

Supplementary Material

Table S1. Nutritional composition of each oral supplement

| | Ensure® Plus Advance (per bottle) | Ensure® Plus High Protein (per bottle) |
|-------------------|--------------------------------------|---|
| Energy (Kcal) | 330 | 275 |
| Proteins (g) | 20 | 17.4 |
| Carbohydrates (g) | 37 | 35 |
| Fats (g) | 11 | 7.3 |
| Water (g) | 168 | 177 |
| Vitamin D3 (mcg) | 13 | 2.4 |
| Leucine (g) | 1.78 | 1.54 |
| Isoleucine (g) | 0.99 | 0.814 |
| Valine (g) | 1.14 | 1.012 |

Table S2. Anthropometric characteristics at baseline

| | HMB Group (n=22) | | | HP Group (n=21) | | | p |
|---------------------------|-------------------|-------------|------------------|------------------|-------------|------------------|-------|
| | Total | Men | Women | Total | Men | Women | |
| BMI (Kg/m ²) | 25.6 ± 4.31 | 26.4 ± 4.34 | 24.2 ± 4.18 | 26.2 ± 3.94 | 26.3 ± 4.56 | 26.1 ± 2.94 | 0.625 |
| %FM | 18.4 [6.15-25.6] | 16.3 ± 9.91 | 19.6 ± 11.5 | 18.8 [8.4-26.1] | 14.4 ± 8.47 | 22.4 ± 9.19 | 0.923 |
| FFMI (Kg/m ²) | 20.8 ± 2.3 | 21.7 ± 1.78 | 19.2 ± 2.32 | 21.4 ± 2.76 | 22.2 ± 2.76 | 20.2 ± 2.39 | 0.403 |
| SMI (Kg/m ²) | 10.8 [9.15- 11.8] | 11.5 ± 1.53 | 8.55 [7.78-9.57] | 10.0 [9.1-11.7] | 11.5 ± 1.96 | 8.65 [7.95-9.55] | 0.644 |
| ASMM (Kg) | 24.4 [19.3-28.2] | 26.4 ± 3.23 | 17.1 [15.8-19.5] | 22.2 [19.2-27.2] | 25.4 ± 5.38 | 19.3 [17.2-22.4] | 0.715 |
| Biceps skinfold (mm) | 6 [4.5-10] | 6.09 ± 2.63 | 9.12 ± 6.29 | 8 [6-10] | 7.88 ± 4.09 | 10.0 ± 4.38 | 0.211 |
| Triceps skinfold (mm) | 12.9 ± 6.38 | 10.9 ± 4.27 | 16 ± 8.18 | 14.4 ± 6.8 | 12 ± 6.78 | 18.2 ± 5.13 | 0.468 |
| MUAC (cm) | 26 ± 4.76 | 27.1 ± 4.64 | 24.2 ± 4.66 | 27.7 ± 3.88 | 27.7 ± 4.43 | 27.8 ± 3.06 | 0.207 |
| MAMC (cm) | 22.2 ± 4.19 | 23.9 ± 3.89 | 19.2 ± 2.84 | 23.2 ± 3.51 | 24.0 ± 3.89 | 22.0 ± 2.58 | 0.381 |
| Calf circumference (cm) | 35 ± 4.57 | 36.4 ± 3.21 | 32.6 ± 5.75 | 36.2 ± 4.14 | 36.8 ± 4.75 | 35.1 ± 2.86 | 0.385 |
| Hand grip (Kg) | 28.9 ± 7.48 | 33.1 ± 5.9 | 21.5 ± 2.39 | 31.7 ± 7.93 | 35.5 ± 6.5 | 25.5 ± 6.07 | 0.240 |

BMI: body mass index, %FM: percentage of fat mass, FFMI: fat-free mass index, SMI: skeletal muscle mass index, ASMM: appendicular skeletal muscle mass, MUAC: mid-upper arm circumference, MAMC: mid-arm muscle-circumference. P: p-value for the comparison between total HMB vs. HP groups.

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Table S3. Laboratory tests at baseline

| | HMB Group (n=22) | HP Group (n=21) | p |
|----------------------------------|---------------------|---------------------|-------|
| Ferritin (ng/ml) | 156.0 [60.9-523.0] | 97.2 [72.4-662] | 0.662 |
| Transferrin (mg/dl) | 218.0 ± 56.6 | 217.0 ± 74.1 | 0.960 |
| Vitamin B12 (pg/ml) | 488.0 [252-778] | 599.0 [389,0-756.0] | 0.161 |
| CRP (mg/dl) | 0.38 [0.15-0.68] | 0.66 [0.16-1.55] | 0.512 |
| Urea (mg/dl) | 29.0 [24.5-42.5] | 28.0 [25.0-34.0] | 0.670 |
| Creatinine (mg/dl) | 0.73 [0.58-0.91] | 0.69 [0.61-0.81] | 0.874 |
| Triglycerides (mg/dl) | 68.0 [51.2-93.2] | 68.0 [54.0-106.0] | 0.496 |
| Total cholesterol (mg/dl) | 172.0 ± 58.9 | 177.0 ± 50.9 | 0.748 |
| HDL-cholesterol (mg/dl) | 50.9 ± 19.6 | 54.6 ± 16.9 | 0.509 |
| LDL-cholesterol (mg/dl) | 106.0 ± 44.6 | 106.0 ± 41.3 | 0.949 |
| APO A1 (mg/dl) | 138.0 ± 43.5 | 143.0 ± 37.3 | 0.694 |
| APO B (mg/dl) | 72.3 [51.3-112] | 70.3 [63.8-86.1] | 0.961 |
| Lipoprotein (a) (mg/dl) | 9.75 [3.21-19.9] | 3.53 [2.07-9.72] | 0.155 |
| Bilirubin (mg/dl) | 1.69 [1.05-2.46] | 1.75 [1.31-2.57] | 0.662 |
| Plasma proteins (g/dl) | 7.20 [6.82-7.40] | 7.20 [6.60-7.40] | 0.644 |
| Albumin (g/dl) | 3.58 ± 0.57 | 3.56 ± 0.62 | 0.913 |
| Prealbumin (mg/dl) | 11.6 [6.38-15.2] | 9.18 [7.62-12.8] | 0.846 |
| ALP (U/L) | 104.0 [93.8-140.0] | 131.0 [112.0-158.0] | 0.138 |
| GGT (U/L) | 64.5 [40.2-100.0] | 98.0 [61.0-126.0] | 0.194 |
| AST (U/L) | 40.5 [30.8-56.5] | 43.0 [32.0-88.0] | 0.248 |
| ALT (U/L) | 23.0 [15.0-28.5] | 30.0 [21.0-41.0] | 0.018 |
| Ammonia (μM) | 56.0 [40.0-83.0] | 55.0 [40.0-76.0] | 0.923 |
| Vitamin D (nmol/L) | 17.5 [10.8-38.2] | 34.1 [16.3-42.6] | 0.195 |
| BAP (U/L) | 24 [19.5-29.9] | 26.8 [23.6-29.1] | 0.325 |
| Osteocalcin (ng/ml) | 7.3 [6.15-11.9] | 7.0 [5.6-9.5] | 0.415 |
| PICP (μg/l) | 123.0 [97.7-175.0] | 118.0 [88.4-145.0] | 0.529 |
| CTX (pg/ml) | 443.0 [285.0-603.0] | 289.0 [250.0-424.0] | 0.033 |
| HMB (μmol/l) | 3.26 [1.54-4.47] | 1.5 [1.19-3.17] | 0.099 |

CRP: C-Reactive Protein, HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, APO A1: Apolipoprotein A1, APO B: Apolipoprotein B, ALP: Alkaline Phosphatase, GGT: Gamma-GlutamylTransferase, AST: Aspartate Transaminase, ALT: Alanine Transaminase, BAP: Bone Alkaline Phosphatase, PICP: Procollagen type I Carboxy-terminal Propeptide, CTX: C-Terminal telopeptide, HMB: β-Hydroxy-β-MethylButyrate

Table S4. Differences in clinical and body composition characteristics between compliers and dropouts

| | Compliers (n=34) | Dropouts (n=9) | p |
|---------------------------------|------------------|------------------|-------|
| Age (Years) | 61.1 (9.09) | 60.1 (8.31) | 0.756 |
| Men (n%) | 13 (38.2%) | 3 (33.3%) | 1.000 |
| Cirrhosis Etiology n (%) | | | |
| Alcohol | 21 (61.8%) | 7 (77.8%) | 0.624 |
| HCV | 4 (11.8%) | 1 (11.1%) | |
| Autoimmune | 3 (8.82%) | 1 (11.1%) | |
| NAFLD | 3 (8.82%) | 0 (0.00%) | |
| HBV+NAFLD | 1 (2.94%) | 0 (0.00%) | |
| PBC | 1 (2.94%) | 0 (0.00%) | |
| Hemochromatosis | 3 (8.82%) | 1 (11.1%) | |
| Ascites | 18 (52.9%) | 3 (33.3%) | 0.457 |
| Child-Pugh | 7.00 [6.00;8.75] | 6.00 [6.00;8.00] | 0.581 |
| MELD | 11.5 [9.25;15.8] | 15.0 [7.00;18.0] | 0.787 |
| SGA | 9.75 [3.21-19.9] | 3.53 [2.07-9.72] | 0.155 |
| Class B | 1.69 [1.05-2.46] | 1.75 [1.31-2.57] | 0.662 |
| Class C | 7.20 [6.82-7.40] | 7.20 [6.60-7.40] | 0.644 |
| BMI | 25.7 (4.32) | 26.5 (3.24) | 0.557 |
| FMI | 5.20 [1.03;7.27] | 4.60 [3.30;6.40] | 0.846 |
| FFMI | 21.0 (2.51) | 21.5 (2.70) | 0.589 |

Data are number (%), median [IQR], or mean \pm SD. p: p-value for the difference. HCV: Hepatitis C Virus, NAFLD: Non-Alcoholic Fatty Liver Disease, HBV: Hepatitis B Virus, PBC: Primary Biliary Cholangitis, MELD: Model for End Stage Liver Disease, SGA: Subjective Global Assessment, BMI: body mass index, FMI: fat mass index, FFMI: fat-free mass index