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

Marie Plante (NCIC)

Jeffrey Goh & Vivek Arora (ANZGOG)

GCIG Meeting Tokyo – November 2015

Specific Hypothesis

- Neoadjuvant chemotherapy (NACT) in node-negative women with stage IB1 (2-4 cm) cervical cancer will enable fertility preservation surgery without compromise in tumour control in good chemo-responders

Primary Objective

- To estimate the rate of fertility preserving surgery in women with node negative, stage IB1 cervical cancer measuring 2-4 cm who receive neoadjuvant chemotherapy (NACT)

Secondary Objectives

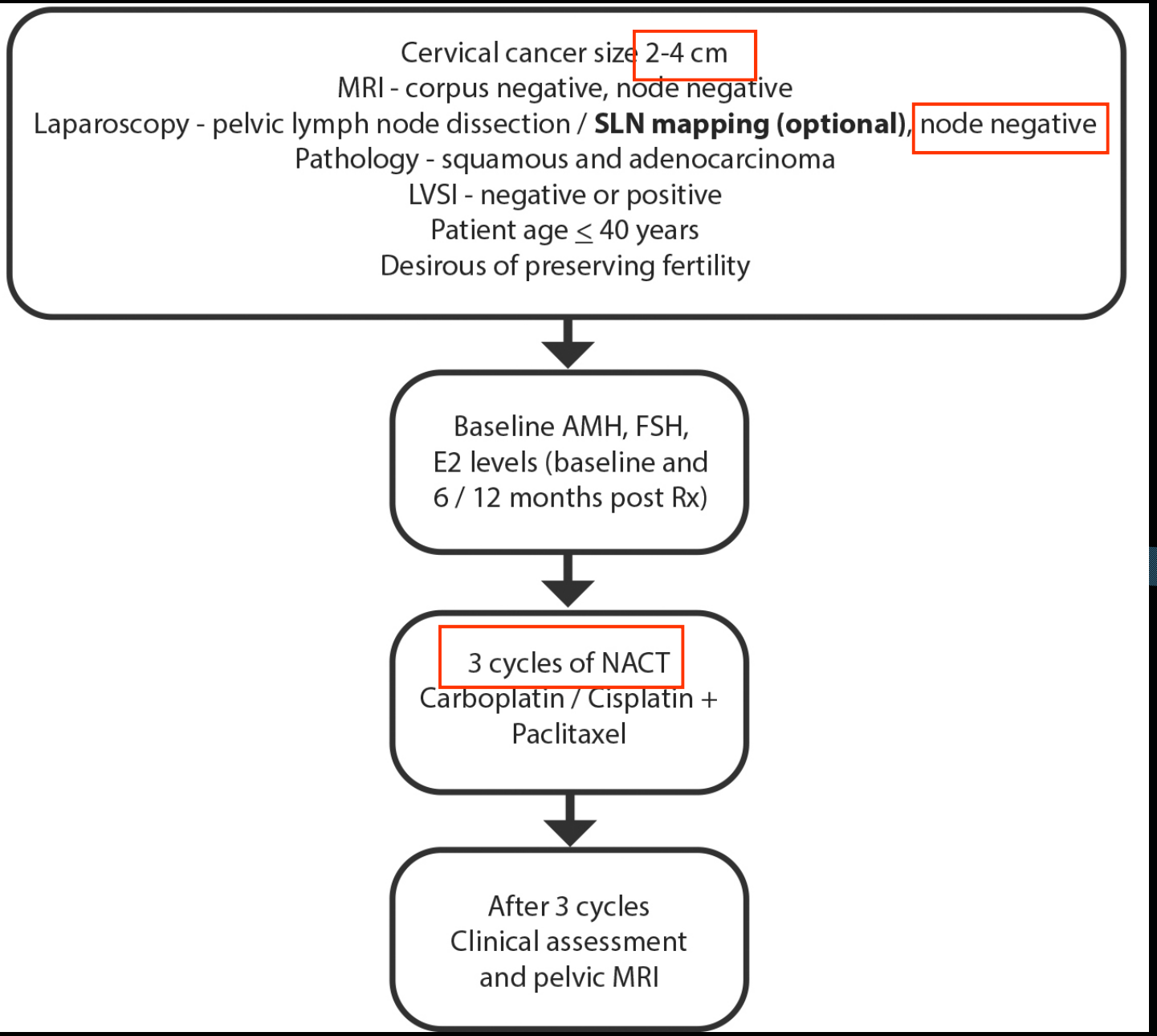
- Chemotherapy response rate
- Chemotherapy related adverse events / safety
- Surgical complication rate
- Requirement for adjuvant radiation therapy (trimodality treatment)
- QOL
- Disease outcomes
- Ovarian function, rates of pregnancy and obstetrical outcomes

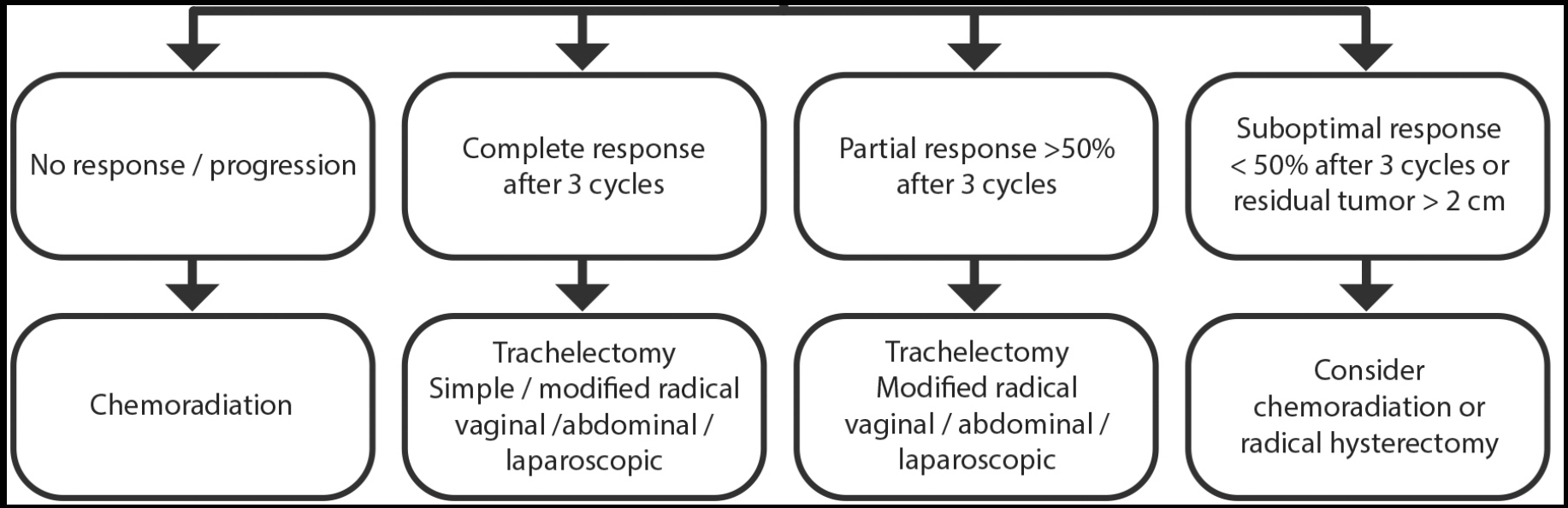
Inclusion criteria

- 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
- Premenopausal status defined by FSH, estradiol and anti mullerian hormone (AMH) levels
- Desire to preserve fertility potential
- PET CT as per standard of practice

Exclusion criteria

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


Cervical cancer size 2-4 cm
MRI - corpus negative, node negative
Laparoscopy - pelvic lymph node dissection / **SLN mapping (optional)**, node negative
Pathology - squamous and adenocarcinoma
LVSI - negative or positive
Patient age ≤ 40 years
Desirous of preserving fertility
Baseline AMH, FSH, E2 levels (baseline and 6 / 12 months post Rx)
3 cycles of NACT
Carboplatin / Cisplatin + Paclitaxel
After 3 cycles
Clinical assessment and pelvic MRI



Adjuvant chemoradiation
(or radical hysterectomy)
Positive margins
Stromal involvement in outer 1 / 2
≥ 5 mm stromal invasion
< 10 mm margin

Primary endpoint

- Rate of fertility sparing surgery (simple or radical trachelectomy) with an intact uterus and without the need for adjuvant radiation therapy

Secondary endpoints

- Response rate to NACT
- Adverse events (CTC AE V 4.0) 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: DFS and OS
- Ovarian function (FSH, estradiol, AMH)
- Pregnancy rates and obstetrical outcomes

Statistical analysis

- The treatment would be considered as
  - **successful** if its **fertility preservation rate** is **50% or higher** (H0) and
  - **not successful** if its fertility preservation rate is **35% or lower** (H1)

Statistical analysis

- Enrol 75 node-negative patients and declare the treatment successful if 32 or more patients had their fertility preserved
- Alpha level (one-sided): 0.10
- Power of the study: 0.91
- Duration of the study: 4 years for accrual

Statistical analysis

- Interim futility analysis
  - When 40 patients have been treated
  - The trial would be stopped if 13 patients or less have preserved fertility

Issues

- Chemotherapy regimen
  - **Taxol 175mg/m2 and Carbo AUC 6 q 3 weeks x 3**
  - Taxol 80mg/m2 and Carbo AUC 2 weekly
  - Taxol 80mg/m2 weekly and Carbo AUC 6 q3 weeks x 3
  - Issues about cisplatin ?

Issues

- Types of fertility-preserving surgery
  - **Simple trachelectomy/cone** in complete or optimal (< 3mm residual) chemo-responders
  - **Modified radical trachelectomy** in sub-optimal chemo-responders (> 3mm residual)

Funding

- NCIC-ANZGOG : lead groups
  - Study to be presented at the upcoming executive NCIC-CTG meeting in November 2015
  - ANZGOG also looking for funding sources

Collaboration

- Survey seeking interest from GCIG cooperative groups and CCRN