

FIGURE S1. Disposition of Patients in a Study of Adjunctive Cannabidiol in Schizophrenia

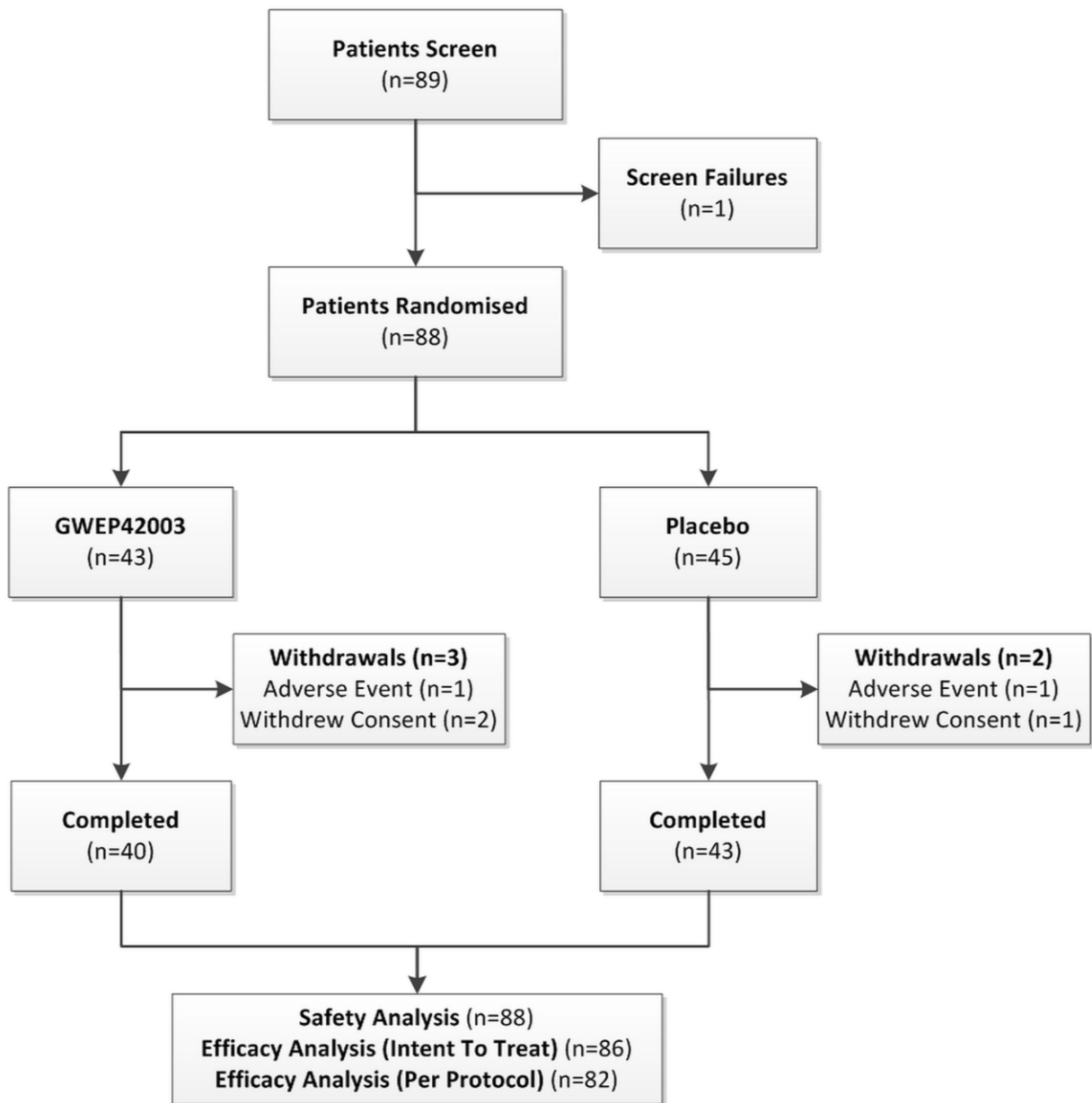


TABLE S1. Schedule of Assessments

| Visit Number | 1 | 2 | 3 | 4 | 5 |
|---|----------|----------|-----------|-----------|-----------|
| Day Number | 1 | 8 | 22 | 43 | 57 |
| Eligibility and safety measures | | | | | |
| Informed consent | X | | | | |
| Demographics | X | | | | |
| Medical history | X | | | | |
| Physical examination | X | | | X | |
| ECG ^a | X | | | X | |
| Vital signs | X | | | X | |
| Concomitant medications review | X | X | X | X | X |
| Pregnancy test (if applicable) | X | | | X | |
| Randomization | X | | | | |
| Blood sampling and urine dipstick tests for safety measures | X | | X | X | |
| Urine drug screen | X | | | X | |
| Investigational medicinal product dispensing | X | X | X | | |
| Investigational medicinal product compliance review | | X | X | X | |
| Adverse Events review | | X | X | X | X |
| Efficacy measures | | | | | |
| Positive and Negative Symptoms Scale (PANSS) questionnaire | X | X | X | X | |
| Scale for the Assessment of Negative Symptoms (SANS) questionnaire | X | X | X | X | |
| Clinician Global Impressions Severity Scale (CGI-S) | X | X | X | X | |
| Clinician Global Impressions Improvement Scale (CGI-I) | | X | X | X | |
| Blood sampling for efficacy measures and determination of cannabinoid plasma levels | X | | X | X | |
| Current substance abuse status (if applicable) | X | | | | |
| Global Assessment of Functioning (GAF) | X | X | X | X | |
| Simpson-Angus Scale questionnaire | X | X | X | X | |
| Brief Assessment of Cognition in Schizophrenia (BACS) questionnaire | X | X | X | X | |
| Participant Global Impression of Change of functioning and sleep (PGIC) | | X | X | X | |
| Caregiver Global Impression of Change of functioning and sleep (CGIC) (if applicable) | | X | X | X | |
| Body weight, BMI, and waist measurement | X | X | X | X | |

^a Additional measurements could be taken at any time during the trial, if clinically indicated.

TABLE S2. Antipsychotic Medication Being Taken by Patients

| Antipsychotic Medication | Patients | | | | | |
|--------------------------|-----------------------|------|-------------------|------|-----------------|------|
| | Cannabidiol (n=43) | | Placebo (n=45) | | Total (n=88) | |
| | n | % | n | % | n | % |
| Aripiprazole | 11 | 25.6 | 13 | 28.9 | 24 | 27.3 |
| Olanzapine | 9 | 20.9 | 12 | 26.7 | 21 | 23.9 |
| Risperidone | 9 | 20.9 | 8 | 17.8 | 17 | 19.3 |
| Amisulpride | 4 | 9.3 | 4 | 8.9 | 8 | 9.1 |
| Quetiapine | 4 | 9.3 | 4 | 8.9 | 8 | 9.1 |
| Flupentixol | 2 | 4.7 | 2 | 4.4 | 4 | 4.5 |
| Clozapine | 1 | 2.3 | 1 | 2.2 | 2 | 2.3 |
| Zuclopentixol acetate | 1 | 2.2 | 1 | 2.2 | 2 | 2.3 |
| Lithium carbonate | 0 | | 1 | 2.2 | 1 | 1.1 |
| Paliperidone | 1 | 2.3 | 0 | - | 1 | 1.1 |
| Ziprasidone | 1 | 2.3 | 0 | - | 1 | 1.1 |

TABLE S3. Global Assessment of Functioning Scores by Visit for CBD and Placebo Patients (Intention to Treat Analysis Set)

| Visit | Global Assessment of Functioning | | | | | | | | | | |
|-------------------------------|----------------------------------|-------|----------------------|------|-------------------|-------|----------------------|------|----------------------|-----------|--------|
| | Cannabidiol (n=42) | | | | Placebo (n=44) | | | | Analysis | | |
| | Score | | Change from Baseline | | Score | | Change from Baseline | | Treatment Difference | | |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | Difference | 95% CI | p |
| Visit 1 (baseline) | 53.2 | 10.53 | NA | NA | 51.7 | 10.60 | NA | NA | | | |
| Visit 2 | 55.7 ^a | 9.27 | 2.4 ^a | 3.93 | 52.1 ^b | 10.68 | 0.8 ^b | 2.8 | | | |
| Visit 3 | 58.0 ^a | 9.60 | 4.8 ^a | 5.92 | 55.1 ^c | 10.06 | 3.9 ^c | 4.67 | | | |
| End of treatment ^d | 60.8 | 11.85 | 7.8 | 9.48 | 56.7 | 10.62 | 4.8 | 6.94 | 3.0 | -0.4, 6.4 | 0.0839 |

^a n=40; ^b n=43; ^c n=42; ^d Visit 4 or withdrawal

TABLE S4. Change in BACS Domain Scores by Treatment Group (Intention To Treat Analysis Set)

| Domain | Range | Cannabidiol | | | | Placebo | | | | Analysis | | |
|--|-------|--------------------------|-------|---|------|--------------------------|-------|---|-------|-------------------------|-------------|-------|
| | | Baseline Value (n=42) | | Change to End of Treatment (n=41) | | Baseline Value (n=44) | | Change to End of Treatment (n=44) | | Treatment Difference | 95% CI | p |
| | | Mean | SD | Mean | SD | Mean | SD | Mean | SD | | | |
| BACS composite score | N/A | 32.21 | 6.04 | 3.48 | 3.03 | 32.91 | 7.16 | 2.14 | 3.44 | 1.31 | -0.10, 2.72 | 0.068 |
| Verbal memory | 0-75 | 34.1 | 11.29 | 2.1 | 6.59 | 36.1 | 10.21 | 2.0 | 6.90 | 0.0 | -2.9, 2.9 | 0.993 |
| Working memory | 0-28 | 15.5 | 3.95 | 1.9 | 3.46 | 15.9 | 4.61 | 0.8 | 3.04 | 1.0 | -0.3, 2.3 | 0.141 |
| Motor speed | 0-100 | 61.5 | 12.99 | 6.1 | 9.82 | 61.0 | 16.60 | 2.1 | 11.74 | 4.2 | 0.1, 8.3 | 0.044 |
| Verbal fluency | > 0 | 31.3 | 10.63 | 4.6 | 6.48 | 35.4 | 10.72 | 3.7 | 6.64 | 0.4 | -2.5, 3.2 | 0.806 |
| Attention and speed information processing | 0-110 | 37.6 | 11.44 | 4.2 | 6.78 | 35.6 | 12.73 | 3.7 | 8.85 | 0.9 | -2.4, 4.2 | 0.592 |
| Executive functions | 0-22 | 13.3 | 4.69 | 2.0 | 4.07 | 13.4 | 4.87 | 0.6 | 4.45 | 1.4 | -0.1, 3.0 | 0.068 |

BACS=Brief Assessment of Cognition in Schizophrenia.