Supplementary Material

Title: A Phase IV, Randomized, Double-Blind, Crossover Study to Compare the Clinical Safety and Efficacy of AbobotulinumtoxinA and OnabotulinumtoxinA in Adult Upper Limb Spasticity

Authors:

Alberto Esquenazi (Corresponding author)

Department of Physical Medicine and Rehabilitation, Jefferson Moss-Magee Rehabilitation, 60 Township Line Rd., Elkins Park, PA 19027, USA

e-mail: alberto.esquenazi@jefferson.edu

Theodore H. Wein

McGill University Health Centre, 1650 Avenue Cedar, Montréal, QC H3G 1A4, Canada

Monica Verduzco-Gutierrez

Long School of Medicine at the University of Texas at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78229, USA

Ziyad Ayyoub

David Geffen School of Medicine, University of California, 10833 Le Conte Ave, Los Angeles, CA 90095, USA

Simon Page · Sarah Harding

Ipsen, 5th Floor The Point, 37 North Wharf Rd, London W2 1AF, UK

Pascal Maisonobe · Mathieu Beneteau

Ipsen, 70 Rue Balard, 75015 Paris, France

Atul Patel

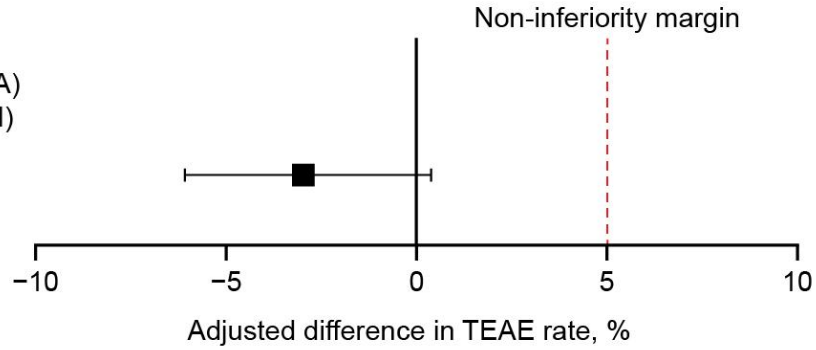
Kansas City Bone & Joint Clinic, 10701 Nall Ave #200, Overland Park, KS 66211, USA

On behalf of the DIRECTION study group*

*Canada: Keith Sequeira, Theodore H. Wein, Masoud Sangani. France: Pierre Blanc, Hélène Cassoudesalle, Emmanuel Amauger, Philippe Gallien, Dominic Pérennou, Jacques Luauté, Ido Ghassan, David Gasq, Anne-Laure Ferrapie, Marie Ève Isner-Horobeti, Raphaël Gross, Simon Butet, Tanguy Le Corre, Florence Angioni, Thibaud Honore. USA: Alberto Esquenazi, Atul Patel, Steven Edgley, Joan Stilling, David Bowers, Kore Liow, David Charles, Vivian Roy, Richard Zorowitz, Heidi Fusco, Karin Goodfriend, Peter Hedera, Khashayar Dashtipour, Ziyad Ayyoub, Ahmet Arac, James Stevens, Joseph Burris, Periminder Bhatia, Daniel Truong, Francois Bethoux, Fatma Gul, Peter McAllister, Edward Dabrowski, Scott Sherman, Anne Hatch, Tuan Vu, Michael Wainberg, Monica Verduzco-Gutierrez, Richard Weiss, Xiaohua Zhou, Johnathan Ho, Mayer Joshua Hasbani, S. Byron Milton III, Yuxi Chen, Wissam Deeb, Robert Balsiger, Brian Copeland, Jonathan Vandenberg, Asare Christian, Natasha Romanoski, Michael Munin, Nirav Patel, Mark Linsenmeyer, Cindy Beth Ivanhoe, Virgilio Evidente, Angeli Mayadev, Bharathy Sundaram, Patricio Espinosa, Warren Spinner, Marissa McCarthy, Michael Saulino, Edwardo Ramos, Dabrowski Edward, Harmony Sierens.

Fig. S1. *S*ensitivity analysis of primary endpoint: forest plot of difference of adjusted TEAE rates from injection to Week 12 (Safety Set)

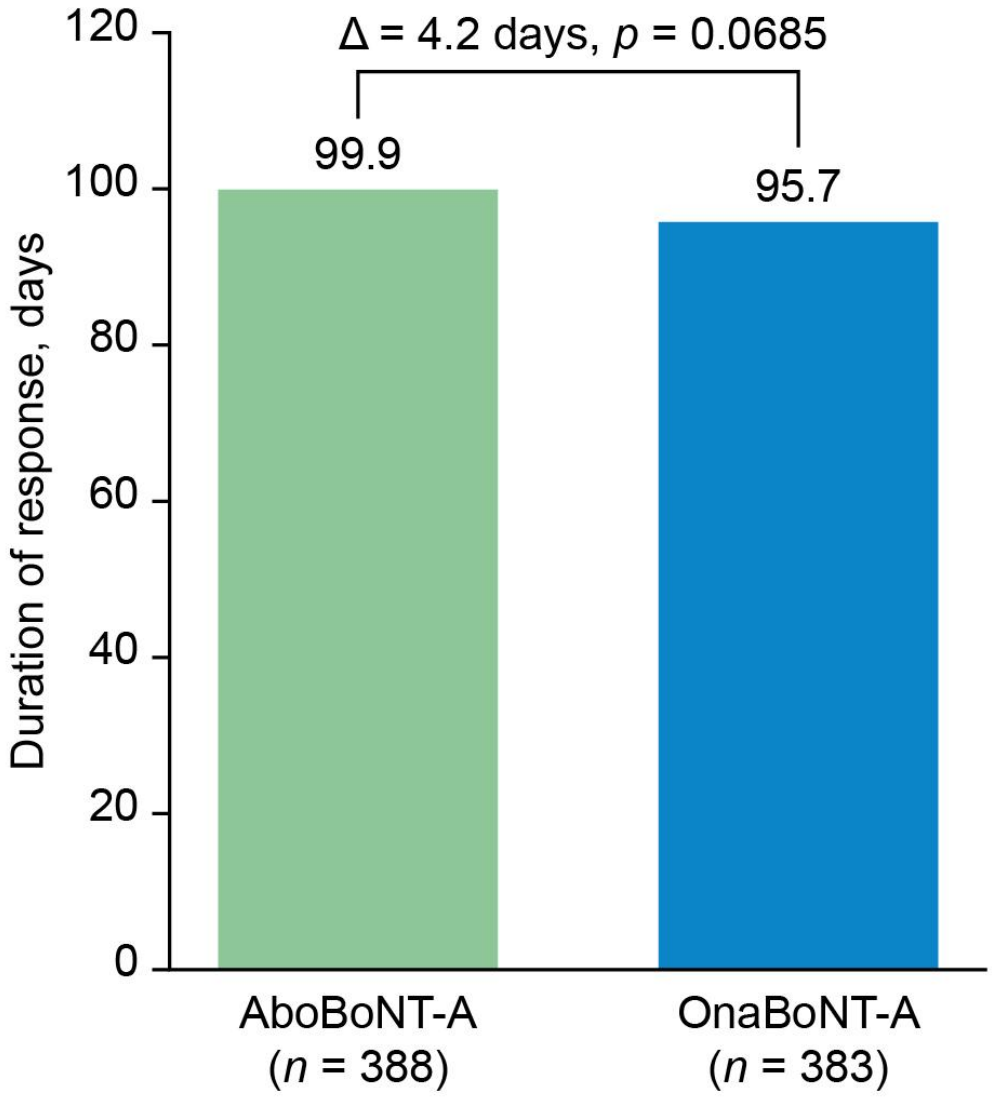
Difference of treatment	Number of patients	Adjusted difference (aboBoNT-A – onaBoNT-A) in TEAE rate (%, 80% CI)
AboBoNT-A – onaBoNT-A	456	−2.9 (−6.1, 0.4)



Patients were classified according to the treatment actually received. Participants treated with aboBoNT-A → aboBoNT-A and onaBoNT-A → onaBoNT-A were excluded. For participants with no safety information and who had not attended any visit in a cycle, the affected cycle of these participants was also excluded.

aboBoNT-A abobotulinumtoxinA, *CI* confidence interval, *onaBoNT-A* onabotulinumtoxinA, *TEAE* treatment-emergent adverse event.

Fig. S2. Post hoc analysis of the secondary endpoint (duration of response based on time to symptom re-emergence; FAS excluding PTMG-related protocol deviations)



AboBoNT-A abobotulinumtoxinA, *FAS* full analysis set, *OnaBoNT-A* onabotulinumtoxinA, *PTMG* primary target muscle group.

Table S1. List of Independent Ethics Committees or Institutional Review Boards

Country Site number Enrolled (Y/N)	Ethics Committee	Approval number
Canada 124002 (Y)	Western University Health Sciences Research Ethics Board (HSRED) Room 5150, Support Services Building, 1393 Western Road London, Ontario, Canada, N6G 1G9	Project ID: 119440
Canada 124003 (Y)	Vancouver Island Health Authority - Clinical Research Ethics Board Queen Alexandra Centre, Main Building, Room 205 - 2400 Arbutus Road, Victoria BC, V8N 1V7	Study Number: C2021-112
Canada 124007 (Y)	"Veritas Independent Review Board McGill University Health Center REB" "3551 St-Charles Blvd, Suite 501, Kirkland, Quebec, H9H 3C4 3801 University Street #686, Montreal, QC, H3A 2B4"	Study ID: (CRU) / 2022-8166
Canada 124011 (Y)	Horizon Health Network Research Ethics Board Saint John Regional Hospital, 2nd floor, 400 University Ave, Sain John, NB, E2L 4L2	RS; 2022-3089
FRA 250001 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250002 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250003 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250004 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250005 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250006 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250007 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250008 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250009 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250010 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250012 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250013 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250014 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250015 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32

FRA 250016 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250017 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250018 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
FRA 250019 (Y)	CHU de Nîmes - Site Serre Cavalier, Place du Pr. Robert Debré, 30029 Nîmes Cedex 9	(IEC/IRB) 2021.07.08 cinq_ 21.01029.000014 EudraCT - 2021-000161-32
USA 840001 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00158115
USA 840002 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00155045
USA 840003 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00153306
USA 840005 (Y)	University of Utah IRB 75 2000 E., Salt Lake City, Utah, USA, 84112	IRB_00143649
USA 840007 (Y)	BRANY Institutional Review Board 1981 Marcus Avenue, Suite 210, Lake Success, NY 11042	WRG Protocol Number: 22-08025138
USA 840008 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00159252
USA 840009 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00167641
USA 840010 (Y)	Human Research Protections Program 3319 West End Ave, Suite 600, Nashville, TN 37203	IRB #220563
USA 840011 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00167266
USA 840012 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00154687
USA 840013 (Y)	NYU Langone Health IRB One Park Avenue, 6th Floor, New York, NY 10016	Study ID: i21-01052_MOD06
USA 840014 (Y)	Medical College of Wisconsin 8701 Watertown Plank Rd, MACC 3rd, Milwaukee, WI 53226	Study ID: PRO00043181
USA 840015 (Y)	University of Louisville Institutional Review Board 300 E. Market Street, Suite 380, Louisville, KY 40202	Study Ref: 736502 IRB #: 21.0450
USA 840016 (Y)	University of Louisville Institutional Review Board 300 E. Market Street, Suite 380, Louisville, KY 40202	IRB# 5220010
USA 840017 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00162377
USA 840018 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00169362
USA 840019 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00158543
USA 840020	Advarra	Protocol Number: (Pro00053962) Approval #: SSU00165868

(Y)	6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	
USA 840021 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00161109
USA 840022 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00158143
USA 840026 (Y)	Cleveland Clinic Institutional Review Board 9500 Euclid Ave, OS-1, Cleveland, OH 44195	IRB 20230808 Study ID: 20230808
USA 840027 (Y)	WCG IRB 1019 39th Ave., SE, Suite 120, Puyallup, WA 98374	Study ID: STU-2021-0659
USA 840028 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00161022
USA 840029 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00158073
USA 840030 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00171368
USA 840031 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00189508
USA 840032 (Y)	WCG IRB 1019 39th Ave., SE, Suite 120, Puyallup ,WA 98374	Study Number: 1327043 20220468
USA 840033 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00171149
USA 840034 (Y)	Mayo Clinic Instiutional Review Board Mayo Clinic 200 First St. SW Rochester, MN 55905"	IRB#: 21-008454
USA 840035 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00197609
USA 840036 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00167641
USA 840037 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00202076
USA 840038 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00176644
USA 840039 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00196114
USA 840040 (Y)	BRANY (Biomedical Research Alliance of New York) 1981 Marcus Avenue, Suite 210, Lake Success, NY 11042	IRB File # 21-02-209-05 Event ID: #194940
USA 840041 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00181852
USA 840043 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00185484
USA 840045 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00183200
USA 840046	BRANY Institutional Review Board	IRB File # 21-02-209-01 Event ID: # 187265

(Y)	1981 Marcus Avenue, Suite 210, Lake Success, NY 11042	
USA 840048 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00165585
USA 840050 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00204283
USA 840051 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00176471
USA 840052 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00170008
USA 840055 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00177033
USA 840057 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00218500
USA 840058 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00175847
USA 840059 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00171852
USA 840060 (Y)	The Human Research Protection Program 101 Technology Center, Suite 205, University Park, PA 16802, USA	Study ID: STUDY00021422
USA 840061 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00196382
USA 840063 (Y)	WCG IRB 1019 39th Ave., SE, Suite 120, Puyallup, WA 98374	Study Number: 1331756 IRB Tracking Number: 20220468
USA 840065 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00182437
USA 840066 (Y)	Committee for the Protection of Human Subject 6410 Fannin Street, Suite 1100, Houston, TX 77030, USA	Reference Number: 244858
USA 840067 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00168221
USA 840071 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00176887
USA 840072 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00181396
USA 840073 (Y)	WCG IRB 1019 39th Ave SE Suite 120, Puyallup, WA 98374, USA	Protocol Number: (Pro00053962) Approval #: SSU00186653
USA 840074 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00187429
USA 840075 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00186653
USA 840076 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00196453
USA 840077 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00206766

USA 840078 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00224523
USA 840079 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00225072
USA 840080 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00224361
USA 840081 (Y)	Advarra 6100 Merriweather Drive, Suite 600, Columbia, Maryland 21044	Protocol Number: (Pro00053962) Approval #: SSU00224787

The study was approved by Advarra as the central ethics committee, with additional approvals obtained from local ethics committees or institutional review boards at participating sites.

Table S2. Summary of related TEAEs from injection to Week 12 and the whole cycle duration by treatment (Safety Set)

TEAE	Injection to Week 12		Whole cycle duration	
	AboBoNT-A (*n* = 427)	OnaBoNT-A (*n* = 424)	AboBoNT-A (*n* = 427)	OnaBoNT-A (*n* = 424)
	n (%); E	*n* (%); E	*n* (%); E	*n* (%); E
Any related TEAE[a]	15 (3.5); 17	15 (3.5); 17	15 (3.5); 17	16 (3.8); 18
Muscular weakness	3 (0.7); 3	2 (0.5); 2	3 (0.7); 3	2 (0.5); 2
Pain in extremity	1 (0.2); 1	2 (0.5); 2	1 (0.2); 1	2 (0.5); 2
Arthralgia	1 (0.2); 1	1 (0.2); 1	1 (0.2); 1	1 (0.2); 1
Joint range of motion decreased	1 (0.2); 1	0	1 (0.2); 1	0
Finger deformity	0	1 (0.2); 1	0	1 (0.2); 1
Myalgia	0	0	0	1 (0.2); 1
Headache	3 (0.7); 3	1 (0.2); 1	3 (0.7); 3	1 (0.2); 1
Hypoaesthesia	2 (0.5); 2	1 (0.2); 1	2 (0.5); 2	1 (0.2); 1
Dystonia	0	1 (0.2); 1	0	1 (0.2); 1
Asthenia	2 (0.5); 2	0	2 (0.5); 2	0
Fatigue	1 (0.2); 1	1 (0.2); 1	1 (0.2); 1	1 (0.2); 1

Injection site pruritus	1 (0.2); 1	0	1 (0.2); 1	0
Injection site pain	0	3 (0.7); 3	0	3 (0.7); 3
Injection site paraesthesia	0	1 (0.2); 1	0	1 (0.2); 1
Injection site rash	0	1 (0.2); 1	0	1 (0.2); 1
Nausea	2 (0.5); 2	0	2 (0.5); 2	0
Diarrhea	0	1 (0.2); 1	0	1 (0.2); 1
Ecchymosis	0	1 (0.2); 1	0	1 (0.2); 1

A TEAE is defined for each treatment cycle as any adverse event that occurs during the cycle if it was not present prior to treatment injection, or if it was present prior to treatment injection but the intensity increased during the cycle. A TEAE was considered related to study treatment or procedure if the TEAE was categorized as definitely, probably, likely or possibly related by the investigator. If the causality was missing, it was considered related to study treatment.

TEAE treatment-emergent adverse event.

Table S3. Summary of TEAEs for the whole cycle duration by treatment (SS)

Event type	**AboBoNT-A (*n* = 427) *n* (%); E**	**OnaBoNT-A (*n* = 424) *n* (%); E**
Any TEAE[a]	96 (22.5); 158	107 (25.2); 194
Severe TEAE	12 (2.8); 14	15 (3.5); 22
Related TEAE[b]	15 (3.5); 17	16 (3.8); 18
Serious TEAE	21 (4.9); 30	20 (4.7); 31
Fatal TEAE[c]	1 (0.2); 1	1 (0.2); 1
TEAE leading to study discontinuation	2 (0.5); 2	2 (0.5); 4
AESIs[d]	7 (1.6); 7	5 (1.2); 6
Of hypersensitivity[e]	5 (1.2); 5	5 (1.2); 6
Of remote spread[f]	2 (0.5); 2	0

[a] A TEAE is defined for each treatment cycle as any adverse event that occurs during the cycle if it was not present prior to treatment injection, or if it was present prior to treatment injection but the intensity increased during the cycle.

[b] A TEAE was considered related to study treatment or procedure if the TEAE was categorized as definitely, probably, likely, or possibly related by the investigator. If the causality was missing, it was considered related to study treatment.

[c] TEAE not related to treatment.

[d] All AEs were monitored by the sponsor to determine if they met the criteria of AESIs.

[e] Hypersensitivity based on standardized Medical Dictionary for Regulatory Activities query.

[f] AESIs of remote spread were included if adjudicated as potential remote spread: one incident of vision blurred and one incident of muscular weakness (one patient each).

AboBoNT-A abobotulinumtoxinA, *AESI* adverse event of special interest, *E* number of events, *OnaBoNT-A* onabotulinumtoxinA, *SS* safety set, *TEAE* treatment-emergent adverse event.

Table S4. Summary of TEAEs from injection to Week 12 by treatment (PPS-Safety)

Event type	AboBoNT-A (*n* = 358) *n* (%); E	OnaBoNT-A (*n* = 358) *n* (%); E
Any TEAE[a]	73 (20.4); 116	82 (22.9); 133
Severe TEAE	6 (1.7); 6	9 (2.5); 12
Related TEAE[b]	14 (3.9); 16	14 (3.9); 16
Serious TEAE	12 (3.4); 18	14 (3.9); 20
TEAE leading to study discontinuation	0	1 (0.3); 1
AESIs[c]	4 (1.1); 4	3 (0.8); 3
Of hypersensitivity[d]	3 (0.8); 3	3 (0.8); 3
Of remote spread[e]	1 (0.3); 1	0

[a] A TEAE is defined for each treatment cycle as any adverse event that occurs during the cycle if it was not present prior to treatment injection, or if it was present prior to treatment injection but the intensity increased during the cycle.

[b] A TEAE was considered related to study treatment or procedure if the TEAE was categorized as definitely, probably, likely, or possibly related by the investigator. If the causality was missing, it was considered related to study treatment

[c] All AEs were monitored by the sponsor to determine if they met the criteria of AESIs.

[d] Hypersensitivity based on standardized Medical Dictionary for Regulatory Activities query.

[e] AESIs of remote spread were included if adjudicated as potential remote spread.

AboBoNT-A abobotulinumtoxinA, *AESI* adverse event of special interest, *E* number of events, *OnaBoNT-A* onabotulinumtoxinA, *PPS-Safety* per-protocol safety set, *TEAE* treatment-emergent adverse event.

Table S5. Health and Well-Being (SF-12) by Treatment (FAS)

Total score	**AboBoNT-A (*n* = 428)**		**OnaBoNT-A (*n* = 424)**	
	Result	**Change from baseline**	**Result**	**Change from baseline**
Baseline				
Physical Functioning (NBS)				
n	416		413	
Mean (SD)	34.58 (9.44)		34.48 (9.29)	
95% CI	33.68, 35.49		33.58, 35.38	
Role Physical (NBS)				
n	418		415	
Mean (SD)	36.14 (9.49)		36.17 (9.5)	
95% CI	35.23, 37.05		35.25, 37.09	
Bodily Pain (NBS)				
n	418		415	
Mean (SD)	46.07 (11.54)		45.60 (11.8)	
95% CI	44.96, 47.18		44.46, 46.74	
General Health (NBS)				
n	418		415	
Mean (SD)	47.09 (10.15)		47.13 (10.27)	
95% CI	46.12, 48.07		46.14, 48.12	

Vitality (NBS)		
n	418	415
Mean (SD)	50.04 (9.72)	50.2 (9.8)
95% CI	49.11, 50.98	49.25, 51.15
Social Functioning (NBS)		
n	418	415
Mean (SD)	44.06 (11.59)	44.18 (11.68)
95% CI	42.95, 45.18	43.05, 45.3
Role Emotional (NBS)		
n	418	415
Mean (SD)	41.1 (14.1)	41.06 (14.25)
95% CI	39.74, 42.45	39.69, 42.44
Mental Health (NBS)		
n	418	415
Mean (SD)	50.67 (9.36)	50.68 (9.56)
95% CI	49.77, 51.57	49.75, 51.6
Utility Index Score		
n	416	413
Mean (SD)	0.67 (0.12)	0.67 (0.12)
95% CI	0.66, 0.68	0.66, 0.68

Week 12

Physical Functioning (NBS)				
n	377	367	377	366
Mean (SD)	36.05 (9.7)	1.14 (9.1)	35.26 (9.5)	0.47 (9.28)
95% CI	35.07, 37.03	0.21, 2.08	34.29, 36.22	−0.48, 1.43
Role Physical (NBS)				
n	378	370	377	368
Mean (SD)	38.4 (9.5)	1.89 (9.65)	38.13 (9.91)	1.55 (10.17)
95% CI	37.44, 39.36	0.91, 2.88	37.12, 39.13	0.51, 2.59
Bodily Pain (NBS)				
n	375	367	376	367
Mean (SD)	47.81 (10.6)	1.29 (11.23)	46.67 (10.97)	0.83 (11.23)
95% CI	46.73, 48.88	0.14, 2.45	45.56, 47.78	−0.32, 1.98
General Health (NBS)				
n	378	370	376	367
Mean (SD)	48.33 (9.46)	1.05 (9.55)	47.61 (9.83)	0.38 (9.71)
95% CI	47.38, 49.29	0.07, 2.02	46.61, 48.61	−0.62, 1.38
Vitality (NBS)				
n	378	370	377	368
Mean (SD)	51.46 (10.51)	1.19 (9.95)	50.03 (10.29)	−0.10 (10.07)
95% CI	50.4, 52.52	0.18, 2.21	48.98, 51.07	−1.13, 0.93
Social Functioning (NBS)				

n	378	370	377	368
Mean (SD)	44.74 (11.97)	0.08 (12.26)	45.23 (11.52)	0.73 (11.14)
95% CI	43.53, 45.95	−1.18, 1.33	44.06, 46.39	−0.41, 1.87
Role Emotional (NBS)				
n	378	370	377	368
Mean (SD)	41.27 (13.97)	−0.23 (14.3)	41.20 (14.15)	−0.08 (14.79)
95% CI	39.86, 42.69	−1.69, 1.23	39.77, 42.64	−1.59, 1.44
Mental Health (NBS)				
n	378	370	377	368
Mean (SD)	51.2 (9.53)	0.35 (8.54)	50.46 (9.59)	−0.15 (9.02)
95% CI	50.23, 52.16	−0.53, 1.22	49.49, 51.43	−1.07, 0.77
Utility Index Score				
n	373	363	376	365
Mean (SD)	0.69 (0.13)	0.01 (0.1)	0.68 (0.12)	0.0 (0.1)
95% CI	0.68, 0.7	0.00, 0.02	0.67, 0.69	−0.01, 0.01

AboBoNT-A abobotulinumtoxinA, *CI* confidence interval, *FAS* full analysis set, *NBS* norm-based score, *OnaBoNT-A* onabotulinumtoxinA, *SD* standard deviation, *SF-12* 12-Item Short Form Health Survey.

Table S6. SQoL-6D by Treatment (FAS)

Total score	**AboBoNT-A (*n* = 428)**		**OnaBoNT-A (*n* = 424)**	
	Result	**Change from baseline**	**Result**	**Change from baseline**
Baseline				
n	424		421	
Mean (SD)	49.82 (17.51)		49.93 (17.69)	
95% CI of Mean	48.14, 51.49		48.24, 51.63	
Median	50.00		50.00	
Q1, Q3	37.50, 62.50		37.50, 62.50	
Min, Max	0.0, 91.7		0.0, 91.7	
Week 4				
n	404	400	402	399
Mean (SD)	59.53 (17.35)	9.69 (16.18)	60.57 (17.61)	10.38 (16.15)
95% CI of Mean	57.83, 61.23	8.10, 11.28	58.85, 62.30	8.79, 11.97
Median	60.42	8.33	62.50	8.33
Q1, Q3	50.00, 70.83	−4.17, 20.83	50.00, 75.00	0.00, 20.83
Min, Max	4.2, 100.0	−50.0, 62.5	4.2, 100.0	−33.3, 62.5
Week 12				
n	378	374	377	374
Mean (SD)	58.43 (17.36)	8.10 (15.95)	58.73 (16.30)	8.28 (15.38)
95% CI of Mean	56.68, 60.19	6.48, 9.72	57.08, 60.38	6.71, 9.84

Median	58.33	8.33	58.33	8.33
Q1, Q3	45.83, 70.83	−4.17, 16.67	45.83, 70.83	0.00, 16.67
Min, Max	4.2, 100.0	−29.2, 75.0	8.3, 100.0	−29.2, 54.2
End of cycle				
n	411	407	414	411
Mean (SD)	56.89 (17.51)	7.21 (16.20)	57.08 (17.13)	7.09 (15.85)
95% CI of Mean	55.20, 58.59	5.63, 8.78	55.42, 58.73	5.56, 8.63
Median	58.33	8.33	58.33	4.17
Q1, Q3	45.83, 70.83	−4.17, 16.67	45.83, 70.83	−4.17, 16.67
Min, Max	4.2, 100.0	−50.0, 79.2	8.3, 100.0	−33.3, 54.2

AboBoNT-A abobotulinumtoxinA, *CI* confidence interval, *FAS* full analysis set, *OnaBoNT-A* onabotulinumtoxinA, *SD* standard deviation, *SQoL-6D* Spasticity-related Quality of Life Tool.

Note: SQoL-6D total score ranges from 0 to 100 with higher score indicating better quality of life.