**Cognitive behavioral therapy for late life depression (CBTlate):**

**results of a multicenter, randomized, observer-blinded, controlled trial**

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**Supplement 2**

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# Description of the interventions

**Cognitive Behavioural Therapy for late life depression (LLD-CBT)** was chosen as the intervention of interest, because CBT in early and midlife is effective in the treatment of depression, treatment is tailored to address late life specific psychological factors, and LLD-CBT program has shown efficacy in comparison with an active control intervention (SUI) in a pilot study. In that pilot study, the individual face-to-face intervention was more effective than LLD-CBT in a group setting [1]. The number of 15 treatment sessions is required to sufficiently work through the 6 sections of the program. The twice-per-week frequency is optimal to engage the subject in the treatment and it also reflects a real-world scenario of the treatment of subjects with moderate to severe depression. The intervention represents the standard of CBT interventions with regard to number and frequency of sessions [2]. The LLD-CBT is guided by a published manual [3]. LLD-CBT is composed of 6 modules which correspond to the basic structure of CBT: (1) Relationship building, history of subject, identification of problems and definition of goals; (2) education of CBT rationale, development of a cognitive-behavioral model of the individual depression, relating interventions to rationale and goals, SOC model, life review; (3) day structuring, life balance, behavioral activation, increasing pleasant activities, decreasing unpleasant activities; (4) detecting, analysing automatic thoughts, understand and change association between way of thinking and mood and behavior, implementing cognitive strategies, socratic dialogues, thought control techniques; (5) detect and overcome skill deficits, training social and interactional skills, problem-solving skills, relaxation skills; (6) stabilizing progress, maintaining learned skills, relapse prevention, crises management and emergency planing. LLD-CBT includes elements such as life review and the SOC model (selection, optimization and compensation) which address the specific needs and topics of depressed patients at higher age. Therapists have to cover all modules but have flexibility how intensive (number of sessions) each module for an individual subject needs to be worked through.

The active control intervention **Supportive unspecific intervention (SUI)** has been successfully applied in a pilot study with older outpatients suffering of major depression. In addition, similar control interventions were applied in randomized, controlled trials with chronic depression, recurrent depression and with bipolar disorder. SUI is described in and guided by a manual. It can be conducted as individual and as group treatment over 12 to 20 sessions. SUI uses supportive, general but non-specific interventions to help patients to overcome their depression by self-reflection and express their emotions to activate their ressources and personal strength. Therapists act patient-centered, are empathic listeners and follow patients, verbalize their expressed feelings, show positive regard and create a warm, understanding therapy atmosphere. Therapists should not interrupt patients but can ask patients giving examples, concrete experiences, and clarification. If patients have questions, (short) educational components with regard to depression are allowed. Treatment sessions are unstructured, content and process are determined by the patient. Not allowed (Non-SUI) are setting agenda, summarizing, giving homework, exercises, role plays, using any kind of material, talking about cognitions and behavioral activation.

1. Hautzinger M, Welz S. Kurz- und längerfristige Wirksamkeit psychologischer Interventionen bei Depressionen im Alter. Z Klin Psychol Psychot. 2008;37:52-60.
2. DGPPN, BÄK, KBV, AWMF, AkdÄ, BPtK, BApK, DAGSHG, DEGAM, DGPM, DGPs, DGRW (Hrsg.) für die Leitliniengruppe Unipolare Depression\*. S3-Leitlinie/Nationale VersorgungsLeitlinie Unipolare Depression – Langfassung. 2.Auflage. Version 4. 2015. Available from: www.depression.versorgungsleitlinien.de; [cited: 02.11.2017]; DOI: 10.
3. Hautzinger M. Depression Im Alter. Psychotherapeutische Behandlung Für Das Einzel- Und Gruppensetting. 2nd ed. Weinheim: Beltz; 2016.

# Adherence to treatment protocols in the CBTlate trial

**Measure**

In order to assess treatment adherence we developed a rating scale. This scale is composed of 20 items, each of which is rated on a 0 to 5 point scale (0 = not characteristic at all, 5 = extremely characteristic). The scale has two sub-scales. Ten items assess therapist behaviours specific to LLD-CBT (e.g. behavioural activation), and form the CBT subscale. Ten items asses therapist behaviours specific for SUI (e.g. focussing on emotions), and form the SUI subscale.

**Raters**

We employed two psychologists (one of them a licensed psychotherapist) to rate treatment adherence. All of the raters were independent to the CBTlate study and received approximately 17 h of training in the use of the scale and introduction to LLD-CBT and SUI. The focus of this training was to be able to identify the presence or absence as well as intensity of the specific LLD-CBT and SUI behaviours in a videotaped therapy session.

**Procedures**

Overall, 66 videos of individual treatment (n = 36 LLD-CBT sessions, n = 30 SUI sessions) were assessed by the raters. In order to assess interrater reliability, twenty videos thereof were rated by both raters. Videotapes of ca. 50 minutes length were randomly selected (two videos per study therapist and therapy type). The raters were given the videos and were not informed which videotapes were of which therapy type. Raters watched the videos and completed the rating scale individually. To prevent rater drift all the raters met on occasion to review the ratings of single rated videos.

**Inter-rater Reliability**

The reliability of the ratings obtained from the two raters was examined by calculating intraclasscorrelation coefficients (ICC), treating the raters as random effects (Strout & Fleiss, 1979, Model 2). The reliability for both subscales CBT and SUI was very high, ICC(2,1) = 0.990, p < 0.001 for the subscale CBT and ICC(2,1) = 0.950, p < 0.001 for the subscale SUI.

**Internal Consistency**

To determine whether the rating scale items were consistent with each other, we calculated Cronbachs α. The alpha for the CBT subscale was α =0.995 and for the SUI subscale α = 0.974, representing an excellent internal consistency.

**Treatment Differences**

In order to assess treatment adherence we looked for treatment differences between the two therapy types by comparing the mean scores for each treatment group on the CBT and SUI subscale. Adherence ratings of the LLD-CBT treatment sessions were significantly higher on the CBT subscale (M = 21.597, SD = 9.859) than on the SUI subscale (M = 15.8611, SD = 6.811), t(35) = 2.171, p <0.05. In addition, adherence ratings of the CBT subscale were significantly higher for LLD-CBT treatment (M = 21.597, SD = 9.859) compared to SUI treatment (M = 0.850, SD = 1.267), t(36.384) = - 12.502, p <0.001. A similar pattern was observed for SUI, with significantly higher adherence ratings for the SUI treatment sessions on the SUI subscale (M = 37.250 SD = 2.093) relative to the CBT subscale (M = 0.850, SD = 1.267), t(29) = 66.116, p <0.001. Furthermore, adherence ratings of the SUI subscale were significantly higher for SUI treatment compared to LLD-CBT treatment, t(47.924) = 17.554, p <0.001.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Baseline** | | | | | | | | **Intermediate (week 5)** | | | | | | | | | **End of Treatment (week 10)** | | | | | | **Follow-up (month 6)** | | | |
|  | **SUI** | | **LLD-CBT** | | | **Overall** | | | **SUI** | | | **LLD-CBT** | | | **Overall** | | | **SUI** | | **LLD-CBT** | | **Overall** | | **SUI** | | **LLD-CBT** | **Overall** |
| **Geriatric Depression Scale (GDS)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n | 108 | | 105 | | | 213 | | | 108 | | | 102 | | | 210 | | | 105 | | 103 | | 208 | | 100 | | 97 | 197 |
| Mean score (SD) | 20.5 (4.2) | | 20.9 (4.3) | | | 20.7 (4.2) | | | 16.9 (5.5) | | | 15.2 (6.4) | | | 16.1 (6.0) | | | 14.1 (7.0) | | 13.1 (7.4) | | 13.6 (7.2) | | 15.0 (6.7) | | 13.8 (7.3) | 14.4 (7.0) |
| **Quick Inventory of Depressive Symptomatology (QIDS-C)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n | 108 | | 105 | | | 213 | | | 108 | | | 102 | | | 210 | | | 105 | | 103 | | 208 | | 99 | | 97 | 196 |
| Mean score (SD) | 14.5 (2.5) | | 14.3 (2.4) | | | 14.4 (2.4) | | | 9.7 (4.2) | | | 8.6 (4.2) | | | 9.1 (4.2) | | | 7.6 (4.8) | | 7.2 (4.7) | | 7.4 (4.8) | | 8.4 (4.6) | | 7.4 (5.4) | 7.9 (5.1) |
| **Geriatric Anxiety Inventory (GAI)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n | 106 | | 103 | | | 209 | | | 106 | | | 100 | | | 206 | | | 101 | | 100 | | 201 | | 94 | | 93 | 187 |
| Mean score (SD) | 11.9 (4.3) | | 11.2 (4.2) | | | 11.6 (4.3) | | | 10.4 (4.5) | | | 8.7 (5.0) | | | 9.6 (4.8) | | | 8.9 (5.2) | | 7.9 (5.2) | | 8.4 (5.2) | | 8.7 (5.2) | | 7.3 (5.2) | 8.0 (5.2) |
| **Patient-Reported Outcome in Major Depressive Disorder (PRO-MDD)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n (%) | 106 | | 103 | | | 209 | | | 106 | | | 99 | | | 205 | | | 101 | | 100 | | 201 | | 94 | | 93 | 187 |
| Mean score (SD) | 139.1 (50.6) | | 140.9 (51.2) | | | 140.0 (50.8) | | | 122.1 (53.1) | | | 111.4 (60.4) | | | 116.9 (56.9) | | | 104.8 (55.7) | | 98.1 (61.5) | | 101.4 (58.6) | | 112.6 (56.8) | | 100.9 (63.6) | 106.8 (60.4) |
| **WHO Quality of Life (WHOQOL-BREF, Global Score)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n (%) | 105 | | 102 | | | 207 | | | 106 | | | 98 | | | 204 | | | 101 | | 98 | | 199 | | 92 | | 92 | 184 |
| Mean score (SD) | 39.4 (17.2) | | 43.4 (17.5) | | | 41.4 (17.4) | | | 57.4 (16.8) | | | 57.8 (20.3) | | | 57.6 (18.5) | | | 58.3 (19.1) | | 58.9 (19.2) | | 58.6 (19.1) | | 60.2 (17.1) | | 59.8 (20.2) | 60.0 (18.7) |
| **WHO Quality of Life (WHOQOL-OLD, Total Score)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n (%) | 106 | | 102 | | | 208 | | | 106 | | | 95 | | | 201 | | | 101 | | 100 | | 201 | | 93 | | 90 | 183 |
| Mean score (SD) | 53.8 (11.7) | | 55.4 (10.8) | | | 54.6 (11.3) | | | 55.2 (12.4) | | | 58.1 (13.2) | | | 56.5 (12.8) | | | 57.6 (12.1) | | 61.4 (13.1) | | 59.5 (12.7) | | 58.6 (12.4) | | 60.9 (13.7) | 59.7 (13.1) |
| **Health Status (SF-36, physical health score)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n (%) | | 104 | | | 101 | | | 205 | | | 104 | | | 99 | | | 203 | | 99 | | 99 | | 198 | | 92 | 89 | 181 |
| Mean score (SD) | | 43.4 (10.8) | | | 44.8 (10.9) | | | 44.1 (10.9) | | | 44.3 (10.6) | | | 44.6 (10.2) | | | 44.5 (10.4) | | 43.7 (11.1) | | 44.9 (11.4) | | 44.3 (11.2) | | 45.6 (10.5) | 44.0 (9.9) | 44.8 (10.2) |
| **Health Status (SF-36, mental health score)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n (%) | | 104 | | | 101 | | | 205 | | | 104 | | | 99 | | | 203 | | 99 | | 99 | | 198 | | 92 | 89 | 181 |
| Mean score (SD) | | 31.7 (8.7) | | | 32.2 (10.5) | | | 31.9 (9.6) | | | 35.6 (9.5) | | | 39.0 (12.9) | | | 37.3 (11.4) | | 39.1 (12.1) | | 41.8 (12.7) | | 40.5 (12.4) | | 37.9 (11.8) | 42.5 (13.1) | 40.2 (12.6) |
| **Insomnia Severity Index (ISI)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n (%) | | 105 | | 102 | | | 207 | | | 106 | | | 99 | | | 205 | | | 101 | | 100 | | 201 | | 93 | 93 | 186 |
| Mean score (SD) | | 14.2 (6.1) | | 13.5 (6.0) | | | 13.8 (6.0) | | | 12.5 (5.9) | | | 11.7 (7.0) | | | 12.2 (6.5) | | | 10.9 (6.4) | | 10.7 (6.6) | | 10.8 (6.5) | | 10.9 (6.5) | 10.1 (6.8) | 10.5 (6.6) |
| **Epworth Sleepiness Scale (ESS)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n (%) | | 105 | | 102 | | | 207 | | | 105 | | | 98 | | | 203 | | | 101 | | 100 | | 201 | | 93 | 92 | 185 |
| Mean score (SD) | | 7.9 (4.7) | | 8.9 (4.4) | | | 8.4 (4.6) | | | 8.1 (4.7) | | | 9.0 (4.7) | | | 8.5 (4.7) | | | 7.0 (4.5) | | 7.9 (4.7) | | 7.5 (4.6) | | 6.8 (3.9) | 8.1 (4.7) | 7.·4 (4.3) |
| **REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ)** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Patients with available data, n (%) | | 107 | | 103 | | | 210 | | | 105 | | | 99 | | | 204 | | | 101 | | 100 | | 201 | | 92 | 91 | 183 |
| Mean score (SD) | | 4·5 (2·8) | | 4.1 (2.1) | | | 4.3 (2.5) | | | 4.6 (2.7) | | | 4.0 (2.6) | | | 4.3 (2.6) | | | 4.1 (2.8) | | 3.6 (2.5) | | 3.9 (2.7) | | 3.9 (2.7) | 3.6 (2.5) | 3.7 (2.6) |

# Table S1: Descriptive summaries of primary and secondary outcome measures (per protocol population)

Data are n (%) or mean (SD). LLD-CBT=cognitive behavioral therapy for late-life depression. SUI = supportive unspecific intervention.

# Table S2: Number (%) of participants recruited per site

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Patients Screened | | | | |
| Site | number (n) | | Percent (%) | |
| Cologne | 65 | | 21.7% | |
| Tuebingen | 22 | | 7.4 % | |
| Berlin | 24 | | 8.0 % | |
| Bonn | 28 | | 9.4 % | |
| Freiburg | 70 | | 23.4 % | |
| Leipzig | 56 | | 18.7 % | |
| Mannheim | 34 | | 11.4 % | |
| Total | 299 | | 100 % | |
| Patients randomized | | | | |
| Site | Randomized (n) | | Treatment (n) | |
|  | No | Yes | CBT | SUI |
| Cologne | 2 | 63 | 31 | 32 |
| Tübingen | 0 | 13 | 7 | 6 |
| Berlin | 0 | 23 | 11 | 12 |
| Bonn | 1 | 22 | 11 | 11 |
| Freiburg | 3 | 64 | 32 | 32 |
| Leipzig | 0 | 41 | 21 | 20 |
| Mannheim | 0 | 25 | 13 | 12 |
| Total | 6 | 251 | 126 | 125 |

In alphabetical order, the psychiatric/psychotherapeutic sites are as follows: Department of Psychiatry and Psychotherapy, University Medical Center Cologne (Site Principal Investigator: Prof. Dr. Frank Jessen); Department of Clinical and Developmental Psychology, University of Tuebingen (Site Principal Investigator: Prof. Dr. Martin Hautzinger); Department of Psychiatry and Psychotherapy, University Medical Center Bonn (Site Principal Investigator: Prof. Dr. Michael Wagner); Department of Psychiatry on Campus Benjamin Franklin, Charité Berlin (Site Principal Investigator: PD Dr. Oliver Peters, MD); Department of Psychiatry and Psychotherapy, University Medical Center Freiburg (Site Principal Investigator: Prof. Dr. Elisabeth Schramm); Institute of Social Health, Occupational Health and Public Health (ISAP), University of Leipzig (Site Principal Investigator: Prof. Dr. Steffi G. Riedel-Heller); Department of Psychiatry, Central Institute for Mental Health Mannheim (Site Principal Investigator: Prof. Dr. Lutz Frölich, MD).

# Table S3: Summary of all adverse events reported during the trial

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Adverse Event (AE) | | Treatment | | Total |
| LLD-CBT | SUI |
| Total Count (n) |  | 113 | 92 | 205 |
| Worsening of symptoms, e.g. generalisation of symptoms | Count (n) | 18 | 16 | 34 |
| % within treatment | 15.9% | 17.4 % | 16.6% |
| Occurrence of new symptoms | Count | 4 | 2 | 6 |
| % within treatment | 3.5 % | 2.2 % | 2.9 % |
| Occurrence of passive suicidal thoughts | Count | 10 | 19 | 29 |
| % within treatment | 8.8% | 20.7% | 14.1% |
| Occurrence of active suicidal intentions or plans | Count | 0 | 2 | 2 |
| % within treatment | 0% | 2.2% | 1.0% |
| Occurrence of problems in the patient-therapist relationship | Count | 0 | 1 | 1 |
| % within treatment | 0% | 1.1% | 0.5% |
| Private problems | Count | 28 | 9 | 37 |
| % within treatment | 24.8% | 9.8% | 18.0% |
| Occupational problems | Count | 4 | 1 | 5 |
| % within treatment | 3.5% | 1.1% | 2.4% |
| Other adverse events (e.g. influenza, fractures etc.) | Count | 49 | 42 | 91 |
| % within treatment | 43.4% | 45.7% | 44.4% |

# Table S4: Summary of intensity of adverse events reported during the trial

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Intensity of AE | | Treatment | | Total |
| LLD-CBT | SUI |
| Total Count (n) |  | 113 | 91 | 204 |
| Unclear | Count (n) | 11 | 6 | 17 |
| % within treatment | 9.7% | 6.6 % | 8.3% |
| Mild | Count | 42 | 33 | 75 |
| % within treatment | 37.2% | 36.3% | 36.8% |
| Moderate | Count | 39 | 39 | 78 |
| % within treatment | 34.5% | 42.9% | 38.2% |
| Severe | Count | 21 | 13 | 34 |
| % within treatment | 18.6% | 14.3% | 16.7% |

# Table S5: Summary of relation of reported adverse events to the study

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Relation of AE to study | | Treatment | | Total |
| LLD-CBT | SUI |
| Total Count (n) |  | 113 | 91 | 204 |
| Uncertain/not determinable | Count (n) | 0 | 3 | 3 |
| % within treatment | 0% | 3.3% | 1.5% |
| Definitely | Count | 0 | 2 | 2 |
| % within treatment | 0% | 2.2% | 1.0% |
| Probably | Count | 3 | 1 | 4 |
| % within treatment | 2.7% | 1.1% | 2.0% |
| Possibly | Count | 2 | 5 | 7 |
| % within treatment | 1.8% | 5.5% | 3.4% |
| Unlikely | Count (n) | 14 | 14 | 28 |
| % within treatment | 12.4% | 15.4% | 13.7% |
| Not related | Count (n) | 94 | 66 | 160 |
| % within treatment | 83.2% | 72.5% | 78.4% |

# Table S6: Summary of all serious adverse events reported during the trial

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Serious Adverse Event (SAE) | | Treatment | | Total |
| LLD-CBT | SUI |
| Total Count (n) |  | 7 | 17 | 24 |
| Death | Count (n) | 0 | 0 | 0 |
| % within treatment | 0% | 0% | 0% |
| Life-threatening | Count | 0 | 1 | 1 |
| % within treatment | 0% | 5.9% | 4.1% |
| Requires inpatient hospitalization or prolongation of existing hospitalization | Count | 5 | 15 | 20 |
| % within treatment | 71·4% | 88.2% | 83.3% |
| Results in persistent or significant disability / incapacity | Count | 0 | 0 | 0 |
| % within treatment | 0% | 0% | 0% |
| Suicide Attempt | Count | 0 | 0 | 0 |
| % within treatment | 0% | 0% | 0% |
| Other reason | Count | 2 | 2 | 4 |
| % within treatment | 28.6% | 11.8% | 16.7% |

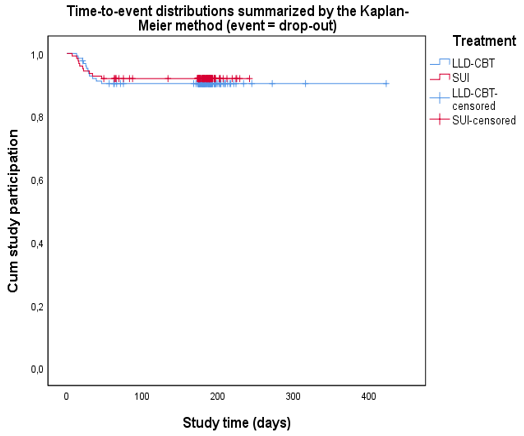
# Table S7: Summary of all reported serious adverse events and adverse events listed by name\*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Treatment | AE-Term  (diagnosis, symptom) | SAE | Intensity of AE | Relation to study | Life-threatening (SAE) | Requires inpatient hospitalization or prolongation of existing hospitalization (SAE) | Results in persistent or significant disability / incapacity (SAE) |
| LLD-CBT | Breast cancer diagnosis | Yes | Mild | Not related | No | Yes | No |
| SUI | Inpatient psychiatric treatment | Yes | Mild | Not related | No | No | No |
| LLD-CBT | Breast cancer surgery | Yes | Moderate | Not related | No | No | No |
| LLD-CBT | Inpatient treatment due to fracture | Yes | Moderate | Not related | No | Yes | No |
| SUI | Inpatient treatment due to fracture | Yes | Moderate | Not related | No | Yes | No |
| SUI | Inpatient treatment due to fracture | Yes | Moderate | Not related | No | Yes | No |
| SUI | Inpatient treatment due to retinal detachment | Yes | Moderate | Not related | No | Yes | No |
| SUI | Inpatient treatment due to ophthalmological surgery | Yes | Moderate | Not related | No | Yes | No |
| SUI | Inpatient treatment due to fall | Yes | Moderate | Not related | No | Yes | No |
| LLD-CBT | Inpatient treatment due to fall | Yes | Severe | Not related | No | Yes | No |
| SUI | Breast cancer diagnosis | Yes | Severe | Not related | No | Yes | No |
| SUI | Inpatient treatment due to pneumonia | Yes | Severe | Not related | No | Yes | No |
| SUI | Inpatient treatment due to fall and hyponatremia | Yes | Severe | Not related | No | Yes | No |
| SUI | Inpatient treatment due to renal failure | Yes | Severe | Not related | No | Yes | No |
| SUI | Inpatient treatment due to cardiac problems | Yes | Severe | Not related | No | Yes | No |
| SUI | Suicidal ideations | Yes | Severe | Not related | No | No | No |
| LLD-CBT | Newly developed psychotic symptoms | Yes | Unclear | Not related | No | No | No |
| LLD-CBT | Inpatient treatment due to back surgery | Yes | Unclear | Not related | No | Yes | No |
| SUI | Inpatient treatment due to Myocarditis | Yes | Unclear | Not related | No | Yes | No |
| SUI | Inpatient treatment due to myocardial infarction | Yes | Unclear | Not related | Yes | Yes | No |
| LLD-CBT | Inpatient treatment due to worsening of depressive symptoms | Yes | Mild | Unlikely | No | Yes | No |
| SUI | Inpatient treatment due to suicidal ideations | Yes | Moderate | Unlikely | No | Yes | No |
| SUI | Inpatient psychiatric treatment due to severity of depressive symptoms | Yes | Severe | Unlikely | No | Yes | No |
| SUI | Day hospital treatment in psychiatric hospital | Yes | Unclear | Unlikely | No | Yes | No |
| SUI | Occurrence of problems in the patient-therapist relationship (patient not satisfied) | No | Mild | Definitely |  |  |  |
| SUI | Worsening of depressive symptoms | No | Moderate | Definitely |  |  |  |
| LLD-CBT | Worsening of depressive symptoms with increased desire to sleep | No | Mild | Possibly |  |  |  |
| LLD-CBT | Feeling of derealisation | No | Mild | Possibly |  |  |  |
| SUI | Worsening of depressive symptoms, resignation | No | Mild | Possibly |  |  |  |
| SUI | Passive suicidal ideations | No | Mild | Possibly |  |  |  |
| SUI | Passive suicidal ideations | No | Mild | Possibly |  |  |  |
| SUI | Increase of agitation | No | Moderate | Possibly |  |  |  |
| SUI | Worsening of depressive symptoms with low energy | No | Severe | Possibly |  |  |  |
| SUI | Low energy and fatigue | No | Mild | Not determinable |  |  |  |
| SUI | Worsening of depressive symptoms | No | Mild | Not determinable |  |  |  |
| SUI | Passive suicidal ideations | No | Moderate | Not determinable |  |  |  |
| LLD-CBT | Worsening of tinnitus | No | Mild | Unlikely |  |  |  |
| LLD-CBT | Back pain | No | Mild | Unlikely |  |  |  |
| LLD-CBT | Interpersonal conflicts | No | Mild | Unlikely |  |  |  |
| LLD-CBT | Passive suicidal ideations | No | Mild | Unlikely |  |  |  |
| LLD-CBT | Passive suicidal ideations | No | Mild | Unlikely |  |  |  |
| SUI | Suspected breast cancer in mammography | No | Mild | Unlikely |  |  |  |
| SUI | Foot injury | No | Mild | Unlikely |  |  |  |
| SUI | Passive suicidal ideations | No | Mild | Unlikely |  |  |  |
| SUI | Nausea | No | Mild | Unlikely |  |  |  |
| SUI | Passive suicidal ideations | No | Mild | Unlikely |  |  |  |
| SUI | Worsening of depressive symptoms | No | Mild | Unlikely |  |  |  |
| LLD-CBT | Passive suicidal ideations | No | Moderate | Unlikely |  |  |  |
| LLD-CBT | Passive suicidal ideations | No | Moderate | Unlikely |  |  |  |
| LLD-CBT | Feeling of drowsiness | No | Moderate | Unlikely |  |  |  |
| LLD-CBT | Worsening of depressive symptoms | No | Moderate | Unlikely |  |  |  |
| LLD-CBT | Passive suicidal ideations | No | Moderate | Unlikely |  |  |  |
| SUI | Passive suicidal ideations | No | Moderate | Unlikely |  |  |  |
| SUI | Interpersonal conflict and passive suicidal ideations | No | Moderate | Unlikely |  |  |  |
| SUI | Passive suicidal ideations | No | Moderate | Unlikely |  |  |  |
| SUI | Passive suicidal ideations | No | Moderate | Unlikely |  |  |  |
| SUI | Passive suicidal ideations | No | Moderate | Unlikely |  |  |  |
| LLD-CBT | Lack of energy | No | Severe | Unlikely |  |  |  |
| LLD-CBT | Interpersonal conflict with wife | No | Severe | Unlikely |  |  |  |
| LLD-CBT | Passive suicidal ideations | No | Unclear | Unlikely |  |  |  |
| SUI | Binge eating (once) | No | Mild | Probably |  |  |  |
| LLD-CBT | Worsening of depressive symptoms | No | Moderate | Probably |  |  |  |
| LLD-CBT | Worsening of depressive symptoms | No | Moderate | Probably |  |  |  |
| LLD-CBT | Worsening of depressive symptoms | No | Moderate | Probably |  |  |  |
| SUI | Worsening of depressive symptoms |  |  |  |  |  |  |

\*the listing includes all SAE independent of their relation to the study and all adverse events exclusive of those that were not related to the study.

# Table S8: Analysis of drop-out during the trial

**Time-to-event distributions summarized by the Kaplan-Meier method (event = drop-out)**



|  |  |  |  |
| --- | --- | --- | --- |
| Means for time-to-event\*(days) | | | |
| Treatment | Mean (SD) | 95% Confidence Interval | |
|  |  | Lower Bound | Upper Bound |
| LLD-CBT | 385.01 (10.41) | 364.68 | 405.49 |
| SUI | 224.41 (5.34) | 213.93 | 234.88 |
| Total | 388.03 (7.12) | 374.06 | 401.99 |

\*event = drop-out

|  |  |  |  |
| --- | --- | --- | --- |
| **Overall Comparisons** | | | |
|  | Chi-Square | df | Sig. |
| Log Rank (Mantel-Cox) | 0.164 | 1 | 0.685 |
| Test of equality of survival distributions for the different levels of treatment. | | | |

# Table S9: Reasons for drop-out per group during the trial

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Reason for drop-out | | | | | | | | | | | |
| Treatment | No. | Number of sessions | Active suicidality | Physical health risk | SAE with therapeutic implication | Occurrence of exclusion criteria | Non-compliance | Relocation of patient / Lost to follow-up | Withdrawal of consent | Protocol violation | Other reason\* |
| LLD-CBT | | | | | | | | | | | |
|  | 1 | 1 | No | No | No | Yes | No | No | No | No | No |
|  | 2 | 1 | No | Yes | No | Yes | No | No | No | No | Yes |
|  | 3 | 1 | No | No | No | No | No | No | Yes | No | No |
| 4 | 4 | No | Yes | No | No | No | No | No | No | Yes |
| 5 | 2 | No | No | No | Yes | No | No | No | No | No |
| 6 | 4 | No | No | No | Yes | No | No | No | No | No |
| 7 | 3 | No | No | No | No | No | No | Yes | No | No |
| 8 | 1 | No | No | No | No | Yes | No | Yes | No | No |
| 9 | 5 | No | No | No | Yes | No | No | No | No | No |
| 10 | 4 | No | No | No | No | Yes | No | No | No | No |
| 11 | 5 | No | No | No | No | No | No | No | No | Yes |
| Total CBT |  | 0 | 2 | 0 | 5 | 2 | 0 | 3 | 0 | 3 |
| SUI | | | | | | | | | | | |
|  | 1 | 0 | No | No | No | No | No | No | No | No | Yes |
|  | 2 | 2 | No | No | No | Yes | No | No | No | No | No |
| 3 | 1 | No | No | No | Yes | No | No | No | No | No |
| 4 | 1 | No | No | No | Yes | No | No | No | No | No |
| 5 | 3 | No | No | No | No | No | No | No | No | Yes |
| 6 | 4 | No | No | Yes | No | No | No | No | No | No |
| 7 | 0 | No | No | No | No | No | No | No | No | Yes |
| 8 | 1 | No | No | No | No | No | No | No | No | Yes |
| 9 | 2 | No | No | No | No | No | No | No | No | Yes |
| 11 | 2 | No | No | No | No | Yes | No | No | No | No |
| Total SUI |  | 0 | 0 | 1 | 3 | 1 | 0 | 0 | 0 | 5 |
| Overall |  |  | 0 | 2 | 1 | 8 | 3 | 0 | 3 | 0 | 8 |

\*other reasons include dropping out due to patient concerns about Covid-19 pandemic (3 cases), physical illnesses (2 cases), change in antidepressive medication (1 case), severe symptoms of a mental illness other than depression (1) and care of a relative (1 case).