Gynecologic Cancer InterGroup (GCIG)

Cervix Cancer Committee
Thursday, June 1, 2017, 3:00 pm – 4:30 pm
LaSalle I Room, DoubleTree Hotel, Chicago
Chair: Brad Monk Co-Chair: Antonio Casado
Harmonization Liaisons: Stonebraker/Keller (Ops), Reuss (Stats)
EORTC

• EORTC GCG 55994
EORTC GCG 55994
Randomized phase III study of neoadjuvant CT followed by surgery vs. concomitant RTX+CT in FIGO stage Ib2, Iia > 4 cm or Iib cervical cancer.

Trial setting: FIGO stage Ib2, Iia > 4 cm or Iib cervical cancer
Study Design: Randomized unblinded 2-arm randomized phase III
Sponsor(s): EORTC GCG
Planned No. of patients: 626 pts (reached in June 2014)

Other important information:
• Primary end-point: OS at 5 years → study closure foreseen at June 2019.
• Data collection and cleaning ongoing.
• No interim analysis foreseen.
• Early publications on trial and treatment characteristics (not related to efficacy):
  • Short term toxicity (presented at IGCS 2016, updated for BGCS 2017)
  • Treatment characteristics (presented at IGCS 2016, updated for BGCS 2017)
• Further planned abstracts under consideration.
EORTC GCG 55994

Randomized phase III study of neoadjuvant CT followed by surgery vs. concomitant RTX+CT in FIGO stage Ib2, Ila > 4 cm or IIb cervical cancer.
EORTC GCG 55994
Randomized phase III study of neoadjuvant CT followed by surgery vs. concomitant RTX+CT in FIGO stage Ib2, Ila > 4 cm or IIb cervical cancer.

SHORT TERM TOXICITY and PRELIMINARY RESULTS FROM EORTC 55994 COMPARING NEOADJUVANT CHEMOTHERAPY FOLLOWED BY SURGERY TO CHEMORADIATION FOR LOCALLY ADVANCED (Stage IB2-IIB ) CERVICAL CANCER


EORTC Study Coordinators: G. Kenter, F. Landoni, S. Greggi

Lisbon, IGCS, nov 2016
KGOG

- TACO
- NRG/KGOG 263
TACO

GCIG/KOG1027/TGCS2012: Randomized Phase III Clinical Trial Comparing Weekly vs Tri-weekly Cisplatin Based Concurrent Chemoradiation in Locally Advanced Cervical Cancer

N= 590. Stage IB2, IIB-IV-A
Primary end-point: OS

NCT01561586
PI: Sang-Young Ryu
Accrual of TACO 2017.05.31 = 252
• Colombia
  - Hospital Las Americas : IRB Process

• Brazil
  - Barretos Cancer Hospital : IRB Process

• USA
  - MD Anderson cancer center : IRB Process
NRG/KGOG 263 (GOG 92 Replacement)

Randomized Phase III Clinical Trial of Adjuvant Radiation vs Chemoradiation In Intermediate Risk, Stage I/IIA Cervical Cancer Treated With Initial Radical Hysterectomy and Pelvic Lymphadenectomy

Stage IA2-IB-IIA: Large, deeply invasive tumors with vascular invasion limited to the cervix after radical hysterectomy

Pelvic Radiation

Pelvic Radiation and Weekly cisplatin (CCRT)

PI = SANG YOUNG RYU
N = 534
Enrollment to date = 252
Primary Endpoint = RFS

NCT01101451
RTOG

• NRG/RTOG 0724
NRG/RTOG 0724

Stage IA2-IB2: Positive nodes, parametrial extension, positive margins after radical hysterectomy

Pelvic Radiation and Weekly cisplatin (CCRT)

Pelvic Radiation and Weekly cisplatin (CCRT) followed by carboplatin + Paclitaxel x 4 cycles

PI = Anuja Jhingran
N = 285
Enrollment to date = 154
Primary Endpoint = DFS
ANZGOG

• OUTBACK
A Phase III trial of adjuvant chemotherapy following chemoradiation as primary treatment for locally advanced cervical cancer compared to chemoradiation alone

Primary Endpoint:
Overall Survival

Planned accrual = 900
MRC-NCRI

• INTERLACE
INTERLACE – induction chemotherapy followed by standard chemoradiation vs standard chemoradiation alone in patients with locally advanced cervical cancer

Randomise

**Carboplatin AUC2 & Paclitaxel 80mg/m^2**
Weeks 1-6

**Standard CRT**

- Standard CRT : 40—50.4Gy in 20-28 fractions plus Intracavitary brachytherapy to give total EQD2 dose of 78-86Gy to point A/volume.
- Weekly cisplatin 40mg/m^2 x 5 weeks

**Follow-up**
- 3 monthly for 2 years; 6 monthly for 3 years
Current status:

Target recruitment – **770 (potential reduction to 630)**

Accrual to date (UK and Mexico) – **215**

Number of sites open – **30**

- **GICOM (Mexico)** – 30 patients recruited since opening in Feb 2016
- **MaNGO (Italy)** – 5 sites in setup

**Sponsor:** University College London
CCTG-NCIC

• SHAPE trial
A RANDOMIZED TRIAL COMPARING RADICAL HYSTERECTOMY AND PELVIC NODE DISSECTION VS SIMPLE HYSTERECTOMY AND PELVIC NODE DISSECTION IN PATIENTS WITH LOW-RISK, EARLY-STAGE CERVICAL CANCER

A Gynecologic Cancer Intergroup (GCIG) Trial led by the CCTG

GCIG Trial Designation: The SHAPE Trial
CCTG Protocol Number: CX.5
Chair: Marie Plante
## Current Status

<table>
<thead>
<tr>
<th>Country</th>
<th># Sites Activated</th>
<th>Country</th>
<th># Patients Accrued</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>17</td>
<td>Canada</td>
<td>124</td>
</tr>
<tr>
<td>France</td>
<td>33</td>
<td>France</td>
<td>57</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>21</td>
<td>United Kingdom</td>
<td>44</td>
</tr>
<tr>
<td>Belgium</td>
<td>8</td>
<td>The Netherlands</td>
<td>43</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>7</td>
<td>Belgium</td>
<td>25</td>
</tr>
<tr>
<td>Austria</td>
<td>7</td>
<td>Austria</td>
<td>15</td>
</tr>
<tr>
<td>South Korea</td>
<td>2</td>
<td>Ireland</td>
<td>10</td>
</tr>
<tr>
<td>Ireland</td>
<td>1</td>
<td>South Korea</td>
<td>8</td>
</tr>
<tr>
<td>China</td>
<td>1</td>
<td>China</td>
<td>2</td>
</tr>
<tr>
<td>Russia</td>
<td>1</td>
<td>Russia</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>98</strong></td>
<td><strong>Total</strong></td>
<td><strong>330 (47%)</strong></td>
</tr>
</tbody>
</table>
Current Status

- We have reached 47% of total accrual
- 50% of patients have been randomized in the past year
- Accrual Rate for past 12 months = 13 pts/month
- 1st CCRN site activated in December 2016
  - Hertzen Moscow Scientific Research Institute of Oncology
  - 2 patients have been enrolled
- We are moving forward with activating 2 CCRN centres in Brazil
G-GOC

- LACC/G-GOC-1001
- ConCerv/G-GOC-1002
Phase III Laparoscopic or Robotic Radical Hysterectomy vs Abdominal Hysterectomy in Early Stage Cervical Cancer

PI: Pedro Ramirez

Trial setting: Cervix, FIGO stage IA1, IA2, or IB1

Study Design: Randomized Phase III

Sponsor(s): None

 Planned No. of patients: 740

Current accrual: 610 as of 04/26/17

Other important information: 27 sites

NCT00614211
LACC Consort Statement as at 26th April 2017

Assessed for Eligibility
n= 1140

Pending
n = 0

Excluded n = 530
Not meeting eligibility criteria (n = 275)
Refused (n = 192)
Other (n = 52)
SHAPE Trial (n = 11)

Randomised
n = 610

Allocated to TARH
n = 302

Allocated to TLRH/TRRH
n = 308

NCT00614211
Conservative Surgery for Women with Low-risk, Early Stage Cervical Cancer

PI: Kathleen Schmeler

Trial setting: Cervix, FIGO stages IA2 or IB1 (Tumor diameter <2 cm on physical exam and on imaging studies)

Study Design: Phase II

Sponsor(s): M.D. Anderson Cancer Center

Planned No. of patients: 100

Current accrual: 73

Other important information:
ConCerv/G-GOC-1002

- Future fertility desired: Cone biopsy and pelvic node dissection
- Future fertility **not** desired: Simple hysterectomy and pelvic node dissection

*SLN only optional*
Preliminary Results

• 73 evaluable patients:
  – 31 simple hysterectomy + nodes (42.5%)
  – 25 cone and nodes (34.2%)
  – 17 cut-through hysterectomy (23.3%)

Not evaluable:
  – 43 ineligible after MD Anderson review
  – 1 cancelled due to + pregnancy test
  – 1 declined surgery
  – 1 patient did not have surgery on protocol due to study hold (amendment was submitted)
NRG Oncology (GOG/RTOG)

Current GCIG Studies in the NRG

1. NRG 278
2. NRG 263 (KGOG 0801)
3. NRG 0724 (RTOG)
4. NRG 0274 (ANZGOG OUTBACK)
5. AIM2CERV/GOG 3009
6. NRG GY006
7. TIME-C (RTOG)
8. NRG 270 (GROINSS-V II)
9. NRG 279
GOG 278

PROTOCOL GOG-0278
EVALUATION OF PHYSICAL FUNCTION AND QUALITY OF LIFE (QOL) BEFORE AND AFTER NON-RADICAL SURGICAL THERAPY (EXTRA FASCIAL HYSTERECTOMY OR CONE BIOPSY WITH PELVIC LYMPHADENECTOMY) FOR STAGE IA1 (LVI+) and IA2-IB1 (≤ 2CM) CERVICAL CANCER

NCI Version Date 09/20/2012

POINTS:
PER CAPITA - 20
MEMBERSHIP - 6

PI = AL COVENS
N = 220
Enrollment to date = 134
Primary Endpoint = QOL
**AIM2CERV / GOG 3009**

- **PI**: THOMAS HERZOG MD
- **N**: 455
- **Enrollment to date**: 
- **Primary Endpoint**: RFS

**Baseline tumor imaging must be performed within 28 days prior to the first study treatment infusion**

**Randomization 1:2 Reference and Treatment Groups**

- **Reference Group**
  - Placebo IV
  - Up to 1 yr

- **Treatment Group**
  - Cisplatin (at least 4 wk exposure) and Radiation (minimum 40Gy external beam radiation therapy)
  - ADXS-HPV (1 x 10^9 cfu)
  - Up to 1 yr

**Follow-up for Overall Survival**
NRG GY006

Newly diagnosed uterine cervix cancer
- Squamous
- Adenosquamous
- Adenocarcinoma

Clinical stage bulky (> 5 cm) IB2, or Clinical stage II, IIIB, or IVA followed by Negative para-aortic nodal staging by PET/CT

Stratify para-aortic node-negative patients by:
- a. Age (≤ 45 years or > 45 years)
- b. Performance status (0, 1, or 2)
- c. Intensity Modulated Radiation Therapy (yes or no)
- d. Stage (≤ clinical stage II, or ≥ clinical stage III)

RANDOMIZE

Arm 1:
- Radiation
- Cisplatin

Arm 2:
- Radiation
- Cisplatin
- Triapine

Radiation: 45 Gy / 25 fractions of 1.8 Gy + 5.4 Gy / 3 fraction parametrium boost + 40 Gy LDR or 30 Gy HDR brachytherapy

Cisplatin: X1 weekly cisplatin 40 mg/m² (maximum 70 mg) days 2, 9, 16, 23, 30 of radiation (5 total infusions; a sixth administration on day 36 is permissible at the treating physician's discretion.)

Triapine: X3 weekly 3-aminopyridine-2-carboxaldehyde thiosemicarbazone (Triapine) 25 mg/m² (maximum 50 mg) days 1, 3, 5, 8, 10, 12, 15, 17, 19, 22, 24, 26, 29, 31, 33 of radiation (15 total infusions)

NTO-1151- Triapine:
Small molecule chelator – inhibits ribonuclease reductase

PI = TREY LEATH MD
N = 188
Enrollment to date = 50
Primary Endpoint = RFS

Primary Endpoint = RFS

NTO-1151- Triapine:
Small molecule chelator – inhibits ribonuclease reductase

PI = TREY LEATH MD
N = 188
Enrollment to date = 50
Primary Endpoint = RFS

Radiation: 45 Gy / 25 fractions of 1.8 Gy + 5.4 Gy / 3 fraction parametrium boost + 40 Gy LDR or 30 Gy HDR brachytherapy

Cisplatin: X1 weekly cisplatin 40 mg/m² (maximum 70 mg) days 2, 9, 16, 23, 30 of radiation (5 total infusions; a sixth administration on day 36 is permissible at the treating physician’s discretion.)

Triapine: X3 weekly 3-aminopyridine-2-carboxaldehyde thiosemicarbazone (Triapine) 25 mg/m² (maximum 50 mg) days 1, 3, 5, 8, 10, 12, 15, 17, 19, 22, 24, 26, 29, 31, 33 of radiation (15 total infusions)
GOG 279

PROTOCOL GOG-0279
A PHASE II TRIAL EVALUATING CISPLATIN (NSC #119875) AND GEMCITABINE (NSC #613327) CONCURRENT WITH INTENSITY-MODULATED RADIATION THERAPY (IMRT) IN THE TREATMENT OF LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE VULVA

NCI Version Date: 11/02/2012
Includes Revision #1

POINTS:
PER CAPITA - 20
MEMBERSHIP – 3

Study Chair: NS Horowitz MD
Target 52 evaluable patients
Enrollment to date = 29
## Total NRG Enrollment into Cervical/Vulvar Cancer Clinical Trials

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Enrollment Goal</th>
<th>Current Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase 3</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0263</td>
<td>534</td>
<td>252</td>
</tr>
<tr>
<td>0274</td>
<td>900</td>
<td>623 US (918 total)</td>
</tr>
<tr>
<td>0724</td>
<td>285</td>
<td>154</td>
</tr>
<tr>
<td>0270</td>
<td>1500 (140)</td>
<td>148 (US)</td>
</tr>
<tr>
<td><strong>Phase 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0278</td>
<td>220</td>
<td>134</td>
</tr>
<tr>
<td>GY006</td>
<td>188</td>
<td>50</td>
</tr>
<tr>
<td>0279</td>
<td>52</td>
<td>29</td>
</tr>
</tbody>
</table>

As of May 30, 2017
- Recurrent, persistent, and/or metastatic cervical cancer
- Progressed within 6 months of the last dose of platinum

REGN2810 350 mg Q3W, for up to 96 weeks
Physicians choice chemotherapy

Pemetrexed 500 mg/m² Q3W
Topotecan 1 mg/m² daily for 5 days, Q21 days
Irinotecan 100 mg/m² days 1, 8, 15, & 22, followed by 2 weeks rest (6-week cycle)
Vinorelbine 30 mg/m² days 1 & 8, Q21 days
Gemcitabine 1000 mg/m² on days 1 & 8, Q21 days

REGN2810, a fully human monoclonal antibody against programmed death-1 (PD-1)
GINECO

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

F Lecuru, M Leitao, P Mathevet, M Plante

<table>
<thead>
<tr>
<th>Coordinating Investigator</th>
<th>PR Fabrice LECURU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Biostatistician</td>
<td>Pr Franck BONNETAIN</td>
</tr>
<tr>
<td>Quality of Life Analysis</td>
<td>Dr Amélie ANOTA</td>
</tr>
<tr>
<td>Trial Management</td>
<td>Nathalie LE FUR</td>
</tr>
<tr>
<td>Sponsor</td>
<td>University Hospital Besançon</td>
</tr>
</tbody>
</table>
Senticol III
Study Design

Inclusion/exclusion criteria

ICF signature

Pre-study procedure

Pelvic examination, SLN mapping + biopsy, Frozen Section on SLN.

950 patients

Patients with bilateral detection without macroscopic suspicious node and negative frozen section on SLN (pN0)

Randomisation 1:1

Arm A (experimental): SLN biopsy only + hysterectomy or tracheectomy

Arm B (reference): SLN biopsy + Pelvic Lymphadenectomy + hysterectomy or tracheectomy

DFS, RFS, QOL, OS

Patients with nodal involvement (pN1)

Followed in a separate cohort to record treatment and outcomes

Surgical & pathological quality assurance
Present status

• Grant for the French part & international coordination
• Sponsor = CHU de Besançon
• Application to French authorities (May 2017)
• 50 sites in France
• 1st inclusion in September
DGOG

- Update GROINSS-V II
- GROINSS-V III
GROINSS-V II

• Multicenter observational study

• Is radiotherapy a safe alternative for lymphadenectomy in patients with a positive SN?

  – SN negative: follow-up
  – SN positive: radiotherapy (50 Gy)

– After protocol amendment:
  • Metastases ≤ 2mm: radiotherapy (50Gy)
  • Metastases > 2mm: inguinofemoral lymphadenectomy +/- radiotherapy
Update GROINSS-V II

1719 registrations

Inclusion every three months
Update GROINSS-V II
Follow-up

Data of 1395 eligible patients:

• SN negative: 1093
  – Groin recurrences: 28 (2.6%)

• SN positive: 304
  – Groin recurrences: 21 (6.9%)
    • Micrometastases: 6 / 150 (4.0%)
    • Macrometastases: 15 / 145 (10.3%)
      – After radiotherapy: 9/45 (20%) (1 PV -> 18% groin rec)
      – After lymphadenectomy +/- RT: 6/100 (6.0%) (incomplete FU)
GROINSS-V III

• Aim: investigate the effectiveness and safety of chemoradiation in patients with a macrometastasis (>2mm) in the sentinel node

• Observational study with stopping rules

• Inclusion criteria:
  
  – Same criteria for SN procedure as in GROINSS-V-II

  – Only patients with positive SN will be included
    • Micrometastasis SN -> Radiotherapy (50Gy)
    • Macrometastasis SN -> Chemoradiation
      – 56 Gy
      – Chemo: Cisplatin weekly (+alternative)
NSGO

- NSGO-CC1-MaRuC
Cervical cancer
- Squamous, Adenosquamous, adenocarcinoma
- Stage 3 & 4 or any stage with para-aortic nodal metastases

Definitive Chemoradiation

Patient in PR or CR

Randomize

Arm A
Rucaparib 600mg BID for 24 mo

Arm B
Placebo BID for 24 mo

n = 162
Randomization: 2:1

Stratification factors
- Histology (squamous vs adenosquamous, adenocarcinoma)
- FIGO stage (3 vs 4)

Enrolment of patients with squamous cell histology will be capped once 60% patients with this histo-type are enrolled

Sponsor
NSGO