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POSTER ABSTRACTS

654.MGUS, AMYLOIDOSIS AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL

A Whole Foods Plant-Based Weight Loss Intervention Improves Quality of Life, Metabolic, Microbiome and Immune Profile in MGUS/SMM As Well As Progression Trajectory in a Subset - the Nutrivention Trial

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Introduction

Obesity, low adiponectin, high leptin, high insulin, and diets lacking plant-based foods are risk factors for plasma cell disorders (PCDs). Patients (pts) with monoclonal gammopathy (MGUS) and smoldering myeloma (SMM) and an elevated body mass index (BMI) are twice as likely to progress to myeloma (MM). There is evidence of microbiome dysbiosis in pts with PCDs and dietary changes can induce large microbial shifts. Therefore, there is a rationale to study a whole food plant-based dietary (WFPBD) intervention to improve modifiable biomarkers and disease trajectory.

Methods

This was a pilot, single-arm trial of WFPBD (self-selected prepared frozen lunch/dinner provided by Plantable with breakfast/snack guidance and no calorie restriction) for 12-weeks (w) and health coaching for 24w (by Plantable coach and a research dietitian) in pts with MGUS/SMM and BMI ≥25 (NCT04920084). The primary endpoint was feasibility (mean BMI reduction ≥5%

and mean dietary adherence [kcal % unprocessed plant food intake] ≥70%) at 12w; secondary endpoints included quality of life (QoL) (EORTC QLQ C30 survey using a linear-mixed effect model), metabolic markers (plasma insulin, adiponectin leptin (AL) ratio via ELISA), gut microbiome (inverse Simpson index α-diversity and relative abundance of butyrate producers (RABP) via stool 16S sequencing), peripheral blood immune profile (leukocyte subsets via 36 color flow cytometry), secreted biomarkers (plasma via Olink inflammation panel) and change in monoclonal (M)-spike concentrations. Rate of change of M-spike/year (y) measured by slope with 95% CI was calculated for up to 20 months (m) pre-intervention and 20m post intervention start (baseline (BL)). A p-value for difference in M-spike rates was calculated.

Results

The study enrolled 23 pts of which 20 completed the 12w intervention and 16 completed 1y. The median age was 62y with 43% male, 43% non-White, 52% MGUS, 74% obese, and 26% prediabetic/diabetic. The study met feasibility endpoints with 90% mean and 92% median adherence during 12w intervention and 77% median at 24w. There was an 8.3% mean and 6.6% median BMI reduction at 12w and 8.6% median at 24w.

There was an improvement in global health status/QoL (median increase 16.7 points, p=0.03), a reduction in dyspnea (median decrease -33.3 points, p=0.001), fatigue (median decrease -11.1 points, p=0.06), and insulin (median decrease 0.791 mU/L; p=0.01), and an increase in AL ratio (median increase 0.09; p=0.0002), α-diversity (median increase 6.18 to 8.42; p= 0.03) and RABP (median increase 0.03 to 0.08; p=0.042) at 12w.

Prelim results at 12w suggest a measurable, albeit not significant change in immune subsets such as an increase in monocytes, regulatory T cells, and a decrease in dendritic cells, trends previously associated with anti-inflammatory diets, as well as increase in butyrate. A decrease in proinflammatory cytokines IL8 (p=0.065), IL12B (p=0.068), and TNFB (p=0.082) and an increase in FGF21 (p=0.043) (promoter of insulin sensitivity) was also observed. Butyrate is known to reduces pro-inflammatory cytokines and increase anti-inflammatory proteins, including FGF21. Further immune and microbiome analysis is ongoing.

Of 16 pts followed for 1y, 2 with significant BMI reduction had significant improvement in M-spike trajectory: Case 1: Mayo Int Risk IgGκ/IgGλ MGUS achieved a 1y BMI reduction of 19%. Pre-intervention M-spike changed +0.28g/dL/y (6 M-spike values), and during intervention M-spike changed +0.03g/dL/y (11 M-spike values); p=0.008. BL M-spike 1.2g/dL and bone marrow plasma cells (BM PC) <5%; 1.5y BM PC 5-9%. Case 2: IMWG Int Risk IgGκ SMM achieved a 1y BMI reduction of 13%. Pre-intervention M-spike changed +0.11g/dL/y (8 M-spike values), and during intervention M-spike changed -0.05g/dL/y (8 M-spike values); p=0.04. BL M-spike 1.2g/dL and BM PC 20-30%; 1y BM PC 10-15%. Two pts without significant BMI reduction (-4% and -1% at 1y) had rising M-spikes. The remaining 12 pts had median 7.5% BMI reduction at 1y with stable M-spike.

Conclusions

This is the first dietary intervention trial in PCDs with insights into the mechanisms by which a WFPBD may delay progression. The intervention improves QoL, metabolic (BMI, insulin resistance), microbiome (α-diversity and butyrate producers) as well as immune (reduced inflammation) profile with potentially slowing progression trajectory in a subset. A larger trial is underway (NCT05640843).

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Figure: Change in gut microbiome A] alpha diversity and B] relative abundance of butyrate producers from baseline to end of 12-week intervention

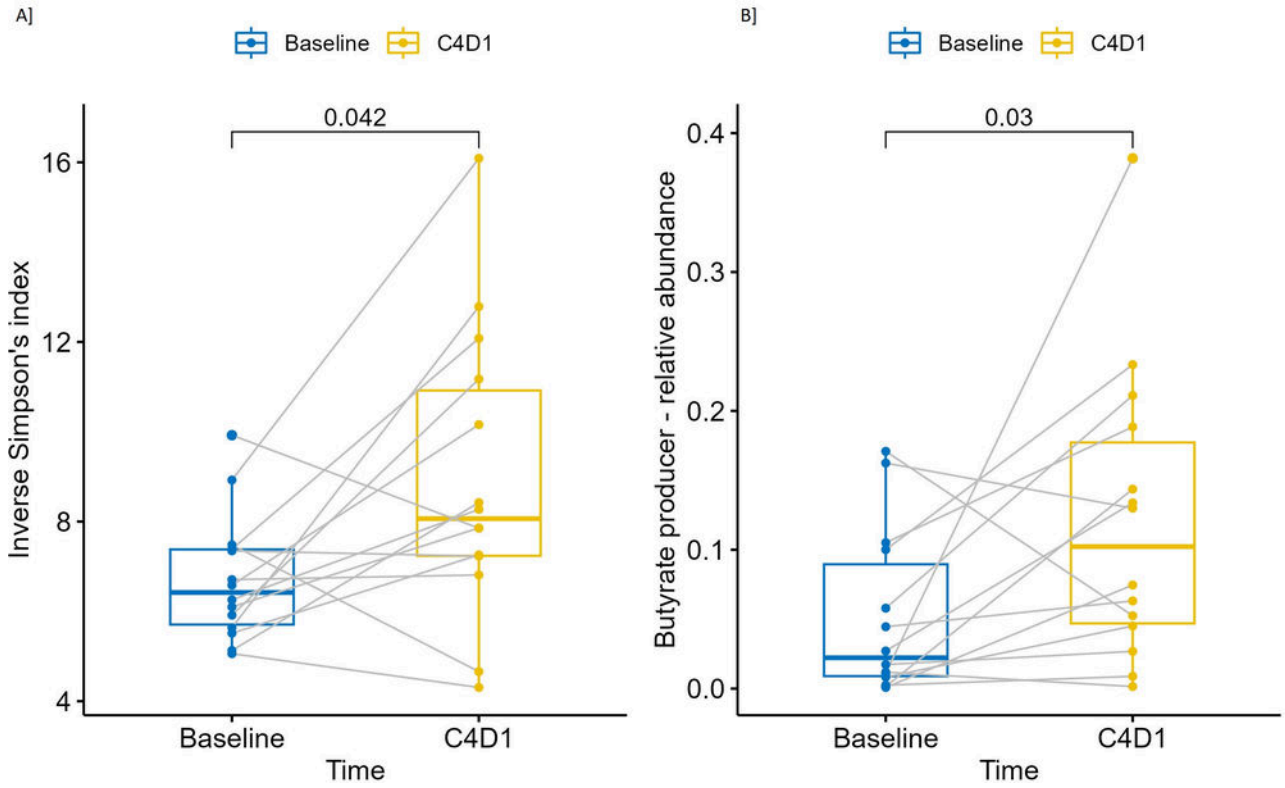

Figure 1

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