Longitudinal Study of Dental Implant Therapy in HIV Positive Patients

Study Protocol & Statistical Analysis Plan

NCT01211288

August 30, 2019

Toni Tien Neumeier, DMD, Principal Investigator
University of Alabama at Birmingham
Birmingham, AL 35294

APPENDIX 1

Protocol

D-2007-51

PROTOCOL SYNOPSIS

Title

Longitudinal Study of Dental Implant Therapy in HIV Positive Patients

Investigator *(Insert here the name, mailing address, email address, and phone number of the Co-ordinating Investigator (for multi-centre studies) or the Principal Investigator (for single-centre studies))*

A. Principle Investigator:
Toni Tien Neumeier, MS, DMD, FAGD, FACD
Prosthodontist, Associate Professor, UAB Comprehensive Dentistry Department
1919 7th Ave South, SDB 530
Birmingham, AL 35294
Neumeier@uab.edu
205-934-5459

B. Co- Investigators:
1. Jeff Hill, DMD
General Dentist, Assistant professor, Director 1917 HIV/AIDS Dental Clinic, UAB Comprehensive Dentistry Department
2. Mike Edwards, DMD, FAGD, MAGD
Assistant clinic professor, UAB Comprehensive Dentistry Department
Private Practice General Dentistry, Wedowee AL.
3. Perng - Ru Liu, DDS, MS, DMD
Prosthodontist, Professor and Chair, UAB Comprehensive Dentistry Department
4. Lance Ramp, DMD, PHD
Prosthodontist, Associate Professor, UAB Comprehensive Dentistry Department
5. Richard Weems, DMD
Radiologist, Associate Professor, Director of Clinical Operations and Dental Radiology, UAB Diagnostic Science Department
6. Patricia Devilliers, DDS, MS
Oral and Maxillofacial Pathologist, Assistant Professor, UAB Anatomic Pathology Department

<>

Study centre(s) and number of subjects planned *(Insert here the address where the study will be conducted, number of patients planned and if applicable distribution of patients per site)*

1. UAB School of Dentistry
Department of Comprehensive Dentistry
1919 7th Ave South
Birmingham, AL 35294

Total 40 patients will be treated in the 2nd floor main clinic
20 HIV (+) patients will be selected from the 1917 Dental Clinic and 20 patients will be selected from UAB School of Dentistry patients.
2. Cone Beam CT scanned at UAB School of Dentistry Periodontal research clinic

<<>>

Study period	*<<Month and year>>*	*<<Month and year>>*
Estimated Start date and End date	January 2010	December 2014
Date of first data available for presentation		December 2011

Objectives *(Insert objectives)*

1. To study the short term and long term osseous integration of implant supported restorations on immunocompromised (HIV positive) patients.
2. Radiographic examination of implant osseous integration using Cone Beam CT and traditional vertical bitewing radiographs.
3. Histologic examination of bone biopsies from each implant surgical site, at the time of initial placement, and from failing implant sites, including histologic examination of the implant-bone interface.

Study design (*Insert a one-sentence summary of study design features*

Provide HIV (+) patients with implant supported restorations, using HIV (-) patients as controls.

<<>>

Target patient population *(Insert a description of target population and indication studied)*

20 HIV (+) patients with the following requirements:
Age 19 and older,
Hemoglobin >8g/dl , Absolute neutrophil count >750/mm3, Platelet count>75,000cells/mm3,
AST< 5 times the upper limit of normal (ULN),
Bilirubin< 2.5 times ULN, Alkaline phosphate < 5 times ULN, Creatinine< 2.5 mg/ml
Non- smoker (quite smoking at least 6 months)
Controlled Type II diabetes
Controlled hypertension
Non bisphosphate user
Non- bruxer
Misch Available Bone classification divisions A, B, C
Misch Bone Density classification D1, D2, D3
Minimal available bone width 5mm
Minimal available bone height 10mm
Minimum bone graft with freeze dried demineralised bone upon implant placement
Extraction site has to be healed up for minimum 3 months for mandibular and 6 months for maxillary before implant placement
Flap or flapless implant placement with surgical stent as guidance
Implant supported restorations are limited to the following edentulous areas:

- Mandibular arches, excluding 3rd molar areas
- Maxillary anterior and premolar areas
- Exclude extensive bone graft involvement and sinus lift
- No immediate implant loading

Total numbers of implant restorations are limited to;

Maximum of 4 units of fixed prosthesis with minimum 2 implants support for maxillary and mandibular anterior region,
3 units bridge with 2 implant supports,
2 units bridge with 2 implant supports,
Single implant support crown

Permanent implant restoration 3 months after implant placement for mandibular and 6 months for maxillary.

All implant supported restorations will be cement-retained restorations.

Dental material: either full metal restoration or porcelain fused with metal restoration.

20 HIV-negative patients following the same requirements as above.

Investigational product/comparator *(State the devices / products that will be investigated / / used and for comparative studies also the comparator/s)*

1. Cone beam CT full facial scan on every patient before and after implant placement on surgical site single arch at 1 year, 2 year, 3 year follow up (i-CAT $600 per patient x40 =$ 24,000)
2. Facilitate Pro software convert Dicom images for implant placement design and surgical stent fabrication ($12,000)
3. Surgical tools for implant placement:
(syringe, needles , elevators, periotomes, extraction forceps #150 & #151, bone spreading chisels, bone grinder, bone trap, bone compactor, bone curette, osteotomes, resorbable and non-resorbable sutures, needle holders, scissors
Surgical stent, two surgical bundles, two surgical trays, one surgical motor, two surgical handpiece heads, two full restorative trays and bundles, surgical saline bags for surgical irrigation, disposable irrigation kits for drill unit, disposable drills. Pulse oximetry) ($ 30,000)
4. Root form implants of various sizes, cover screws ($250 per implant x est. 80=$ 20,000)
5. Freeze dried demineralised bone as bone graft material ($ 100/ 0.5cc vial x est.20 = $ 2,000)
6. Resorbable membrane ($ 100/ membrane x est. 20= $ 2,000)
7. Poly vinyl siloxane impression materials ($ 4,000)
8. Prosthodontic instrument kits plus laboratory fee (impression transfer material, implant abutments, implant analogues, Cresco Precision system)
($ 400 per implant restoration x est. 80 = $32,000)
9. Two WhipMix Semi- adjustable articulators ($ 800 x 2 =$1,600)
10. Half-time patient coordinator ($ 18,000 or neg.)
11. Computer for information storage and portable printer ($ 3,000)
12. SLR camera with Macro-lens and flash ($ 2,500)
13. Histological examination of 40 bone biopsies processed at UAB Anatomic Pathology Lab, including special stains and decalcification ($ 8,000)
14. Processing of failed implants at the UAB Bone Core facility with subsequent histologic examination of implant-bone interface ($200.00 per failed implant x est. 5 =$1,000)
15. Journal publication expenses ($2000.00)
16. Travel expenses to national and/or international meetings by the PI investigator and one co-investigator ($ 4000.00)

Total budget: $166,000

Outcome variables (Indicate which variable is the primary variable for the study)

Efficacy *(List all efficacy variables and indicate clearly your primary outcome variable*

The primary variable examined will be the treatment outcome as measured according to the Albrektsson and Zarb criteria for implant success. Patients will be examined at each interval for the presence of pain, infection, mobility, and radiographic bone height of each implant

Additional clinical assessments *(Describe use of any additional clinical assessments e.g. clinical photographs etc.*

1. All selected patients will have prior medical authorization to have surgical procedure performed. Patients with undergo complete oral clinical examination as well as cone beam CT scan, selected periapical and vertical bitewing radiographs on planning implant placement site, full mouth photography, diagnostic casts, and surgical stint before implant placement.
2. Cone Beam CT on the implant sites of arches at 1 year, 2 years and 3 years post placement follow-up (Cone Beam CT provides 1:1 ratio image, view in 3- dimensions, limited radiation exposure). The images will be evaluated by the dental radiologist.
Compare accuracy and efficiency of Cone Beam CT image of alveolar bone around implant in 3-dimensions vs. of conventional standard X-ray examination of bone lost around implant in 2-dimensions.
3. Histologic examination of the bone biopsy from the implant sites will provide scientific evidence of the bone changes that may occur in the process of implant osteointegration under immunocompromised conditions.
4. Photograph during implant restoration procedure and after complete restoration.
5. Patient post-implant restoration survey (such as: general satisfaction, social life, mastication on hard food, comfort).

Statistical methods *(Describe as relevant the statistical methods to be used, the populations to be analysed (e.g. intention to treat, per-protocol), and any interim analyses)*

Descriptive statistics will be applied to acquire the mean parameter values, range, and implant success rate as determined by the Albrektsson and Zarb criteria.

With rigorous inclusion/exclusion criteria proposed, parametric data will be analysed using ANOVA methods. Nonparametric (yes/no) criteria will be analyzed with the Chi-Square method.

Publications / Presentations *(Describe your plans with regard to publications or public presentations i.e. what journals or conferences/meetings)*

Peer reviewed journals such as: Journal of American Dental Association, Journal of Prosthodontics, Journal of General Dentistry.

Oral platform presentations at various national and international dental meetings at Astra's discretion

APPENDIX 2 - **Details of products to be provided:**

Investigator name: Toni Neumeier, UAB
Study Title: Longitudinal Study of Dental Implant Therapy in HIV Positive Patients

Astra Tech reference no.: D-2007-51

Product	Ref. no.	Quantity
Restorative Instrument Kit	24879	2
Restorative Tray	22495	2
Torque Wrench Kit	24100	2
Torque Wrench Bit,Locator-15mm	24490	2
Wrench Adapter	24572	2
Implant Unit SI-915, 115 V	24360	2
Cont Ang.W&H WS-75 E/KM AE	22903	2
Surgical Instrument Kit	24878	2
Driver Handle	24358	2
Surgical Tray	24349	2
Ratchet Wrench	24357	2
Hex Screwdriver, Short	22514	4
Hex Screwdriver, Intermediate	22515	4
Osteotome Kit	22956	2
SP Drill Kit, Short	22898	24
SP Drill Kit, Long	22899	24
SP Twist Drill, 3.35 mm, Short	22908	12
SP Twist Drill, 3.35 mm, Long	22909	12
SP Twist Drill, 3.7 mm, Short	22910	24
SP Twist Drill, 3.7 mm, Long	22911	24
SP Conical Drill, 4.5mm, Short	22921	24
SP Conical Drill, 4.5mm, Long	22922	24
SP Conical Drill, 5.0mm, Short	22923	24
SP Conical Drill, 5.0mm, Long	22924	24
OsseoSpeed 3.5 S - 9 mm	24611	8
OsseoSpeed 3.5 S - 11 mm	24612	8
OsseoSpeed 3.5 S - 13 mm	24613	8
OsseoSpeed 4.0 S - 9 mm	24621	8
OsseoSpeed 4.0 S - 11 mm	24622	10
OsseoSpeed 4.0 S - 13 mm	24623	8
OsseoSpeed 4.5 - 9 mm	24631	8
OsseoSpeed 4.5 - 11 mm	24632	10
OsseoSpeed 4.5 - 13 mm	24633	8
OsseoSpeed 5.0 - 9 mm	24641	8

OsseoSpeed 5.0 - 11 mm	24642	8
OsseoSpeed 5.0 - 13 mm	24643	8
Implant Transfer 3.5/4.0 Short	24547	30
Implant Transfer 3.5/4.0 Long	24548	20
Fixt. Transfer 4.5/5.0,Short	22433	30
Fixt. Transfer 4.5/5.0, Long	22485	20
Implant Replica 3.5/4.0	24276	50
Implant Replica 4.5/5.0	22509	50
Ti-Zir Design 3.5/4.0 Try-in	24847	4
Ti-Zir Design 4.5/5.0 Try-in	24849	4
TiDesign 3.5/4.0 - Ø 5.5,1.5mm	24287	12
TiDesign 3.5/4.0 - Ø 5.5, 3mm	24288	12
TiDesign 4.5/5.0 -Ø5.5,1.5 mm	24235	12
TiDesign 4.5/5.0 -Ø5.5, 3mm	24236	12
ZirDesign 3.5/4.0 Ø 4.5 1.5 mm	24702	8
ZirDesign 3.5/4.0 Ø 5.5 1.5 mm	24704	8
ZirDesign 4.5/5.0 Ø 5.5 1.5 mm	24707	8
ZirDesign 4.5/5.0 Ø 5.5 3 mm	24708	8
Dir.Abutm.API 3.5/4.0-Ø5, 1mm	24555	4
Dir.Abutm.API 3.5/4.0-Ø5,2.5mm	24556	4
Dir.Abutm.API 4.5/5.0-Ø5, 1mm	24559	4
Dir.Abutm.API 4.5/5.0-Ø5,2.5mm	24560	4
Dir.Abutm.API 4.5/5.0-Ø6, 1mm	24562	4
Dir.Abutm.API 4.5/5.0-Ø6,2.5mm	24563	4
Cover Screw 3.5/4.0 - 0 mm	24328	40
Cover Screw 4.5/5.0 - 0mm	24447	40
Healing Abutm.3.5/4.0-Ø4,2mm	24574	12
Healing Abutm.3.5/4.0-Ø4.5,4mm	24575	12
Healing Abutm.3.5/4.0-Ø5.5,2mm	24577	12
Healing Abutm.3.5/4.0-Ø5.5,4mm	24578	12
Healing Abutm.4.5/5.0-Ø5.5,2mm	24582	12
Healing Abutm.4.5/5.0-Ø5.5,4mm	24583	12
Healing Abutm.4.5/5.0-Ø6.5,2mm	24585	12
Healing Abutm.4.5/5.0-Ø6.5,4mm	24586	12
Bone Trap	22179	8
Disposable Irrigation Set	22176	8
Periotome,straight/curved edge	24274	2
Periotome, curved/straight	24275	2
Grinding Handle	22740	2
Bowl, Titanium	22137	4
Forceps 94	22437	4

Facilitate Instrument Kit	24819	2
Direct Abutment 3.5/4.0 Try-in	24848	4
Direct Abutment 4.5/5.0 Try-in	24850	4

Products will be distributed to the below contact person and address:
Dr. Toni Tien Neumeier
Comprehensive Dentistry Department
1919 7th Ave South SDB 530
Birmingham, Al 35294