Informed Consent Form – Information Sheet

Study Title:：**Efficacy and Safety of Sapylin Versus Dexamethasone Atomized Inhalation for Concurrent Chemoradiotherapy-Induced Oral Mucositis in Patients With Nasopharyngeal Carcinoma: A Randomized, Parallel, Non-inferiority Clinical Trial**

Institution：Affiliated Hospital of Guangdong Medical University

Principal Investigator (Responsible Study Physician):Haiqing Luo

Dear Patient (Subject),

You have been diagnosed with nasopharyngeal carcinoma. We invite you to participate in a randomized controlled study titled: "A Non-inferiority, Parallel-Design, Randomized Controlled Study of Sapylin versus Dexamethasone Nebulized Inhalation for the Prevention and Treatment of Radiation-Induced Oral Mucositis in Nasopharyngeal Carcinoma." Protocol Number: LCYJ2021A002.This study protocol has been reviewed and approved by the Institutional Review Board/Ethics Committee of the Affiliated Hospital of Guangdong Medical University. Clinical research may proceed following this approval.

Before you decide whether to participate in this study, please read the following information as carefully as possible. It will help you understand the study, why it is being conducted, the procedures and duration involved, as well as the potential benefits, risks, and discomforts associated with participation. If you wish, you may also discuss this with your family or friends, or ask the study doctor for further explanation to assist you in making your decision.

1. Study Background

Radiotherapy is the primary treatment modality for nasopharyngeal carcinoma (NPC). At the time of diagnosis, 70% of patients are already in the advanced stage. For locally advanced nasopharyngeal carcinoma (LA-NPC), the standard treatment regimen is induction chemotherapy combined with concurrent chemoradiotherapy (CCRT). Despite this, over 20% of patients with LA-NPC experience treatment failure, with a survival rate of less than 5 years. Furthermore, during radiotherapy, radiation causes varying degrees of damage to the normal tissues surrounding the tumor, leading to adverse reactions such as xerostomia and radiation-induced oral mucositis. These side effects can reduce patient compliance and diminish the efficacy of CCRT, resulting in unfavorable clinical outcomes. The INT0099 trial showed that 37% of patients receiving CCRT discontinued treatment prematurely due to excessive toxicity. Therefore, finding methods to

enhance the efficacy of CCRT and reduce the incidence and severity of toxicities associated with radiotherapy and chemotherapy has become an urgent research priority.Currently, clinical practice guidelines related to mucositis issued by the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO), the updated ESMO guidelines for the prevention and management of oral mucositis, and the 2019 Chinese Expert Consensus on Prevention and Management Strategies for Radiation-Induced Oral Mucositis by the Chinese Society of Radiation Oncology agree that the focus for radiation-induced oral mucositis (RTOM) is on prevention, with good oral hygiene and care being primary measures. However, there is currently no specific drug for the prevention and treatment of RTOM. Treatment primarily aims to alleviate symptoms and reduce complications. Moreover, there is still no standardized prevention and treatment protocol applicable to all NPC patients.In recent years, domestic and international studies have indicated that the biologic immunomodulator Sapylin, administered via nebulized inhalation, may enhance chemotherapy efficacy and improve immune function in lung cancer patients.

2. Study Objectives

This study aims to explore, via nebulized inhalation, the impact of Sapylin inhalation on the incidence and severity of Radiation-Induced Oral Mucositis (RTOM), and to assess the safety profile of Sapylin inhalation as well as its effect on the efficacy of concurrent chemoradiotherapy (CCRT) in patients with nasopharyngeal carcinoma. This research seeks to provide nasopharyngeal carcinoma specialists and patients with an effective and low-toxicity method to enhance CCRT efficacy and improve the management of RTOM.

3. Study Procedures

If you agree to participate in this study, we will engage in detailed communication with you to explain all relevant aspects of the research. We will also ask you to provide information related to your medical condition, including the course of the disease, family medical history, previous medical consultations, and the results of any prior examinations. Each participant will be assigned a unique identification number, and a medical record file will be created. Regular follow-up visits will be scheduled.

4. Risks and Discomforts

Although existing evidence suggests that Sapylin Nebulized Inhalation has satisfactory efficacy, this does not guarantee that it will definitely be effective for you. The Sapylin Nebulized Inhalation used in this study is also not the only method to improve the incidence and severity of RTOM and enhance the efficacy of concurrent chemoradiotherapy for nasopharyngeal carcinoma. If Sapylin Nebulized

Inhalation is ineffective for your condition or you are dissatisfied with the treatment results, you may inquire with your doctor about other potential alternative treatment options.

(1) The following adverse reactions may occur after Sapylin Nebulized Inhalation:

① Systemic reactions: Allergic reactions, including anaphylactic shock.

② Hematological adverse reactions: There may be a mild, temporary decrease in hemoglobin or red blood cells, and a mild, temporary increase in white blood cells.

③ Increase in serum alkaline phosphatase, AST (GOT), and ALT (GPT).

④ Gastrointestinal adverse reactions: Symptoms such as loss of appetite, nausea, vomiting, and diarrhea.

(2) When dexamethasone is used at physiological doses for replacement therapy, there are no significant adverse reactions. Adverse reactions mostly occur at pharmacological doses and are closely related to the duration of treatment, dosage, type of medication, administration method, and route. Common adverse reactions mainly include the following categories:

① Adverse reactions caused by long-term use: Iatrogenic Cushing's syndrome (manifested as moon face, central obesity, etc.), weight gain, lower limb edema, purple striae, increased tendency to bleed, poor wound healing, acne, menstrual disorders, osteoporosis and fractures, muscle weakness, muscle atrophy, gastrointestinal irritation (nausea, vomiting), peptic ulcer or perforation, inhibition of growth in children, glaucoma, cataracts, impaired glucose tolerance, and exacerbation of diabetes. Glucocorticoids can suppress the body's immune function. Long-term use of dexamethasone can often induce or aggravate infections, causing latent infections to spread or dormant infections to reactivate.

② Patients may experience psychiatric symptoms: Euphoria, agitation, delirium, disorientation, or may present with depression. Psychiatric symptoms are more likely to occur in individuals with chronic wasting diseases or a history of mental illness.

③ Infection, a major adverse reaction of adrenal corticosteroids, primarily involving fungi, tubercle bacilli, staphylococci, proteus, pseudomonas aeruginosa, and various herpes viruses.

④ Glucocorticoid withdrawal syndrome. Sometimes after discontinuation, patients may experience dizziness, fainting tendencies, low-grade fever, loss of appetite, nausea, vomiting, muscle or joint pain, and general weakness. If adrenal insufficiency and recurrence of the original disease can be ruled out after careful examination, it may be considered a dependency syndrome on glucocorticoids.

(3) If you experience any discomfort, changes in your condition, or any unexpected events during the study, regardless of whether they are related to the research, you should notify your doctor promptly. He/she will assess the situation and provide appropriate medical management. Participation in the study

requires you to attend follow-up visits at the hospital on schedule for examinations, which will take up some of your time and may cause inconvenience or trouble.

5. Benefits

All patients participating in this study will be examined by the responsible study physician, who will answer your questions and provide timely and attentive medical services. The study results may potentially contribute to the further treatment of this type of disease in the future, but they may also be of no direct benefit.

6. Requirements for Participation

(1) You must come to the hospital for appointments at the scheduled follow-up times, bringing your medical records, test, and examination results (during the follow-up phase, the doctor may contact you via telephone or home visit to understand your condition). Your follow-up is crucial because the doctor needs to assess whether the treatment you are receiving is truly effective and to provide you with timely guidance.

(2) You must take the medication as instructed by the doctor and promptly and objectively complete your medication record. At each follow-up visit, you must return any unused medication along with its packaging, and bring any other medications you are currently taking, including those for other concurrent conditions. During the study period, you must not self-administer any other drugs related to the treatment of nasopharyngeal carcinoma. If you require other treatments, please contact your doctor in advance.

(3) During the research process, you may be required to cooperate with multiple blood tests at initial hospitalization and after treatment. You must inform the study doctor whether you have recently participated, or are currently participating, in any other research studies.

7. Privacy and Confidentiality

If you decide to participate in this study, your participation and all personal data collected during the trial will be kept confidential. The Principal Investigator and other research staff will have access to your medical information for research purposes. This information may include your name, medical history, and data obtained during your study visits. Your records will be stored in a locked cabinet accessible only to authorized research personnel. To ensure the study is conducted in accordance with regulations, representatives from relevant government regulatory authorities or the Ethics Review Board may, if necessary and as stipulated by regulations, inspect your personal data at the research site. Should the results of this study be published, no personally identifiable information will be disclosed.

8.How to Obtain More Information?

You may ask any questions concerning this study at any time. Your doctor will provide you with his/her contact number to address your inquiries. If any significant new information arises

during the study that might affect your willingness to continue participation, your doctor will notify you promptly.

9.Voluntary Participation and Right to Withdraw

Participation in this study is entirely voluntary. You may choose not to participate or to withdraw from the study at any time without penalty or loss of benefits to which you are otherwise entitled. Your relationship with your doctor or the quality of your medical care will not be affected. Additionally, the Principal Investigator or study staff may discontinue your participation at any time if it is deemed to be in your best interest.

10. What Happens Now?

The decision to participate is yours alone. You are encouraged to discuss this with your family or friends before deciding. Before making your decision, please feel free to ask your doctor any questions until you fully understand all aspects of this study. Thank you for taking the time to read this information. Please keep this document for your records.

11. Related Costs

Each patient enrolled in this study will receive a transportation subsidy of 100 RMB. After enrollment, costs associated with concurrent chemoradiotherapy, Sapylin or Dexamethasone nebulized inhalation, and related examinations (such as head/neck MRI) will be the responsibility of the patient. In the event that a patient experiences a serious adverse event requiring withdrawal from the study, costs incurred for managing the adverse reaction will also be borne by the patient; however, all the aforementioned expenses are eligible for medical insurance reimbursement.

12. Ethics Committee Approval

This study has been reviewed and approved by the Institutional Review Board/Ethics Committee of the Affiliated Hospital of Guangdong Medical University. For any matters concerning ethics or your rights and welfare during the study, you may contact the Ethics Committee at: 0759-2386971 (Affiliated Hospital of Guangdong Medical University).

Informed Consent Form – Consent and Signature Page

Study Title: Efficacy and Safety of Sapylin Versus Dexamethasone Atomized Inhalation for Concurrent Chemoradiotherapy-Induced Oral Mucositis in Patients With Nasopharyngeal Carcinoma: A Randomized, Parallel, Non-inferiority Clinical Trial

Institution Responsible for the Study: Affiliated Hospital of Guangdong Medical University

Collaborating Institution(s):_____

Study/Task Identification Number: ___LCYJ2021A002_____

Consent Statement

I have read the above information regarding this study and have had the opportunity to discuss it with the doctor and ask questions. All of my questions have been satisfactorily answered. I understand the potential risks and benefits associated with participating in this study. I am aware that participation is voluntary. I confirm that I have had sufficient time to consider this and understand that:

- I may consult the doctor for further information at any time.
- I may withdraw from this study at any time without facing discrimination or retaliation, and my medical treatment and rights will not be affected.

I also understand that if I withdraw from the study, especially due to the study intervention or medication, it would be very helpful to the overall study if I inform the doctor of any changes in my condition and complete the corresponding physical and laboratory examinations.

If any additional medication is required due to changes in my condition, I will seek the doctor's opinion in advance or truthfully inform the doctor afterward.

I agree that representatives from national health authorities, drug regulatory agencies, the ethics committee, or the study sponsor may review my research data.

I will receive a signed and dated copy of this informed consent form.

Finally, I have decided to agree to participate in this study and will make every effort to follow the doctor's instructions.

Patient (Subject) Signature: _____ Date :_____

Patient (Subject) Contact Phone Number: _____

(Note: If the patient is unable to sign, the legal representative must sign. The relationship between the patient and the legal representative should be clarified. If the patient is unable to read or write, an impartial witness must sign.)

Lgal Representative Signature (if applicable): _____

Relationship to Patient (Subject):_____ Date :_____

Contact Phone Number:_____

Witness Signature (if applicable): _____ Date : _____

Contact Phone Number: _____

I confirm that I have explained the details of this trial to the patient (subject), including their rights, potential benefits, and risks, and have provided them with a signed copy of the informed consent form.

Investigator Signature:_____ Date: _____

Investigator Contact Information: _____