RADICAL Trial – RADiotherapy or Imiquimod in Complex lentigo mALigna

A randomised controlled multicentre trial of imiquimod versus radiotherapy for lentigo maligna (LM) when staged surgical excision with 5mm margins is not possible, is refused, or fails

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Background and Rationale
To date, there have been no prospective studies or randomised controlled trials (RCT) conducted to form the basis of any recommendations for the management of LM. LM is difficult to diagnose and to treat, which translates to high recurrence rates and high morbidity. Surgery by staged excision is recognised worldwide as the gold standard treatment as it provides a definitive pathology report that rules out the risk of invasive melanoma. Surgery however may also result in major disfigurement to the face and neck. Medical treatments have been proposed to address these recurrences and cosmetic issues treating a larger field. Currently radiotherapy is sometimes used for the treatment of LM when surgical margins are inadequate or surgery is not possible, however only Level 3 evidence supports its use. Although imiquimod use is becoming increasingly common worldwide its efficacy has only been reported through case series.

In order to establish the optimum management for these patients and to accurately evaluate these treatments a prospective randomised controlled clinical trial is required.

Study Objectives
To compare the rate of LM treatment failure at 6 months (as determined by systemic biopsy) and at 12 and 24 months (as determined by Dermoscopy) following treatment with topical imiquimod 5% cream or radiotherapy as non-surgical treatment in patients who are unable to undergo surgery, refuse surgery or have failed surgery (incomplete excision or excision margins less than 1mm). Treatment failure includes both the recurrence and persistence of LM, and is defined as the presence of LM cells within the original field of treatment confirmed by histopathology.

Study Hypothesis
That topical imiquimod is superior to radiotherapy and will result in significantly improved cure rates and cosmesis.

Study Design
Multi-centre, randomised, controlled, open-label, 2-arm parallel Phase III trial.
**Schema**

**Patient Accrual**
The pilot phase of this study will see 80 participants recruited to the study in 3 years from sites across Australia. Total patient accrual for this trial will be 266 patients accrued over five years.

**Inclusion Criteria**
Patients may be included in the study only if they meet all of the following criteria:
- Aged 18 years or older.
- A biopsy-proven LM. This includes treatment failures of LM that are diagnosed as biopsy-proven LM.
- LM that is in a location amenable to treatment with imiquimod and radiotherapy.
- Willing and able to comply with study requirements.
- Written informed consent.

**Exclusion Criteria**
Patients will be excluded from the study for any of the following reasons:
- Invasive melanoma.
- Medical or psychiatric condition that compromises the ability of the patient to complete protocol treatment or follow-up assessments.
- Patients who are pregnant or lactating. Women of child bearing potential must have a confirmed negative urine pregnancy test at study entry.
- Life expectancy of less than 2 years.
- Radiotherapy sensitivity syndrome.