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

1	**Sponsor:** CHU de Bordeaux
2	**Naming of the experimental drug(s):** Zopiclone, Zolpidem, or Benzodiazepines
3	**Naming of the experimental active(s) substance(s):** Zopiclone, Zolpidem, or Benzodiazepines
4 4.1 4.2 4.3	**Study identification** **Official Title:** Self-help program for hypnotics withdrawal in chronic insomniac patients: A randomized controlled clinical trial. **Acronym:** PROPERSOM **Unique Protocol ID:** CHUBX 2014/35
5.1 5.2	**ID EudraCT:** 2015-000691-94 **ID NCT :** NCT02720458
6	**Investigator(s):** Pr Pierre PHILIP - Clinique du sommeil – Hôpital Pellegrin - CHU Bordeaux pierre.philip@chu-bordeaux.fr
7	**Location(s):** - **Clinique du Sommeil -** Hospital Pellegrin – CHU de Bordeaux - **Unité de Sommeil -** APHP Hôpital Raymond Poincaré - 92380 GARCHES - **Service de Neurophysiologie Clinique -**Hôpital Roger Salengro - CHRU de Lille - 59037 LILLE Cedex - **Unité de Sommeil –** Neurologie - Hopital Gui de Chauliac - 34295 MONTPELLIER Cedex 5 - **Centre du Sommeil et de la Vigilance -** APHP Hôtel-Dieu de Paris - 75181 PARIS Cedex 04 - **Service de Psychiatrie adultes -** APHP Hôpital Pitié-Salpétrière - 75013 PARIS
8	**Paediatric regulatory details if necessary: ☐yes / ☒no**
9 9.1	**Trial status / Results Analysis stage:** ☒prematurely ended (Terminated) ☐withdrawn ☐no subjects recruited ☒only partial results are available ☐trial transitioned to CTIS and its results will be posted there **Detailed reason:** Target number of subject not reached
10 10.1 10.2	**Notification of the end of the trial to the NCA : ☒yes / ☐no** **ANSM: Decembre 26 2019** **RRF (Résumé du Rapport Final): March 26 2024**
11 11.1 11.2 11.3	**Study duration** - First inclusion: October 4 2016 - Primary completion date: November 25 2019 - Study completion date: November 25 2019
12. **Clinical Trial Phase / Type:** IV	
13 13.1 13.2 13.3	**Population of trial subjects / Enrollment** - **Number of subjects expected:** 256 - **Actual Number of subjects included in the trial: 62** - **Actual Number of subjects analysed in the trial: 61**
14	**Main objective:** To evaluate whether a short-term simple self-help program delivered by internet (sleep restriction therapy + stimulus control) facilitates hypnotic taper-to-abstinence in chronic hypnotic users (intermediate half-life benzodiazepines or Z-drugs in monotherapy) still reporting sleep complaints and enables an hypnotic abstinence during 2 weeks.

14.1	**Secondary objectives:** 1) To evaluate the long-term effect of a short-term simple self-help program (sleep restriction therapy + stimulus control) on hypnotic cessation: Percentage of patients free of hypnotics at three months 2) To evaluate the short- and long-term effects of a short-term simple self-help program (sleep restriction therapy + stimulus control) on anxiety and depression, 3) To evaluate the short- and long-term effects of a short-term simple self-help program (sleep restriction therapy + stimulus control) on total sleep time objectively and subjectively measured, 4) To evaluate the short- and long-term effect of a short-term simple self-help program (sleep restriction therapy + stimulus control) on insomnia severity measured by The Insomnia Severity Scale, 5) To evaluate the efficiency of a short-term simple self-help program (sleep restriction therapy + stimulus control) on quality of life, 6) To evaluate, on the whole sample, the efficiency of a short-term simple self-help program (sleep restriction therapy + stimulus control) on withdrawal Symptoms. 7) To evaluate, in each group separately, whether pretreatment outcome expectancies predict successful tapering, 8) To evaluate the reasons for non-compliance. 9) To evaluate acceptability of the program and patient's satisfaction
15	**Research strategy:** Comparative randomized parallel groups multicentre clinical trial of superiority: - Group 1: standardized gradual hypnotic taper and short-term simple self-help program (restriction of time in bed and stimulus control). - Group 2: standardized gradual hypnotic taper (no access to the self-help program).
16	**Medical condition or disease studied:** Insomnia
16.1	**Inclusion Criteria:** - Patient complaining of persistent insomnia without co morbidities (DSM-5) and treated for at least 1 months with **monotherapy** of: • Zopiclone or Zolpidem with usual doses (3,5 doses per week at least to a maximum of 14 per week, see appendix 2) **OR** • Intermediate half-life benzodiazepines included in the appendix 1 list with usual doses (3,5 doses per week at least to a maximum of 14 per week, see appendix 2) - Motivated to stop hypnotic treatment (score >5 on a 1 to 10 degrees VAS) - 18 to 75 years old - Man or woman, - Having an Internet connection, - Affiliated to a national health service, - Having given written informed consent to participate in the trial.
16.2	**Exclusion Criteria:** - Patient with 2 psychotropic drugs or more taken daily for insomnia complaints (antidepressant, anxiolytic and antihistamine treatments will be allowed if they are prescribed for a stabilized mood and/or anxiety disorder) - Patient not believing in self-help program - Night and shift-workers, - Insomnia with comorbidities other than a stabilized mood and/or anxiety disorder - Current Psychiatric disorder: mood disorder (depression, bipolar disorder) with a BDI score > 19, anxiety disorder, psychosis - All sleep disorders other than persistent insomnia, - Progressive neurological diseases that include restless legs syndrome, - Unstable cardiovascular disease, - Unstable respiratory or endocrinological diseases, - Drug addiction, alcohol addiction during the previous 6 months, - Having undertaken trans-meridian travel (± 3H) in the previous 1 month, - Pregnant or lactating woman. - Current participation in psychotherapy.
17	**Experimental drug(s) studied (name, dose, route of administration, lot number):** short-term simple self-help program with gradual hypnotic taper as : week 1 : 100 % of initial weekly dose week 2 : about 75% of initial weekly dose

	week 3 : about 50 % of initial weekly dose week 4 : about 25 % of initial weekly dose week 5 : about 12,5% of initial weekly dose From the 6th week (W6), patients will not take hypnotic anymore.
18	**Treatment duration:** Duration of withdrawal± self-help program: 5 weeks Duration of follow-up (including withdrawal): 17 weeks
19	**Reference Experimental drug(s) (name, dose, route of administration, lot number):** gradual hypnotic taper as the Experimental arm, without access to the self-help program
20 20.1 20.2	**Evaluation criteria** **Primary endpoint / Outcome:** Achievement of 2 weeks continuous hypnotic abstinence from the end of the gradual taper measured by: - urinary hypnotics screening - medical interview **Secondary endpoints / Outcomes:** 1) Achievement of 3 months continuous hypnotic abstinence from the end of the gradual taper (urinary hypnotics screening) 2) Score on depression and anxiety scales (Beck Depression Inventory and the Beck Anxiety Inventory), 3) Total sleep time, Sleep efficiency, Wake after sleep onset, Sleep latency assessed by Sleep diary and actimetry, 4) Scores on insomnia scales (Insomnia Severity Scale, Leeds), 5) Score on quality of life questionnaire (Short-Form SF-36 Health Survey), 6) Score on Benzodiazepine Withdrawal Symptoms Questionnaire 7) Score on Self-efficacy VAS 8) Reasons for non-compliance (loss of information, loss of motivation, obstacles). 9) Score on Acceptability E-Scale (French version EAPI) and Client Satisfaction Questionnaire (CSQ-8)
21	**Statistical analysis of the data** The 95% confidence intervals (exact binomial distribution) in each group will be calculated. These 2 proportions will be compared with a Chi² test or a Fisher's exact test, according to the size of the expected values under the hypothesis of independence. Logistic regression model will be used to adjust the analysis for stratification factor and other major confounding factors. Assumption of the models (log-linearity of the associations) will be systematically checked.
22 22.1 22.2	**Trial Summary – Results** - **Outcomes / Efficacy evaluation:** This study did not demonstrate the effectiveness of the personalized program compared to the standardized program in achieving abstinence from hypnotic use 2 months after the intervention (medical interview and urine test). The same lack of efficacy was observed at 3 months. No effect was observed on the assessment of secondary endpoints (sleep measured by actigraphy, mood, emotions, withdrawal symptoms, etc.) - **Adverses events / Security evaluation:** In total, two serious adverse events were reported to the sponsor; both were considered by the investigator and the sponsor to be unrelated to the study protocol.
23	**Conclusion** It should be noted that only 61 of the 256 planned participants could be included, which implies low statistical power to demonstrate the program's effectiveness.
24	**<u>More Information</u>**: *Global Substantial Amendments:* *Global Interruptions and re-starts:* *Limitations & Caveats:*
25	**Publication(s):**
26	**Establishment date:** 28/07/2026