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Evolution of COVID-19 patients treated with a combination of nutraceuticals to reduce symptomatology and improve prognosis: a multi-centred, retrospective cohort study

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Abstract

Although a vast knowledge has already been gathered on the pathophysiology of COVID-19, there are still limited, non-optimal treatment options. In this context, agents that can act on prophylaxis or as adjuvants to the therapies are of high value. In this paper, we describe a multicentre, retrospective, observational study to describe the course of SARS-CoV-2 disease in patients treated with Immuno Formulation (IF), an add-on therapy developed to decrease duration of clinical symptoms. In parallel, a group of patients that did not receive IF was used for comparison (using standard of care treatment). A total of 39 patients were evaluated for their recovery rate, general symptoms and their severity, and adverse reactions. Throughout the observational period, 90% of patients recovered in the IF cohort and 47.4% in the Control cohort (p=0.0057). From the symptoms with statistically significant differences, the duration of symptoms (i.e., the time to recover from it) was shorter in the IF cohort than in control cohort (in days, average), especially for fever (2.25 x 21.78), dry cough (4.38 x 24.00), dyspnoea (3.67 x 20.00), headache (2.00 x 26.50), diarrhoea (5.25 x 25.25), and weakness (1.92 x 23.30). This demonstrates a potential promising role of IF as adjuvant therapy on the evolution of symptomatology to COVID-19 patients.

Keywords: COVID-19; SARS-CoV-2; Transfer Factor; Clinical Study.

Introduction

The coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has being spread worldwide for more than 1 year. Although a vast knowledge has been gathered throughout this period, there are still limited, non-optimal treatment options. In this context, agents that can act on prophylaxis or as adjuvants to the therapies are of high value.

When it comes to the pathological mechanisms of the SARS-CoV-2, it is now clear the major involvement of the immune system with consequent (hyper) inflammatory effects. In fact, some authors consider that the disease presents itself in three stages: (I) Mild (early infection, viremia phase), (II) Moderate (Pulmonary Involvement with and without Hypoxia; pneumonia phase, inflammation in the lung), and (III) Severe (Systemic Hyper inflammation) or Recovery phase [1].

In general, the three main findings common to all phases are lymphopenia (T-cell and, more specifically, CD8+ T cells), imbalance between Th1 and Th2 responses (leading to cytokine storm and inflammasome activation), and decreased circulating eosinophil numbers [2].

CD8+ lymphopenia (with raised C-reactive protein, D-dimer and ferritin) has been linked to the severe progression of the disease, and it is shown to be reversible after patient recovery, notably for mild cases [3-5]. When we consider previously known coronaviruses such as SARS-CoV-1 and MERS-CoV, it is also understood that T cell immunity can play a decisive role in recovery and long-term protection of patients [6]. In addition, it seems that T cell-mediated immune response is paramount for a good prognosis, as antibody responses in coronaviruses (SARS-CoV-1) are short-lived and can even aggravate lung pathology [6-8]. This reduction in T cells subsets are also reported to be followed by an exhaustion of effector T cells, which contributes to the defective immune response against the virus [9, 10].

The dysfunctional immune response related to the reduced functional diversity of T cells in peripheral blood is also a key parameter to predict severity, as ICU/Stage III patients tend to show a more marked Th2 profile [3, 11]. This triggers a cytokine storm which, in turn, leads to inflammatory cell infiltration and consequent secretion of proteases and reactive oxygen species (oxidative stress), which altogether contribute to the lung damage and COVID-19 severity [12-14]. This raise in inflammatory cytokines

can be observed in peripheral blood [15], as well as a reduced level of IFN-γ, which is currently linked to a faster resolution of the infection [3, 16].

This knowledge brings up the concept of three points of action for improvement of symptomatology and faster recovery: regulation of the immune system, decrease of hyper inflammation and decrease of oxidative stress. Some treatments target on those have been already described and tested, but we focus here on a blend of ingredients that were first described by Ferreira et al. and with positive responses in isolated patients [17, 18]. This blend (further referred to as Imuno Formulation, IF) can potentially play a role in the prevention and/or support treatment of the symptomatology associated with COVID-19. The IF consist of: transfer factors (oligo- and polypeptides from porcine spleen, ultra-filtered at <10 kDa – Imuno TF®) 100 mg, 800 mg anti-inflammatory natural blend (*Uncaria tomentosa*, *Endopleura uchi* and *Haematoccocus pluvialis* - Miodesin™), 60 mg zinc orotate, 48 mg selenium yeast (equivalent to 96 µg of Se), 20,000 IU cholecalciferol, 300 mg ascorbic acid, 480 mg ferulic acid, 90 mg resveratrol, 800 mg spirulina, 560 mg N-acetylcysteine, 610 mg glucosamine sulphate potassium chloride, and 400 mg maltodextrin-stabilized orthosilicic acid (equivalent to 6 mg of Si – SiliciuMax®). The quantities correspond to the daily intake of the IF, which can be split into 3 doses, taken every 8 hours.

Thus, given the lack of gold-standard treatments, the knowledge on the virus mechanisms, and the theoretical potential benefit of the above referred adjuvant therapy, we have clinically evaluated the added value of IF for mild cases of COVID-19. In this preliminary report, we describe the course of SARS-CoV-2 disease in the patients that did or did not receive IF, based on the duration of clinical symptoms, as the basis for future clinical trials.

Materials and Methods

Study design: This is a multicentre, retrospective, observational study to describe the course of SARS-CoV-2 disease in patients treated with IF. In parallel, a group of patients that did not receive IF during the course of the SARS-CoV-2 disease was used for comparison. All patients attended either one of two private clinics (Clinic Bascoy and Clínica Arvila Magna, Barcelona, Spain) from March to May 2020. Data were collected from medical registers from 02 July 2020 to 29 September 2020. All patients/participants provided written informed consent. All steps of the study were conducted in accordance with the Good Clinical Practice Guideline as defined by the International Conference on Harmonisation, the Declaration of Helsinki, and all applicable federal and local regulations and institutional review board guidelines. Ethical approval for was granted by the Medicinal Product Research Ethics Committee of Hospital de Mar, once the private clinics where the study was conduct do not possess their own Ethics Committee, and once this is a reference centre for clinical studies in the region.

Secondary objectives were: (i) to describe the profile of patients (age, sex, comorbidities, concomitant medications and potential risk factors for contagion); (ii) to describe the course of SARS-CoV-2 disease in patients treated or not with IF based on the presence of symptoms at the time of the visit, two weeks and one month after the first visit for symptoms of the disease; (iii) to describe the course of SARS-CoV-2 disease in patients treated or not with IF based on the severity of the symptoms at the time of the visit, two weeks and one month after the first visit for symptoms of the disease; and (iv) to describe the adverse reactions (serious and non-serious) recorded in the patients' medical records during treatment with IF.

Study population: It was planned to collect data from approximately 40 patients who had tested positive in a diagnostic test for SARS-CoV-2: 20 patients who have had treated with IF and these results were compared with 20 patients who had received standard care only. Both cohorts were included without restrictions on the adjuvant treatment received.

All patients who met the screening criteria and gave their informed consent to participate were included consecutively. Inclusion criteria: patients aged 18 years or older; patients who give written informed consent to participate in the study; patients who have consulted their physician for symptoms associated with SARS-CoV-2 infection between March 2020 and May 2020; patients who have tested positive in a diagnostic test for SARS-CoV-2; patients with onset of COVID-19 symptoms ≥ 5 days prior to diagnosis of SARS-CoV-2; patients with data in the medical record from the first visit due to disease symptoms until recovery, or at least 1 month of follow-up of symptoms, whichever occurs first. Exclusion criteria included any medical or psychological condition that, in the physician's opinion, could compromise the patient's ability to give informed consent; patients requiring hospital admission due to the disease.

Sample size calculation was established according to the ICH guidelines, where it was specified that the number of patients should be sufficient to provide a safe response about the issues raised. According to Lechien et al. (2020), the mean duration of mild/moderate symptoms of COVID-19 was 11.5 ± 5.7 days [19]. A sample of 18 patients would be sufficient to estimate, with a 95% confidence and a precision of ± 2.8 days, a mean duration of symptoms with a standard deviation of 5.7 days. Assuming a loss of 10% of patients, the sample size was 20 patients. The calculations were performed with the help of the PASS package, version 2011.

Data Processing and Debugging: Study data were collected in a CRD and inserted the data in a database specifically designed for the study. The database included internal consistency ranges and rules to ensure data quality control. Data recorded during the study were checked. If incomplete responses or abnormal values were seen, a query was issued to the investigator to resolve the discrepancy. When all data have been recorded and all discrepancies

resolved, the database was locked the analysis was performed by the statistics department.

Data Analysis and Statistical Tests: The analyses of the primary and secondary objectives were performed from a single evaluable patient sample, including all patients meeting the inclusion criteria and none of the exclusion criteria. This sample of evaluable patients (EVAL set) for the description of the course of the disease was also be used for the description of the sample and the variables. Safety analyses of the secondary objective were performed on patients who have signed the informed consent (SAF set).

For comparisons between periods of continuous variables, parametric (Student's t test for paired data) and non-parametric (Wilcoxon) tests were used, as appropriate, according to the characteristics of the study variables (assumption of normality), while categorical variables were compared using the McNemar test. The statistical tests used for comparison of the variables depended on the nature of the latter and based on the characteristics of the study variables and the number of groups to compare. The comparison between groups of quantitative variables were made using parametric (Student's t or ANOVA) or non-parametric tests (Mann-Whitney or Kruskal-Wallis); comparison between groups of qualitative variables were made using chi-square test or Fisher test. Statistical significance level of 0.05 was used for all statistical tests. All calculations were performed using the SAS statistical software package, version 9.4.

Results

A total of 40 patients were recruited (20 in the ImmunoFormulation cohort / 20 in the Control cohort). Finally, 39 patients were Evaluable (EVAL set) (20 ImmunoFormulation cohort / 19 Control cohort) for efficacy variables (Figure 1). The control cohort received standard care only, while the ImmunoFormulation cohort received standard care and the IF, prepared by a local compounding pharmacy (concomitant medication during the observational study is summarized in Table S1). The median time between the first consultation for symptomatology and positive diagnosis test for SARS-CoV-2 was 6.00 days in the IF and 15.00 days in the Control cohort, observing statistically significant differences (p=0.0004) (Table 1, which also describes the population's sociodemographic data and the profile of comorbidities).

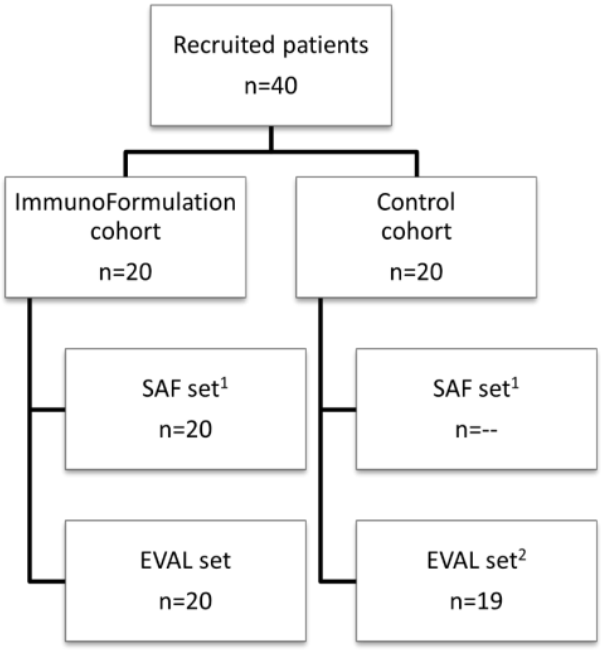

Figure 1: Flow chart of the study. [1]Description of adverse reactions only were analysed in the ImmunoFormulation cohort. [2]One patient did not meet Inclusion Criterion (patients with onset of COVID-19 symptoms ≥ 5 days prior to diagnosis of SARS-CoV-2). SAF = Safety. EVAL = Evaluable patients.

Overall, most common first symptoms were (Table S2): weakness (53.8%), fever (51.3%), dry cough (41.0%), dyspnoea (30.8%) and headache (17.9%). In the ImmunoFormulation cohort the most common first symptoms were: weakness (60.0%), headache (30.0%), abdominal pain (20.0%) and general discomfort (20.0%). In the Control cohort the most common first symptoms were: fever (89.5%), dry cough (68.4%), dyspnoea (57.9%), weakness (47.4%) and hypoxemia (21.1%). Statistically significant differences between cohorts were observed in fever (p<0.0001), dry cough (p=0.0011), dyspnoea (p=0.0004) and hypoxemia (p=0.0471). Patients were classified for the severity of their first severity symptoms according to the most common first symptoms: In the ImmunoFormulation cohort the 50.0% of the patients were classified as mild, 30.0% as moderate and 20.0% as severe (Table 1). In the Control cohort 36.8% of the patients were classified as mild, 26.3% as moderate and 36.8% as severe. No statistically significant differences between cohorts were observed (p=0.4927). Detailed information on each symptom can be found in Table S3.

Table 1: Patient's characteristics upon the first consultation for symptomatology associated with SARS-CoV-2 infection.

Characteristics	ImmunoFormulation cohort (n=20)	Control cohort (n=19)
Age, year [mean (SD)] *	54.25 (14.24)	81.16 (11.30)
Male gender, n (%)	9 (45.0)	3 (15.8)
Time between first consultation for symptomatology and positive diagnosis for SARS-CoV-2, days [median (25; P75)] *	6.00 (5.00; 6.00)	15.00 (6.00; 21.00)
Time between the start date of the first symptom and start date of the ImmunoFormulation treatment, days [median (25; P75)]	6.00 (5.00; 6.00)	-
Type of patient according to the most common severity first symptom[a]		
Predominance of mild severity, n (%)	10 (50.0)	7 (36.8)
Predominance of moderate severity, n (%)	6 (30.0)	5 (26.3)
Predominance of severe severity, n (%)	4 (20.0)	7 (36.3)
Comorbidities* (n= 8 patients with 14 relevant comorbidities)		
Cardiac disorders, n (%)	0 (0.0)	11 (21.2)
Vascular disorders, n (%)	4 (28.6)	14 (26.9)
Endocrine disorders, n (%)	1 (7.1)	0 (0.0)
Musculoskeletal disorders, n (%)	1 (7.1)	4 (7.7)
Neoplasms, n (%)	3 (21.4)	0 (0.0)
Nervous system disorders, n (%)	0 (0.0)	1 (1.9)
Psychiatric disorders, n (%)	0 (0.0)	5 (9.6)
Renal disorders, n (%)	0 (0.0)	2 (3.8)
Respiratory disorders, n (%)	2 (14.3)	4 (7.7)

[a]single patient could have more than one symptom. In this case, the most common first symptom was analysed. When groups would be directly compared, characteristics indicated by asterisk are statistically different ($p < 0.05$).

Throughout the observational period, 90% of patients recovered in the ImmunoFormulation cohort and 47.4% in the Control cohort (p=0.0057) (Figure 2). According to the most severe first symptoms, in the ImmunoFormulation cohort, the mean (SD) days with some symptoms from the start of IF treatment to the end of the observational period was 11.22 (10.06) days in mild symptoms, 17.57 (8.36) days in moderate symptoms and 16.00 (8.76) days in severe symptoms. In the Control cohort, the mean (SD) days with some symptoms to the end of the observational period (end observational period - start first symptom) was 28.00 (4.47) days in mild symptoms, 28.00 (4.47) days in moderate symptoms and 25.42 (5.52) days in severe symptoms (Table S4).

The duration of symptoms in both cohorts (time to recover from start of the first symptom), as well as the percentage of recovery of each symptom by the end of the observational period is described in Table 2. From the symptoms with statistically significant differences, the duration of symptoms (i.e., the time to recover from it) was shorter in the ImmunoFormulation cohort, especially for fever, headache, and weakness, which ended in less than 2 days. As for the adverse reactions' evaluation, no patient presented adverse drug reactions (Table 3).

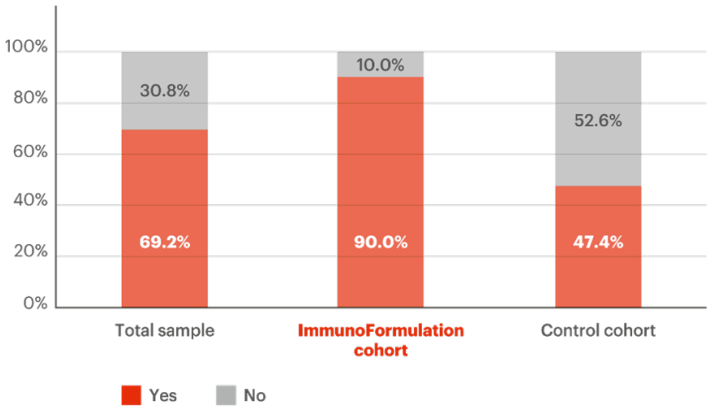

Figure 2: Patients Recovered From Start of the First Symptom to the End of the Observational Period.

Table 2: Total Recovery Duration of Symptoms Associated with COVID-19 Stratified by the Most Common Symptoms.

Symptom	ImmunoFormulation cohort		Control cohort
	Time to recover from start of the first symptom / patients recovered by the end of the observational period	Time to recover from start of treatment	Time to recover from start of the first symptom / patients recovered by the end of the observational period
Fever*	3.35 (2.87) / 100.0%	2.25 (0.91) / 100.0%	21.78 (7.75) / 66.7%
Dry cough*	6.15 (6.52) / 100.0%	4.38 (6.31) / 100.0%	24.00 (7.39) / 53.3%
Dyspnoea*	5.67 (6.35) / 100.0%	3.67 (2.08) / 100.0%	20.00 (7.29) / 71.4%
Loss of taste and smell	21.55 (7.27) / 90.9%	19.73 (4.67) / 90.9%	26.50 (4.95) / 0.0%
Headache*	6.25 (1.98) / 100.0%	2.00 (1.31) / 100.0%	26.50 (4.95) / 0.0%
Diarrhoea*	8.75 (4.35) / 100.0%	5.25 (5.85) / 100.0%	25.25 (3.20) / 25.0%
Weakness*	7.42 (1.08) / 100.0%	1.92 (0.67) / 100.0%	23.30 (9.37) / 50.0%

*$p < 0.05$ (ImmunoFormulation x Control cohorts, in relation to time to recover from start of first symptom). Only symptoms present in more than 2 patients in each group are shown (full overview is shown in Tables S5 and S6).

Discussion

The lack of standard treatment for COVID-19 creates the need for investigation of strategies that can either target SARS-CoV-2 to eliminate it or to improve the symptomatology and strengthen the natural defences. We aimed on this second option and evaluated the use of an add-on therapy described previously on literature [17, 18]. Comparing the two cohorts, a clear difference was seen in the resolution of most symptoms, including fever, dry cough, dyspnoea, headache, diarrhoea, and weakness. Overall, the reduction in time for the resolution of the symptoms indicate a possible positive effect for IF as an add-on therapy for COVID-19 [19].

Robust studies showing the time for recovery of symptoms are still lacking, as most of them focus on the time for symptom onset and in the rate of recovery/complications. The time from exposure to symptom onset is usually reported as is in average 11.5 days, and the time between symptom onset and hospital admission about 7 days [20, 21]. Usually the first symptoms (Stage I: fever, dry cough, headache, diarrhoea) appear between 0 to 4 days; the Stage II symptoms (hypoxia) in 5-13 days; and Stage III symptoms (ARDS, cardiac failure, shock) after 14 days of infection [1]. This is in concordance with what was found by Wang et al, a median 5 days (range 2-8 days) for the progression from mild-moderate cases to severe condition, and a hospital stay range from 14 to 22 days [22].

Table 3. Adverse drug reactions in the ImmunoFormulation cohort.

Patients with adverse drug reactions	ImmunoFormulation cohort, n (%)
Patients with adverse drug reactions	0 (0.0%)
Patients without adverse drug reactions	20 (100.0%)

As an attempt for comparison, Carfi *et al*. evaluated a population similar to our IF cohort in sociodemographic terms: patients with mean age of 56.5 (± 14.6) years, and 63% were men; the difference is that they evaluated hospitalized patients [23]. They assessed the patients for a mean of 60.3 days after onset of the first COVID-19 symptom and observed that only 12.6% were completely free of any COVID-19–related symptom, while 32% had 1 or 2 symptoms and 55% had 3 or more [24]. A report from Imperial College of London showed that the mean time for recovery after symptom onset is 20.51 (± 6.69) days. In contrast, 90.0% of the IF cohort of the present study recovered during the observational period (30 days), and the most common symptoms were resolved within around 2 to five days (except for loss of taste and smell, which is known to be a long-lasting or irreversible complication of COVID-19 [25].

A similar population studied was also reported by Chen *et al*. patients with mild cases, a median of 51 years, and a percentage of 50.6% men [26]. In this study, the estimated median duration of fever was 10 days (CI: 8-11 days), after onset of symptoms – in our findings, the duration of fever was 3.35 days after the onset of symptoms and 2.25 days after the start of treatment.

Obtaining fast patient recovery is important, as the persistence of symptoms can reflect the worsening in his prognosis. For example, for severe cases, the symptoms can last for more than 28 days, leading to hyperinflammation/hypercoagulation responses and pulmonary fibrosis formation [27].

The improvement in the time needed for recovery of the symptoms in the IF cohort can be related to the multiple mechanisms that the components of the IF theoretically acts on as described earlier by Ferreira et al [17]. We will highlight four. First, immune system regulation. This can be related to macrophage activation by Imuno TF® and spirulina, to development of neutrophils by Spirulina and Zinc, to activation of NK-cells by Imuno TF®, Spirulina, Zinc, Vitamin C, and Resveratrol to the increase in T-cells functions by Spirulina, Vitamin C and Vitamin D3, and to CD4+ cells activation by Imuno TF® and Selenium, which can regulate the antigenic stimulus triggering CD4+ Th1 cells to produce IFN-γ, IL-1 and TNF- α [28-44]. In addition, Imuno TF® positively regulates Th1 cytokines, while decreases the release of Th2 cytokines (IL-4, IL-5, IL-6, IL-13) [45]. This is relevant once there is evidence that the

Th2 overresponse are linked to bronchoconstriction, dyspnea and exacerbations of allergic airways diseases [46].

Secondly, targeting the virus itself: Resveratrol have demonstrated DPP4R inhibitory effect (also observed with the use of N-acetylcysteine) and potential to block the ACE2' binding site; and Zinc (high concentration, intracellular) can inhibit the RNA polymerase [47-49]. In addition, N-acetylcysteine, Selenium, and Glucosamine can amplify the signalling functions of TLR7 [50]. Recently, *U. tomentosa* bark extract (one of the components of Miodesin™) has shown antiviral effect against SARS-CoV-2 on Vero E6 cells [51].

Third, the IF effects on the inflammatory process generated by the infection. Vitamin D3 possesses anti-inflammatory properties and can decrease the cytokines storm, notably decreasing the IL-6 effect, a marker of severity in COVID-19 patients [52-59]. Vitamin C is related to an increase in lymphocytes B and T proliferation and differentiation [40, 60, 61]. Resveratrol and Ferulic acid were reported to inhibit the TLR4 signalling pathway – Ferulic acid can also diminish the serological concentration of TNF-α and IL-1β [50, 62, 63]. Another ingredient, Miodesin™, was shown recently to decrease inflammation through inhibition of the release of cytokines (IL-1β, IL-6, IL-8, and TNF-α) and chemokines (CCL2, CCL3, and CCL5) and the expression of NF-κB, inflammatory enzymes (COX-1, COX-2, PLA2, iNOS), and chemokines (CCL2, CCL3, and CCL5) [64].

Finally, the add-on treatment provided was idealized to also act on the oxidative stress. Phase 2 inductive nutraceuticals as Ferulic acid and Resveratrol induce various peroxidase enzymes and promote synthesis of glutathione. Glutathione production can also be promoted by administration of N-acetylcysteine. Selenium supplementation might also be appropriate in this context [50]. Besides, other nutraceuticals with antioxidant properties such as Vitamin C, Spirulina and Astaxanthin can also contribute to reduce the oxidative stress [50, 60, 61, 65-68].

As a limitation of our study, we can point out the differences in age of the cohorts. Therefore, we can understand the data as a description of the fast times needed to recover from the most common COVID-19 symptoms, rather than a direct comparison between the cohorts.

Conclusions

This retrospective observational study demonstrates a potential promising role of ImmunoFormulation as adjuvant therapy on the evolution of symptomatology to COVID-19 patients. Specially for the symptoms fever, dry cough, dyspnoea, headache, diarrhoea and weakness, the recovery time for the treated cohort was significant shorter in comparison to the control cohort. A controlled, double-blind, randomized clinical trial in a larger population is therefore currently being conducted.

Supplementary Materials: Table S1. Concomitant medication by maximum degree of severity in the initial symptomatology, Table S2. First symptomatology associated with SARS-CoV-2 infection by absence/presence, Table S3. First symptomatology associated with SARS-CoV-2 infection by severity, Table S4. Recovery duration of each symptom associated with COVID-19 by symptoms, Table S5. Recovery duration of each symptom associated with COVID-19 by symptoms.

Author Contributions: Conceptualization, methodology, investigation, M.D.H., J.U., L.B.; writing—original draft preparation, writing—review and editing, M.D.H., J.U. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by Medicinal Product Research Ethics Committee of Hospital de Mar (protocol No. 2020/9310, June 23th 2020).

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Table S1. Concomitant medication by maximum degree of severity in the initial symptomatology

	Total n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	p[1]
Total sample					
Patients with concomitant medication	**39 (100.0%)**	**11 (100.0%)**	**12 (100.0%)**	**16 (100.0%)**	**0.0353(f)**
Yes	34 (87.2%)	10 (90.9%)	8 (66.7%)	16 (100.0%)	
No	5 (12.8%)	1 (9.1%)	4 (33.3%)	0 (0.0%)	
N=34 patients with n=173 concomitant medications	**173 (100.0%)**	**32 (100.0%)**	**41 (100.0%)**	**100 (100.0%)**	**0.7336**
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	8 (4.6%)	2 (6.3%)	3 (7.3%)	3 (3.0%)	
ALL OTHER THERAPEUTIC PRODUCTS	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	
ANALGESICS	27 (15.6%)	10 (31.3%)	5 (12.2%)	12 (12.0%)	
ANTI-ACNE PREPARATIONS	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	
ANTIBACTERIALS FOR SYSTEMIC USE	33 (19.1%)	3 (9.4%)	8 (19.5%)	22 (22.0%)	
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	
ANTIDIARRHEALS. INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	17 (9.8%)	2 (6.3%)	7 (17.1%)	8 (8.0%)	
ANTIEPILEPTICS	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	5 (2.9%)	0 (0.0%)	1 (2.4%)	4 (4.0%)	
ANTINEOPLASTIC AGENTS	1 (0.6%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	
ANTITHROMBOTIC AGENTS	3 (1.7%)	0 (0.0%)	0 (0.0%)	3 (3.0%)	
BETA BLOCKING AGENTS	8 (4.6%)	0 (0.0%)	2 (4.9%)	6 (6.0%)	
CALCIUM CHANNEL BLOCKERS	2 (1.2%)	1 (3.1%)	0 (0.0%)	1 (1.0%)	
CORTICOSTEROIDS. DERMATOLOGICAL PREPARATIONS	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	
DIURETICS	11 (6.4%)	1 (3.1%)	2 (4.9%)	8 (8.0%)	
DRUGS FOR ACID RELATED DISORDERS	4 (2.3%)	0 (0.0%)	1 (2.4%)	3 (3.0%)	
DRUGS FOR CONSTIPATION	4 (2.3%)	1 (3.1%)	0 (0.0%)	3 (3.0%)	
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	17 (9.8%)	5 (15.6%)	4 (9.8%)	8 (8.0%)	
DRUGS USED IN DIABETES	9 (5.2%)	2 (6.3%)	2 (4.9%)	5 (5.0%)	
ENDOCRINE THERAPY	1 (0.6%)	0 (0.0%)	1 (2.4%)	0 (0.0%)	
LIPID MODIFYING AGENTS	3 (1.7%)	1 (3.1%)	1 (2.4%)	1 (1.0%)	
OPHTHALMOLOGICALS	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	
PSYCHOANALEPTICS	7 (4.0%)	2 (6.3%)	1 (2.4%)	4 (4.0%)	
PSYCHOLEPTICS	2 (1.2%)	1 (3.1%)	1 (2.4%)	0 (0.0%)	
THYROID THERAPY	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	
UROLOGICALS	1 (0.6%)	0 (0.0%)	1 (2.4%)	0 (0.0%)	
VASOPROTECTIVES	3 (1.7%)	0 (0.0%)	1 (2.4%)	2 (2.0%)	
ImmunoFormulation cohort					
Patients with concomitant medication	**20 (100.0%)**	**9 (100.0%)**	**7 (100.0%)**	**4 (100.0%)**	**0.0844(f)**
Yes	15 (75.0%)	8 (88.9%)	3 (42.9%)	4 (100.0%)	

No	5 (25.0%)	1 (11.1%)	4 (57.1%)	0 (0.0%)	
N=15 patients with n=34 concomitant medications	**34 (100.0%)**	**15 (100.0%)**	**6 (100.0%)**	**13 (100.0%)**	**0.5904**
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	2 (5.9%)	1 (6.7%)	1 (16.7%)	0 (0.0%)	
ANALGESICS	13 (38.2%)	7 (46.7%)	3 (50.0%)	3 (23.1%)	
ANTI-ACNE PREPARATIONS	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	
ANTIBACTERIALS FOR SYSTEMIC USE	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	
ANTINEOPLASTIC AGENTS	1 (2.9%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	
ANTITHROMBOTIC AGENTS	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	
CALCIUM CHANNEL BLOCKERS	2 (5.9%)	1 (6.7%)	0 (0.0%)	1 (7.7%)	
CORTICOSTEROIDS. DERMATOLOGICAL PREPARATIONS	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	
DIURETICS	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	
DRUGS FOR CONSTIPATION	2 (5.9%)	1 (6.7%)	0 (0.0%)	1 (7.7%)	
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	3 (8.8%)	3 (20.0%)	0 (0.0%)	0 (0.0%)	
ENDOCRINE THERAPY	1 (2.9%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	
LIPID MODIFYING AGENTS	3 (8.8%)	1 (6.7%)	1 (16.7%)	1 (7.7%)	
THYROID THERAPY	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	
Control cohort					
Patients with concomitant medication	**19 (100.0%)**	**2 (100.0%)**	**5 (100.0%)**	**12 (100.0%)**	**--**
Yes	19 (100.0%)	2 (100.0%)	5 (100.0%)	12 (100.0%)	
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
N=19 patients with n=139 concomitant medications	**139 (100.0%)**	**17 (100.0%)**	**35 (100.0%)**	**87 (100.0%)**	**0.9656**
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	6 (4.3%)	1 (5.9%)	2 (5.7%)	3 (3.4%)	
ALL OTHER THERAPEUTIC PRODUCTS	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	
ANALGESICS	14 (10.1%)	3 (17.6%)	2 (5.7%)	9 (10.3%)	
ANTIBACTERIALS FOR SYSTEMIC USE	32 (23.0%)	3 (17.6%)	8 (22.9%)	21 (24.1%)	
ANTIDIARRHEALS. INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	17 (12.2%)	2 (11.8%)	7 (20.0%)	8 (9.2%)	
ANTIEPILEPTICS	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	5 (3.6%)	0 (0.0%)	1 (2.9%)	4 (4.6%)	
ANTITHROMBOTIC AGENTS	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (2.3%)	
BETA BLOCKING AGENTS	8 (5.8%)	0 (0.0%)	2 (5.7%)	6 (6.9%)	
DIURETICS	10 (7.2%)	1 (5.9%)	2 (5.7%)	7 (8.0%)	
DRUGS FOR ACID RELATED DISORDERS	4 (2.9%)	0 (0.0%)	1 (2.9%)	3 (3.4%)	
DRUGS FOR CONSTIPATION	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (2.3%)	
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	14 (10.1%)	2 (11.8%)	4 (11.4%)	8 (9.2%)	

DRUGS USED IN DIABETES	9 (6.5%)	2 (11.8%)	2 (5.7%)	5 (5.7%)	
OPHTHALMOLOGICALS	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	
PSYCHOANALEPTICS	7 (5.0%)	2 (11.8%)	1 (2.9%)	4 (4.6%)	
PSYCHOLEPTICS	2 (1.4%)	1 (5.9%)	1 (2.9%)	0 (0.0%)	
UROLOGICALS	1 (0.7%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	
VASOPROTECTIVES	3 (2.2%)	0 (0.0%)	1 (2.9%)	2 (2.3%)	
[1]Chi-square test or Fisher's exact test (f)					

Table S2. First symptomatology associated with SARS-CoV-2 infection by absence/presence[a]

	Total sample n (%)	ImmunoFormulation cohort n (%)	Control cohort n (%)	p[1]
1.Fever	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**<0.0001(f)**
Absence	19 (48.7%)	17 (85.0%)	2 (10.5%)	
Presence	20 (51.3%)	3 (15.0%)	17 (89.5%)	
2.Dry cough	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.0011(f)**
Absence	23 (59.0%)	17 (85.0%)	6 (31.6%)	
Presence	16 (41.0%)	3 (15.0%)	13 (68.4%)	
3.Dyspnea	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.0004(f)**
Absence	27 (69.2%)	19 (95.0%)	8 (42.1%)	
Presence	12 (30.8%)	1 (5.0%)	11 (57.9%)	
4.Loss of taste and smell	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.6050(f)**
Absence	35 (89.7%)	17 (85.0%)	18 (94.7%)	
Presence	4 (10.3%)	3 (15.0%)	1 (5.3%)	
5.Headache	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.0915(f)**
Absence	32 (82.1%)	14 (70.0%)	18 (94.7%)	
Presence	7 (17.9%)	6 (30.0%)	1 (5.3%)	
6.Diarrehea	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absence	35 (89.7%)	18 (90.0%)	17 (89.5%)	
Presence	4 (10.3%)	2 (10.0%)	2 (10.5%)	
7.Abdominal pain	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.1060(f)**
Absence	35 (89.7%)	16 (80.0%)	19 (100.0%)	
Presence	4 (10.3%)	4 (20.0%)	0 (0.0%)	
8.Dermatological findings	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absence	38 (97.4%)	19 (95.0%)	19 (100.0%)	
Presence	1 (2.6%)	1 (5.0%)	0 (0.0%)	
9.1. General discomfort[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.1060(f)**
Absence	35 (89.7%)	16 (80.0%)	19 (100.0%)	
Presence	4 (10.3%)	4 (20.0%)	0 (0.0%)	
9.2. Throat lesion[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absence	38 (97.4%)	19 (95.0%)	19 (100.0%)	
Presence	1 (2.6%)	1 (5.0%)	0 (0.0%)	
9.3. Vomiting[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absence	38 (97.4%)	19 (95.0%)	19 (100.0%)	
Presence	1 (2.6%)	1 (5.0%)	0 (0.0%)	

9.4. Weakness[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.5273(f)**
Absence	18 (46.2%)	8 (40.0%)	10 (52.6%)	
Presence	21 (53.8%)	12 (60.0%)	9 (47.4%)	
9.5. Sore throat[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absence	38 (97.4%)	19 (95.0%)	19 (100.0%)	
Presence	1 (2.6%)	1 (5.0%)	0 (0.0%)	
9.6. Muscular pain[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absence	37 (94.9%)	19 (95.0%)	18 (94.7%)	
Presence	2 (5.1%)	1 (5.0%)	1 (5.3%)	
9.7. Dehydration[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absence	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Presence	1 (2.6%)	0 (0.0%)	1 (5.3%)	
9.8. Emesis[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.2308(f)**
Absence	37 (94.9%)	20 (100.0%)	17 (89.5%)	
Presence	2 (5.1%)	0 (0.0%)	2 (10.5%)	
9.9. Hypoxemia[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.0471(f)**
Absence	35 (89.7%)	20 (100.0%)	15 (78.9%)	
Presence	4 (10.3%)	0 (0.0%)	4 (21.1%)	
9.10. Dysuria[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.1060(f)**
Absence	36 (92.3%)	20 (100.0%)	16 (84.2%)	
Presence	3 (7.7%)	0 (0.0%)	3 (15.8%)	
9.11. Pollakiuria[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.2308(f)**
Absence	37 (94.9%)	20 (100.0%)	17 (89.5%)	
Presence	2 (5.1%)	0 (0.0%)	2 (10.5%)	
9.12. Sleepiness[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absence	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Presence	1 (2.6%)	0 (0.0%)	1 (5.3%)	
9.14. Apathy[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absence	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Presence	1 (2.6%)	0 (0.0%)	1 (5.3%)	
9.14. Disorientation[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absence	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Presence	1 (2.6%)	0 (0.0%)	1 (5.3%)	
9.15. Anorexia[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.2308(f)**
Absence	37 (94.9%)	20 (100.0%)	17 (89.5%)	
Presence	2 (5.1%)	0 (0.0%)	2 (10.5%)	
9.16. Myalgia[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absence	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Presence	1 (2.6%)	0 (0.0%)	1 (5.3%)	
9.17. Nasal congestion[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absence	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Presence	1 (2.6%)	0 (0.0%)	1 (5.3%)	

[1]Fisher exact test (f)
[2]Other symptoms: According to MedDRA 23.0 (LLT)

Table S3. First symptomatology associated with SARS-CoV-2 infection by severity

	Total sample	ImmunoFormulation cohort	Control cohort	p[1]
1.Fever	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**<0.0001(f)**
Absent	19 (48.7%)	17 (85.0%)	2 (10.5%)	
Mild	10 (25.6%)	1 (5.0%)	9 (47.4%)	
Moderate	3 (7.7%)	0 (0.0%)	3 (15.8%)	
Severe	7 (17.9%)	2 (10.0%)	5 (26.3%)	
2.Dry cough	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.0026(f)**
Absent	23 (59.0%)	17 (85.0%)	6 (31.6%)	
Mild	4 (10.3%)	1 (5.0%)	3 (15.8%)	
Moderate	5 (12.8%)	0 (0.0%)	5 (26.3%)	
Severe	7 (17.9%)	2 (10.0%)	5 (26.3%)	
3.Dyspnea	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.0004(f)**
Absent	27 (69.2%)	19 (95.0%)	8 (42.1%)	
Mild	4 (10.3%)	0 (0.0%)	4 (21.1%)	
Moderate	4 (10.3%)	0 (0.0%)	4 (21.1%)	
Severe	4 (10.3%)	1 (5.0%)	3 (15.7%)	
4.Loss of taste and smell	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absent	35 (89.7%)	17 (85.0%)	18 (94.7%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	1 (2.6%)	1 (5.0%)	0 (0.0%)	
Severe	3 (7.7%)	2 (10.0%)	1 (5.3%)	
5.Headache	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.1065(f)**
Absent	32 (82.1%)	14 (70.0%)	18 (94.7%)	
Mild	5 (12.8%)	4 (20.0%)	1 (5.3%)	
Moderate	2 (5.1%)	2 (10.0%)	0 (0.0%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
6.Diarrehea	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absent	35 (89.7%)	18 (90.0%)	17 (89.5%)	
Mild	3 (7.7%)	1 (5.0%)	2 (10.5%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	1 (2.6%)	1 (5.0%)	0 (0.0%)	
7.Abdominal pain	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.1649(f)**
Absent	35 (89.7%)	16 (80.0%)	19 (100.0%)	
Mild	3 (7.7%)	3 (15.0%)	0 (0.0%)	
Moderate	1 (2.6%)	1 (5.0%)	0 (0.0%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
8.Dermatological finding	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absent	38 (97.4%)	19 (95.0%)	19 (100.0%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	1 (2.6%)	1 (5.0%)	0 (0.0%)	
9.1. General discomfort[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.2238(f)**

Absent	35 (89.7%)	16 (80.0%)	19 (100.0%)	
Mild	1 (2.6%)	1 (5.0%)	0 (0.0%)	
Moderate	1 (2.6%)	1 (5.0%)	0 (0.0%)	
Severe	2 (5.1%)	2 (10.0%)	0 (0.0%)	
9.2. Throat lesion[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absent	38 (97.4%)	19 (95.0%)	19 (100.0%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	1 (2.6%)	1 (5.0%)	0 (0.0%)	
9.3. Vomiting[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absent	38 (97.4%)	19 (95.0%)	19 (100.0%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	1 (2.6%)	1 (5.0%)	0 (0.0%)	
9.4. Weakness[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.2063(f)**
Absent	18 (46.2%)	8 (40.0%)	10 (52.6%)	
Mild	12 (30.8%)	8 (40.0%)	4 (21.1%)	
Moderate	2 (5.1%)	2 (10.0%)	0 (0.0%)	
Severe	7 (17.9%)	2 (10.0%)	5 (26.3%)	
9.5. Sore throat[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absent	38 (97.4%)	19 (95.0%)	19 (100.0%)	
Mild	1 (2.6%)	1 (5.0%)	0 (0.0%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
9.6. Muscular pain[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**1.0000(f)**
Absent	37 (94.9%)	19 (95.0%)	18 (94.7%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	1 (2.6%)	1 (5.0%)	0 (0.0%)	
Severe	1 (2.6%)	0 (0.0%)	1 (5.3%)	
9.7. Dehydration[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absent	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	1 (2.6%)	0 (0.0%)	1 (5.3%)	
9.8. Emesis[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.2308(f)**
Absent	37 (94.9%)	20 (100.0%)	17 (89.5%)	
Mild	1 (2.6%)	0 (0.0%)	1 (5.3%)	
Moderate	1 (2.6%)	0 (0.0%)	1 (5.3%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
9.9. Hypoxemia[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.0471(f)**
Absent	35 (89.7%)	20 (100.0%)	15 (78.9%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	4 (10.3%)	0 (0.0%)	4 (21.1%)	

Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
9.10. Dysuria[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.1060(f)**
Absent	36 (92.3%)	20 (100.0%)	16 (84.2%)	
Mild	2 (5.1%)	0 (0.0%)	2 (10.5%)	
Moderate	1 (2.6%)	0 (0.0%)	1 (5.3%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
9.11. Pollakiuria[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.2308(f)**
Absent	37 (94.9%)	20 (100.0%)	17 (89.5%)	
Mild	1 (2.6%)	0 (0.0%)	1 (5.3%)	
Moderate	1 (2.6%)	0 (0.0%)	1 (5.3%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
9.12. Sleepiness[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absent	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	1 (2.6%)	0 (0.0%)	1 (5.3%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
9.13. Apathy[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absent	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	1 (2.6%)	0 (0.0%)	1 (5.3%)	
9.14. Disorientation[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absent	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Mild	1 (2.6%)	0 (0.0%)	1 (5.3%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
9.15. Anorexia[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.2308(f)**
Absent	37 (94.9%)	20 (100.0%)	17 (89.5%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	2 (5.1%)	0 (0.0%)	2 (10.5%)	
9.16. Myalgia[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absent	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	1 (2.6%)	0 (0.0%)	1 (5.3%)	
9.17. Nasal congestion[2]	**39 (100.0%)**	**20 (100.0%)**	**19 (100.0%)**	**0.4872(f)**
Absent	38 (97.4%)	20 (100.0%)	18 (94.7%)	
Mild	1 (2.6%)	0 (0.0%)	1 (5.3%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
[1]Fisher exact test (f)				

Table S4. Recovery duration of each symptom associated with COVID-19 by symptoms

	Total Sample	Immuno Formulation cohort	Control cohort	p[1]
TOTAL RECOVERY FROM START OF THE FIRST SYMPTOM[a]				
1. Fever				
Days with some symptoms to the end of the observational period				
Mean (SD)	12.08 (10.90)	3.35 (2.87)	21.78 (7.75)	<0.0001
95%CI	(8.50 ; 15.66)	(2.01 ; 4.69)	(17.92 ; 25.63)	
Median (P25 ; P75)	10.00 (2.00 ; 24.00)	2.00 (2.00 ; 3.00)	24.00 (14.00 ; 30.00)	
(Min ; Max)	(1.00 ; 31.00)	(1.00 ; 13.00)	(11.00 ; 31.00)	
N valid	38	20	18	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**38 (100.0%)**	**20 (100.0%)**	**18 (100.0%)**	**0.0067(f)**
Yes	32 (84.2%)	20 (100.0%)	12 (66.7%)	
No	6 (15.8%)	0 (0.0%)	6 (33.3%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	9.22 (8.96)	3.35 (2.87)	19.00 (6.71)	<0.0001
95%CI	(5.99 ; 12.45)	(2.01 ; 4.69)	(14.73 ; 23.27)	
Median (P25 ; P75)	3.00 (2.00 ; 14.00)	2.00 (2.00 ; 3.00)	18.50 (13.00 ; 24.50)	
(Min ; Max)	(1.00 ; 30.00)	(1.00 ; 13.00)	(11.00 ; 30.00)	
N valid	32	20	12	
2. Dry Cough				
Days with some symptoms to the end of the observational period				
Mean (SD)	15.71 (11.37)	6.15 (6.52)	24.00 (7.39)	<0.0001
95%CI	(11.30 ; 20.12)	(2.22 ; 10.09)	(19.91 ; 28.09)	
Median (P25 ; P75)	16.50 (4.00 ; 27.50)	4.00 (2.00 ; 6.00)	25.00 (20.00 ; 30.00)	
(Min ; Max)	(2.00 ; 30.00)	(2.00 ; 25.00)	(6.00 ; 30.00)	
N valid	28	13	15	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**28 (100.0%)**	**13 (100.0%)**	**15 (100.0%)**	**0.0069(f)**
Yes	21 (75.0%)	13 (100.0%)	8 (53.3%)	
No	7 (25.0%)	0 (0.0%)	7 (46.7%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	11.29 (9.49)	6.15 (6.52)	19.63 (7.50)	0.0025
95%CI	(6.96 ; 15.61)	(2.22 ; 10.09)	(13.35 ; 25.90)	
Median (P25 ; P75)	6.00 (3.00 ; 20.00)	4.00 (2.00 ; 6.00)	20.50 (16.00 ; 24.00)	
(Min ; Max)	(2.00 ; 30.00)	(2.00 ; 25.00)	(6.00 ; 30.00)	
N valid	21	13	8	

3. Dyspnea				
Days with some symptoms to the end of the observational period				
Mean (SD)	17.47 (8.94)	5.67 (6.35)	20.00 (7.29)	0.0315
95%CI	(12.88 ; 22.07)	(0.00 ; 21.44)	(15.79 ; 24.21)	
Median (P25 ; P75)	20.00 (12.00 ; 24.00)	2.00 (2.00 ; 13.00)	20.50 (13.00 ; 25.00)	
(Min ; Max)	(2.00 ; 30.00)	(2.00 ; 13.00)	(7.00 ; 30.00)	
N valid	17	3	14	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**17 (100.0%)**	**3 (100.0%)**	**14 (100.0%)**	**0.5412(f)**
Yes	13 (76.5%)	3 (100.0%)	10 (71.4%)	
No	4 (23.5%)	0 (0.0%)	4 (28.6%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	17.31 (9.23)	5.67 (6.35)	20.80 (6.78)	0.0341
95%CI	(11.73 ; 22.89)	(0.00 ; 21.44)	(15.95 ; 25.65)	
Median (P25 ; P75)	20.00 (12.00 ; 24.00)	2.00 (2.00 ; 13.00)	22.00 (20.00 ; 25.00)	
(Min ; Max)	(2.00 ; 30.00)	(2.00 ; 13.00)	(7.00 ; 30.00)	
N valid	13	3	10	
4. Loss of taste and smell				
Days with some symptoms to the end of the observational period				
Mean (SD)	22.31 (7.04)	21.55 (7.27)	26.50 (4.95)	0.4860
95%CI	(18.05 ; 26.56)	(16.66 ; 26.43)	(0.00 ; 70.97)	
Median (P25 ; P75)	23.00 (15.00 ; 29.00)	23.00 (14.00 ; 29.00)	26.50 (23.00 ; 30.00)	
(Min ; Max)	(11.00 ; 31.00)	(11.00 ; 31.00)	(23.00 ; 30.00)	
N valid	13	11	2	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**13 (100.0%)**	**11 (100.0%)**	**2 (100.0%)**	**0.0385(f)**
Yes	10 (76.9%)	10 (90.9%)	0 (0.0%)	
No	3 (23.1%)	1 (9.1%)	2 (100.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	20.60 (6.92)	20.60 (6.92)	--	--
95%CI	(15.65 ; 25.55)	(15.65 ; 25.55)		
Median (P25 ; P75)	21.50 (14.00 ; 26.00)	21.50 (14.00 ; 26.00)		
(Min ; Max)	(11.00 ; 31.00)	(11.00 ; 31.00)		
N valid	10	10		
5. Headache				
Days with some symptoms to the end of the observational period				
Mean (SD)	10.30 (8.87)	6.25 (1.98)	26.50 (4.95)	0.0467
95%CI	(3.95 ; 16.65)	(4.59 ; 7.91)	(0.00 ; 70.97)	

Median (P25 ; P75)	7.00 (6.00 ; 8.00)	7.00 (5.50 ; 7.50)	26.50 (23.00 ; 30.00)	
(Min ; Max)	(2.00 ; 30.00)	(2.00 ; 8.00)	(23.00 ; 30.00)	
N valid	10	8	2	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**10 (100.0%)**	**8 (100.0%)**	**2 (100.0%)**	**0.0222(f)**
Yes	8 (80.0%)	8 (100.0%)	0 (0.0%)	
No	2 (20.0%)	0 (0.0%)	2 (100.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	6.25 (1.98)	6.25 (1.98)	--	--
95%CI	(4.59 ; 7.91)	(4.59 ; 7.91)		
Median (P25 ; P75)	7.00 (5.50 ; 7.50)	7.00 (5.50 ; 7.50)		
(Min ; Max)	(2.00 ; 8.00)	(2.00 ; 8.00)		
N valid	8	8		
6. Diarrhea				
Days with some symptoms to the end of the observational period				
Mean (SD)	17.00 (9.50)	8.75 (4.35)	25.25 (3.20)	0.0294
95%CI	(9.06 ; 24.94)	(1.83 ; 15.67)	(20.16 ; 30.34)	
Median (P25 ; P75)	18.00 (9.50 ; 24.00)	9.50 (5.50 ; 12.00)	24.00 (23.50 ; 27.00)	
(Min ; Max)	(3.00 ; 30.00)	(3.00 ; 13.00)	(23.00 ; 30.00)	
N valid	8	4	4	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**8 (100.0%)**	**4 (100.0%)**	**4 (100.0%)**	**0.1429(f)**
Yes	5 (62.5%)	4 (100.0%)	1 (25.0%)	
No	3 (37.5%)	0 (0.0%)	3 (75.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	11.80 (7.79)	8.75 (4.35)	24.00 (.)	0.2888
95%CI	(2.13 ; 21.47)	(1.83 ; 15.67)	(. ; .)	
Median (P25 ; P75)	11.00 (8.00 ; 13.00)	9.50 (5.50 ; 12.00)	24.00 (24.00 ; 24.00)	
(Min ; Max)	(3.00 ; 24.00)	(3.00 ; 13.00)	(24.00 ; 24.00)	
N valid	5	4	1	
7. Abdominal pain				
Days with some symptoms to the end of the observational period				
Mean (SD)	6.80 (2.17)	6.80 (2.17)	. (.)	--
95%CI	(4.11 ; 9.49)	(4.11 ; 9.49)	(. ; .)	
Median (P25 ; P75)	8.00 (7.00 ; 8.00)	8.00 (7.00 ; 8.00)	. (. ; .)	
(Min ; Max)	(3.00 ; 8.00)	(3.00 ; 8.00)	(. ; .)	
N valid	5	5	0	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**5 (100.0%)**	**5 (100.0%)**	**--**	**--**

Yes	5 (100.0%)	5 (100.0%)		
No	5 (100.0%)	5 (100.0%)		
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	6.80 (2.17)	6.80 (2.17)	--	--
95%CI	(4.11 ; 9.49)	(4.11 ; 9.49)		
Median (P25 ; P75)	8.00 (7.00 ; 8.00)	8.00 (7.00 ; 8.00)		
(Min ; Max)	(3.00 ; 8.00)	(3.00 ; 8.00)		
N valid	5	5		
8. Dermatological findings				
Days with some symptoms to the end of the observational period				
Mean (SD)	31.00 (.)	31.00 (.)	. (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	31.00 (31.00 ; 31.00)	31.00 (31.00 ; 31.00)	. (. ; .)	
(Min ; Max)	(31.00 ; 31.00)	(31.00 ; 31.00)	(. ; .)	
N valid	1	1	0	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**1 (100.0%)**	**--**	**--**
Yes	0 (0.0%)	0 (0.0%)		
No	1 (100.0%)	1 (100.0%)		
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	--	--	--	--
95%CI				
Median (P25 ; P75)				
(Min ; Max)				
N valid				
9.1. General discomfort[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	15.75 (10.37)	15.75 (10.37)	. (.)	--
95%CI	(0.00 ; 32.25)	(0.00 ; 32.25)	(. ; .)	
Median (P25 ; P75)	12.00 (9.50 ; 22.00)	12.00 (9.50 ; 22.00)	. (. ; .)	
(Min ; Max)	(8.00 ; 31.00)	(8.00 ; 31.00)	(. ; .)	
N valid	4	4	0	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**4 (100.0%)**	**4 (100.0%)**	**--**	**--**
Yes	3 (75.0%)	3 (75.0%)		
No	1 (25.0%)	1 (25.0%)		
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	10.67 (2.52)	10.67 (2.52)	--	--
95%CI	(4.42 ; 16.92)	(4.42 ; 16.92)		
Median (P25 ; P75)	11.00 (8.00 ; 13.00)	11.00 (8.00 ; 13.00)		
(Min ; Max)	(8.00 ; 13.00)	(8.00 ; 13.00)		

N valid	3	3		
9.2. Throat lesion[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	13.00 (.)	13.00 (.)	. (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	13.00 (13.00 ; 13.00)	13.00 (13.00 ; 13.00)	. (. ; .)	
(Min ; Max)	(13.00 ; 13.00)	(13.00 ; 13.00)	(. ; .)	
N valid	1	1	0	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**1 (100.0%)**	**--**	**--**
Yes	1 (100.0%)	1 (100.0%)		
No	0 (0.0%)	0 (0.0%)		
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	13.00 (.)	13.00 (.)	--	--
95%CI	(. ; .)	(. ; .)		
Median (P25 ; P75)	13.00 (13.00 ; 13.00)	13.00 (13.00 ; 13.00)		
(Min ; Max)	(13.00 ; 13.00)	(13.00 ; 13.00)		
N valid	1	1		
9.3. Vomiting[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	13.00 (.)	13.00 (.)	. (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	13.00 (13.00 ; 13.00)	13.00 (13.00 ; 13.00)	. (. ; .)	
(Min ; Max)	(13.00 ; 13.00)	(13.00 ; 13.00)	(. ; .)	
N valid	1	1	0	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**1 (100.0%)**	**--**	**--**
Yes	1 (100.0%)	1 (100.0%)		
No	0 (0.0%)	0 (0.0%)		
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	13.00 (.)	13.00 (.)	. (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	13.00 (13.00 ; 13.00)	13.00 (13.00 ; 13.00)	. (. ; .)	
(Min ; Max)	(13.00 ; 13.00)	(13.00 ; 13.00)	(. ; .)	
N valid	1	1	0	
9.4. Weakness[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	14.64 (10.19)	7.42 (1.08)	23.30 (9.37)	0.0060
95%CI	(10.12 ; 19.15)	(6.73 ; 8.11)	(16.60 ; 30.00)	
Median (P25 ; P75)	8.00 (7.00 ; 26.00)	7.00 (7.00 ; 8.00)	27.50 (21.00 ; 30.00)	
(Min ; Max)	(6.00 ; 30.00)	(6.00 ; 10.00)	(6.00 ; 30.00)	

N valid	22	12	10	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**22 (100.0%)**	**12 (100.0%)**	**10 (100.0%)**	**0.0096(f)**
Yes	17 (77.3%)	12 (100.0%)	5 (50.0%)	
No	5 (22.7%)	0 (0.0%)	5 (50.0%)	
PATIENT RECOVERED- Days with some symptoms to the end of the observational period				
Mean (SD)	11.47 (7.93)	7.42 (1.08)	21.20 (8.98)	0.0464
95%CI	(7.39 ; 15.55)	(6.73 ; 8.11)	(10.05 ; 32.35)	
Median (P25 ; P75)	8.00 (7.00 ; 10.00)	7.00 (7.00 ; 8.00)	24.00 (21.00 ; 26.00)	
(Min ; Max)	(6.00 ; 29.00)	(6.00 ; 10.00)	(6.00 ; 29.00)	
N valid	17	12	5	
9.5. Sore throat[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	7.00 (.)	7.00 (.)	. (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	7.00 (7.00 ; 7.00)	7.00 (7.00 ; 7.00)	. (. ; .)	
(Min ; Max)	(7.00 ; 7.00)	(7.00 ; 7.00)	(. ; .)	
N valid	1	1	0	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**1 (100.0%)**	**--**	**--**
Yes	1 (100.0%)	1 (100.0%)		
No	0 (0.0%)	0 (0.0%)		
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	7.00 (.)	7.00 (.)	. (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	7.00 (7.00 ; 7.00)	7.00 (7.00 ; 7.00)	. (. ; .)	
(Min ; Max)	(7.00 ; 7.00)	(7.00 ; 7.00)	(. ; .)	
N valid	1	1	0	
9.6. Muscular pain[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	10.50 (3.54)	8.00 (.)	13.00 (.)	--
95%CI	(0.00 ; 42.27)	(. ; .)	(. ; .)	
Median (P25 ; P75)	10.50 (8.00 ; 13.00)	8.00 (8.00 ; 8.00)	13.00 (13.00 ; 13.00)	
(Min ; Max)	(8.00 ; 13.00)	(8.00 ; 8.00)	(13.00 ; 13.00)	
N valid	2	1	1	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**2 (100.0%)**	**1 (100.0%)**	**1 (100.0%)**	**--**
Yes	2 (100.0%)	1 (100.0%)	1 (100.0%)	
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	
PATIENT RECOVERED- Days with some symptoms to the end of the observational period				

Mean (SD)	10.50 (3.54)	8.00 (.)	13.00 (.)	--
95%CI	(0.00 ; 42.27)	(. ; .)	(. ; .)	
Median (P25 ; P75)	10.50 (8.00 ; 13.00)	8.00 (8.00 ; 8.00)	13.00 (13.00 ; 13.00)	
(Min ; Max)	(8.00 ; 13.00)	(8.00 ; 8.00)	(13.00 ; 13.00)	
N valid	2	1	1	
9.7. Dehydration[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	31.00 (.)	. (.)	31.00 (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	31.00 (31.00 ; 31.00)	. (. ; .)	31.00 (31.00 ; 31.00)	
(Min ; Max)	(31.00 ; 31.00)	(. ; .)	(31.00 ; 31.00)	
N valid	1	0	1	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**-**	**1 (100.0%)**	**--**
Yes	0 (0.0%)		0 (0.0%)	
No	1 (100.0%)		1 (100.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	--	--	--	--
95%CI				
Median (P25 ; P75)				
(Min ; Max)				
N valid				
9.8. Emesis[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	27.00 (4.24)	. (.)	27.00 (4.24)	--
95%CI	(0.00 ; 65.12)	(. ; .)	(0.00 ; 65.12)	
Median (P25 ; P75)	27.00 (24.00 ; 30.00)	. (. ; .)	27.00 (24.00 ; 30.00)	
(Min ; Max)	(24.00 ; 30.00)	(. ; .)	(24.00 ; 30.00)	
N valid	2	0	2	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**2 (100.0%)**	**--**	**2 (100.0%)**	**--**
Yes	1 (50.0%)		1 (50.0%)	
No	1 (50.0%)		1 (50.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	24.00 (.)	--	24.00 (.)	--
95%CI	(. ; .)		(. ; .)	
Median (P25 ; P75)	24.00 (24.00 ; 24.00)		24.00 (24.00 ; 24.00)	
(Min ; Max)	(24.00 ; 24.00)		(24.00 ; 24.00)	

N valid	1		1	
9.9. Hypoxemia[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	22.50 (8.10)	. (.)	22.50 (8.10)	--
95%CI	(9.61 ; 35.39)	(. ; .)	(9.61 ; 35.39)	
Median (P25 ; P75)	24.50 (17.50 ; 27.50)	. (. ; .)	24.50 (17.50 ; 27.50)	
(Min ; Max)	(11.00 ; 30.00)	(. ; .)	(11.00 ; 30.00)	
N valid	4	0	4	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**4 (100.0%)**	**--**	**4 (100.0%)**	**--**
Yes	3 (75.0%)		3 (75.0%)	
No	1 (25.0%)		1 (25.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	20.00 (7.81)	--	20.00 (7.81)	--
95%CI	(0.60 ; 39.40)		(0.60 ; 39.40)	
Median (P25 ; P75)	24.00 (11.00 ; 25.00)		24.00 (11.00 ; 25.00)	
(Min ; Max)	(11.00 ; 25.00)		(11.00 ; 25.00)	
N valid	3		3	
9.10. Dysuria[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	25.67 (3.79)	. (.)	25.67 (3.79)	--
95%CI	(16.26 ; 35.07)	(. ; .)	(16.26 ; 35.07)	
Median (P25 ; P75)	24.00 (23.00 ; 30.00)	. (. ; .)	24.00 (23.00 ; 30.00)	
(Min ; Max)	(23.00 ; 30.00)	(. ; .)	(23.00 ; 30.00)	
N valid	3	0	3	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**3 (100.0%)**	**--**	**3 (100.0%)**	**--**
Yes	2 (66.7%)		2 (66.7%)	
No	1 (33.3%)		1 (33.3%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	23.50 (0.71)	--	23.50 (0.71)	--
95%CI	(17.15 ; 29.85)		(17.15 ; 29.85)	
Median (P25 ; P75)	23.50 (23.00 ; 24.00)		23.50 (23.00 ; 24.00)	
(Min ; Max)	(23.00 ; 24.00)		(23.00 ; 24.00)	
N valid	2		2	
9.11. Pollakiuria[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	27.00 (4.24)	. (.)	27.00 (4.24)	--

95%CI	(0.00 ; 65.12)	(. ; .)	(0.00 ; 65.12)	
Median (P25 ; P75)	27.00 (24.00 ; 30.00)	. (. ; .)	27.00 (24.00 ; 30.00)	
(Min ; Max)	(24.00 ; 30.00)	(. ; .)	(24.00 ; 30.00)	
N valid	2	0	2	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**2 (100.0%)**	**--**	**2 (100.0%)**	**--**
Yes	1 (50.0%)		1 (50.0%)	
No	1 (50.0%)		1 (50.0%)	
PATIENT RECOVERED- Days with some symptoms to the end of the observational period				
Mean (SD)	24.00 (.)	--	24.00 (.)	--
95%CI	(. ; .)		(. ; .)	
Median (P25 ; P75)	24.00 (24.00 ; 24.00)		24.00 (24.00 ; 24.00)	
(Min ; Max)	(24.00 ; 24.00)		(24.00 ; 24.00)	
N valid	1		1	
9.12. Sleepiness[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	30.00 (.)	. (.)	30.00 (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	30.00 (30.00 ; 30.00)	. (. ; .)	30.00 (30.00 ; 30.00)	
(Min ; Max)	(30.00 ; 30.00)	(. ; .)	(30.00 ; 30.00)	
N valid	1	0	1	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**--**	**1 (100.0%)**	**--**
Yes	0 (0.0%)		0 (0.0%)	
No	1 (100.0%)		1 (100.0%)	
PATIENT RECOVERED- Days with some symptoms to the end of the observational period				
Mean (SD)	--	--	--	--
95%CI				
Median (P25 ; P75)				
(Min ; Max)				
N valid				
9.13. Apathy[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	24.00 (.)	. (.)	24.00 (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	24.00 (24.00 ; 24.00)	. (. ; .)	24.00 (24.00 ; 24.00)	
(Min ; Max)	(24.00 ; 24.00)	(. ; .)	(24.00 ; 24.00)	
N valid	1	0	1	

PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**--**	**1 (100.0%)**	**--**
Yes	1 (100.0%)		1 (100.0%)	
No	0 (0.0%)		0 (0.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	24.00 (.)	--	24.00 (.)	--
95%CI	(. ; .)		(. ; .)	
Median (P25 ; P75)	24.00 (24.00 ; 24.00)		24.00 (24.00 ; 24.00)	
(Min ; Max)	(24.00 ; 24.00)		(24.00 ; 24.00)	
N valid	1		1	
9.14. Disorientation[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	24.00 (.)	. (.)	24.00 (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	24.00 (24.00 ; 24.00)	. (. ; .)	24.00 (24.00 ; 24.00)	
(Min ; Max)	(24.00 ; 24.00)	(. ; .)	(24.00 ; 24.00)	
N valid	1	0	1	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**--**	**1 (100.0%)**	**--**
Yes	1 (100.0%)		1 (100.0%)	
No	0 (0.0%)		0 (0.0%)	
PATIENT RECOVERED-Days with some symptoms to the end of the observational period				
Mean (SD)	24.00 (.)	--	24.00 (.)	--
95%CI	(. ; .)		(. ; .)	
Median (P25 ; P75)	24.00 (24.00 ; 24.00)		24.00 (24.00 ; 24.00)	
(Min ; Max)	(24.00 ; 24.00)		(24.00 ; 24.00)	
N valid	1		1	
9.15. Anorexia[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	25.33 (1.15)	26.00 (.)	25.00 (1.41)	1.0000
95%CI	(22.46 ; 28.20)	(. ; .)	(12.29 ; 37.71)	
Median (P25 ; P75)	26.00 (24.00 ; 26.00)	26.00 (26.00 ; 26.00)	25.00 (24.00 ; 26.00)	
(Min ; Max)	(24.00 ; 26.00)	(26.00 ; 26.00)	(24.00 ; 26.00)	
N valid	3	1	2	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**3 (100.0%)**	**1 (100.0%)**	**2 (100.0%)**	**--**
Yes	3 (100.0%)	1 (100.0%)	2 (100.0%)	
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	

PATIENT RECOVERED- Days with some symptoms to the end of the observational period				
Mean (SD)	25.33 (1.15)	26.00 (.)	25.00 (1.41)	1.0000
95%CI	(22.46 ; 28.20)	(. ; .)	(12.29 ; 37.71)	
Median (P25 ; P75)	26.00 (24.00 ; 26.00)	26.00 (26.00 ; 26.00)	25.00 (24.00 ; 26.00)	
(Min ; Max)	(24.00 ; 26.00)	(26.00 ; 26.00)	(24.00 ; 26.00)	
N valid	3	1	2	
9.16. Myalgia[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	21.50 (12.02)	. (.)	21.50 (12.02)	--
95%CI	(0.00 ; 129.50)	(. ; .)	(0.00 ; 129.50)	
Median (P25 ; P75)	21.50 (13.00 ; 30.00)	. (. ; .)	21.50 (13.00 ; 30.00)	
(Min ; Max)	(13.00 ; 30.00)	(. ; .)	(13.00 ; 30.00)	
N valid	21.50 (12.02)	. (.)	21.50 (12.02)	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**2 (100.0%)**	**--**	**2 (100.0%)**	**--**
Yes	0 (0.0%)		0 (0.0%)	
No	2 (100.0%)		2 (100.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	--	--	--	--
95%CI				
Median (P25 ; P75)				
(Min ; Max)				
N valid				
9.17. Nasal congestion[3]				
Days with some symptoms to the end of the observational period				
Mean (SD)	30.00 (.)	. (.)	30.00 (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	30.00 (30.00 ; 30.00)	. (. ; .)	30.00 (30.00 ; 30.00)	
(Min ; Max)	(30.00 ; 30.00)	(. ; .)	(30.00 ; 30.00)	
N valid	1	0	1	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**--**	**1 (100.0%)**	**--**
Yes	0 (0.0%)		0 (0.0%)	
No	1 (100.0%)		1 (100.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	--	--	--	--
95%CI				
Median (P25 ; P75)				
(Min ; Max)				

N valid				
9.18. Chest pain[3,4]				
Days with some symptoms to the end of the observational period				
Mean (SD)	6.00 (4.24)	3.00 (.)	9.00 (.)	--
95%CI	(0.00 ; 44.12)	(. ; .)	(. ; .)	
Median (P25 ; P75)	6.00 (3.00 ; 9.00)	3.00 (3.00 ; 3.00)	9.00 (9.00 ; 9.00)	
(Min ; Max)	(3.00 ; 9.00)	(3.00 ; 3.00)	(9.00 ; 9.00)	
N valid	2	1	1	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**2 (100.0%)**	**1 (100.0%)**	**1 (100.0%)**	**1.0000(f)**
Yes	1 (50.0%)	1 (100.0%)	0 (0.0%)	
No	1 (50.0%)	0 (0.0%)	1 (100.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	3.00 (.)	3.00 (.)	--	--
95%CI	(. ; .)	(. ; .)		
Median (P25 ; P75)	3.00 (3.00 ; 3.00)	3.00 (3.00 ; 3.00)		
(Min ; Max)	(3.00 ; 3.00)	(3.00 ; 3.00)		
N valid	1	1		
9.19. Hyporexia[3,4]				
Days with some symptoms to the end of the observational period				
Mean (SD)	16.50 (12.02)	25.00 (.)	8.00 (.)	--
95%CI	(0.00 ; 124.50)	(. ; .)	(. ; .)	
Median (P25 ; P75)	16.50 (8.00 ; 25.00)	25.00 (25.00 ; 25.00)	8.00 (8.00 ; 8.00)	
(Min ; Max)	(8.00 ; 25.00)	(25.00 ; 25.00)	(8.00 ; 8.00)	
N valid	2	1	1	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**2 (100.0%)**	**1 (100.0%)**	**1 (100.0%)**	**1.0000(f)**
Yes	1 (50.0%)	0 (0.0%)	1 (100.0%)	
No	1 (50.0%)	1 (100.0%)	0 (0.0%)	
PATIENT RECOVERED- Days with some symptoms to the end of the observational period				
Mean (SD)	8.00 (.)	--	8.00 (.)	--
95%CI	(. ; .)		(. ; .)	
Median (P25 ; P75)	8.00 (8.00 ; 8.00)		8.00 (8.00 ; 8.00)	
(Min ; Max)	(8.00 ; 8.00)		(8.00 ; 8.00)	
N valid	1		1	
9.20. Lymphedema3,4				
Days with some symptoms to the end of the observational period				
Mean (SD)	4.00 (.)	4.00 (.)	. (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	4.00 (4.00 ; 4.00)	4.00 (4.00 ; 4.00)	. (. ; .)	
(Min ; Max)	(4.00 ; 4.00)	(4.00 ; 4.00)	(. ; .)	

N valid	1	1	0	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**1 (100.0%)**	**--**	**--**
Yes	1 (100.0%)	1 (100.0%)		
No	0 (0.0%)	0 (0.0%)		
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	4.00 (.)	4.00 (.)	--	--
95%CI	(. ; .)	(. ; .)		
Median (P25 ; P75)	4.00 (4.00 ; 4.00)	4.00 (4.00 ; 4.00)		
(Min ; Max)	(4.00 ; 4.00)	(4.00 ; 4.00)		
N valid	1	1		
9.21. Orthopnea3,4				
Days with some symptoms to the end of the observational period				
Mean (SD)	9.00 (.)	. (.)	9.00 (.)	--
95%CI	(. ; .)	(. ; .)	(. ; .)	
Median (P25 ; P75)	9.00 (9.00 ; 9.00)	. (. ; .)	9.00 (9.00 ; 9.00)	
(Min ; Max)	(9.00 ; 9.00)	(. ; .)	(9.00 ; 9.00)	
N valid	1	0	1	
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**	**--**	**1 (100.0%)**	**--**
Yes	0 (0.0%)		0 (0.0%)	
No	1 (100.0%)		1 (100.0%)	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period				
Mean (SD)	--	--	--	--
95%CI				
Median (P25 ; P75)				
(Min ; Max)				
N valid				

[a] In patients who presented each symptom
[1] Mann–Whitney U test or Fisher exact test (f)
[2] Variable generated by statistical programming.
[3] Other symptoms: According to MedDRA 23.0 (LLT)
[4] These symptoms were not first symptoms

Table S5. Recovery duration of each symptom associated with COVID-19 by symptoms

	ImmunoFormulation cohort
TOTAL RECOVERY FROM START OF IMMUNOFORMULATION TREATMENT[a]	
1. Fever	
Days with some symptoms to the end of the observational period	
Mean (SD)	2.25 (0.91)
95%CI	(1.82 ; 2.68)
Median (P25 ; P75)	2.00 (2.00 ; 3.00)
(Min ; Max)	(1.00 ; 5.00)
N valid	20
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**20 (100.0%)**
Yes	20 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	2.25 (0.91)
95%CI	(1.82 ; 2.68)
Median (P25 ; P75)	2.00 (2.00 ; 3.00)
(Min ; Max)	(1.00 ; 5.00)
N valid	20
2. Dry Cough	
Days with some symptoms to the end of the observational period	
Mean (SD)	4.38 (6.31)
95%CI	(0.57 ; 8.19)
Median (P25 ; P75)	2.00 (2.00 ; 4.00)
(Min ; Max)	(1.00 ; 25.00)
N valid	13
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**13 (100.0%)**
Yes	13 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	4.38 (6.31)
95%CI	(0.57 ; 8.19)
Median (P25 ; P75)	2.00 (2.00 ; 4.00)
(Min ; Max)	(1.00 ; 25.00)
N valid	13
3. Dyspnea	
Days with some symptoms to the end of the observational period	
Mean (SD)	3.67 (2.08)
95%CI	(0.00 ; 8.84)
Median (P25 ; P75)	3.00 (2.00 ; 6.00)
(Min ; Max)	(2.00 ; 6.00)
N valid	3

PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**3 (100.0%)**
Yes	3 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	3.67 (2.08)
95%CI	(0.00 ; 8.84)
Median (P25 ; P75)	3.00 (2.00 ; 6.00)
(Min ; Max)	(2.00 ; 6.00)
N valid	3
4. Loss of taste and smell	
Days with some symptoms to the end of the observational period	
Mean (SD)	19.73 (4.67)
95%CI	(16.59 ; 22.87)
Median (P25 ; P75)	20.00 (14.00 ; 23.00)
(Min ; Max)	(14.00 ; 26.00)
N valid	11
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**11 (100.0%)**
Yes	10 (90.9%)
No	1 (9.1%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	19.70 (4.92)
95%CI	(16.18 ; 23.22)
Median (P25 ; P75)	20.50 (14.00 ; 23.00)
(Min ; Max)	(14.00 ; 26.00)
N valid	10
5. Headache	
Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (1.31)
95%CI	(0.91 ; 3.09)
Median (P25 ; P75)	2.00 (1.00 ; 2.00)
(Min ; Max)	(1.00 ; 5.00)
N valid	8
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**8 (100.0%)**
Yes	8 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (1.31)
95%CI	(0.91 ; 3.09)
Median (P25 ; P75)	2.00 (1.00 ; 2.00)
(Min ; Max)	(1.00 ; 5.00)
N valid	8
6. Diarrhea	
Days with some symptoms to the end of the observational period	

Mean (SD)	5.25 (5.85)
95%CI	(0.00 ; 14.56)
Median (P25 ; P75)	2.50 (2.00 ; 8.50)
(Min ; Max)	(2.00 ; 14.00)
N valid	4
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**4 (100.0%)**
Yes	4 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	5.25 (5.85)
95%CI	(0.00 ; 14.56)
Median (P25 ; P75)	2.50 (2.00 ; 8.50)
(Min ; Max)	(2.00 ; 14.00)
N valid	4
7. Abdominal pain	
Days with some symptoms to the end of the observational period	
Mean (SD)	2.80 (1.30)
95%CI	(1.18 ; 4.42)
Median (P25 ; P75)	2.00 (2.00 ; 3.00)
(Min ; Max)	(2.00 ; 5.00)
N valid	5
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**5 (100.0%)**
Yes	5 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	2.80 (1.30)
95%CI	(1.18 ; 4.42)
Median (P25 ; P75)	2.00 (2.00 ; 3.00)
(Min ; Max)	(2.00 ; 5.00)
N valid	5
8. Dermatological findings	
Days with some symptoms to the end of the observational period	
Mean (SD)	20.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	20.00 (20.00 ; 20.00)
(Min ; Max)	(20.00 ; 20.00)
N valid	1
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**
Yes	0 (0.0%)
No	1 (100.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	**--**
Mean (SD)	
95%CI	

Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.1. General discomfort[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	8.00 (8.16)
95%CI	(0.00 ; 20.99)
Median (P25 ; P75)	5.00 (3.00 ; 13.00)
(Min ; Max)	(2.00 ; 20.00)
N valid	4
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**4 (100.0%)**
Yes	3 (75.0%)
No	1 (25.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	4.00 (2.00)
95%CI	(0.00 ; 8.97)
Median (P25 ; P75)	4.00 (2.00 ; 6.00)
(Min ; Max)	(2.00 ; 6.00)
N valid	3
9.2. Throat lesion[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	2.00 (2.00 ; 2.00)
(Min ; Max)	(2.00 ; 2.00)
N valid	1
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**
Yes	1 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	2.00 (2.00 ; 2.00)
(Min ; Max)	(2.00 ; 2.00)
N valid	1
9.3. Vomiting[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	2.00 (2.00 ; 2.00)
(Min ; Max)	(2.00 ; 2.00)
N valid	1
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**

Yes	1 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	2.00 (2.00 ; 2.00)
(Min ; Max)	(2.00 ; 2.00)
N valid	1
9.4. Weakness[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	1.92 (0.67)
95%CI	(1.49 ; 2.34)
Median (P25 ; P75)	2.00 (1.50 ; 2.00)
(Min ; Max)	(1.00 ; 3.00)
N valid	12
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**12 (100.0%)**
Yes	12 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED-Days with some symptoms to the end of the observational period	
Mean (SD)	1.92 (0.67)
95%CI	(1.49 ; 2.34)
Median (P25 ; P75)	2.00 (1.50 ; 2.00)
(Min ; Max)	(1.00 ; 3.00)
N valid	12
9.5. Sore throat[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	2.00 (2.00 ; 2.00)
(Min ; Max)	(2.00 ; 2.00)
N valid	1
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**
Yes	1 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	2.00 (2.00 ; 2.00)
(Min ; Max)	(2.00 ; 2.00)
N valid	1
9.6. Muscular pain3	
Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (.)

95%CI	(. ; .)
Median (P25 ; P75)	2.00 (2.00 ; 2.00)
(Min ; Max)	(2.00 ; 2.00)
N valid	1
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**
Yes	1 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	2.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	2.00 (2.00 ; 2.00)
(Min ; Max)	(2.00 ; 2.00)
N valid	1
9.7. Dehydration3	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**--**
Yes	
No	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	--
Mean (SD)	
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.8. Emesis[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**--**
Yes	
No	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	**--**
Mean (SD)	
95%CI	
Median (P25 ; P75)	

(Min ; Max)	
N valid	
9.9. Hypoxemia[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	--
Yes	
No	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	**--**
Mean (SD)	
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.10. Dysuria[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	--
Yes	
No	
PATIENT RECOVERED-Days with some symptoms to the end of the observational period	--
Mean (SD)	
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.11. Pollakiuria[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**--**

Yes	
No	
PATIENT RECOVERED- Days with some symptoms to the end of the observational period	--
Mean (SD)	
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.12. Sleepiness[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**--**
Yes	
No	
PATIENT RECOVERED- Days with some symptoms to the end of the observational period	--
Mean (SD)	--
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.13. Apathy3	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**--**
Yes	
No	
PATIENT RECOVERED-Days with some symptoms to the end of the observational period	**--**
Mean (SD)	
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.14. Disorientation3	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)

95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**--**
Yes	
No	
PATIENT RECOVERED-Days with some symptoms to the end of the observational period	**--**
Mean (SD)	
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.15. Anorexia[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	26.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	26.00 (26.00 ; 26.00)
(Min ; Max)	(26.00 ; 26.00)
N valid	1
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**
Yes	1 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	26.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	26.00 (26.00 ; 26.00)
(Min ; Max)	(26.00 ; 26.00)
N valid	1
9.16. Myalgia[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**--**
Yes	
No	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	**--**
Mean (SD)	
95%CI	
Median (P25 ; P75)	

(Min ; Max)	
N valid	
9.17. Nasal congestion[3]	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**--**
Yes	
No	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	**--**
Mean (SD)	
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.18. Chest pain[3,4]	
Days with some symptoms to the end of the observational period	
Mean (SD)	3.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	3.00 (3.00 ; 3.00)
(Min ; Max)	(3.00 ; 3.00)
N valid	1
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**
Yes	1 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	
Mean (SD)	3.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	3.00 (3.00 ; 3.00)
(Min ; Max)	(3.00 ; 3.00)
N valid	1
9.19. Hyporexia[3,4]	
Days with some symptoms to the end of the observational period	
Mean (SD)	24.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	24.00 (24.00 ; 24.00)
(Min ; Max)	(24.00 ; 24.00)
N valid	1
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**
Yes	0 (0.0%)

No	1 (100.0%)
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	**--**
Mean (SD)	
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	
9.20. Lymphedema[3,4]	
Days with some symptoms to the end of the observational period	
Mean (SD)	4.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	4.00 (4.00 ; 4.00)
(Min ; Max)	(4.00 ; 4.00)
N valid	1
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**1 (100.0%)**
Yes	1 (100.0%)
No	0 (0.0%)
PATIENT RECOVERED-Days with some symptoms to the end of the observational period	
Mean (SD)	4.00 (.)
95%CI	(. ; .)
Median (P25 ; P75)	4.00 (4.00 ; 4.00)
(Min ; Max)	(4.00 ; 4.00)
N valid	1
9.21. Orthopnea[3,4]	
Days with some symptoms to the end of the observational period	
Mean (SD)	. (.)
95%CI	(. ; .)
Median (P25 ; P75)	. (. ; .)
(Min ; Max)	(. ; .)
N valid	0
PATIENTS RECOVERED TO THE END OF THE OBSERVATIONAL PERIOD, n (%)	**--**
Yes	
No	
PATIENT RECOVERED - Days with some symptoms to the end of the observational period	**--**
Mean (SD)	
95%CI	
Median (P25 ; P75)	
(Min ; Max)	
N valid	

[a] In patients who presented each symptom
[1] Mann–Whitney U test
[2] Variable generated by statistical programming.
[3] Other symptoms: According to MedDRA 23.0 (LLT)
[4] These symptoms were not first symptoms