Cover Page

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ClinicalTrials.gov ID: NCT07033585

Unique Protocol ID: ANDA219975 + ANDA220011

Brief Title: Generic Drugs (Dapagliflozin and Saxagliptin) Treat Type 2 Diabetes Patients with Controlled Cancers (GD-T2D)

Official Title: Generic Drugs (Dapagliflozin and Saxagliptin) Treat Type 2 Diabetes Patients with Controlled Cancers

Secondary IDs: NPI-1831468511 [Registry ID: HHS, Health Care Provider Individual]
NPI-1023387701 [Registry ID: HHS, Health Care Provider Organization]
FWA00015357 [Registry ID: HHS, Human Protections Administrator]
IORG0007849 [Registry ID: HHS, IORG]
IRB00009424 [Registry ID: HHS, IRB]
ANDA219975 [Registry ID: FDA, ANDA]
ANDA220011 [Registry ID: FDA, ANDA]

Contents

21 CFR §312.23 (a)(3)

(3) Introductory statement and general investigation plan.

(i) A brief introductory statement giving the name of the drug and all active ingredients, the drug's pharmacological class, the structural formula of the drug (if known), the formulation of the dosage form(s) to be used, the route of administration, and the broad objectives and planned duration of the proposed clinical investigation(s).

The names of the drugs and all active ingredients:

Oral Mix Prescription - 1:
NDC 0310-6210-30 (FARXIGA - dapagliflozin tablet, film coated) (NDA202293) (Mix-1)
NDC 0310-6105-30 (ONGLYZA - saxagliptin tablet, film coated) (NDA022350) (Mix-1)
NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) (ANDA077880) (Mix-1)

Oral Mix Prescription - 2:
China Import - dapagliflozin tablet (**ANDA 219975**) (Mix-2)
China Import - saxagliptin tablet (**ANDA 220011**) (Mix-2)
NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) (ANDA077880) (Mix-2)

The drug's pharmacological class:
Antidiabetics

The structural formula of the drug:
LABEL: FARXIGA - dapagliflozin tablet, film coated (https://dailymed.nlm.nih.gov)
LABEL: ONGLYZA - saxagliptin tablet, film coated (https://dailymed.nlm.nih.gov)
LABEL: METFORMIN HYDROCHLORIDE - metformin tablet (https://dailymed.nlm.nih.gov)

The formulation of the dosage form(s) to be used:

Usual Approach Group: 300 type 2 diabetes patients with Controlled Cancers
Oral Mix Prescription - 1:

NDC 0310-6210-30 (FARXIGA - dapagliflozin tablet, film coated) -- 10 mg orally once daily
NDC 0310-6105-30 (ONGLYZA - saxagliptin tablet, film coated) -- 5 mg orally once daily
NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

Study Approach Group: 300 type 2 diabetes patients with Controlled Cancers
Oral Mix Prescription - 2:
China Import - dapagliflozin tablet (**ANDA 219975**) -- 10 mg orally once daily
China Import - saxagliptin tablet (**ANDA 220011**) -- 5 mg orally once daily
NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

The route of administration:
Usual Approach Group: Oral Administration = OS
Study Approach Group: Oral Administration = OS

The broad objectives of my proposed clinical investigation:

Generic Drugs Treat Type 2 Diabetes Patients with Controlled Cancers (GD-T2D).

The planned duration of my proposed clinical investigation:

90 days -- Phase 2 **ANDA** Diabetes Clinical Investigation **NCT07033585**

(ii) A brief summary of previous human experience with the drug, with reference to other IND's if pertinent, and to investigational or marketing experience in other countries that may be relevant to the safety of the proposed clinical investigation(s).

LABEL: FARXIGA - dapagliflozin tablet, film coated (https://dailymed.nlm.nih.gov)
LABEL: ONGLYZA - saxagliptin tablet, film coated (https://dailymed.nlm.nih.gov)
LABEL: METFORMIN HYDROCHLORIDE - metformin tablet (https://dailymed.nlm.nih.gov)
Nan Fang Yi Ke Da Xue Xue Bao: 2019 Nov 30; 39(11): 1305-1311.

(iii) If the drug has been withdrawn from investigation or marketing in any country for any reason related to safety or effectiveness, identification of the country(ies) where the drug was withdrawn and the reasons for the withdrawal.

The drugs above have **never** been withdrawn from investigation or marketing in any country for any reason related to safety or effectiveness.

(iv) A brief description of the overall plan for investigating the drug product for the following year. The plan should include the following: (*a*) The rationale for the drug or the research study; (*b*) the indication(s) to be studied; (*c*) the general approach to be followed in evaluating the drug; (*d*) the kinds of clinical trials to be conducted in the first year following the submission (if plans are not developed for the entire year, the sponsor should so indicate); (*e*) the estimated number of patients to be given the drug in those studies; and (*f*) any risks of particular severity or seriousness anticipated on the basis of the toxicological data in animals or prior studies in humans with the drug or related drugs.

90 days -- Phase 2 **ANDA** Diabetes Clinical Investigation **NCT07033585**

(a) The rationale for the drug and the research study:

- **LABEL:** FARXIGA - dapagliflozin tablet, film coated (https://dailymed.nlm.nih.gov)
- **LABEL:** ONGLYZA - saxagliptin tablet, film coated (https://dailymed.nlm.nih.gov)
- **LABEL:** METFORMIN HYDROCHLORIDE - metformin tablet (https://dailymed.nlm.nih.gov)

(*b*) the indication(s) to be studied -- **follow up DAILYMED Labels**:

- **LABEL:** FARXIGA - dapagliflozin tablet, film coated (https://dailymed.nlm.nih.gov)
- **LABEL:** ONGLYZA - saxagliptin tablet, film coated (https://dailymed.nlm.nih.gov)
- **LABEL:** METFORMIN HYDROCHLORIDE - metformin tablet (https://dailymed.nlm.nih.gov)
- Dapagliflozin plus Saxagliptin plus Metformin Oral Mix Prescription Treat Type 2 Diabetes Patients with Controlled Cancers

(*c*) the general approach to be followed in evaluating the drug:

- The usual approach to be followed in evaluating above drugs -- Oral Mix Prescription - 1
- The study approach to be followed in evaluating above drugs -- Oral Mix Prescription - 2

(*d*) the kinds of clinical trials to be conducted in the first year following the submission (if plans are not developed for the entire year, the sponsor should indicate so):

90 days -- Phase 2 **ANDA** Diabetes Clinical Trial **NCT07033585**

(*e*) the estimated number of patients to be given the drug in those studies; …

- The usual approach group: 300 type 2 diabetes patients with Controlled Cancers
- The study approach group: 300 type 2 diabetes patients with Controlled Cancers

(*f*) any risks of particular severity or seriousness anticipated on the basis of the toxicological data in animals or prior studies in humans with the drug and related drugs.

- **LABEL:** FARXIGA - dapagliflozin tablet, film coated (https://dailymed.nlm.nih.gov)
- **LABEL:** ONGLYZA - saxagliptin tablet, film coated (https://dailymed.nlm.nih.gov)
- **LABEL:** METFORMIN HYDROCHLORIDE - metformin tablet (https://dailymed.nlm.nih.gov)

The General Investigational plan [21 CFR 312.23(a)(3)]

Dapagliflozin plus Saxagliptin plus Metformin Oral Mix Prescription Treat Type 2 Diabetes Patients with Controlled Cancers

- Criteria:
  - ✧ Select 600 type 2 diabetes patients with controlled cancers.
  - ✧ Dosage Duration at least 90 days

- Inclusion Criteria:

1. Clinical diagnosis of type 2 diabetes
2. Controlled cancers
3. Suitable for enough blood-drawing
4. Random and double blind
5. Measurable disease
6. Adequate organ functions
7. Adequate performance status
8. Age 24 years old and over
9. Sign an informed consent form
10. Receive blood-drawing

- Exclusion Criteria:

1. Uncontrolled cancer
2. Pregnancy
3. Breast-feeding
4. The patients with other serious intercurrent illnesses or infectious diseases
5. Have more than one different kind of cancer at the same time
6. Serious Allergy to Drugs
7. Serious Bleed Tendency
8. Serious Risks or Serious Adverse Events of the drug product
9. The prohibition of drug products
10. Have no therapeutic effects

The expected accrual populations:

- ✧ Select 600 type 2 diabetes patients with controlled cancers.

The primary efficacy and safety endpoints:

- ➢ Detect Hemoglobin A1c (HbA1c)
- ➢ Detect fasting blood glucose (FBG)
- ➢ Detect 2-hour postprandial blood glucose (2 hPBG)
- ➢ Detect fasting insulin (FINS)
- ➢ Detect 2-hour postprandial insulin (2 hPINS)

The dose range (The statistical table):

- ✧ The usual approach randomization-double-blinding active treatment concurrent control group:
  Oral Mix Prescription - 1:
  NDC 0310-6210-30 (FARXIGA - dapagliflozin tablet, film coated) -- 10 mg orally once daily
  NDC 0310-6105-30 (ONGLYZA - saxagliptin tablet, film coated) -- 5 mg orally once daily
  NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

- ✧ The study approach randomization-double-blinding active treatment concurrent control group:
  Oral Mix Prescription - 2:
  China Import - dapagliflozin tablet (**ANDA 219975**) -- 10 mg orally once daily
  China Import - saxagliptin tablet (**ANDA 220011**) -- 5 mg orally once daily
  NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

The analysis plans (The statistical analysis plan):

- ➢ Detect Hemoglobin A1c (HbA1c)
- ➢ Detect fasting blood glucose (FBG)
- ➢ Detect 2-hour postprandial blood glucose (2 hPBG)
- ➢ Detect fasting insulin (FINS)
- ➢ Detect 2-hour postprandial insulin (2 hPINS)

The potential limitations of my proposed clinical trial:

Dapagliflozin plus Saxagliptin plus Metformin Oral Mix Prescription Treat Type 2 Diabetes Patients with Controlled Cancers

I (Han Xu, M.D., Ph.D. i.e., Sponsor i.e., Sponsor-Investigator) as IRB Chair of our IRB (IRB00009424) will organize the IRB meeting only but give up my voting power in the IRB determination, when I conduct my clinical investigation **(NCT07033585)**.

Reference:

LABEL: FARXIGA - dapagliflozin tablet, film coated (https://dailymed.nlm.nih.gov)
LABEL: ONGLYZA - saxagliptin tablet, film coated (https://dailymed.nlm.nih.gov)
LABEL: METFORMIN HYDROCHLORIDE - metformin tablet (https://dailymed.nlm.nih.gov)
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21 CFR 56.102(g)

Institutional Review Board (IRB) means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects.

According to 21 CFR 56.102(g), Institutional Review Board (IRB) (IRB00009424) can approve the initiation of and can conduct periodic review of biomedical research involving human subjects (NCT07033585).

21 CFR 56.102(m)

IRB approval means the determination of the IRB that the clinical investigation has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

According to 21 CFR 56.102(m), IRB approval means the determination of our IRB (IRB00009424) that my clinical investigation (NCT07033585) has been reviewed and may be conducted at our institution (Medicine Invention Design Incorporation) within the constraints set forth by our IRB (IRB00009424) and by other institutional and Federal requirements.

21 CFR 56.107(e)

No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

According to 21 CFR 56.107(e), I (Han Xu, M.D., Ph.D., FAPCR, Sponsor-Investigator) as IRB Chair of our IRB (IRB00009424) will only organize the IRB meeting but give up my voting power in the determination of IRB, when I conduct my clinical investigation (NCT07033585).

The investigation (**NCT07033585**) will be conducted in compliance with the requirements for **21 CFR Part 56** as follows:

21 CFR § 56.102 (k)

Sponsor-investigator means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., it does not include a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.

I (Han Xu, **sponsor-investigator**) will actually conduct, with online-referral clinical investigators, the clinical investigation (NCT07033585), i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject.

Our investigation (**NCT07033585**) will be conducted in compliance with the requirements for **21 CFR Part 50** as follows:

21 CFR § 50.3 (f)

Sponsor-investigator means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., corporation or agency.

I (Han Xu, **sponsor-investigator**) will actually conduct, with online-referral clinical investigators, the clinical investigation (NCT07033585), i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject.