Unification of treatments and interventions for tinnitus patients

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Deliverable D7.2:
Midterm Recruitment Report

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1 Introduction

This document summarizes the current recruitment progress at half time of the UNITI Randomized Clinical Trial (RCT), which is conducted within the work package 7 of the proposal.
Over the course of the UNITI-RCT a 12-week treatment trial for chronic tinnitus patients using 4 different types of interventions (hearing aids, sound therapy, structured counseling, cognitive behavioral therapy) either as a single treatment or a combination of two treatments is performed. The RCT is harmonized over five clinical centers across the EU and aims to investigate 500 tinnitus patients. Detailed information about the RCT design and the used interventions and assessments can be found in Schoisswohl et al. (2021)

1.1 Clinical sites

The UNITI-RCT is conducted at five clinical sites across the European Union. Below the clinical sites and the respective responsible principal investigators are listed:

(1) University of Regensburg, Regensburg, Germany (RCT coordinator)

- Prof. Dr. Berthold Langguth
- PD Dr. Winfried Schlee
- PD Dr. Martin Schecklmann
- Dr. Stefan Schoisswohl

(2) Charité – Universitaetsmedizin Berlin, Berlin, Germany

- Prof. Dr. Birgit Mazurek
- Dr. Benjamin Böcking

(3) Ethniko Kai Kapodistriako Panepistimo Athinon, Athens, Greece

- Dr. Dimitris Kikidis
- Assoc. Prof. Dr. Athanasios Bibas

(4) Hospital Universitario Virgen de las Nieves/Hospital Clinico Universitario San Cecilio, Granada, Spain

- PD. Dr. Jose Antonio López Escámez
- Dr. Juan Manuel Espinosa-Sanchez
- Dr. Patricia Perez Carpena
- Marta Martinez-Martinez

(5) Katholieke Universiteit Leuven, Leuven, Belgium

- Asst. Prof. Dr. Rilana Cima
- Prof. Dr. Johan Vlaeyen

1.2 Sample of tinnitus patients

In total 500 tinnitus patients will be recruited during the UNITI-RCT. Potential patients are recruited via e.g., newspaper or social media announcements, individually at the clinical sites through information sheets as well as conversations with ENTs with respect to the following inclusion and exclusion criteria as outlined in **Table 1**.

Table 1. *Inclusion and exclusion criteria*

Inclusion criteria
- Primary complaint tinnitus
- Chronic tinnitus (≥ six months)
- Age between 18 and 80 years
- A score of ≥ 18 in the Tinnitus Handicap Inventory (THI; Newman et al., 1996) – at least mild tinnitus distress
- A score of > 22 in the Montreal Cognitive Assessment (MoCa; Nasreddine et al., 2005) – absence of mild cognitive impairment
- Ability and willingness to use the UNITI mobile applications on smartphones
- Openness to use a HA (if indication and allocation to HA group)
- Ability to understand and consent to the research (hearing ability, intellectual capacity)
- Ability to participate in all relevant visits (no plans for e.g., long-term holidays or pregnancy)
- Existing drug therapies with psychoactive substances (e.g., antidepressants or anticonvulsants) must be stable for at least 30 days at the beginning of the therapeutic intervention. The drug therapy should remain constant during the course of the study. Necessary changes do not constitute an exclusion criterion per se, but need to be recorded.
Exclusion criteria
- Objective tinnitus or heartbeat-synchronous tinnitus as primary complaint
- Otosclerosis / acoustic neuroma or other relevant ear disorders with fluctuation hearing
- Present acute infections (acute otitis media, otitis externa, acute sinusitis)
- Meniere's disease or similar syndromes (but not vestibular migraine)
- Serious internal, neurological or psychiatric conditions
- Epilepsy or other disorders of the central nervous system (e.g., brain tumor or encephalitis)
- Clinically relevant drug, medication or alcohol abuse up to 12 weeks before study start
- Severe hearing loss – inability to communicate properly in the course of the study
- One deaf ear
- Missing written informed consent
- Start of any other tinnitus related treatments, especially hearing aids, structured counseling, sound therapy (with special devices; expecting long term effects) or cognitive behavioral therapy in the last 3 months before the start of the study**

***** Due to specific standards of the local ethics committee at the clinical site in Granada, Spain (Servicio Andaluz de Salud) with respect to the conduction of RCTs, all female participants will be tested with regards to an existing pregnancy

** If a HA has already been worn three months before screening, eligible candidates are allowed to participate, but are automatically assigned to the group with no HA indication.

2 Current state of recruitment

With the 10th of March 2022 a total number of 634 potential study participants were screened for the UNITI-RCT, from which 392 met the inclusion criteria and were successfully included in the trial (randomized + baseline visit, **Figure 1A).** Currently 239 tinnitus patients already completed the 12-week intervention phase with a successful end of treatment visit (**Figure 1B**). Up to now 63 patients cancelled their participation in the trial (16.07% of drop-outs; **Figure 1D**). 73 patients already completed the mandatory part of the trial with follow-up visit 1 which is conducted 36 weeks after the baseline visit (**Figure 1C**). No additional voluntary follow-up visits 48 weeks after baseline were conducted so far. For an overview, please see **Figure 1**.

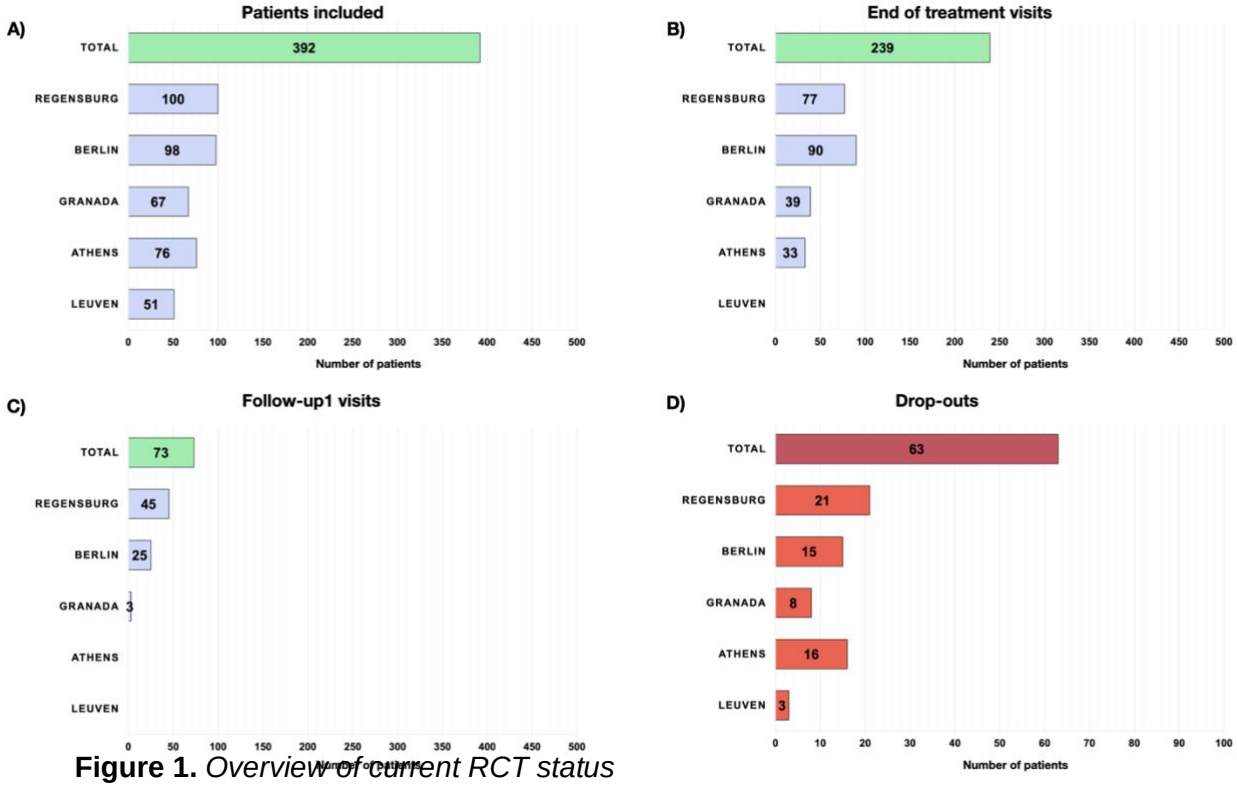

Figure 1. *Overview of current RCT status*

In the following section the current RCT recruitment status is described per clinical site in more detail, including the quantity of recruited patients per treatment arm as well as the already successful performed study visits.

2.1 Regensburg

Patient screening at the clinical site in Regensburg started in April 2021 and was successfully finished with the inclusion (randomization + baseline measurements) of the last patient (N = 100) on the 12th of January 2022. A total number of 285 patients were screened. Currently 89 interim visits were performed. 77 patients already finished the treatment phase, 45 patients successfully finished all mandatory visits for RCT participation (follow-up 1). Currently 21 patients dropped out (21%) from the trial. For a detailed overview of the current status at the clinical site in Regensburg see **Table 2** below.

Table 2. *Recruitment status Regensburg*

Treatment arm	Baseline visits	Interim visits	End of treatment visits	Follow-up 1	Follow-up 2	Drop-outs
HA	12	12	11	5	-	-
ST	12	12	11	6	-	3
SC	12	11	11	7	-	1
CBT	12	9	6	2	-	5
HA + ST	6	5	4	2	-	1
HA + SC	4	4	3	2	-	-
HA + CBT	4	3	3	1	-	1
ST + SC	14	11	10	6	-	3
ST + CBT	12	12	10	6	-	3
SC + CBT	12	10	8	8	-	4
Total	**100**	**89**	**77**	**45**	**-**	**21**

2.2 Berlin

The screening phase started during April 2021 and is currently in its final phase. Already 98 tinnitus patients were successfully included in the trial in Berlin. By now N = 129 patients were screened. Interims visits and end of treatment visits were successfully conducted for 90 patients. 25 patients already finished their trial participation with the mandatory follow-up 1. At the clinical site in Berlin, 15 patients dropped out from the RCT (15.31%). For a detailed overview of the current status at the clinical site in Berlin see **Table 3** below.

Table 3. *Recruitment status Berlin*

Treatment arm	Baseline visits	Interim visits	End of treatment visits	Follow-up 1	Follow-up 2	Drop-outs
HA	11	11	11	4	-	1
ST	11	10	11	4	-	1
SC	12	10	11	3	-	2
CBT	12	11	12	3	-	2
HA + ST	6	6	5	1	-	-
HA + SC	4	4	3	1	-	-
HA + CBT	4	3	4	1	-	3
ST + SC	14	14	13	3	-	1
ST + CBT	12	12	9	3	-	1
SC + CBT	12	9	11	2	-	4
Total	**98**	**90**	**90**	**25**	**-**	**15**

2.3 Athens

Patient's screening started in June 2021 and is currently ongoing. By now 79 patients were screened from which 76 were included in the trial. 46 patients participated in the interim assessments, whereas 33 patients already finished the treatment phase with the end of treatment visit. No follow-up measurements were conducted so far. 16 patients are considered as drop-outs (21.05%). For a detailed overview of the current status at the clinical site in Athens see **Table 4** below.

Table 4. *Recruitment status Athens*

Treatment arm	Baseline visits	Interim visits	End of treatment visits	Follow-up 1	Follow-up 2	Drop-outs
HA	9	6	3	-	-	1
ST	9	6	6	-	-	1
SC	9	5	3	-	-	3
CBT	9	5	4	-	-	1
HA + ST	3	2	2	-	-	-
HA + SC	3	-	-	-	-	1
HA + CBT	3	-	-	-	-	2
ST + SC	12	11	8	-	-	2
ST + CBT	9	5	3	-	-	4
SC + CBT	10	6	4	-	-	1
Total	**76**	**46**	**33**	**-**	**-**	**16**

2.4 Granada

The clinical site in Granada started with screening of potential patients during June 2021. From 82 patients screened, 67 patients were included in the trial. 53 patients already participated in the interim assessment visits, whereas 39 of which successfully completed the 12-week intervention phase by participating in the end of treatment visit. 3 mandatory follow-up measurements were executed up to now. 8 drop-outs (11.94%) were reported by the team in Granada. For a detailed overview of the current status at the clinical site in Granada see **Table 5** below.

Table 5. *Recruitment status Granada*

Treatment arm	Baseline visits	Interim visits	End of treatment visits	Follow-up 1	Follow-up 2	Drop-outs
HA	12	11	8	-	-	1
ST	6	4	3	-	-	-
SC	7	6	4	1	-	-
CBT	9	5	2	1	-	2
HA + ST	6	6	6	-	-	-
HA + SC	4	4	2	1	-	-
HA + CBT	4	3	2	-	-	1
ST + SC	7	5	5	-	-	2
ST + CBT	6	3	3	-	-	1
SC + CBT	6	6	4	-	-	1
Total	**67**	**53**	**39**	**3**	**-**	**8**

2.5 Leuven

The screening phase in Leuven started during November 2021. By now 59 potential patients were screened from which 51 were successfully included in the trial. 18 interim assessments were already performed. 3 patients are considered as drop-outs in Leuven (5.88%). Currently no patient finished the 12-week treatment phase. For a detailed overview of the current status at the clinical site in Leuven see **Table 6** below.

Table 6. Recruitment status Leuven

Treatment arm	Baseline visits	Interim visits	End of treatment visits	Follow-up 1	Follow-up 2	Drop-outs
HA	7	4	-	-	-	
ST	6	2	-	-	-	
SC	6	3	-	-	-	
CBT	7	0	-	-	-	
HA + ST	3	2	-	-	-	
HA + SC	3	1	-	-	-	
HA + CBT	2	1	-	-	-	
ST + SC	5	2	-	-	-	
ST + CBT	5	1	-	-	-	
SC + CBT	7	2	-	-	-	
Total	**51**	**18**	**-**	**-**	**-**	

3 Summary

Per 10th of March 2022 392 out of 500 planned tinnitus patients (78.4%) were successfully recruited for the UNITI-RCT. No major problems were identified during the recruitment process at any of the involved clinical centers.

4 References

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