Cervix cancer committee

SENTICOL III: International prospective validation trial of sentinel node biopsy in cervical cancer

A Gynecologic Cancer interGroup (GCIG) trial, lead by the GINECO

F Lecuru, M Leitao, P Mathevet, M Plante.

Advances and Concepts in Cervical Cancer Trials

A Road Map for the Future

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and On behalf of the participants of the Gynecologic Cancer InterGroup Cervix Cancer brainstorming day

Objective: Cervical cancer is responsible for more than a quarter of a million deaths globally each year, mostly in developing countries, making therapeutic advances in all health care settings a top priority. The Gynecologic Cancer InterGroup (GCIG) is a worldwide collaboration of leading national research groups that develops and promotes multinational trials in gynecologic cancer. In recognition of the pressing need for action, the GCIG convened an international meeting with expert representation from the GCIG groups and selected large sites in low- and middle-income countries.

Methods: The focus was to develop a consensus on several concepts for future clinical trials, which would be developed and promoted by the GCIG and launched with major international participation. The first half of the meeting was devoted to a resume of the current state of the knowledge and identifying the gaps in need of new evidence, validating control arms for present and future clinical trials and identifying national and international barriers for studies of cervix cancers. The second half of the meeting was concerned with achieving consensus on a path forward.

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Objectives

- Main objective:

« co-primary » disease free survival and health related quality of life

  - non-inferiority of SLN biopsy vs lymphadenectomy for DFS
  - superiority of SLN biopsy for QoL

The hypothesis is that SLN biopsy alone provides similar survival and better quality of life.

- Secondary objectives:
- **- Outcome of pN1 patients according to the size of metastasis and treatment (isolated tumor cells and micrometastases),**
- **- Evaluation of mapping with indocyanine green (ICG),**
- - Surgical morbidity and mortality,
- - Longitudinal and other dimensions of health related Quality of life.
- - Positive and negative predictive values of SLN biopsy.
- - Overall survival.
- - Recurrence free survival.
- A cost analysis will be developed in some countries.
- A tumor bank will be built by collection of cervical specimen. A translational research will be performed in a subsequent study to investigate predictors of recurrence in low risk patients.

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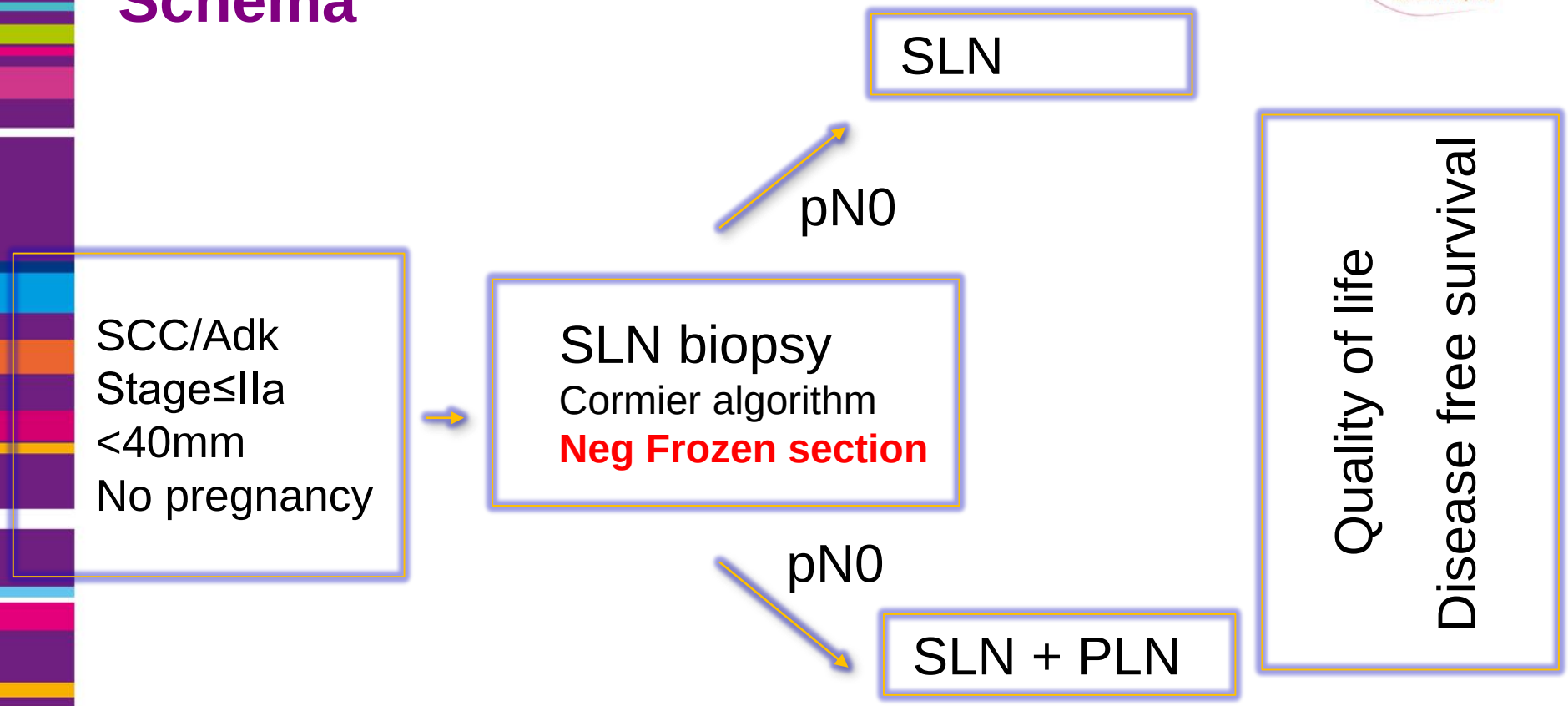
Schema



Randomized study

Surgical & pathological quality assurance

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❖ Inclusion criteria:

- Squamous or adenocarcinoma of the cervix (proven by biopsy or cone biopsy)
- Stage Ia1 with lymphovascular emboli to IIa1 (clinical stage)
- Maximum diameter ≤40mm on MRI
- No suspicious node on pelvic and abdominal MRI (small axis ≥ 8-10mm and morphologic criteria)
- Informed consent given

❖ Exclusion criteria:

- Age <18 years
- Pregnancy
- Previous pelvic of abdominal cancer
- Previous chemo and/or radiation therapy for the cervical cancer
- Allergy to blue dye, isotope or Indocyanine green

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Statistics

- **1-DFS**
- With a 3 years-disease free survival of 85% to demonstrate a non-inferiority of SLN biopsy vs SLN biopsy + lymphadenectomy with a non-inferiority margin of 5% (80 vs 85%, HR = 1.373). With a unilateral alpha error of 5%, and a power of 80%, 900 patients in 3 years, with 4 years of follow-up should be included to observe the required 219 DFS events. An interim analysis is planned when at least 110 events will be observed to reject H0 or H1 using O Brien Fleming and alpha spending function.

- **2-HRQoL**
- We target 3 HRQoL dimensions global health, pain and physical functioning of EORTC QLQC 30 compared at 3 years.
- To demonstrate a superiority of at least one of the 3 targeted dimensions without significant deterioration in at least one with a minimal important difference in mean score of at least 5 points (SD: 20), and a bilateral alpha type one error of 0.015 (Bonferroni adjustment it would be required to have 815 patients with available HRQoL scores to reach 85% statistical power.

- **950 patients have to be randomized**
- **An international collaboration is requested**

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Participating & interested groups

- AGO
- NOGGO
- DGOG
- G-GOC
- MITO
- MANGO
- NCIC
- And….

- Patients association « 1000 femmes – 1000 vies »

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Thank you

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Agenda

- GCIG June 2016
  - Final acceptation of the study and validation of the design
- June to sept 2016
  - Protocol writing
- Sept 2016
  - Full protocol submitted to INCa for funding
- Nov – dec 2016
  - Response of INCa
- 2017 KICK-OFF meeting ?