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Novartis CTRD Results Template

Sponsor Novartis
Generic Drug Name AQW051
Therapeutic Area of Trial L-dopa induced dyskinesia in Parkinson's patients
Approved Indication Investigational
Protocol Number CAQW051A2209
Title A multi-centre, randomized, double-blind, placebo-controlled, parallel-group, multiple oral dose study to assess the efficacy, safety and tolerability of AQW051 in reducing L-dopa induced dyskinesias in Parkinson's patients with moderate to severe L-dopa induced dyskinesias
Phase of Development Phase II
Study Start/End Dates 15-Sep-2011 to 21-Feb-2013
Study Design/Methodology This was an exploratory, multi-center, double-blind, randomized, placebo-controlled, parallel group, multiple-dose Proof-of-Concept study in PD-LID patients of moderate to severe severity. The study population comprised of male or female Parkinson's disease patients with L-dopa induced dyskinesia of moderate or severe intensity.
Centres 28 Centers, USA (7), France (11), Germany (8), Italy (2)

Publication

None

Outcome measures

Primary outcome measures(s)

- To assess the anti-dyskinetic efficacy of multiple doses of AQW051 in Parkinson's patients with moderate to severe L-dopa induced dyskinesias using the modified Abnormal Involuntary Movement Scale (mAIMS).
- To assess the anti-parkinsonian effect of multiple doses of AQW051 in combination with L-dopa in Parkinson's patients with moderate to severe L-dopa induced dyskinesias using the Unified Parkinson's Disease Rating Scale (UPDRS) – part III.
- To assess the safety and tolerability of multiple doses of AQW051 in combination with L-dopa in Parkinson's patients with moderate to severe L-dopa induced dyskinesias.

Secondary outcome measures(s)

- Lang-Fahn Activities of Daily Living Dyskinesia Scale (LFADLDS) : change from baseline to day 28
- UPDRS(32-33): change from baseline to day 28
- Track-PD: change from baseline to day 28
- Cogstate: change from baseline to day 28
- Pharmacokinetics: blood collection at:
- Days 1, 8, 16, 21 (pre-dose sample collected only from patients who took dose in the clinics)
- Day 28 (pre-dose and 1,3,5,8, and 12h post dose
- Day 32 (pre and immediately post efficacy assessment)

Test Product (s), Dose(s), and Mode(s) of Administration

50 mg AQW051 (2 oral capsules each 25mg) once each morning for 28 days
10 mg AQW051 (2 oral capsules each 5mg) once each morning for 28 days
placebo (2 oral capsules) once each morning for 28 days

Statistical Methods

The modified Abnormal Involuntary Movement Scale (mAIMS) consists of 6 separate items (face, neck and trunk, and four limbs). Each item was rated as 0, 1, 2, 3, or 4; higher values correspond to worse disease status. A sum score, ranging from 0 to 24 points, was calculated and this was one of two the primary target variables in this study.

mAIMS was performed in the morning 1 hr post L-dopa dose and in the afternoon at a patient specific timepoint. The mean of these two values (mean sum score) was used in the calculation of changes from baseline, summary statistics and statistical analyses.

The Unified Parkinson's Disease Rating Scale (UPDRS) part III consisted of 14 separate items (UPDRS items 18-31). Each item was rated 0, 1, 2, 3 or 4; more points corresponded to worse disease status. A sum score, ranging from 0 to 108 points, was calculated and this sum score was the second primary endpoint in this study.

UPDRS part III was performed in the morning 1 hr post L-dopa dose and in the afternoon at a patient specific timepoint. The mean of these two values (mean sum score) was used in the calculation of changes from baseline, summary statistics and statistical analyses.

An analysis of covariance (ANCOVA) was performed for the statistical evaluation of the two primary endpoints, mAIMS mean sum score and UPDRS part III mean sum score. The absolute change from baseline (day -2) to day 28 was used as the outcome measure. The statistical model included treatment group as a fixed factor and the respective baseline value as a continuous covariate. The effect over placebo was estimated within this model for each active dose using a Dunnett adjustment. No further adjustment was applied in this study. Least square means (LSmeans), p-values and two-sided 95% confidence intervals were presented.

If the two-sided 95% confidence interval for one or both of the two primary endpoints at day 28 did not include zero this was interpreted as a strong signal for a beneficial drug effect.

Although there was no evidence of violation of the MAR assumption the analyses of the main variables were also performed under the last observation carried forward (LOCF) method, in order to investigate possible missing data effects.

The two sum scores (mAIMS and UPDRS part III) were also summarized descriptively and their time course displayed graphically by treatment over time (days). Further, an appropriate linear mixed effects model for repeated measurements, including data from day 1 to day 28, helped determine any differences between treatment profiles over time. The absolute change from baseline (day -2) to day 28 was used as the outcome measure. The statistical model included subjects as a random factor, treatment as a fixed factor, visit as a repeated factor (fitted using an unstructured covariance matrix), the visit by treatment interaction and the respective baseline value as a continuous covariate. LSmeans, p-values and two-sided 95% confidence intervals were presented for each visit.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion criteria:

1. Male and female, non-smoking patients between 30 and 85 years of age (both inclusive).
2. Written informed consent had to be obtained before any assessment is performed.
3. Patients with idiopathic Parkinson's disease diagnosed by UK Parkinson's disease Society Brain Bank criteria.
4. Patients with L-dopa induced dyskinesia greater than 20% (UPDRS item of 32, rating ≥1) of moderate to severe (complete disabling) intensity (UPDRS item 33 rating ≥ 2).
5. Patients with dyskinesias for at least 3 months before randomization.
6. Patients had to be on L-dopa treatment for at least 3 years prior to randomization and the L-dopa treatment had to be stable for at least 1 month prior to randomization (i.e. the total daily dose and dosing regimen could vary among patients but had to be stable for individual patients). Other concomitant anti-parkinsonian medication (e.g. pramipexole, cabergoline, ropinirole) was allowed but the total daily dose and dosing regimen had to be stable for at least one month prior to randomization.
7. Patients treated with amantadine, antidepressants (except as indicated in Appendix 16.1.1-Protocol-Appendix 3), and/or benzodiazepines were allowed to enter the study provided that they were on a stable regimen for at least 4 weeks prior to randomization.
8. Other than related to Parkinson's disease, patients had to be in good health as determined by past medical history, physical examination, vital signs, electrocardiogram, and routine laboratory tests (hematology, biochemistry, and urinalysis) at screening and baseline.
9. Patients had to weigh at least 45 kg to participate in the study, and had a body mass index (BMI) within the range of 18 - 32 kg/m^2. See (Appendix 16.1.1-Protocol-Appendix 5) of this protocol for BMI ranges.
10. Able to communicate well with the investigator, to understand and comply with the requirements of the study.

Exclusion criteria

1. Patients with a prior surgery for Parkinson's disease (e.g. pallidotomy).
2. Patients with a Hoehn and Yahr score of 5 when 'off'.
3. Patients with atypical Parkinson's disease (Progressive Supranuclear Palsy (PSP), Multi Systemic Atrophy (MSA).
4. Patients who were under deep brain stimulation.
5. Patients with cognitive impairment (MMSE score of less than 24).
6. Patients with a presence of psychosis, confusional states and/or repeated hallucinations.
7. Patients who participated in an anti-dyskinetic clinical study in which drugs were administered within 3 months prior to randomization, or longer if required by local regulations, and any other limit on participation based on local regulations.
8. Patients who received neuroleptics or antipsychotics during 2 months before randomization.
9. Use of other investigational drugs at the time of enrollment, or within 30 days or 5 half-lives of enrollment, whichever was longer; or longer if required by local regulations, and for any other limitation of participation in an investigational trial based on local regulations.
10. History of hypersensitivity to any of the study drugs or to drugs of similar chemical classes.
11. History of seizures.
12. Patients using (or had used within 5 half-lives prior to first treatment with AQW051) concomitant medication that are strong inhibitors of CYP3A4 and CYP1A2 (See (Appendix 16.1.1-Protocol-Appendix 3) for a list of medication and food that were not allowed during the study).
13. A history or presence of clinically significant ECG abnormalities at Screening or Baseline.
14. History of malignancy of any organ system (other than localized basal cell carcinoma of the skin), treated or untreated, within the past 5 years, regardless of whether there was evidence of local recurrence or metastases.
15. Pregnant or nursing (lactating) women.
16. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, had to use effective contraception during the study. Effective contraception was defined as either

- Barrier method: Condom or Occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/vaginal suppository

Spermicides alone were not a barrier method of contraception and should not be used alone.
The following methods were considered more effective than the barrier method and were also acceptable:

- Total abstinence: When this is in line with the preferred and usual lifestyle of the subject. [Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception].
- Female sterilization: have had surgical bilateral oophorectomy (with or without hysterectomy) or tubal ligation at least six weeks before taking study treatment. In case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment
- Male partner sterilization (with the appropriate post-vasectomy documentation of the absence of sperm in the ejaculate). [For female subjects on the study, the vasectomised male partner should be the sole partner for that subject].
- Use of established oral, injected or implanted hormonal methods of contraception**,** intrauterine device (IUD) or intrauterine system (IUS).
- Women are considered post-menopausal and not of child bearing potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. age appropriate, history of vasomotor symptoms) or have had surgical bilateral oophorectomy (with or without hysterectomy) or tubal ligation at least six weeks ago. In the case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment is she considered not of child bearing potential.

17. Smokers (use of tobacco products in the previous 3 months). Urine cotinine levels were measured during screening and at baseline for all subjects. Smokers were defined as any subject who reported tobacco use and/or who had a urine cotinine ≥ 500 ng/mL.
18. Donation or loss of 400 ml or more of blood within eight (8) weeks prior to initial dosing, or longer if required by local regulation.
19. Significant illness within two (2) weeks prior to initial dosing.
20. Recent (within the last three [3] years) and/or recurrent history of autonomic dysfunction (e.g., recurrent episodes of fainting, palpitations, etc).
21. Recent (within the last three [3] years) and/or recurrent history of acute or chronic bronchospastic disease (including asthma and chronic obstructive pulmonary disease, treated or not treated).
22. Any surgical or medical condition which significantly altered the absorption, distribution, metabolism, or excretion of drugs, or which jeopardized the subject in case of participation in the study. The Investigator made this determination in consideration of the subject's medical history and/or clinical or laboratory evidence.
23. History or presence of impaired renal function as indicated by clinically significantly abnormal creatinine or BUN and/or urea values, or abnormal urinary constituents (e.g., albuminuria).
24. Evidence of urinary obstruction or difficulty in voiding at screening.
25. History of immunodeficiency diseases, including a positive HIV (ELISA and Western blot) test result.
26. A positive Hepatitis B surface antigen (HBsAg) or Hepatitis C test result.
27. History of drug or alcohol abuse within the 12 months prior to dosing, or evidence of such abuse as indicated by the laboratory assays conducted during screening or baseline.

Participant Flow

Subject disposition - n (%) of subjects

Disposition reason	AQW051 50 mg N=24 n (%)	AQW051 10 mg N=24 n (%)	Placebo N=23 n (%)	Total N=71 n (%)
Completed	21 (87.5)	23 (95.8)	23 (100.0)	67 (94.4)
Discontinued	3 (12.5)	1 (4.2)	0 (0.0)	4 (5.6)
- Adverse Event(s)	1 (4.2)	1 (4.2)	0 (0.0)	2 (2.8)
- Patient withdrew consent	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
- Administrative problems	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)

Baseline Characteristics

Demographic summary by treatment group

		AQW051 50 mg N=24	AQW051 10 mg N=24	Placebo N=23	Total N=71
Age(years)	Mean(SD)	65.5 (10.26)	64.2 (8.30)	63.3 (10.01)	64.4 (9.46)
	Median	65.0	64.0	65.0	65.0
	Range	44, 83	47, 79	45, 81	44, 83
Sex-n(%)	Male	15 (62.5%)	11 (45.8%)	13 (56.5%)	39 (54.9%)
	Female	9 (37.5%)	13 (54.2%)	10 (43.5%)	32 (45.1%)
Race-n(%)	Caucasian	23 (95.8%)	22 (91.7%)	23 (100.0%)	68 (95.8%)
	Asian	0 (0.0%)	1 (4.2%)	0 (0.0%)	1 (1.4%)
	Other	1 (4.2%)	1 (4.2%)	0 (0.0%)	2 (2.8%)
Ethnicity-n(%)	Hispanic/Latino	0 (0.0%)	3 (12.5%)	1 (4.3%)	4 (5.6%)
	Indian (India subc)	0 (0.0%)	1 (4.2%)	0 (0.0%)	1 (1.4%)
	Other	24 (100.0%)	20 (83.3%)	21 (91.3%)	65 (91.5%)
	Unknown	0 (0.0%)	0 (0.0%)	1 (4.3%)	1 (1.4%)
Weight (kg)	Mean(SD)	73.19 (15.811)	70.71 (12.622)	71.65 (14.462)	71.85 (14.188)
	Median	74.50	69.20	76.00	72.30
	Range	45.0, 105.0	49.0, 101.0	48.0, 99.0	45.0, 105.0
Height (cm)	Mean(SD)	171.1 (10.72)	166.5 (9.29)	169.9 (9.74)	169.2 (9.99)
	Median	168.8	168.0	170.0	169.5
	Range	153, 194	147, 182	155, 190	147, 194
BMI (kg/m^2)	Mean(SD)	24.825 (3.8041)	25.424 (3.4286)	24.684 (3.8964)	24.982 (3.6733)
	Median	25.350	25.625	23.720	25.090
	Range	16.71, 31.92	18.73, 31.88	19.57, 35.01	16.71, 35.01
L-dopa equivalent dose (mg)	Mean(SD)	919.6 (523.00)	681.7 (389.49)	767.4 (368.00)	789.9 (438.44)
	Median	750.0	550.0	750.0	700.0
	Range	300, 2725	125, 1600	300, 2000	125, 2725
Amantadine taken	No	15 (62.5%)	20 (83.3%)	15 (65.2%)	50 (70.4%)

	Yes	9 (37.5%)	4 (16.7%)	8 (34.8%)	21 (29.6%)
PD Mild cognitive impairment (MCI)	No	9 (37.5%)	9 (37.5%)	7 (30.4%)	25 (35.2%)
	Yes	15 (62.5%)	15 (62.5%)	16 (69.6%)	46 (64.8%)

Outcome measures

Primary Outcome Result(s)

Results from analysis of change from baseline to day 28 in mAIMS mean sum score (PD analysis set)

Treatment	N	Baseline mAIMS mean sum score	LSmean for change from baseline (SE)	Difference in LSmean vs Placebo (SE)	Adjusted 95% CI	Adjusted P-value
AQW051 50 mg	19	11.30	-1.92 (0.924)	1.22 (1.278)	(-1.67, 4.12)	0.534
AQW051 10 mg	23	9.38	-3.22 (0.852)	-0.07 (1.244)	(-2.89, 2.75)	0.997
Placebo	21	11.48	-3.14 (0.887)	0 (0.0)	0 (0.0)	0 (0.0)

Results from analysis of change from baseline to day 28 in UPDRS part III mean sum score (PD analysis set)

Treatment	N	Baseline UPDRS part III mean sum score	LSmean for change from baseline (SE)	Difference in LSmean vs Placebo (SE)	Adjusted 95% CI	Adjusted P-value
AQW051 50 mg	19	14.41	-0.44 (1.413)	1.48 (1.945)	(-2.93, 5.89)	0.667
AQW051 10 mg	23	17.65	-1.32 (1.281)	0.60 (1.848)	(-3.60, 4.79)	0.928
Placebo	21	16.64	-1.92 (1.334)	0 (0.0)	(0.0)	0.0

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Summary of hematology: ABSNEU ABSEOS ABSLYM ABSBAS ABSMON
Safety analysis set

Treatment: AQW051 50mg

Visit		ABSNEU (10E9/L)	ABSEOS (10E9/L)	ABSLYM (10E9/L)	ABSBAS (10E9/L)	ABSMON (10E9/L)
SCR	n	24	24	24	24	24
	mean	4.27	0.16	1.58	0.04	0.41
	SD	1.510	0.088	0.490	0.050	0.133
	minimum	1.3	0.1	0.6	0.0	0.2
	median	4.40	0.10	1.60	0.00	0.40
	maximum	7.4	0.4	2.9	0.1	0.8
BAS-2	n	24	24	24	24	24
	mean	4.11	0.16	1.55	0.03	0.44
	SD	1.280	0.097	0.441	0.046	0.272
	minimum	1.9	0.0	0.5	0.0	0.2
	median	4.00	0.10	1.40	0.00	0.40
	maximum	7.5	0.4	2.3	0.1	1.6
DAY8	n	22	22	22	22	22
	mean	3.85	0.14	1.55	0.05	0.39
	SD	1.130	0.059	0.558	0.051	0.127
	minimum	2.0	0.1	0.6	0.0	0.2
	median	3.95	0.10	1.50	0.00	0.40
	maximum	6.4	0.3	3.2	0.1	0.8
DAY16	n	24	24	24	24	24
	mean	3.99	0.15	1.52	0.03	0.44
	SD	1.165	0.093	0.528	0.046	0.166
	minimum	1.8	0.0	0.7	0.0	0.1
	median	3.90	0.10	1.40	0.00	0.40
	maximum	6.4	0.4	3.3	0.1	0.9

Treatment: AQW051 50mg

Visit		ABSNEU (10E9/L)	ABSEOS (10E9/L)	ABSLYM (10E9/L)	ABSBAS (10E9/L)	ABSMON (10E9/L)
DAY21	n	22	22	22	22	22
	mean	3.97	0.15	1.63	0.04	0.44
	SD	1.269	0.074	0.704	0.050	0.150
	minimum	1.7	0.0	0.6	0.0	0.2
	median	3.65	0.10	1.50	0.00	0.40
	maximum	6.3	0.3	4.3	0.1	0.8
DAY28	n	20	20	20	20	20
	mean	3.89	0.15	1.53	0.03	0.41
	SD	1.379	0.076	0.583	0.047	0.112
	minimum	1.5	0.1	0.6	0.0	0.2
	median	3.75	0.10	1.50	0.00	0.40
	maximum	7.0	0.4	3.4	0.1	0.6
EOS	n	23	23	23	23	23
	mean	4.12	0.17	1.65	0.03	0.41
	SD	1.082	0.093	0.692	0.047	0.146
	minimum	1.9	0.1	0.5	0.0	0.2
	median	4.40	0.20	1.50	0.00	0.40
	maximum	5.7	0.5	4.0	0.1	0.8

Treatment: AQW051 10mg

Visit		ABSNEU (10E9/L)	ABSEOS (10E9/L)	ABSLYM (10E9/L)	ABSBAS (10E9/L)	ABSMON (10E9/L)
SCR	n	24	24	24	24	24
	mean	4.32	0.14	1.55	0.06	0.40
	SD	1.317	0.088	0.468	0.072	0.110
	minimum	2.5	0.0	0.8	0.0	0.2
	median	4.55	0.10	1.50	0.05	0.40
	maximum	8.4	0.3	3.0	0.3	0.7
BAS-2	n	24	24	24	24	24
	mean	4.33	0.16	1.53	0.03	0.38
	SD	1.593	0.071	0.532	0.044	0.117
	minimum	2.1	0.1	1.0	0.0	0.2
	median	4.00	0.15	1.35	0.00	0.40
	maximum	9.9	0.3	3.0	0.1	0.6
DAY8	n	24	24	24	24	24
	mean	4.20	0.15	1.47	0.04	0.39
	SD	1.031	0.078	0.396	0.050	0.128
	minimum	2.3	0.1	0.8	0.0	0.2
	median	4.20	0.10	1.45	0.00	0.40
	maximum	6.1	0.3	2.3	0.1	0.7
DAY16	n	22	22	22	22	22
	mean	4.39	0.15	1.53	0.03	0.40
	SD	1.529	0.096	0.403	0.048	0.111
	minimum	2.4	0.0	1.0	0.0	0.3
	median	4.00	0.10	1.45	0.00	0.40
	maximum	8.9	0.4	2.7	0.1	0.7

Treatment: AQW051 10mg

Visit		ABSNEU (10E9/L)	ABSEOS (10E9/L)	ABSLYM (10E9/L)	ABSBAS (10E9/L)	ABSMON (10E9/L)
DAY21	n	22	22	22	22	22
	mean	4.01	0.15	1.45	0.04	0.38
	SD	1.230	0.074	0.446	0.050	0.105
	minimum	2.6	0.1	0.8	0.0	0.3
	median	3.90	0.10	1.40	0.00	0.30
	maximum	7.7	0.3	2.8	0.1	0.6
DAY28	n	23	23	23	23	23
	mean	4.18	0.18	1.68	0.05	0.40
	SD	1.532	0.089	0.550	0.051	0.122
	minimum	1.8	0.1	1.2	0.0	0.2
	median	4.10	0.20	1.40	0.00	0.40
	maximum	8.3	0.4	3.5	0.1	0.6
EOS	n	24	24	24	24	24
	mean	4.50	0.16	1.48	0.03	0.41
	SD	1.908	0.088	0.438	0.048	0.142
	minimum	2.5	0.1	0.8	0.0	0.2
	median	4.05	0.10	1.40	0.00	0.40
	maximum	10.5	0.4	2.6	0.1	0.7

Treatment: Placebo

Visit		ABSNEU (10E9/L)	ABSEOS (10E9/L)	ABSLYM (10E9/L)	ABSBAS (10E9/L)	ABSMON (10E9/L)
SCR	n	23	23	23	23	23
	mean	4.60	0.13	1.68	0.04	0.41
	SD	1.237	0.103	0.473	0.050	0.108
	minimum	3.0	0.0	0.6	0.0	0.1
	median	4.00	0.10	1.70	0.00	0.40
	maximum	7.1	0.4	2.7	0.1	0.6
BAS-2	n	23	23	23	23	23
	mean	4.29	0.14	1.71	0.05	0.41
	SD	1.155	0.079	0.467	0.051	0.101
	minimum	2.4	0.0	0.9	0.0	0.2
	median	4.00	0.10	1.60	0.10	0.40
	maximum	6.3	0.3	2.5	0.1	0.6
DAY8	n	21	21	21	21	21
	mean	4.51	0.17	1.77	0.05	0.47
	SD	1.468	0.101	0.404	0.051	0.135
	minimum	2.8	0.1	1.1	0.0	0.3
	median	4.10	0.10	1.80	0.00	0.50
	maximum	8.1	0.5	2.6	0.1	0.7
DAY16	n	21	21	21	21	21
	mean	4.35	0.15	1.74	0.03	0.43
	SD	1.222	0.087	0.392	0.048	0.106
	minimum	2.3	0.0	1.1	0.0	0.2
	median	4.50	0.10	1.60	0.00	0.40
	maximum	6.8	0.3	2.4	0.1	0.6

Treatment: Placebo

Visit		ABSNEU (10E9/L)	ABSEOS (10E9/L)	ABSLYM (10E9/L)	ABSBAS (10E9/L)	ABSMON (10E9/L)
DAY21	n	23	23	23	23	23
	mean	4.35	0.16	1.83	0.04	0.45
	SD	1.314	0.084	0.464	0.050	0.131
	minimum	2.3	0.0	1.2	0.0	0.3
	median	4.10	0.20	1.70	0.00	0.40
	maximum	7.4	0.3	3.0	0.1	0.7
DAY28	n	23	23	23	23	23
	mean	3.79	0.17	1.79	0.03	0.42
	SD	1.111	0.122	0.400	0.049	0.120
	minimum	2.1	0.1	1.0	0.0	0.3
	median	3.60	0.10	1.90	0.00	0.40
	maximum	6.2	0.6	2.5	0.1	0.7
EOS	n	23	23	23	23	23
	mean	4.23	0.18	1.79	0.04	0.47
	SD	1.353	0.175	0.441	0.050	0.118
	minimum	1.5	0.0	1.2	0.0	0.3
	median	4.40	0.10	1.60	0.00	0.50
	maximum	6.6	0.8	2.7	0.1	0.8

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Summary of biochemistry: SOD POT MAG CHLOR CALC PHOS
Safety analysis set

Treatment: AQW051 50mg

Visit		SOD (mmol/L)	POT (mmol/L)	MAG (mmol/L)	CHLOR (mmol/L)	CALC (mmol/L)	PHOS (mmol/L)
SCR	n	24	24	24	24	24	24
	mean	142.3	4.32	0.851	103.9	2.273	1.093
	SD	2.48	0.293	0.0663	2.86	0.0943	0.1357
	minimum	136	3.7	0.70	97	2.05	0.85
	median	142.0	4.30	0.855	104.0	2.255	1.115
	maximum	147	4.9	0.99	108	2.48	1.34
BAS-2	n	24	24	24	24	24	24
	mean	142.2	4.35	0.850	103.8	2.309	1.081
	SD	2.93	0.416	0.0682	2.63	0.1146	0.1614
	minimum	137	3.9	0.74	99	2.11	0.88
	median	141.5	4.30	0.845	103.5	2.315	1.055
	maximum	148	5.6	1.00	110	2.60	1.42
DAY8	n	24	24	24	24	24	24
	mean	141.7	4.42	0.838	103.5	2.292	1.106
	SD	2.97	0.435	0.0593	2.70	0.1145	0.1550
	minimum	136	3.7	0.75	98	2.03	0.89
	median	141.0	4.40	0.830	103.0	2.285	1.105
	maximum	147	5.5	0.99	108	2.59	1.52
DAY16	n	24	24	24	24	24	24
	mean	141.8	4.38	0.823	103.4	2.273	1.131
	SD	2.77	0.397	0.0588	2.69	0.1149	0.1451
	minimum	137	3.9	0.70	98	1.94	0.79
	median	141.5	4.40	0.820	103.0	2.265	1.140
	maximum	148	5.6	0.96	108	2.50	1.38

Summary of biochemistry: SOD POT MAG CHLOR CALC PHOS
Safety analysis set

Treatment: AQW051 50mg

Visit		SOD (mmol/L)	POT (mmol/L)	MAG (mmol/L)	CHLOR (mmol/L)	CALC (mmol/L)	PHOS (mmol/L)
DAY21	n	22	21	22	22	22	22
	mean	142.2	4.34	0.831	103.6	2.287	1.138
	SD	2.82	0.436	0.0718	2.65	0.0912	0.1475
	minimum	137	3.7	0.67	98	2.05	0.91
	median	142.5	4.30	0.820	103.0	2.285	1.145
	maximum	147	5.5	0.97	112	2.47	1.47
DAY28	n	21	19	21	21	21	21
	mean	141.9	4.26	0.840	103.8	2.278	1.140
	SD	2.70	0.332	0.0489	2.96	0.1048	0.1790
	minimum	137	3.7	0.75	98	2.09	0.94
	median	142.0	4.30	0.830	104.0	2.280	1.080
	maximum	148	4.9	0.94	111	2.47	1.52
EOS	n	23	23	23	23	23	23
	mean	141.8	4.32	0.831	103.4	2.275	1.111
	SD	2.77	0.424	0.0447	2.73	0.0884	0.1670
	minimum	135	3.6	0.74	98	2.05	0.78
	median	142.0	4.30	0.830	103.0	2.300	1.120
	maximum	146	5.4	0.91	108	2.45	1.45

NOVARTIS

Summary of biochemistry: SOD POT MAG CHLOR CALC PHOS
Safety analysis set

Treatment: AQW051 10mg

Visit		SOD (mmol/L)	POT (mmol/L)	MAG (mmol/L)	CHLOR (mmol/L)	CALC (mmol/L)	PHOS (mmol/L)
SCR	n	23	23	23	23	23	23
	mean	142.7	4.31	0.808	104.2	2.273	1.130
	SD	2.79	0.439	0.0694	3.41	0.0822	0.1594
	minimum	138	3.4	0.68	97	2.10	0.86
	median	143.0	4.30	0.820	105.0	2.260	1.110
	maximum	148	5.5	0.92	110	2.43	1.48
BAS-2	n	24	23	24	24	24	24
	mean	142.2	4.28	0.796	104.4	2.265	1.165
	SD	2.65	0.397	0.0636	2.89	0.0856	0.1925
	minimum	138	3.3	0.69	99	2.11	0.85
	median	142.0	4.30	0.800	104.5	2.265	1.165
	maximum	147	5.0	0.91	110	2.42	1.62
DAY8	n	24	24	24	24	24	24
	mean	142.0	4.38	0.790	104.6	2.278	1.173
	SD	2.40	0.527	0.0577	2.86	0.0980	0.1880
	minimum	137	3.5	0.67	100	2.12	0.92
	median	142.5	4.30	0.785	105.0	2.280	1.135
	maximum	146	6.0	0.90	110	2.46	1.73
DAY16	n	24	24	24	24	24	24
	mean	142.8	4.28	0.802	105.0	2.268	1.156
	SD	2.49	0.432	0.0626	2.98	0.0914	0.1708
	minimum	137	3.5	0.70	99	2.13	0.78
	median	143.0	4.30	0.805	105.0	2.260	1.185
	maximum	148	5.3	0.91	110	2.52	1.50

Summary of biochemistry: SOD POT MAG CHLOR CALC PHOS
Safety analysis set

Treatment: AQW051 10mg

Visit		SOD (mmol/L)	POT (mmol/L)	MAG (mmol/L)	CHLOR (mmol/L)	CALC (mmol/L)	PHOS (mmol/L)
DAY21	n	23	22	23	23	23	23
	mean	142.4	4.36	0.804	104.4	2.258	1.191
	SD	2.33	0.349	0.0623	3.00	0.0840	0.1448
	minimum	139	3.7	0.69	97	2.11	0.83
	median	142.0	4.40	0.810	104.0	2.230	1.230
	maximum	149	5.2	0.90	110	2.41	1.39
DAY28	n	23	22	23	23	23	23
	mean	143.0	4.26	0.804	105.3	2.261	1.147
	SD	2.44	0.367	0.0670	2.88	0.0917	0.1918
	minimum	139	3.4	0.65	100	2.10	0.81
	median	143.0	4.20	0.800	105.0	2.260	1.110
	maximum	148	5.3	0.91	110	2.50	1.54
EOS	n	24	23	24	24	24	24
	mean	142.6	4.35	0.795	105.3	2.251	1.168
	SD	2.38	0.399	0.0593	3.07	0.0749	0.2379
	minimum	138	3.6	0.69	100	2.04	0.69
	median	142.0	4.30	0.800	106.0	2.275	1.205
	maximum	148	5.3	0.91	112	2.35	1.86

NOVARTIS

Summary of biochemistry: SOD POT MAG CHLOR CALC PHOS
Safety analysis set

Treatment: Placebo

Visit		SOD (mmol/L)	POT (mmol/L)	MAG (mmol/L)	CHLOR (mmol/L)	CALC (mmol/L)	PHOS (mmol/L)
SCR	n	23	23	23	23	23	23
	mean	141.8	4.34	0.809	103.1	2.267	1.220
	SD	2.89	0.351	0.0687	3.36	0.0871	0.0860
	minimum	134	3.5	0.60	93	2.11	1.01
	median	142.0	4.40	0.810	103.0	2.240	1.230
	maximum	147	5.1	0.91	109	2.43	1.35
BAS-2	n	23	23	23	23	23	23
	mean	141.2	4.35	0.820	103.4	2.266	1.203
	SD	3.04	0.364	0.0739	3.24	0.0983	0.1336
	minimum	132	3.5	0.63	94	2.08	0.93
	median	142.0	4.30	0.810	103.0	2.270	1.210
	maximum	146	5.2	0.95	108	2.45	1.59
DAY8	n	23	23	23	23	23	23
	mean	141.3	4.31	0.823	103.5	2.278	1.143
	SD	3.35	0.405	0.0707	3.58	0.0895	0.1663
	minimum	130	3.7	0.60	92	2.13	0.76
	median	142.0	4.20	0.810	105.0	2.280	1.170
	maximum	146	5.2	0.93	108	2.45	1.37
DAY16	n	22	22	22	22	22	22
	mean	141.6	4.36	0.806	103.9	2.257	1.136
	SD	2.89	0.305	0.0776	2.75	0.0764	0.2522
	minimum	132	3.8	0.54	96	2.14	0.66
	median	142.0	4.40	0.805	105.0	2.265	1.095
	maximum	145	4.9	0.91	108	2.39	2.02

Summary of biochemistry: SOD POT MAG CHLOR CALC PHOS
Safety analysis set

Treatment: Placebo

Visit		SOD (mmol/L)	POT (mmol/L)	MAG (mmol/L)	CHLOR (mmol/L)	CALC (mmol/L)	PHOS (mmol/L)
DAY21	n	23	23	23	23	23	23
	mean	141.6	4.31	0.812	103.7	2.269	1.172
	SD	3.50	0.345	0.0660	3.37	0.0887	0.1220
	minimum	129	3.7	0.61	93	2.12	0.94
	median	142.0	4.30	0.820	105.0	2.250	1.190
	maximum	146	5.0	0.95	108	2.42	1.40
DAY28	n	23	23	23	23	23	23
	mean	141.7	4.29	0.804	103.9	2.273	1.215
	SD	3.72	0.359	0.0679	3.58	0.1136	0.1585
	minimum	129	3.6	0.58	91	2.05	0.81
	median	142.0	4.30	0.810	104.0	2.280	1.230
	maximum	148	5.1	0.88	109	2.48	1.56
EOS	n	23	23	23	23	23	23
	mean	141.7	4.26	0.793	103.3	2.271	1.159
	SD	2.99	0.361	0.0727	3.07	0.1036	0.1250
	minimum	131	3.7	0.57	95	2.07	0.72
	median	142.0	4.30	0.790	104.0	2.260	1.180
	maximum	145	5.0	0.91	108	2.43	1.30

NOVARTIS

Summary of biochemistry: CREA UREA UACID ALB TPROT GLUC
Safety analysis set

Treatment: AQW051 50mg

Visit		CREA (umol/L)	BUN (mmol/L)	UACID (umol/L)	ALB (g/L)	TPROT (g/L)	GLUC (mmol/L)
SCR	n	24	24	24	24	24	24
	mean	80.1	6.86	276.1	43.7	66.7	5.256
	SD	15.48	1.789	86.13	2.44	3.60	0.5848
	minimum	50	3.9	119	36	58	4.30
	median	77.0	6.80	295.0	44.0	67.0	5.300
	maximum	114	10.8	488	48	73	6.55
BAS-2	n	24	24	24	24	24	24
	mean	82.3	7.30	278.8	44.3	67.9	5.487
	SD	19.43	1.735	88.01	2.37	3.28	0.8890
	minimum	55	4.8	161	39	63	4.50
	median	81.0	7.10	285.0	44.0	68.0	5.350
	maximum	145	12.1	446	50	75	7.66
DAY8	n	24	24	24	24	24	24
	mean	83.9	7.17	270.4	44.3	68.0	5.388
	SD	19.17	1.886	84.39	2.35	3.36	0.7887
	minimum	49	4.3	143	38	62	3.60
	median	82.0	6.85	275.0	45.0	68.0	5.350
	maximum	132	11.1	440	48	77	6.90
DAY16	n	24	24	24	24	24	24
	mean	84.1	7.30	275.6	43.8	67.1	5.572
	SD	27.06	2.161	91.22	2.73	2.89	0.8966
	minimum	48	4.2	120	38	62	4.30
	median	78.0	6.95	285.0	44.0	66.5	5.400
	maximum	186	13.3	440	50	74	7.88

Summary of biochemistry: CREA UREA UACID ALB TPROT GLUC
Safety analysis set

Treatment: AQW051 50mg

Visit		CREA (umol/L)	BUN (mmol/L)	UACID (umol/L)	ALB (g/L)	TPROT (g/L)	GLUC (mmol/L)
DAY21	n	22	22	22	22	22	22
	mean	82.4	6.96	267.2	44.0	67.6	5.104
	SD	21.63	1.909	91.79	2.02	3.23	1.0299
	minimum	50	3.5	113	39	63	3.40
	median	79.0	6.15	265.0	44.0	68.0	4.900
	maximum	146	10.6	464	47	76	7.16
DAY28	n	21	21	21	21	21	21
	mean	82.0	6.88	268.2	43.7	67.0	5.678
	SD	24.83	2.340	102.68	1.79	3.91	1.0315
	minimum	48	4.1	130	39	61	4.00
	median	79.0	6.40	250.0	44.0	66.0	5.400
	maximum	174	12.8	460	47	75	8.60
EOS	n	23	23	23	23	23	23
	mean	79.8	6.98	265.7	43.5	66.5	5.917
	SD	17.02	1.819	87.46	2.19	3.16	1.3669
	minimum	47	3.8	130	38	61	4.00
	median	77.0	7.00	250.0	43.0	66.0	5.600
	maximum	126	11.1	410	48	72	10.30

NOVARTIS

Summary of biochemistry: CREA UREA UACID ALB TPROT GLUC
Safety analysis set

Treatment: AQW051 10mg

Visit		CREA (umol/L)	BUN (mmol/L)	UACID (umol/L)	ALB (g/L)	TPROT (g/L)	GLUC (mmol/L)
SCR	n	23	23	23	23	23	23
	mean	73.0	7.07	251.0	43.8	67.7	5.476
	SD	12.43	2.000	54.05	1.85	2.84	0.9337
	minimum	52	4.4	160	41	62	3.90
	median	74.0	6.40	250.0	44.0	67.0	5.300
	maximum	94	12.2	340	48	74	8.30
BAS-2	n	24	24	24	24	24	24
	mean	73.5	7.15	244.6	43.5	66.7	5.986
	SD	13.69	1.895	48.27	1.86	3.70	1.5915
	minimum	47	5.4	130	40	58	4.30
	median	74.0	6.55	250.0	44.0	67.0	5.750
	maximum	101	12.8	320	46	72	12.20
DAY8	n	24	24	24	24	24	24
	mean	72.1	6.97	236.4	43.7	67.1	5.635
	SD	14.59	1.658	56.65	1.81	2.88	1.2391
	minimum	46	4.6	110	39	62	4.20
	median	76.0	6.75	235.0	44.0	67.0	5.400
	maximum	96	11.0	350	47	73	10.70
DAY16	n	24	24	24	24	24	23
	mean	72.8	6.95	239.3	43.9	66.9	5.693
	SD	13.35	1.621	55.56	1.95	2.89	1.8895
	minimum	47	4.2	120	41	61	4.10
	median	74.0	6.85	237.0	43.0	66.5	5.300
	maximum	94	11.5	330	49	73	13.70

Treatment: AQW051 10mg

Visit		CREA (umol/L)	BUN (mmol/L)	UACID (umol/L)	ALB (g/L)	TPROT (g/L)	GLUC (mmol/L)
DAY21	n	23	23	23	23	23	23
	mean	74.4	6.95	241.4	43.3	66.8	5.844
	SD	16.65	1.312	54.75	1.61	2.68	1.6157
	minimum	51	4.8	140	40	61	3.90
	median	74.0	6.90	250.0	43.0	68.0	5.600
	maximum	103	10.5	340	46	71	9.30
DAY28	n	23	23	23	23	23	23
	mean	73.9	7.12	246.6	43.4	66.9	5.703
	SD	13.74	1.827	61.93	2.29	3.62	1.4871
	minimum	53	4.2	130	40	61	3.70
	median	70.0	6.70	250.0	44.0	66.0	5.500
	maximum	102	12.3	370	49	76	11.40
EOS	n	24	24	24	24	24	24
	mean	73.7	7.08	245.6	43.4	66.3	5.663
	SD	13.94	1.547	51.37	1.95	2.99	1.5768
	minimum	50	5.4	170	40	61	3.40
	median	74.5	6.30	240.0	43.0	66.0	5.450
	maximum	95	10.4	360	48	75	11.20

NOVARTIS

Summary of biochemistry: CREA UREA UACID ALB TPROT GLUC
Safety analysis set

Treatment: Placebo

Visit		CREA (umol/L)	BUN (mmol/L)	UACID (umol/L)	ALB (g/L)	TPROT (g/L)	GLUC (mmol/L)
SCR	n	23	23	23	23	23	23
	mean	70.0	6.68	280.2	44.0	68.2	5.477
	SD	13.92	1.570	86.30	1.81	3.59	0.9205
	minimum	51	3.6	172	40	62	3.90
	median	70.0	6.40	260.0	44.0	69.0	5.160
	maximum	102	10.4	452	48	74	7.94
BAS-2	n	23	23	23	22	23	23
	mean	70.2	6.62	269.1	43.7	68.0	5.895
	SD	13.00	1.771	82.07	1.78	3.62	1.2601
	minimum	52	3.3	150	40	61	4.50
	median	70.0	6.40	240.0	43.5	68.0	5.400
	maximum	100	10.5	404	46	75	8.55
DAY8	n	23	23	23	23	23	23
	mean	72.0	6.16	277.5	44.3	68.6	5.541
	SD	16.19	1.591	85.83	2.16	3.75	1.4443
	minimum	44	2.8	160	41	62	3.40
	median	72.0	6.50	240.0	44.0	69.0	5.100
	maximum	105	9.2	470	48	76	10.10
DAY16	n	22	22	22	22	22	22
	mean	72.0	6.68	278.9	43.8	67.8	5.520
	SD	14.98	1.778	81.32	2.58	3.38	1.1034
	minimum	43	3.0	180	39	60	3.70
	median	72.0	7.00	265.0	44.0	68.0	5.500
	maximum	94	9.3	440	49	75	8.60

Summary of biochemistry: CREA UREA UACID ALB TPROT GLUC
Safety analysis set

Treatment: Placebo

Visit		CREA (umol/L)	BUN (mmol/L)	UACID (umol/L)	ALB (g/L)	TPROT (g/L)	GLUC (mmol/L)
DAY21	n	23	23	23	23	23	23
	mean	71.9	6.52	271.7	44.1	68.2	5.513
	SD	14.72	1.477	79.10	2.05	3.37	1.1637
	minimum	52	3.5	167	41	63	3.30
	median	70.0	6.80	270.0	44.0	68.0	5.400
	maximum	111	8.7	420	47	78	8.50
DAY28	n	23	23	23	23	23	23
	mean	70.9	6.25	268.3	43.7	67.7	5.678
	SD	15.93	1.460	78.83	2.58	4.68	1.7207
	minimum	49	4.0	161	38	58	4.20
	median	70.0	6.40	250.0	44.0	67.0	5.300
	maximum	100	8.8	420	49	78	12.80
EOS	n	23	23	23	23	23	23
	mean	70.1	6.40	259.2	43.9	67.8	5.176
	SD	14.03	1.649	76.48	2.34	3.42	0.9651
	minimum	51	3.3	161	38	60	2.50
	median	68.0	6.50	240.0	44.0	68.0	5.200
	maximum	104	9.8	410	48	76	6.80

NOVARTIS

Summary of biochemistry: TBIL DBIL IBIL SGOT SGPT GGT ALKPHS
Safety analysis set

Treatment: AQW051 50mg

Visit		TBIL (umol/L)	DBIL (umol/L)	IBIL (umol/L)	SGOT (U/L)	SGPT (U/L)	GGT (U/L)	ALKPHS (U/L)
SCR	n	24	0	0	24	24	24	24
	mean	8.8			19.5	15.2	31.2	75.9
	SD	5.79			5.28	8.86	37.54	19.60
	minimum	3			12	7	7	29
	median	7.0			19.5	13.0	17.0	71.5
	maximum	24			36	52	164	119
BAS-2	n	24	1	1	24	23	24	24
	mean	9.1	11.0	26.0	22.4	16.9	41.8	79.1
	SD	7.68			10.25	11.92	55.73	20.76
	minimum	3	11	26	13	5	7	33
	median	6.5	11.0	26.0	20.5	13.0	18.0	75.5
	maximum	37	11	26	63	58	206	129
DAY8	n	24	0	0	24	24	24	24
	mean	9.1			21.2	16.4	36.8	78.5
	SD	5.83			6.96	10.19	43.44	20.94
	minimum	4			11	4	6	30
	median	7.5			20.5	13.0	20.5	75.0
	maximum	29			37	52	184	122
DAY16	n	24	1	1	24	24	24	24
	mean	9.1	12.0	37.0	20.9	16.2	38.8	77.1
	SD	9.37			6.59	10.54	59.93	24.13
	minimum	3	12	37	11	5	6	33
	median	6.5	12.0	37.0	20.0	14.0	20.0	74.5
	maximum	49	12	37	37	57	289	154

Summary of biochemistry: TBIL DBIL IBIL SGOT SGPT GGT ALKPHS
Safety analysis set

Treatment: AQW051 50mg

Visit		TBIL (umol/L)	DBIL (umol/L)	IBIL (umol/L)	SGOT (U/L)	SGPT (U/L)	GGT (U/L)	ALKPHS (U/L)
DAY21	n	22	1	1	19	21	22	22
	mean	9.1	11.0	31.0	21.8	16.7	36.6	78.7
	SD	8.35			7.07	12.18	52.17	19.83
	minimum	3	11	31	11	7	7	52
	median	6.5	11.0	31.0	21.0	13.0	19.5	74.5
	maximum	42	11	31	40	61	237	138
DAY28	n	21	0	0	19	19	21	21
	mean	9.1			19.8	15.4	35.9	76.2
	SD	6.02			7.47	6.75	51.86	20.39
	minimum	5			11	7	6	48
	median	7.0			19.0	12.0	20.0	69.0
	maximum	27			45	34	236	140
EOS	n	23	1	1	22	23	23	23
	mean	9.0	11.0	22.0	20.6	16.5	39.3	76.7
	SD	6.60			7.96	13.13	63.36	20.75
	minimum	3	11	22	12	6	7	33
	median	7.0	11.0	22.0	18.5	12.0	18.0	74.0
	maximum	33	11	22	38	58	256	122

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Summary of biochemistry: TBIL DBIL IBIL SGOT SGPT GGT ALKPHS
Safety analysis set

Treatment: AQW051 10mg

Visit		TBIL (umol/L)	DBIL (umol/L)	IBIL (umol/L)	SGOT (U/L)	SGPT (U/L)	GGT (U/L)	ALKPHS (U/L)
SCR	n	23	0	0	22	23	23	23
	mean	6.7			19.3	15.8	31.7	79.3
	SD	3.11			3.98	5.88	33.95	19.44
	minimum	3			13	7	7	48
	median	6.0			20.0	15.0	24.0	80.0
	maximum	15			28	28	170	118
BAS-2	n	24	0	0	23	23	24	24
	mean	6.5			20.0	15.3	31.3	80.0
	SD	3.02			5.56	5.23	29.38	18.56
	minimum	3			11	6	6	47
	median	6.0			19.0	16.0	20.5	82.0
	maximum	15			30	27	128	115
DAY8	n	24	0	0	23	24	24	24
	mean	6.7			21.7	15.8	29.6	78.3
	SD	2.33			7.47	6.45	26.27	17.37
	minimum	4			10	6	6	47
	median	6.5			22.0	16.0	21.0	79.5
	maximum	12			47	28	111	107
DAY16	n	24	0	0	23	24	24	24
	mean	8.0			20.0	15.5	29.1	78.8
	SD	5.03			4.61	5.58	26.23	16.44
	minimum	4			9	7	6	48
	median	6.5			21.0	15.0	21.5	81.5
	maximum	23			29	28	117	108

Summary of biochemistry: TBIL DBIL IBIL SGOT SGPT GGT ALKPHS
Safety analysis set

Treatment: AQW051 10mg

Visit		TBIL (umol/L)	DBIL (umol/L)	IBIL (umol/L)	SGOT (U/L)	SGPT (U/L)	GGT (U/L)	ALKPHS (U/L)
DAY21	n	23	0	0	22	22	23	23
	mean	7.4			19.1	14.9	28.2	77.1
	SD	4.27			4.45	5.80	24.16	16.71
	minimum	3			9	7	6	49
	median	6.0			19.0	13.0	20.0	78.0
	maximum	22			26	28	101	116
DAY28	n	23	0	0	22	22	23	23
	mean	7.8			20.0	15.5	29.7	77.5
	SD	5.79			5.51	6.07	26.29	17.62
	minimum	2			11	7	7	43
	median	6.0			20.0	15.5	21.0	78.0
	maximum	29			36	28	115	117
EOS	n	24	0	0	23	23	24	24
	mean	7.5			19.5	15.2	28.4	77.1
	SD	3.02			4.07	5.75	25.89	17.83
	minimum	3			10	8	6	42
	median	7.0			19.0	15.0	20.5	80.5
	maximum	15			26	27	102	116

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Summary of biochemistry: TBIL DBIL IBIL SGOT SGPT GGT ALKPHS
Safety analysis set

Treatment: Placebo

Visit		TBIL (umol/L)	DBIL (umol/L)	IBIL (umol/L)	SGOT (U/L)	SGPT (U/L)	GGT (U/L)	ALKPHS (U/L)
SCR	n	23	0	0	23	23	23	23
	mean	7.1			19.4	16.1	28.2	77.3
	SD	1.89			5.12	8.92	32.56	28.25
	minimum	3			10	6	10	39
	median	7.0			19.0	15.0	19.0	75.0
	maximum	11			31	46	170	172
BAS-2	n	23	0	0	23	23	23	23
	mean	7.9			18.7	16.0	26.6	77.0
	SD	3.11			4.88	8.96	23.84	25.00
	minimum	3			11	5	10	42
	median	8.0			19.0	13.0	17.0	75.0
	maximum	15			30	39	125	162
DAY8	n	23	0	0	23	23	23	23
	mean	8.0			20.0	16.9	29.3	82.4
	SD	3.04			5.66	7.67	27.26	26.62
	minimum	4			13	7	10	42
	median	7.0			19.0	17.0	19.0	79.0
	maximum	15			37	37	125	181
DAY16	n	22	0	0	22	22	22	22
	mean	7.3			19.5	16.0	25.7	79.8
	SD	2.53			6.03	8.71	20.08	26.24
	minimum	4			10	4	9	40
	median	7.0			18.0	13.5	18.0	77.5
	maximum	13			32	38	98	171

Summary of biochemistry: TBIL DBIL IBIL SGOT SGPT GGT ALKPHS
Safety analysis set

Treatment: Placebo

Visit		TBIL (umol/L)	DBIL (umol/L)	IBIL (umol/L)	SGOT (U/L)	SGPT (U/L)	GGT (U/L)	ALKPHS (U/L)
DAY21	n	23	0	0	23	23	23	23
	mean	7.0			19.0	16.5	25.7	78.9
	SD	2.64			4.77	9.00	22.88	28.10
	minimum	3			10	6	10	42
	median	7.0			19.0	14.0	18.0	78.0
	maximum	14			29	40	120	180
DAY28	n	23	0	0	22	23	23	23
	mean	8.0			20.6	16.6	24.5	79.0
	SD	3.52			6.37	9.08	21.07	31.50
	minimum	3			10	4	9	42
	median	7.0			20.5	13.0	18.0	75.0
	maximum	19			31	35	112	192
EOS	n	23	0	0	23	23	23	23
	mean	7.3			20.0	15.2	27.8	79.5
	SD	2.57			4.70	7.66	33.12	32.01
	minimum	3			13	4	11	39
	median	7.0			19.0	13.0	18.0	76.0
	maximum	12			34	34	172	182

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Summary of biochemistry: LDH LIPASE AMY CK TRIGLY TCHOL
Safety analysis set

Treatment: AQW051 50mg

Visit		LDH (U/L)	LIPASE (U/L)	AMY (U/L)	CK (U/L)	TRIGLY (mmol/L)	TCHOL (mmol/L)
SCR	n	24	24	24	24	24	24
	mean	168.3	39.3	60.0	133.0	1.110	4.918
	SD	30.90	20.21	24.20	85.91	0.5288	1.0006
	minimum	113	18	23	50	0.31	3.46
	median	163.5	34.0	55.5	100.5	1.040	4.660
	maximum	249	110	107	432	2.05	6.88
BAS-2	n	24	24	24	24	24	24
	mean	177.6	68.1	70.3	133.8	1.271	5.000
	SD	34.13	154.33	49.22	97.57	0.5960	1.1128
	minimum	116	19	30	52	0.32	3.11
	median	176.0	35.0	53.5	102.0	1.210	4.715
	maximum	257	790	270	483	2.53	7.03
DAY8	n	24	24	24	24	24	24
	mean	172.6	40.0	61.8	135.9	1.161	4.955
	SD	31.85	19.71	21.22	99.84	0.5902	1.1212
	minimum	103	19	22	51	0.28	3.09
	median	175.0	38.0	62.0	111.5	1.175	4.685
	maximum	230	97	96	535	2.92	7.16
DAY16	n	24	24	24	24	24	24
	mean	173.2	43.6	61.5	129.1	1.188	4.810
	SD	36.00	23.26	27.83	83.67	0.5543	1.0566
	minimum	102	18	26	52	0.44	3.32
	median	173.0	35.5	56.0	103.0	1.105	4.465
	maximum	246	105	142	436	2.46	7.27

Summary of biochemistry: LDH LIPASE AMY CK TRIGLY TCHOL
Safety analysis set

Treatment: AQW051 50mg

Visit		LDH (U/L)	LIPASE (U/L)	AMY (U/L)	CK (U/L)	TRIGLY (mmol/L)	TCHOL (mmol/L)
DAY21	n	21	22	22	22	22	22
	mean	178.0	41.8	65.8	141.6	1.327	4.878
	SD	37.02	28.96	28.38	93.07	0.8192	1.0623
	minimum	111	18	25	48	0.35	3.07
	median	168.0	34.0	57.5	110.0	0.990	4.530
	maximum	261	158	140	472	3.36	7.04
DAY28	n	19	21	21	20	21	21
	mean	169.4	39.9	66.6	136.4	1.203	5.019
	SD	35.86	22.95	30.33	137.01	0.5661	1.2168
	minimum	103	20	23	43	0.24	3.65
	median	164.0	36.0	63.0	97.0	1.120	4.490
	maximum	245	125	129	670	2.25	7.18
EOS	n	23	23	23	23	23	23
	mean	168.6	38.9	63.9	141.2	1.518	5.039
	SD	31.42	15.48	26.43	169.39	1.0063	1.0194
	minimum	114	20	24	43	0.27	3.91
	median	169.0	37.0	59.0	100.0	1.300	4.730
	maximum	224	84	117	863	4.72	7.33

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Summary of biochemistry: LDH LIPASE AMY CK TRIGLY TCHOL
Safety analysis set

Treatment: AQW051 10mg

Visit		LDH (U/L)	LIPASE (U/L)	AMY (U/L)	CK (U/L)	TRIGLY (mmol/L)	TCHOL (mmol/L)
SCR	n	23	23	23	23	23	23
	mean	184.9	34.2	63.9	128.8	1.098	5.467
	SD	38.12	16.27	20.86	46.05	0.6054	0.9301
	minimum	114	15	18	67	0.40	3.09
	median	191.0	30.0	61.0	119.0	0.960	5.400
	maximum	255	76	116	263	3.27	7.56
BAS-2	n	23	24	24	24	24	24
	mean	183.2	35.0	64.1	138.9	1.344	5.340
	SD	33.60	15.01	19.77	88.11	1.0576	0.6617
	minimum	122	16	16	55	0.54	4.24
	median	184.0	30.0	63.5	122.0	1.010	5.285
	maximum	247	68	111	426	5.57	6.85
DAY8	n	24	24	24	24	24	24
	mean	187.9	38.1	67.4	151.9	1.228	5.390
	SD	32.60	20.74	23.13	85.97	0.9474	0.7332
	minimum	126	15	17	54	0.54	4.06
	median	190.5	31.5	64.5	139.5	0.865	5.335
	maximum	253	111	106	430	4.60	7.01
DAY16	n	24	24	24	24	24	24
	mean	189.2	38.8	65.4	149.9	1.390	5.323
	SD	35.06	22.45	20.76	78.25	1.3891	0.6950
	minimum	123	15	17	67	0.50	4.17
	median	193.0	30.5	61.5	126.0	0.880	5.165
	maximum	257	111	107	386	6.81	7.32

Summary of biochemistry: LDH LIPASE AMY CK TRIGLY TCHOL
Safety analysis set

Treatment: AQW051 10mg

Visit		LDH (U/L)	LIPASE (U/L)	AMY (U/L)	CK (U/L)	TRIGLY (mmol/L)	TCHOL (mmol/L)
DAY21	n	22	23	23	22	23	23
	mean	181.3	42.7	65.4	129.8	1.335	5.256
	SD	30.84	37.19	21.44	49.75	1.1938	0.7076
	minimum	127	15	18	59	0.44	4.09
	median	182.5	33.0	63.0	117.0	1.010	5.040
	maximum	224	197	102	266	5.55	7.11
DAY28	n	22	23	23	23	23	23
	mean	180.2	38.3	66.3	184.2	1.293	5.338
	SD	31.72	19.00	22.24	272.08	1.1330	0.7716
	minimum	123	18	21	51	0.45	4.11
	median	181.0	32.0	60.0	112.0	0.960	5.230
	maximum	253	89	124	1403	5.05	7.08
EOS	n	23	24	24	24	24	24
	mean	185.2	36.3	64.3	146.5	1.266	5.210
	SD	36.27	15.70	22.34	76.36	0.8446	0.8307
	minimum	127	16	18	51	0.46	2.86
	median	185.0	33.0	60.0	128.0	1.015	5.155
	maximum	254	83	107	357	3.72	7.35

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Summary of biochemistry: LDH LIPASE AMY CK TRIGLY TCHOL
Safety analysis set

Treatment: Placebo

Visit		LDH (U/L)	LIPASE (U/L)	AMY (U/L)	CK (U/L)	TRIGLY (mmol/L)	TCHOL (mmol/L)
SCR	n	23	23	23	23	23	23
	mean	182.9	39.0	58.9	150.0	1.007	4.915
	SD	48.60	25.76	26.45	75.97	0.2620	0.7748
	minimum	81	15	34	46	0.46	3.51
	median	178.0	34.0	53.0	143.0	1.010	4.950
	maximum	322	112	162	354	1.62	6.22
BAS-2	n	23	23	23	23	23	23
	mean	178.2	44.0	62.8	119.3	1.106	4.866
	SD	43.32	46.03	37.73	67.41	0.3732	0.8291
	minimum	73	15	35	50	0.52	3.20
	median	174.0	32.0	55.0	94.0	1.000	5.040
	maximum	292	239	221	284	1.86	6.35
DAY8	n	23	23	23	23	23	23
	mean	180.3	38.0	55.7	155.3	1.132	4.809
	SD	47.43	21.05	14.51	172.93	0.4606	0.8703
	minimum	70	15	33	55	0.49	3.06
	median	177.0	37.0	54.0	116.0	1.090	4.840
	maximum	297	97	90	907	2.62	6.58
DAY16	n	22	22	22	22	22	22
	mean	186.5	38.6	58.5	139.0	1.264	4.714
	SD	62.01	21.65	18.09	106.17	0.5040	0.7083
	minimum	78	16	34	56	0.38	3.42
	median	181.5	36.0	57.5	100.5	1.255	4.630
	maximum	373	102	98	546	2.36	6.16

Summary of biochemistry: LDH LIPASE AMY CK TRIGLY TCHOL
Safety analysis set

Treatment: Placebo

Visit		LDH (U/L)	LIPASE (U/L)	AMY (U/L)	CK (U/L)	TRIGLY (mmol/L)	TCHOL (mmol/L)
DAY21	n	23	23	23	23	23	23
	mean	184.6	36.7	58.6	136.8	1.122	4.904
	SD	53.09	20.28	17.90	71.82	0.3501	0.7886
	minimum	73	15	32	48	0.44	3.43
	median	170.0	34.0	57.0	120.0	1.140	4.800
	maximum	299	115	104	302	1.84	6.62
DAY28	n	23	23	23	23	23	23
	mean	184.8	34.3	55.9	148.9	1.083	4.908
	SD	49.58	16.41	17.03	104.92	0.4584	0.8491
	minimum	84	18	33	43	0.36	3.24
	median	196.0	33.0	53.0	126.0	1.030	4.960
	maximum	282	95	89	482	2.27	6.55
EOS	n	23	23	23	23	23	23
	mean	186.7	48.3	61.3	155.3	1.127	4.759
	SD	52.79	38.13	20.53	93.19	0.3959	0.7741
	minimum	73	18	29	50	0.60	3.32
	median	179.0	37.0	58.0	145.0	1.070	4.710
	maximum	332	165	104	418	2.13	6.51

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Summary of vital signs
Safety analysis set

Treatment: AQW051 50mg

Visit		Weight (kg)	Body temp 35-37.5 (°C)	Sitting Blood pressure syst. 90-140 (mmHg)	Sitting Blood pressure dias. 50-90 (mmHg)	Sitting Pulse rate 40-90 (bpm)
DAY16	n	0	0	24	24	24
	mean			121.9	72.0	75.0
	SD			12.56	10.16	12.53
	minimum			100	52	54
	median			120.0	70.0	80.0
	maximum			150	92	103
DAY21	n	0	0	22	22	22
	mean			117.9	72.0	79.3
	SD			13.40	9.94	13.42
	minimum			95	60	54
	median			119.5	70.5	80.0
	maximum			152	93	108
DAY28	n	0	0	21	21	21
	mean			122.3	72.6	74.0
	SD			15.70	10.94	13.77
	minimum			90	56	52
	median			124.0	72.0	70.0
	maximum			150	90	109
DAY32	n	0	0	22	22	22
	mean			126.5	75.1	75.1
	SD			22.83	12.84	8.27
	minimum			101	55	63
	median			121.5	70.5	74.0
	maximum			210	100	93

Treatment: AQW051 50mg

Visit		Weight (kg)	Body temp 35-37.5 (°C)	Sitting Blood pressure syst. 90-140 (mmHg)	Sitting Blood pressure dias. 50-90 (mmHg)	Sitting Pulse rate 40-90 (bpm)
EOS	n	24	22	24	24	24
	mean	72.83	36.30	122.0	74.1	78.0
	SD	15.626	0.606	12.59	10.80	11.66
	minimum	45.0	35.0	100	58	60
	median	72.35	36.20	121.5	74.0	78.0
	maximum	105.0	37.6	143	92	103

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Treatment: AQW051 10mg

Visit		Weight (kg)	Body temp 35-37.5 (°C)	Sitting Blood pressure syst. 90-140 (mmHg)	Sitting Blood pressure dias. 50-90 (mmHg)	Sitting Pulse rate 40-90 (bpm)
SCR	n	24	22	24	24	24
	mean	70.71	36.50	124.2	75.8	77.4
	SD	12.622	0.544	13.15	9.74	7.87
	minimum	49.0	35.2	90	60	56
	median	69.20	36.50	125.5	73.0	79.5
	maximum	101.0	37.7	141	95	96
BAS-2	n	24	22	23	23	23
	mean	70.90	36.45	126.6	76.9	75.9
	SD	12.796	0.437	22.10	14.86	7.86
	minimum	49.0	35.3	99	49	59
	median	69.45	36.50	120.0	73.0	76.0
	maximum	101.0	37.4	190	111	89
DAY1	n	0	0	24	24	24
	mean			120.0	72.8	73.9
	SD			17.71	11.87	11.13
	minimum			90	55	52
	median			120.0	75.5	74.0
	maximum			150	90	100
DAY8	n	0	0	22	22	22
	mean			121.4	71.5	70.7
	SD			15.85	9.41	7.50
	minimum			94	54	57
	median			124.0	70.0	69.5
	maximum			151	90	85

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Treatment: AQW051 10mg

Visit		Weight (kg)	Body temp 35-37.5 (°C)	Sitting Blood pressure syst. 90-140 (mmHg)	Sitting Blood pressure dias. 50-90 (mmHg)	Sitting Pulse rate 40-90 (bpm)
DAY16	n	0	0	22	22	23
	mean			125.0	75.4	75.1
	SD			14.06	11.79	11.00
	minimum			105	58	54
	median			125.0	73.5	77.0
	maximum			148	110	94
DAY21	n	0	0	22	22	22
	mean			123.8	72.0	74.0
	SD			12.88	10.60	8.11
	minimum			105	48	58
	median			120.0	75.0	75.5
	maximum			152	90	86
DAY28	n	0	0	22	22	22
	mean			129.0	77.3	74.3
	SD			13.82	7.48	10.21
	minimum			101	65	52
	median			130.0	77.5	76.5
	maximum			166	96	92
DAY32	n	0	0	21	21	22
	mean			125.2	72.9	76.4
	SD			16.20	11.15	9.62
	minimum			100	58	60
	median			120.0	70.0	78.0
	maximum			155	95	94

Treatment: AQW051 10mg

Visit		Weight (kg)	Body temp 35-37.5 (°C)	Sitting Blood pressure syst. 90-140 (mmHg)	Sitting Blood pressure dias. 50-90 (mmHg)	Sitting Pulse rate 40-90 (bpm)
EOS	n	24	21	24	24	24
	mean	70.46	36.16	123.3	73.0	73.1
	SD	12.558	0.485	15.72	10.44	8.32
	minimum	48.5	35.2	95	50	55
	median	68.45	36.30	124.0	73.5	74.0
	maximum	103.0	36.9	160	91	90

Treatment: Placebo

Visit		Weight (kg)	Body temp 35-37.5 (°C)	Sitting Blood pressure syst. 90-140 (mmHg)	Sitting Blood pressure dias. 50-90 (mmHg)	Sitting Pulse rate 40-90 (bpm)
SCR	n	23	23	23	23	23
	mean	71.65	36.32	122.7	73.6	76.7
	SD	14.462	0.556	18.87	13.67	9.12
	minimum	48.0	35.0	86	50	59
	median	76.00	36.50	121.0	74.0	76.0
	maximum	99.0	37.4	155	106	95
BAS-2	n	22	22	22	22	22
	mean	71.68	36.21	123.5	73.5	77.7
	SD	14.802	0.665	21.13	15.74	11.68
	minimum	48.0	34.8	89	40	60
	median	76.65	36.25	120.0	71.5	77.5
	maximum	100.7	37.3	186	118	101
DAY1	n	0	0	23	23	23
	mean			120.4	71.2	76.0
	SD			17.64	12.77	10.15
	minimum			90	52	58
	median			120.0	70.0	76.0
	maximum			159	109	92
DAY8	n	0	0	23	23	23
	mean			119.3	71.6	74.4
	SD			19.00	13.15	9.56
	minimum			81	55	56
	median			120.0	70.0	74.0
	maximum			150	102	97

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Treatment: Placebo

Visit		Weight (kg)	Body temp 35-37.5 (°C)	Sitting Blood pressure syst. 90-140 (mmHg)	Sitting Blood pressure dias. 50-90 (mmHg)	Sitting Pulse rate 40-90 (bpm)
DAY16	n	0	0	23	23	23
	mean			123.5	73.4	75.6
	SD			18.42	10.55	10.17
	minimum			94	57	59
	median			117.0	70.0	74.0
	maximum			166	98	98
DAY21	n	0	0	23	23	23
	mean			122.0	72.4	76.5
	SD			16.60	11.00	10.80
	minimum			90	60	58
	median			124.0	70.0	77.0
	maximum			160	97	94
DAY28	n	0	0	23	23	23
	mean			124.0	71.6	74.0
	SD			15.91	7.20	9.78
	minimum			95	60	60
	median			126.0	71.0	72.0
	maximum			145	86	104
DAY32	n	0	0	23	23	23
	mean			119.6	72.4	75.7
	SD			18.09	10.78	9.91
	minimum			90	57	57
	median			120.0	70.0	76.0
	maximum			150	105	93

Treatment: Placebo

Visit		Weight (kg)	Body temp 35-37.5 (°C)	Sitting Blood pressure syst. 90-140 (mmHg)	Sitting Blood pressure dias. 50-90 (mmHg)	Sitting Pulse rate 40-90 (bpm)
EOS	n	21	22	23	23	23
	mean	70.91	36.23	124.3	73.5	75.3
	SD	13.572	0.546	13.45	10.77	14.38
	minimum	49.0	35.0	103	51	53
	median	76.00	36.30	125.0	74.0	75.0
	maximum	93.0	37.0	160	100	122

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Summary of ECG intervals
Safety analysis set

Treatment: AQW051 50mg

Visit		Heart rate (bpm)	PR interval (msec)	RR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcB interval (msec)	QTcF interval (msec)
SCR	n	24	24	24	24	24	24	24
	mean	67.3	175.6	917.3	92.2	388.6	408.0	401.2
	SD	11.17	23.52	164.64	7.14	32.45	20.93	19.46
	minimum	50	138	725	79	326	373	363
	median	70.0	173.5	854.5	90.5	392.5	409.0	401.0
	maximum	83	228	1194	104	459	446	433
BAS-2	n	24	24	24	24	24	24	24
	mean	69.4	175.7	888.5	93.2	382.5	408.4	399.2
	SD	11.65	26.91	152.21	8.91	21.83	20.52	14.07
	minimum	47	140	623	76	336	373	374
	median	70.0	168.0	856.0	93.0	384.0	412.0	399.5
	maximum	96	238	1264	117	420	444	423
DAY8	n	23	23	23	23	23	23	23
	mean	70.0	178.8	883.6	91.9	388.6	416.1	406.2
	SD	12.30	23.20	166.33	8.54	29.00	21.66	17.91
	minimum	45	143	676	74	324	371	368
	median	68.0	173.0	888.0	91.0	397.0	416.0	405.0
	maximum	89	229	1329	108	430	454	437

Summary of ECG intervals
Safety analysis set

Treatment: AQW051 50mg

Visit		Heart rate (bpm)	PR interval (msec)	RR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcB interval (msec)	QTcF interval (msec)
DAY16	n	24	24	24	24	24	24	24
	mean	71.0	175.4	860.9	94.1	382.9	413.9	403.0
	SD	9.83	26.35	122.88	7.76	27.60	15.19	15.78
	minimum	54	136	655	82	321	385	365
	median	71.0	174.0	841.0	93.0	382.5	412.0	405.0
	maximum	92	232	1114	108	426	447	429
DAY21	n	22	22	22	22	22	22	22
	mean	69.8	177.9	877.8	92.0	387.7	415.6	405.9
	SD	10.45	28.74	131.86	7.19	26.92	18.00	16.00
	minimum	53	135	661	81	343	378	369
	median	69.5	175.0	862.0	93.0	378.5	418.5	408.0
	maximum	91	242	1129	105	448	454	431
DAY28	n	21	21	21	21	21	21	21
	mean	68.9	176.4	892.4	90.0	389.7	414.3	405.7
	SD	11.35	30.03	135.52	8.23	28.37	18.39	16.88
	minimum	53	137	622	74	328	382	365
	median	67.0	169.0	893.0	90.0	392.0	416.0	407.0
	maximum	97	235	1129	107	433	447	439

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Summary of ECG intervals
Safety analysis set

Treatment: AQW051 50mg

Visit		Heart rate (bpm)	PR interval (msec)	RR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcB interval (msec)	QTcF interval (msec)
DAY32	n	22	22	22	22	22	22	22
	mean	70.0	173.6	880.0	93.6	386.3	413.5	403.9
	SD	11.89	26.35	142.03	7.41	29.76	11.28	12.82
	minimum	51	134	639	82	326	395	378
	median	67.5	170.0	891.0	95.0	392.0	411.0	406.0
	maximum	94	220	1179	107	444	442	422
EOS	n	23	23	23	23	23	23	23
	mean	71.3	175.5	863.9	91.8	381.1	412.3	401.2
	SD	12.43	27.15	144.41	6.17	26.46	16.47	13.12
	minimum	56	140	610	79	333	380	377
	median	68.0	170.0	880.0	92.0	388.0	414.0	399.0
	maximum	98	227	1073	103	423	447	419

Treatment: AQW051 10mg

Visit		Heart rate (bpm)	PR interval (msec)	RR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcB interval (msec)	QTcF interval (msec)
SCR	n	24	24	24	24	24	24	24
	mean	70.2	173.0	869.1	95.6	388.8	418.4	408.2
	SD	7.91	25.67	113.30	14.24	23.83	21.38	19.07
	minimum	48	133	707	77	341	383	369
	median	70.5	166.5	853.5	92.5	391.5	420.0	411.0
	maximum	85	252	1259	153	443	453	440
BAS-2	n	24	24	24	24	24	24	24
	mean	70.2	168.0	866.4	94.7	393.2	423.7	413.2
	SD	7.99	23.17	109.37	13.67	21.63	17.33	15.14
	minimum	50	124	725	81	361	391	388
	median	71.0	167.5	842.5	92.5	391.5	422.5	411.0
	maximum	83	239	1200	147	429	454	438
DAY8	n	24	24	24	24	24	24	24
	mean	69.2	169.3	879.0	95.5	393.7	421.0	411.5
	SD	8.25	22.17	107.37	13.09	24.65	18.54	17.55
	minimum	53	130	694	81	353	385	374
	median	69.5	174.0	862.0	94.5	397.5	421.5	410.5
	maximum	86	229	1122	149	442	466	455

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Treatment: AQW051 10mg

Visit		Heart rate (bpm)	PR interval (msec)	RR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcB interval (msec)	QTcF interval (msec)
DAY16	n	24	23	24	23	23	22	22
	mean	70.6	165.3	870.9	92.3	389.2	420.0	409.9
	SD	10.79	25.38	144.02	12.76	28.11	20.74	16.76
	minimum	47	124	624	79	338	382	376
	median	71.0	168.0	848.0	90.0	389.0	422.5	412.0
	maximum	96	236	1274	140	451	450	439
DAY21	n	23	23	23	23	23	23	23
	mean	70.8	172.7	858.9	94.8	389.7	421.4	410.4
	SD	8.32	22.19	105.33	18.86	28.07	22.18	21.32
	minimum	54	137	678	81	345	376	370
	median	73.0	173.0	827.0	92.0	387.0	419.0	409.0
	maximum	88	241	1121	177	450	460	445
DAY28	n	22	22	22	22	22	22	22
	mean	70.0	173.8	866.2	95.7	392.2	422.3	411.8
	SD	7.54	24.59	95.21	13.68	21.34	15.92	14.87
	minimum	55	120	682	80	351	388	380
	median	70.5	169.0	848.5	93.5	395.5	424.0	415.0
	maximum	88	243	1084	149	434	449	442

Treatment: AQW051 10mg

Visit		Heart rate (bpm)	PR interval (msec)	RR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcB interval (msec)	QTcF interval (msec)
DAY32	n	23	23	23	23	23	23	23
	mean	71.4	170.6	848.8	93.1	389.0	423.1	411.1
	SD	8.05	23.55	94.23	14.29	23.68	19.35	18.07
	minimum	57	127	693	77	349	380	369
	median	71.0	175.0	848.0	91.0	392.0	425.0	411.0
	maximum	87	241	1053	150	430	457	442
EOS	n	24	24	24	24	24	24	24
	mean	67.2	169.2	909.2	93.6	397.3	418.0	410.8
	SD	8.91	26.40	122.34	13.05	27.29	18.59	17.87
	minimum	52	117	694	76	354	376	377
	median	65.5	169.5	917.0	92.5	393.5	415.5	410.0
	maximum	86	236	1155	143	442	453	446

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Treatment: Placebo

Visit		Heart rate (bpm)	PR interval (msec)	RR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcB interval (msec)	QTcF interval (msec)
SCR	n	23	22	23	23	23	23	23
	mean	70.9	165.7	858.3	97.6	382.0	413.6	402.6
	SD	8.23	19.35	102.53	13.57	18.65	18.29	14.66
	minimum	55	135	706	83	352	370	376
	median	70.0	163.5	851.0	95.0	381.0	412.0	400.0
	maximum	85	205	1094	135	428	454	434
BAS-2	n	23	22	23	23	23	23	23
	mean	74.9	167.5	816.2	97.1	377.9	420.4	405.7
	SD	11.53	19.08	113.02	15.29	22.82	23.87	18.55
	minimum	58	135	593	77	343	392	382
	median	72.0	166.5	837.0	94.0	372.0	415.0	400.0
	maximum	101	205	1027	140	426	494	453
DAY8	n	23	22	23	23	23	23	23
	mean	71.5	161.8	864.3	97.4	382.4	414.2	403.0
	SD	12.47	20.70	147.36	13.92	24.94	21.62	15.75
	minimum	54	127	620	74	335	363	367
	median	73.0	159.5	827.0	97.0	379.0	413.0	401.0
	maximum	97	205	1115	137	428	468	436

Treatment: Placebo

Visit		Heart rate (bpm)	PR interval (msec)	RR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcB interval (msec)	QTcF interval (msec)
DAY16	n	23	21	23	23	23	23	23
	mean	72.8	164.0	842.0	97.2	379.8	414.6	402.4
	SD	10.97	18.66	134.35	14.37	23.27	20.48	17.30
	minimum	52	134	624	78	333	367	375
	median	73.0	161.0	818.0	96.0	384.0	412.0	398.0
	maximum	96	198	1148	142	416	454	434
DAY21	n	22	21	22	22	22	22	22
	mean	73.8	166.3	839.4	97.1	382.2	420.8	407.1
	SD	15.24	20.89	151.25	13.77	25.88	22.73	14.91
	minimum	53	135	491	83	336	384	385
	median	70.5	165.0	850.5	95.5	384.0	419.0	405.5
	maximum	122	206	1128	140	436	480	438
DAY28	n	23	22	23	23	23	23	23
	mean	70.1	169.9	870.3	98.5	389.3	419.4	408.8
	SD	10.27	16.69	111.97	13.46	19.32	22.60	16.13
	minimum	56	137	565	79	350	391	388
	median	69.0	173.0	867.0	96.0	389.0	414.0	405.0
	maximum	106	197	1072	139	429	499	452

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Summary of ECG intervals
Safety analysis set

Treatment: Placebo

Visit		Heart rate (bpm)	PR interval (msec)	RR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcB interval (msec)	QTcF interval (msec)
DAY32	n	23	22	23	23	23	23	23
	mean	73.0	162.5	852.5	96.0	382.3	417.3	404.8
	SD	15.38	19.51	155.16	12.33	26.44	23.61	16.45
	minimum	49	129	478	83	333	384	378
	median	72.0	162.0	831.0	93.0	373.0	418.0	401.0
	maximum	126	195	1224	127	428	481	441
EOS	n	23	22	23	23	22	22	22
	mean	70.7	166.5	877.0	97.8	388.2	411.0	403.1
	SD	15.06	20.41	141.94	14.42	26.23	17.25	17.32
	minimum	54	138	464	82	336	382	377
	median	67.0	161.5	901.0	93.0	385.5	407.0	399.0
	maximum	129	217	1121	143	437	457	449

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
SCR	Wish to be dead or not wake up	No	23 (95.8)	22 (91.7)	23 (100.0)
		Yes	1 (4.2)	2 (8.3)	0 (0.0)
	Non specific thoughts	No	22 (91.7)	21 (87.5)	23 (100.0)
		Yes	2 (8.3)	3 (12.5)	0 (0.0)
	Specific thoughts of method	No	2 (8.3)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	2 (8.3)	0 (0.0)
	Some intent to act, no plan	No	2 (8.3)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	2 (8.3)	0 (0.0)
	Specific plan and intent	No	2 (8.3)	2 (8.3)	0 (0.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Most severe ideation	Type 2	1 (4.2)	1 (4.2)	0 (0.0)
		Type 3	0 (0.0)	1 (4.2)	0 (0.0)
		Type 4	0 (0.0)	1 (4.2)	0 (0.0)
		Type 5	1 (4.2)	0 (0.0)	0 (0.0)
	Frequency of thoughts	Less than once a week	2 (8.3)	1 (4.2)	0 (0.0)
		Once a week	0 (0.0)	1 (4.2)	0 (0.0)

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Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
SCR	Frequency of thoughts	2-5 times a week	0 (0.0)	1 (4.2)	0 (0.0)
	Duration of thoughts	Fleeting few seconds or minutes	1 (4.2)	0 (0.0)	0 (0.0)
		Less than 1 hour/some of the time	0 (0.0)	2 (8.3)	0 (0.0)
		1-4 hours/a lot of time	0 (0.0)	1 (4.2)	0 (0.0)
		More than 8 hours/persistent or continuous	1 (4.2)	0 (0.0)	0 (0.0)
	Controllability of thoughts	Easily able to control thoughts	2 (8.3)	1 (4.2)	0 (0.0)
		Can control thoughts with little difficulty	0 (0.0)	1 (4.2)	0 (0.0)
		Can control thoughts with some difficulty	0 (0.0)	1 (4.2)	0 (0.0)
	Deterrents	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
		Deterrents definitely stopped you from attempting suicide	2 (8.3)	2 (8.3)	0 (0.0)
	Reasons	Does not apply	1 (4.2)	0 (0.0)	0 (0.0)
		Mostly to end or stop the pain	0 (0.0)	3 (12.5)	0 (0.0)
		Completely to end or stop the pain	1 (4.2)	0 (0.0)	0 (0.0)
	Made suicide attempts	No	24 (100.0)	22 (91.7)	23 (100.0)
		Yes	0 (0.0)	2 (8.3)	0 (0.0)
	Interrupted attempts	No	24 (100.0)	24 (100.0)	23 (100.0)

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
SCR	Interrupted attempts	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Aborted attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Preparatory actions	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Any suicidal behavior	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non-suicidal self-injurious behaviors	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
BAS-2	Wish to be dead or not wake up	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non specific thoughts	No	24 (100.0)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Specific thoughts of method	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Some intent to act, no plan	No	0 (0.0)	1 (4.2)	0 (0.0)

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Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
SCR	Interrupted attempts	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Aborted attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Preparatory actions	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Any suicidal behavior	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non-suicidal self-injurious behaviors	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
BAS-2	Wish to be dead or not wake up	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non specific thoughts	No	24 (100.0)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Specific thoughts of method	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Some intent to act, no plan	No	0 (0.0)	1 (4.2)	0 (0.0)

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
BAS-2	Some intent to act, no plan	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Specific plan and intent	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Most severe ideation	Type 1	0 (0.0)	1 (4.2)	0 (0.0)
	Frequency of thoughts	2-5 times a week	0 (0.0)	1 (4.2)	0 (0.0)
	Duration of thoughts	Fleeting few seconds or minutes	0 (0.0)	1 (4.2)	0 (0.0)
	Controllability of thoughts	Does not attempt to control thoughts	0 (0.0)	1 (4.2)	0 (0.0)
	Deterrents	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
	Reasons	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
	Made suicide attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Interrupted attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Aborted attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Preparatory actions	No	24 (100.0)	24 (100.0)	23 (100.0)

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Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
BAS-2	Preparatory actions	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Any suicidal behavior	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Completed suicide	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non-suicidal self-injurious behaviors	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
DAY8	Wish to be dead or not wake up	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non specific thoughts	No	24 (100.0)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Specific thoughts of method	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Some intent to act, no plan	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Specific plan and intent	No	0 (0.0)	1 (4.2)	0 (0.0)

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY8	Specific plan and intent	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Most severe ideation	Type 1	0 (0.0)	1 (4.2)	0 (0.0)
	Frequency of thoughts	2-5 times a week	0 (0.0)	1 (4.2)	0 (0.0)
	Duration of thoughts	Fleeting few seconds or minutes	0 (0.0)	1 (4.2)	0 (0.0)
	Controllability of thoughts	Does not attempt to control thoughts	0 (0.0)	1 (4.2)	0 (0.0)
	Deterrents	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
	Reasons	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
	Made suicide attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Interrupted attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Aborted attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Preparatory actions	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Any suicidal behavior	No	24 (100.0)	24 (100.0)	23 (100.0)

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Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY8	Any suicidal behavior	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Completed suicide	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non-suicidal self-injurious behaviors	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
DAY16	Wish to be dead or not wake up	No	24 (100.0)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Non specific thoughts	No	24 (100.0)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Specific thoughts of method	No	0 (0.0)	2 (8.3)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Some intent to act, no plan	No	0 (0.0)	2 (8.3)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Specific plan and intent	No	0 (0.0)	2 (8.3)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Most severe ideation	Type 1	0 (0.0)	2 (8.3)	0 (0.0)

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY16	Frequency of thoughts	Once a week	0 (0.0)	1 (4.2)	0 (0.0)
		2-5 times a week	0 (0.0)	1 (4.2)	0 (0.0)
	Duration of thoughts	Fleeting few seconds or minutes	0 (0.0)	1 (4.2)	0 (0.0)
		1-4 hours/a lot of time	0 (0.0)	1 (4.2)	0 (0.0)
	Controllability of thoughts	Does not attempt to control thoughts	0 (0.0)	1 (4.2)	0 (0.0)
		Can control thoughts with some difficulty	0 (0.0)	1 (4.2)	0 (0.0)
	Deterrents	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
		Deterrents definitely stopped you from attempting suicide	0 (0.0)	1 (4.2)	0 (0.0)
	Reasons	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
		Mostly to end or stop the pain	0 (0.0)	1 (4.2)	0 (0.0)
	Made suicide attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Interrupted attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Aborted attempts	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

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Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY16	Preparatory actions	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Any suicidal behavior	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Completed suicide	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non-suicidal self-injurious behaviors	No	24 (100.0)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
DAY21	Wish to be dead or not wake up	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non specific thoughts	No	22 (91.7)	22 (91.7)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Specific thoughts of method	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Some intent to act, no plan	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY21	Specific plan and intent	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Most severe ideation	Type 1	0 (0.0)	1 (4.2)	0 (0.0)
	Frequency of thoughts	2-5 times a week	0 (0.0)	1 (4.2)	0 (0.0)
	Duration of thoughts	Fleeting few seconds or minutes	0 (0.0)	1 (4.2)	0 (0.0)
	Controllability of thoughts	Does not attempt to control thoughts	0 (0.0)	1 (4.2)	0 (0.0)
	Deterrents	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
	Reasons	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
	Made suicide attempts	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Interrupted attempts	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Aborted attempts	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Preparatory actions	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

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Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY21	Any suicidal behavior	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Completed suicide	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non-suicidal self-injurious behaviors	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
DAY28	Wish to be dead or not wake up	No	20 (83.3)	23 (95.8)	23 (100.0)
		Yes	1 (4.2)	0 (0.0)	0 (0.0)
	Non specific thoughts	No	21 (87.5)	22 (91.7)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Specific thoughts of method	No	1 (4.2)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Some intent to act, no plan	No	1 (4.2)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Specific plan and intent	No	1 (4.2)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY28	Most severe ideation	Type 1	1 (4.2)	1 (4.2)	0 (0.0)
	Frequency of thoughts	Less than once a week	1 (4.2)	0 (0.0)	0 (0.0)
		2-5 times a week	0 (0.0)	1 (4.2)	0 (0.0)
	Duration of thoughts	Fleeting few seconds or minutes	1 (4.2)	1 (4.2)	0 (0.0)
	Controllability of thoughts	Does not attempt to control thoughts	1 (4.2)	0 (0.0)	0 (0.0)
		Easily able to control thoughts	0 (0.0)	1 (4.2)	0 (0.0)
	Deterrents	Does not apply	1 (4.2)	1 (4.2)	0 (0.0)
	Reasons	Does not apply	1 (4.2)	1 (4.2)	0 (0.0)
	Made suicide attempts	No	21 (87.5)	23 (95.8)	22 (95.7)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Interrupted attempts	No	21 (87.5)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Aborted attempts	No	21 (87.5)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Preparatory actions	No	21 (87.5)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

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Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY28	Any suicidal behavior	No	21 (87.5)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Completed suicide	No	21 (87.5)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non-suicidal self-injurious behaviors	No	21 (87.5)	23 (95.8)	22 (95.7)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
DAY32	Wish to be dead or not wake up	No	22 (91.7)	22 (91.7)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Non specific thoughts	No	22 (91.7)	22 (91.7)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Specific thoughts of method	No	0 (0.0)	2 (8.3)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Some intent to act, no plan	No	0 (0.0)	2 (8.3)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Specific plan and intent	No	0 (0.0)	2 (8.3)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY32	Most severe ideation	Type 1	0 (0.0)	2 (8.3)	0 (0.0)
	Frequency of thoughts	Less than once a week	0 (0.0)	1 (4.2)	0 (0.0)
		2-5 times a week	0 (0.0)	1 (4.2)	0 (0.0)
	Duration of thoughts	Fleeting few seconds or minutes	0 (0.0)	1 (4.2)	0 (0.0)
		Less than 1 hour/some of the time	0 (0.0)	1 (4.2)	0 (0.0)
	Controllability of thoughts	Easily able to control thoughts	0 (0.0)	2 (8.3)	0 (0.0)
	Deterrents	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
		Deterrents definitely stopped you from attempting suicide	0 (0.0)	1 (4.2)	0 (0.0)
	Reasons	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
		Mostly to end or stop the pain	0 (0.0)	1 (4.2)	0 (0.0)
	Made suicide attempts	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Interrupted attempts	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Aborted attempts	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

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Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
DAY32	Preparatory actions	No	21 (87.5)	23 (95.8)	23 (100.0)
		Yes	1 (4.2)	0 (0.0)	0 (0.0)
	Any suicidal behavior	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Completed suicide	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non-suicidal self-injurious behaviors	No	22 (91.7)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
EOS	Wish to be dead or not wake up	No	23 (95.8)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non specific thoughts	No	23 (95.8)	23 (95.8)	23 (100.0)
		Yes	0 (0.0)	1 (4.2)	0 (0.0)
	Specific thoughts of method	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Some intent to act, no plan	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
EOS	Specific plan and intent	No	0 (0.0)	1 (4.2)	0 (0.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Most severe ideation	Type 1	0 (0.0)	1 (4.2)	0 (0.0)
	Frequency of thoughts	2-5 times a week	0 (0.0)	1 (4.2)	0 (0.0)
	Duration of thoughts	Fleeting few seconds or minutes	0 (0.0)	1 (4.2)	0 (0.0)
	Controllability of thoughts	Does not attempt to control thoughts	0 (0.0)	1 (4.2)	0 (0.0)
	Deterrents	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
	Reasons	Does not apply	0 (0.0)	1 (4.2)	0 (0.0)
	Made suicide attempts	No	23 (95.8)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Interrupted attempts	No	23 (95.8)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Aborted attempts	No	23 (95.8)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Preparatory actions	No	23 (95.8)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

Summary of Columbia-Suicidality Severity Rating Scale (C-SSRS)
Safety analysis set

Visit	Question	Response	AQW051 50mg N=24	AQW051 10mg N=24	Placebo N=23
EOS	Any suicidal behavior	No	23 (95.8)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Completed suicide	No	23 (95.8)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)
	Non-suicidal self-injurious behaviors	No	23 (95.8)	24 (100.0)	23 (100.0)
		Yes	0 (0.0)	0 (0.0)	0 (0.0)

Secondary Outcome Result(s)

Results from analysis of change from baseline to day 28 in LFADLDS sum score (PD analysis set)

Treatment	N	Baseline LFADLDS sum score	LSmean for change from baseline (SE)	Difference in LSmean vs Placebo (SE)	Adjusted 95% CI	Adjusted P-value
AQW051 50 mg	19	9.55	-1.73 (0.622)	-0.88 (0.865)	(-2.84, 1.08)	0.494
AQW051 10 mg	23	9.17	-0.96 (0.566)	-0.11 (0.828)	(-1.98, 1.77)	0.987
Placebo	21	10.43	-0.85 (0.597)	0 (0.0)	(0.0)	0.0

Results from analysis of change from baseline to day 28 in UPDRS(32-33) mean sum score (PD analysis set)

Treatment	N	Baseline UPDRS(32-33) mean sum score	LSmean for change from baseline (SE)	Difference in LSmean vs Placebo (SE)	Adjusted 95% CI	Adjusted P-value
AQW051 50 mg	19	4.48	-1.01 (0.309)	0.12 (0.427)	(-0.84, 1.09)	0.940
AQW051 10 mg	23	4.58	-0.95 (0.280)	0.18 (0.406)	(-0.74, 1.10)	0.867
Placebo	21	4.62	-1.14 (0.294)	0 (0.0)	(0.0)	0.0

Results from analysis of change from baseline to day 28 in mean primary outcomes from Track PD motor assessments with LOCF (PD analysis set)

Motor assessment	Primary outcome	Treatment	N	Baseline result	LSmean for change from baseline (SE)	Difference in LSmean vs Placebo (SE)	Adjusted 95% CI	Adjusted P-value
Manumotography & Dyskinesiography	Position-index (right hand) (cm/sec)	AQW051 50mg	7	2.40	-0.14 (0.633)	0.61 (0.909)	(-1.54, 2.77)	0.720
		AQW051 10mg	10	2.73	0.61 (0.527)	1.37 (0.831)	(-0.60, 3.34)	0.193
		Placebo	7	3.54	-0.76 (0.638)			
	Position-index (left hand) (cm/sec)	AQW051 50mg	7	2.76	-0.23 (0.789)	-0.50 (1.081)	(-3.06, 2.06)	0.856
		AQW051 10mg	10	3.23	0.22 (0.660)	-0.06 (0.989)	(-2.40, 2.29)	0.998
		Placebo	8	3.19	0.27 (0.737)			
	Grip force variability (right hand) (%)	AQW051 50mg	7	7.66	-0.37 (0.987)	-0.26 (1.509)	(-3.81, 3.30)	0.977
		AQW051 10mg	10	7.93	-0.40 (0.825)	-0.29 (1.396)	(-3.58, 3.01)	0.967
		Placebo	7	12.35	-0.12 (1.061)			
	Grip force variability (left hand) (%)	AQW051 50mg	7	8.98	-0.72 (0.964)	0.26 (1.338)	(-2.91, 3.42)	0.973
		AQW051 10mg	10	8.82	-0.12 (0.810)	0.85 (1.233)	(-2.07, 3.77)	0.714
		Placebo	8	10.89	-0.97 (0.915)			
Digitomotography	Speeded-taping inter-onset-inteval-rthnd (sec)	AQW051 50mg	8	0.0291	0.0023 (0.00757)	0.0080 (0.01084)	(-0.0173, 0.0333)	0.676
		AQW051 10mg	13	0.0298	0.0087 (0.00594)	0.0144 (0.00974)	(-0.0084, 0.0371)	0.253
		Placebo	8	0.0379	-0.0057 (0.00766)			
	Speeded-taping inter-onset-inteval-lthnd (sec)	AQW051 50mg	8	0.0401	0.0062 (0.00825)	0.0154 (0.01167)	(-0.0119, 0.0426)	0.324
		AQW051 10mg	13	0.0504	-0.0039 (0.00652)	0.0053 (0.01065)	(-0.0196, 0.0302)	0.831
		Placebo	8	0.0340	-0.0092 (0.00831)			
Dysdiadochomotography	Pron-supin-inter-onset-interva-var-rthnd (sec)	AQW051 50mg	8	0.0793	-0.0055 (0.01922)	-0.0050 (0.02828)	(-0.0710, 0.0610)	0.976

Motor assessment	Primary outcome	Treatment	N	Baseline result	LSmean for change from baseline (SE)	Difference in LSmean vs Placebo (SE)	Adjusted 95% CI	Adjusted P-value
		AQW051 10mg	13	0.0617	0.0124 (0.01546)	0.0129 (0.02683)	(-0.0497, 0.0756)	0.837
		Placebo	7	0.0915	-0.0006 (0.02109)			
	Pron-sup-inter-onset-interv-variab-lthnd (sec)	AQW051 50mg	8	0.0590	0.0000 (0.01183)	0.0152 (0.01749)	(-0.0258, 0.0561)	0.585
		AQW051 10mg	12	0.0710	0.0024 (0.00955)	0.0176 (0.01583)	(-0.0195, 0.0546)	0.433
		Placebo	7	0.0823	-0.0152 (0.01264)			
Pedomotography	Foot-tap-inter-onset-interv-variab-rtft (sec)	AQW051 50mg	8	0.2018	-0.0673 (0.06809)	-0.0440 (0.10019)	(-0.2786, 0.1907)	0.863
		AQW051 10mg	12	0.2026	-0.0078 (0.05561)	0.0156 (0.09216)	(-0.2002, 0.2314)	0.978
		Placebo	7	0.2764	-0.0234 (0.07317)			
	Foot-tap-inter-onset-interv-variab-ltft (sec)	AQW051 50mg	8	0.1974	-0.0706 (0.06100)	-0.0846 (0.08939)	(-0.2941, 0.1248)	0.534
		AQW051 10mg	12	0.2227	0.0749 (0.04971)	0.0609 (0.08191)	(-0.1310, 0.2528)	0.669
		Placebo	7	0.2347	0.0140 (0.06515)			

Cogstate:

Summary of Effect Size and Statistical Significance for Overall Differences Between AQW051 50 mg and AQW051 10 mg Versus Placebo at Day 28 for the Pharmacodynamic Population Analyses for All Data

Outcome Variable	Dose	Cohen's d (ANCOVA with LOCF)	p-value (ANCOVA with LOCF)	Cohen's d (Repeated Measures)	p-value (Repeated Measures)
ISLT	AQW051 50 mg	0.486	0.213	0.530	0.104
	AQW051 10 mg	0.416	0.309	0.454	0.149
Detection[a]	AQW051 50 mg	-0.111	0.914	0.040	0.902
	AQW051 10 mg	-0.322	0.460	-0.300	0.328
Identification[a]	AQW051 50 mg	-0.304	0.509	-0.283	0.361
	AQW051 10 mg	-0.239	0.659	-0.207	0.451
One Card Learning	AQW051 50 mg	-0.203	0.733	-0.259	0.413
	AQW051 10 mg	0.214	0.695	0.191	0.517
One Back[a]	AQW051 50 mg	-0.353	0.407	-0.346	0.292
	AQW051 10 mg	-0.071	0.967	-0.055	0.864
GMLT[a]	AQW051 50 mg	-0.417	0.410	-0.395	0.303
	AQW051 10 mg	-0.033	0.993	-0.088	0.816
COWAT	AQW051 50 mg	-0.308	0.521	-0.320	0.348
	AQW051 10 mg	-0.272	0.601	-0.265	0.399
PSY-ATT	AQW051 50 mg	-0.223	0.690	-0.128	0.686
	AQW051 10 mg	-0.337	0.431	-0.315	0.299
EF COMP 1	AQW051 50 mg	-0.572	0.127	-0.453	0.160
	AQW051 10 mg	-0.076	0.956	-0.046	0.882
EF COMP 2	AQW051 50 mg	-0.363	0.397	-0.253	0.429
	AQW051 10 mg	0.022	0.996	0.062	0.837
MEM COMP 1	AQW051 50 mg	0.520	0.170	0.585	0.067
	AQW051 10 mg	0.435	0.265	0.491	0.109
MEM COMP 2	AQW051 50 mg	0.231	0.674	0.231	0.465
	AQW051 10 mg	0.373	0.370	0.399	0.193

[a]Scores for tasks with speed or error as the primary outcome variable have been reversed (multiplied by -1) so that, for all tasks, benefit of AQW051 versus placebo is indicated by a positive effect size.
Note: ISLT= International Shopping List Task GMLT= Groton Maze Learning Test, COWAT= Controlled Oral Word Association Test, PSY-ATT COMP= Psychomotor-Attention Composite, EF COMP = Executive Function Composite, MEM COMP= Memory Composite.

Steady state pharmacokinetics of AQW051

Parameter	10 mg/day (N=23)	50 mg/day (N=18)
Tmax (h)	5.00 (2.92 – 11.9)	4.99 (3.00 – 8.00)
Cmax (ng/mL)	8.62 (4.00)	38.7 (18.7)
AUC0-24h,ss (ng*h/mL)	160 (86.8)	686 (407)
CL/F (L/h)	88.8 (68.4)	102 (59.2)

Values are mean (SD), except for Tmax which is presented as median (range).

Safety Results

Incidence of AEs by primary system organ class (Safety set)

	AQW051 50 mg N=24 n (%)	AQW051 10 mg N=24 n (%)	Placebo N=23 n (%)	Total N=71 n (%)
Subjects with AE(s)	15 (62.5)	18 (75.0)	18 (78.3)	51 (71.8)
System organ class				
Nervous system disorders	12 (50.0)	10 (41.7)	8 (34.8)	30 (42.3)
Psychiatric disorders	8 (33.3)	5 (20.8)	8 (34.8)	21 (29.6)
Infections and infestations	3 (12.5)	5 (20.8)	7 (30.4)	15 (21.1)
Musculoskeletal and connective tissue disorders	4 (16.7)	5 (20.8)	5 (21.7)	14 (19.7)
Gastrointestinal disorders	1 (4.2)	7 (29.2)	4 (17.4)	12 (16.9)
General disorders and administration site conditions	3 (12.5)	5 (20.8)	2 (8.7)	10 (14.1)
Investigations	5 (20.8)	3 (12.5)	1 (4.3)	9 (12.7)
Injury, poisoning and procedural complications	3 (12.5)	4 (16.7)	1 (4.3)	8 (11.3)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	2 (8.3)	3 (13.0)	5 (7.0)
Skin and subcutaneous tissue disorders	0 (0.0)	3 (12.5)	1 (4.3)	4 (5.6)
Vascular disorders	2 (8.3)	2 (8.3)	0 (0.0)	4 (5.6)
Metabolism and nutrition disorders	0 (0.0)	0 (0.0)	2 (8.7)	2 (2.8)
Blood and lymphatic system disorders	0 (0.0)	1 (4.2)	0 (0.0)	1 (1.4)
Ear and labyrinth disorders	0 (0.0)	1 (4.2)	0 (0.0)	1 (1.4)
Eye disorders	0 (0.0)	1 (4.2)	0 (0.0)	1 (1.4)
Renal and urinary disorders	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Reproductive system and breast disorders	0 (0.0)	1 (4.2)	0 (0.0)	1 (1.4)

10 Most Frequently Reported AEs Overall by Preferred Term n (%)

Incidence of AEs by preferred term - n (%) of subjects

	AQW051 50 mg N=24 n (%)	AQW051 10 mg N=24 n (%)	Placebo N=23 n (%)	Total N=71 n (%)
Subjects with AE(s)	15 (62.5)	18 (75.0)	18 (78.3)	51 (71.8)
Preferred term				
Back pain	1 (4.2)	2 (8.3)	2 (8.7)	5 (7.0)
Dizziness	1 (4.2)	2 (8.3)	1 (4.3)	4 (5.6)
Dyskinesia	6 (25.0)	1 (4.2)	3 (13.0)	10 (14.1)
Fall	3 (12.5)	2 (8.3)	1 (4.3)	6 (8.5)
Fatigue	2 (8.3)	2 (8.3)	2 (8.7)	6 (8.5)
Headache	1 (4.2)	2 (8.3)	1 (4.3)	4 (5.6)
Muscle spasms	0 (0.0)	3 (12.5)	1 (4.3)	4 (5.6)
Myalgia	1 (4.2)	0 (0.0)	3 (13.0)	4 (5.6)
Nasopharyngitis	1 (4.2)	1 (4.2)	2 (8.7)	4 (5.6)
Nausea	1 (4.2)	5 (20.8)	0 (0.0)	6 (8.5)
Nightmare	0 (0.0)	2 (8.3)	3 (13.0)	5 (7.0)
On and off phenomenon	2 (8.3)	1 (4.2)	3 (13.0)	6 (8.5)
Somnolence	3 (12.5)	0 (0.0)	1 (4.3)	4 (5.6)

Arranged alphabetically for terms with >5% overall incidence

Serious Adverse Events and Deaths

	AQW051 (50 mg) N=24	AQW051 (10 mg) N=24	Placebo N=23
No. (%) of subjects with AE(s)	15 (62.5)	18 (75.0)	18 (78.3)
Number (%) of subjects with serious or other significant events	2 (8.3)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)
SAE(s)	2 (8.3)	0 (0.0)	0 (0.0)
Discontinued due to SAE(s)	0 (0.0)	0 (0.0)	0 (0.0)

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Date of Latest Update