Clinical Trial Summary Attachment (based on RRF)	**SA**

1	**Sponsor:** CHU de Bordeaux	
2	**Naming of the experimental drug(s):** BOTOX-A	
3	**Naming of the experimental active(s) substance(s):** Botulinic Toxin type A	
4 4.1 4.2 4.3	**Study identification:** **Official Title:** **A Prospective** Pilot Study to Assess the Efficacy of Botox-A in Patients With Low Anterior Resection Syndrome (LARS>20) and Refractory Medical Treatment After Rectal Resection **Acronym:** BOTOX-TME **Unique Protocol ID:** CHUBX 2020/64	
5.1 5.2	**ID EudraCT:** 2021-000593-29 **NCT**04991688	
6	**Investigator(s):** Pr Eric RULLIER, main investigator, service de chirurgie colorectale - CHU de Bordeaux Pr Franck ZERBIB, Co-coordonnator, service d'hépato gastroentérologie – CHU de Bordeaux	
7	**Location(s):** CHU de Bordeaux	
8	**Paediatric regulatory details if necessary: ☐yes / ☒no**	
9 9.1	**Trial status:** ☒prematurely ended ☐no subjects recruited ☒only partial results are available ☐trial transitioned to CTIS and its results will be posted there **Detailed reason:** Halted prematurely because of organizational difficulties	
10 10.1 10.2	**Notification of the end of the trial to the NCA : ☒yes / ☐no** **ANSM: 18/04/2023** **RRF (Résumé du Rapport Final): 30/05/2024**	
11 11.1 11.2 11.3	**Study duration:** - First inclusion: 01/09/2021 - Primary completion date: 07/01/2023 - Study completion date: 03/03/2023	12. **Clinical Trial Phase /Type:** II
13 13.1 13.2 13.3	**Population of trial subjects:** - **Number of subjects expected:** 20 patients with symptoms of Low Anterior Resection Syndrome (LARS>20) and refractory to medical treatment at 3 months after surgery - **Actual Number of subjects included in the trial: 11** - **Actual Number of subjects analysed in the trial: 8**	
14 14.1	**Main objective:** Assess the efficacy of Botox-A on the proportion of patients with a good digestive function (no LARS, i.e. score ≤ 20) at 3 months after injection. **Secondary objectives:** Evaluate: - Compliance and Tolerance to treatment - Functional outcome (LARS) at 0,1, 2, 3 and 6 months after injection	

	- Faecal incontinence (WEXNER) at 0,1, 2, 3 and 6 months - Quality of life (QLQ-C30 and QLQ-CR29) at 0, 1, 3 and 6 months - Anxiety at 0, 1, 3 and 6 months - Rectal physiology (Manometry) at 0,1,3 and 6 months - Rectal compliance (Barostat) at 0,1,3 and 6 months - Efficacy of Botox-A at 6 months
15	**Research strategy:** This is a monocentric, prospective, observational, cohort study evaluating effects of Botox-A in patients with symptoms of Low Anterior Resection Syndrome (LARS>20) and refractory to medical treatment.
16	**Medical condition or disease studied:** The goal of this study is to test intra-rectal BOTOX-A on functional outcomes and quality of life of patients with LARS refractory to medical treatment at 3 months after surgery.
16.1	**Inclusion Criteria:** • Patient: male and female, age ≥18 years • Tumour: rectal cancer • Surgery: anterior resection (high or low) with colorectal or coloanal anastomosis, or intersphincteric resection, or pull-through • Symptoms: Low Anterior Resection Syndrome (LARS score >20) refractory to medical treatment at 3 months after rectal surgery (or after temporary stoma closed) • Straight or pouch colonic reconstruction • Surgery alone or with neoadjuvant therapy (chemoradiotherapy, short course radiotherapy, induction chemotherapy) • Signed and dated informed consent • Patient affiliated to a social security system or beneficiary of the same • Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures
16.2	**Exclusion Criteria**: • Anal cancer • Anal surgery in the last 3 months • Acute/painful perianal disease • Ongoing adjuvant treatment • Contraindication for BOTOX-A (known hypersensitivity to botulinum toxin type A or to albumin, infection at the proposed injection site, severe myasthenia) • Have received BOTOX-A in perianal region in the previous 3 months • General anaesthesia performed less than a month • Impossibility of performing a rectoscopy (eg: anal stenosis) • Recent history (<12 months) of myocardial infarction and / or arrhythmias not reduced by appropriate treatment • Subject with a significant deficit of clinical or subclinical neuromuscular transmission (myasthenia or Lambert-Eaton syndrome) or with peripheral motor neuropathy (such as amyotrophic lateral sclerosis or motor neuropathy) • Treatment that directly or indirectly interferes with neuromuscular transmission (aminoglycosides, curare, anticholinesterase, aminoquinoline, cyclosporine, etc.) • History of neuromuscular disorders • Anal clinical examination suggesting the presence of an anorectal abscess • Pregnant woman or breastfeeding woman • Women of child-bearing potential (WOCBP)* not using effective contraception (oestrogen-progesteron combined contraceptives or intra uterine device) since at least 7 days and during all the duration of the study • Persons deprived of their liberty or under measure of judicial protection (curatorship or guardianship) or unable to give their consent • Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol or follow-up schedule, as assessed by investigator.
17	**Experimental drug(s) studied (name, dose, route of administration, lot number):** 1 injection of BOTOX-A (Allergan): 10 intra-rectal injections of 20 U of botulinic toxin
18	**Treatment duration**: 1 injection
19	**Reference Experimental drug(s) (name, dose, route of administration, lot number):** Non applicable

20	**Evaluation criteria:** Efficacy
20.1	**Primary endpoint:** Proportion of patients with LARS ≤ 20 at 3 months after injection
20.2	**Secondary endpoints:** - Compliance and tolerance to treatment: proportion of patients receiving full treatment - Functional outcome with LARS score at 0, 1, 2, 3 and 6 months - Faecal incontinence with Wexner score at 0, 1, 2, 3 and 6 months - Quality of life (QLQ-C30 and QLQ-CR29) at 0, 1,3 and 6 months - Anxiety at 0, 1, 3 and 6 months - Evaluation and comparison of physiologic tests (manometry and barostat) at 0, 1, 3 and 6 months - Proportion of patients with LARS ≤ 20 at 6 months - Correlation between LARS and physiologic tests will be analysed
21	**Statistical analysis of the data:** Functional data will be studied by descriptive analyses. Correlation tests will be performed between LARS score and physiology (manometry and barostat).
22	**Trial Summary:** The number of patients to be included at the beginning of the trial was evaluated as 20. At least, 54 patients were pre-screened during the study, then 19 were screened, 11 were include and 3 were exclude. At the end, the data of only 8 patients were analysed.
22.1	- **Outcomes / Efficacy evaluation** The primary objective of the study was to evaluate the efficacy of BOTOX A in reducing the proportion of patients with a LARS score > 20 at 3 months after injection. The LARS score at 3 months was recorded for 7 of the 8 patients included in the analysis. All 7 participants showed an improvement in their LARS score at 3 months. Only one participant had a LARS score <20 at 3 months. Of the 7 participants, 6 maintained a LARS score > 20 at 3 months. We have complete LARS score data at 6 months for 6 of the 8 patients, only 5 of whom had data at both 3 and 6 months. Four of these five participants showed a stable or improved LARS score at 6 months. Analysis of the secondary endpoints shows that all 8 patients included in the analysis received the full course of treatment. Analysis of the questionnaires (LARS, WEXNER, QLQ-C30, QLQ-CR29, and STAI-Y) administered 1 month, 2 months, 3 months, and 6 months after injection showed no significant changes compared to the questionnaires completed at baseline. Similarly, for manometry and barostat examinations, no significant changes were observed between the baseline measurement and the measurements at 1, 2, 3, and 6 months.
22.2	- **Adverses events / Security evaluation:** During the study, a single serious adverse event was reported; however, the investigator and the sponsor determined that it was not related to the study treatment (chest pain that resolved on the day it occurred, with no evidence suggesting a cardiac emergency). No safety concerns were identified during the study.
23	**Conclusion**: The target of 20 patients to be included in the study was not met. Only eight participants were included, with heterogeneous demographic characteristics. Most participants were men (75%), aged 44 to 67 years. The approach to rectal excision and neorectal reconstruction was also heterogeneous. All participants, with the exception of one, received neoadjuvant therapy About the study primary objective, it is worth pointing out that all participants with complete data on the LARS score at 3 months (7 out of 8) showed an improvement in their score. One participant's LARS score improved by 71%, and four participants' scores improved by 23%. However, only one participant had a LARS score <20 (i.e., there was no low anterior resection syndrome). About the secondary outcomes, we did not observe any trend toward improvement or worsening in the physiological studies or the quality-of-life questionnaires. It is important to note that data for some participants were missing because the questionnaires were incomplete or incorrectly filled out.

	In conclusion, most participants showed an improvement in their LARS score and some reported a significant improvement in their symptoms, but no physiological changes were observed following the injection of BOTOX-A.
24	**More Information**: *Global Substantial Amendments: None* *Global Interruptions and re-starts: None* *Limitations & Caveats: None*
25	**Publication(s)**:
26	Establishment date: 18/06/2026