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Progenalen™

Human Observational Study

Summary

In collaboration with Living Well Health group under Dr. Sharon Montes in Loveland, CO, Imagine Pharma commissioned a 90-day human study to investigate the safety and efficacy of Progenalen as a wellness and longevity supplement in 20 patients. Quantitative laboratory biomarkers (telomere length, lipid profile, hs CRP, fasting glucose and HbA1c), questionnaire, and clinical assessment were performed on this cohort before and at 90 days after initiation of oral Progenalen (200 µg/day). The study has since expanded to include a broader qualitative assessment of reported symptomatic changes in a cohort of 40 more patients. These 40 patients would be given oral Progenalen and would report monthly their perception of symptomatic changes with Progenalen.

This interim report documents the findings thus far in this study, led by the CO team, but performed in both Loveland, CO and Pittsburgh, PA in the quantitative (N=15) and qualitative (38) cohorts of patients. The completion of this study is projected to be the end of November. The organization of the report serves as the basic framework for a manuscript to be submitted for publication in an academic medical or supplement journal.

Both the quantitative and qualitative cohorts demonstrated that Progenalen is very safe for human consumption. Liver and kidney biomarkers, longstanding standard for examining toxicity, were unchanged from their normal values before and after Progenalen therapy in the quantitative group. As further supporting evidence, there were no reported side-effects in the 38 patients in the qualitative cohort accrued to date.

Moreover, Progenalen appeared to demonstrate beneficial effects as measured by laboratory values listed above. Improvements in total cholesterol, LDL cholesterol, hs CRP and fasting blood glucose were seen in a majority of patients (>50%), notably with lower fasting blood glucose seen in 93% and inflammation reduction (hs CRP) in 73% of the patients. A minority of the 15 quantitative cohorts (<50%) exhibited improvements in triglycerides, HDL, HbA1C. Triglyceride improvement was seen in 33% of the patients.

Telomerase activity and telomere length studies performed on 8 patients showed activated telomerase activity and increased telomere length in peripheral blood of 6 (75%) after 90 days of Progenalen therapy. These findings strongly suggest Progenalen possesses anti-aging and regenerative effects. Interestingly, there was strong correlation between increased telomere length and reduction of the inflammation marker, hs CRP.

These findings confirm the efficacy of Progenalen as a supplement for managing patients with pre-diabetes, the metabolic syndrome and cardiovascular vulnerability because of its improvement in certain lipid profile, glucose utilization and inflammation. Furthermore, this study validates the potential of Progenalen as an anti-aging and longevity remedy.

Introduction

Progenalen is a 293-amino acid polypeptide primarily known as a structural protein in the ribosomes of every cell. However, used exogenously as a oral drug or supplement, Progenalen shows efficacy in treating the metabolic syndrome, regenerating multiple organ cell types and maintaining health, perhaps even slowing aging. These multiple indications and benefits render Progenalen an ideal therapeutic in the growing supplement market for the treatment of pre-diabetes, cardiovascular health and wellness and longevity. The lower FDA regulatory hurdle in the supplement field enables a faster delivery of Progenalen and these benefits to the general patients.

This study was commissioned with the goal of assessing Progenalen as a supplement. The aims were three-fold:

1. To assess the safety of Progenalen in clinical human subjects
2. To assess the efficacy of Progenalen in the treatment of disease-related laboratory biomarkers (cholesterol, hs crp, HbA1c, comprehensive metabolic panel, CBC) in human subjects
3. To assess patients' qualitative perspective of Progenalen through a point-based Multi-System Questionnaire (MSQ), and their perceptions on the efficacy of Progenalen on their health and symptoms

Methods

This clinical observation study aims to examine the safety and efficacy of oral Progenalen in human patients. The study is comprised of two cohorts, quantitative and qualitative, as shown below.

Quantitative:	Progenalen dose 200 µg/day PO Goal N=20 pts, ≥90-day study Labs pre- and at 90 days (CMP, hs crp, HgBA1C) Multiple System Questionnaire and interview pre- and post Blood for telomere length pre- and 90 days
Qualitative:	Progenalen dose 200 µg/day PO Random distribution Feedback monthly by telephone interview Some with voluntary labs before and after Progenalen

Results

1. Progenalen is very safe for human consumption

Markers of liver function (bilirubin, AST, ALT, alkaline phosphatase) remained normal and did not change in value before and at 90-days after Progenalen use. Similarly, renal function (BUN and creatinine) remained normal and unchanged after Progenalen use.

2. Progenalen therapy shows beneficial effects in lipid profiles (total cholesterol, HDL, LDL, Triglycerides)

In this cohort of 15 patients, Progenalen treatments resulted in:

lower total cholesterol in 9/15 (60%) patients
lower LDL in 8/15 (53%)
increase HDL in 6/15 (40%)
lower TG in 5/15 (33%)

When those patients (N=6) with initial elevated cholesterol (>200 mg/dL) were examined, the benefits of Progenalen appears to be greater:

5/6 patients had lower cholesterol
1/6 patients had higher cholesterol

3. Progenalen therapy decreases overall inflammation in 73% of patients

In this 15-patient cohort, after 90-days of Progenalen therapy, 11/15 (73%) patients had a reduction in hs crp suggesting lower body inflammation. Stratified to those with initial abnormal crp (>1), 6/7 (86%) pts showed improvement in crp.

4. Progenalen therapy reduces fasting blood glucose and HgBA1c

13/14 ((93%) patients showed decreased fasting blood glucose
6/15 (40%) had a reduction in HgBA1c

5) Progenalen therapy shows telomerase activity and increased telomere length

Peripheral blood mononuclear cells from 8 patients pre- and post-Progenalen therapy were sent to Pittsburgh for detection of telomerase activity and measurement of telomere length.

6/8 (75%) patients had detectable telomerase enzyme activity
6/8 (75%) patients had increased telomere length

6) Progenalen activates telomerase and increases telomere length in strong negative correlation with hs CRP

Multiple associations were conducted between anti-aging effects (telomere length/ telomerase activity) and the other biomarkers measured: a strong negative correlation was found between telomere interaction and hs CRP.

6 patients with detectable telomerase and increased telomere length had decreased hs CRP
2 patients with undetectable telomerase and no change in telomere length had no improvement or slightly increased hs CRP

7) Patients reported overall benefits as reflected by the Multi-System Questionnaire

MSQ is a points-based questionnaire developed by Dr. Sharon Montes that assesses patient scoring of multiple symptoms in many body systems (eg. Mental status, GI, Energy, Mind, Emotion). Scores for a particular symptom range from 0-4 from better to worse. Total scores were compiled for each system as well as the overall questionnaire. The lower the score, the better overall status of symptomology.

N=15*	Improvement (score ↓)	Worse (score ↑)	Same
Overall	11	0	4
GI	6	2	6
MS	6	0	7
Energy	6	3	6
Emotion	8	2	5

*incomplete data for GI and MS in 1 and 2 patients, respectively

8) Qualitative reports by 38 patients showing various benefits after >30 days of taking Progenalen

38	Total (varying states of health, symptoms)
0	adverse effects
38	increased energy
19	improved joint pain
7	improved BG, lower insulin or HgBA1C
6	enhanced hair, nail growth
5	increased libido
7	resolution of IBS (constipation or diarrhea)
3	improved cholesterol

9) Index patients examples

Middle age gentleman with Type 2 DM, elevated fasting BG=313, HgbA1c=14.0, and elevated cholesterol =263. Patient refused referral to endocrinologist for management of diabetes and metabolic syndrome. Progenalen at 200 µg PO QD was started. 3 month later laboratory values showed HgbA1c=12.0, reduction of 2%. Fasting BG was 145 mg/dL, and total cholesterol reduced by 44 points (263↓219). Hs CRP also reduce by 0.9. Patient also reported feeling great.

Young woman with long-standing Type 1 DM, brittle diabetic on insulin pump and continuous glucose monitor with renal insufficiency, retinopathy and neuropathy secondary to diabetes. After 1 month of Progenalen 200 µg PO QD, patient reported lower insulin requirement as recorded by pump, less variability with glucose swings, greater energy and greater sense of health and well-being: “I feel great. Progenalen realy helps. It has given me more good days than bad”.

Conclusion

This interim report in 53 total patients has already revealed very interesting and compelling results into the benefits of Progenalen for pre-diabetes, metabolic syndrome and longevity and anti-aging. Most important, Progenalen is very safe: it does not have any effects on liver or renal function as measured by liver and renal function studies. There were no reports of side-effects seen in the qualitative cohort.

Progenalen provides improvement in cholesterol, fasting blood glucose, hs crp in a majority of patients with laboratory monitoring, especially in the inflammation marker (hs CRP) where Progenalen reduced C-reactive Protein in 73% of patients. Overall body inflammation, and relationship to oxidative stress, has been associated with cardiovascular diseases, insulin resistance (diabetes), lipd disregulation as well as arthritic pain. The improvement in the metabolic syndrome and glucose utilization and qualitative amelioration of joint pain is consistent with this reduction in inflammation. Progenalen is also a known anti-oxidant.

Furthermore, activation of telomerase and increased telomere length may reflect an anti-aging effect through bodily tissue and organ regeneration by progenitor cells – a known property of Progenalen shown by Imagine's scientific team. These progenitor cells enhance the body's repair and healing mechanism which may also explain the improvement in joint pain, and is particularly highlighted by the accelerated hair and nail growth. Regeneration of enterocytes by progenitor cells by Progenalen may also explain its unexpected benefit for irritable bowel syndrome. Progenalen may perform this function by strengthen the gut mucosa, and enhancing the barrier against food, toxins, and pathogens.

These findings create a compelling argument for Progenalen as a highly effective supplement with a diverse beneficial profile for patients seeking longevity, wellness or normalizing against the metabolic syndrome. The underlying mechanism for Progenalen's normalizing effects may lie in its function as an agent of regeneration.

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Imagine Pharma is a biotechnology company focused on the development of its Progenalen polypeptide. Research and development efforts have led to the development of three distinctive platforms each with first-in-class programs that address multiple disease states in large underserved markets.