

PsyCHovid : CPZ Protocol for Covid-19 and Psychosis		
Phase 1 : Subjects Enrollment		
Inclusion Criteria		Exclusion Criteria
1	Patients already treated for psychosis admitted to hospital.	History of severe hypersensitivity to CPZ or any other phenothiazine.
2	Age 18 and 65; Hospitalized on an acute care ward due to COVID-19.	Active use of anti-viral therapies directed at SARS-CoV-2, except for remdesivir at the discretion of the treating physician. Antibiotics not directed at SARS-CoV-2 are allowed.
3	Gender: both males and females.	History of congenital long QT syndrome or known history of prolonged QT interval corrected by the Fridericia correction formula (QTcF) > 500 msec on electrocardiogram performed within 60 days of randomization.
4	Positive RT-PCR assay for SARS-CoV-2 on a nasopharyngeal swab sample.	Patients who have been hospitalized for COVID-19 for more than 72 hours, including the hospitalization time at another hospital for patients who were transferred.
5		Use of hydroxychloroquine, chloroquine or azithromycin within 30 days of Day 1.
6	The subject (or legally acceptable representative if applicable) must provide written informed consent for the trial.	Enrollment in another investigational study within 30 days of Day 1.
7		Known psychiatric or substance abuse disorder that would interfere with the requirements of the trial.
8		Unwilling or unable to comply with the study protocol.
9		Any condition, which in the opinion of the investigator, would preclude participation in the trial.
10		Healthy volunteers not allowed to participate.

Appendix. PsyCHovid : CPZ Protocol for Covid-19 and Psychosis

Phase 2 : Subjects Randomization (Two Groups)		Intervention\Treatment
Group A : <u>Placebo Arm</u>	Placebo Comparator: BSC No active, only best supportive care (BSC).	Other: TAU
Group B : <u>Interventional Arm</u>	Experimental: CPZ+ BSC Chlorpromazine tablets.	Drug: CPZ
Protocol Parameters		
Baseline :	Patients already treated for psychosis and receiving antipsychotic medication.	
Interventional Protocol :	1- Add-on CPZ and decrease their current antipsychotic and sleep pills. 2- Randomization will be between two groups of trial; One will receive CPZ and decrease the antipsychotic and Experimental Oral Psychoses Adult: 25 mg at night 3 days then 50 mg 3 days and; may be given as a single 75 mg dose at night.	
Comparison group :	No change.	
Treatment Variables :	CPZ, Antipsychotic medications, and doses.	
Contraindications :	<i>Subjects with the following Conditions\Diseases:</i> Hypersensitivity to phenothiazine; Preexisting CNS Depression, Coma, Bone-Marrow Suppression; Phaeochromocytoma; Lactation, History of Neuroleptic Malignant Syndrome.	
Special Precautions :	<i>Subjects should be careful if they have the following Conditions\Diseases:</i> Parkinson's Disease; CV Disease; Renal or Hepatic Impairment; Jaundice; DM; Hypothyroidism; Paralytic ileus; Prostatic Hyperplasia or Urinary Retention; Epilepsy or History of Seizures; Myasthenia Gravis; Pregnancy; <i>Subjects they should avoid:</i> direct sunlight.	
Timeline :	Depends on the outcomes, if primary outcomes present on the subject, time frame will be: 15 days, if secondary outcomes present on the subject, time frame : will be through study completion/discharge (an average of 30 days with a maximum of 4 months).	
Maintenance :	25-100 mg night increased to 300mg daily as required in psychotic patients (25-100mg tid). With a decrease of their usual night medication. The decrease of the current antipsychotics will be based on the Chlorpromazine equivalent table. For instance if a patient took 6 mg of risperidone, the CPZ equivalent is 300mg, so the adjusted dosage of risperidone after randomization to experimental CPZ harm at 100mg will be 4 mg.	
For Research Purposes :	<p>CPZeq method is set in 300 mg/day of chlorpromazine as a maintenance dose.</p> <p><i>The concept of CPZeq was derived from the potency for Dopamine receptor blockade, which was determined empirically to judge the dose equivalence between different Antipsychotic agents.</i></p> <p>-Shih-Ku LinLin, Shih-Ku, et al. "Comparison of the Defined Daily Dose and Chlorpromazine Equivalent Methods in Antipsychotic Drug Utilization in Six Asian Countries." (2018): 1847-1852.</p>	
Outcome Measures :		
A. Primary Outcome Measures :	<p>1. A composite endpoint of mortality.</p> <p>2. Ongoing need for hospitalization.</p> <p>3. Requirement for mechanical ventilation/extracorporeal membrane oxygenation (ECMO) at Day 15 after randomization.</p> <p>-Time Frame : 15 days.</p> <p>- Determine if : CPZ + best supportive care (BSC) as compared to TAU + BSC reduces the composite endpoint of mortality, ongoing need for hospitalization, or requirement for mechanical ventilation/extracorporeal membrane oxygenation (ECMO) at Day 15 after randomization.</p>	

<p>B. Secondary Outcome Measures :</p>	<p>1. Time to Clinical Improvement. -Time Frame : Through study completion/discharge (an average of 30 days with a maximum of 4 months). -Determine if : CPZ + BSC as compared to TAU + BSC reduces time to clinical improvement as defined by a decline of 2 categories or more from the baseline on the modified 7-category ordinal scale of clinical status of hospitalized influenza patients.</p> <p>2. Inpatient mortality. -Time Frame : Through study completion/discharge (an average of 30 days with a maximum of 4 months). - Determine if : CPZ + BSC as compared to TAU + BSC reduces inpatient mortality.</p> <p>3. Duration of hospitalization. -Time Frame : Through study completion/discharge (an average of 30 days with a maximum of 4 months). -Determine if : CPZ + BSC as compared to TAU + BSC shortens the duration of hospitalization.</p> <p>4. Duration of intubation for mechanical ventilation. -Time Frame : Through study completion/discharge (an average of 30 days with a maximum of 4 months). -Determine if : CPZ + BSC as compared to TAU + BSC shortens the duration of intubation for mechanical ventilation.</p> <p>5. Time to normalization of temperature. - Time Frame : Through study completion/discharge (an average of 30 days with a maximum of 4 months). -Determine if : CPZ + BSC as compared to TAU + BSC reduces the time to normalization of temperature (T < 37.5 for 48 hours).</p> <p>6. Maximum severity of COVID19 illness. -Time Frame : Through study completion/discharge (an average of 30 days with a maximum of 4 months). -Determine if : CPZ + BSC as compared to TAU + BSC reduces the maximum severity of COVID-19 illness based on the modified 7-category ordinal scale of clinical status of hospitalized influenza patients. <i>(Score range 1-7, higher scores equals worse outcome).</i></p>

	<p>7. Biochemical Responses:</p> <p>A. <i>Airal load of SARS-CoV-2 on a nasopharyngeal sample.</i> -Time Frame: day 7 from randomization.</p> <p>B. <i>Serum viral load of SARS-CoV-2.</i> -Time Frame: day: Day15.</p> <p>C. <i>Biochemical response: C-reactive protein (CRP).</i> -Time Frame: Days: 3,15.</p>
	<p>8. Rates of Serious Adverse Events. -Time Frame : Days 7, 15.</p>
	<p>9. Rates of Non-Serious Side Effects. -Time Frame : Days 7,15.</p>
	<p>10. Extrapiramidal Assessment: ESRS Scale. -Time Frame : Days 7,15.</p>
	<p>11. Subjective Cognitive Complains: SSTICS. -Time Frame : Days 7,15.</p>
	<p>12. Prolactine Level. -Time Frame : Days 15, 30.</p>
	<p>13. Psychiatric Symptoms Assessment: SSPI (Peter Liddle) Time : Days 7, 15, 30</p>