

Oncothermia in HIV Positive and Negative Locally Advanced Cervical Cancer Patients in South Africa



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INTRODUCTION:

The investigation of technologies which can increase cancer treatment efficacy is driven by:

- The high prevalence of Human Immunodeficiency Virus (HIV) and cervical cancer in South Africa^{1,2}
- The growing concerns that HIV infection and certain Antiretroviral Therapies (ARTs) increase the sensitivity to radiation therapy (RT) and chemotherapy,^{3,4,5}
- The economic impact of cancer on the already over-burdened healthcare system and economy in Africa⁶

AIM: To investigate the clinical and economic benefits of the addition of oncothermia to standard treatment protocols for HIV positive and negative locally advanced cervical cancer patients in public healthcare in South Africa and to study the radiosensitising effects of the technology on a cellular level in these patients.

OBJECTIVES

PRIMARY:

Evaluate the effect of the addition of oncothermia on:

- Local disease control at 6 months (assessed by PET scans);
- Progression free survival at 12, 18 and 24 months;
- Overall survival at 2 years (and the cause of death)

SECONDARY:

- Evaluate adverse effects that can be directly attributed to oncothermia
- Evaluate the effects of oncothermia on tolerability and toxicity of the prescribed treatments
- Evaluate the economic impact of the addition of oncothermia in public healthcare (based on quality adjusted life years)
- Evaluate the effect of the addition of oncothermia on the quality of life of patients
- To evaluate the effect, if any, of oncothermia treatments on the HIV disease status of HIV positive and negative patients:
 - CD4 count
 - HIV viral load
 - Concurrent AIDS-defining conditions
- To describe cervical cancer recurrence patterns in both groups

RADIOBIOLOGY RESEARCH

- To evaluate thermoradiosensitivity by measuring DNA damage (double strand breaks), using Micronucleus (MN) assays, in response to ionising radiation combined with oncothermia before and after completing treatment in HIV positive and negative patients.
- To investigate the molecular markers for thermoradiosensitivity. This will be done by comparing gene expression profiles of cells extracted from biopsies of thermoradiosensitive and thermoradioresistant tumours. Gene profiling of tumour samples will be used to identify potential molecular markers in the tumour cells which are associated with increased response or with resistance to radiochemotherapy combined with oncothermia. This may eventually result in individualised treatment schedules and may be useful in separating patients with and without recurrence following oncothermia.

METHODOLOGY:

Study Type: Phase III randomised clinical trial. **Sample:** 236 HIV negative and HIV positive stage IIb-IV locally advanced cervical cancer patients will be recruited. This is based on the estimated required sample size for a two-sample comparison of survivors' functions at two years. The statistical significance is defined as a two-sided alpha < 0.05 for a log-rank test, with a constant Hazard ratio of 0.5693, a statistical power of 90%, a 15% withdrawal rate and an estimated 140 events. We anticipate at least 50% of recruited participants will be in Stage III of the disease and around 30% of these participants will be HIV positive. **Randomisation:** The participants will be divided into a control group (N=118) and a study group (N=118) and the sampling method used will be stratified random sampling (stratum: HIV status). In each stratum there will be a random selection in order to ensure equal numbers of HIV positive and HIV negative women in each group. **Location:** The trial will be conducted at the Charlotte Maxeke Johannesburg Academic Hospital, Gauteng, South Africa. **Treatment:** Participants from both groups will receive 3 doses of cisplatin (80mg/m²), external beam radiation (50Gy administered over 25 fractions of 2Gy) and 3 HDR intracavitary brachytherapy treatments of 8Gy each. The study group will receive two 60 minute oncothermia treatments per week during the external beam radiation therapy. **Duration:** The study is scheduled to start in January 2013 and the recruitment is expected to take two years. Participants will be monitored for two years after completion of the treatment protocols. The total study duration is therefore expected to be 4 years.

EXPECTED OUTCOMES:

- The addition of oncothermia to standard treatment protocols will result in improved local disease control and two year survival rates in HIV positive and negative locally advanced cervical cancer patients without increasing the treatment toxicity.
- We hypothesise that the addition of oncothermia will result in a reduction in healthcare costs associated with the treatment of cervical cancer. This would significantly benefit the already over-burdened healthcare system and economy of South Africa and other developing countries.

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