EXCISE – EXcisional treatment Comparison for In Situ Endocervical adenocarcinoma

Excisional treatment in women with cervical adenocarcinoma-in-situ (AIS): a prospective randomised controlled non-inferiority trial to compare AIS recurrence after loop electrosurgical excision procedure (LEEP) to cold knife cone biopsy (CKC).

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Background and rationale

- AIS is the precursor to invasive cervical adenocarcinoma
- AIS on cervical cytology and/or cervical biopsy → a diagnostic excisional procedure to exclude invasive adenocarcinoma
- CKC or LEEP?
- There are NO prospective randomised studies to inform practice

Loop electrosurgical excision procedure (LEEP)

Against LEEP

- Incomplete excision
- Thermal artefact
- Greater risk of a positive endocervical margin

In favour of LEEP

- Avoid general anaesthesia
- Outpatient setting
- Lower morbidity, and reduced rates of obstetric complications

EXCISE

- Aim: to determine if the treatment of cervical AIS by LEEP is non-inferior to CKC with regard to 5-year recurrence rate in women managed conservatively
- Hypothesis: LEEP will not be inferior to CKC with regard to AIS persistence and recurrence in conservatively managed women
- Primary objective: to compare the 5-year recurrence rate of cervical AIS following LEEP to that after CKC, in conservatively managed women.

Secondary Objectives

- Margin status and specimen dimensions
- Early and late complications
- QoL
- Cost-effectiveness

EXCISE

- Study population:
  - women aged 18 to 45 years diagnosed with AIS on cervical screening and/or colposcopically directed biopsy who are to receive excisional treatment
- Inclusion criteria:
  - Lesion amenable to single pass excision (serial endocervical excisions including 'top-hat' will not be permitted in accordance with ASCPP recommendations)
  - Patients able to comply with follow-up evaluations and complete QOL assessments

Exclusion Criteria

- Previous excisional or ablative treatment
- Cytological or clinical suspicion of invasion
- On immunosuppressive agents
- Pregnancy
- Lesion considered unsuitable for single pass excision by treating specialist

Procedures

- Randomization:

  Randomization will be 1:1 (CKC: LEEP). Sequence generation will be by computer with no blocking or stratification.

- Blinding:

  Study investigators and participants will not be blinded to the intervention. Those conducting data analysis will be blinded to the intervention.

Sample Size

- Estimated using a 2 group test of non-inferiority of proportions
- Primary end point is the AIS recurrence rate at 5 years and the comparison will be between CKC and LEEP, based on a 1-sided test for non-inferiority
- Assumes an 8% rate of AIS recurrence at 5 years after CKC, and a 5% non-inferiority margin (upper 95% confidence rate of AIS recurrence of 13% is still within the non-inferiority margin).
- Sample size needed is 730 (365 per group). Assuming a 10% drop-out rate, a total sample size of 810 participants (405 per group) would need to be randomised. (One-sided Type I error is set at 5% with 80% power.)

Questions??

Or can contact Dr Paul Cohen [Paul.Cohen@sjog.org.au] for more information

Protecting against sources of bias

- The requirement for a single-pass specimen will limit surgical performance bias.
- Each site to have a lead pathologist who will perform histopathological review of all procedures conducted at their site.
- Detection bias: possible central pathology review by a histopathologist who will be blinded to the original treatment allocation. This strategy will limit detection bias.
- Ascertainment bias: incidence of long term outcomes including obstetric and neonatal morbidity will be determined by Data Linkage utilising a number of national and state health information registries.