Phase 3 study of ADXS11-001 administered following chemoradiation as adjuvant treatment for high risk locally advanced cervical cancer: AIM2CERV (Advaxis IMmunotherapy 2 prevent CERVical recurrence)

Published: 27-02-2017
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Primary objective:- Disease free survival (DFS)Secondary objective:- Safety & tolerability- Overall survival (OS)Exploratory objective:- Association between HPV subtypes and efficacy- Patient reported outcomes (PRO)Please refer to section 1 in...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON47237

Source
ToetsingOnline

Brief title
AIM2CERV study in patients with locally advanced cervical cancer

Condition

- Reproductive neoplasms female malignant and unspecified
- Cervix disorders (excl infections and inflammations)

Synonym
1)cervical cancer 2) A malignant tumor of the cervix, the lowermost part of the uterus

Research involving
Human

Sponsors and support

Primary sponsor: Advaxis, Inc
Source(s) of monetary or material Support: Advaxis;Inc

Intervention

Keyword: ADXS11-001, locally advanced cervical cancer, phase 3

Outcome measures

Primary outcome

The primary endpoint for this study is DFS measured from the time of

randomization to recurrence or death.

Secondary outcome

- The safety objective of this study is to determine and compare the frequency

and severity of AEs as assessed by NCI CTCAE v 4.03 for the regimens

administered on this study.

- The exploratory endpoint are patient reported outcomes

Study description

Background summary

As noted in the protocol section2.1, subjects with nodal disease, either pelvic or para-aortic, and subjects with FIGO stage III and IV represent a subset of subjects with LACC who are at greatest risk for recurrence and death from the disease, and represent the population of LACC with the highest unmet need. Therefore, by restricting the study population to high risk disease, as determined by conventional and accepted diagnostic standards, we are focusing our evaluation of ADXS11-001 on those subjects who would have the highest potential to benefit and where the benefit/ risk ratio is acceptable for

treatment with experimental therapies.

Hypothesis: ADXS11-001 administered in the adjuvant setting, following definitive therapy with CCRT, will significantly improve DFS rate as compared with placebo.

Study objective

Primary objective:

- Disease free survival (DFS)

Secondary objective:

- Safety & tolerability
- Overall survival (OS)

Exploratory objective:
- Association between HPV subtypes and efficacy
- Patient reported outcomes (PRO)

Please refer to section 1 in the protocol page 12-13

Study design

This is a double-blind, placebo-controlled randomized study of ADXS11-001 administered in the adjuvant setting after completion of cisplatin-based CCRT in subjects with locally advanced cervical cancer at higher risk for recurrence (HRLACC), or death. The study will enroll subjects with high-risk disease as determined by prognostic factors such as tumor staging, nodal involvement, extent of nodal involvement, and location of nodal involvement. All eligible subjects will have received CCRT administered with curative intent according to institutional/national guidelines as well as meeting the minimum standards defined in the protocol. Subjects must initiate the Screening period within 10 weeks after the completion of CCRT. Baseline radiographic assessments and clinical laboratory assessments must be completed no longer than 28 days prior to and 3 days prior to the first study treatment infusion, respectively.
Eligible subjects will be randomized 1:2 to receive either placebo or ADXS11-001 (1 x 109 CFU infused over approximately 60 minutes). Subjects will receive 1 infusion of study treatment (placebo or ADXS11-001, 1 x 109 CFU) administered every 3 weeks for 3 doses (Weeks 1, 4 and 7) for the first 3 months. This is called the Prime Phase at the study. Thereafter, subjects will receive study treatment every 8 weeks (Weeks 15, 23, 31, 39, and 47) for a total of 5 doses or until disease recurrence. This is called the Maintenance Phase. Subjects will receive a 7-day course of an oral antibiotic (e.g. trimethoprim/sulfamethoxazole (Bactrim) or Ampicillin; Bactrim is drug of

choice but Ampicillin may be used in specific cases (e.g. sulfa allergy) or placebo starting 72 hours following the completion of study treatment administration during the Prime and Maintenance phases. The total treatment period will be approximately 1 year.

Lm Surveillance Period
Subjects will enter a 3-year Lm surveillance period beginning at the completion of study treatment or at the time of study discontinuation. This period is intended to help ensure the eradication of Lm bacteria in the body. It consists of a 6-month course of trimethoprim/sulfamethoxazole, ampicillin or placebo and a 2.5 year follow-up which will involve blood testing. The initiation of antibiotic therapy will begin either 72 hours following the completion of the last dose of study treatment or immediately following study discontinuation.

Follow-up and Post-Disease Recurrence Period
Subjects will continue to participate in the study and be followed for disease recurrence after the completion of the study treatment period. In addition, information regarding anticancer treatment(s) and interventions as well as survival following confirmed disease recurrence will also be collected. This period will last for a total of 5 years or death, whichever occurs earlier.

Intervention

ADXS11-001 (1 x 10 9) CFU or placebo IV infusion over 60 minutes.
1 dose administered every 3 weeks (Weeks 1, 4 and 7) for 3 doses (Prime Phase), thereafter, subjects will receive 1 dose every 8 weeks (Weeks 15, 23, 31, 39, and 47) (Maintenance Phase)

AND
80 mg Trimethoprim/ 400 sulfamethoxazole (or 500 mg ampicillin) or placebo administered once daily for 7 consecutive days or ampicillin administered four times daily for 7 consecutive days

The 7-day courses of antibiotics or placebo are given after each scheduled infusion of ADXS11-001, and a 6-month course of antibiotics or placebo is given during the Lm surveillance monitoring period.

Please also refer to table 5 in the protocol (page 31)

Study burden and risks

Participation in this study will take a maximum of approximately 6 years. This duration will include a 1-year treatment period and a 5-year follow-up period which will include a study visit approximately every 3 months for the first year and then every 6 months for the remaining 4 years. All visits to the hospital will last between 2 and 6 hours. The subject will also receive a phone

calls every 3 months during the Post-Disease Recurrence phase

The following procedures will be done during the different visits:

19x full physical examination, 3x focused physical examination, 2x check medical history, demographics, surgical history, 10x vital signs measurement, 17x pelvic examination, 10x performance status assessment, 22x blood drawn, 9x urine pregnancy test (for women of childbearing potential), 18x completion of quality of life forms, 8x administration of pre-medications, 8 x infusion of IMP, 8x IV infusion of hydration fluid before each treatment 8x 7 day course of antibiotics (after each IMP infusion), 17x CT scan of chest and abdomen and MRI of pelvis, 6 month antibiotic course during Lm surveillance monitoring, 12x blood draw during Lm surveillance monitoring.

during all visits concomitant medication use is discussed as well as (serious) adverse events

The most common side effects with the use of ADXS11-001 are: Headache, Chills, Fever, Nausea, Vomiting, Feeling physically or mentally exhausted (Fatigue), Low hemoglobin blood count (Anemia), Pain (abdominal).

Please refer to the patient information leaflet and investigator Brochure for less common side effects of the IMP and other medications used in this study as well as Risks Associated With Study Procedures.

Contacts

Public
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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Subjects with:
o Histological diagnosis of squamous cell, adenocarcinoma or adenosquamous carcinoma of the cervix who have undergone definitive therapy with a curative intent;• Subjects may have:
o Stage IB2, IIA2, IIB with any of the following pelvic lymph node metastases criteria:
- Biopsy proven pelvic node(s)
- 2 or more positive nodes by MRI/CT >=1.5 cm shortest dimension
- 2 or more positive pelvic nodes by PET with standard uptake value >=2.5
OR
o All Stage IIIA, IIIB, IVA
OR
o Any FIGO stage with para-aortic lymph node metastases criteria (defined by 1 of the following):
- Biopsy proven para-aortic node(s)
- 1 or more positive para-aortic node(s) by MRI/CT >1.5 cm shortest dimension
- 1 or more positive para-aortic node(s) by PET with SUV >2.5;Subjects must have received definitive therapy with curative intent, which consist of at least 4 weeks of treatment with cisplatin and a minimum of 40 Gy external beam radiation therapy (EBRT). NOTE: Brachytherapy is permitted.;• Subjects must be:
o Age 18 years or older
o GOG performance status 0 - 1
o ANC >=1000 x 109/L
o Platelets >=75 x 109/L
o Bilirubin <=1.5 x ULN
o AST or ALT <=2.5 x ULN
o Serum creatinine or measured creatinine clearance <=1.5 xULN
o Toxicities resulting from definitive therapy must resolve to <=Grade 1 prior to randomization, with the exception of peripheral neuropathy (sensory and motor) which must resolve to <=Grade 2.

Exclusion criteria

• Subjects who have not achieved disease-free status (e.g. no evidence of measurable disease or non-measurable disease per RECIST 1.1) after completion of CCRT administered with curative intent.
• Subjects with FIGO stage IVB
• Histologies other than described above (neuroendocrine cancers are excluded)
• Subjects who have undergone a previous hysterectomy defined as removal of the entire uterus or will have a hysterectomy as part of their initial cervical cancer therapy NOTE: Women who have had a partial/subtotal hysterectomy are eligible to participate in the study.
• Has implanted medical device(s) that pose a high risk for colonization and/or cannot be easily removed (e.g., prosthetic joints, artificial heart valves, pacemakers, orthopedic screw(s), metal plate(s), bone graft(s), or other exogenous implant(s)). NOTE: More common devices and prosthetics which include arterial and venous stents, dental and breast implants and venous access devices (e.g. Port-a-Cath or Mediport) are permitted. Sponsor must be contacted prior to consenting any subject who has any other device and/or implant.
• Who are receiving, plan, or anticipate on receiving PI3K or TNF* inhibitors
• Has a contraindication (sensitivity or allergy) to trimethoprim/sulfamethoxazole and ampicillin.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	6
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Genetic modified organism
Product type:	Medicine
Brand name:	Ampicillin

Ethics review

Approved WMO Date:	27-02-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-11-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-06-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-06-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2015-004844-20-NL
ClinicalTrials.gov	NCT02853604
CCMO	NL57159.000.17