Stage IB1 (2-4 cm) Cervical cancer treated with Neoadjuvant chemotherapy followed by fertility sparing Surgery (CONTESSA)

Dre Marie Plante

Neo-Adjuvant Chemotherapy and Conservative Surgery in Cervical Cancer to Preserve Fertility (NEOCON-F)

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Preliminary Proposal

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Dr Frédéric Amant
CONTESSA / NEOCON-F

CONTESSA

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Study Coordinator CGOA/NCI:
Nienke van Trommel
Historical background

🔗 Contessa was developed out of the cervical cancer brainstorming day (Melbourne 10/2014)
🔗 Proposal was put on hold 6/2016 (funding issues)
🔗 Proposal reactivated 10/2017 (PMH Consortium)
🔗 Recent opportunity to join forces with NEOCON protocol (Netherlands)
Background

upertino radical trachelectomy: “standard of care” for the management of early-stage cervical in women who wish to preserve fertility (NCCN guideline 2017)
- Validated for lesions < 2 cm

Limited data in the literature regarding the optimal management of women with larger size lesions (2-4 cm) who wish to preserve fertility
Background

NACT followed by FPS

- NACT been shown to be effective in reducing the size of cervical cancer (70%)
- High rates of fertility preservation (80%)
- Limited data in the literature (few series / small #); no standardized approach
Specific Hypothesis

Neoadjuvant chemotherapy (NACT) in node-negative women with stage IB1 (2-4 cm) cervical cancer will enable fertility preserving surgery without compromising oncologic outcome in good chemo-responders.
Primary Objective #1

To evaluate the safety (PFS) of NACT in women with node negative, stage IB1 cervical cancer with lesions measuring 2-4 cm
Primary Objective #2

To evaluate the rate of fertility preserving surgery (FPS) following neoadjuvant chemotherapy (NACT)
Secondary Objectives

- Chemotherapy related adverse events / safety
- Surgical complication rate of FPS
- Requirement for adjuvant radiation therapy (trimodality treatment)
- Requirement for definitive hysterectomy
- Quality of Life
- Ovarian function, rates of pregnancy and obstetrical outcomes
Inclusion criteria

- Invasive cervical cancer
  - adenocarcinoma, adenosquamous or squamous
- LVSI allowed
- Grade 1, 2 and 3
- Stage IB1 measuring 2-4 cm (clinical exam and MRI)
- Age ≤ 40
- No evidence of Premature Ovarian Failure
- Desire to preserve fertility potential
Exclusion criteria

-Uterine corpus invasion or extracervical disease (based on MRI)
-Lymph node metastasis
  -Pre-study laparoscopy to exclude LN mets
    • sentinel lymph node mapping
    • pelvic lymphadenectomy
CONTESSA

Cervical cancer size 2–4 cm
MRI - corpus negative, node negative
Laparoscopy - pelvic lymph node dissection / SLN mapping, node negative
Pathology - squamous, adenosquamous or adenocarcinoma
LVSI - negative or positive
Patient age ≤ 40 years
Desirous of preserving fertility
No evidence of premature ovarian failure (Baseline AMH, FSH, E2 levels)

NACT x 3 cycles
Carboplatin / Paclitaxel

After 3 cycles
Clinical assessment and pelvic MRI

No response / progression
Chemoradiation or radical hysterectomy

Complete response
Simple Trachelectomy / Conisation

Partial response residual tumor < 2 cm
Simple Trachelectomy / Conisation

Suboptimal response residual tumor ≥ 2 cm
Chemoradiation or radical hysterectomy

Adjuvant chemoradiation or radical hysterectomy
Positive margins or < 5 mm margin
Stromal involvement in outer 1/2 (?)
Trial design

- **Screening phase:** Laparoscopy
  - SLN mapping + pelvic LND
  - Await final pathology analysis

- **Study phase (If LN-):** NACT x 3 cycles
  - Weekly Taxol 80 mg/m² & Carbo AUC2
  - Q3 weeks Taxol 175 mg/m² & Carbo AUC6

- **Pelvic MRI** and clinical exam
  - If residual tumor < 2 cm

- **Fertility Preserving Surgery (FPS)**
  - Large cone / simple trachelectomy
Primary endpoints

☞ Recurrence rate/PFS at 2 years (#1)
☞ Intact functional uterus following NACT and FPS (#2)
Secondary endpoints

- Response rate to NACT
- Adverse events and safety
- Surgical complication rate
- Rates of definitive hysterectomy
- Requirement for adjuvant radiation therapy (trimodality treatment)
- QOL: EORTC QLQ C30 and QLQ CX 24
- Disease Outcomes: PFS at 2 years
- Ovarian function (FSH, estradiol, AMH)
- Pregnancy rates and obstetrical outcomes
Statistical analysis

 Phase II study
 Prospective, multi-center, international trial
Statistics: PRELIMINARY

- **N=119** patients
- **Expected response rate to NACT: 75%**
  - 90 patients should proceed to FPS
- **First phase of accrual: 40 patients**
  - At least 27 must have responded
- **Second phase of accrual: 79 patients**
  - At least 83 must have responded
Safety: defined as number of recurrences within two years in the group receiving FPS (7% recurrence rate expected)

Patients will be monitored continuously in a Bayesian manner and stopping rules will apply when the percentage of recurrences exceeds 12% at two years.
Translational research

Assessment of **tumor response**

- Circulating tumor DNA (ctDNA) (PMH)
- Hypermethylated DNA (Netherlands)
Funding

PMH Consortium
- Per case funding for Canadian patients
- Data collection and data monitoring

Netherlands (CGOA/NCI)
- Per case funding for Dutch patients
- Data collection and data monitoring

Other groups
- Will have to secure own funding
Summary

- Feasible study
- Count on international collaboration
- Will provide solid data as to the safety of this approach and standardize the procedure
- In the process of finalizing the “merging” of the 2 protocols