Study title: Safety and effectiveness of BIOMODULINA T ® in protective therapy in local transmission events of COVID-19. Intervention study.

FLOW OF PARTICIPANTS
From a universe of 1,474 older adults belonging to three polyclinics in the municipality of Arroyo Naranjo (Eléctrico, Mantilla and Párraga), out of a total of seven CMF , 1,460 were included . Six elderly people from the Mantilla Polyclinic were outside their area of residence and A total of 17 individuals refused to participate: eleven from the Mantilla polyclinic and six from the Reparto Eléctrico. The health areas of Párraga and Mantilla were the ones that contributed the most patients, taking into account the greater extension of these localities.

Table 1. Distribution of elderly included by CMF.

Polyclinic	# CMF	Total	
		N	**%**
Electric	17	128	8.8
paraga	76	726	49.7
Mantilla	30	606	41.5
Total		**1,460**	100.0

The elderly were mostly included in Group I treatment (62.0 vs 38.0%). This assertion was more or less similar in all the clinics except in the CMF # 14 of Mantilla, where there was a slight predominance of inclusion in Group II. However, in CMF # 16 of this same polyclinic, very few were included in Group II. (Table 2).
In general, 16.7% were included in group I because they were older than 80 years. Most, 83.3% of the elderly included in this treatment group were due to presenting comorbidities

Table 2. Distribution by treatment groups according to CMF.

Polyclinic	# CMF	Group I		Group II		Total	
		N	**%**	**N**	**%**	**N**	**%**
Electric	17	68	53.1	60	46.9	128	100.0
paraga	9	43	71.7	17	28.3	60	100.0
	eleven	145	59.4	99	40.6	244	100.0
	17	190	67.4	92	32.6	282	100.0
	22	111	79.3	29	20.7	140	100.0
Mantilla	14	181	42.2	248	57.8	429	100.0
	16	167	94.4	10	5.6	177	100.0
Total		**905**	62.0	**555**	38.0	**1,460**	100.0

Of the total included, 100% of the elderly in Group II complied with the complete regimen, and within Group I, 900 individuals (99.4%) completed the complete regimen, with five patients abandoning the study

with only seven doses administered. In this way, 99.7% of those included (1,455 of 1,460) completed the intervention.

According to the distribution of those included, a total of 14,190 doses should have been applied [(905*12) + (555*6)]. 14 165 doses were applied [(900*12) + (5*7) + (555*6)], fulfilling 99.8% of the forecast.

The foregoing demonstrates the great adherence to the treatment under study, which was undoubtedly influenced by the excellent work of the basic health teams.

BASELINE CHARACTERISTICS

Next, the distribution of the descriptive variables, age (Table 3) and skin color (Table 4) according to sex are summarized in the study patients.

In the entire sample, a predominance of the female sex was observed, with a mean age of 69.7 ± 8.7 years, without differences with the mean age of men of 69.3 ± 7.3 years, although within the females the age range it extended up to 108 years and in men up to 95. When making the distribution by age groups, for both sexes, the group of 60 to 69 years prevailed, in correspondence with the data of the country.

Regarding skin color, the distribution was similar in both sexes, with a predominance of white skin in general, followed by mestizo and black, in that order. The greater frequency of white skin color is in accordance with the censuses of our population. However, if we add the group of black and mestizo people, it is more frequent, in correspondence with the peculiarities of the area in question.

Table 3. Distribution by age groups according to sex.

Age		Male		Feminine		Total	
		.	%	.	%	.	%
60-69		372	57.6	468	57.5	840	57.5
70-79		215	33.3	238	29.2	453	31.0
80-89		53	8.2	85	10.4	138	9.5
90-99		6	0.9	twenty	2.5	26	1.8
100 and more		0	0.0	3	0.4	3	0.2
Total		**646**	44.2	**814**	55.8	**1,460**	100.0
Half		69.3		69.7		69.5	
Standard deviation		7.3		8.7		8.1	
95% CI		68.7-69.8		69.1-75.7		69.1-69.9	
min		60		60		60	
Max		95		108		108	
Percentiles	25	63		63		63	
	fifty	68		68		68	
	75	74		75		74	

Table 4. Skin color according to sex.

Skin color	Male		Feminine		Total	
	.	%	.	%	.	%
White	261	40.4	3. 4. 5	42.4	606	41.5
mestizo	200	31.0	256	31.4	456	31.2

black	184	28.5	209	25.7	393	26.9
Yellow	1	0.2	4	0.5	5	0.3
Total	**646**	100	**814**	100	**1,460**	100

When the PPAs of the study patients are analyzed (Table 5), 64.7% of those included presented at least one chronic disease, but only 5.8% were comorbid , that is, they presented 3 or more pathologies.

The most frequent disease was hypertension, present in 50.5% of the sample.

For DM and Asthma, somewhat lower percentages were obtained than those reported in the yearbook of 17.2 and 7.3%, respectively. In general, the females presented a worse state of health than the men, in congruence with the statistics of the same yearbook.

Table 5. Personal Pathological History according to sex

APP	Male	%	Feminine	%	Total	%
With at least one APP	**373**	57.7	**572**	70.3	945	64.7
AHT	281	43.5	457	56.1	738	50.5
DM	63	9.8	155	19.0	218	14.9
IQ	53	8.2	96	11.8	149	10.2
Bronchial asthma	22	3.4	63	7.7	85	5.8
Cancer	10	1.5	13	1.6	23	1.6
COPD	4	0.6	17	2.1	twenty-one	1.4
CVD	16	2.5	13	1.6	29	2.0
Obesity	5	0.8	6	0.7	eleven	0.8
bedridden	9	1.4	6	0.7	fifteen	1.0
CKD	4	0.6	7	0.9	eleven	0.8
Malnutrition	0	0.0	two	0.2	two	0.1
Other diseases	27	4.2	40	4.9	67	4.6
CM	19	2.9	65	8.0	84	5.8

PRIMARY AND SECONDARY OUTCOMES

COVID-19 infection

Up to one month after the end of the treatment, none of the elderly was diagnosed with COVID-19. This is a very positive result, taking into account the complex epidemiological situation of the locality where the intervention was carried out. In this context, people aged 60 were contributing the largest number of cases and deaths. In this municipality, 65% of the confirmed cases had been asymptomatic at diagnosis and an average of 800 PCR tests per day were being carried out among its inhabitants.

osteoarticular pain and sleep disorders.

During the development of the Phase IV Clinical Trial with BIOMODULINA T ® , carried out in older adults from all nursing homes in the country, using the product for the prevention of infections including COVID-19, the health personnel of these institutions reported that in the elderly had improved appetite,

slept better, and complained of less osteoarticular pain . For these reasons, these indicators were investigated in this study. 1,051 of those included responded in this regard. Table 6 shows the absolute and percentage values of those who reported improvement according to the treatment group in which they were included. The improvement of the three parameters was remarkable in nearly three quarters of the treated patients. All three variables improved in both treatment groups similarly.

Table 6. Effect of treatment on appetite/joint pain/sleep disorders according to treatment group.

IMPROVED SYMPTOMS	Group I N= 673		Group II No.= 378		Total N= 1051	
	N	%	N	%	N	%
Appetite	562	83.5	330	87.3	892	84.9
Osteoarticular pain	573	85.1	328	86.8	901	85.7
Sleep disorders	478	71.0	306	81.0	784	74.6
Improvement of the three	433	64.3	293	77.5	726	69.1
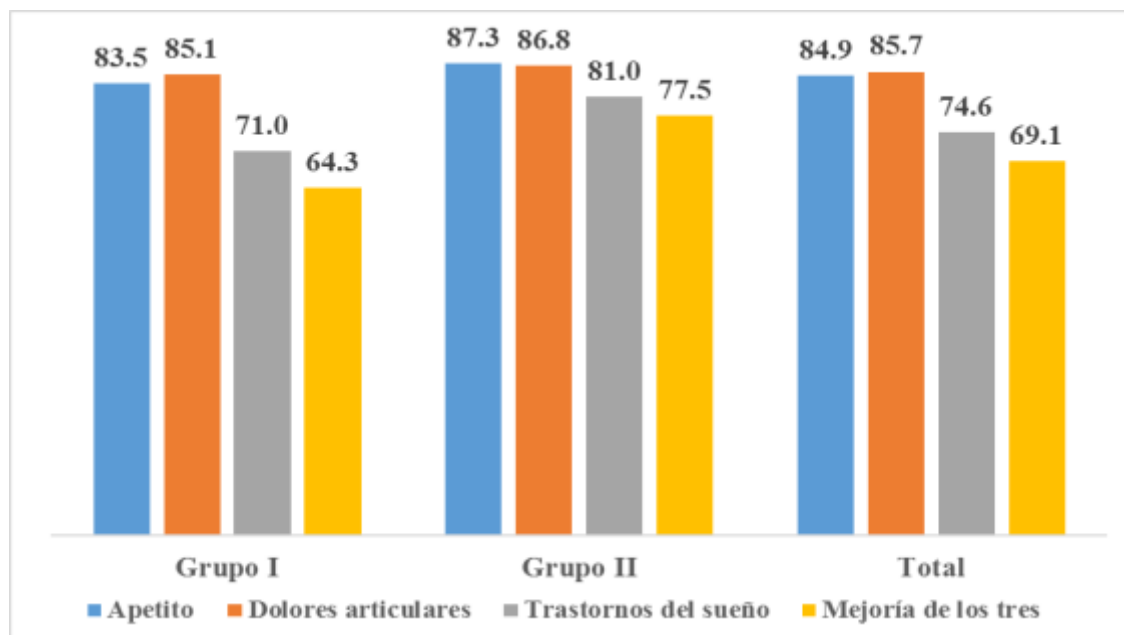
Graph 1. Effect of BIOMODULINA T ® on appetite / joint pain / sleep disorders according to treatment group.

ADVERSE EVENTS
During the intervention, no related adverse events were reported, that is, no ADRs were reported. This is reliable data considering that the research team visited the elderly at home once or twice a week according to the indicated schedule and the municipal health directorate issued reports to CITED-BioCen with the same frequency. The treatment had great acceptability among the elderly, with adherence to it being very favorable.

GENERAL CONCLUSIONS

❖ The excellent safety profile of BIOMODULINA T $^{® \text{ was once again demonstrated}}$, as no adverse reactions were recorded with the product.

❖ Treatment with BIOMODULINA T $^®$ contributed to the control of COVID-19 in local transmission events in the Arroyo Naranjo municipality, as no older adult treated was diagnosed with this disease, in a very complex epidemiological context.

❖ osteoarticular pain and sleep disorders observed in the elderly treated with BIOMODULINA T $^®$ open the way to new lines of research and provide a better quality of life for the elderly.