Chlorpheniramine Intranasal Spray to Accelerate COVID-19 Clinical Recovery in an Outpatient Setting: ACCROS TRIALS

Fernando Valerio-Pascua[a], Mari L. Tesch[b], Natalia Garcia[c] , Estela Jackeline Pineda Mejía[a], Franck F. Rahaghi[d]

[a] Department of Critical Care, Hospital CEMESA Cortés, San Pedro Sula, Honduras, [b] Aventura Hospital Pulmonary and Critical Care Fellowship, Aventura, FL, USA , FL, USA, Clínica Universitaria Unión Médica, DR [d] Department of Pulmonary and Critical Care Medicine, Cleveland Clinic, Weston, FL, USA

INTRODUCTION

The main goal of the present studies was to examine the effectiveness of Chlorpheniramine Maleate (CPM) intranasal spray as part of the early treatment of mild to moderate COVID-19. A three-part research study was conducted to collect evidence.

- **Part I:** Accelerating COVID-19 Clinical Recovery in an Outpatient Setting (ACCROS-I) A randomized, double-blind, placebo-controlled Trial
- **Part II:** A retrospective cohort study (ACCROS-II) in patients with COVID-19 infection.
- **Part III:** Accelerating COVID-19 Clinical Recovery in an Outpatient Setting (ACCROS-III) A randomized, double-blinded, placebo-controlled trial

METHODS

Part I & III:
Subjects were randomized to receive either CPM internasal spray or placebo. Both groups administer two spray doses in each nostril, three times a day. The atomizer was used at a 12-15º angle to enhance medication deposition in the nasopharynx, the primary site of viral infection.

- The IP group concentrations:
  - **Part I** used a concentration of 1.0% CPM
  - **Part III** used a concentration of 0.4% CPM

Part II:
Data from June 2021 to July 2022 were collected from COVID-positive subjects' medical records to compare patients that received CPM nasal spray and standard of care (CPM+SoC) vs. SoC alone. They were evaluated by the total number of days with COVID-19 symptoms, including cough, nasal congestion, ageusia, and anosmia. The rate of hospitalization among the cohorts was also evaluated.

OUTCOMES

Part I & III:
Main outcome: The improvement of clinical recovery Change from baseline to day 7 in symptoms measured daily symptoms score (DSS) and a Visual Analog Scale (VAS) in COVID-19 symptoms.

Part II:
Main outcome: The improvement of clinical recovery, collected as the total number of days with manifestation and symptoms from the beginning of treatment. Secondary outcomes included the rate of hospitalization.

SUBJECTS CHARACTERISTICS

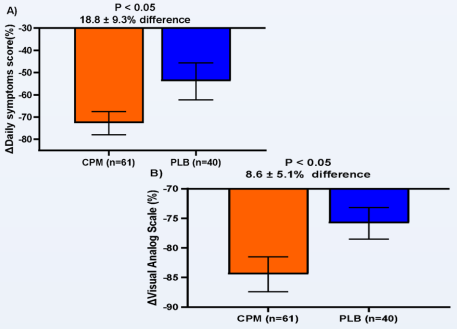
Subjects Characteristics Part I (ACCROS I)* (N = 101; CPM = 61; PLB = 40)			
Sex	Male	52	51.5%
	Female	49	48.5%
Past Medical History	Hypertension	30	29.7%
	Rhinitis	7	6.9%
	Diabetes	11	10.9%
	Asthma	2	2.0%
	Chronic Sinusitis	0	0.0%
	Other Conditions	3	2.9%
	Vaccination Status	100	99.0%
	Smoker	5	5.0%
Age	46.16 ± 15.68		

Subjects Characteristics Part II (ACCROS II)* (N = 660; CPM = 330; PLB = 330)			
Sex	Male	311	47.0%
	Female	349	53.0%
Past Medical History	Hypertension	185	28.0%
	Rhinitis	46	7.0%
	Diabetes	65	9.8%
	Asthma	86	13.0%
	Chronic Sinusitis	15	2.3%
	Other Conditions	21	3.2%
	Vaccination Status	595	90.2%
	Smoker	32	4.9%
Age	46.23 ± 0.70		

Subjects Characteristics Part III (ACCROS III)* (N = 136; PLB = 65; CPM = 71)			
Sex	Male	73	53.7%
	Female	63	46.3%
Past Medical History	Hypertension	45	33.6%
	Rhinitis	10	9.3%
	Diabetes	17	14.0%
	Asthma	7	6.5%
	Chronic Sinusitis	1	0.9%
	Other Conditions	1	0.9%
	Vaccination Status	108	99.1%
	Smoker	7	6.5%
Age	46.23 ± 0.70		

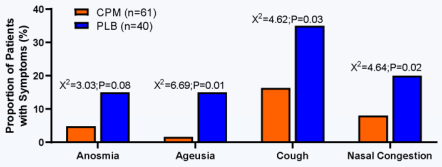
RESULTS

Part I: Student t-tests show the statistically significant differences observed between the groups over the study period (Day 1 to Day 7) **Figure 1 A**: DSS Δ% Change **Figure 1 B:** VAS Δ% Change

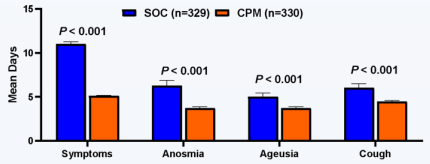


RESULTS CONT.

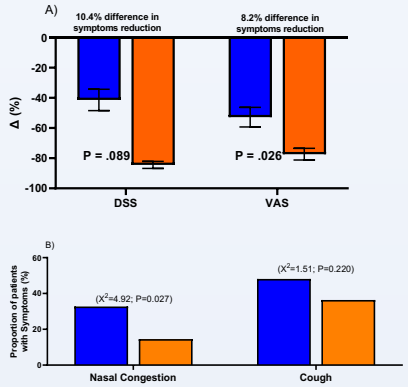
Figure 2. ACCROS I: COVID-19-related sensory and upper respiratory symptoms in response to 7 days of treatment.



Part II: Figure 3. Part II (ACCROS II)COVID-19-related sensory and upper respiratory symptoms in response to Intranasal CPM treatment.

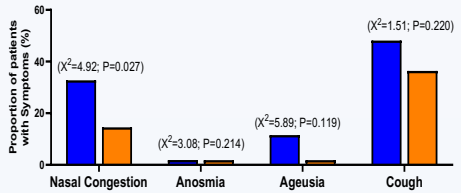


Part III:
There was a difference in the rate of clinical recovery such that the treatment group reported fewer symptoms than the placebo (Figure A). The proportion of patients who reported upper respiratory symptoms on day 7 was significantly lower in the treatment group vs the placebo group for nasal congestion but not for cough (Figure B).



RESULTS CONT.

C) Part III. ACCROS III COVID-19-related sensory and upper respiratory symptoms in response to 7 days of treatment



CONCLUSIONS

The findings from this three-part study strongly support the efficacy of intranasal CPM as an antiviral agent for the treatment of COVID-19-induced symptoms. Intranasal CPM demonstrated accelerated clinical recovery and reduced upper respiratory symptoms in patients with mild to moderate COVID-19. The implications of this study are significant, including a faster return to daily activities, reduced economic burdens at both individual and community levels, and decreased healthcare utilization. Further investigation is warranted to explore the effectiveness of intranasal CPM in treating other viral-induced upper respiratory symptoms and cough.

FUNDING

The study medication and delivery device were provided by Dr. Ferrer Biopharma.

CONFLICT OF INTEREST

All the authors report no conflict of interest.

ETHICS APPROVAL

- **ACCROS I & ACCROS III:** The study was approved following the statutes of the Declaration of Helsinki by the Institutional Ethics Committee and Investigation of the Department of Education and Research Masters in Zoonotic and Infectious Diseases of the Universidad Nacional Autonoma de Honduras and the IRB of the Hospital CEMESA.
- **ACROSS II:** The study was approved by the following the statutes of the Declaration of Helsinki by the Institutional Ethics Committee, and the investigation department of Clínica Universitaria Unión Médica.