Study for Dexamethasone Mouthwash in Lowering Episodes of Oral Mucositis among Patients with Cancer: The SMILE Study

Sponsor: Foundation for Woman's

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I. Table of Contents

I. Background *3*

II. Study Objectives *3*

III. Study Design *3*

a. Endpoints **4**

b. Subject Population **4**

c. Eligibility criteria **4**

Inclusion criteria 4

Exclusion criteria 4

d. Study Timeline and Procedures **5**

IV. Recruitment *5*

a. Recruitment Process: **5**

b. Partial Waiver of HIPAA Authorization: **5**

V. Consent Process *5*

a. Informed Consent Process **5**

b. Consent Procedures **6**

VI. Risks *6*

VII. Benefits *6*

a. Possible Direct Benefits **6**

b. Possible Indirect Benefits **6**

VIII. Withdrawal of Participation and Subject Complaints *7*

IX. Compensation to Research Subjects *7*

X. Sponsorship and Cost to Subjects *7*

XI. Data *7*

a. Statistical Analysis Plan **7**

b. How records/data will be kept confidential **8**

c. Data usage and sharing of Results with participants **8**

XII. Adverse Events Management and Data Safety Monitoring *8*

XIII. References *9*

I. Background

Oral mucositis, or chemotherapy-induced stomatitis, can be a side effect of cancer therapies, including cytotoxic chemotherapy and targeted treatments such as mechanistic target of rapamycin (mTOR) inhibitors. In patients with breast and/or gynecologic cancer, especially those receiving anthracycline-based chemotherapy or everolimus-based regimens, severe oral mucositis can adversely affect quality of life and treatment continuity.

Recent research has shown that topical corticosteroids, specifically dexamethasone mouthwash, may reduce the incidence and severity of this condition. The SWISH trial, a phase 2 study in women undergoing everolimus and exemestane treatment for metastatic breast cancer, found that prophylactic use of dexamethasone mouthwash reduced the incidence of grade ≥2 oral mucositis (2% compared to 33% in historical controls), resulting in fewer treatment interruptions and improved tolerability.[1] Another group conducted a randomized controlled trial in patients with early-stage breast cancer receiving anthracycline-based chemotherapy and found that dexamethasone mouthwash reduced the incidence of moderate-to-severe oral mucositis by 17% compared to controls.[2]

Despite these results, questions remain regarding optimal dosing schedules, prophylactic versus reactive use, and generalizability across cancer subtypes and treatment protocols. The MIST trial, which compared prophylactic versus reactive dexamethasone administration, was underpowered but pointed to the importance of timing in maximizing benefit.[3] Other observational studies and reviews advocate for proactive, standardized interventions that integrate corticosteroid rinses into clinical workflows.[4-6] The current study proposes to evaluate the prophylactic efficacy and tolerability of dexamethasone mouthwash in patients with cancer undergoing chemotherapy at Woman's Cancer Pavilion. Given the safety profile and patient acceptability reported in prior trials, we hypothesize that dexamethasone mouthwash will reduce the incidence and severity of oral mucositis in this population compared to historical rates.

II. Study Objectives

- To evaluate the efficacy of prophylactic dexamethasone mouthwash in reducing the incidence of grade ≥2 oral mucositis in patients with cancer receiving chemotherapy regimens known to be associated with oral mucositis, including anthracyclines and taxanes.
- To assess the severity of oral mucositis symptoms (graded per CTCAE criteria) in patients using dexamethasone mouthwash compared to historical controls
- To evaluate the impact of oral mucositis on treatment adherence, including chemotherapy dose modifications, delays, or discontinuations, and on patient quality of life using the Oral Mucositis Weekly Questionnaire (OMWQ)

III. Study Design

This is a single-arm prospective study utilizing a historical comparison group to evaluate the effectiveness of prophylactic dexamethasone mouthwash in reducing oral mucositis among patients with cancer receiving chemotherapy associated with an increased risk of oral mucositis.

Prospective Intervention Group: At least 45 patients with cancer scheduled to receive chemotherapy (e.g., anthracyclines, taxanes) at Woman's Cancer Pavilion will be prospectively enrolled. Participants will receive a standardized dexamethasone mouthwash protocol (e.g., 10mL alcohol free dexamethasone 0.5 mg per 5mL oral solutions; swish for 2 minutes then spit; 4 times daily for 8 weeks; can continue to additional 8 weeks if clinically indicated) initiated the first week of chemotherapy and continued throughout the first chemotherapy cycle, or longer, depending on the regimen. Participants will be monitored for the development and severity of oral mucositis, mouthwash adherence, adverse events, and chemotherapy treatment modifications. They will also be given a survey (OMWQ) to

complete during their infusion appointments to assess the severity of mouth and throat soreness, pain, and how these symptoms affect daily activities such as eating, drinking, and speaking.

Historical Control Group: The comparison group will consist of patients with cancer treated at Woman's Cancer Pavilion with similar chemotherapy regimens, who did not receive prophylactic dexamethasone mouthwash. Retrospective data will be collected from electronic medical records, including demographic variables, chemotherapy regimen, incidence and grade of oral mucositis (as per CTCAE criteria), and treatment interruptions.

a. Endpoints

- Primary endpoint: Incidence of grade ≥2 oral mucositis during chemotherapy
- Secondary endpoints: Oral mucositis severity, chemotherapy delays/reductions, adverse events related to mouthwash, patient-reported pain or discomfort, intervention adherence, OMWQ responses

b. Subject Population

The study will enroll at least 45 adult participants in the prospective intervention group. All participants will be patients with a confirmed cancer diagnosis who are scheduled to begin chemotherapy regimens known to be associated with oral mucositis, including anthracyclines and taxanes.

- Number of Participants: 45 (prospectively enrolled for intervention group)
- Age Range: ≥18 years (adult population only)
- Health Status: Participants must have a confirmed cancer diagnosis and be healthy enough to receive chemotherapy.

c. Eligibility criteria

Inclusion criteria:

- ≥18 years old
- Confirmed cancer diagnosis
- Scheduled to receive or receiving chemotherapy known to be associated with oral mucositis (e.g., anthracyclines and taxanes)
- Ability to provide informed consent
- Ability to comply with study procedures

Exclusion criteria:

- Current tobacco usage or usage within the past 6 weeks.
- HIV/AIDS
- Gastrointestinal disorder (such as Crohn's disease, ulcerative colitis, or celiac disease)
- History of cold sores (herpes simplex virus)
- Herpes zoster (oral shingles) within the past 6 weeks
- Active oral infections at the time of enrollment (e.g., candidiasis)
- Known sensitivity or allergy to dexamethasone
- Inability to self-administer or tolerate mouthwash protocol
- Concurrent enrollment in conflicting clinical trials
- Existing oral ulcers or oral mucositis at enrollment
- Pregnant
- Uncontrolled diabetes mellitus as defined by HbA1c unknown or >8% in the past 3 months despite adequate therapy

d. Study Timeline and Procedures

This study will span approximately 18 months and involve the prospective enrollment of at least 45 patients with cancer scheduled to undergo chemotherapy. Participants will be followed for up to ten chemotherapy cycles, with additional follow-up if clinically indicated. The study will also include the use of a retrospective historical control group, which will not require direct participant involvement.

IV. Recruitment

Participants will be recruited through healthcare team referral within the Woman's Cancer Pavilion or collaborating healthcare organization (e.g., Mary Bird Perkins and Our Lady of the Lake). Staff will identify potentially eligible patients based on diagnosis and treatment plan, and will introduce the study during clinical visits. If this referrer is not the patient's medical oncologist, s/he will be contacted prior to recruitment to approve approaching their patient.

a. Recruitment Process:

- Healthcare Provider Identification: Healthcare providers will assess patients for preliminary eligibility. If the patient appears appropriate for the study, the physician will inform them of the research opportunity and/or provide their information to the study team for approach.
- Study Introduction: A member of the research team (e.g., clinical research coordinator and/or nurse patient navigator) will contact potential participants to provide study details, answer questions, and conduct eligibility screening.
- Informed Consent and HIPAA Authorization: Eligible patients who agree to participate will provide informed consent and HIPAA authorization before any study procedures begin.

b. Partial Waiver of HIPAA Authorization:

To facilitate identification of potentially eligible participants, the research and/or healthcare teams may review electronic medical records (EMRs). This process may involve access to limited protected health information (PHI), including contact information, diagnosis, chemotherapy regimen, and demographic information.

- A partial waiver of HIPAA authorization is requested to allow screening of medical records prior to patient's provision of HIPAA authorization.
- PHI collected during screening will be used solely for the purpose of assessing eligibility.
- PHI for individuals who are found to be ineligible or who decline participation will be destroyed and not retained for future use.
- No study-specific procedures will be performed until the subject has documented consent and HIPAA authorization.

V. Consent Process

a. Informed Consent Process

The process of obtaining, documenting, and maintaining informed consent will be conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines and the Declaration of Helsinki. An IRB-approved informed consent form (ICF) describing the study, study procedures, potential risks, and participant rights will be provided to each potential participant. Written informed consent must be obtained and documented prior to the initiation of any study-specific procedures. The participant will sign and date the ICF, and a copy will be provided to them for their records. Documentation of the consent process, including the date, will be maintained in the source documents.

Participants will be informed that their participation is entirely voluntary, that they may withdraw at any time without penalty or prejudice, and that refusal to participate will not affect the quality of their medical care. The rights and welfare of participants will be protected throughout the process.

b. Consent Procedures

The informed consent process will begin prior to enrollment and will continue throughout the duration of participation. The IRB-approved ICF will be provided to participants for review. Research staff will conduct the consent discussion, explain the study objectives, procedures, risks, and participant rights, and respond to any questions. A verbal explanation will be tailored to the participant's level of comprehension. Participants will be afforded adequate time to review the document, ask questions, and, if they wish, consult with family members or legally authorized representatives before making a decision.

VI. Risks

Participants in this study may be exposed to minimal risks, primarily related to the use of dexamethasone mouthwash as an investigational prophylactic intervention. The risks associated with participation can be categorized as follows:

- **Oral side effects**: The most commonly reported adverse event with dexamethasone mouthwash is oral candidiasis (thrush). A small number of participants may experience a burning or unpleasant taste during rinsing.
- **Steroid-related effects**: Risks include minor alterations in blood glucose or local immune suppression within the oral cavity.

VII. Benefits

Participation in this study may offer direct clinical benefits to enrolled subjects, as well as potential indirect benefits to future patients and the broader medical community.

a. Possible Direct Benefits:

- Participants in the prospective arm of the study will receive dexamethasone mouthwash, which has been shown in previous clinical trials to reduce the incidence and severity of oral mucositis.
- Preventing or lessening oral mucositis may result in improved comfort, nutritional intake, ability to communicate, and overall quality of life during chemotherapy treatment.
- Reducing oral discomfort may also help participants complete their chemotherapy regimens without interruption, minimizing dose delays or reductions and potentially enhancing treatment efficacy.

b. Possible Indirect Benefits:

- Even if no direct clinical benefit is experienced, participants will contribute to important scientific knowledge about the prevention of oral mucositis in patients with cancer.
- The findings may help refine supportive care practices and inform future standard-of-care interventions, especially for patients receiving taxane and/or anthracycline-based therapies.
- Participants will also receive regular oral assessments and symptom monitoring, which may help identify and address oral complications promptly, regardless of their relationship to the study intervention.

VIII. Withdrawal of Participation and Subject Complaints

Participants can request withdrawal from the study to research@womans.org or call the research department where removal of study data can be performed securely via REDCap database. Instructions for how to withdraw will be included in the study ICF. Upon receipt of withdrawal request, the record will be deleted from the REDCap database.

Instructions to submit a research complaint along with contact information is posted on the main womans.org/research webpage, as well as included in the consent form: "You can also call the research office at Woman's if you cannot reach the study team, have questions about your rights as a research participant, or want to speak to someone not directly involved with this study: call Ericka Seidemann, Human Protections Administrator, at 225-231-5296 or email research@womans.org.".

IX. Compensation to Research Subjects

Patients will not be compensated for participation in this study.

X. Sponsorship and Cost to Subjects

The study costs are being paid by a grant from the Foundation for Woman's.

XI. Data

a. Statistical Analysis Plan

Data collected will be analyzed using standard statistical software (e.g., SPSS, R, or SAS). Descriptive statistics will be used to summarize demographic variables, cancer diagnosis, oral mucositis, etc. Continuous variables will be summarized using means and standard deviations; categorical variables will be reported as frequencies and percentages.

This study will use identifiable information obtained from both prospectively enrolled participants and a retrospective historical control group. The data will be collected from clinical records and physician assessments. No biological specimens or genetic information will be collected or analyzed in this study.

Prospective Cohort: For participants enrolled in the dexamethasone mouthwash intervention group, the following research materials will be collected:

- Sociodemographic data: height, weight, race, ethnicity, date of birth, education, income, language spoken, health insurance type, etc.
- Medical history and diagnosis: type and stage of cancer, comorbid conditions
- Chemotherapy regimen: drug name, dose, schedule, start dates
- Oral mucositis data: incidence, grade (using CTCAE criteria), duration of symptoms, OMWQ responses
- Adverse event data: type, severity, timing, and relationship to mouthwash use
- Mouthwash adherence: frequency and consistency of use (via self-report and staff monitoring)

Historical Control Group: This group will include patients with cancer previously treated at Woman's Cancer Pavilion who received standard chemotherapy without dexamethasone mouthwash. Data will be abstracted from the hospital's electronic medical records (EMR), including but not limited to:

- Demographic data: height, weight, race, ethnicity, date of birth, education, income, language spoken, health insurance type, etc.
- Medical history and diagnosis: type and stage of cancer, comorbid conditions
- Chemotherapy regimen: drug name, dose, schedule, start dates
- Oral mucositis data: incidence, grade (using CTCAE criteria), and duration of symptoms

- Relevant adverse events or treatment delays due to oral mucositis

b. How records/data will be kept confidential

Protected health information (PHI) will not be used in publications resulting from information in the study. Study data, i.e. data extracted from the medical record, will be stored in REDCap or excel and will be accessible only through password-protected login and permissioned projects. The research team will have access to the data, and the Principal Investigator will be responsible for receipt and transmission of the data. All electronic records will be kept behind Woman's Hospital firewalls in order to maintain security. Permission to use PHI collected in the study for future contact will be obtained from participants via the consent form and is strictly voluntary. Data will not be stored on portable devices, such as laptops or USBs. Protected Health Information (PHI) will not be used in any publications of the study results.

c. Data usage and sharing of Results with participants

The results of the study will be analyzed and published in a peer-reviewed medical journal, but no identifying data will be published. Individual nor aggregated results will not be shared with individual participants. A summary of the study results will be prepared in lay language for distribution to the study participants at the end of the trial and its analysis.

XII. Adverse Events Management and Data Safety Monitoring

Adverse event reporting will be limited to events that are reasonably related to the study intervention (dexamethasone mouthwash). Investigators will monitor for any local or systemic reactions that may result from the use of the mouthwash, including but not limited to allergic reactions or unexpected side effects. Only serious adverse events (SAEs), suspected unexpected serious adverse reactions (SUSARs), and serious adverse drug reactions (SADRs) that are deemed related to the study mouthwash will be reported to the Woman's Hospital Foundation Institutional Review Board (IRB), in accordance with applicable federal regulations, local HRPP policies, and IRB requirements. We will collect the following information at minimum for each of these events:

- Appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number.
- A detailed description of the adverse event, incident, experience, or outcome.
- An explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem.
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

To satisfy the requirement for prompt reporting, unanticipated problems will be reported using the following timeline:

- Unanticipated problems that are serious adverse events will be reported to the IRB and the study coordinator within 2 business days of becoming aware of the event.
- Any other unanticipated problem will be reported within 2 weeks of the investigator becoming aware of the problem.

XIII. References

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