Efficiency of AV2® antiviral drug in the treatment of HPV-associated precancerous lesions of the uterine cervix: A Randomized Placebo-controlled Clinical Trial

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NCT02346227

Research Team

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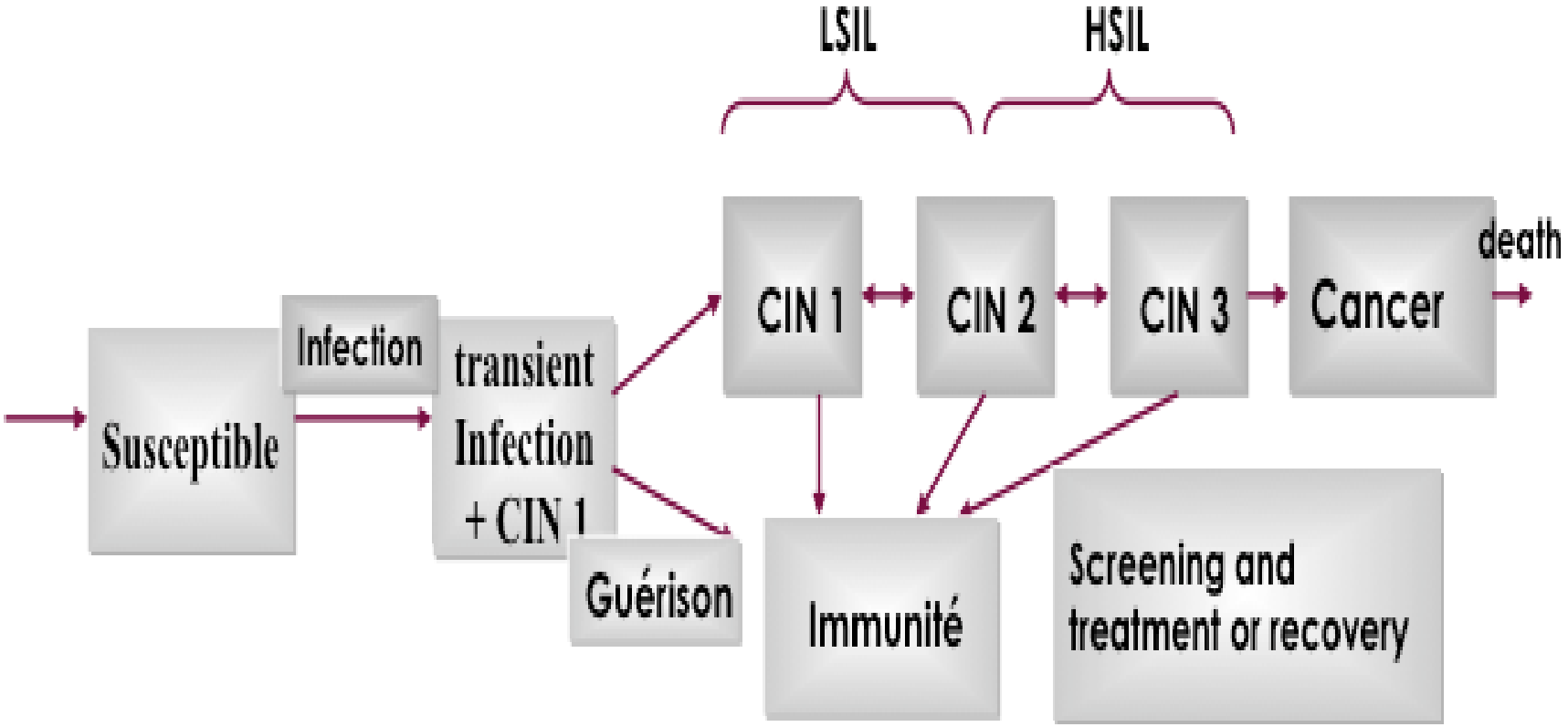
Natural history of HPV infection



Main Objective

To evaluate the clinical efficacy of Antivirus AV2® in the regression of cervical lesions related to HPV infection.

Hypothesis

The viricidal spray AV2® is more effective than placebo in the treatment of HPV-associated precancerous lesions of the cervix.

Methods

- **Study type :** randomized placebo-controlled phase 3 clinical trial.
- **Sites**:
  - Centre Hospitalier du Mont-Amba (University of Kinshasa)

Population

- **Women aged 25 and over:**

•no upper limit (first screening contact for the majority of women).

•not < 25 years (high HPV prevalence, spontaneous resolution after some years)

- **Inclusion criteria:**

•Sexually-active women;

•with intact uterine cervix;

•written informed consent to participate;

Investigational product: AV2®

A synergistic combination of FDA-approved organic compounds mixed in equal volumes diluted 70% in olive oil.

1a. D--carvone 2.5%
1b. L--carvone 2.5%
2. Eugenol 2.5%
3. Trans-Geraniol 2.5%
4. Cis/Trans-Nerolidol 5.0 %
5. D-Glucose 15.0 %
6. Olive Oil 70.0 %

AV2®

- highly effective broad-spectrum anti-viral effect.
- deactivates the HPV virus outside the cell by preventing endocytosis. (e.g. Parvo, HSV Clinical Trials)
- possibly stops exit new virions from basal cells without formation of new lesions
- cervical lesions can regress due to deactivation of the virus.

• Results in:

  - Rapid clearing of the lesions
  - Slow shrinking of the warts

Thus, medical treatment of cervical dysplasia with AV2 could offer a minimally invasive treatment with minor morbidity and time constraints.

AV2®

- **Side effects:**

  - Orally: no side effect.
  - Topically: warming/burning
    (similar to disinfecting alcohol on very sensitive areas such as Labia minora and this for about 30-60 seconds.

- **Application: One time Spray** of AV2® directly on the cervical lesions

  - as a topical spray to the cervix while the subject is in the lithotomic position and fitted with a speculum.
  - The manual spray applicator is positioned inside the anterior of the vagina and two pumps are applied. Each pump delivers 100 microliters of the solution.

Placebo

- consists of 10% lemon (citrus limon) and 10% lime (citrus aurantifolia) essential oils in 80% olive oil.

  The oils are included to provide a fragrance

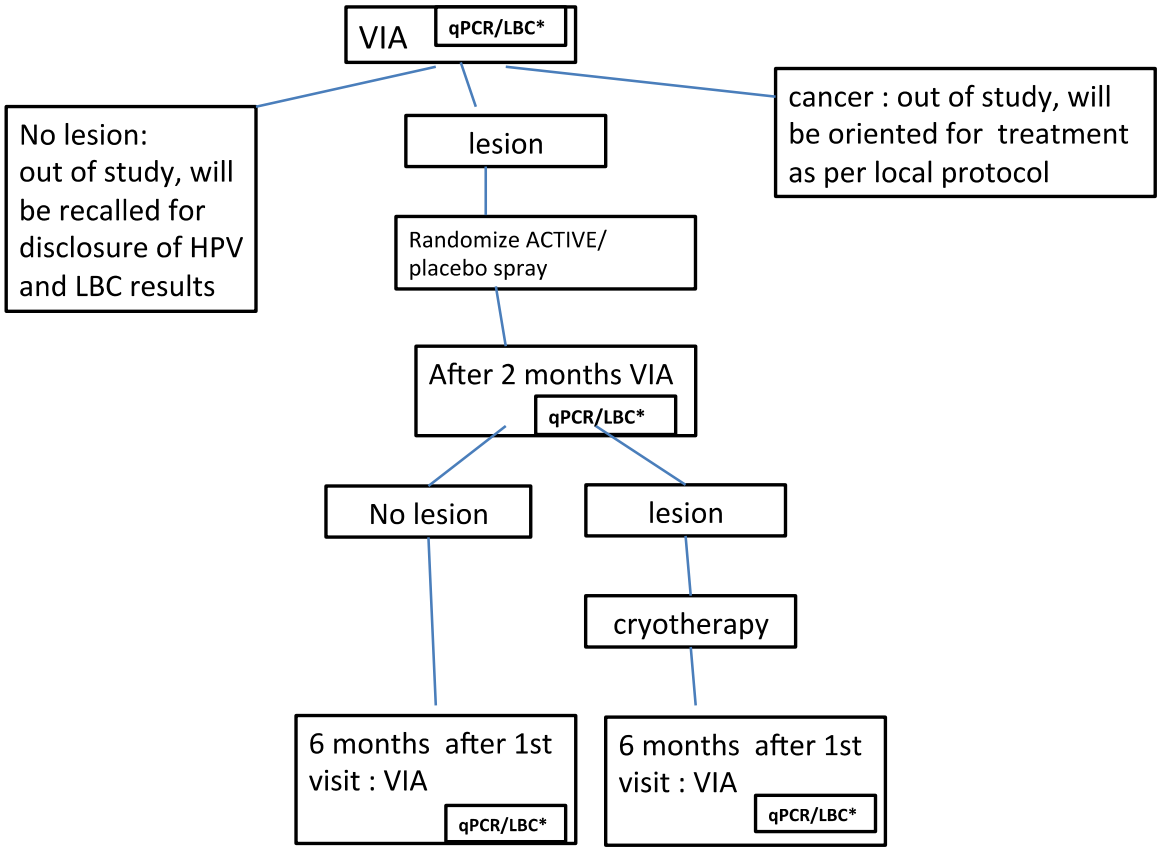
  to the placebo, similar to AV2®.

- similar appearance, identical glass container, identical labeling vs AV2®.

Mexican trial :Phase 2

- Randomized, double-blind, placebo-controlled trial comparing the clinical efficacy of AV2® and placebo over a 60-days period
- > 50% reduction for 21/28 patients (75%) in AV2® groupe vs 0% reduction in comparable placebo group.
- Failed to respond positively : 2 % of participants AV2® group versus 80% in the placebo group.

Study flowchart



* qPCR and LBC for later analysis not available at radnomisation or treatment

Screening and HPV testing

- Visual inspection with acetic acid (VIA): cervical lesions
- **ThinPrep® Pap test** (Hologic Corporation, Marlborough, MA): cytologic evaluation
- Panther system (Luminex): HPV genotyping

Assessment of outcomes

- **Primary outcome**: change in lesion size 2 months after treatment with AV2®.

- **Secondary outcomes**:
  - absence of HPV DNA at month 2,
  - changes in HPV viral particle load at month 6,
  - number of participants with adverse effects.

Adverse effects

- Adverse effect (AE) : unfavourable and unintended sign, symptom, or disease temporally associated with the use of the virucide administered.

Ethical issues

Regulatory Authorities and Ethical Review Committee

- IRB approval: OK

  - UZA Ethisch comité : OK
    Belgisch Registratienummer: **B300201423066**

  - Kinshasa School of Public Health EC: OK
    Registration Number: **ESP/CE/019/14**

- ClinicalTrials.gov registration: **NCT02346227**

Funding

- VLIR-UOS: ZRDC2014MP083

Insurance

No-fault liability insurance: taken by the Sponsor to cover study site.

Status

- Start Date: 2nd july 2015
- Status: Ongoing
- Screened: 942
- Recruited: 179 women
- Adverse Events or SAEs: None
- Compliance to control visits: good (only 122 out of 143)

Thank You