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Efficacy and Safety of Sovateltide in Patients with Acute Cerebral Ischemic Stroke: A Randomized, Double-blind, Placebo-controlled, Multicentre, Phase III Clinical Trial

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Supplementary Table 2: Details of each Patient unable to complete 90-day follow-up.

Standard Treatments + Saline					Standard Treatments + Sovateltide				
Subject Number	**Date of Enrolment**	**Date of Exclusion / Withdrawal / Death**	**Reason of Exclusion / Withdrawal / Death**	**Details**	**Subject Number**	**Date of Enrolment**	**Date of Exclusion / Withdrawal / Death**	**Reason of Exclusion / Withdrawal / Death**	**Details**
01-006	09-Jan-2020	15-Feb-2020	Lost to Follow-up	This patient was enrolled, and the first dose was administered on 09-Jan-2020 at 14:00 hrs, and then the rest of the doses were administered as per protocol. The subject was discharged on 18-Jan-2020. On 21-Jan-2020, the subject came to the site to complete visit 2 as per protocol, and for the next scheduled visit 3, the patient was called, but the phone was switched off. Several attempts were made to contact the subject. On 15-Feb-2020, the subject was considered lost to follow-up from the study.	01-008	27-Jan-2020	28-Jan-2020	Consent withdrawn	This patient was enrolled and successfully received all three doses. On Visit-1 (Day 2), the consent was withdrawn and Discharge Against Medical Advice (DAMA) was taken.
01-021	25-Jan-2022	25-Feb-2022	Consent Withdrawn	This patient was enrolled and completed visit 2. On the scheduled visit 3 (Day 30 +5), the patient did not come to the site; the study site coordinator tried to call, but the patient did not pick up the call. However, after several tries, the patient picked up the call and reported feeling better. Then, the study coordinator asked him to come to the site for a scheduled visit, but he didn't want to continue with the study and wanted to withdraw from it.	03-006	28-Nov-2019	30-Nov-2019	Consent Withdrawn	This patient was enrolled, and as per protocol, the first dose of the study drug was given, the patient complained of breathlessness (Dyspnea) and refused to take the 2nd dose of the study drug; the scheduled dose was not given. The event was self-resolved after 10-15 minutes; therefore, no medication was required. The patient was not willing to continue with the study and withdrew consent.
02-002	19-Jan-2020	31-Jan-2020	Consent Withdrawn	This patient was enrolled, and during visit 2 the patient wanted to withdraw consent to continue as a participant in the study and refused to do any follow-up visits. At the patient's request, this patient was withdrawn from the study.	03-013	06-Feb-2020	07-Feb-2020	Consent Withdrawn	This patient was enrolled and received all 3 doses of the study drug on visit 1 (Day 1) as per protocol; after that, they did not want to continue management in this hospital and wanted to shift to another hospital. Therefore, this patient was considered consent withdrawn from the study.
06-004	25-Feb-2020	27-Feb-2020	Consent Withdrawn	This patient was enrolled and received all 3 doses of study drug on visit 1 (Day 1) as per protocol. However, on visit 1 (Day 3), the consent was withdrawn from the study.	03-016	29-Feb-2020	01-Mar-2020	Consent Withdrawn	This patient was enrolled and received all 3 doses of the study drug on visit 1 (Day 1) as per protocol; however, the patient did not want to continue management in this hospital and wanted to shift to another hospital. This patient was considered to have withdrawn from the study.
08-001	01-Jan-2020	10-Jan-2020	Death	This patient was admitted with a complaint of sudden fall and weakness and pain of the right side of the body with complete loss of speech. The patient had a known case of accelerated hypertension with IHD and LVD and had an ejection fraction (EF) of 25%. After admission, patient was immediately shifted to ICU, and an emergency CT scan was suggested with the	04-012	26-Aug-2020	27-Aug-2020	Consent Withdrawn	This patient was enrolled and received all 3 doses of the study drug on visit 1 (Day 1) as per protocol. However, the patient requested the investigator for consent withdrawal from the study, and the subject took discharge from the hospital against medical advice.

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				clinical diagnosis of acute ischemic stroke. Vitals were: B.P-180/100 mmHg; Heart rate-138 beats per minute; Respiratory rate-38 breaths per minute. CT Scan showed chronic infarct of the left occipital region, chronic lacunar infarct, chronic ischemic and cerebral atrophic changes. Subtype of Ischemic Stroke: Large Artery Atherosclerosis. Different scores quantified the patient's stroke severity. NIHSS: 19; mRS: 4; BI: 5. The Patient met the eligibility criteria and was enrolled in the study after obtaining consent from LAR. The patient received all the 9 doses of the study drug as per protocol. The patient was not thrombolysed because the patient was old and frail. On day 2, the scoring was NIHSS: 19; mRS: 4; and BI: 5. The patient was responding to oral commands with the left hand of the body. Carotid doppler revealed bilateral diffuse intimal thickening common carotid artery (CCA), no significant plaque or stenosis seen, bilateral 30-40% plaque seen in the ICA, 30% plaque seen in the right external carotid artery (RECA) and 30-40% plaque seen in the left internal carotid artery (LICA). 2D color doppler echocardiography report revealed severe global hypokinesia of the left ventricle (LV), severe LV systolic dysfunction, dilated left atrium (LA) and LV with LV eject fraction of 20%, mild tricuspid regurgitation (TR), Pulmonary arterial systolic pressure (PASP) 40 mg, mild mitral regurgitation (MR). On day 3, the scoring was NIHSS: 19; mRS: 4; and BI: 5. The general condition was deteriorating. CT Scan (head) was repeated and showed a very large parietotemporal hemorrhagic infarct with mass effect, and the midline was shifted to the right. On day 4 (04-Jan-2020) – The Patient was conscious but not oriented. Central catheterization was done in					

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				aseptic precaution under local anaesthesia in the right-side internal jugular vein. Back flow was checked, and CVP was 3 cm. Motion were not passed. Passive physiotherapy was advised. GCS (Morning): $E_4V_1M_5$ -10/15; GCS (Evening): $E_3V_1M_5$ -10/15. On day 5 (05-Jan-2020) – The Patient was semiconscious. CVP was 4 cm. Motion were not passed. Passive physiotherapy was advised. GCS (Morning): $E_4V_1M_5$ -9/15. The repeat CT Scan (Head) showed a very large parietotemporal hemorrhagic infarct with mass effect, and a midline was shifted to the right. On day 6 (06-Jan-2020), the scoring was NIHSS: 30; mRS: 5; BI: 5; and EuroQOL: 20. The patient's condition was explained to the attendants. Neurosurgical consultation was taken from Neurosurgeon and had advised the attendants for a craniotomy to decompress the brain from almost full half brain cerebral edema. The attendants did not consent to surgery because of age and previously existing cardiac ischemic cardiomyopathy, and poor general condition. Patient was continued on treatment antibiotic Inj. Piperacillin 4 gm + Tazobactam 500 mg (4.5 gm) IV 8 hourly, Mannitol IV 8 hourly, Syp. Sucralfate + Oxetacaine and Inj. Dexamethasone 8 mg 8 hourly to decrease brain edema along with the SOC. On day 7 (07-Jan-2020) - CVP was 1 cm. Motion were not passed. On day 8 (08-Jan-2020) – The Patient was drowsy; motions were not passed. The patient's condition was deteriorating, and a poor prognosis was explained to patient attendants. CVP was 1 cm. On 09-Jan-2020 - NIHSS scale worsened, and had respiratory depression and was put on a ventilator. Patient CT scan (head) repeated on ventilator showed a very large area of hypodensity in the left cerebral hemisphere with					

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				gross mass effect likely suggestive of infarct with hemorrhagic transformation, chronic ischemic white matter changes, and midline shift. Despite all efforts and standard treatment patient's death occurred because of the progression of the present illness, i.e., acute ischemic stroke and severe global hypokinesia and dysfunction of LV leading to respiratory depression and cardiac arrest. The event (death) was not related to study drug (investigational product) or study procedures.					
17-003	23-Jul-2020	23-Jul-2020	Consent Withdrawn	This patient was enrolled and received all 3 doses of the study drug on visit 1 (Day 1). However, the patient withdrew consent to participate in the study later that day.	04-014	25-Sep-2020	27-Sep-2020	Death	This patient visited the emergency department with the complaint of sudden onset of weakness in legs, unable to walk, slurring of speech, shortness of breath, and sudden fall on 25-Sep-2020 morning at 08:30 hours. The clinical examination showed left hemiparesis with dense lower limb weakness and numbness with a suspicion of right anterior cerebral artery (ACA) stroke. The patient's general condition was poor, and afebrile, and vitals were: SBP-100 mmHg, DBP-70 mmHg, Pulse rate-80 per minute, Respiratory rate-20 breaths per minute. The Patient's CT scan showed an acute infarct in the left Middle Cerebral Artery (MCA) territory. Subtype of Ischemic Stroke: Small Vessel Occlusion. ECG showed abnormal T wave, anterolateral Loeys-Dietz syndrome (LDS), and considered ischemia changes, with a QTc interval of 456 msec. The medical history provided by relatives was type-II Diabetes mellitus (T2DM), hypertension, severe alcoholic from the past 20 years, and an ex-smoker. The patient was diagnosed with an ongoing stroke. The Alteplase (rtPA) as intravenous thrombolysis (IVT) therapy was administered at 11:20 hours after consent. After IVT, sensorium was normal; however, the neurological deficit was fluctuating. The investigator considered the patient suitable for enrollment in this study. PI approached the patient to participate in this study, and LAR gave consent. The

<table>
<tr><th colspan="5">Standard Treatments + Saline</th><th colspan="5">Standard Treatments + Sovateltide</th></tr>
<tr><th>Subject Number</th><th>Date of Enrolment</th><th>Date of Exclusion / Withdrawal / Death</th><th>Reason of Exclusion / Withdrawal / Death</th><th>Details</th><th>Subject Number</th><th>Date of Enrolment</th><th>Date of Exclusion / Withdrawal / Death</th><th>Reason of Exclusion / Withdrawal / Death</th><th>Details</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>patient's laboratory investigation showed high blood sugar (378 mg/dl). Other abnormal values reported were WBC count (11900 cells/cumm) Neutrophils (84%), Lymphocytes (10%), PCV (36.7 %), MCH (27.8 pg), ESR (58 mm/hour), bilirubin (1.2 mg/dl), potassium (5.0 mmol/l) and SGOT (83 IU/L). The patient's chest X-ray was normal. Stroke severity was assessed with scales: NIHSS-7, mRS-4, BI- 25, EQ-5D-5L (EURO-QoL)- [Mobility-5, Selfcare-4, Usual activities (e.g., work, study, housework, family or leisure activities)-5, Pain/discomfort-2, Anxiety/depression-2] Patient health score-50. The patient was randomized in this study.
Study Drug Administration on Day 1:
<table>
<tr><td>Date→</td><td colspan="3">Day-1 (25 Sept 2020)</td></tr>
<tr><td>Dose No.</td><td>Start Time (HH:MM)</td><td>Stop Time (HH:MM)</td><td>Total dose Administered (ml)</td></tr>
<tr><td>Dose 1</td><td>18:20</td><td>18:21</td><td>3.5</td></tr>
<tr><td>Dose 2</td><td>21:25</td><td>21:26</td><td>3.5</td></tr>
<tr><td></td><td colspan="3">Day-1 (26 Sept 2020)</td></tr>
<tr><td>Dose 3</td><td>00:25</td><td>00:26</td><td>3.5</td></tr>
</table>
On 26-Sep-2020, almost 24 hours post thrombolysis, the patient was conscious, coherent, and obeying commands. Limb movements were better, whereas slurring of speech was mild. Post rtPA as routine practice, MRI and Magnetic resonance angiography (MRA) was advised by the investigator. MRI Showed acute infarct (restriction on DWI & ADC) in left capsuloganglionic region, corpus callosum, and bilateral frontal lobes. Mild ischemic changes in bilateral periventricular and fronto-parietal white matter, diffuse cerebral atrophy; MRA showed "Decreased flow noted in bilateral A2 branches. Atheromatous changes noted in the bilateral intracranial internal carotid artery (ICA's), hypoplastic right vertebral artery and A1 segment of the right</td></tr>
</table>

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									anterior cerebral artery (ACA)." The patient's general condition was moderately sick, and stroke severity scales scores were: NIHSS- 7 mRS- 4. The 2D ECHO was performed at the bedside at 12:00 noon of 26 Sep 2020 by the cardiologist and diagnosed as ischemic heart disease and left ventricular dysfunction (IHD-LVD) with EF - 40%. The patient continued to receive SOC from the time of hospital admission, including Injection Ceftrixone 2 gm BD, Injection Piracetam 15 mL TID, Injection Metoclopramide 2cc TID, Injection Thiamine OD, Injection Levetiracetam 500 mg TID, Tablet Aspirin 325 mg OD, Tablet Atrovastatin 80 mg OD, Injection Enoxaparin 40 mg in 0.4 mL S/C BD, Tablet Clopidogrel 75 mg OD, Tablet Isosorbide mononitrate 10 mg BD. At 22:30, the patient had one episode of vomiting associated with sweating. The patient was conscious, oriented, and obeying commands. The patient reported no chest pain and no haematemesis. Vitals were recorded as: Pulse rate- 76 per minute, SBP- 120 mmHg, DBP- 80 mmHg, random blood glucose – 260 mg/dL, SpO_2 94% at room atmosphere and 98% on 4 lit. O_2 supply. ECG showed abnormal T wave and anterolateral LDS and considered ischemic changes, with a QTc interval of 460 msec. The intensivist was informed, and the patient was administered Injection Esomeprazole, Injection Metoclopramide 2cc stat, Injection Hydrocortisone 100 mg IV stat, IVF Normal Saline at the rate of 50 mL/hour. Repeat CT of the brain was advised. On 27 Sep 2020: At 00:30 hours, vitals were: Pulse rate- 106 per minute, SBP- 100 mmHg, DBP- 70 mmHg. Arterial Blood Gases (ABG) test reported a base deficit of -6.2 and oxygen saturation of 96%. Repeat CT of the brain showed no fresh changes except ventricular system dilated. On 27 Sep 2020: At 02:30 hours, vitals were recorded as Pulse rate- 112 per minute, SBP- 100 mm of Hg, DBP- 60 mm of Hg, Respiratory rate- 24 breaths per

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									minute, Body temperature- 98.6 °F, Oxygen saturation- 99%. At 3:30 hours, patient vitals were Pulse rate- 89 per minute, SBP- 80 mmHg, DBP- not recordable, Respiratory rate- 32 breaths per minute, Body temperature- 98.6 °F, SpO_2- 89%. At 04:30 on 27 Sep 2020, the patient had sudden breathlessness (tachypnea) and sweating. Vitals were: Pulse rate-110 per minute (tachycardia), SBP- 80 mmHg (on noradrenaline support) (Hypotension), DBP- 70 mmHg, respiratory rate- 38 breaths per minute, bilateral crept present, SpO_2- 93% on 6-liter oxygen support. Repeat ECG was taken, which showed sinus tachycardia and marked ischemic changes. An emergency cardiologist's opinion was taken and diagnosed as IHD with pulmonary edema. Injection noradrenaline was administered at 15 mL/hour, Injection Dobutamine at mL/hour, Injection Furosemide intravenous infusion at 10 mL/hour for the first 1 hour followed by 3 mL/hour, Injection Mephentermine at 5 mL/hour, and Injection Carnisure 1 gm IV stat. At 5:00 hours, Pulse rate- 67 per minute, SBP- 80 mmHg (on noradrenaline support), DBP- not recordable, respiratory rate- 14 breaths per minute, SpO2- 87%. Due to poor GCS score ($E_2V_TM_4 = 7$) and desaturation, the patient was intubated and supported with a ventilator. At 6:40 hours, the patient had sudden bradycardia; therefore, CPR was started. Injection Atropine 2 cc IV stat and Injection adrenaline IV stat were administered. CPR effort was continued in spite of vitals recorded as Pulse rate- zero, BP- Not recordable, Pupils- Dilated, and ECG was flat at 07:30 hours of 27 Sep 2020. The patient was continuously receiving SOC right from hospital admission, and the study drug was administered as add-on therapy. Medical history included Type-II Diabetes mellitus (T2DM), hypertension, and severely alcoholic from the past 20 years, an ex-smoker, and present condition includes

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									ischemic stroke and IHD with LVD (Ejection fraction 40%) and pulmonary edema. Unfortunately, despite all efforts and continuous SOC patient's death occurred due to the progression of underlying conditions, that is, ischemic stroke and IHD with LVD and pulmonary edema leading to cardiorespiratory arrest. The event (Death) was not related to the study drug (investigational product) or study procedures and was associated with the progression of existing illness i.e., ischemic stroke and IHD with LVD (Ejection fraction 40%) and pulmonary edema leading to cardiorespiratory arrest.
24-011	12-Jan-2022	14-Jan-2022	Consent Withdrawn	This patient was enrolled and received all 3 doses of the study drug on visit 1 (Day 1). However, on visit 1 (Day 2), the patient withdrew consent to participate in the study.	05-002	08-Jan-2020	08-Jan-2020	Consent Withdrawn	This patient was enrolled in the study on 08-Jan-2020. However, no study drug was given as the patient refused to take the first dose of study drug and withdrew consent from the study on the same day, i.e., visit 1 (Day 1) just after randomization. Therefore, at the patient's request, this patient was considered consent withdrawn from the study.
26-012	13-Jan-2022	17-Mar-2022	Death	Patient admitted to the emergency department on 12-Jan-2022 at 22:42 Hrs. Patient presented with complaints of right limb weakness since 17:00 Hrs. on the day of hospitalization after waking up from sleep along with slurring of speech. Provisional diagnosis was 1. CVA left MCA infarct-small vessel disease, 2. Diabetes Mellitus, 3. Hypertension. The patient had a history of Type-II diabetes mellitus since 2014, on regular insulin (32 U – 22 U) + Oral hypoglycemic agent, Systemic hypertension since (2019) on Tab. Amlong 5 mg, and chronic kidney disease (left atrophic kidney). The patient had a history of hysterectomy 10 years back. The patient was awake and alert; general appearance was sick, with no pallor, icterus, or cyanosis. Patient's BP 160/100 mmHg, Pulse rate 106/min, Body Temperature 96.9 °F. CVS: S1 S2 heard, Respiratory System: Bilateral air entry present P/A: Soft, normal CNS: Awake, alert, Bilateral	05-003	15-Jan-2020	07-Feb-2020	Death	This patient was admitted to the emergency department on 14-Jan-2020 at 15:39 hours with complaints of sudden onset of weakness of the right upper and lower limb of the body, deviation of mouth to the right side, giddiness prior to the episode and slurred speech. This was a case of acute ischemic stroke involving the Left Middle Cerebral Artery Territory (MCA) infarct. On 14-Jan-2020, an urgent CT head with CT angiography was done, which showed acute non-hemorrhagic left middle cerebral artery territory infarct with chronic infarcts involving bilateral supratentorial parenchyma and lipid-rich plaque involving the left proximal ICA causing severe luminal stenosis. Thrombotic/stenotic occlusion of the left middle cerebral artery with non-visualization of its distal branches. Subtype of Ischemic Stroke: Large Artery Atherosclerosis. The patient was within the window period, i.e., 4.5 hours, and was thrombolysed with intravenous alteplase (rt-PA). The patient was suffering from Diabetes mellitus Type 2 and hypertension. The patient

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<tr><td></td><td></td><td></td><td></td><td>pupils equal and reacting to light, right UMN facial palsy present, right hemiparesis present, left gaze-evoked nystagmus present and sensory-normal. Stroke severity quantified by neurologic examination stroke scale: NIHSS: 08, mRS: 3, BI: 70, MRI brain with angiogram done on 12-Jan-2022 showed multiple acute lacunar infarcts in the left thalamus, posterior limb of the left internal capsule, and left superior temporal lobe white matter. No obvious mass effect/hemorrhagic transformation. Discrete diffusion non-restricted sub-cortical flair hyperintensities noted-small vessel ischemic changes. Right CP angle arachnoid cyst (non-significant). Subtype of Ischemic Stroke: Small Vessel Occlusion.
ECG was done on 12-Jan-2022, which showed a normal study. Chest X-Ray was done on 13-Jan-2022 and had a normal impression. HRCT-Chest was done on 13-Jan-2022 and showed subpleural /dependent atelectasis with an admixture of ground glass haze in bilateral lower lobe basal segments-CORADS 2. Calcified plaques in LAD, LCX, and RCA. ECHO cardiography done on 13-Jan-2022 showed normal left ventricular systolic function (LVEF: 65%), Normal wall and chambers, LVDD E/A: 0.6, No RWMA, Mild IAS thinned out, No color flow across the IAS, Normal pericardium, No thrombus, IVC: 1.5 cm, No collapse. USG Abdomen on 13-Jan-2022: Right Kidney was normal in size with a mild increase in cortical echotexture. CM differentiation was maintained -suggestive of Medical Renal Disease, right kidney hydronephrosis-? Partial Pelvi Ureteric Junction obstruction. Left Kidney: Not Visualized, well distended urinary bladder with thickening and floating internal echoes-to rule</td><td></td><td></td><td></td><td></td><td>provided a history of cerebrovascular accident (CVA or Stroke) two months back and Glaucoma. Digital Subtraction Angiography of the brain was done, which showed left ICA origin 70% stenosis. Occlusion of the superior division of left M1. 90% stenosis of the left vertebral origin. The patient was meeting the eligibility criteria and was randomized in this study. The consent was obtained from patients LAR on 15th Jan 2020 at 11:28 hours. On day 1, as per protocol, blood samples were taken, ECG and X-ray were done. The patient's stroke scales (NIHSS, mRS, BI, EuroQoL) were assessed, and doses were given. The study drug administration details are as follows.

<table>
<tr><td>Date→</td><td>15 Jan 2020</td><td>17 Jan 2020</td><td>20 Jan 2020</td></tr>
<tr><td>Dose 1</td><td>12:30</td><td>12:32</td><td>12:35</td></tr>
<tr><td>Dose 2</td><td>14:40</td><td>14:44</td><td>14:54</td></tr>
<tr><td>Dose 3</td><td>16:55</td><td>17:00</td><td>17:05</td></tr>
</table>

The patient's repeat MRI brain was done on 18-Jan-2020, which showed a large area of restricted diffusion showing hyperintensities on T2 FLAIR is noted involving left fronto-parieto temporal and occipital parenchyma and left globus pallidus, suggestive of an acute infarct. There were few punctate foci of blooming on SWI images involving bilateral basal ganglia and parieto-temporal parenchyma, suggestive of microbleeds. On day 3, vital assessment and scales (NIHSS, mRS, BI, and EuroQoL) were done along with standard treatment. The patient's condition worsened and got intubated and on SIMV mode of the ventilator. On day 6, vital assessment and scales (NIHSS, mRS, BI, and EuroQoL) were done. The patient had a lower respiratory tract infection (consolidation in the posterior basal segment of the right lower lobe), as evidenced by the HRCT chest on 18 Jan 2020, and a respiratory physician's consultation</td></tr>
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<tr><td></td><td></td><td></td><td></td><td>out cystitis. The right lower ureter was dilated, and bladder outflow obstruction. Trace right pleural effusion. Significant postvoid residual urine of 415 ml. Color Duplex Doppler Examination of Carotid and Vertebral Arteries on 13-Jan-2022 showed atherosclerotic changes in the form of diffuse thickening of Intima-Media Complex in both common carotid arteries. Hyperechoic plaque in the right CCA. As per study protocol, the patient met all the eligibility criteria and was randomized in the study on 13-Jan-2022 at 16:20 hours after receiving the consent. The patient successfully received all nine doses of the study drug as follows:
<table>
<tr><td>Date→</td><td colspan="3">Day-1 (13-Jan-2022)</td></tr>
<tr><td>Dose No.</td><td>Start Time (HH:MM)</td><td>Stop Time (HH:MM)</td><td>Total dose Administered (ml)</td></tr>
<tr><td>Dose 1</td><td>16:40</td><td>16:41</td><td>2.5</td></tr>
<tr><td>Dose 2</td><td>19:00</td><td>19:01</td><td>2.5</td></tr>
<tr><td>Dose 3</td><td>21:30</td><td>21:31</td><td>2.5</td></tr>
</table>
<table>
<tr><td>Date→</td><td colspan="3">Day-3 (15-Jan-2022)</td></tr>
<tr><td>Dose No.</td><td>Start Time (HH:MM)</td><td>Stop Time (HH:MM)</td><td>Total dose Administered (ml)</td></tr>
<tr><td>Dose 1</td><td>17:00</td><td>17:01</td><td>2.5</td></tr>
<tr><td>Dose 2</td><td>19:20</td><td>19:21</td><td>2.5</td></tr>
<tr><td>Dose 3</td><td>21:40</td><td>21:41</td><td>2.5</td></tr>
</table>
<table>
<tr><td>Date→</td><td colspan="3">Day-6 (18-Jan-2022)</td></tr>
<tr><td>Dose No.</td><td>Start Time (HH:MM)</td><td>Stop Time (HH:MM)</td><td>Total dose Administered (ml)</td></tr>
</table></td><td></td><td></td><td></td><td></td><td>was taken. Antibiotics were upgraded to meropenem and polymyxin. In view of low GCS, the patient was intubated and put on ventilatory support. The Patient's CT chest was done, which showed small consolidation in the posterior basal segment of the right lower lobe. The patient completed visit 2 (12+2 day) evaluation on 28 Jan 2020 during the hospital stay. On 29 Jan 2020, a tracheostomy was done in view of the difficulty in weaning from the ventilator. LAR took LAMA on 02 Feb 2020. Condition of the Patient and grave prognosis due to severe clinical condition: Acute left MCA territory infarct, recurrent stroke, lower respiratory tract infection, and sepsis; coexisting diseases: Hypertension, Diabetes mellitus type 2 and right eye glaucoma was explained in detail to the relatives. The patient had a tracheostomy tube in situ. The site coordinator followed the patient telephonically to find out the patient's condition, as he was unwell during LAMA. On 12-Feb-2020 the site coordinator was informed about the patient's death on 7-Feb-2020 at 7:00 AM at home. The cause of death was unknown as the patient died at home. This patient was in the hospital for almost 18 days because of a health condition and was discharged from the hospital on LAMA. The patient's death occurred at home after 5 days of discharge from the hospital. A causal association of the event (death) with the suspect product (study drugs or study procedure) cannot be proved. However, the patient's death might occur due to worsening of health condition even after receiving continuous standard treatment. This is also to be noted that this patient was suffering from coexisting diseases like hypertension, Diabetes mellitus type 2, and right eye glaucoma.
The patient died due to the progression of the underlying condition of acute left MCA territory infarct, recurrent stroke, hemorrhagic transformation of stroke, lower respiratory tract infection, and sepsis.</td></tr>
</table>

Standard Treatments + Saline					Standard Treatments + Sovateltide				
Subject Number	**Date of Enrolment**	**Date of Exclusion / Withdrawal / Death**	**Reason of Exclusion / Withdrawal / Death**	**Details**	**Subject Number**	**Date of Enrolment**	**Date of Exclusion / Withdrawal / Death**	**Reason of Exclusion / Withdrawal / Death**	**Details**
				<table><tr><td>Dose 1</td><td>18:00</td><td>18:01</td><td>2.5</td></tr><tr><td>Dose 2</td><td>20:30</td><td>20:31</td><td>2.5</td></tr><tr><td>Dose 3</td><td>22:45</td><td>22:46</td><td>2.5</td></tr></table> The patient continued receiving standard treatment for ischemic stroke from admission to the hospital and throughout stay in the hospital as per the study protocol, and the IP was an add-on treatment. Patient conservatively managed with loading dose C stat., Tab. Aspirin + Clopidogrel (75/75 mg) (OD), Tab. Atorvastatin 40 mg (HS), Inj. Pantoprazole 40 mg I.V (OD), Syrup. (Potassium Citrate + magnesium Citrate + Vitamin B6) 10 mL in the morning, 10 mL (BD), Inj. KCl 40 mEq in 100 mL/hour, Inj. Human insulin s/c (TID), Tab. Metformin 1gm + Teneligliptin 20 mg (OD), Tab. Gliclazide 60 mg (OD), Tab. Methylcobalamine 1500mcg + Multivitamin (HS), Tab. Ranitidine 300 mg (OD). This patient was discharged from the hospital on 16-Jan-2022 at 15:00 hours. The patient was clinically stable at the time of discharge. Discharge instructions included: Tab. Aspirin + Clopidogrel (75/75 mg) (OD), Tab. Atorvastatin 40 mg (HS), Tab. Metformin 1gm + Teneligliptin 20 mg (OD), Tab. Gliclazide 60 mg (OD), Tab. Methylcobalamine 1500 mcg + Multivitamin (HS), Tab. Ranitidine 300 mg (OD), Tab Azelnidipine 16 mg (HS). On 25-Jan-2022 at 12:00 Hrs. The patient came to the hospital for planned visit as per protocol. The patient was stable. No AE/SAE or recurrence of stroke was reported on this visit. Patient continued on the same discharge medication. On 01-Feb-2022 at 13:20 Hrs, the patient visited the hospital as an unscheduled visit. BP-192/117 mmHg (Sitting Position), Heart Rate-115 beats/minute, and BP – 199/128 mmHg					

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				(Standing Position), Heart rate-112 beats/minute, and the same was recorded as an adverse event. On examination: No edema, No pallor CVS: S1 and S2 heard. Respiratory system: Bilateral Normal Vesicular Breath Sound present. P/A: Soft and Bowl sound present. CNS: Moving all 4 limbs, and no recurrence of stroke occurred during this period. Patient was advised Tab. Bethanechol 25 mg BD, Tab Amoxycillin 500 mg + Clavulanic Acid 125 mg (625 mg) TDS and Tab. Prazosin Hydrochloride 2.5 mg TDS, salt-restricted diet (sodium less than 2g/day) Foley's tube was removed, and continued rest of the previous medication. On 12-Feb-2022 at17:00 Hrs. (Visit-3, Day 30): Patient came to the hospital for scheduled visit as per protocol. The patient was awake, alert, catheterized, and weakness in the right side was getting better. No AE/SAE or recurrence of stroke occurred during this period. On 07-Mar-2022 at 10:00 Hrs. Visit-4, Day 60 (Telephonic Visit); Study investigator performed a telephonic visit as per protocol; the patient was stable and had a good improvement and good compliance with concomitant medication. All neurological or study-related assessments were done telephonically. No AE/SAE or recurrence of stroke occurred during this period. On 16-Mar-2022 at 22:00 Hrs.: This Patient was presented to the emergency ward with complaints of sudden onset of giddiness and fall at around 19:30 Hrs, followed by dysarthria, and became unresponsive within 30 minutes. No history of seizure, vomiting, or bleeding manifestation. On examination: General appearance- the patient was unconscious with no pallor, icterus, cyanosis, or clubbing. BP was 190/100 mmHg, Heart rate was 80 beats/minute,					

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				respiratory rate was 24 breaths/minute, and body temperature was 98.2 °F. RBS 266 mg/dl and oxygen saturation 100% on room air. CVS- S1, S2 heard. Respiratory System- Bilateral air entry present. Abdomen- Soft, no organomegaly. CNS- GCS: 3/15; Bilateral pupil asymmetric right 3.5 mm and not reacting to light; left 2.5 mm not reacting to light and mild flexor posturing to painful stimuli. At 22:30 Hrs.: On examination: the Patient's GCS was 3/15, Bilateral pupil asymmetric right 3.5 mm and not reacting to light; left 2.5 mm not reacting to light. CVS- S1 S2 present, Respiratory system- Bilateral air entry present, BP- 190/100 mmHg, pulse rate-80/minute, respiratory rate 24 breaths/minute, body temperature 98.2 °F, and involuntary myoclonic jerks present. In view of low GCS, the patient was intubated with a 7mm ET tube at 22:35 Hrs. and mechanically ventilated. Ryle's tube 16 size was introduced at 22:45 Hrs. and the patient was evaluated further with routine blood investigations and CT brain. CT brain revealed acute intracerebral hemorrhage of volume approx. 60-65 cc at the right ganglio-thalamo-capsular region extending to the right frontal, temporoparietal lobes with surrounding edema. There was a mass effect with a midline shift of 9 mm to the left side and intraventricular extension of hemorrhage. A hypodense lesion of 15-30 HU at the right CP angle and right anterior aspect of posterior fossa-differentials; epidermoid, an arachnoid cyst. NC/HRCT Chest had a normal impression. Patient was managed with Inj. Labetalol 10 mg IV, Inj. Midazolam 3mg IV, Inj. Atracurium 30 mg IV, Inj. Atropin 0.6mg IV Inj. Mannitol 100ml IV, Inj. Tranexamic Acid 1g IV and Inj. Levetiracetam 1g IV. The patient's lab					

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Subject Number	**Date of Enrolment**	**Date of Exclusion / Withdrawal / Death**	**Reason of Exclusion / Withdrawal / Death**	**Details**	**Subject Number**	**Date of Enrolment**	**Date of Exclusion / Withdrawal / Death**	**Reason of Exclusion / Withdrawal / Death**	**Details**
				investigations were performed on 17-Mar-2022 at 00:30 Hrs. ECG on 17-March-2022 at 00:33 Hrs showed sinus tachycardia, nonspecific ST, and T-wave abnormality. On 17-March-2022 at 01:00 Hrs.: Visual Infusion Phlebitis (VIP) score – 0/5, Barden score – 18/23, Morse fall score – 95/125, and Wells score -1/6. At 01:15 Hrs. The patient was diagnosed with right intracranial hemorrhage with midline shift and hypokalemic and shifted to IMCU from the emergency department for further management. While in ICU, the patient was unconscious and mechanically ventilated. BP was 150/80 mmHg, pulse rate 80 /minute, respiratory rate 24 breaths/minute, and oxygen saturation-100% on mechanical ventilation support. Respiratory System- Bilateral air entry present. Abdomen- Soft, no organomegaly. CNS- GCS: E_1 V_T M_1, Pupil asymmetric right 3.5 mm and not reacting to light; left 2.5 mm not reacting to light. Involuntary jerks present. The Patient's RBG was 299 mg/dl. At 07:00 Hrs: On examination: GCS – E_1 V_T M_1, pupil- Asymmetrical, BP was 170/100 mmHg (Mean Arterial Pressure 130 mmHg), Heart rate 102 beats/minute, respiratory rate 20 breaths/minute, oxygen saturation 100% on mechanical ventilation support (FiO2-50%, PEEP-5 and TV-350 ml), potassium correction. Input/output was 300 ml/625 ml, respectively. Visual Infusion Phlebitis (VIP) score 0/5, Barden score 18/23, Morse fall score 115/125, and Wells score 1/6. At 07:40 Hrs, vitals are as follows: BP-140/90 mmHg and Heart rate- 94 beats/minute. On examination: GCS – E_1 V_T M_1, the bilateral pupil was not reflecting to light, and the patient continued on mechanical ventilation support and					

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				potassium correction. At 08:30 Hrs, the patient experienced acute neurovascular syndrome; BP was 144/92 mmHg. On examination, the patient was unconscious, pupils right 3.5 mm and not reacting to light; left 2.5 mm not reacting to light, Doll's Eye Movement was negative, mild flexor posturing to deep pain. At 13:00 Hrs: Visual Infusion Phlebitis (VIP) score 0/5, Barden score 18/23, Morse fall score 115/125, and Wells score 1/6. The patient was on continuous mechanical ventilation support. GCS E_1 V_T M_1, intravenous infusion of normal saline at 100/hr was started. At 15:40 Hrs.: The Patient's heart rate was 60 beats/minutes, the patient developed bradycardia and went into sudden desaturation and became unresponsive. ACLS protocol was initiated, CPR was given, and 2 ampoules of Injection Adrenaline were injected during the CPR process. At 15:44 Hrs. Injection Adrenaline first dose was administered, and CPR continued, no carotid pulse was felt, and the patient didn't respond. At 15:47 Hrs. Injection Adrenaline second dose was administered, and CPR continued, no carotid pulse was felt, and the patient didn't respond. At 15:50 Hrs, despite the above resuscitative measure's patient couldn't be revived. ECG showed asystole. The patient was declared dead on 17-Mar-2022 at 15:50 Hrs. The causal association of the event (death) with the suspect product (study drugs or study procedures) cannot be proved. However, the patient had a history of diabetes mellitus (since 2014), hypertension (Since 2019), and chronic kidney disease (left atrophic kidney). The patient was on antiplatelet medications aspirin and clopidogrel since 13-Jan-2022. Therefore, intracranial hemorrhage most likely resulted from antiplatelet drugs and the patient's underlying disease conditions, diabetes mellitus, diabetic vasculopathy, hypertension,					

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				and chronic kidney disease (left atrophic kidney) as contributory factors. The event (Death) was not related to the study drug or study procedure and was due to brain stem dysfunction due to underlying condition mass effect resulting from right intra-cranial hemorrhage.					
					06-009	08-Feb-2021	11-Mar-2021	Consent Withdrawn	This patient was enrolled in the study and completed visit 2 (Day 12). On 11-Mar-2021, visit 3 (Day 30). However, the patient withdrew consent from the study because of concerns about the high number of COVID-infected patients in the hospital. Therefore, this patient was considered consent withdrawn from the study on 11-Mar-2021.
					07-002	16-Mar-2020	19-Mar-2020	Consent Withdrawn	This patient was enrolled and received all 3 doses of the study drug on visit 1 (Day 1). However, on 19-Mar-2020, visit 1 (Day 3), the patient withdrew consent to continue participating in the study and denied doing any investigations or sharing any further details from 19-Mar-2020.
					08-005	15-Feb-2020	16-Feb-2020	Consent Withdrawn	This patient was enrolled and received all 3 doses of the study drug on visit 1 (Day 1). However, on 16-Feb-2020, visit 1 (Day 2), the patient withdrew consent to participate in the study and took Leave Against Medical Advice from the hospital. Therefore, this patient was considered consent withdrawn from the study on 16-Feb-2020.
					17-007	15-Jan-2021	28-Jan-2021	Death	This patient was initially taken to the hospital on 14th Jan 2021 family with complaints of sudden onset of weakness of both proximal and distal Upper Limbs > Lower Limbs associated with numbness of the right side of the body since 14th Jan 2021 from 16:00 hours. The patient underwent MRI, which showed "acute non-haemorrhagic infarcts in the left insular cortex, perisylvian parenchyma and frontal region, chronic lacunar infarcts in the bilateral capsuloganglonic regions, ischemic changes in bilateral periventricular and fronto-parietal white matter and diffuse cerebral atrophy." MR-Angiogram showed Right Middle Cerebral Artery (MCA), Interior Cerebral Artery (ICA), bilateral Anterior Cerebral Artery (ACA), and Posterior Cerebral Artery (PCA) were not visualized –

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									occlusions. Subtype of Ischemic Stroke: Large Artery Atherosclerosis. The patient's family decided to bring the patient to another hospital for further treatment. On admission at 00:40 hours of 15th Jan 2020, the patient was afebrile, conscious, but not comprehending, and vitals were: BP-150/90 mm of Hg, Pulse rate 90 per minute with SpO_2 99% at room air (RA). The patient had right hemiparesis, right side upper motor neuron (UMN) palsy with global aphasia, and right planter extensor. The patient was diagnosed with acute ischemic stroke, confirmed from the MRI & MRA performed. Patient had type II diabetes mellitus (from the last 7 years) and hypertension. ECG was within normal limits, and chest x-ray was found to be normal. The patient was eligible to enroll in this study, and the consent was obtained from LAR. Stroke severity was assessed with scales: NIHSS-12, mRS-4, BI-10, EQ-5D-5L (Euro QoL) - [Mobility-4, Selfcare- 4, Usual activities (e.g. work, study, housework, family or leisure activities) - 4, Pain/discomfort- 3, Anxiety/depression- 3; Patient health score- 40]. The patient was randomized in the study on 15-Jan-2021 at 13:54 hours. The patient received the standard treatment in I.C.U from the time of hospitalization, including: Tab. Aspirin 150 mg OD, Tab. Clopidogrel 75 mg OD, Tab. Atorvastatin 40mg OD, Tab. Telmisartan 40 mg OD, Tab. Metformin 500 mg TDS and Inj. Human insulin S.C TDS. Patient laboratory reports (14-Jan-2021 at 20:38 hours) showed few abnormal values: MCH (26.3 pg), ESR (25 mm/hour). On 15-Jan-2021, the laboratory report showed: Random blood glucose (273 mg/dl) and serum calcium (7.6 mg/dl). The patient received the study drug on day 1 as follows: Date→ | Day-1 (15 Jan 2021)

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Dose No.	Start Time (HH:MM)	Stop Time (HH:MM)	Total dose Administered (ml)
Dose 1	14:00	14:01	2.25
Dose 2	17:00	17:01	2.25
Dose 3	20:00	20:01	2.25

At 18:30 hours, the patient was conscious with the right plantar extensor, and BP was 150/080 mmHg. At 19:00, GRBS was 277 mg/dl. On 16-Jan-2021, at 07:00 hours- the patient was conscious, comprehending with right hemiparesis, right side UMN palsy, global aphasia, and right plantar extensor. Vitals were recorded as BP 130/080 mmHg, Pulse rate 74 per minute, Respiratory rate 13 per minute with SpO_2 100% at room air. At 14:15 hours the patient was conscious, occasionally comprehending with right hemiparesis. Vitals were recorded as BP 120/080 mmHg, Pulse rate 76 per minute, Body temperature 98.4 °F with SpO_2 99% at room air (RA). The NIHSS was 12, and mRS was 4. At 16:30 hours, the patient's BP was recorded as 140/100. On 17-Jan-2021, at 07:00 hours, the patient's BP was recorded as 130/090. At 10:00 hours, the patient was conscious, comprehending right side UMN palsy with right hemiparesis having power 0/5 of both upper limb and lower limb of the right side. The BP of the Patient was 130/080, Pulse rate- was 80 per minute. The patient received the study drug on day 3 as follows:

Date→	Day-3 (17 Jan 2021)		
Dose No.	Start Time (HH:MM)	Stop Time (HH:MM)	Total dose Administered (ml)
Dose 1	14:20	14:21	2.25
Dose 2	17:25	17:26	2.25
Dose 3	20:20	20:21	2.25

<table>
<tr><th colspan="5">Standard Treatments + Saline</th><th colspan="5">Standard Treatments + Sovateltide</th></tr>
<tr><th>Subject Number</th><th>Date of Enrolment</th><th>Date of Exclusion / Withdrawal / Death</th><th>Reason of Exclusion / Withdrawal / Death</th><th>Details</th><th>Subject Number</th><th>Date of Enrolment</th><th>Date of Exclusion / Withdrawal / Death</th><th>Reason of Exclusion / Withdrawal / Death</th><th>Details</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>At 19:00 hours- the GRBS was 276 mg/dl. On 18-Jan-2021, the patient was conscious, having a GCS score of 10 ($E_4V_1M_5$). The BP was recorded as 150/090 mmHg with GRBS 193 mg/dl. The patient had global aphasia with right hemiparesis, right extensor plantar and left plantar flexor, and right-side UMN palsy. An ultrasound abdomen was done and found to be normal. At 19:00- the GRBS was 243 mg/dl. On 19-Jan-2021, the patient was conscious, comprehending having a right side UMN palsy, global aphasia, and right hemiparesis. Vitals were recorded as BP 130/080, pulse rate 92 per minute with SpO_2 97% at room air, and the GRBS was 208 mg/dl. At 19:00 hours the patient was conscious, and vitals were stable. The GRBS was 136 mg/dl. On 20-Jan-2021, the patient was conscious, having global aphasia, right side UMN palsy, and right hemiparesis. On examination, cardiovascular system S_1S_2 is normal and respiratory system- normal vesicular breath sound present. The patient had bilateral plantar flexor response, and the pupil was normal in size and reactive to light. BP was recorded as 130/070 mmHg, and GRBS was 240 mg/dl. The patient received the study drug on day 6 as follows:
<table>
<tr><td>Date→</td><td colspan="3">Day-6 (20 Jan 2021)</td></tr>
<tr><td>Dose No.</td><td>Start Time (HH:MM)</td><td>Stop Time (HH:MM)</td><td>Total dose Administered (ml)</td></tr>
<tr><td>Dose 1</td><td>14:30</td><td>14:31</td><td>2.25</td></tr>
<tr><td>Dose 2</td><td>17:35</td><td>17:36</td><td>2.25</td></tr>
<tr><td>Dose 3</td><td>20:30</td><td>20:31</td><td>2.25</td></tr>
</table>
At 17:00 hours the BP was recorded as 150/100 mmHg. At 18:09 hours- the HbA_{1C} was 8.7 %, and the mean blood glucose was 226 mg/dl. On 21-Jan-2021, the patient was conscious, having global aphasia and, right-side UMN palsy, right hemiparesis. On examination, the cardiovascular system S_1S_2 is normal, and the respiratory system normal vesicular breath</td></tr>
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									sound present. The patient was having right plantar mute and left plantar flexor response, and the pupil was normal in size and reactive to light. BP was recorded as 110/070 mmHg, and GRBS was 135 mg/dl. At 19:00 hours the GRBS was 253 mg/dl. The patient was stable and shifted to the ward. On 22-Jan-2021, the patient was stable, having global aphasia, right side UMN palsy, and right hemiparesis with power 0/5 in both upper and lower limb of the right side and 4/5 in both upper limb and lower limb of the left side. The GCS score was 9 ($E_5V_1M_3$). On examination cardiovascular system and the respiratory system were normal. The fasting blood sugar was 220 mg/dl. At 13:00 hours- the GRBS was 284 mg/dl. On 23-Jan-2021, the patient's condition was stable, and patient was discharged from the hospital with the advice of the following medications for 2 weeks: Tab Aspirin 150 mg OD, Tab Clopidogrel 75 mg OD, Tab Atorvastatin 40 mg H/S, Tab Citicoline 500 mg BD, Tab Metformin 500 mg TID, Tab pantoprazole 40 mg OD, Inj. Human Insulin /Human Isophane (30/70) SC 16U-0-16U and Inj. Basal insulin 8U. On 28-Jan-2021, the patient was apparently well till 01:45 hours, and then patient developed abnormal movement in the left upper limb, which after some time involved the whole of the body, followed by loss of consciousness. Later, patient was brought to the hospital at 03:11 hours and declared dead at 03:31 hours as BP, pulse rate, and SpO2 were not recordable, and pupils were not reactive to light. ECG (12 Lead) showing no electrical activity of the heart (in any lead). The event (Death) was not related to the study drug or study procedure and most likely due to underlying condition: ischemic stroke and/or metabolic causes leading to left focal seizures with secondary generalization with aspiration pneumonitis and cardiopulmonary arrest.

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					26-015	04-Feb-2022	12-Apr-2022	Death	This case refers to a patient admitted to the emergency department on 03-Feb-2022 at 20:29 Hours. He presented with complaints of sudden onset of right limb weakness since 12:00 hours with difficulty in speaking and facial deviation to the left side. Provisional diagnosis was 1. CVA left MCA infarct, 2. Hypertension. The patient had hypertension for the last 3 years (2018) and coronary artery disease (CAD) for 4 months. The general appearance was normal, with no pallor, no icterus, or cyanosis. Patient's BP 130/90 mmHg, Pulse rate 67/min, Respiratory Rate 16 breaths/minute, Body Temperature 98.6°F. Patient in room air with 99% of oxygen saturation. CVS: S1 S2 heard. Respiratory System: Bilateral air entry present P/A: Soft, bowel sound present CNS: Awake, alert, Bilateral pupils equal and reacting to light (PERL), extraocular movement (EOM) full, dysarthria present, severe right hemiplegia present, upper limb (UL) > lower limb (LL) and limb ataxia present limb sensation decrease in right side. Stroke severity quantified by neurologic examination stroke scale: NIHSS score: 11, mRS: 4, BI: 20. NCCT Head with DWI-MR done on 03-Feb-2022 at 15:05 hours showed acute left MCA territory, Left MCA-PCA (middle carotid artery-posterior carotid artery) watershed territory infarct involving left frontal cortical, left parietal, left occipital region, left centrum semiovale and left external capsule. Bilateral peripheral microangiopathic changes. Age-related atrophy changes of the prominence of bilateral ventricles, sulci, and cisterns. Subtype of Ischemic Stroke: Large Artery Atherosclerosis. ECG was done on 03-Feb-2022, which showed sinus rhythm, sinus bradycardia, Q in III, aVF, V5, V6, Right bundle branch block, Heart rate- 59 beats/min. Chest X-Ray done on 03-Feb-2022 had a normal impression. ECHO cardiography done on 04-Feb-2022 showed RWMA-mild hypokinesia of inferior, inferoseptal

<table>
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<tr><th>Subject Number</th><th>Date of Enrolment</th><th>Date of Exclusion / Withdrawal / Death</th><th>Reason of Exclusion / Withdrawal / Death</th><th>Details</th><th>Subject Number</th><th>Date of Enrolment</th><th>Date of Exclusion / Withdrawal / Death</th><th>Reason of Exclusion / Withdrawal / Death</th><th>Details</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>territory. Mild MR (mitral regurgitation, normal left ventricular function (LVEF: 55%). No AR/AS. Mild TR (Tricuspid Regurgitation), normal RV function TAPSE: 20mm. No LA/LV clot. Normal Pericardium. Impression: Old IWMI, normal LV function. Advice to send Trop-I –it was positive (158.2 pg/mL). As per study protocol, the patient met all the inclusion criteria and was randomized in the study on 04-Feb-2022 at 23:26 hours after receiving the consent. This patient successfully received all nine doses of the study drug, and the last dose was administered on 09-Feb-2022 at 17:16 hours. The dosing details are given below.
<table>
<tr><td>Date→</td><td colspan="3">Day-1 (04-FEB-2022)</td></tr>
<tr><td>Dose No.</td><td>Start Time (HH:MM)</td><td>Stop Time (HH:MM)</td><td>Total dose Administered (ml)</td></tr>
<tr><td>Dose 1</td><td>11:45</td><td>11:46</td><td>3</td></tr>
<tr><td>Dose 2</td><td>14:00</td><td>14:01</td><td>3</td></tr>
<tr><td>Dose 3</td><td>16:30</td><td>16:31</td><td>3</td></tr>
<tr><td>Date→</td><td colspan="3">Day-3 (06-FEB-2022)</td></tr>
<tr><td>Dose No.</td><td>Start Time (HH:MM)</td><td>Stop Time (HH:MM)</td><td>Total dose Administered (ml)</td></tr>
<tr><td>Dose 1</td><td>12:30</td><td>12:31</td><td>3</td></tr>
<tr><td>Dose 2</td><td>15:00</td><td>15:01</td><td>3</td></tr>
<tr><td>Dose 3</td><td>17:20</td><td>17:21</td><td>3</td></tr>
</table>
The patient was managed conservatively with a loading dose of C stat. (Aspirin 350 mg + Atorvastatin 80 mg + Clopidogrel 300 mg), Tab. Aspirin + Clopidogrel (75/75 mg) (OD), Tab. Atorvastatin 40 mg (HS), Tab. Folic Acid 1.5 mg + Levocarnitine 500 mg + Mecobalamin 1500 mcg (OD), IV fluids, and other supportive measures. This patient was discharged from the hospital on 07-Feb-2022 at 19:00 hours. The patient was clinically stable at the time of discharge. Discharge medication includes Tab. Aspirin + Clopidogrel (75/75) (OD), Tab Atorvastatin 40 mg HS and Tab. Tab. Folic Acid 1.5 mg + Levocarnitine 500 mg +</td></tr>
</table>

<table>
<tr><th colspan="5">Standard Treatments + Saline</th><th colspan="5">Standard Treatments + Sovateltide</th></tr>
<tr><th>Subject Number</th><th>Date of Enrolment</th><th>Date of Exclusion / Withdrawal / Death</th><th>Reason of Exclusion / Withdrawal / Death</th><th>Details</th><th>Subject Number</th><th>Date of Enrolment</th><th>Date of Exclusion / Withdrawal / Death</th><th>Reason of Exclusion / Withdrawal / Death</th><th>Details</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>Mecobalamin 1500 mcg (OD) for 20 days. Health education was given to the patient and relatives regarding diet, medicines, and personal hygiene. On 09-Feb-2022 at 12:00 hours (visit-1; Day-6): The Patient came to the hospital for study drug administration as per protocol. The patient was stable, and no AE/SAE was reported. Vitals were: BP 140/70 mmHg, heart rate 84 beats/min, respiratory rate 19 breaths/min, and body temperature 97.2 °F. Day 6 dosing details are as follows:
<table>
<tr><td>Date→</td><td colspan="3">Day-6 (09-Feb-2022)</td></tr>
<tr><td>Dose No.</td><td>Start Time (HH:MM)</td><td>Stop Time (HH:MM)</td><td>Total dose Administered (ml)</td></tr>
<tr><td>Dose 1</td><td>12:45</td><td>12:46</td><td>3</td></tr>
<tr><td>Dose 2</td><td>15:00</td><td>15:01</td><td>3</td></tr>
<tr><td>Dose 3</td><td>17:15</td><td>17:16</td><td>3</td></tr>
</table>
The patient continued on the same discharge medication. The patient continued receiving standard treatment for an ischemic stroke right from admission to the hospital and throughout stay in the hospital as per the study protocol, and the IP was an add-on treatment. On 16-Feb-2022 at 16:30 hours (Visit-2, Day 12 +2), the patient came to the hospital for scheduled visit as per protocol. The patient was feeling better and had no fresh complaints. Sleep and appetite were normal. No AE/SAE or recurrence of stroke occurred during this period. The patient's vitals were: BP 128/71 mmHg, Heart Rate 52 beats/minute, Respiratory Rate 19 breaths/minute, and body temperature was 97.6 °F. He was continued on the same discharge medication. On 06-Mar-2022 at 11:50 Hours (Visit-3, Day 30), the patient came to the hospital for a scheduled visit as per protocol. The patient was stable but had a complaint of tiredness. No AE/SAE or recurrence of stroke occurred during this period. The patient's vitals were: BP 110/60 mmHg, Heart rate 56 beats/minute, Respiratory rate 19</td></tr>
</table>

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									breaths/minute, and Body temperature was 97.1 °F. On examination, CVS: S1, S2 heard, Respiratory system: Bilateral air entry present, P/A: soft, bowl sound present, CNS: No fresh CNS sign. ECG done on 06-Mar-2022 shows sinus bradycardia. Stroke severity quantified by neurologic examination stroke scale: NIHSS score: 2, mRS: 2, BI: 90, EQ-5D-5L (EuroQoL) Score: 90, SSQOL scale score: 223, Medication Advised: Suspension Bandy Plus (Albendazole-400mg + Ivermectin-3 mg), Tab. (Ferric Pyrophosphate 30 mg + Vitamin C 50 mg + Curcuma longa 5 mg + Folic Acid 200 mcg + Vitamin B12 0.75 mcg), Tab. Aspirin + Clopidogrel 75/75 mg), Tab. Atorvastatin 40 mg, Tab. Folic Acid 1.5 mg + Levocarnitine 500 mg + Mecobalamin 1500 mcg. On 29-Mar-2022 at 10:00 Hours Visit-4, Day 60 (Telephonic Visit); the Study investigator performed a telephonic visit as per protocol, the patient was stable and able to walk independently, with good compliance with medications. No fresh complaints. No AE/SAE or recurrence of stroke occurred during this period. The patient was advised to contact if any problem occurred, and a reminder was given for next planned schedule visit 5. On 12-Apr-2022, this patient was presented to the emergency ward with complaints of abdominal pain associated with fatigue, sweating, and decreased urine output since 11:00 hours. No history of nausea or vomiting. No history of chest pain, breathing difficulty, burning micturition, fever, or trauma. Known case of hypertension, CAD, CVA-Left MCA infarct on DAPT. The patient is not aware of any drug allergy. On examination: General appearance- pallor present, no icterus, cyanosis, or clubbing. BP was 80/50 mmHg, Heart rate was 120 beats/minute, respiratory rate was 22 breaths/minute, and body temperature was 98.6 °F. RBS 228 mg/dl and oxygen saturation 100% on room air. CVS S1, S2 heard. Respiratory System- Bilateral air entry present. Abdomen- distended grossly,

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									tenderness present: epigastrium, right hypochondrium: guarding present. CNS- drowsy, arousable. ECG: sinus tachycardia, old inferior wall MI. Bedside ECHO on 12-Apr-2022 showed Mild Left ventricular hypertrophy. Provisional Diagnosis: Acute abdomen with hypovolemic shock. Lab investigation was performed on 12-Apr-2022. At 14:45 Hours, the patient was conscious and oriented with a complaint of severe abdominal pain. Vital were: BP 50/20 mmHg, Heart rate 130 beats/min, SPO_2 88%. Bedside ultrasound abdomen showed: Bilateral increased renal echoes. Simple left renal cyst. Moderate free fluid abdomen. Prostatomegaly. Well-defined hyperechoic area/lesion inferior to the left lobe of liver. No obvious intralesional vascularity. The patient was conservatively managed with the infusion of 100 ml/hr of normal saline. and ringer lactate 100 ml/hr., inj. Pantoprazole 40 mg, inj. Ondansetron 1 amp with 1 unit of normal saline, inj. Noradrenalin 8mg with 42 ml of normal saline at the rate of 5ml/hr. onflow. At 15:30 Hours: Adopting aseptic precaution central line was inserted in the right IJV. BP was- 120/80 mmHg (on Noradrenalin support at 8ml/hr.), Heart rate 122 beats/min., Respiratory rate 22 breaths/min. SPO_2 100 % on 5 L oxygen support., RBG 191 mg/dl, P/A Tense/Tender. At 16:30 Hours, the plain and CECT abdomen had the impression: Well, defined heterogeneously enhancing mass lesion of size 6.0 X 6.2 X 6.4 cm (CC X AP X TR) in left lobe in segment II of the liver-? Hepatoma. The lesion was partly exophytic and showed non-enhancing hypodense (likely necrotic) areas within. No obvious intralesional calcification. Loss of fat plane between the lesion and gastric cardia/lesser curvature. The capsular breach with active contrast extravasation/arterial blush from the posteroinferior aspect of the lesion. Heterodense hematoma of size ≈ 13.0 X 1.5 cm in hepato-gastric region. Moderate volume hemoperitoneum. Bilateral

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									Bosniak type I renal cysts. The patient's condition was explained to the patient attendant. Vitals were: BP 120/70 mmHg on Noradrenalin support, pulse rate 125/minute. GCS was 15/15. At 17:20 hours: the patient was restless and pallor, having SBP 90 mmHg DBP not recordable, Heart rate 130 beats/min. he was administered with fresh frozen plasma (1 unit) and Packed cells (2 units). In view of refractory hypovolemic shock, general surgeon consultation was obtained. The guarded prognosis was explained to the patient's family. At 17:35 the patient had altered sensorium. Vitals were BP 90/50 mmHg, Heart Rate 136 beats/min, SPO_2 92% with 5L of oxygen. P/A-grossly distended, diffuse tenderness present, and bowel sound absent. The poor prognosis was explained to the patient's attendant. At 19:15 hours: the patient developed desaturation and bradycardia. Vitals were: SBP 60 mmHg DBP not recordable, Pulse rate 30 beats/min. As per ACLS protocol, CPR started, and 3 ampoules of Injection Adrenaline were injected during the CPR process at 19:16 hours, 19:20 hours, and 19:24 hours. Carotid pulse not felt, BP was not recordable CPR resumed. In spite of maximum resuscitation efforts, a return of spontaneous circulation was not obtained. ECG showed asystole. The patient was declared dead on 12-Apr-2022 at 19:35 hours. The patient's provisional diagnosis was acute abdomen with refractory hypovolemic shock. The cause of death was refractory hypovolemic shock due to massive internal bleeding from the mass in the left lobe of the liver. The event (Death) was not related to the study drug or study procedure and was due to hypovolemic shock secondary to massive internal bleeding from a mass in the left lobe of the liver.