2. SYNOPSIS

<table>
<tr><td colspan="2">Name of Sponsor: I.R.I.S., 50 rue Carnot - 92284 Suresnes Cedex - France</td><td rowspan="2">(For National Authority Use only)</td></tr>
<tr><td colspan="2">Test drug
Name of Finished Product:
NA
Name of Active Ingredient:
S44819</td></tr>
<tr><td>Individual Study Table Referring to Part of the Dossier</td><td>Volume:</td><td>Page:</td></tr>
<tr><td colspan="3">Title of study: Randomized Efficacy and Safety Trial with Oral S44819 after Recent ischemic cerebral Event International, multi-centre, randomized, double-blind placebo-controlled phase II study.
Protocol No.: CL2-44819-004
EudraCT No.: 2016-001005-16
The description of the study protocol given hereafter includes the modifications of the seven substantial amendments (3 international and 4 local amendments) to the protocol.</td></tr>
<tr><td colspan="3">International coordinator
No international coordinator was assigned.</td></tr>
<tr><td colspan="3">Study countries:
In all, 14 countries included a total of 585 patients: 40 patients in Australia, 20 patients in Belgium, 34 patients in Brazil, 9 patients in Canada, 1 patient in the Czech Republic, 52 patients in France, 33 patients in Germany, 101 patients in Hungary, 16 patients in Italy, 25 patients in the Republic of South Korea, 3 patients in the Netherlands, 58 patients in Poland, 121 patients in Spain and 72 patients in the United Kingdom.</td></tr>
<tr><td colspan="3">Publication (reference):
Not applicable</td></tr>
<tr><td colspan="2">Studied period:
Initiation date: 19 December 2016 (first visit first patient).
Completion date: 10 March 2019 (last visit last patient).</td><td>Phase of development of the study:
Phase II</td></tr>
<tr><td colspan="3">Objectives:
The purpose of this trial was to assess the efficacy and safety of S44819 (150 or 300 mg twice a day) versus placebo in ischaemic stroke recovery.
The primary objective of the study was to demonstrate the superiority of at least one of the two doses of S44819 versus placebo on functional recovery from ischaemic stroke measured with the modified Rankin Scale (mRS) after 90 days of treatment.
The secondary objectives were:
- To assess the efficacy of the two doses of S44819 versus placebo in stroke recovery using neurological evaluation [National Institutes of Health Stroke Scale (NIHSS)], activities of daily living test [Barthel Index (BI)], and cognitive performance tests [Montreal Cognitive Assessment scale (MoCA), Trail Making Test (TMT)].
- To assess the safety and tolerability of S44819.
Exploratory objectives were:
- To assess the pharmacokinetics (PK) of S44819 and metabolites (if applicable).
- To evaluate patient benefit through sub-dimensions of Quality of Life (QOL) using a Visual Analogue Scale (VAS).
- To perform a pharmacogenomic (PG) analysis of inter-patient variation in genes encoding for proteins involved in absorption/distribution/metabolism/excretion (ADME) (optional part).</td></tr>
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Methodology:
This was a phase II, randomised, double-blind, international, multi-centre, parallel-groups, placebo-controlled study with a 90-day treatment period followed by a 15-day period with no treatment.
This study included patients who suffered from an acute ischaemic stroke that occurred between 72 hours (3 days) and 192 hours (8 days) (both inclusive) before inclusion.
The treatment (S44819 150 mg bid, S44819 300 mg bid or placebo) was assigned at the inclusion visit (D0) by a balanced, non-adaptive randomisation, with stratification by country and previous revascularisation therapy (thrombolysis and / or endovascular therapy).

This study was performed in strict accordance with Good Clinical Practice.

The effect of S44819 in post-stroke recovery was not demonstrated in this phase II study. Due to the Sponsor's decision to stop the S44819 development, an abbreviated clinical study report was written.

Number of patients:
Planned: approximately 580 patients (approximately 194 patients in each group).
Included: 585 patients (197 patients in the S44819 150 mg bid group, 195 in the S44819 300 mg bid group and 193 in the placebo group).

Diagnosis and main criteria for inclusion:
Patients, aged 18-85 years (both inclusive), with a recent (between 72 hours (3days) and 192 hours (8 days) cortical or combined cortical-subcortical ischaemic stroke, with NIHSS 7-20 (both inclusive) and with no previous disability (*i.e.* neither physical nor pre-stroke cognitive impairment).

Test drug:
Name - Dosage form - Doses: S44819 - sachet of 150 mg - 150 or 300 mg twice a day.

Mode of administration: The study medication was administered in the morning and in the evening (during or within 30 minutes following the meal). The interval between two intakes of the study treatment was to be at least 8 hours. Three methods of sachet administration were possible:

- With a glass of water.
- With thickened water, yoghurt, stewed fruit or mashed food.
- Through a nasogastric tube or a percutaneous feeding tube.

Batch Nos. [redacted]

Comparator (placebo):
Name - Dosage form: Placebo - sachet.

Mode of administration: 2 sachets of placebo were administered in the morning and in the evening (during or within 30 minutes following the meal). The interval between two intakes of the study treatment was to be at least 8 hours. Three methods of sachets administration were possible:

- With a glass of water.
- With thickened water, yoghurt, stewed fruits or mashed food.
- Through a nasogastric tube or a percutaneous feeding tube.

Batch Nos. [redacted]

Duration of treatment:
Selection period: period of maximum 144 hours (6 days), without study drug intake.

Treatment period: period of 90 days (Days D0-D90).

Follow-up period: period of 15 days, without study drug intake.

Criteria for evaluation:

Efficacy measurements:

Primary criterion:

The primary efficacy endpoint was the modified Rankin Scale (mRS) score at the D90 visit.

Secondary criteria:

- NIHSS total score.
- BI total score.
- MoCA total score.
- TMT: time for part A and time for part B.

Safety measurements:

- Adverse Events (AEs).
- Laboratory parameters (haematology and biochemistry).
- Vital signs [supine for Systolic and Diastolic Blood Pressure (SBP and DBP)].
- Body weight.
- 12-lead Electrocardiogram (ECG).
- Columbia-Suicide Severity Rating Scale (C-SSRS).

Pharmacokinetic measurements:

Blood samples were collected at the D5, D30, D60 and D90 visits and samples concentrations were measured. Due to the Sponsor's decision to stop the S44819 development, other PK analyses planned in the protocol were not performed.

Pharmacogenomic measurements (optional):

Blood samples were collected at the D5 visit (or before if the patient left the recruiting centre earlier) from patients who signed the specific Informed Consent Form, but due to the Sponsor's decision to stop the S44819 development, analysis was not performed.

Other measurements:

VAS on sub-dimensions of QOL (appetite, sleep, day-time alertness, mood, anxiety, pain).

Statistical methods:

Analysis Sets:

Randomised Set (RS): all included patients to whom a therapeutic unit was randomly assigned using IRS.

Full Analysis Set (FAS): all patients of the RS having taken at least one dose of Investigational Medicinal Product (IMP) and having at least a value of the primary efficacy endpoint after D5 (excluded). Of note, patients deceased after D5 are included in the FAS.

Efficacy analysis:

Primary endpoint:

The primary efficacy endpoint was defined as the mRS score expressed as value at the D90 visit.

<u>*Primary analysis*</u>: each dose of S44819 was compared to placebo on the primary efficacy endpoint in the FAS, using an ordinal logistic regression (also called «shift analysis») to assess the odds of shifting from one category to the next in the direction of a better outcome, assuming categories 5 and 6 of the mRS scale are combined [Saver, 2009]. The analysis included the fixed, categorical effects of treatment, country and previous revascularisation therapy (thrombolysis and / or endovascular therapy *versus* none).

Missing data at D90 were imputed with the Last Observation Carried Forward (LOCF) approach. In order to take into account the multiplicity of comparisons, the step-down Holm procedure was used for comparison of each S44819 dose to placebo.

<u>*Sensitivity to adjustment factors*</u>: to assess the robustness of the primary analysis results to adjustment factors, the same analysis as the primary analysis was performed in the FAS, including in addition the continuous fixed, covariates of age and baseline NIHSS total score.

<u>*Sensitivity to missing data handling*</u>: to assess robustness to the method for handling missing data, a multiple imputation (MI) using a Copy Increment from Reference (CIR) approach was performed.
This method assumes that after discontinuation, patients discontinued from the S44819 group will exhibit an evolution of the disease similar to patients in the placebo group but starting from the benefit already obtained.

Statistical methods: (Cont'd)
Efficacy analysis: **(Cont'd)**
Secondary endpoints:

As this is an abbreviated study report, secondary endpoints are not described in the present report.

Study patients: disposition baseline characteristics and treatments analysis: descriptive statistics were provided in the RS.

Safety analysis: descriptive statistics were provided in the Safety Set.

Pharmacokinetic analysis: not performed.

Pharmacogenomic analysis: not performed.

SUMMARY - CONCLUSIONS
DISPOSITION OF PATIENTS AND ANALYSIS SETS

	S44819 150 mg bid (N = 197)	**S44819 300 mg bid (N = 195)**	**Placebo (N = 193)**	**ALL (N = 585)**
Included/Randomised	**197**	**195**	**193**	**585**
Withdrawn due to	**44 (22.3)**	**36 (18.5)**	**39 (20.2)**	**119 (20.3)**
- Lost to follow-up	-	-	-	-
- Adverse event	18 (9.1)	16 (8.2)	25 (13.0)	59 (10.1)
- Lack of efficacy	1 (0.5)			1 (0.2)
- Non-medical reason	16 (8.1)	17 (8.7)	11 (5.7)	44 (7.5)
- Protocol deviation	9 (4.6)	3 (1.5)	3 (1.6)	15 (2.6)
Completed	**153 (77.7)**	**159 (81.5)**	**154 (79.8)**	**466 (79.7)**
Full Analysis Set (FAS)	**189 (95.9)**	**188 (96.4)**	**191 (99.0)**	**568 (97.1)**
Per Protocol Set (PPS)	**136 (69.0)**	**147 (75.4)**	**145 (75.1)**	**428 (73.2)**
Safety Set (SS)	**195 (99.0)**	**194 (99.5)**	**193 (100)**	**582 (99.5)**

N number of patients by group
n number of patients
% Expressed as percentage of the patients from the Included/Randomised Set

BASELINE CHARACTERISTICS
Demographics and other baseline characteristics in the Randomised Set were in accordance with the target population.
At baseline, in the RS, the mean (± SD) age was 67.2 ± 11.7 years. Most patients (62.1%) were aged from 65 to 84 years with a slightly higher rate in the S44819 300 mg bid (69.2% of the patients) than in the S44819 150 mg bid group (59.4%) and the placebo group (57.5%). More than half of the patients were male (54.9%) and about 90% were white, without relevant differences between the treatment groups.

The current stroke (*i.e.,* the stroke that happened between 3 to 8 days before inclusion) had been diagnosed 5.1 ± 1.5 days on average before inclusion, without any relevant differences between the groups. The majority of the patients did not receive any acute stroke treatment like intravenous (IV) thrombolysis (59.0%) or endovascular therapy (66.0%), without any relevant differences between the groups. Regarding the history of a previous stroke, most patients reported neither previous ischaemic (87.9% of the patients) nor haemorrhagic (99.1% of the patients) stroke, without any relevant differences between the groups.

At baseline, the majority of patients (77.3%) had mild to moderate stroke severity ($7 \leq$ NIHSS ≤ 14). The other patients (except one patient in deviation to the protocol with NIHSS score of 6) had a more severe stroke ($15 \leq$ NIHSS ≤ 20). The mean ± SD total NIHSS score was 11.3 ± 3.8. No relevant differences between the groups were observed regarding the total NIHSS score at baseline.

No relevant difference between groups was observed regarding BMI [mean ± SD = 27.3 ± 5.1 kg/m², overweight patients ($\geq$ 30 kg/m²) = 25.0% overall], blood pressures (mean ± SD SBP/DBP = 136.0 ± 18.7/77.7 ± 11.3 mmHg) and heart rate (mean ± SD = 74.4 ± 16.6 bpm).

SUMMARY - CONCLUSIONS (Cont'd)

BASELINE CHARACTERISTICS (Cont'd)

As regards to ECG parameters at baseline, no relevant difference between groups was observed in mean values. A total of 87 patients (15.6%) had a QTcF value within the]450; 480] ms range with a higher frequency in the S44819 300 mg bid group (18.2%) compared to the S44819 150 mg bid group (13.8%) and the placebo group (14.8%). Few patients (3) had QTcF value above 480 ms (2 patients in the S44819 150 mg bid group and one patient in the S44819 300 mg bid group). Significant ECG abnormalities were reported in a total of 69 patients (12.4%) with a slightly higher frequency in the S44819 300 mg bid group (15.0%) than in the S44819 150 mg bid (10.1%) and placebo (12.1%) groups.

In the RS, 98.6% of patients had at least one medical history in addition to stroke, without relevant differences between the groups. The most frequent medical history was hypertension (76.6%) without relevant differences between the groups. At least one surgical or medical procedure was reported by 39.7% of patients overall, without relevant differences between the groups.

Overall, at inclusion, 98.3% of patients received at least one concomitant treatment without relevant differences between the groups. The most frequently reported pharmacological class was antithrombotic agents (92.6%). During the treatment period, most of the patients (93.3%) had a rehabilitation therapy without relevant differences between the groups.

EXTENT OF EXPOSURE

In the FAS, the mean ± SD treatment duration was 80.9 ± 24.7 days (median of 90.0 days). Almost all patients (86.2%) were treated for at least 60 days. The overall compliance was good with a mean ± SD of 91.6 ± 14.2 %. There were no relevant differences between the groups. Similar results were observed in the SS.

EFFICACY RESULTS

Primary efficacy endpoint

In the FAS, the main analysis failed to demonstrate a statistically significant superiority of at least one of the two doses of S44819 (150 mg bid or 300 mg bid) *versus* placebo on functional recovery after ischaemic stroke using the modified Rankin Scale (mRS) score at D90 (primary efficacy endpoint). The estimates of the odds ratio (OR) between the S44819 150 mg bid group and the placebo group and between the S44819 300 mg bid group and the placebo group did not show a statistically significant difference between the groups:

- S44819 150 mg bid group compared to the placebo group:
  Estimate of the OR = 0.91, 95% CI [0.64; 1.31], p = 0.800.
- S44819 300 mg bid group compared to the placebo group:
  Estimate of the OR = 1.17, 95% CI [0.81; 1.67], p = 0.800.

These results were confirmed by sensitivity analyses.

The effect of S44819 in post-stroke recovery has not been demonstrated in this study. The Sponsor has decided to stop any further development of S44819.

SUMMARY - CONCLUSIONS (Cont'd)
EFFICACY RESULTS (Cont'd)
Primary efficacy endpoint (Cont'd)

Distribution of mRS score at D90 and difference between S44819 doses and placebo - Primary analysis - FAS (N = 568)

			S44819 150 mg bid (N = 189)	S44819 300 mg bid (N = 188)	Placebo (N = 191)
Descriptive Statistics					
D90		n (*)	189	188	191
	0	n (%)	-	10 (5.3)	7 (3.7)
	1	n (%)	26 (13.8)	24 (12.8)	23 (12.0)
	2	n (%)	47 (24.9)	47 (25.0)	54 (28.3)
	3	n (%)	55 (29.1)	51 (27.1)	44 (23.0)
	4	n (%)	44 (23.3)	35 (18.6)	40 (20.9)
	5-6	n (%)	17 (9.0)	21 (11.2)	23 (12.0)
Statistical analysis					
Primary statistical analysis	Comparison to placebo	E (1)	0.91	1.17	
		95% CI (2)	[0.64; 1.31]	[0.81; 1.67]	
		p-value (3)	0.800	0.800	
Sensitivity to adjustment factors	Comparison to placebo	E (1')	0.97	1.20	
		95% CI (2)	[0.67; 1.42]	[0.82; 1.76]	
		p-value (3)	0.884	0.680	
Sensitivity to missing data handling	Comparison to placebo	E (1")	0.93	1.17	
		95% CI (2)	[0.65; 1.34]	[0.81; 1.69]	
		p-value (3)	0.797	0.797	

(*) Last Observation Carried Forward (LOCF) approach for imputing missing data taking into account that for dead patients, mRS equals 6 after their death
(1) Estimate of the Odds Ratio of mRS score between treatment groups at D90 using an Ordinal Logistic Regression including the categorical fixed covariates of country and previous revascularisation therapy with a LOCF approach
(1') Estimate of the Odds Ratio of mRS score between treatment groups at D90 using an Ordinal Logistic Regression including the categorical fixed covariates of country and previous revascularisation therapy and in addition the continuous fixed covariates of age and baseline NIHSS total score with a LOCF approach
(1") Estimate of the Odds Ratio of mRS score between treatment groups at D90 using an Ordinal Logistic Regression including the categorical fixed covariates of country and previous revascularisation therapy with a Multiple Imputation (MI) approach for missing data
(2) Two-sided 95% Confidence Interval of the estimate without Holm adjustment
(3) Two-sided adjusted p-value taking into account Holm adjustment (to be compared to 0.05)

Secondary efficacy endpoints
As this is an abbreviated study report, none of the planned analyses related to secondary criteria are described in the present report.

SUMMARY - CONCLUSIONS (Cont'd)
SAFETY RESULTS

- **Adverse events**

Overall summary for adverse events in the Safety Set

		S44819 150 mg bid (N = 195)	S44819 300 mg bid (N = 194)	Placebo (N =193)
Patients having reported at least one:				
EAE	n (%)	154 (79.0%)	139 (71.6%)	152 (78.8%)
Treatment-related EAE	n (%)	22 (11.3%)	20 (10.3%)	29 (15.0%)
Serious AE (including death)	n (%)	74 (37.9%)	58 (29.9%)	66 (34.2%)
Serious EAE (including death)	n (%)	71 (36.4%)	56 (28.9%)	65 (33.7%)
Treatment-related serious EAE	n (%)	2 (1.0%)	2 (1.0%)	11 (5.7%)
EAE leading to treatment withdrawal	n (%)	17 (8.7%)	12 (6.2%)	25 (13.0%)
Serious EAE leading to treatment withdrawal	n (%)	11 (5.6%)	6 (3.1%)	19 (9.8%)
Treatment-related EAE leading to treatment withdrawal	n (%)	5 (2.6%)	3 (1.5%)	11 (5.7%)
Treatment-related serious EAE leading to treatment withdrawal	n (%)	-	-	8 (4.1%)
Patients who died	n (%)	7 (3.6%)	9 (4.6%)	5 (2.6%)

In the Safety Set, the percentage of patients who reported at least one emergent adverse event (EAE) was similar or lower in the S44819 groups than in the placebo group (79.0% in the 150 mg bid dose group and 71.6% in the 300 mg bid dose group *versus* 78.8% in the placebo group).

Among the most frequently reported EAEs in the S44819 groups (in at least 3% of patients in any group), the frequency was higher in the S44819 150 mg bid and/or 300 mg bid groups than in the placebo group for: constipation (12.3% and 6.7% *versus* 9.3%, respectively), depression (6.7% and 6.7% *versus* 5.2%, respectively), nausea (3.6% and 5.7% *versus* 3.1%, respectively), hypotension (4.1% and 4.6% *versus* 3.1%, respectively), atrial fibrillation (6.7% and 3.6% *versus* 3.6%, respectively), dehydration (3.6% and 3.6% *versus* 0.5%, respectively) and hypokalaemia (0.5% and 3.6% *versus* 2.1%, respectively).
There was no increase of frequency of adverse events with the dose.

The rate of severe EAEs was higher in the S44819 150 and 300 mg bid groups (5.7% and 6.7%, respectively) than in the placebo group (3.7%). The severe EAEs more frequently reported in the S44819 groups than in the placebo group were pneumonia (3 patients in the S44819 300 mg bid group *versus* none) and deep vein thrombosis (1 patient in the S44819 150 mg bid group and 3 patients in the S44819 300 mg bid group *versus* none).

The percentage of patients with at least one treatment-related EAE was lower in the S44819 150 mg bid and 300 mg bid groups (11.3% and 10.3%, respectively) than in the placebo group (15.0%). However, nausea was more frequently reported in the S44819 300 mg bid group than in the placebo group (2 and 4 patients in the S44819 150 and 300 mg bid groups *versus* none in the placebo group).

Overall, 21 patients died during the study including one patient in the placebo group following a non-emergent adverse event.
During the treatment period, deaths following EAEs were more frequent in the S44819 groups than in the placebo group: 7 patients (3.6%) and 9 patients (4.6%) in the S44819 150 mg bid and 300 mg bid groups, respectively *versus* 4 patients (2.1%) in the placebo group. EAEs leading to death were each reported only once in any group.

None of the deaths in the S44819 150 mg bid and 300 mg bid groups was due to an EAE considered as related to the treatment.

SUMMARY - CONCLUSIONS (Cont'd)
SAFETY RESULTS (Cont'd)

- **Adverse events (Cont'd)**

The percentage of patients who experienced a serious emergent adverse event was slightly higher in the S44819 150 mg bid group (36.4%) than in the placebo group (33.7%), but was lower in the S44819 300 mg bid group than in the placebo group (28.9% *versus* 33.7% respectively).
The following SEAEs were more frequently reported in the S44819 150 mg bid group than in the placebo group: sepsis, syncope and cerebrovascular accident (all reported by 3 patients *versus* none, respectively). In the S44819 300 mg bid group, no cerebrovascular accident was reported whereas sepsis and syncope were each reported by 1 patient.

Overall 2 patients (1.0%) in each S44819 group reported at least one SEAE considered as related to the treatment with a lower rate than in the placebo group (11 patients, 5.7%): 3 events in the S44819 150 mg bid group (stroke in evolution, nausea and vomiting) and 2 events in the S44819 300 mg bid group (epilepsy and hypotension).

The percentage of patients with at least one EAE leading to treatment withdrawal was lower in the S44819 150 mg bid and 300 mg bid groups (8.7% and 6.2%, respectively) than in the placebo group (13.0%). There was no relevant difference between the S44819 and placebo groups regarding the number of EAEs leading to treatment withdrawal.

- **Laboratory tests**

In the Safety Set during the treatment period, emergent Potentially Clinically Significant Abnormal (PCSA) biochemical values were more frequent in at least one of the S44819 groups than in the placebo group for high sodium (1.7% of the patients in the S44819 300 mg bid group *versus* none in the placebo group), high GGT (8.8% in the S44819 150 mg bid group *versus* 7.1% in the placebo group), high urate (6.0% in the S44819 150 mg bid group *versus* 4.3% in the placebo group), high alkaline phosphatase (2.2% in the S44819 150 mg bid group *versus* 0.5% in the placebo group) and low albumin (3.3% in the S44819 150 mg bid group *versus* 1.6% in the placebo group).
Regarding haematological parameters, emergent PCSA values were more frequent in at least one of the S44819 groups than in the placebo group for low erythrocytes (2.3% of the patients in the S44819 150 mg bid group *versus* none in the placebo group), low haematocrit ratio (6.2% in the S44819 150 mg bid group *versus* 1.7% in the placebo group) and high eosinophils/leukocytes ratio (3.8% in the S44819 150 mg bid group *versus* 1.1% in the placebo group).
To note that except for sodium, emergent PCSA values were less or similarly reported in the 300 mg bid group than in the placebo group.
No trend for an increase in PCSA values with the dose of 44819 was observed for any parameter.

- **Vital signs, weight and BMI**

Neither clinically relevant changes from baseline nor differences between the groups were detected in blood pressures, weight and BMI during the treatment period.

- **Electrocardiogram**

There were no clinically relevant mean changes in ECG parameters between baseline and post baseline visits except for a slight decrease in heart rate throughout the study in the S44819 300 mg bid group: -0.5 ± 14.8 bpm, -2.0 ± 16.3 bpm, -2.7 ±16.2 bpm and -3.3 ± 16.3 bpm at the D5, D30, D60 and D90 visits, respectively. At the last post-baseline value under treatment, the mean ± SD change was -2.9 ± 15.9 bpm.
Bradycardia and/or sinus bradycardia were reported by 2 patients in the S44819 150 mg bid group and 3 patients in the S44819 300 mg bid group *versus* none in the placebo group. None of them were considered as related to the treatment.

QTcF prolongations, defined as at least one post-baseline QTcF value > 500 ms or at least one change from baseline > 60 ms under treatment, were reported in all groups, with a lower rate in the S44819 groups than in the placebo group (4.7% and 3.7% in the S44819 150 mg bid and 300 mg bid groups, respectively, *versus* 6.3% in the placebo group).

The percentage of patients with QTcF last post-baseline values under treatment in the]480-500] ms range was higher in the S44819 300 mg bid group than in the placebo group (0.5%, 2.6% *versus* none in the S44819 150 mg bid, 300 mg bid and placebo groups, respectively) as was the percentage of patients with changes in QTcF from baseline to the last post-baseline value in the [30-60] ms range (3.8%, 8.8% *versus* 5.5%, respectively).
The percentage of patients with QTcF values > 500 ms (last post-baseline value under treatment) was higher in the S44819 150 mg bid group than in the placebo group (2.6% *versus* 0.5%, respectively) but the percentage of patients with QTcF values > 500 ms was lower in the S44819 300 mg bid group (1.1%) than in the 150 mg bid group.

- **C-SSRS**

No relevant differences between the groups were observed regarding suicidal ideation during the treatment period. No patient reported suicidal behaviour**.**

CONCLUSION

This international phase II, randomised, double-blinded, multicentre, parallel groups, placebo controlled study conducted in patients who suffered from a recent ischaemic stroke and treated for a 90 - day treatment period either with S44819 150 mg bid, S44819 300 mg bid or placebo, failed to demonstrate a statistically significant superiority of at least one of the two doses of S44819 *versus* placebo on functional recovery after ischaemic stroke using the modified Rankin Scale (mRS) score at D90 (primary efficacy endpoint).
The effect of S44819 in post-stroke recovery has therefore not been demonstrated in this study. The Sponsor has decided to stop any further development of S44819.
No concerns were observed regarding the safety profile of S44819.

Date of the report: 15 October 2019

Version of the report: Final version