AdiStem™

Summary of Type II Diabetes Efficacy

PROTOCOL FOR AUTOLOGOUS ADIPOSE-DERIVED ADULT STEM CELL TRANSPLANT

SUBMISSION BY: **DR. FLORENCIO LUCERO**

FOR: **HUMAN ETHICS APPROVAL**

TO: **HOSPITAL INSTITUTE REVIEW BOARD**

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STATEMENT OF PURPOSE

This submission, the Protocol for Autologous Adipose-derived Adult Stem Cell Transplant, is for medical and surgical ethics approval by the Committee on Research, at Manila Doctors Hospital; and will consist of the following:

(a) Statement of General Principles for Research/Medical and Surgical Procedures using Human Subjects in Autologous Adipose-derived Adult Stem Cell Transplant. This includes the following ***general*** ethical considerations:

1. Moral and religious concerns
2. Respect
3. Beneficence
4. Non-maleficence
5. Justice

(b) Statement of Specific Principles on Research/Medical and Surgical Procedures using Human Subjects in Autologous Adipose-derived Adult Stem Cell Transplant. This includes the following ***specific*** ethical considerations:

1. Biological safety and risks
2. Medical safety and risks
3. Surgical safety and risks
4. Product safety and risks
5. Statistics collected.

This submission, endeavors to comply with the ***International Ethical Guidelines for Biomedical Research involving Human subjects (2002)***,[1] prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO); and the ***International Guidelines for Ethical Review in Epidemiological studies (1991)*** [2]– currently being revised by CIOMS.

APPENDIX 2

Presented at: 6th World Congress on Anti-Aging Medicine, Paris 2008.

Title: Stem cells in cosmetic medicine and surgery.

Authors: Florencio Q. Lucero[1,2], Emerita A. Barrenechea[3], Leticia Lucero-Palma[1], Kribah Krishnan[1], Bill Paspaliaris[1]

1 Adistem Ltd, Hong Kong
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Presenter: Dr. Florencio Q. Lucero

Abstract:
Stem cell therapies hold great promise for anti-aging benefits as they are regenerative in nature. Autologous adipose-derived stem cell transplants hold even more potential as they have no ethical barriers and require no out-of-surgery culture requirements. We have devised a method that entails the isolation of stem cells from fat derived from a mini-liposuction procedure, their activation from a quiescent stage to an active stage, and their reintroduction back into the patient via intravenous mode. This method has now been performed on 167 subjects over a two year period with no adverse effect. The anti-aging benefits that have been observed and reported include increased energy level, vigor, stamina and desire for physical activity, improved short-term memory and powers of attention and concentration, better moods, improvement in sleeping patterns, enhanced sexual function and potency, better appetite and improved digestion, improved hearing and eyesight, improved skin vitality, hair thickness and blackening. Benefits were also observed on a variety of degenerative disease types; however, they were on a small sample number. A clinical trial was then performed to assess the efficacy of the therapy on 37 patients with type II diabetes mellitus. An initial follow up of these patients after three months post-operation has shown a significant and sustained reduction in fasting glucose levels (from 10.36$\pm$4.39 mmol/l to 7.11$\pm$2.07 mmol/l; p=0.005), and glycosylated haemoglobin (from 9.12$\pm$1.90% to 7.55+0.91%; p=0.0003), and triglycerides (from 2.09$\pm$0.87 to 1.43$\pm$0.81; p=0.0003). There was no change in C-peptide levels, total cholesterols and other CBC, LFT and KFT values. The results of the trial to date suggest that the autologous adipose derived stem cell therapy appears to help type II diabetes patients by decreasing their resistance to insulin and decreasing their overall cardiovascular risk factors. We believe that the stem cell transplant is probably acting by positively affecting the autonomic nervous system in these subjects but this is yet to be proven. Most patients noticed the anti-aging benefits reported above and an improvement in their neuropathy.

APPENDIX 3

Safety and efficacy of autologous adipose derived stem cell therapy in Type II diabetes mellitus: preliminary 3 month post-operative results.

Investigators: Florencio Q. Lucero[1,2], Emerita A. Barrenechea[3], Leticia Lucero-Palma[1], Kribah Krishnan[1], Bill Paspaliaris[1]

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DIABETES PARAMETERS

Fasting Blood Sugar (mmol/L)

Baseline	2 weeks po	9 weeks po	p value	n
10.36+4.39	7.29+2.70**	7.11+2.07**	*0.005*	21

Glycosalated Haemoglobin (HbA1c %)

Baseline	9 weeks po	p value	n
9.12+1.90	7.55+0.91***	*0.0003*	19

C-Peptide (ng/ml)

Baseline	9 weeks po	p value	n
2.48+1.29	2.39+1.75	0.79	18

HAEMOTOLOGICAL PARAMETERS

Haemoglobin

Baseline	9 weeks po	p value	n
139+16	137+17	0.21	18

Haematocrit

Baseline	9 weeks po	p value	n
0.41+0.04	0.41+0.04	0.85	18

Red Blood Cell

Baseline	9 weeks po	p value	n
4.77+0.43	4.75+0.50	0.73	18

White Blood Cell

Baseline	9 weeks po	p value	n
7.71+2.63	7.26+1.93	0.41	18

UROLOGICAL PARAMETERS

BUN

Baseline	9 weeks po	p value	n
4.58+1.43	4.73+1.93	0.74	18

Creatinine

Baseline	9 weeks po	p value	n
73+22	71+30	0.40	18

HEPATIC PARAMETERS

Total Cholesterol

Baseline	9 weeks po	p value	n
5.21+1.13	5.03+1.04	0.49	18

Triglycerides

Baseline	9 weeks po	p value	n
2.09+0.87	1.43+0.81***	*0.0003*	18

SGOT

Baseline	9 weeks po	p value	n
23+7	26+10	0.12	18

SGPT

Baseline	9 weeks po	p value	n
49+16	50+27	0.77	18

Analysis of AdiStem's Diabetes Type II Trial

Statistical Results:

There were 35 patients included in the analysis, 3 of whom where Type I and 32 Type II. The mean age of the sample was 52±11.49 with 14 (40%) males and 21 (60%) females. The details of the baseline characteristics of the Type II diabetes patients are shown in Table 1.

Due to the very small number (n=3) of type I diabetes patients, no test of significance was applied to the data (not included). Type II group, Table 2.2, showed significant decrease in FBS all observation periods except on the 6th month wherein there was observable decrease but was not statistically significant.

The Type II group showed statistically significant decrease in all observation periods as shown in Tables 3.2.

Significant decrease was observed on the 3rd and 9th month of the Type II group in C peptide values, while an increase was observed on the 6th and 12th month but not statistically significant, Table 4.2.

In Type II group, significant increase in RBC at 6th and 9th month were observed, Table 5.2A, while significant decrease in Triglyceride on month 3, Table 5.2B.

Statistical Tests:

Paired t-test was used to determine the mean change in from baseline to follow-up months. McNemar test was used to test the change in urine laboratory results. A $p \leq 0.050$ was considered significant.

Table 1. Baseline Characteristics of Patients

Characteristics	mean	sd
Type II (n=32)		
Age (years)	54	9.13
FBS	9.53	3.89
C-peptide	2.78	0.99
HBA1C	9.02	2.03
Gender	No.	%
Male	12	37.5
Female	20	62.5
Both Sexes	32	100

Table 2.2 Assessment of FBS Response from Baseline to Different Observation Periods Type II

Observation Periods	FBS		
	mean	SD	SE
Baseline	9.53	3.89	0.69
3 months	7.67	2.32	0.41
Difference (n=32)	1.87	4.01	0.71
p-value	0.013 *		
Baseline	9.53	3.89	0.69
6 months	8.39	2.82	0.50
Difference (n=32)	1.14	3.51	0.62
p-value	0.075 NS		
Baseline	9.18	3.41	0.61
9 months	7.08	2.18	0.39
Difference (n=31)	2.10	3.65	0.66
p-value	0.003**		
Baseline	9.21	3.50	0.65
12 months	7.00	2.04	0.38
Difference (n=29)	2.21	3.27	0.61
p-value	0.001 ***		

Table 3.2 Assessment of HBA_1C from Baseline to Different Observation Periods Type II

Observation Periods	HBA_1C		
	mean	SD	SE
Baseline	9.02	2.03	0.36
3 months	7.70	1.20	0.21
Difference (n=32)	1.32	1.42	0.25
p-value	0.000 ***		
Baseline	9.02	2.03	0.36
6 months	8.03	1.82	0.32
Difference (n=32)	0.99	1.57	0.28
p-value	0.001 ***		
Baseline	8.89	1.92	0.34
9 months	7.51	1.40	0.25
Difference (n=31)	1.38	1.47	0.26
p-value	0.000 ***		
Baseline	8.78	1.93	0.36
12 months	7.88	1.84	0.34
Difference (n=29)	0.90	1.25	0.23
p-value	0.001 ***		

Table 4.2 Assessment of C-Peptide from Baseline to Different Observation Periods Type II

Observation Periods	C-Peptide		
	mean	SD	SE
Baseline	2.80	1.00	0.18
3 months	2.29	1.38	0.25
Difference (n=31)	0.51	1.26	0.23
p-value	.033 *		
Baseline	2.81	1.00	0.18
6 months	2.84	1.29	0.23
Difference (n=31)	0.03	1.12	0.20
p-value	0.887 NS		
Baseline	2.63	0.91	0.18
9 months	2.31	1.14	0.22
Difference (n=27)	0.32	0.82	0.16
p-value	0.050 *		
Baseline	2.76	1.02	0.19
12 months	2.81	2.93	0.55
Difference (n=30)	0.06	2.86	0.54
p-value	0.783 NS		

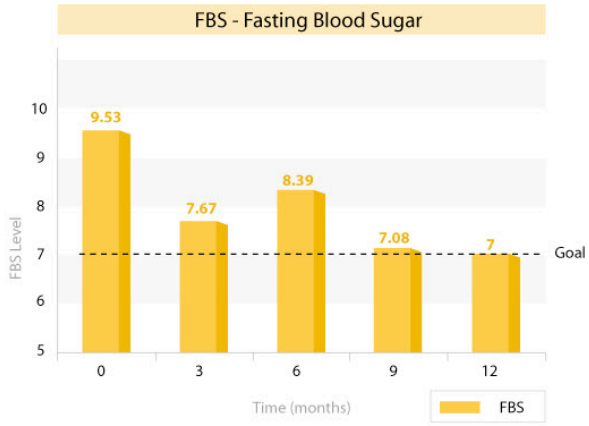
AdiStem®
Technology

Fat Stem Cell Treatment for Diabetes - 1 Year Results

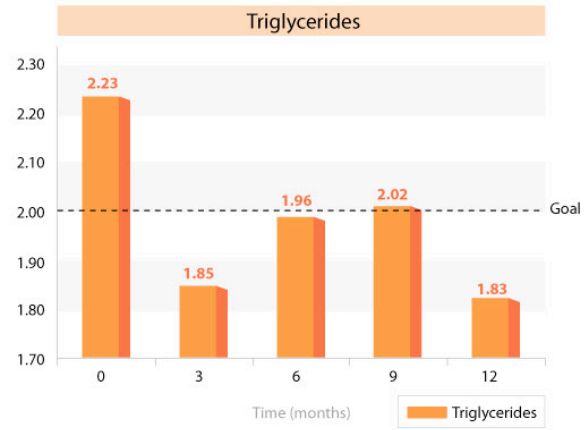
Clinical Trial for Diabetes Summary

Total patients	35	patients
Type I Diabetic	3	patients
Type II Diabetic	32	patients
Males	14	patients (40%)
Females	21	patients (60%)

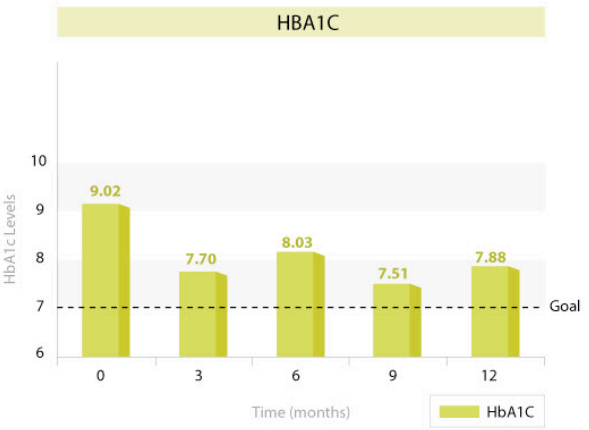
The mean age of the patients was 52±11.49



Fasting blood sugar declined to near diabetic goal of 7.



Trigliceride levels fluctuate, but were reduced over time, indicating improved overall health.



HBA1C levels showed a general decline, indicating improved metabolic function.

Table 5.2A. Assessment of Laboratory Results at Different Observation Periods Type II

Laboratory/Observation Period		Mean	Sd	p-value
Hemoglobin	• Baseline	140.06	14.23	0.626
	3 months(n=32)	139.41	14.87	NS
	• Baseline	140.06	14.23	0.905
	6 months (n=32)	139.88	16.24	NS
	• Baseline	140.03	14.46	0.225
	9 months (n=31)	138.48	16.14	NS
	• Baseline	138.48	13.59	0.236
	12 months (n=29)	136.38	15.03	NS
Hematocrit	• Baseline	0.41	0.04	0.214
	3 months(n=32)	0.42	0.04	NS
	• Baseline	0.41	0.04	0.005
	6 months (n=32)	0.42	0.04	**
	• Baseline	0.41	0.04	0.000
	9 months (n=31)	0.43	0.04	***
	• Baseline	0.41	0.04	0.315
	12 months (n=29)	0.41	0.04	NS
RBC	• Baseline	4.69	0.53	0.274
	3 months(n=32)	4.74	0.60	NS
	• Baseline	4.69	0.53	0.020
	6 months (n=32)	4.81	0.58	*
	• Baseline	4.70	0.53	0.007
	9 months (n=31)	4.83	0.61	**
	• Baseline	4.65	0.51	0.338
	12 months (n=29)	4.71	0.50	NS
WBC	• Baseline	7.70	2.08	0.873
	3 months(n=32)	7.64	1.69	NS
	• Baseline	7.70	2.08	0.539
	6 months (n=32)	7.51	1.61	NS
	• Baseline	7.72	2.11	0.938
	9 months (n=31)	7.69	2.20	NS
	• Baseline	7.59	2.11	0.940
	12 months (n=29)	7.62	1.57	NS
BUN	• Baseline	4.96	1.49	0.418
	3 months(n=32)	5.19	1.58	NS
	• Baseline	4.96	1.49	0.559
	6 months (n=32)	5.09	1.74	NS
	• Baseline	4.89	1.45	0.642
	9 months (n=31)	5.02	2.03	NS
	• Baseline	4.93	1.49	0.089
	12 months (n=29)	5.32	1.75	NS

Table 5.2B. Assessment of Laboratory Results at Different Observation Periods Type II (continued)

Laboratory/Observation Period	Mean	sd	p-value
Creatinine ● Baseline	75.16	20.75	0.052
3 months(n=32)	71.31	25.88	NS
● Baseline	75.16	20.75	0.531
6 months (n=32)	73.72	23.82	NS
● Baseline	73.90	19.82	0.695
9 months (n=31)	74.64	24.26	NS
● Baseline	72.55	19.29	0.221
12 months (n=29)	75.00	22.86	NS
Cholesterol ● Baseline	5.27	1.26	0.85
3 months(n=32)	5.11	1.19	NS
● Baseline	5.27	1.26	0.090
6 months (n=32)	4.94	1.24	NS
● Baseline	5.23	1.25	0.919
9 months (n=31)	5.20	1.30	NS
● Baseline	5.21	1.29	0.913
12 months (n=29)	5.25	1.72	NS
Triglyceride ● Baseline	2.23	1.51	0.032
3 months(n=32)	1.85	1.59	*
● Baseline	2.23	1.51	0.359
6 months (n=32)	1.96	1.30	NS
● Baseline	2.26	1.53	0.128
9 months (n=31)	2.02	1.22	NS
● Baseline	2.29	1.56	0.088
12 months (n=29)	1.83	1.04	NS
SGPT ● Baseline	48.81	17.64	0.350
3 months(n=32)	52.31	27.44	NS
● Baseline	48.81	17.64	0.351
6 months (n=32)	52.28	28.56	NS
● Baseline	49.29	17.72	0.337
9 months (n=31)	53.03	27.28	NS
● Baseline	49.86	18.19	0.747
12 months (n=29)	50.93	22.29	NS
SGOT ● Baseline	23.34	8.43	0.106
3 months(n=32)	25.84	10.91	NS
● Baseline	23.34	8.43	0.068
6 months (n=32)	26.34	12.46	NS
● Baseline	23.61	8.43	0.759
9 months (n=31)	24.39	15.72	NS
● Baseline	23.59	8.69	0.837
12 months (n=29)	23.21	10.03	NS

Safety and Efficacy of Autologous Adipose-Derived Stem Cell Transplantation in Type 2 Diabetics

The recruitment status of this study is unknown because the information has not been verified recently.

Verified June 2008 by Adistem Ltd.
Recruitment status was Active, not recruiting

Sponsor:
Adistem Ltd

Information provided by:
Adistem Ltd

ClinicalTrials.gov identifier:
NCT00703612

First received: June 19, 2008
Last updated: June 28, 2008
Last verified: June 2008
History of Changes

Purpose

The purpose of this study is to determine whether intravenous administration of autologous adipose-derived stem cells is of benefit in the management of types 2 diabetics.

Condition	Intervention	Phase
Type 2 Diabetes Mellitus	Procedure: Autologous Adipose-derived Stem cells	Phase 1 Phase 2

Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Phase I/II Study of Intravenous Administration of Activated Autologous Adipose-Derived Stromal Vascular Fraction in Patients With Type 2 Diabetes

Resource links provided by NLM:

MedlinePlus related topics: Diabetes Diabetes Type 2

U.S. FDA Resources

Further study details as provided by Adistem Ltd:

Primary Outcome Measures:

- Lowering of blood glucose be it fasting, random or post prandial [Time Frame: At 2, 4, 12, 24, 36, and 48 weeks] [Designated as safety issue: Yes]

Secondary Outcome Measures:

- Decrease in anti-hyperglycemic medication dosages. [Time Frame: At 2, 4, 12, 24, 36, and 48 weeks.] [Designated as safety issue: Yes]
- Improvement in the general well-being of patients. [Time Frame: At 2, 4, 12, 24, 36, and 48 weeks.] [Designated as safety issue: Yes]
- Lowering of glycosylated hemoglobin (HbA1C). [Time Frame: At 4, 12, 24, 36, and 48 weeks] [Designated as safety issue: Yes]

Enrollment:	34
Study Start Date:	November 2007
Estimated Study Completion Date:	January 2009
Estimated Primary Completion Date:	December 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Treatment Group This is the only arm and that is the treatment group.	Procedure: Autologous Adipose-derived Stem cells Intravenous administration of autologous activated stromal vascular fraction derived from 100-120 ml lipoaspirate following mini-liposuction of abdominal adipose tissue.

Detailed Description:

Diabetes Mellitus is of large epidemic proportions worldwide. It is proliferating at such a fast rate that new novel drugs and other therapeutic approaches are required. The purpose of this Phase 1/Phase 2 study is to determine whether the intavenous administration of activated adipose-derived stromal vascular fraction as a single procedure is safe to and can benefit the disease pathology of patients with Type 2 Diabetes Mellitus (insulin resistance). Patients will be observed over 12 months following the procedure, with a 2 week, 1 month and then tri monthly diagnostics and life style questionaires.

Eligibility

Ages Eligible for Study:	40 Years to 70 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Confirmed diagnosis of Type II diabetes for at least 2 years
- Type 2 diabetics on oral hypoglycemic agents and/or insulin
- Fasting blood sugar of >200mg% on at least two occasions
- Willing to keep a weekly diary and undergo observation for 12 months

Exclusion Criteria:

- Presence of of previous and/or acute diabetic complications such as myocardial infarction, CVA or nephropathy

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00703612

Locations

Philippines

Beverly Hills Medical Group
Makati City, Manila, Philippines, 1223

Veterens Memorial Medical Centre
Quezon City, Manila, Philippines, 1229

Sponsors and Collaborators

Adistem Ltd

Investigators

Principal Investigator:	Emeritta A Barrenechea, MD	Veterens Memorial Medical Centre, Philippines
Principal Investigator:	Florencio Q Lucero, MD	University of Philippines, College of Medicine.
Study Director:	Letitia Lucero-Palma, MD	Far Eastern University-NRMF Hospital, Quezon City, Philippines
Study Chair:	Bill Paspaliaris, PhD	**Adistem** Ltd

More Information

Additional Information:

NIH website describing basic facts on adult stem cells

Publications:

Gimble JM, Katz AJ, Bunnell BA. Adipose-derived stem cells for regenerative medicine. Circ Res. 2007 May 11;100(9):1249-60. Review.

Responsible Party:	Bill Paspaliaris / Director, Adistem Ltd
ClinicalTrials.gov Identifier:	NCT00703612 History of Changes
Other Study ID Numbers:	Adis-002
Study First Received:	June 19, 2008
Last Updated:	June 28, 2008
Health Authority:	Philippines: Department of Health

Keywords provided by Adistem Ltd:
Diabetes Mellitus
Adipose-derived stem cells
Adipose stromal vascular fraction
Autologous
Hyperglycemia

Additional relevant MeSH terms:
Diabetes Mellitus
Diabetes Mellitus, Type 2
Glucose Metabolism Disorders
Metabolic Diseases
Endocrine System Diseases

ClinicalTrials.gov processed this record on November 06, 2012