Table 2. study characteristics, outcome measures and results for cerebral spasticity

Study; design	Sample size	Type and characteristics BoNTA	Type and characteristic Placebo	Outcomes of interest reported Study quality assessment	Length of follow-up	Remarks regarding sponsoring
1. Studies evaluating after single injection cycle						
Lindsay, 2021 RCT	93	onabotulinumtoxin-A injections to six muscles of the affected arm in predetermined doses + Electrical stimulation to the wrist extensors, n = 45	Placebo (0.9 mg of sodium chloride injection) + Electrical stimulation to the wrist extensors n = 48	- ARAT (active arm-hand ability) Moderate risk of bias	12 weeks	Allergan provided study drug; no other role within this study.
Wallace, 2020 RCT	28	onabotulinumtoxin-A + standardized physiotherapy with 10 sessions in 4 weeks n= 14	Placebo injection (saline) + standardized physiotherapy with 10 sessions in 4 weeks n = 14	- 9-HPT (active arm-hand ability) - ARAT (active arm-hand ability) Low risk of bias	5 weeks	Study funded by the UK Stroke Association
Rosales, 2012 RCT	163	abobotulinumtoxinA 500 U n = 80	Placebo (visually identical) n = 83	- Barthel index (ADL) - Motor Assessment Score Moderate risk of bias	4 weeks, 12 weeks,	Study was funded by Ipsen
Kerzoncuf, 2020 RCT	40	onabotulinumtoxin-A injection, maximum dose 300 U n = 23	Placebo (physiologic serum) n = 26	- Walking speed - Balance and sway area Moderate risk of bias	4-6 weeks	Study was funded by the Protocole Hospitalier de Recherche Clinique.
Kaji, 2010 RCT	120	onabotulinumtoxin-A single injection of 300 U + 75 U into 4 muscles n = 58	Placebo (visually identical, same amount of injection) n = 62	- Change in time on 10m walking test Moderate risk of bias	4 weeks, 12 weeks	Study sponsored by GlaxoSmithKline
Prazeres, 2018	40	onabotulinumtoxin-A (dose not reported) + physical therapy	Placebo (saline solution) + physical therapy	- Timed-Up-and-Go test (TUG); - 6-min walking test	12 weeks	Study funded by the Brazilian National Institutes of Science, CAPES,

RCT		according to a standardized protocol including muscle strength, flexibility, endurance and functional training twice a week n = 20	according to a standardized protocol including muscle strength, flexibility, endurance and functional training twice a week n = 20	Low risk of bias		and UFBA and authors declared no conflicts of interest
2. **Studies evaluating after (single and) multiple injection cycles**						
Masakado, 2020 RCT	100	Incobotulinumtoxin-A injections n1 (high 400 U) = 44 n2 (low 250 U) = 23	2 groups: high dose placebo, n=22 low dose placebo, n=11	- MAS (OLEX) - DAS (OLEX) - Adverse events (OLEX) High risk of bias	4 weeks, 12 weeks OLEX: 24 weeks, 36 weeks, 48 weeks	Study funded by Merz Pharmaceuticals GmbH, and three authors are either employee or consultant for the company
McCrory, 2009 RCT	96	Abobotulinumtoxin-A, with a total dose range of 750-1000 U, re-treatment at week 12. n = 54	Placebo (visually identical) n = 42	- MMAS (active skills and abilities) *(also assessed after single injection)* - MAS (muscle tone) - VAS (pain) - Adverse events Low risk of bias	20 weeks	Study funded by Ipsen, who had no influence on the interpretation of data and the final conclusions drawn.
Masakado, 2022 RCT	208	single injection cycle of incobotulinumtoxin-A 400 U in the plantar flexors n = 104	Placebo (visually identical) n = 104	- Change in time 10m walking test *(also assessed after single injection)* - MAS AUC change (muscle tone, OLEX) - Patient's Assessment of Spasticity, Pain and Spasms scale (pain, OLEX) - Adverse events	4 weeks, 12 weeks OLEX: 24 weeks, 36 weeks, 48 weeks	Study funded by Merz Pharmaceuticals GmbH, conflicts of interests were not reported, but three authors were employees at Merz Pharmaceuticals GmbH.

				Moderate risk of bias		
Wein, 2018 RCT	468	onabotulinumtoxin-A 300 U, with optional additional =<100 U n = 233	Placebo (0.9 mg of sodium chloride injection) n = 235	- Walking speed *(also assessed after single injection)* - MAS (muscle tone, in OLEX) Moderate risk of bias	4 weeks, 12 weeks OLEX: 24 weeks, 36-42 weeks, 60 weeks	Study was funded by Allergan plc;. two of the authors were Allergan employees
Gracies, 2017 RCT	381	one lower limb injection abobotulinumtoxin-A 1000 U (n = 125); abobotulinumtoxin-A 1500 U) (n = 128)	Placebo (not reported) n = 128	- Speed on 10m walking test (*also assessed after single injection)* - MAS (muscle tone, in OLEX) - adverse events (OLEX) High risk of bias	4 weeks, 12 weeks, OLEX: 24 weeks, 36 weeks, 48 weeks	Study was sponsored by Ipsen; four of the authors were Ipsen employees
Ward, 2014 RCT	273	onabotulinumtoxin -A, maximum dose of 800 U. Combined with standard of care. Optional re-injection at 12-24 weeks n = 139	Placebo + standard of care (SC), which could be more intensive care than prior to study, such as physical therapy, occupational therapy and SC focused on active functional goal achievement n= 134	- REPAS-26 (muscle tone) - Adverse events High risk of bias	12 weeks after first injection, 10 weeks after second injection, OLEX: 12 months	Allergan employees were involved in: (i) the design and conduct of the study; and (ii) the collection, management, analysis, and interpretation of the study data. The authors had sole control over the preparation, review, and approval of this manuscript.

Abbreviations: ARAT= Action Research Arm Test; AS= Ashworth score; DAS= Disability Assessment scale; LS = least squares analysis; MAS = Modified Ashworth score; MMAS = Modified Motor Assessment Scale NHPT= Nine-hole peg test; TUG= Timed up-and-go test; VAS= Visual Analogue Scale