LEIDEN UNIVERSITY MEDICAL CENTER

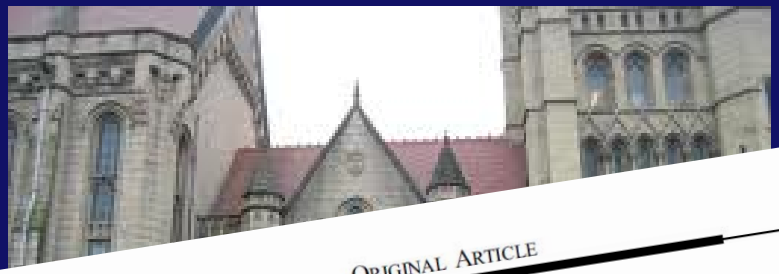
GCIG Endometrial Cancer Clinical Trials Planning Meeting

Welcome to Leiden!

Carien Creutzberg

Endometrial Cancer CTPM 2006

MANCHESTER 1824
The University of Manchester



ORIGINAL ARTICLE

Endometrial Cancer State of the Science Meeting

Henry C. Kitchener, Edward L. Trimble,†*
and for the Endometrial Cancer Working Group of the Gynecologic Cancer Intergroup

Abstract: There is a pressing need to improve our understanding of endometrial cancer (EC) and uterine carcinosarcoma and to develop new treatment strategies to improve outcomes. In recognition of this, a State of the Science meeting on EC was held last November 28 and 29, 2006, in Manchester, United Kingdom. The meeting was cosponsored by the National Cancer Research Institute (UK), the National Cancer Institute (US), and the Gynecological Cancer Intergroup.

The objectives of the meeting were as follows:

1. To review current knowledge and understanding of EC and its treatments.
2. To identify key issues for translational research and clinical trials.
3. To identify the most important trials for women with endometrial carcinoma and uterine carcinosarcoma, both those already underway or to be done, for which the Gynecological Cancer Intergroup might facilitate international cooperation.

Key Words: Endometrial cancer, Clinical trials, Translational research

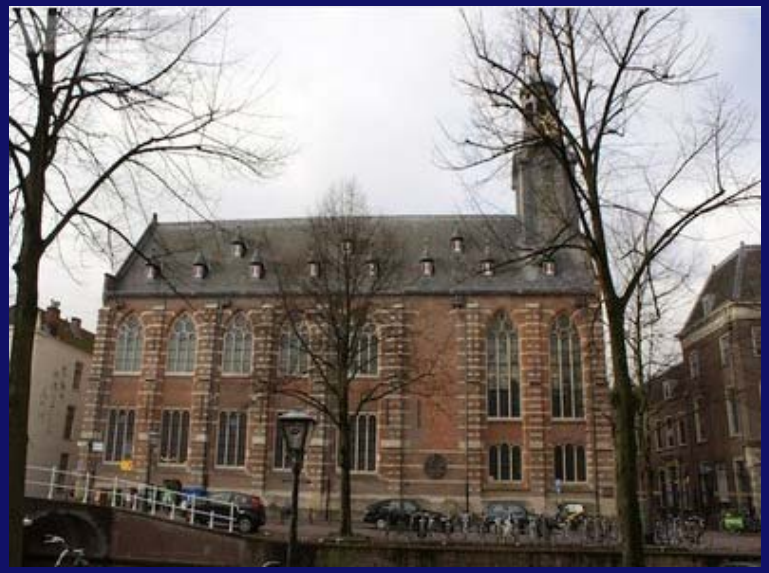
(*Int J Gynecol Cancer* 2009;19: 134–140)

Endometrial cancer (EC), the second most common gynecologic cancer worldwide, has now become the most common gynecologic cancer in developed countries. Its rising incidence is related to increasing life expectancy, tamoxifen use, and the epidemic of obesity. The last is also responsible for comorbidity, notably adult-

(US), and the Gynecological Cancer Intergroup (GCIG). A multidisciplinary group of 75, drawing on surgeons, gynecologic oncologists, radiation (clinical) oncologists, medical oncologists, pathologists, translational scientists, and patient advocates from 18 countries and representing 14 trial groups attended.

The objectives of the meeting were as follows:

Sponsors



GYNECOLOGIC CANCER INTERGROUP

An Organization of International Cooperative Groups for Clinical Trials in Gynecologic Cancers

Nucletron
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DUTCH GOG
Dutch Gynaecological Oncology Group

Program

GCIG Endometrial Cancer Clinical Trials Planning Meeting
Chairs: Henry Kitchener and Carien Creutzberg

8:30 h	**Welcome, Objectives** Carien Creutzberg
8:40 h	**Review of 2006 Endometrial State of Science Meeting** Henry Kitchener
8:55 h	**Main surgical issues and ongoing trials** Fabio Landoni
9:10 h	**Report from the NCI Lymphadenectomy Trial Working Group** Gillian Thomas
9:15 h	**Review of systemic therapy and radiation issues and ongoing trials** Melanie Powell
9:30 h	**Review of histological types and "lump vs split" issues** Michael Birrer
9:45 h	**Review of translational research and targeted therapy issues** Karen Lu
10:00 h	**Short report from the PORTEC3 translational research meeting** Carien Creutzberg
10:05 h	**Coffee Break**

Program

10:30 h	**Working group sessions I**
	Surgery – Chair: Michael Quinn; Rapporteur: Richard Edmonson
	Systemic therapy and RT- Chair: Gillian Thomas; Rapporteur: Carol Aghajanian
	Translational research - co-Chairs: Mike Birrer & Paul Goodfellow
	Rapporteur: Helga Salvesen
12:00 h	**Report from the working groups** I (each group 10 mins)
	Richard Edmonson; Carol Aghajanian; Helga Salvesen
12:30 h	**Lunch Break**
13:30 h	**Working group sessions II**
	Summary and priorities of key issues and concepts for new trials
14:30 h	**Tea Break I** (+ preparing reports)
15:00 h	**Report from the working groups** II (each group 10 mins)
	Richard Edmonson; Carol Aghajanian; Helga Salvesen
15:30 h	**Discussion; integration of translational and clinical issues**
	Chair: Michael Quinn
16:30 h	**Tea Break II**
16:50 h	**Consensus session** – Chairs: Henry Kitchener & Carien Creutzberg
	final discussion and consensus on 3-4 trials
17:30 h	**Closure** - transport to Holiday Inn for GCIG dinner

GYNECOLOGIC CANCER INTERGROUP

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Translational research

- Prospective markers
  - to detect high risk within early stage disease
  - no biomarker for prime time
  - Further markers need to be validated in retrospective studies prior to prospective validation/implementation studies - GOG210 or/and MoMaTEC (ENITEC)
  - Committee for evaluating evidence for proposed biomarker panel
- Predictive markers
  - no validated predictive biomarkers for targeted therapy
  - define hypotheses and biomarkers for assessment
  - evaluate reponse PET-CT (PET-MRI, f-MRI)

➢ GCIG Early Phase consortium Program

GCIG Early Phase consortium Program

- series of early phase trials
- chemo naive vs. chemo resistant
- international design
- control arm uniformly the same (carboplatin/paclitaxel)
- randomise against different agents in different countries
- dropping arms that are no good, add new arms based on biomarker hypotheses
- mandatory tissue collection and biomarker studies fully integrated
- tissue collection (FFPE of primary and metastastic nodes; blood/plasma/serum) mandatory at trial entry; tissue sampling at relapse strongly encouraged

GCIG Translational research consortium

- New approach in GCIG
- New direction from phase III collaborative trials to such early phase 1-2 trials
- Should collect update of current trials in each group
- Start with 'rolling trial approach' in endometrial cancer
- ? Approach for several tumor types eventually
- Propose concept to GCIG
- Propose to spend a GCIG November meeting 1st "brainstorming" day on this topic for all tumor sites (year after next?)

Conservative therapy trial

- Obese, overweight group (possibly randomized)
- Fertility sparing group (one arm, registry)

- Obese group: aim is to lower the rate of hysterectomies in morbidly obese patients with surgical risk factors
  - Mirena with surgery on progression (vs surgery)
  - include secondary prevention program with life style intervention (randomised?)
  - Include bariatric surgery in phase 2 program as feasibility study
  - Add Metformin? (Mirena +/- Metformin and exercise)
- Fertility sparing group: inventory of current approaches; define common approach and registry
- Sequential FFPE tissue sampling and biomarker studies
- Should be ER/PR positive

Lymphadenectomy trial

NCI working group concept

- for high-risk endometrial cancer (>15% risk)
- grade 3, not serous, not clear cell, not carcinosarcoma
- ? Grade 2 with deep invasion – PET-CT/MRI/Ca125
- strong support for SN within LA arm
- LA - node negative arm :
  - no further treatment or brachytherapy alone
- LA - node positive arm
  - RT plus chemo (common arm of GOG258 & PORTEC3)
  - or chemo alone / RT+chemo - at group's discretion
- no LA arm ("nodes unknown")
  - same as in Node+ arm
  - chemo alone / RT+chemo - at group's discretion
- ? post-Sx not high risk
- integral mandatory biomarker component

Lymphadenectomy trial

- To be further discussed in groups
- strong support for the concept and need to answer this question
- surgical group consensus on extent of LA, QA, SN
- not delay study until results from trials become available
- design best current approach and amend if clear evidence becomes available on best adjuvant therapy
- support for mandatory biomarker component

- GCIG groups to discuss the concept
- Finalize trial design

Carcinosarcoma trial

- need to have a prospective trial
- most would favor chemotherapy – and RT?
- Australian approach early stage carcinosarcoma
  - chemoradiation + adjuvant chemo phase 2 trial
- for early stage: work towards common approach and common database
- PMH: carbo/taxol with radiation (as control arm)
- separate stage I-II from advanced stage disease
- NSGO proposal for advanced disears, in combined group of high risk tumours – phase 1-2 based on amplifications

➢ proposal for endometrial group to explore trial for early stage carcinosarcoma (including biomarker studies)

Endometrial Cancer CTPM - Conclusions

- Move from traditional trials to era of biomarker directed therapy
- GCIG Translational research consortium with collaborative early phase program
- Mandatory tissue collection in GCIG trials
- Priorities for trials
  - Lymphadenectomy trial for high-risk EC
    - strongly supported, to be further developed
  - Conservative therapy trials
    - morbidly obese – fertility sparing
  - Carcinosarcoma trial for early stage
  - Biomarker studies integral part of all trials