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Effect and Safety of Viusid® on Quality of Life in Patients with Chronic Kidney Disease Undergoing Haemodialysis

Dagoberto Semanat Vaillant[1*], Esther Ibars Bolaños[2], Yanitza Roja Guerra[1], Iamara Yaicel Castro Licea[1], José Antonio Álvarez Ramírez[2], Alicia Vargas Batista[3], Rolando Uranga Piña[4], Ivis Cristina Mendoza Hernández[3], David Márquez Soriano[5]

[1]Haemodialysis Department, Hermanos Ameijeiras Surgical Clinical Hospital (HA), Havana, Cuba
[2]Haemodialysis Department, Dr. Abelardo Bush López Institute of Nephrology (INEF), Havana, Cuba
[3]Clinical Trials Department, National Coordinator of Clinical Trial Centre (CENCEC), Havana, Cuba
[4]Biostatistics Department, National Coordinator of Clinical Trial Centre (CENCEC), Havana, Cuba
[5]Scientific Department, CATALYSIS S.L., Madrid, Spain
Email: *dago.semanat@infomed.sld.cu

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Abstract

Introduction: The primary goal in the treatment of patients with Chronic Kidney Disease (CKD) undergoing dialysis is to optimise parameters that support an improved Quality of Life (QoL). Nutritional supplements have been widely used for this purpose. **Objective:** To evaluate the effect and safety of the nutritional supplement **Viusid®** in a cohort of patients with stage 5 CKD undergoing haemodialysis. **Material and methods:** This was an open-label, multicentre, prospective, uncontrolled study. Sixty patients from the Dr. Abelardo Bush López Institute of Nephrology and the Hermanos Ameijeiras Surgical Clinical Hospital in Havana, Cuba, were included. Patients received one vial of **Viusid®** daily for six months and were evaluated at three time points. Clinical and sociodemographic data were collected from each patient. The primary outcome was quality of life, assessed using the SF-36 QoL questionnaire. Secondary outcomes included the presence and severity of symptoms and signs, anthropometric measurements, haematological, biochemical and immunological profiles, and safety. **Results:** The mean age was 49.27 ± 1.64 years, with a predominance of male patients. Hypertension was the leading cause of kidney damage (33.3%). The sample size decreased from 60 to 43 patients who completed all evaluations. Significant absolute increases were observed in each of the eight SF-36 QoL dimensions, exceeding the non-inferiority margin ($\delta = -5$), indicating that scores either remained stable or improved from baseline (month 0) to month 6. Improvements were observed in symptoms such as cramps, pain, and sleep disturbances, along with stabilisation in nutritional categories.

Haemoglobin and haematocrit levels remained outside normal ranges, with no additional deviations attributable to treatment. Albumin, total protein, transferrin, and C-Reactive Protein (CRP) levels showed improvement. The proportion of adverse events was 33% related to haemodialysis and 20% related to **Viusid**®. **Conclusions:** Improvement or maintenance of SF-36 QoL scores was achieved, particularly in the domains of general health, physical functioning, social functioning, and bodily pain. **Viusid**® was found to be safe, with a low incidence of adverse events.

Keywords

Chronic Kidney Disease, Haemodialysis, Nutritional Supplement, Antioxidant, Quality of Life

1. Introduction

Chronic Kidney Disease (CKD) is a serious global health concern. According to statistics from the World Health Organization (WHO), up to 600 million people worldwide may suffer from end-stage CKD, of whom more than 1.5 million are undergoing dialysis treatment and nearly 500,000 have received a kidney transplant [1]. The global burden of stage 5 CKD requiring Renal Replacement Therapy (RRT), either dialysis or kidney transplantation, is increasing by 6% to 20% annually, with over 2.5 million patients currently receiving dialysis. This figure is expected to double over the next decade [2].

In Cuba, the prevalence rate of CKD across its various stages is 3,550 per million inhabitants, and the mortality rate ranges between 100 and 120 per million [3].

Prior to the advent of renal replacement therapy techniques, CKD was an irreversible and terminal condition within a relatively short timeframe. It was only from the 1960s onwards, with the development of dialysis methods, that the survival of these patients began to improve [1]-[4], transforming stage 5 CKD into a long-term illness, despite its debilitating and catastrophic nature [4].

These patients often exhibit immunodeficiency, particularly in the more advanced stages of RRT via haemodialysis or peritoneal dialysis, which manifests through alterations in both innate and adaptive immunity [5] [6]. In addition to this secondary immunodeficiency, caused by uraemia, diabetes, and other risk factors [7], malnutrition is a significant contributing factor. Furthermore, oxidative stress and a severe chronic inflammatory state, induced by haemodialysis [8], lead to both subclinical and clinical infections, which are associated with increased cardiovascular risk and mortality due to cardiac causes and sepsis [8]-[11].

For decades, the primary objective in the treatment of patients undergoing dialysis has been to optimise parameters that enable the achievement of an optimal Quality of Life (QoL). Nutritional supplements have been widely used for this purpose, highlighting the importance of evaluating the potential beneficial effects and safety of the oral solution **Viusid**® in patients with stage 5 CKD on haemodi-

alysis [12] [13].

Viusid®, manufactured by Catalysis S.L., is a nutritional supplement presented in oral solution form. It comprises various substances that help reduce oxidative stress in patients with CKD, while also acting as a natural immunomodulator. The product contains active ingredients that support both immune system function and liver metabolism. Among its components is pyridoxal, which is essential for the formation of antibodies and red blood cells. It also plays a critical role in the proper absorption of vitamin B12, the immune response, and the formation of CD4 lymphocytes [13]-[18].

In addition to pyridoxal, **Viusid**® contains several bioactive compounds with potential relevance in CKD. L-arginine supports urea cycle function and immune modulation through thymic maturation and nitric oxide synthesis [19] [20]. L-glycine, a precursor of glutathione, contributes to antioxidant defence and mucosal protection [21] [22]. Vitamin C enhances innate and adaptive immunity and improves iron absorption [23]. Folic acid and vitamin B12 aid haematopoiesis, DNA synthesis, and epithelial integrity [24]-[26]. Zinc acts as a cofactor in immune responses and has antiviral properties [27] [28], while glucosamine and glycyrrhizin modulate inflammatory responses and protect mucosal and hepatic tissues [29] [30].

Alternative therapeutic approaches, such as the nutritional supplement **Viusid**®, may prove beneficial for patients with stage 5 CKD, as it contributes to reducing blood and urinary urea levels. Additionally, this product enhances the immune system by increasing CD4 and CD8 lymphocyte counts, thereby boosting immune responsiveness and improving control over opportunistic infections. As an immunonutrient, it is particularly suitable for immunosuppressed patients, such as those suffering from CKD [13]-[18].

For these reasons, we aimed to evaluate the effect and safety of the nutritional supplement **Viusid**® in a sample of patients with stage 5 chronic kidney disease undergoing haemodialysis.

2. Materials and Methods

2.1. Clinical Sites

The study was conducted in the haemodialysis programmes of the Nephrology Services at the Dr Abelardo Bush López Institute of Nephrology and the Hermanos Ameijeiras Surgical Clinical Hospital, Havana, Cuba.

2.2. Study Design

This is an open-label, multicentre, uncontrolled, prospective study conducted over a six-month period. Each patient underwent three scheduled assessments: an initial evaluation at baseline (Month 0), a midpoint evaluation after three months of treatment (Month 3) and a final evaluation at the end of the observation period (Month 6). The study aimed to assess the clinical and quality-of-life outcomes associated with the administration of **Viusid**® in patients undergoing regular hae-

modialysis. Each participant served their own control, allowing for intra-individual comparisons across the three time points.

2.3. Study Sample

A total of 60 patients with Chronic Kidney Disease (CKD) undergoing regular haemodialysis (30 per centre) were included. All participants were over 18 years of age and received 2 to 3 dialysis sessions per week between December 2023 and April 2024. For each patient, sex, age, primary cause of renal function loss, and associated comorbidities were recorded.

Exclusion criteria included:

- Active infection at the time of inclusion;
- Pregnancy or breastfeeding;
- Active immunological disease or mental disability;
- Ongoing chemotherapy or radiotherapy;
- Known hypersensitivity to products similar to **Viusid**® oral solution.

2.4. Dialysis Regimen

Patients remained on haemodialysis with a dose adjusted according to recommendations (Kt/V = 1.4). Low-flow polysulphone dialysers (PolySulphone©, Fresenius AG, Germany) and glucose-free bicarbonate buffer were used as the dialysis solution, infused at a flow rate adjusted to 500 mL/min. Blood flow was maintained between 300 and 350 mL/min, depending on vascular access conditions.

2.5. Concomitant Treatment

All patients included continued treatment with recombinant human erythropoietin (EPOhur©, CIGB—Centre for Genetic Engineering and Biotechnology, Havana, Cuba) for the prevention and management of anaemia.

2.6. Treatment Administration

Viusid® was administered as a single-dose oral solution (a vial of 30 mL) once daily for six months. It was prescribed one hour after dialysis sessions and, on non-dialysis days, at a similar time of day where possible.

2.7. Patient Follow-Up and Evaluation

Each patient was followed for six months. Adverse events related to haemodialysis and the nutritional supplement were recorded. Each patient served as their own control (pre-/post-treatment comparison).

2.8. Working Hypothesis

"With the administration of the nutritional supplement **Viusid**®, it is expected that the score on the Quality-of-Life scale in treated patients will remain stable or improve compared to the baseline value." To test this hypothesis, a non-inferiority version of the signed rank test was applied to the relative change in scale dimen-

sions from Month 0 to Month 6.

2.9. Parameters Evaluated

2.9.1. Main Variable

- **Quality-of-Life (QoL).** Assessed using the SF-36 Quality-of-Life questionnaire, consisting of 36 items covering eight dimensions [31]. Changes in dimension scores at Month 6 were compared to baseline values (Month 0).

2.9.2. Secondary Variables

- **Symptoms And Signs.** Evaluated using the Palliative Care Outcome Symptom Scale (POS-S Renal), comprising 17 items across two dimensions [32]. Changes in symptom scores were assessed at Month 6 relative to baseline values.
- **Anthropometric Assessment.** Height (m) and weight (kg) were measured using standardised procedures at the end of the dialysis session. The Body Mass Index (BMI) was calculated from the recorded height and weight and stratified as follows: Underweight: BMI < 18.5 kg/m^2; Normal weight: 18.5 kg/m^2 ≤ BMI < 25.0 kg/m^2; Overweight: BMI ≥ 25.0 kg/m^2. Obesity was defined as BMI ≥ 30.0 kg/m^2. Measurements were taken at Months 0, 3 and 6.
- **Laboratory Profile.** The following parameters were recorded for each patient: haemoglobin (g/dL), ferritin (ng/mL), transferrin (g/L), albumin (g/L), prealbumin (g/L), C-reactive protein (mg/L), lymphocytes (cells × 10^9/L), neutrophil leukocytes (cells × 10^9/L), and platelets (cells × 10^9/L). Platelet-to-lymphocyte and neutrophil-to-lymphocyte ratios were calculated. Data were collected at all three time points.
- **Safety.** Adverse Events (AEs) were documented at Months 3 and 6, including type of AE, intensity, severity, causality, attitude towards treatment, and outcome. Patient interviews, physical examinations, and supplement batch tracking were conducted. Treatment discontinuations and their causes were also analysed.

2.10. Criteria for Evaluating Response

Treatment was considered successful if **Viusid**® administration resulted in improvement or maintenance of SF-36 QoL scores compared to baseline.

2.11. Handling of Missing Values

Mean values for QoL, nutritional status, and laboratory variables at each assessment point were calculated using the available case method. Mean increases in response variables were calculated using the complete case method.

2.12. Data Collection and Processing

Data were recorded using a dedicated data collection booklet and processed using automated computing systems: SAS for Windows version 9.3, S-PLUS version 6.2, and SPSS version 25.

2.13. Statistical Analysis

Descriptive statistics (mean, standard error, 95% confidence interval for the mean, median, minimum, and maximum) were reported for quantitative variables. Absolute and relative frequencies were reported for qualitative variables. Before-after comparisons of quantitative variables were performed using the paired Student's *t*-test or the non-parametric Wilcoxon signed-rank test if the normality assumption was not met. Correlations for qualitative variables before and after treatment were analysed using the Kappa index. Time-dependent variables were visualised using average profile plots.

The non-inferiority margin ($\Delta = -5$) was selected to test whether the observed improvements in SF-36 scores were significantly greater than a minimal reference value. Given that SF-36 scores range from 0 to 100, a margin of −5 was considered sufficiently small to represent a clinically negligible difference. A sensitivity analysis using $\Delta = -1$ yielded comparable results, supporting the robustness of the findings. The hypothesis test employed was a non-inferiority adaptation of the signed-rank test.

2.14. Ethical Aspects

The study was conducted in accordance with the Declaration of Helsinki as adopted at the 64th World Medical Association General Assembly in Fortaleza, Brazil, October 2013 [33] and with current Cuban state regulations for nutritional supplements issued by the National Institute of Hygiene, Epidemiology, and Microbiology (INHEM) [34]. Informed consent was obtained from all patients prior to enrolment. The study protocol was reviewed and approved by the Research Ethics Committees (REC) of the participating institutions (INEF and HA), and its initiation was duly notified to the INHEM.

3. Results

3.1. Baseline Characteristics and Intergroup Comparisons

The study was conducted between January and October 2024. Table 1 summarises the baseline socio-demographic and clinical characteristics of the 60 patients included. The mean age was 49.27 ± 1.64 years (range: 20 to 80 years), with a predominance of male patients (male-to-female ratio: 1.61). The leading cause of renal impairment was hypertension (33.3%), followed by diabetes mellitus (8.33%). The most frequent comorbidities were arterial hypertension (95.0%) and cardiovascular diseases (43.33%). Haemodialysis was performed via an arteriovenous fistula in 93.33% of patients, and the same proportion were receiving at least one concomitant medication.

An analysis of group homogeneity revealed differences between the two study centres. The proportion of female patients was 27.0% in the HHA group and 50.0% in the INEF group, a difference approaching statistical significance ($p = 0.0551$). Statistically significant differences were observed in the prevalence of cardiovascular disease (70.0% in HHA vs 17.0% in INEF; $p < 0.0001$), allergic conditions

(0.0% in HHA vs 20.0% in INEF; p = 0.0119), and other comorbidities (83.0% in HHA vs 30.0% in INEF; p < 0.0001).

Table 1. Distribution of patients by centre according to sociodemographic and clinical variables (n = 60).

Variable	HHA (n = 30)	INEF (n = 30)	Total (n = 60)	p-value
Age (years) Mean ± SD (min-max)	**49.9 ± 2.28** (20 - 76)	**49.6 ± 2.40** (25 - 80)	**49.27 ± 1.64** (20 - 80)	0.39
Gender, n (%)				
Male	**22** (73.33%)	**15** (50.0%)	**37** (61.67%)	0.06
Female	**8** (26.67%)	**15** (50.0%)	**23** (38.33%)	
Ethnic background, n (%)				
White Caribbean	**11** (36.67%)	**13** (43.33%)	**24** (40.00%)	
Black Caribbean	**7** (23.33%)	**7** (23.33%)	**14** (23.33%)	0.84
Mixed Caribbean	**12** (40.0%)	**10** (33.33%)	**22** (36.67%)	
Cause of CKD, n (%)*				
Hypertension	**10** (33.33%)	**10** (33.33%)	**20** (33.33%)	0.61
DM	**4** (13.33%)	**1** (3.33%)	**5** (8.33%)	0.18
Other causes	**17** (56.6%)	**20** (66.67%)	**37** (61.67%)	0.30
Comorbidities, n (%)				
Hypertension	**30** (100.0%)	**27** (90.0%)	**57** (95.00%)	0.12
Cardiovascular disease	**21** (70.0%)	**5** (16.67%)	**26** (43.33%)	0.00
DM	**5** (16.67%)	**3** (10.0%)	**8** (13.33%)	0.35
COPD	**0** (0.00%)	**1** (3.33%)	**1** (1.67%)	0.50
Asthma	**0** (0.00%)	**3** (10.0%)	**3** (5.00%)	0.12
Allergic diseases	**0** (0.00%)	**6** (20.0%)	**6** (10.00%)	0.01
Cerebrovascular disease	**0** (0.00%)	**1** (3.33%)	**1** (1.67%)	0.50
Rheumatic Diseases	**2** (6.67%)	**1** (3.33%)	**3** (5.00%)	0.5
Neurological diseases	**0** (0.00%)	**2** (6.67%)	**2** (3.33%)	0.25
Other comorbidities	**25** (83.33%)	**9** (30.0%)	**34** (56.67%)	0.00
Vascular Access, n (%)				
FAV	**30** (100.00%)	**26** (86.67%)	**56** (93.33%)	0.06
Venous catheter	**0** (0.00%)	**4** (6.67%)	**4** (6.67%)	
Treatment at Inclusion, n (%)				
Yes	**29** (96.67%)	**27** (90.00%)	**56** (93.33%)	0.31
No	**1** (3.33%)	**3** (10.00%)	**4** (6.67%)	

Abbreviations: AVF = Arteriovenous Fistula; COPD = Chronic Obstructive Pulmonary Disease; DM = Diabetes Mellitus; HHA = Hermanos Ameijeiras Hospital; HTA = high blood pressure; INEF = Institute of Nephrology; max = maximum value; min = minimum value; SD = Standard Deviation. **Source:** Medical records. **Note:** *Two patients reported two causes of CKD: HA10 HTA and focal segmental glomerulosclerosis and INEF28 DM and HTA.

3.2. Quality of Life (SF-36) after Six Months of Viusid® Supplementation

Of the 67 patients initially screened, 60 were enrolled and received treatment, and 43 completed the six-month follow-up (Figure 1). Sample Size (SS) available at each assessment point for the eight SF-36 dimensions is shown in Table 2. Initially, all 60 patients completed the questionnaire. By month 6, 17 patients had discontinued, resulting in a final SS of 43 patients, with one additional patient not completing the "Emotional Role" and "Physical Role" items. For relative change analysis, SS ranged from 35 to 43 patients due to missing data and baseline zero values.

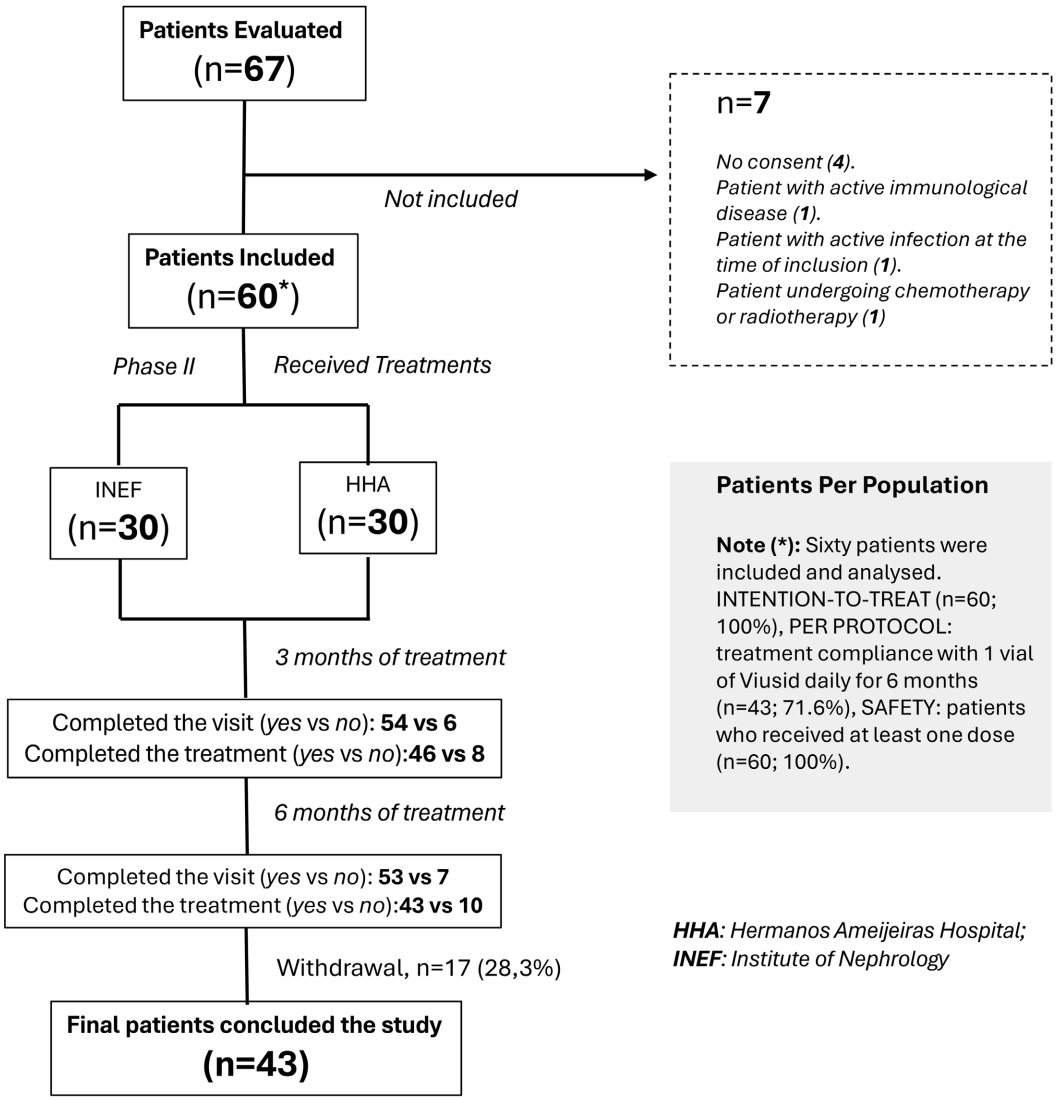

Figure 1. Patient flow throughout the study. Flowchart showing the number of patients evaluated, included, and followed up at each stage of the study. Of the 67 patients initially assessed, 60 were included and received treatment (30 at INEF and 30 at HHA). A total of 43 patients completed the six-month treatment period and were included in the per-protocol analysis. Reasons for exclusion and withdrawal are detailed, along with treatment compliance and population definitions (intention-to-treat, per-protocol, and safety).

Table 2. Sample Size (SS) available for assessment of the SF-36 Quality of Life dimensions.

Dimension	Initial SM	SM month 6	Null initial values	TM for Relative Increase
General Health	60	43	1	42
Physical Functioning	60	43	2	42
Vitality	60	43	0	43
Social Functioning	60	43	2	41
Emotional Role	60	42	10	38
Mental Health	60	43	0	43
Physical Pain	60	43	0	43
Physical Role	60	42	15	35

Note. The relative increase of a variable is defined as the difference between the final value and initial value, divided by the initial value and multiplied by 100. This calculation requires that the initial value is not zero. Therefore, the Total Measurements (TM) for relative increase includes missing data and zero initial values. There were 17 discontinuations, resulting in a sample size of 43 patients at month 6, except for the dimensions "Emotional Role" and "Physical Role", where patient INEF02, although not discontinued, did not complete the corresponding questionnaire items (questions 13 - 16 for physical role, and 17 - 19 for emotional role). The MT for absolute increase variables coincides with the MT at month 6.

Results of the non-inferiority hypothesis test applied to the SF-36 scores with a non-inferiority margin (δ) of -5 points were established (Table 3). All eight dimensions (General Health, Physical Functioning, Vitality, Social Functioning, Emotional Role, Mental Health, Bodily Pain, Physical Role) showed absolute increases significantly greater than the δ, indicating that QoL scores either remained stable or improved over the six-month period. However, relative increases in the dimensions of Vitality, Mental Health, and Physical Role did not reach statistical significance.

Table 3. Evaluation of Quality of Life response after six months of treatment.

Dimension	**Baseline (n = 60)** mean ± SD (IC 95%)	**Month 6*** mean ± SD (IC 95%)	**Absolute Change** Mean ± SD (IC 95%)	p**	**Relative Change (%)** Mean ± SD (IC 95%))	**P ****
General Health	**42.17 ± 2.56** (37.04 - 47.30)	**48.37 ± 2.79** (42.74 - 54.01)	**2.79 ± 2.69** (−2.65 - 8.23)	**0.0027**	**41.42 ± 29.77** (−18.71 - 101.55)	**0.0177**
Physical Functioning	64.67 ± 3.54 (57.59 - 71.74)	**72.78 ± 3.43** (65.86 - 79.70)	**0.22 ± 1.76** (−3.32 - 3.76)	**0.0006**	**3.91 ± 4.00** (−4.17 - 11.99)	**0.0028**
Vitality	**65.33 ± 2.89** (59.55 - 71.11)	**69.38 ± 3.16** (63.00 - 75.76)	**−0.74 ± 2.08** (−4.94 - 3.47)	**0.0309**	**5.80 ± 6.35** (−7.01 - 18.62)	0.0961
Social Functioning*	**79.38 ± 3.41** (72.55 - 86.20)	**83.14 ± 3.92** (75.23 - 91.05)	**1.45 ± 4.33** (−7.28 - 10.19)	**0.0136**	**6.14 ± 6.87** (−7.75 - 20.03	**0.0222**
Emotional Role**	**78.89 ± 5.01** (68.87 - 88.91)	**82.54 ± 5.48** (71.48 - 93.60)	**−5.56 ± 5.89** (−17.46 - 6.35)	**0.0010**	**−10.96 ± 5.19** (−21.49 - −0.04)	**0.0064**
Mental Health	**77.93 ± 2.49** (72.95 - 82.92)	**78.70 ± 2.74** (73.17 - 84.23)	**−1.4 ± 2.49** (−6.43 - 3.64)	**0.0243**	**2.13 ± 5.54** (−9.05 - 13.31)	0.0512

Continued

Bodily Pain	**67.17 ± 3.35** (60.47 - 73.86)	**73.95 ± 3.28** (67.33 - 80.57)	**3.72 ± 2.84** (−2.02 - 9.46)	**0.0004**	**20.59 ± 8.92** (2.59 - 38.59)	**0.0001**
Physical role***	**70.42 ± 5.59** (59.23 - 81.60)	**73.81 ± 6.32** (61.05 - 86.56)	**−4.76 ± 4.84** (−14.53 - 5.01)	**0.0167**	**−4.05 ± 10.35** (−25.08 - 16.98)	0.1041

Note. The relative change of a variable is defined as the difference between the final and initial values, divided by the initial value and multiplied by 100. (*) Sample sizes for each dimension at month 6 are detailed in Table 2; (**) p-value refers to the non-inferiority version of the Wilcoxon signed-rank test. Non-inferiority margin: $\delta = 5$ points. The hypothesis tested is that the relative increase exceeds $-\delta$ **(***)** Patient INEF02 did not complete items 13 - 16 of the SF-36 questionnaire (Physical Role). **Abbreviations:** IC 95%: 95% confidence interval.

Although all final means were higher than initial means, some mean changes were negative due to the influence of missing data. For instance, the Emotional Role dimension had an initial mean of 78.89 points, and a final mean of 82.54; nevertheless, the absolute mean change was −5.56 and the relative change was -10.96. This discrepancy is explained by the fact that the initial mean was calculated on the full sample (n = 60), while the final mean was based on a reduced subsample (n = 42). The relative change was further affected by excluding patients with baseline scores of zero.

The absolute change was calculated using the same subsample of 42 patients, while the relative change was calculated using a subsample of 38 patients (excluding those patients with zero baseline Emotional Role scores as explained in Table 2). Consequently, in the full sample of 60 patients, the 18 additional patients (relative to the Month 6 subsample) shifted the mean downward.

Therefore, it can be asserted that there is a robust tendency towards stability or improvement in quality-of-life scores, despite some negative mean changes. This is because the mean is not always the most appropriate summary statistic; an alternative that is more robust to data variability is the median, and in the present context, an even more informative indicator is the relative frequency.

Limitation of mean-based analysis by presenting medians and relative frequencies is presented in Table 4. In none of the eight dimensions did the median decrease from Month 0 to Month 6. For instance, the initial median for Emotional Role remained at 100 points. Furthermore, of these 42 patients, 36 (85.71%) reported equal or higher scores at Month 6 compared to baseline ($p = 0.000$), strongly supporting the hypothesis of stability or improvement with **Viusid**® administration. The negative mean change is attributable to the distribution of individual changes: six patients experienced a decrease in their Emotional Role score; 33 patients remained unchanged, and three patients showed an improvement. This highlights the limitations of the mean as a summary statistic in the presence of skewed distributions and missing data.

In summary, Table 4 confirms that the majority of patients with CKD experienced either stability or improvement in QoL across all eight dimensions with **Viusid**® supplementation ($p < 0.05$ in all cases). This is further supported by the upward trend in mean scores from baseline to Month 6, as shown in Table 3.

A consistent improvement in perceived quality of life was observed across all eight SF-36 dimensions following six months of **Viusid**® supplementation, particularly in General Health, Bodily Pain, and Physical Role (Figure 2).

Table 4. Categorical response in SF-36 dimensions after six months of treatment with **Viusid**® compared to baseline.

SF-36 dimension	Baseline Median	Month 6 Median	Same or Improved	%	p
General health	45.0	50.0	32/43	74.42	**0.0014**
Physical Functioning	80.0	80.0	30/43	69.77	**0.0095**
Vitality	70.0	70.0	30/43	69.77	**0.0095**
Social Functioning	100.0	100.0	34/43	79.07	**0.0001**
Emotional Role	100.0	100.0	36/42	85.71	**0.0000**
Mental Health	80.0	80.0	28/43	65.12	**0.0474**
Bodily Pain	70.0	70.0	36/43	83.72	**0.0000**
Physical Role	100.0	100.0	34/42	80.95	**0.0001**

Note. Categorical response was defined as maintaining or improving the score in each SF-36 dimension at month 6 compared to baseline. Missing data were handled using the **Complete Case** method: only patients with both baseline and final assessments for each dimension were included in the analysis. P-values were calculated using the non-parametric Wilcoxon signed-rank test.

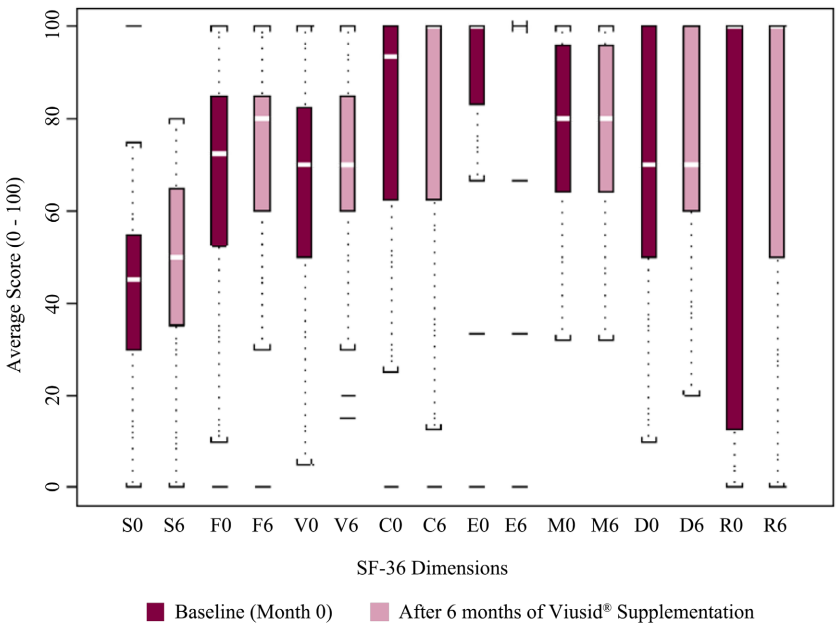

Figure 2. Improvement in SF-36 quality of life scores after six months of **Viusid**® Supplementation. Average scores across the eight SF-36 dimensions at baseline (Month 0) and after six months of treatment (Month 6). Abbreviations. S: General health, F: Physical Functioning, V: Vitality, C: Social Functioning, E: Emotional Role, M: Mental Health, D: Bodily Pain, R: Physical Role.

3.3. Symptom Burden Assessment (POS-S Renal)

Table 5 presents the evolution of symptom burden using the Palliative Care Outcome Symptom Scale (POS-S Renal). Of the 17 items assessed, 9 items (52.94%) showed improvement at the end of 6 months of administering **Viusid**®. Statisti-

cally significant improvements were observed in symptoms such as cramps, pain, and sleep problems. The analysis considered both the presence and absence of symptoms at baseline and follow-up.

Table 5. Improvement in symptoms assessed by the POS-S renal scale after six months of treatment with **Viusid**®.

Symptom (Absence of)	Initial Assessment		Final Assessment		p-value
	N/Total	%	N/Total	%	
Cramps	35/60	58.33	36/42	85.71	0.01
Skin changes	44/60	73.33	37/42	88.1	0.18
Weakness	38/60	63.33	32/43	74.42	0.25
Difficulty breathing	48/60	80.0	39/43	90.07	0.13
Pain	34/59	57.63	33/41	80.49	0.04
Constipation	50/60	83.33	39/43	90.7	0.49
Itching	35/60	58.33	31/41	75.61	0.23
Restless legs	53/60	88.33	38/42	90.48	0.12
Sleep problems	35/60	58.33	34/41	82.93	0.01

Note. Symptom improvement was defined as the absence of the symptom at the final assessment compared to baseline. The POS-S Renal (Palliative Care Outcome Symptom Scale—Renal) was used to evaluate symptom burden. P-values were calculated using non-parametric tests for paired categorical data. Sample sizes vary due to missing responses in individual items.

3.4. Nutritional Status Remained Stable throughout the Study

The evolution of anthropometric and nutritional status assessments, shown in Table 6 and Table 7, indicates that patients maintained stable nutritional parameters throughout the study period. No significant changes were observed in weight, height, or Body Mass Index (BMI) from baseline to Month 6, as the confidence intervals for the mean differences include zero (Table 6).

Similarly, the distribution of patients across BMI categories (underweight, normal weight, overweight, and obesity) remained unchanged at Month 3 and Month 6 compared to baseline (Table 7). Most patients remained within the same nutritional status category throughout the study. No significant shifts were observed ($p > 0.05$) indicating that nutritional status was preserved during the administration of **Viusid**®.

Table 6. Evaluation of nutritional status after six months of treatment with **Viusid**®.

Variable	Baseline (n = 60) Mean ± SD (IC 95%)	Month 6 (n = 53) Mean ± SD (IC 95%)	Difference (IC 95%)	Relative Increase (IC 95%)
Weight (kg)	**68.47 ± 2.08** (64.30 - 72.64)	**67.57 ± 2.22** (63.12 - 72.02)	**−0.48 ± 0.40** (−1.28 - 0.32)	−0.56 ± 0.57 (−1.70 - 0.59)
Height (m)	**1.67 ± 0.01** (1.64 - 1.70)	**1.67 ± 0.01** (1.64 - 1.70)	**0**	0.0
Body Mass Index	**24.36 ± 0.56** (23.24 - 25.49)	**24.18 ± 0.62** (22.93 - 25.44)	**−0.09 ± 0.15** (−0.39 - 0.22)	−0.28 ± 0.60 (−1.49 - 0.93)

Note. Relative increase is calculated as the difference between final and initial values, divided by the initial value and multiplied by 100. Only patients with complete data at both time points were included in the analysis. **Abbreviations:** IC 95%: 95% confidence interval.

Table 7. Non-parametric signed-rank test of nutritional status (baseline, month 3 and month 6).

Nutritional Status	Start		Month 3		Month 6	
	n	%	n	%	n	%
Underweight	**5**	8.33	**4**	7.41	**5**	9.43
Normal weight	**29**	48.33	**27**	50.00	**26**	49.06
Overweight	**21**	35.00	**19**	35.18	**16**	30.19
Obese	**5**	8.33	**4**	7.41	**6**	11.32
Total	**60**	100.00	**54**	100.00	**53**	100.00

Note. Nutritional status was categorised into four groups: underweight, normal weight, overweight, and obese. The non-parametric signed-rank test was applied to assess changes over time. Missing data were handled using the Complete Case method: only patients with available data at each time point were included.

3.5. Evolution of Laboratory Parameters and Inflammatory Markers

Significant changes were observed in several laboratory parameters over the course of the study (Table 8). Haematocrit and pre-albumin decreased significantly from Month 0 to Month 3. Conversely, albumin levels significantly increased during the same period. Haematocrit, Total Leukocyte Count (TLC), and lymphocytes significantly decreased from Month 0 to Month 6, while neutrophils, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and total protein increased significantly. These trends were consistent across both evaluation points.

Transferrin levels showed a positive trend, with mean values increasing from baseline to Month 3 and Month 6, although these changes did not reach statistical significance. Similarly, C-Reactive Protein (CRP) levels increased at Month 3 and decreased at Month 6, without statistically significant variation. These findings are summarised in Table 8, with p-values used as descriptive indicators of statistical, not clinical, significance.

Table 8. Evaluation of response in haematological, biochemical and inflammatory indicators after six months of treatment.

Variable	Baseline (n = 60) mean ± SD (IC 95%)	Month 3 (n = 54) mean ± SD (IC 95%)	Month 6 (n = 43) mean ± SD (IC 95%)	Diff M0-M3	p	Diff M0-M6	p
Haemoglobin (g/dL)	**97.72 ± 2.83** (92.03 - 103.40)	**92.41 ± 2.70** (86.99 - 97.83)	**90.93 ± 2.44** (85.99 - 95.87)	−4.833	0.089	−5.113	0.103
Haematocrit (%)	**0.33 ± 0.01** (0.31 - 0.35)	**0.28 ± 0.01** (0.27 - 0.30)	**0.30 ± 0.01** (0.28 - 0.31)	−0.043	**0.000**	−0.028	**0.007**
Total Leukocyte Count (×10⁹ cells/L)	**5.09 ± 0.19** (4.70 - 5.47)	**4.86 ± 0.37** (4.11 - 5.61)	**3.90 ± 0.23** (3.43 - 4.38)	−0.298	0.456	−1.054	**0.000**
Neutrophils (×10⁹ cells/L)	**55.11 ± 1.83** (51.44 - 58.76)	**56.37 ± 1.72** (52.93 - 59.82)	**64.91 ± 1.49** (61.91 - 67.91)	0.686	0.780	10.22	**0.000**
Lymphocytes (×10⁹ cells/L)	**30.37 ± 1.56** (27.23 - 33.50)	**33.99 ± 1.76** (30.45 - 37.53)	**24.67 ± 1.36** (21.92 - 27.41)	3.029	0.194	−6.230	**0.003**

Continued

Platelets (×10⁹ cells/L)	**195.58 ± 8.07** (179.43 - 211.73)	**208.87 ± 10.62** (187.57 - 230.17)	**205.70 ± 13.01** (179.04 - 232.07)	10.67	0.260	5.818	0.572
Neutrophil/Lymphocyte Ratio	**2.50 ± 0.33** (1.83 - 3.17)	**2.35 ± 0.33** (1.70 - 3.01)	**3.25 ± 0.25** (2.73 - 3.76)	−0143	0.780	1.077	**0.000**
Platelet/lymphocyte Ratio	**160.52 ± 5.59** (11.84 - 136.80)	**176.39 ± 16.01** (144.26 - 208.50)	**274.29 ± 27.25** (219.29 - 329.29)	21.52	0.244	118.5	**0.000**
Total proteins (g/L)	**69.53 ± 1.10** (67.33 - 71.73)	**71.26 ± 1.19** (68.87 - 73.66)	**70.17 ± 2.10** (65.82 - 74.51)	1.618	0.092	4.476	**0.028**
Albumin (g/L)	**41.45 ± 0.55** (40.36 - 42.55)	**43.53 ± 0.61** (42.31 - 44.75)	**42.03 ± 1.09** (39.84 - 44.22)	2.143	**0.001**	0.891	0.494
Prealbumin (g/L)	**0.30 ± 0.01** (0.28 - 0.32)	**0.26 ± 0.01** (0.24 - 0.28)	**0.28 ± 0.01** (0.26 - 0.31)	−0.038	**0.007**	−0.010	0.390
Transferrin (g/L)	**2.08 ± 0.09** (1.91 - 2.26)	**4.84 ± 2.68** (0.54 - 10.23)	**2.38 ± 0.09** (2.20 - 2.57)	3.194	0.314	0.177	0.128
C-reactive protein (mg/L)	**7.88 ± 1.88** (4.12 - 11.64)	**10.86 ± 3.88** (3.07 - 18.66)	**8.93 ± 1.76** (5.38 - 12.48)	3.104	0.495	−0.238	0.926

Abbreviations: IC 95%: 95% confidence interval.

3.6. Discontinuations and Safety Profile

A total of 17 patients (28.32%) discontinued the study, including 14 voluntary withdrawals (23.33%) and 3 deaths (4.99%). Neither of deaths was related to the administration of the supplement **Viusid**®.

At study completion, the proportion of adverse events attributed to haemodialysis was 33.0%, and to **Viusid**® was 20.0%. In both cases, the probability of adverse events occurring was significantly lower than 50.0%, haemodialysis ($p = 0.0098$) and **Viusid**® ($p < 0.0001$).

A total of 51 adverse events were reported: 33 (64.7%) related to haemodialysis and 18 (35.3%) related to **Viusid**®. The most frequent events associated with haemodialysis were pyrogenic reactions and chills (4 reports each, 7.8%). The most common adverse events related to **Viusid**® were diarrhoea (9 reports, 17.4%), cramps (2 reports, 3.9%), and abdominal pain (2 reports, 3.9%). Two sudden deaths (3.9%) were reported, likely secondary to cardiovascular events related to haemodialysis.

Mild adverse events predominated among those attributed to **Viusid**® (78.0%), compared to 33.0% for haemodialysis. Overall, mild (49.0%) and non-serious (86.0%) adverse events were most frequent. In most cases, events were not influenced by **Viusid**® administration (63.0%), and 69.0% of patients recovered. Regarding causality, 51.0% were classified as very likely or certain. Treatment was required in 67.0% of cases.

4. Discussion

The ageing population, and the consequent rise in chronic non-communicable

diseases, particularly Diabetes Mellitus (DM) and Hypertension (HTA), as leading causes of CKD, alongside obstructive nephropathy in males, have increasingly positioned nephrology as a geriatric specialty. A growing number of elderly patients are surviving thanks to Renal Replacement Therapies (RRT). In Cuba, the average age of patients at initiation of RRT has increased from 51.8 years in 2004 to 54.6 years in 2014, slightly above the mean age observed in our study population (49.27 ± 1.64 years; range: 20 - 80 years; **Table 1**). Despite the wide age range, the low standard deviation suggests a clustering of values around the mean, reflecting a concentration of patients in middle adulthood.

CKD-T affects men and women equally, and in countries where both sexes have equitable access to replacement therapy, no significant gender differences are typically observed in patient numbers [2]-[4] [34]. However, in our sample, male patients predominated, accounting for 61.67% of the total population (**Table 1**).

Hypertension and diabetes together account for approximately 55-70% of all CDK cases. In most countries, diabetes is the leading cause of RRT initiation, representing up to 50% of cases in certain regions [5] [6] [9]. These data are consistent with our findings, where hypertension was the leading cause of CKD (33.3%) and the most prevalent comorbidity (95.0%), followed by cardiovascular disease (43.3%) and diabetes mellitus (13.3%) (**Table 1**).

In the developed countries, chronic diseases are the principal contributors to morbidity and mortality. Although these conditions are treatable, they are not curable. Consequently, healthcare professionals must consider not only objective clinical outcomes but also patients' self-reported assessments of their physical, mental, and social functioning, as well as the broader impact of disease and treatment on wellbeing and quality of life. It is therefore essential to therapeutic strategies that enhance overall health and improve quality of life [35].

Dialysis therapies replace only the kidneys' filtering function, without restoring other essential roles such as immune regulation, endocrine secretion, metabolic balance, or the excretion of hormones involved in erythropoiesis, bone metabolism, sexual function, and nutritional homeostasis. This limitation predisposes patients to a range of complications that, over time, negatively affect their physical health, mental wellbeing, and family and social dynamics [36].

This condition affects the emotional, economic, and social health of patients who, upon entering renal replacement therapy programmes, must adhere to strict treatments and significantly modify their social routines. Studies of patients with CKD have concluded that the disease, particularly its medical aspects, is associated with a reduction in Quality of Life (QoL) [37].

The study results show that emotions, mood disturbances, and psychological factors are not the primary contributors to the limitations experienced in daily life by these patients. This finding is broadly consistent with a 2011 study conducted in the same haemodialysis unit [12], whose results across all dimensions validate the effectiveness and superiority of those found in the current research. The dimensions previously identified as most affected (physical functioning and physi-

cal pain) showed better baseline results in the present study, with statistically significant improvements. For instance, 74.42% of patients reported equal or improved scores in General Health, and 83.72% in Bodily Pain after six months of **Viusid**® supplementation (Table 4).

Contreras *et al.*, in a study of patients with chronic renal failure undergoing haemodialysis, reported that social functioning was the best-preserved dimension, while physical role, general health, bodily pain, and emotional role were the most impaired [38].

Renal patients are known to experience a high symptom burden, which contributes to increased suffering and diminished QoL. The Palliative Care Outcome Scale-Symptoms Renal (POS-S Renal), used in a previous study to assess symptomatology in haemodialysis patients, demonstrated a reduction in total symptom scores at six months of administering **Viusid**®, although no further improvement was observed at twelve months compared to baseline. Fatigue or lack of energy showed sustained improvement, while changes in other symptoms were variable. The study concluded that regular assessment of patient-reported symptoms is feasible in routine dialysis practice and may support the evaluation of clinical interventions [39].

Patients with CKD frequently present with impaired nutritional status, secondary to anorexia induced by uraemia and dialysis procedures, as well as the dietary restrictions they must adhere to and an accelerated catabolic state. Moreover, haemodialysis is associated with significant losses of amino acids, blood, calories, and other micronutrients [12].

Anaemia, which is also prevalent among patients undergoing dialysis, is closely associated with both malnutrition and inflammation. Elevated levels of inflammatory markers and biochemical indicators of malnutrition (such as low serum albumin and prealbumin) have been linked to a diminished response to erythropoiesis-stimulating agents [40] [41]. Inflammation further disrupts hepatic synthesis of functional proteins, resulting in reduced circulating transferrin levels and elevated ferritin concentration [42]-[44].

Inflammation and malnutrition frequently coexist in CKD patient population, leading to overlap in the biomarkers used to assess these conditions. Thus, parameters such as serum albumin, prealbumin, total lymphocyte count, and C-Reactive Protein (CRP) serve as useful indicators for both nutritional and inflammation status. In addition, the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Lymphocyte Ratio (NLR) have been proposed as potential markers of systemic inflammation, with NLR also being associated with endothelial dysfunction [45] [46].

In the analysed sample, symptom burden showed a favourable evolution following **Viusid**® supplementation. Statistically significant improvements were observed in cramps (absence increased from 58.33% to 85.71%, $p = 0.01$), pain (from 57.63% to 80.49%, $p = 0.04$), and sleep problems (from 58.33% to 82.93%, $p = 0.01$), as shown in Table 5. Other symptoms (including skin changes, weakness,

difficulty breathing, constipation, itching, and restless legs) also showed improvement, albeit without statistical significance. Nutritional status remained stable throughout the study period, with no significant changes in weight, height, or BMI categories (Table 6 and Table 7). Although some laboratory parameters, such as haemoglobin and haematocrit, remained outside normal ranges, which is typical in patients with CKD undergoing haemodialysis, no additional deviations attributable to treatment with the nutritional supplement **Viusid**® were observed. Meanwhile, several indicators, including albumin, total protein, transferrin, and CRP, showed improvement within clinically acceptable ranges (Table 8). The observed decrease in lymphocyte count and increase in the Neutrophil-to-Lymphocyte Ratio (NLR) may suggest changes in inflammatory status. However, given the limited sample size and incomplete data availability for these parameters, definitive conclusions cannot be drawn. These markers are influenced by multiple factors and tend to evolve over longer periods. Future studies with larger cohorts and extended follow-up are needed to clarify their clinical relevance.

The dropout rate reported in the study may be related to the expectations of this patient group, who, as is well known, often anticipate significant short-term results from dialysis programmes. It is also worth noting that the literature identifies patient retention as a major challenge in many clinical trials, with some trial designers accounting for dropout rates of up to 30% in their calculations.

The open-label, uncontrolled design of this study represents a key limitation. Although the sample was appropriately selected and procedures were standardised across both institutions, the absence of a placebo control group precludes definitive attribution of the observed improvements in quality of life to **Viusid**® administration. These findings should be interpreted as preliminary and hypothesis-generating, warranting confirmation in future randomised controlled trials.

The choice of a per-protocol analysis for the primary outcome, rather than an intention-to-treat approach, may introduce attrition bias given the 28.3% dropout rate. However, multiple imputation was applied as an alternative method for handling missing data, and yielded similar results, supporting the reliability of the findings. Future studies should consider intention-to-treat analyses to enhance generalisability and reduce bias.

Post-marketing pharmacovigilance data confirms the good tolerability of **Viusid**®. However, allergic reactions to components of the formulation may occur, potentially linked to hypersensitivity to the product. In a study combining the use of the nutritional supplement **Viusid**® with ribavirin and IFNα in patients with chronic hepatitis, most adverse events reported were mild and transient [16]. Among the CKD patients treated in the present study, a low proportion of adverse events were observed, with only 20.0% attributed to **Viusid**®. Mild reactions predominated (78.0%), and no serious events related to the product were reported. The most frequent **Viusid**®-related symptoms were diarrhoea (17.4%), cramps (3.9%) and abdominal pain (3.9%) (Result section). Dialysis-related complications occurred at expected rates.

Regarding the prevention of nosocomial transmission, one of the Quality Indicators for compliance with hemodialysis protocols, it is worth noting that the number of seroconversions to hepatitis C and hepatitis B viruses remained at 0% throughout the study period. No fungal infections were reported, and in the case of bacterial sepsis, the reported number of only four events, with clinical manifestations of pyrogenic crisis and no major complications, is practically negligible during the period evaluated. These findings suggest that a positive association was observed during **Viusid**® administration with respect to immune system regulation in the treated patients.

Literature reports describe an incidence of Sudden Death (SD) of 16.7 cases per 1000 patient-years, slightly lower than the 17 to 28 cases per 1,000 patient-years reported in haemodialysis patients. It is well established that the risk of SD increases proportionally with declining renal function. Cardiovascular disease is a leading cause of death in patients with Chronic Kidney Disease (CKD), with a high percentage of these deaths occurring suddenly and unexpectedly. Ischaemic, structural, and electrophysiological cardiac changes are common in CKD, and when combined with hyperkalaemia, sudden electrolyte shifts, and haemodynamic instability associated with haemodialysis, patients are at an increased risk of developing lethal arrhythmias [45] [46]. With the exception of the two reported sudden death events (HA21 and INEF08) and one patient who suffered an acute myocardial infarction (HA27), no other cardiovascular events were described during the treatment period, which could suggest that the use of **Viusid**® does not favor the occurrence of cardiovascular events.

In our experience with the use of **Viusid**® in this study, the safety of the nutritional supplement stands out, as it was well tolerated with few undesirable effects. Adverse events related to the dialysis procedure occurred as expected.

5. Conclusion

Treatment with the nutritional supplement **Viusid**® was associated with either improvement or maintenance of quality of life, as assessed by the SF-36 scale. Particularly notable were the positive changes observed in the dimensions of General Health, Physical Functioning, Social Functioning, and Bodily Pain. Furthermore, a favourable safety profile was observed during **Viusid**® administration in a population characterised by high symptom burden and nutritional vulnerability. The incidence of adverse events was low, with no serious events attributable to **Viusid**®, and dialysis-related complications remained within expected clinical parameters range.

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Author Contributions

DSV and EIB were the principal investigators of this trial. DSV, EIB, ABV, and ICMH conceived the study, designed the trial and the study protocol, and were involved in data analysis and interpretation. RUP was involved in statistical analysis of data. DSV, YRJ, ABV, RUP, ICMH and DMS wrote the manuscript, and the rest of authors provided paper feedback. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors D. S. V., E. I. B., Y. R. G., I. Y. C. L., J. A. A. R., A. V. B., R. U. P., I. C. M. H. and D. M. S. declare no conflicts of interest related to this study. The investigational product (**Viusid**®) was provided by the manufacturer, but the sponsor had no role in the study design, data collection, statistical analysis, interpretation of results, or manuscript preparation.

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