The ARMOR Trial
Commensal Oral Microbiota as a Trigger of Oral Mucositis Severity

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NIDCR Medical Monitor: Kevin McBryde, MD

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Version 11

STATEMENT OF COMPLIANCE

The study will be conducted in accordance with the International Council for Harmonisation guidelines for Good Clinical Practice (ICH E6), the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), and the NIDCR Clinical Terms of Award. All personnel involved in the conduct of this study have completed human subjects protection training.

SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

Principal Investigator or Clinical Site Investigator:

Signed:  Date: January 19, 2022

Name: Dr. Patricia Corby

Title: Principal Investigator

Signed: 

Date: January 19, 2022

Name: Dr. Alexander Lin

Title: Co-Principal Investigator

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LIST OF ABBREVIATIONS

ADL	Activities of Daily Living
AE	Adverse Event/Adverse Experience
AJCC - TNM	American Joint Committee on Cancer - TNM Classification of Malignant Tumors
ANC	Absolute Neutrophil Count
ARMOR	Commensal Oral Microbiota as a Trigger of Oral Mucositis Severity
CBC	Complete Blood Count testing
CFR	Code of Federal Regulations
chemoRT	Chemoradiation therapy
CMP	Clinical Monitoring Plan
CROMS	Clinical Research Operations and Management Support
CTCAE	Common Terminology Criteria for Adverse Events
CQMP	Clinical Quality Management Plan
DHHS	Department of Health and Human Services
DSMB	Data and Safety Monitoring Board
EORTC QLQ-C-30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
EORTC QLQ-H&N35	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire with the additional Head & Neck specific module
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GEE	General Estimating Equation
H&N	Head and Neck
HIV	Human Immunodeficiency Virus
HNSCCs	Head and Neck Squamous Cell Carcinomas
ICH	International Council for Harmonisation
IMRT	Intensity-modulated radiation therapy
IRB	Institutional Review Board
MASCC/ISOO	Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology
MOP	Manual of Procedures
MSD	MesoScale Discovery

NIDCR	National Institute of Dental and Craniofacial Research, NIH, DHHS
NIH	National Institutes of Health
NYU	New York University
UPenn	University of Pennsylvania, School of Dental Medicine
OCTOM	Office of Clinical Trials Operations and Management
OHRP	Office for Human Research Protections
OM	Oral Mucositis
OMDP-IG	Oral Mucosal Deterging and Dental Prophylaxis (Intervention Group)
PHI	Protected Health Information
PI	Principal Investigator
QM	Quality Management
QOL	Quality of life
RT	Radiation Therapy
SAE	Serious Adverse Event/Serious Adverse Experience
SOC-OH	Standard of Care Oral Hygiene (Control Group)
SOC	Standard of Care
US	United States
WHO	World Health Organization

PROTOCOL SUMMARY

Title: The ARMOR Trial: Commensal Oral Microbiota as a Trigger of Oral Mucositis Severity

Précis: This is a prospective, single blind, two arm, randomized, controlled trial to test the efficacy of an oral care protocol to treat oral mucositis (OM) in patients receiving radiation (RT) or chemoradiation (chemoRT) for head and neck cancer. This trial will also measure salivary proinflammatory cytokines, and evaluate other clinical effects of the intervention during cancer therapy. In addition, oral mucosal swabs will be collected for the future characterization of changes in the microbiome associated with OM severity.

Patients will be randomized in a 1:1 ratio to two different oral care protocols within 4 strata defined by type of RT (Proton beam therapy (Protons)) vs intensity-modulated radiation therapy (IMRT) and cancer treatment (RT versus chemoRT). Eligible subjects will be assigned to receive either the **Oral Mucosal Deterging and Dental Prophylaxis** protocol (OMDP) or a **Standard of Care Oral Hygiene** protocol (SOC-OH). Prior to randomization, all enrolled subjects will receive a baseline dental prophylaxis and fluoride varnish application prior to start of RT or chemoRT to ensure that all subjects enter the study with comparable oral health. **Subjects assigned to OMDP** will receive the OMDP Protocol (*Oral Mucosal Deterging and Dental Prophylaxis*) at weekly intervention visits. **Subjects randomized to the SOC-OH** will receive oral health instructions following the *American Dental Association Guidelines*[1] and will have their teeth cleaned (brushed) during weekly intervention visits; no treatment to the oral mucosa will be provided to this group.

At each bi-weekly study visit, study assessments will include the collection of saliva and oral mucosal swabs, an oral exam and OM assessment, and the completion of questionnaires. During the course of the study, subjects will attend one baseline visit, up to 9 intervention visits, and follow-up visits approximately 1 month and 3 months after completion of RT. Local supportive care, including normal saline rinses, topical anesthetics, mixed medication mouthwashes (e.g. Magic Mouthwash), feeding tubes, and pain management will be allowed according to each recruitment site's standard of care procedures.

Objectives:

Primary Objective: To test the efficacy of the OMDP protocol compared to SOC-OH on OM severity in head and neck cancer patients undergoing RT or chemoRT.

The primary outcome measure is OM severity as measured by the World Health Organization's Oral Toxicity Scale (WHO OTS).

Secondary Objectives:

1) To compare changes in salivary **proinflammatory cytokines** between the OMDP and SOC-OH groups.
2) To evaluate differences between the OMDP and SOC-OH groups in the following clinical indicators: a) duration of and time to onset of severe OM, b) salivary hypofunction, c) average mouth and throat soreness [MTS], and d) quality of life and function [EORTC QLQ 30 and EORTC QLQ HN35].

The secondary outcome measures are changes in: salivary proinflammatory cytokines, duration and time to onset of severe OM, OM severity as measured by the Common Terminology Criteria for Adverse Events (CTCAE), salivary hypofunction, symptoms, quality of life, and function.

Exploratory Objective. To estimate progression-free survival and overall survival by intervention group.

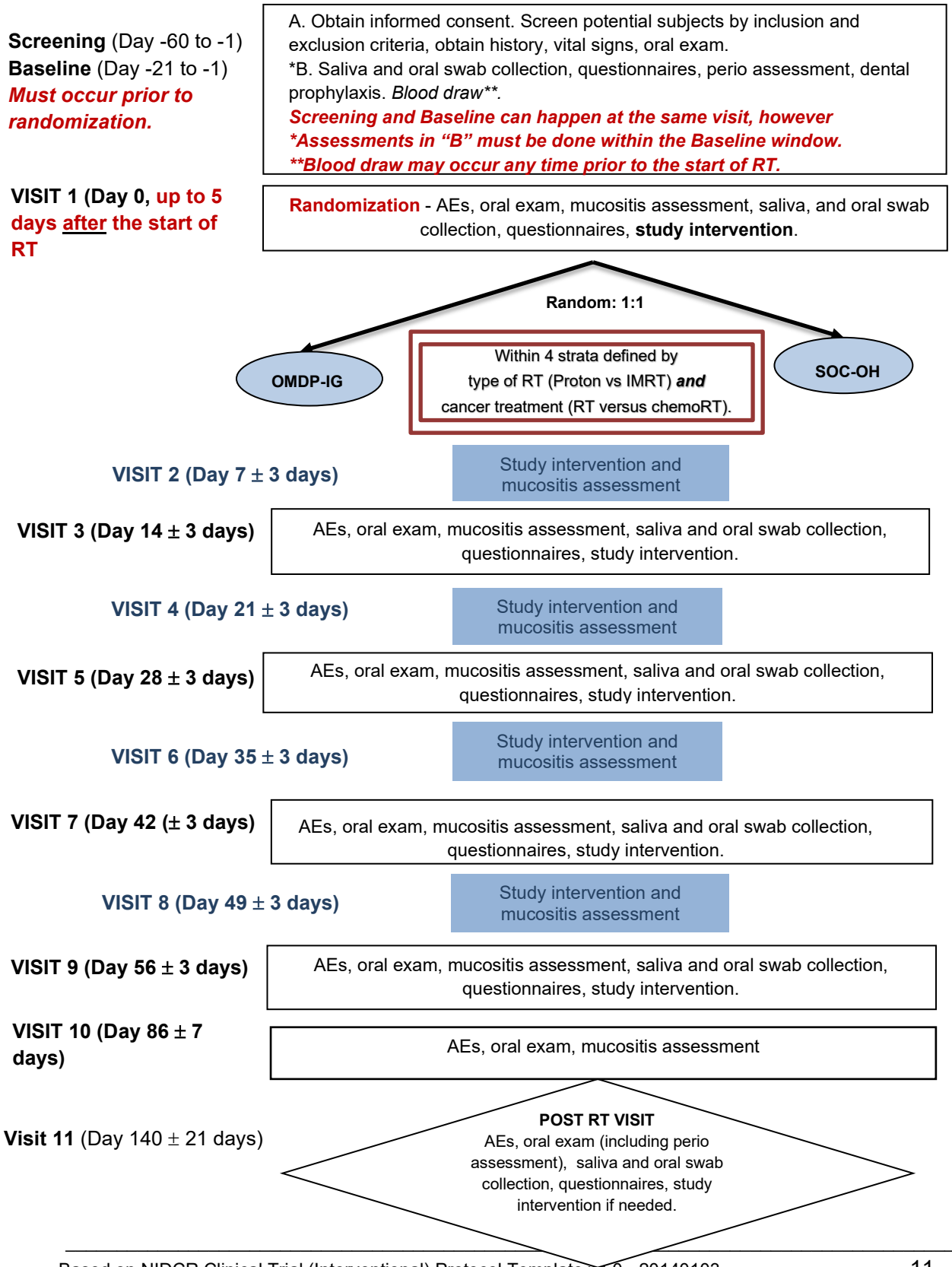
The central hypothesis is that a weekly regimen of targeted professional oral care during anti-cancer treatment prevents harmful ecological shifts in the oral cavity and consequently reduces the duration and severity of OM, reduces OM local inflammation, and improves oral health, thereby improving overall quality of life during cancer treatment. The rationale is that the cleansing of dead, damaged, or infected oral mucosa tissues in combination with mechanical removal of dental plaque and calculus in the oral cavity to facilitate biofilm disruption and endotoxin flushing during RT/chemoRT treatment, improves the healing potential of the oral tissues and suppresses OM severity.

Population: A total of 120 male and female subjects (N=120) aged 18 years and older who will undergo different modalities of RT [IMRT or Protons] with or without combined chemotherapy for head and neck cancer will be enrolled.

Phase: II

Clinical Center (s):	Hospital of the University of Pennsylvania Perelman Center for Advanced Medicine 3400 Civic Center Blvd Philadelphia, PA 19104 Perelman School of Medicine, University of Pennsylvania Department of Oral & Maxillofacial Surgery Perelman Center for Advanced Medicine 3400 Civic Center Blvd., 4th Floor South Pavilion Philadelphia, PA 19104 School of Dental Medicine, University of Pennsylvania
Number of Core Laboratories:	Two core laboratories: The Forsyth Institute National Institute of Nursing Research (NINR)
Statistical Center:	NYU Langone Health, School of Medicine
Description of Intervention:	The study intervention will consist of weekly visits during which a dental professional will administer the OMDP intervention protocol. The OMDP comprises a professional dental prophylaxis including periodontal surface debridement (*a light-touch, gentle form of instrumentation performed with an ultrasonic instrument to promote plaque removal, to facilitate biofilm disruption and endotoxin flushing, but yet with the preservation of the periodontal cementum*) followed by *cleansing and deterging* of the oral mucosal surfaces using a soft bristled manual toothbrush and a deterging agent. The standard of care intervention for the control group will consist of weekly visits at which subjects will receive oral health instructions and have their teeth brushed.
Study Duration:	Approximately 5 years
Subject Participation Duration:	Approximately 5 months
Estimated Time to Complete Enrollment:	Approximately 3.5 years

SCHEMATIC OF STUDY DESIGN:



1. KEY ROLES AND CONTACT INFORMATION

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