231).

Keywords Stroke, Gait, Balance, Hands-free, Overground exoskeleton, Rehabilitation, Safety

Background

Stroke or cerebro-vascular accident (CVA) is the second cause of death and third leading cause of disability in adults in the world [1, 2]. A commonly recognized consequence of stroke is motor impairment of upper and/or lower limb, affecting approximately 80% of persons [3]. Gait dysfunction, muscle weakness, spasticity, and proprioceptive deficits affect 62% of individuals following stroke. These lead to asymmetrical gait patterns, disrupted motor control, inappropriate postural responses, balance issues, and altered temporospatial, kinematic, kinetic, and electromyographic parameters, potentially increasing the risks of falls [4].

Gait rehabilitation, like other aspects of motor rehabilitation, should begin as early as possible. The therapeutic methods should vary depending on the stage of recovery, incorporating both manual and instrumental techniques, with a preference for combining these approaches [5]. Multiple rehabilitation techniques, such as spasticity management, goal-oriented and task-specific physical therapy, balance rehabilitation, treadmill training, and various other specific methods, have proven effective in enhancing motor function and quality of life for people post-stroke [6–10].

Electromechanical-assisted methods of rehabilitation, including end-effector devices, fixed and overground robotic-assisted gait training (RAGT), have been suggested as promising tools for rehabilitation of gait and balance post-stroke, allowing task oriented high-intensity training [11]. Various types of robots, with and without body-weight support, are described to allow early mobilization, verticalization, and individually tailored settings. RAGT is safe to use in post-stroke people, with low drop-out rates and few reported adverse events such as pain, skin irritation, fatigue, hypotension, which are generally mild and quickly resolve with appropriate treatment [11–13]. The efficacy of RAGT for gait recovery was explored in multiple randomized-controlled clinical trials. When used solely, RAGT has not been shown to significantly improve walking independence in post-stroke people [14–16]. However, when combined with conventional rehabilitation, RAGT could lead to significant improvements in walking ability [17–20] and in gait parameters such as walking speed, step length, stride duration, stance duration on the unaffected side, cadence and symmetry [21]. Although most studies have not proved superiority of RAGT over conventional rehabilitation, it has been suggested that non-ambulatory persons could benefit of RAGT more than ambulatory people with better odds of reaching independent walking ability [11]. Trunk control and balance were improved as well [20, 22]. However, the role of the type of device, and dose-effectiveness relationship is not clear, and other randomized controlled trials are necessary to disentangle the clinical efficacy as well as neurophysiological mechanisms involved in the recovery post-stroke [22]. It is important to recall that post-stroke individuals often present with upper limb motor impairment. Therefore, not all RAGT devices are appropriate to use in severely impaired people, especially when requiring crutches. The hands-free feature of the Atalante exoskeleton [23] allows for gait training without the need for hand support, while also providing the flexibility to engage the upper limbs in rehabilitation exercises, all while maintaining full support for gait and balance training. The aim of this study was to assess the safety of a hands-free Atalante overground robotic assisted gait training (RAGT) in post-stroke subjects, unable or with limited ability to walk. We hypothesized that hands-free RAGT will be safe to use in this population. Additionally, the effects of this rehabilitation on gait and balance dysfunction were explored using standard clinical tests.

Methods

Study design

This study (CIP002) was a prospective, multicenter safety study performed in 6 rehabilitations centers located in France, Belgium and Luxembourg. It was sponsored by Wandercraft and granted approvals by local Ethics Committees in France, Belgium, and Luxembourg (Comite de Protection des Personnes Ouest IV– Nantes, on March 11th, 2021, Comité d'Ethique Hospitalo-Facultaire Saint Luc– UCL March 8th, 2021 and Comité National d'Ethique de Recherche on March 17th 2021), registered under ID RCB: 2020-A02437-32, B403202000079, and 202010/03, respectively. It was authorised by the French, Belgium and Luxembourg competent authorities (Agence Nationale de Sécurité du Médicament et des produits de Santé [ANSM], Agence Fédérale des Médicaments et des Produits de Santé [AFMPS], and Comité National d'Ethique de Recherche [CNER]), and registered in a public trials' registry (Trial Registration: ClinicalTrials.gov NCT04694001). This study, based on 'Evaluating the

Indego Exoskeleton for Persons With Hemiplegia Due to CVA' (ClinicalTrials.gov NCT03054064) clinical trial, aimed to demonstrate the safety of the hands-free Atalante exoskeleton, as a part of the Food and Drug Administration (FDA) clearance submission process.

Participants

Participants were recruited according to following inclusion criteria:

- Diagnosis of hemiplegia due to cerebrovascular accident (≥ two weeks), with completed etiological evaluation of stroke;
- Functional Ambulatory Category [24] score of 0, 1, 2 or 3;
- Age of 18 years or older, able to read and write in at least one of the languages of the country.

Exclusion criteria included:

- Severe spasticity of adductor muscles, hamstring, quadriceps or triceps surae (> 3 on Modified Ashworth scale [25];
- History of osteoporotic fracture and /or pathology or treatment causing secondary osteoporosis;
- Pressure Ulcer of Grade I or higher according to the International NPUAP/EPUAP pressure ulcer classification system, in areas of contact with the Atalante system,
- Severe aphasia;
- Cardiac or respiratory contraindication to physical exertion;
- Cognitive impairment (Mini Mental State Examination Score < 18) [26];
- Morphological contraindications to the use of the Atalante exoskeleton [23], with maximum user weight of 90 kg, and minimal height of 155 cm, and.
- Previous history of uncontrolled all-cause vertigo.

Intervention– Hands-free Atalante overground exoskeleton

The hands-free overground exoskeleton used in this study, Atalante, is a Class IIa medical device (CE) (Fig. 1) [23]. The exoskeleton is operated by certified operators. A total of 30 operators were certified to use Atalante device in this study, all of whom completed a 12-hour training program focused on using the Atalante exoskeleton, including both theoretical and hands-on instruction. The training was designed to ensure the safe and effective use of the device, with refresher sessions provided as needed. The exoskeleton provides various gait training modalities: forward, lateral and backwards gait, with two independent modes: *EarlyGait* (short passive steps) and *RealGait*, (mimicking physiological gait). The gait speed, and step length could be modified in the *CustomGait* mode. Numerous actuators allow Atalante to perform a U-turn and to change trajectory during walking. In the *RealGait* mode, the exoskeleton operator can adjust the level of robotic assistance during gait, ranging from fully passive gait (passive steps) to active gait (active steps), with assistance levels varying from 100% to -25% resistance. These settings can be adjusted independently for each leg, with lower assistance values indicating reduced robotic assistance.

An exercise mode is available, allowing to perform squats and weight shifts, and various task-oriented exercises/physical activities.

The image shows various parts of the Atalante exoskeleton, a motorized device with two articulated legs and 12 actuators: 3 in each hip, 1 in each knee, and 2 in each ankle. Mechanical and software stops protect joints from exceeding physiological motion limits. Trunk support is provided through plastic shell back, and the subject's trunk is attached to the back of the exoskeleton with a vest. The back is attached to the lower limbs of the exoskeleton, equipped with adjustable straps at the thigh, knee, and ankle, allowing to strap the lower limbs of the participant. The exoskeleton is mechanically adjustable to fit the user's anthropometric measurements through length adjustable segments. Additionally, plastic wedges can be attached to the feet to compensate for limited range of motion. The exoskeleton application on a tablet connects users to Atalante and the Wandercraft server, generating subject-specific movement trajectories based on individual measurements and range of motion. Atalante is to be used in combination with a safety rail. The exoskeleton is operated through two interfaces: a keyboard for the certified exoskeleton operator and a remote control, which can be used by either the operator or the participant. The stop button is available on both interfaces. Gait modes are selected and adjusted via the tablet application by the operator, who also manages mode transitions (installation, sit-to-stand, sitting). The motion of the exoskeleton is triggered by the participant through trunk flexion to initiate standing, sitting, or walking, or through sideways leaning to initiate turning. The inertial sensor (IMU) placed on the vest detects the participant's intent. Either the operator or the participant can control the remote to trigger actions such as starting or stopping gait, turns, and activating the exercise mode.

Procedure

The rehabilitation program consisted of five rehabilitation sessions with the exoskeleton, performed over three weeks, in combination with conventional rehabilitation. This conventional rehabilitation was in accordance with the standard of care in each center. The RAGT sessions included 10 min of donning and doffing, and

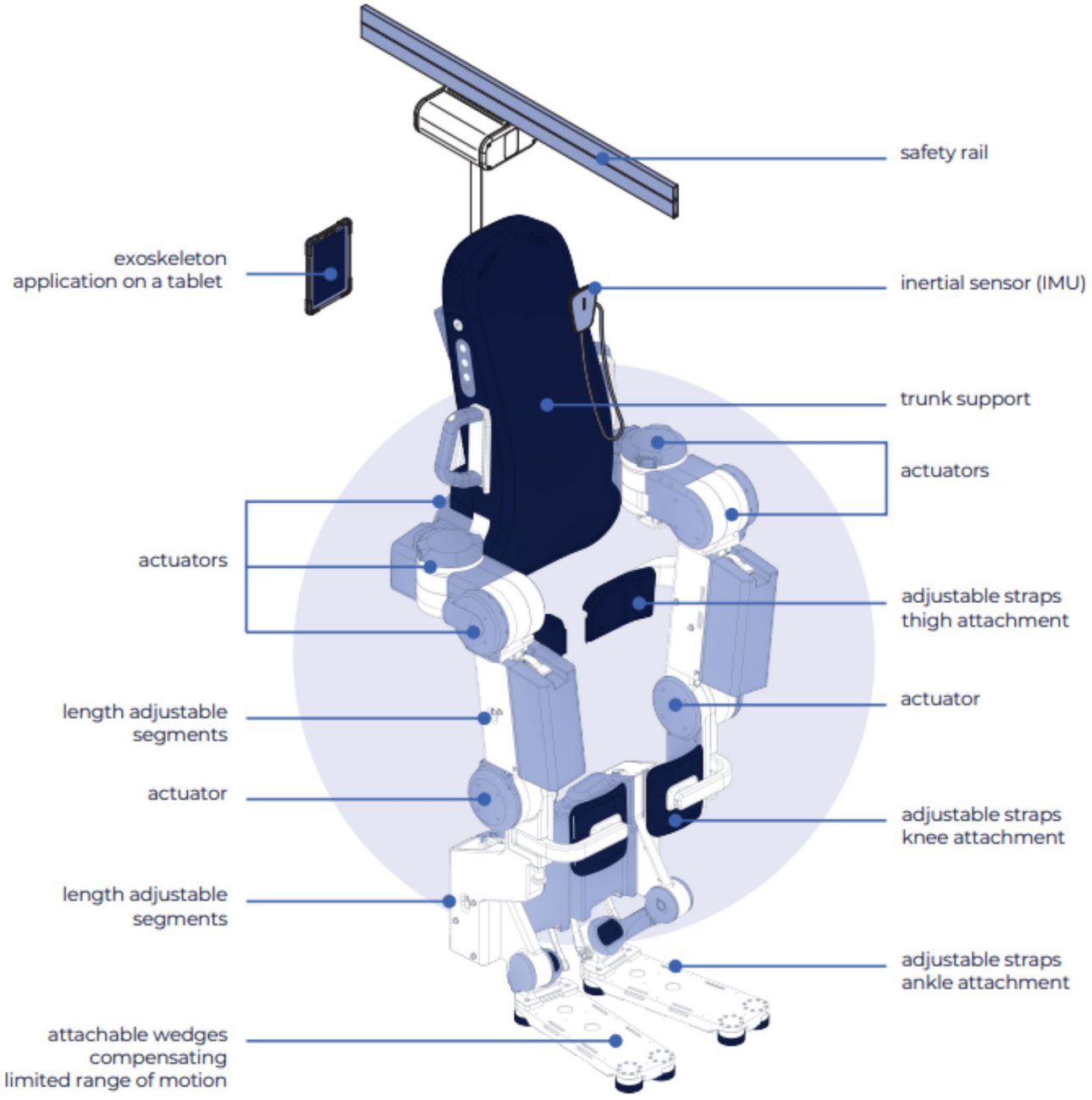

Fig. 1 Atalante exoskeleton

up to 40 min of exercises in the exoskeleton, the latter depending on the participant's abilities. The exoskeleton operators could choose between different types of gait patterns, with or without robotic assistance adjustment to gait, exercise mode, and working with the additional equipment.

Outcome measures

Primary outcome measure

The primary outcome measure was the safety of the exoskeleton, assessed through the occurrence of both serious (SAE) and non-serious Adverse Events (AEs), whether linked or not to the device and/or the study procedure, and including both anticipated and unanticipated events. The classification of the AEs was made according to internationally acknowledged standards [27, 28]. Pain and skin condition were monitored before and after each training session, directly related to adverse event reporting. An independent Clinical Event Committee (CEC) was constituted of three independent experts (academic physiatrist, psychologist and engineer). They assessed all relevant events to determine if they were related to the

device and/or study procedure, and decided whether to continue the study with or without a recommendation or to stop the study prematurely.

Secondary outcome measures

Secondary device-related outcomes included rehabilitation session data (gait performance) and a filmed usability test during the final training session (S05). In this test, participants' success was measured based on three tasks: walking straight for 5 m, performing side steps, and walking backward, all while avoiding lines on the floor. Each task was rated as Success (1) or Failure (0), with a total success score ranging from 0 to 3. The time taken to complete the tasks was also recorded. After the completion of five training sessions with the device, participants responded to a 7-point Likert type exoskeleton use questionnaire. This questionnaire was a modified version of an existing instrument [29] and included 48 statements organized into the following key domains: general satisfaction, overall satisfaction with the training program, learning, robotic device perception, training program perception, health benefits and risks, and overall general perception of RAGT (Additional file 1).

Clinical outcomes, assessed without the device, comprised gait speed during the 10 m Walk Test (10MWT) [30, 31], walking distance during 6-minute walk test (6MWT) [32], the walking capacity by Functional Ambulation Category [24], balance with Berg Balance Scale (BBS) [33], spasticity of adductor muscles, hamstrings, quadriceps, and triceps surae by modified Ashworth scale (m-Ashworth) [25], and depression and anxiety by Hospital Anxiety and Depression Scale (HADS) [34]. These outcomes were assessed before (Baseline) and after performing five rehabilitation sessions with the device (Post-training) with an overall participation duration of four weeks.

Statistical analysis

The primary outcome was analyzed by using a proportion calculation for each session with 95% confidence interval (Wilson method) [35], as well as the average AE rate per trial [36].

A sample of thirty participants allowed to estimate the AE rate within a distance between 12% and 18% (i.e. the width of the 95% confidence interval) of the supposed AE rate proportion, between 0% and 5%. To account for potential premature dropouts, we planned to include up to 50 participants. Descriptive statistics were expressed as mean ± standard deviation (SD). A gait speed of 0 m/s, and 6MWT distance of 0 m, was assigned for non-ambulatory participants having completed the Post-training visit. The changes in the clinical scores between Baseline and Post-training visit were assessed using the non-parametric Wilcoxon tests or sign test. Within group differences for rehabilitation sessions were analysed by Friedman's test, followed by post-hoc Nemenyi test, when applicable. All statistical analyses were performed using the XLSTAT (version 2022.1). Results were considered significant at $p < 0.05$.

Results

Participants

Between April 2021 and April 2022, 43 persons with a stroke were screened and forty were included in six rehabilitation centers, according to inclusion criteria. All study participants gave their informed, written consent to participate in line with ethical guidelines. Thirty-one subjects completed the trial, while nine discontinued their participation. The flow-chart of participants through the trial and reasons for drop-outs are displayed in Fig. 2. The baseline characteristics of included participants are available in Table 1.

Primary outcome measure: safety

Overall, the investigators reported 2 serious adverse events (SAEs) and 6 adverse events (AEs). The CEC examination of reported events concluded that no SAEs were linked to the use of the device or the study procedure but recommended adding vertigo to the non-inclusion criteria. The estimated per-session non-serious average AEs rate possibly linked to the device or the study procedure was of 2.5 ± 1.4%, which totals four AEs (knee pain [$n = 1$] and skin lacerations on the lower limbs [$n = 3$, knee and heels]) with severity categorized as negligible to minor. Aside from previously reported skin lacerations, only two subjects developed skin redness after training, located at the knees. No participants showed signs of bruising, burns, or pressure sores.

Pain monitoring before and after RAGT revealed that 88% of subjects did not experience any pain at either time. A total of 12% did experience pain, with 7% of subjects reporting pain both before and after the sessions, while 5% developed pain only after the sessions (detailed distribution available in Table 2). Pain, when present, was located in the shoulders, gluteal region, hips, knees, ankles, and lumbar spine, and was rated as low to moderate on average using a visual analogue scale. One event of knee pain was reported as an AE and led to study discontinuation.

A complete list of adverse events can be found in Table 3.

Secondary outcome measures

Hands-free Atalante exoskeleton training sessions

Data were available for 155 out of the 200 expected sessions across 40 patients. Sessions were managed by one operator who could be accompanied by additional personnel, including Adapted Physical Activity Monitors

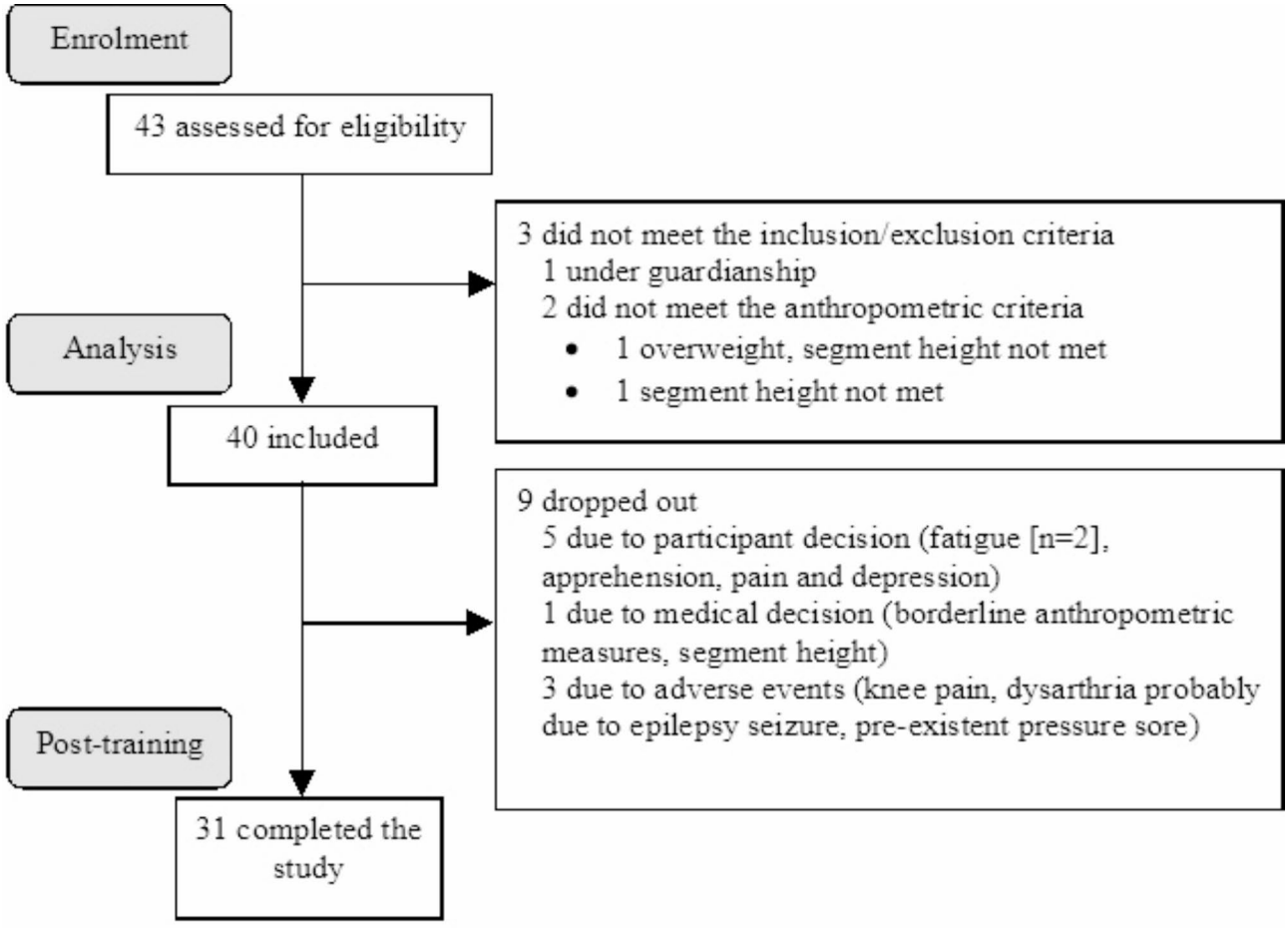

Fig. 2 Flowchart of the trial

Table 1 Baseline characteristics of included participants

N **= 40**	
Men/Women	23/17
Age (years), mean ± SD	62.0 ± 10
Time after stroke (months), mean ± SD	10.2 ± 12.1
Subjects in subacute phase (≥ two weeks and < six months) (*n* = 28)	2.4 ± 1.2
Subjects in chronic phase (≥ 6 months) (*n* = 12)	29.1 ± 50.7
FAC, median [IQR]	1 [0–2]

FAC - Functional Ambulation Category, IQR - interquartile range

Table 2 Pain monitoring before and after the training sessions

	S01 (*n* = 39)	**S02 (*n* = 38)**	**S03 (*n* = 35)**	**S04 (*n* = 32)**	**S05 (*n* = 29)**
No pain	82%	87%	88%	88%	94%
Pain present after the session	3%	8%	6%	6%	3%
Pain present before and after the session	15%	5%	6%	6%	3%

(APAM), psychomotor therapists, physical therapists, occupational therapists, and health professional trainees, depending on the session. Operators used passive gait in 98%, active gait in 25%, and exercise mode in 59% of the sessions, respectively. The average duration of the overall training sessions and verticalization time were 30.5 ± 12.2 min and 21.9 ± 8.6 min, respectively, with an average of 439 ± 274 steps performed. The overall training duration remained stable over five training sessions (Friedmans' test; training duration: p = ns), while verticalization duration and the number of steps increased with training (Friedmans' test; verticalization time, number of

Table 3 Adverse events in the study

Session / number of active subjects	Number of observed AEs / Subject number	Event description / AE classification	Treatment / Resolution	Severity level / causal link to the device / causal level to the study	CEC decision and recommendation (if applicable)/ Subjects study continuation status	Proportion (%) of occurrence per session (95%CI)
S01 ($n=40$)	1 / 01-PL-01	Knee pain / NSAE	Local treatment of the knee by icing / resolved without sequalae	Negligible / NA / Causal	Study continuation, follow up the subject's pain /Discontinued the study due to AE	5%[#] (1.4%; 16.5%)
	1 / 01-GJ-07	Vertigo, nausea, vomiting / Non-expected SAE	E.R. visit, received symptomatic treatment / resolved without sequalae	Minor / Not related / Not related	Study continuation, with addition of exclusion criteria*/ Continued the study following AE and later discontinued because of fatigue	
	1 / 03-MJ-03[#]	Pressure sore[#] / NSAE	Local treatment / resolved without sequalae	Minor / Not related / Not related	Study continuation without recommendation/ Discontinued the study due to AE	
S02 ($n=38$)	0	-	-	-	-	0% (0%; 9.2%)
S03 ($n=35$)	1 / 02-MD-07	Bilateral heels skin laceration / NSAE	No treatment required / resolved without sequalae	Minor / Possible / Possible	Study continuation without recommendation/ Continued the study	2.9% (0.5%; 14.5%)
S04 ($n=32$)	1 / 02-PA-05	Knee skin laceration / NSAE	No treatment required / resolved without sequalae	Negligible / Possible / Probable	Study continuation without recommendation/ Continued the study	9.4% (3.2%; 24.2%)
	1 / 06-DT-07	SARS-CoV-2 virus / NSAE	Isolation and appropriate treatment / resolved without sequalae	Negligible / Not related / Not related	Study continuation without recommendation	
		Dysarthria (due to possible epilepsy crises) / Non-expected SAE	Hospitalization / Resolution with cognitive sequelae	Serious / Not related / Not related	Study continuation without recommendation/ Discontinued the study due to AE	
S05 ($n=31$)	1 / 06-MM-03	Knee skin laceration / NSAE	No treatment required / resolved without sequalae	Minor / Possible / Possible	Study continuation without recommendation/ Continued the study	3,2% (0.6%; 16.2%)
Post training ($n=31$)	0	-	-	-	-	0% (0%; 11%)

AE = adverse event; NSAE = non-serious adverse event; SAE = serious adverse event; NA = not applicable; CEC = clinical evaluation committee; CI = confidence interval; MD = medical doctor

*Previous history of all-cause vertigo, uncontrolled at the time of inclusion

[#] The participant already presented a pressure sore before the first training session with the exoskeleton. Only adverse events occurred after the session are taken into account when calculating the percentage of occurrence of adverse events. Therefore, this event was not included in the computation of the adverse event proportion.

steps, $p < 0.05$, respectively). Post-hoc analysis (Nemenyi post-hoc test) revealed a significant increase in verticalization duration between the 1st and 3rd, and 1st and 4th session ($p < 0.05$), while steps number increased between 1st and 3rd, 4th, as well 5th training sessions ($p < 0.05$) (Fig. 3). The average duration of exercise mode was 3.3 ± 2.3 min. When active gait mode was employed, the average robotic assistance was 78.2 ± 17.0% for the left leg and 73.6 ± 29.4% for the right leg, with an average time of 13.9 ± 8.0 min spent in active mode.

Usability test and satisfaction with hands-free RAGT

Of the 23 available and validated videos of the Atalante exoskeleton remote usability test, 19 were successfully completed, representing 82.6% of the participants. Twenty-two of 23 individuals (95.7%) were successful in walking forward and sideway without touching the obstacle area line, while 19 of 23 (82.6%) were successful in performing backward walking. The overall score of the usability questionnaire was 2.7 ± 0.7 points, representing high usability performance. The average time required to perform the task was 3 ± 1.6 min. The exoskeleton use questionnaire indicated high general satisfaction, while other dimensions of the questionnaire indicated good satisfaction with the training program, good learnability, positive perception of the robotic device, neutral perception of health benefits, low perceived risks, and very high motivation to engage in RAGT (Table 4).

Clinical gait and balance disorders, anxiety and depression

These outcomes were analyzed for participants having completed the study ($n = 31$, mean ± SD: age of 61.0 ± 11.0 years, 19 men and 12 women, 10.2 ± 9.2 months post stroke). Gait speed (10MWT), walking distance (6MWT), and walking capacity (FAC) without the device from Baseline to Post-training increased significantly by 0.05 ± 0.08 m/s, 13 ± 18.8 m, and 0.6 ± 1.0 points, respectively (Wilcoxon signed rank test, $p < 0.05$, Table 5). BBS score significantly increased by 6.2 ± 8.1 points (Wilcoxon signed rank test, $p = 0.0001$, Table 5). Overall, 55%, 45%, 29% and 74% of subjects increased their gait speed, walked distance, ambulatory capacities, and balance, respectively. Spasticity of targeted muscles measured by m-Ashworth scale, as well as anxiety and depression measured by HADS, remained unchanged at Post-training, relative to Baseline ($p > 0.05$, respectively).

Discussion

The primary aim of this study was to evaluate the safety of the hands-free Atalante exoskeleton for rehabilitation of gait and balance disorders in people with post-stroke hemiplegia. The results indicate that Atalante can be safely used in this population, with high overall satisfaction and opinion about the RAGT. Clinical assessments suggested improvements in gait and balance disorders with positive evolution of walking capacity, walked distance, gait speed, and balance, following RAGT combined with conventional rehabilitation.

Our trial had no SAEs linked to the study or procedure. When looking at non-serious AEs, four were judged as possibly linked to the device and/or study procedure (knee pain and 3 cases of skin lacerations). These events were previously reported in the literature when using robotic devices and are described as mild and temporary [11, 13, 37]. A recent exploration of hazardous situations when using exoskeletons points to the role of misalignments in 60% of skin damages, while mechanical issues cause 73.8% of observed damages [38]. Another possible explanation for the observed AEs related to the study and/or study procedure is use error. According to the FDA, the overall rate of use errors could be prevented by training and practice with the device and improving usability testing [38]. With 43% of operators having less than 6 months and 57% more than 6 months of experience post-device certification, device-related AEs remained low in the present study, suggesting that effective operator training played a key role in mitigating risks, as supported by other studies [38, 39]. We observed nine dropouts, five of which were based on the participant's decision (fatigue [$n = 2$], apprehension [$n = 1$], depression [$n = 1$] and pain [$n = 1$]), one based on medical decision (borderline anthropometric measures), and three because of AEs (SAEs: dysarthria, AEs: knee pain, pre-existent pressure sore). The population included in our trial had severe ambulatory deficits, which could have affected participants' physical capacities and caused exacerbated fatigue, known to be frequent in post-stroke individuals, as is the case of anxiety, depression, and pain [40, 41]. Overall, our dropout rate of 22.5% percent is similar to what has been previously reported in robotic gait training literature [11]. The use of exoskeletons in stroke rehabilitation has previously been reported both in pilot studies and in randomized controlled trials in acute, subacute, and chronic stages with good safety and performance results as well as promising results in gait and balance improvements [42].

Although the primary objective of this study was to assess safety, secondary clinical outcomes explored the effects of RAGT, combined with conventional rehabilitation, on gait, balance, spasticity, anxiety, and depression. The results show favorable changes in gait and balance that would motivate a future clinical efficacy trial. These observations may be related intensive, task-oriented repetitive training that mirrors natural human gait in an individually tailored environment provided by the exoskeleton device [42–44].

RAGT was suggested effective in improving FAC score regardless of post-stroke phases, and initial walking

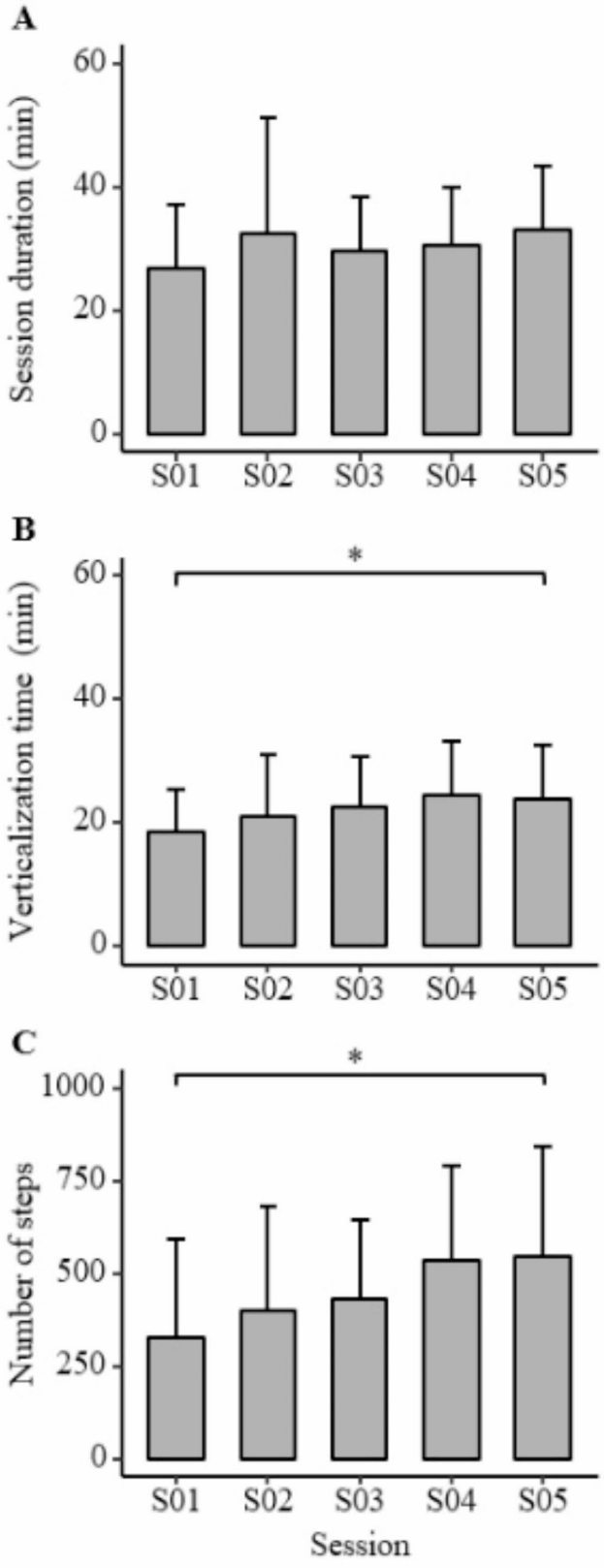

Fig. 3 Training session duration (**A**), verticalization time (**B**) and number of steps (**C**) in post-stroke subjects. The graphs represent the mean and standard deviation, from top to bottom, in training session duration (**A**), verticalization time (**B**) and number of steps (**C**) after the 1st (S01), 2nd (S02), 3rd (S03), 4th (S04) and 5th (S05) training sessions. * $p < 0.05$ Friedmans' test

Table 4 Exoskeleton use questionnaire

	Negative perception (%)	Neutral perception (%)	Positive perception (%)
General satisfaction	2 ± 2.3	2 ± 2.3	90 ± 0
Robotic gait device	14 ± 9.6	5 ± 4.3	74 ± 12.5
Learning	25 ± 20.3	6 ± 2.6	62 ± 21.8
Training program	19 ± 14.2	11 ± 6.4	66 ± 13.9
Perceived effects on health	2 ± 3.8	62 ± 12.3	26 ± 12.9
Perceived risks	19 ± 7.5	6 ± 2.9	65 ± 8.6
Overall general perception	6 ± 4.6	2 ± 2.3	82 ± 6.8

Data are presented as mean and standard deviation (SD). Due to missing responses, category percentages may not sum to 100%. A total of 91% ± 2% of the data were available and analyzed, while 9% ± 2% were missing. Percentages for positive, neutral, and negative perceptions were based on Likert scale responses: 5-6-7 for positive, 4 for neutral, and 1-2-3 for negative. For dimensions where responses did not evolve in the same direction, scores were adjusted to ensure consistency

Table 5 Gait and balance related clinical outcomes

N = 31	Baseline	Post-training	*P*-value
10MWT (m/s)	0.12 ± 0.18	0.17 ± 0.18	0.001*
6MWT (m)	32.5 ± 44.3	45.5 ± 47.9	0.002*
FAC	1 ± 1.1	1.6 ± 1.4	0.001*
BBS	18.7 ± 13.3	25 ± 15.8	0.0001*

10MWT = 10-meter walk test; 6MWT = 6-minute walk test; FAC - Functional Ambulation Category; BBS - Berg Balance Scale. The data represent the mean and standard deviation. *p 0.05 for within-group changes between Baseline and Post-training

status [44]. In our study, 42.5% of included participants were non-ambulatory, and 25% needed continuous manual assistance while walking. Hence, our preliminary results would suggest that hands-free RAGT is beneficial in non-ambulatory or minimally ambulatory population.

Gait speed can be significantly improved with RAGT in similar populations [45, 46], and RAGT leads to an increase in the number of steps in a day [45]. A recent meta-analysis showed that gait speed is sensitive to small changes after intervention [44], as observed in our study (+ 0.05 ± 0.08 m/s). The observed change would correspond to a small meaningful change estimate defined between 0.04 and 0.06 m/s [47], while minimal clinically important difference (MCID) is set at 0.16 m/s [48]. Walking speed, in particular, is a crucial indicator of post-stroke walking independence, encompassing activities of daily living and community participation [49]. In summary, walking capacity may serve as a predictor for community-dwelling activities [49].

Our study suggested a positive change in walked distance (+ 11.6 ± 18 m), although below the MCID of 44 m for people in subacute phase post-stroke with gait speed < 0.40 m/s [50]. The effects of RAGT on walked distance (6MWT) were analyzed in several metanalysis, showing mostly limited effectiveness of intervention on this variable [11, 44, 51]. Some pre-stroke factors, including low levels of activity before the stroke and older age, are predictive of diminished walking activity following a stroke, and should be taken into account in rehabilitation [52].

Our study implies improvement in balance function, reaching a minimal detectable threshold of + 6 points on the Berg Balance Scale [53]. Balance improvements were also reported in a recent meta-analysis after RAGT [22, 51]. This result is important, since balance plays a fundamental role not only in walking but also in numerous activities of daily life, and is commonly assessed when evaluating the risk of falls [22]. Additionally, a recent meta-analysis points to the role of trunk balance on walking ability [54]. The data from the literature suggest that RAGT may be effective in treating gait and balance dysfunction in post-stroke participants, particularly when combined with conventional rehabilitation [21, 22, 51].

The present study involved only five sessions of RAGT combined with conventional rehabilitation. The components, duration, and intensity of the conventional physical therapy received by participants were not recorded. Therefore, the effects of RAGT on gait and balance in this study should be interpreted with caution, as the primary focus was on safety rather than efficacy.

Some studies do not recommend the use of RAGT but 'this recommendation may not apply to non-ambulatory individuals' undergoing stroke rehabilitation [55]. Indeed, it has been suggested that non-ambulatory people could benefit more from robotic-assisted gait training [11].

When discussing motor and functional improvements, it is important to consider post-stroke phases. Our study sample included 70% subacute and 30% chronic post-stroke participants. This heterogeneity is crucial to address because spontaneous motor recovery occurs in the early stages post-stroke [6, 56], although functional improvements can still be observed even in the chronic stages of post-stroke recovery [57]. Therefore, there is still a possibility that the improvements observed in our study are due to spontaneous recovery, since the majority of included participants were in a subacute phase post-stroke.

Overall, these results support the importance of rehabilitation in post-stroke subjects and the positive usability of hands-free RAGT, combined with conventional rehabilitation in clinical practice.

Limitations

As this was a safety study, our trial is subject to a number of limitations, including the absence of a control group and a blinded assessor, as well as a small and heterogeneous sample size. Further, larger controlled studies are essential to examine the effectiveness of hands-free robotic-assisted gait training, with increased training frequency and intensity, in a homogenous group of people post-stroke.

Conclusions

This safety study shows that RAGT with the hands-free Atalante exoskeleton is safe and well-received for addressing gait and balance disorders in post-stroke individuals when combined with conventional rehabilitation. Future studies should further explore the clinical efficacy of RAGT in treating gait and balance disorders in post-stroke individuals.

Abbreviations

APAM	Adapted Physical Activity Monitors
FAC	Functional Ambulation Category
AEs	Adverse events
CEC	Clinical evaluation committee
10MWT	10-meter walk test
6MWT	6-minute walk test
BBS	Berg Balance Scale
SAE	Serious adverse events
NSAE	Non serious adverse event
CVA	Cerebro-vascular accident
RAGT	Robotic-assisted gait training
ANSM	Agence Nationale de Sécurité du Médicament et des produits de Santé
AFMPS	Agence Fédérale des Médicaments et des Produits de Santé
CNER	Comité National d'Ethique de Recherche
FDA	Food and Drug Administration
IMU	Inertial sensor
m-Ashworth	Modified Ashworth scale
SD	Standard deviation
IQR	Interquartile range
HADS	Hospital Anxiety and Depression Scale
MCID	Minimal clinically important difference
CI	Confidence interval
MD	Medical doctor
PT	Physical therapist
Pt	Psychomotor therapist
Ph.D	Doctor of philosophy

Supplementary Information

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Supplementary Material 1

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Author contributions

T.L, JG.P, S.T, T.D and Ja.K, were responsible for the conception and design of the study. T.L, JG.P, S.T, T.D, Ja.K, F.J, B.P, S.D, C.C, S.SP, and J.K performed clinical investigations and acquired clinical data. C.C, S.P, S.D, B.P, J.K performed training sessions. The data were analysed by VP. Writing original draft, review and editing: T.L, D.N. S.D, JG.P, C.C, T.D, J.K, B.P, V.P, S.SP, F.J, S.T and Ja.K. All authors reviewed the manuscript and give final approval of the version to be submitted. The study was supervised by Ja.K. Project administration: T.L, JG.P, T.D. S.T, and Ja.K.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was performed in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines and was approved by the local ethics committee (CPP Ouest-IV, CE Hospitalo-Facultaire Saint Luc, and CNER, registered under ID RCB: 2020-A02437-32, B403202000079, and 202010/03, respectively). It was authorized by the French, Belgium and Luxembourg competent authorities (ANSM, AFMPS, and CNER). The study was promoted by the Wandercraft (CIP002) and registered in a public trial registry (Trial Registration: NCT04694001 ClinicalTrials.gov). All participants had agreed to participate and provided written informed consent.

Consent for publication

Not applicable.

Competing interests

Prof Thierry LEJEUNE, MD, PhD*; Stéphanie DEHEM, PhD; Jean-Gabriel PREVINAIRE, MD; Céline CUENOT, Pt; Jerome KAPS, PT; Bérénice PAUL, PT; Sergi SANZ PEREZ, PT, MSc; Fanny JUHEL, MD; Soultana TATSIDOU, MD, Jacques KERDRAON, MD have no conflict to declare. Vincent PÉAN, PhD received compensation by Wandercraft to perform the independent statistical analysis of the data. Dijana NUIC, PhD is employed by Wandercraft. Thierry DEBUGNE, MD is a speaker for Coloplast-AbbVie.

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