

GCIG CERVIX CANCER BRAINSTORMING DAY

Thursday, 6 November, 2014

Melbourne, Australia

Satoru Sagae (JGOG)

Bradley Monk (GOG)



Chair: Satoru Sagae (Cx Ca Comm. Chair & JGOG)

Co-Chair: Brad Monk (Cx Ca Comm. Co-Chair & GOG)

Core Scientific Committee:

Eric Pujade-Lauraine (GCIG Chair & GINECO),

Bill Small (GCIG Chair-elect & RTOG),

Dave Gaffney (CCRN RT QA & RTOG),

Kailash Narayan (OUTBACK & ANZGOG).

Scientific and Planning Committee:

Sang Ryu (TACO Chair & KGOG),

Mary McCormack (INTERLACE Chair & MRC NCRI),

Marie Plante (SHAPE Chair & NCIC CTG),

Antonio Casado (EORTC GCG),

Alexander Reuss (Stats & AGO-Ovar),

and Adriana Chavez (Ops & GICOM).

Participants: (as of Oct. 26/2014 TOTAL 99 persons)

Member Groups: (53 persons) 28 groups

ACRIN, AGO–Au, AGO–De, ANZGOG, BGOG, COGi, DGOG, EORTC–GCG
GEICO, GICOM, GINECO, G–GOC, GOG, GOTIC, ICORG, JGOG, KGOG
MaNGO, MITO, MRC–NCRI, NCIC CTG, NOGGO, NSGO, PMHC, RTOG
SGCTG, SGOG, NCI US

Industry Partners: (5 persons)

AZ, Elekta/Nucletron, Pharmamar, Roche, Zeria

Speakers: (9 persons)

Nam (KGOG), Jhingran (RTOG), Temkin for Trimble (NCI US), Mileskin (ANZGOG),
Berns, Scholl (EORTC–GCG), Doll (NCIC CTG), Rustum (GOG), Lecuru (GINECO)

Added Harmonization reps (Breakout groups): (3 persons)

Martyn (ANZGOG), Aotani (JGOG), Hamano (GOTIC).

Executive Officers: (3 persons)

Quinn, Kitchener, Stuart.

Non-voting Observers/Guests: (13 persons)

Thai, Brazil, Viet Nam, Bangladesh, Argentina, Russia, S.Africa, Singapore
India, LACOG/INCA, Chile, ISSTD, Israel

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Objectives:

- To validate control arms for present and future clinical trials involving cervix cancers;
- To identify national & international barriers for trials dedicated to cervix cancers;
- To summarize and prioritize key issues for research and agree new set of trial concepts to address the key issues.

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8:50 – 9:00 Surrogate Markers (as endpoints) --- A. Reuss

Session 1: Local Disease Cervical Cancer– Chair: S. Sagae

9:00 – 9:25 Prognostic Groupings (speaker: **Narayan**)

9:25 – 9:45 Should we include developing countries or do we need more than one study?
Role of CCRN? (guest speaker: **Kitchener**)

9:45 – 10:00 What is the control arm & endpoint? (speaker: **B.H Nam**)

10:00 – 10:15 Is there a place for standard RT vs IMRT and IGBT in clinical trials?
(speaker: **A. Jhingran**)

Session 2: Metastatic Cervical Cancer– Chair: B. Monk

10:30 – 10:50 Can we do targeted therapy trials in developing countries?

What are the barriers of shipping investigational agents
across international lines? (guest speaker: **Sarah Temkin for Trimble**)

10:50 – 11:10 What is the control arm? Should it include bevacizumab? (speaker: **Eric Pujade**)

11:10 – 11:30 Is an assay directed trial feasible? (speaker: **L.Mileshkin**)

11:30 – 11:50 What is the appropriate endpoint? Should we do phase II or phase III studies?
(speaker: **Chavez**)

CURRENT ACTIVE/NEAR ACTIVATION RANDOMIZED GCIG TRIALS 2014,11

1.Surgery plus Radiation + / – CT post operative radiation

KGOG–0801/GOG263 (RTOG): RT vs CCRT in intermediate risk cervix cancer after hysterectomy

Ryu 145→170 /480

RTOG–0724 (GOG): ChemoRT with and without adjuvant chemotherapy in high risk cervix cancer after hysterectomy

Small <100? /400

NAC+surgery VS CCRT

EORTC 55994: Randomized phase III study of NAC followed by RH vs CCRT in FIGO stage Ib2, Ila>4 cm or IIb cervical cancer

Casado completed June 2014/625

KGOG 1029 A Randomized Controlled Trial Comparing Radical Hysterectomy plus Tailored Adjuvant Therapy versus Primary Chemoradiation Therapy in Bulky Early–stage Cervical Cancer?

Park too early?/409

Paraaortic Lymphadenectomy

G–GOC LiLACS Lymphadenectomy in Locally Advanced Cervix Study

Stage IB2–IVA Cervical Cancer PET (+) Pelvic Nodes/ (–) Paraaortic Nodes

Laparoscopic Paraaortic Lymphadenectomy /Tailored ChemoXRT (Experimental) vs Whole Pelvic Chemoradiation Therapy (Standard of Care)

Frumovitz 20 /600

2. Chemoradiation related trials:

KGOG–Thai TACO: (RTOG, GICOM) (CCRN – Viet Nam, Thailand) Randomized Clinical Trial of Weekly versus Tri–Weekly Cisplatin based Chemoradiation in Locally Advanced Cervical cancer

Ryu 75→130 /590

ANZGOG OUTBACK: (GOG, RTOG) (CCRN – India) :

Chemoradiotherapy +/- adjuvant chemotherapy Mileskin 254→432 /780

NCRI: INTERLACE: (CCRN – Romania, Belarus) INduction ChemoThERapy in Locally Advanced Cervical Cancer.
McCormack 14 →38 /700

RTOG: A RANDOMIZED PHASE III STUDY OF STANDARD VS. IMRT PELVIC RADIATION FOR POST–OPERATIVE TREATMENT OF ENDOMETRIAL AND CERVICAL CANCER: TIME–C

Small too early?/284

histology

JGOG1074 ; A New Protocol Concept for Advanced Cervical Adenocarcinoma of the Uterine Cervix CCRT–P (RT + CDDP 40 mg/m² weekly) VS CCRT–TP (RT + CDDP 30 mg/m² + PTX 50 mg/m² weekly)
Fujiwara just started /240

3. minimal invasive surgery related trials:

NCIC-CTG CX 5 SHAPE: (DGOG,) (CCRN -) A RANDOMIZED TRIAL COMPARING RADICAL HYSTERECTOMY AND PELVIC NODE DISSECTION VS SIMPLE HYSTERECTOMY AND PELVIC NODE DISSECTION IN PATIENTS WITH LOW RISK EARLY STAGE CX CA:

Plante 11->50 /700

G-GOC ConCerv Conservative Surgery for Early Stage Cervical Cancer: Tailoring Radicality to Risk Factors CONE+PLN, SH+PLN, cut-through hyst Schmeler 48 /100

G-GOC LACC A Phase III Randomized Clinical Trial of Laparoscopic or Robotic Radical Hysterectomy versus Abdominal Radical Hysterectomy in Patients with Early Stage Cervical Cancer

Ramirez 357 /740

GOG-0278 Conservative surgery (cone/nodes or hyst/(nodes) in early stage cervical cancer. (evaluation of physical function and QOL)

Monk 9->? /220

4. Vulvar Cancer

DGOG GROINSS-V II (EORTC, GOG) : Groningen International Study on Sentinel Nodes in Vulvar Cancer Creutzberg for van der Zee 1,037 cases

GOG-0279 Phase II Trial Evaluating Cisplatin (NSC #119875) and Gemcitabine (NSC #613327) Concurrent with Intensity-Modulated Radiation Therapy (IMRT) in Treatment of Locally Adv. SC C of the Vulva Monk 9->? /52

Lunch

Breakout Working Groups:

#1 – Topic: Translational Research: Casado/McCormack/E.Aotani/T.Hamano

E. Bern, S.Scholl, C.Doll

- liquid biopsies and possibly biomarkers
- an overview on solid biopsies (genomics), biomarkers and DNA vaccines
- PI3K pathway/PIK3CA mutational status in cervical cancer. Immunotherapy??

#2 – Topic: International Obstacles and Approaches: Ryu/Small/A.Chavez/B.H.Nam

S.Ryu, Sarah Temkin for Trimble, H.Kitchener

- CCRN survey, NCI–US report, Founder’s comments

#3– Topic: Fertility sparing/preserving,node studies:

Plante/E.Pujade–Lauraine/J.Martyn/A.Reuss

M.Plante, N.Abu–Rustum, F. Lecuru

How to best manage women with larger size lesions / bulky IB1–IB2 (Plante)

How to manage women with low volume lymph node metastasis (Lecuru)

Is there a place for a SLN mapping trial in early–stage cervical cancer (Abu–Rustum)

Plenary – REPORTS from Breakout Working groups (10 minutes each)

Plenary: Consensus Session: locally advanced and metastatic disease – Chair: Monk

Proposed Trials

Proposed Trials from CCRN group

As Palliative Radiation

- RT fractionation
 - 10 Gy vs. 5 Gy X 4.
 - Endpoint one month PRO

For Curative Patients

- Hypofractionation.
 - 3 weeks vs 5 weeks EBRT
 - Possible 2 vs 4 brachytherapy fractions

Proposals from TR group

Proposal 1

- High risk pts- node+ / large vol/corpus +
- Maintenance trial-
 rand observation v targeted agent
(PI3K inhibitor, PD1, Immunotherapy, anti-HPV, anti-Angio etc)
- Tissue/ sera, plasma at different time points over course disease

Proposal 2

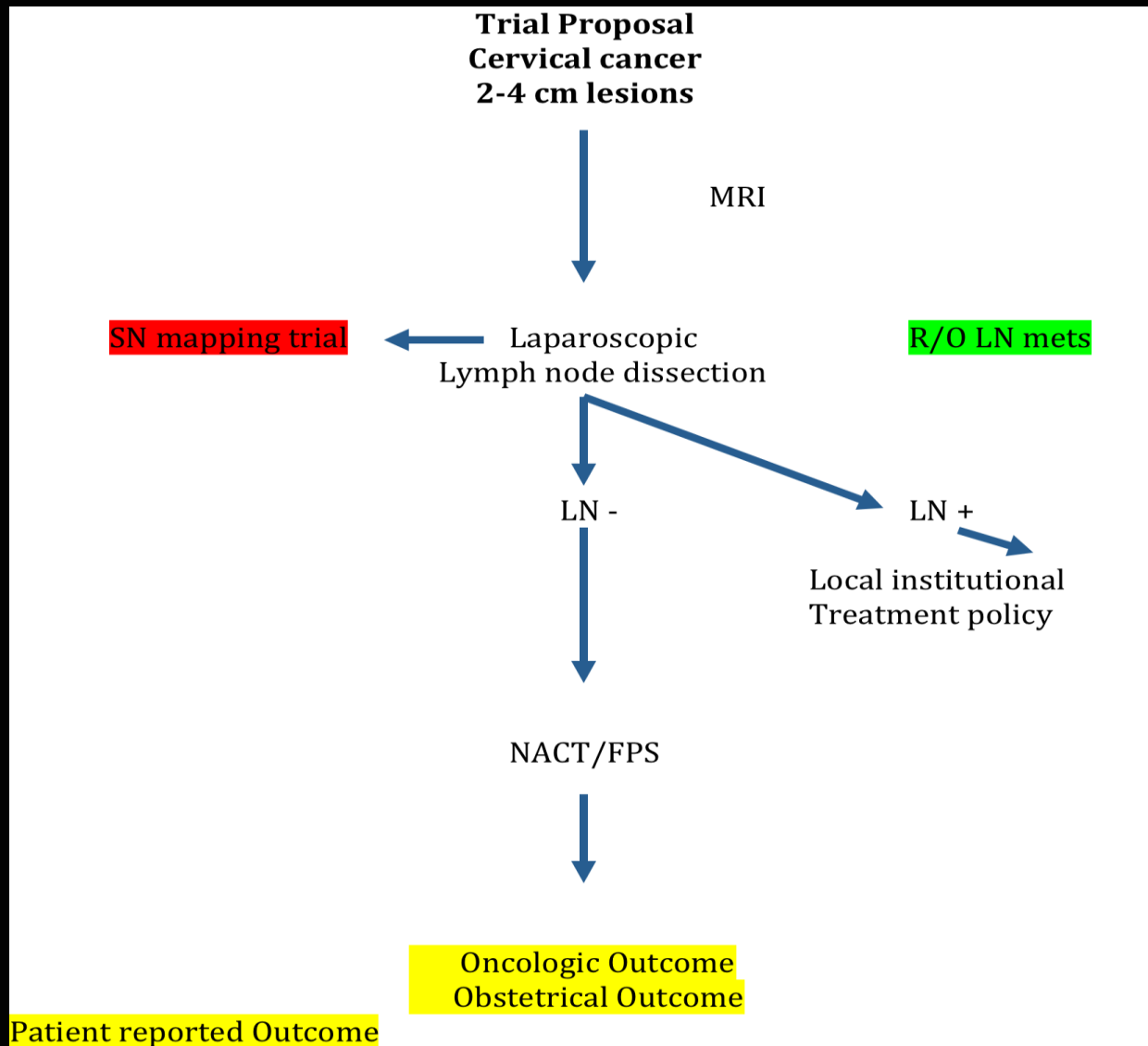
- Relapsed/met disease
- Rand Carbo/Taxol +/- PI3K inhibitor

Fertility Sparing Brainstorming Session

❧ 3 Clinical Issues

- How to best manage women with **larger size lesions** / bulky IB1-IB2 (Plante)
- How to manage women with **low volume lymph node metastasis** (Lecuru)
- Is there a **place for a SLN mapping trial** in early-stage cervical cancer (Abu-Rustum)

Proposal #1



Proposal #2 SLN algorithm validation trial

∞Laparoscopy – SLN biopsy

- No routine lymphadenectomy (cf Algorithm)
- Similar to the **GROINS** trial

∞Observational study with stopping rules

- For pelvic lymph node recurrence

∞Inclusion criteria

- Stage I-IIA (< 4 cm)
- Trachelectomy, rad hyst
- Sites with **prior experience** in SLN mapping (30 cases/center)

Proposal #3: Registry for the management of low volume metastasis

⇒ **Standardization** of the definition of low-volume metastasis (LVM)

- ITC and micrometastasis

⇒ Define **minimal requirements** for pathology infrastructure (serial sectioning, CK staining)

⇒ Management of ptes with ITC

- Observation
- Adjuvant treatment
- Patterns of recurrence

Thank you so much
for your participation and wonderful discussion