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. NRG 270 (GROINSS-V II)
8. NRG 279
9. GOG 3016
10. GOG 2024

GYNECOLOGIC CANCER INTERGROUP

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

GOG® FOUNDATION, INC.

NRG ONCOLOGY™

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 (LVSI+) and IA2-IB1 (≤ 2CM) CERVICAL CANCER

NCI Version Date 09/20/2012

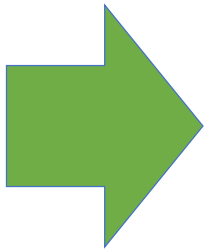
POINTS:
PER CAPITA - 20
MEMBERSHIP - 6

PI = AL COVENS
N = 220
Enrollment to date = 172
Primary Endpoint = QOL

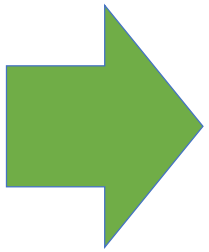
NRG/RTOG 0724

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

R A N D O M I Z E



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 = 184
Primary Endpoint = DFS

NRG GY006

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

PI = TREY LEATH MD
N = 188
Enrollment to date = 150
Primary Endpoint = RFS

Will transition into phase 3 study N=348

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

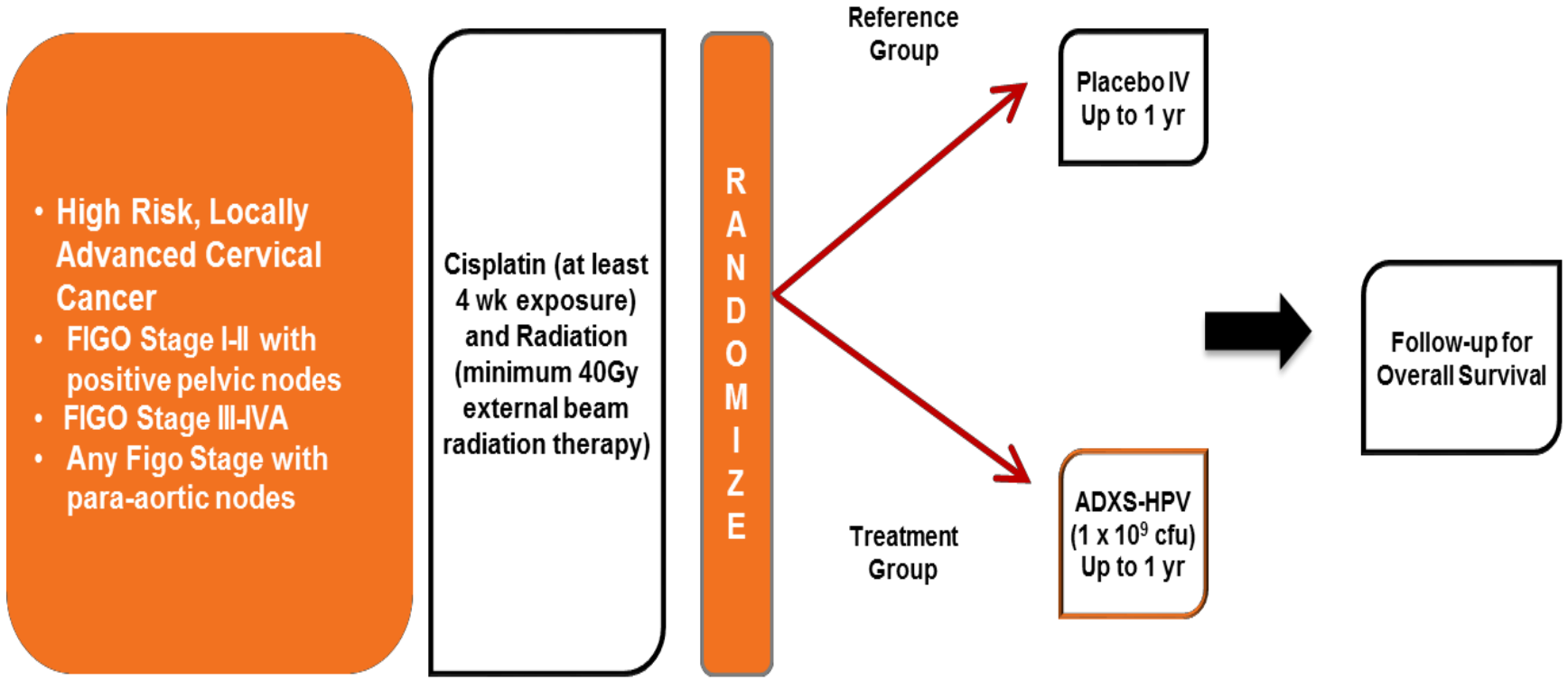
Arm 2:
- Radiation
- Cisplatin
- Triapine

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/m^2 (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/m^2 (maximum 50 mg) days 1, 3, 5, 8, 10, 12, 15, 17, 19, 22, 24, 26, 29, 31, 33 of radiation (15 total infusions)

AIM2CERV / GOG 3009



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

Randomization 1:2 Reference and Treatment Groups

Primary Objective is Progression Free Survival

PI = THOMAS HERZOG MD
N = 455
Enrollment to date = 99
Primary Endpoint = RFS

GOG-3016 (R2810-ONC-1676)

Empower Cervical 1

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

RANDOMIZE

→ 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

PI = Krishnansu S. Tewari, MD
N = 436
Primary Endpoint = OS
Enrollment = 160

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

Empower Cervical 1:
R2810-ONC-1676/GOG-3016/ENGOT CX9/GEICO 72-C
GCIG Meeting

Ana Oaknin, MD PhD
Head of Gynecologic Cancer Program. Vall d´Hebron Institute of Oncology(VHIO).
Vall d´Hebron University Hospital.
GEICO Vice-Chairman
Barcelona, Spain

Empower Cervical 1 Review

1. Participant Groups / Countries
2. Sample Size: Recruitment update
3. ENGOT Groups Study Timelines

Empower Cervical 1 Review
ENGOT Participant Groups / Countries

ENGOT Lead Group:	GEICO (Spain), PI Dr. Ana Oaknin
BGOG (Belgium)	PGOG (Poland)
MaNGO (Italy)	HeCOG (Greece)
MITO (Italy)	NCRI (UK)

Empower Cervical 1 Review

ENGOT Groups' Participation

▪ **GEICO**:	10 sites,	40 patients	PI: Dr. Ana Oaknin
▪ **PGOG**:	03 sites,	12 patients	PI: Dr. Radoslaw Madry*
▪ **BGOG**:	06 sites,	24 patients	PI: Dr. Ignace Vergote
▪ **MaNGO**:	05 sites,	20 patients	PI: Dr. Domenica Lorusso*
▪ **MITO**:	06 sites,	24 patients	PI: Dr. Domenica Lorusso
▪ **HeCOG:**	06 sites,	24 patients	PI: Dr. Flora Zagouri
▪ **NCRI:**	06 sites,	24 patients	PI: Dr. Azmat Sadozye

42 sites, 168 patients

* PGOG's PI needS to confirm his participation in the Study

*Italy(MITO&MANGO)will have a common PI.

Empower Cervical 1 Review
ENGOT Groups Study Timelines

GROUP	Submission Planned	SIV-FPI Planned
GEICO Dr. Ana Oaknin	Amendment for news sites addition planned for Nov 2018	1st SIV-FPI for the new sites planned in January / February 2019
BGOG Dr. Ignace Vergote	Submission planned for November 2018	1st SIV-FPI planned in January / February 2019
MaNGO Dr. Domenica Lorusso	Submission planned for November 2018	1st SIV-FPI planned in February / March2019
MITO Dr. Domenica Lorusso	Submission planned for November 2018	1st SIV-FPI planned in February / March2019
HeCOG Dr. Flora Zagouri	Submission planned for January 2019	1st SIV planned in April / May 2019
NCRI Dr. Azmat Sadozye	Submission already done: 31Aug2018	1st SIV-FPI planned in January / February 2019

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

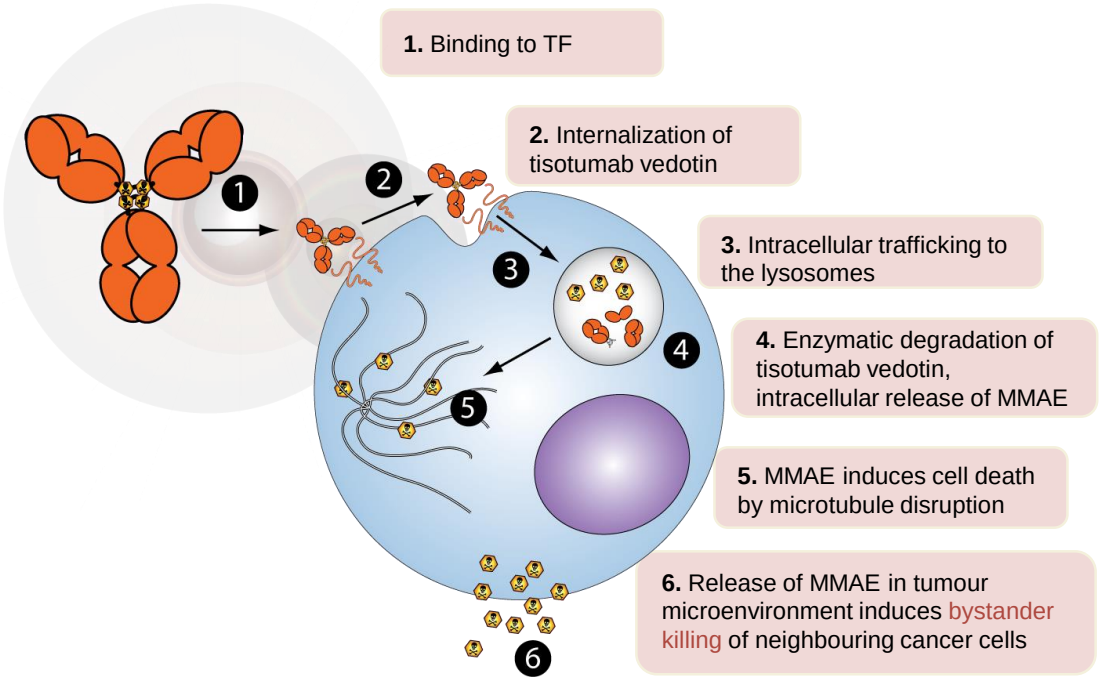
Includes Revision #1

POINTS:
PER CAPITA - 20
MEMBERSHIP – 3

Study Chair: NS Horowitz MD
Target 52 evaluable patients
Enrollment to date = 40

Mechanism of action Tisotumab Vedotin

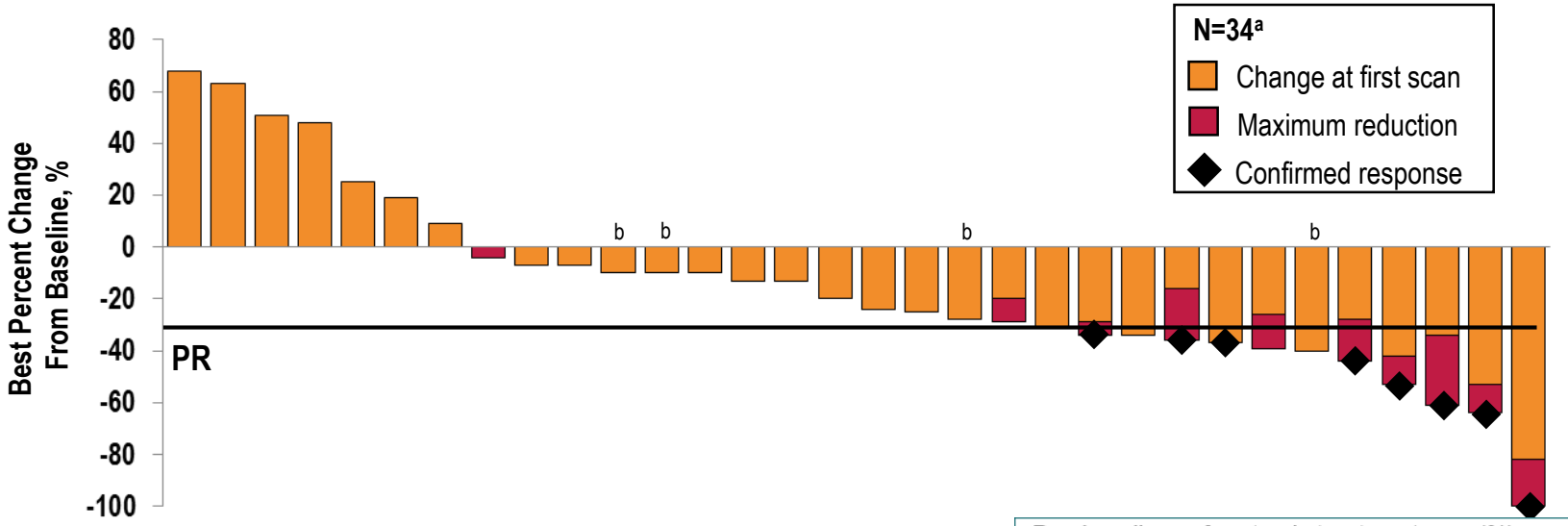
- Tisotumab vedotin is an Antibody-Drug Conjugate (ADC) composed of a human mAb specific for Tissue Factor (TF= TROMBOPLASTIN), a protease-cleavable linker, and the microtubule disrupting agent MMAE[1,a,b]
- TF is a transmembrane protein that is the main physiological initiator of coagulation and is involved in angiogenesis, cell adhesion, motility, and cell survival[3]
- TF is aberrantly expressed in a broad range of solid tumours, including cervical cancer, and is associated with poor prognosis[4,5]



ADC=antibody-drug conjugate; mAb=monoclonal antibody; MMAE=monomethyl auristatin E.
[a]Tissue factor is known as TF, CD142, and thromboplastin.
[b]MMAE-based ADC technology was licensed from Seattle Genetics, Inc., in a license and collaboration agreement.
1. Breij EC et al. *Cancer Res.* 2014;74(4):1214-1226. **2.** De Goeij BE et al. *Mol Cancer Ther*. 2015;14(5):1130-1140. **3.** Chu AJ. *Int J Inflam*. 2011;2011. doi: 10.4061/2011/367284.
4. Förster Y et al. *Clin Chim Acta*. 2006;364(1-2):12-21. **5.** Cocco E et al. *BMC Cancer*. 2011;11:263.

Phase I expansion in ≥ 2nd line recurrent Cxca (Vergote et al ESMO 2017)

32% OF PATIENTS WITH RECURRENT/ADVANCED CERVICAL CANCER ACHIEVED RESPONSE WITH TISOTUMAB VEDOTIN



- 50% (17 of 34 patients; 95% CI, 35%-65%) clinical benefit after 12 wks (DCR)[c,d]
- 32% (11 of 34 patients; 95% CI, 17%-50%) response (ORR)[d]
  - 8 PR, confirmed
  - 3 PR, unconfirmed[e]

Previous lines of systemic treatments, no (%)	
0[a]	3 (9%)
1	13 (38%)
2	11 (32%)
3	4 (12%)
4	3 (9%)

CI=confidence interval; CR=complete response; CT=computed tomography; DCR=disease control rate; ORR=overall response rate; PD=progressive disease; PR=partial response; RECIST=Response Evaluation Criteria in Solid Tumors; SD=stable disease.

[a]Two patients were withdrawn prior to CT scan, and so are not represented in the graph. [b]PD due to new lesion at same scan. [c]Clinical benefit was defined as the DCR rate, the proportion of patients who achieved a CR, PR, or SD after 12 weeks. [d]Response was as assessed by investigators using standard RECIST 1.1 criteria. [e]One of which is still ongoing. Data cutoff date July 24, 2017.

GOG 3024 / ENGOT-cx6: Tisotumab Vedotin in Previously treated recurrent or metastatic cervical cancer

STUDY DESIGN

Patients with recurrent or metastatic cervical cancer who have received **at least one prior line** of systemic therapy.

Enrollment →

N ~ 100

Treatment	Design
• **Tisotumab vedotin (TV) 2.0 mg/kg 1Q3W** • Imaging every **6 weeks** first 30 weeks and every 12 weeks thereafter. • Imaging assessed locally (by PI) and centrally (by IRC*).	• Continue TV treatment **until IRC verified PD or until pt. fulfils other treatment discontinuation criteria** e.g. unacceptable adverse events. • Pt. is followed up for survival and new anti-cancer treatment until the pt. dies or until withdrawal from the trial.

ENGOT Model C

*IRC: Independent review committee

- Data obtained from central IRC review will be used in the analysis and reporting of trial results.

Enrollment = 18 as of Oct 15, 2018 (33 active sites)

GOG263: RANDOMIZED CLINICAL TRIAL OF ADJUVANT RADIATION VERSUS CHEMORADIATION IN INTERMEDIATE RISK, STAGE I/IIA CERVICAL CANCER TREATED WITH INITIAL RADICAL HYSTERECTOMY AND PELVIC LYMPHADENECTOMY

Trial setting: Post radical hysterctomy cervical cancer, Intermediate risk, Stage I/IIA
Study Design: Adjuvant RT vs CRT

Sponsor(s): NCI-NRG

Planned No. of patients: 360

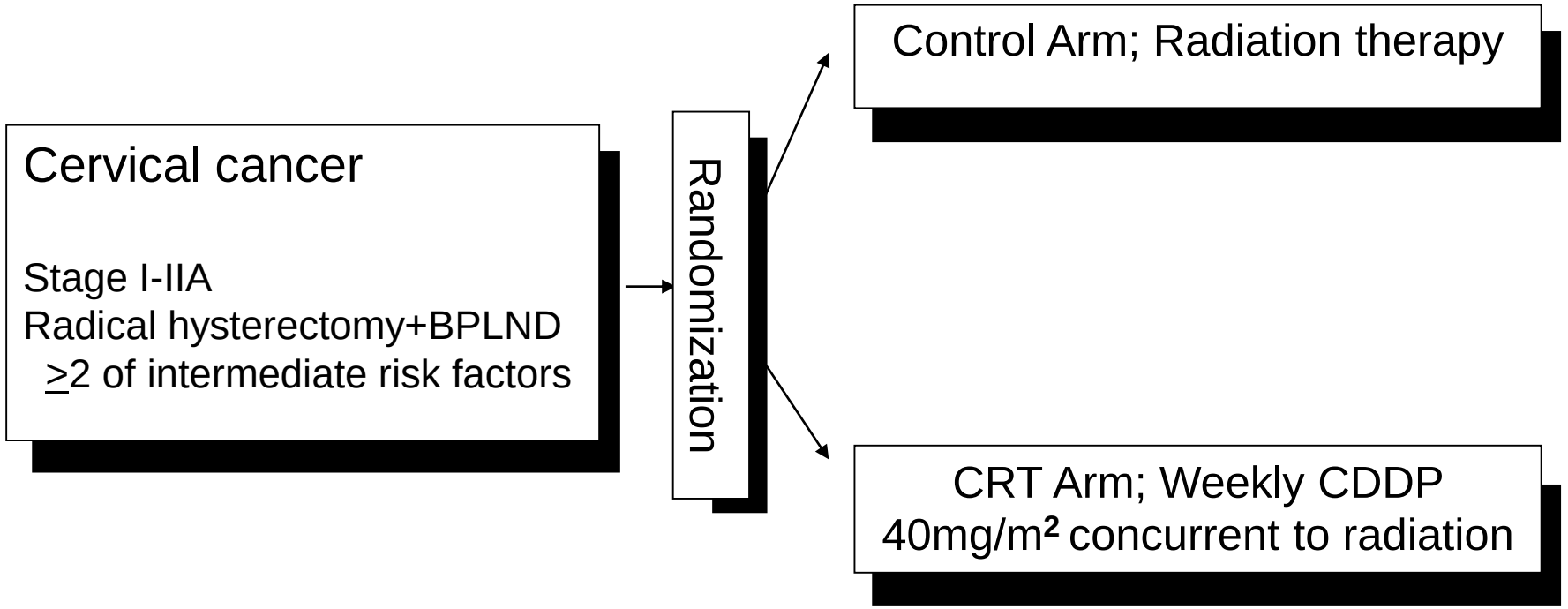
Current accrual: 280

Revision:

Update (11/2017): Based on the observed accrual rate through November 2017, power analysis and sample size calculations using the Gompertz model suggest that enrolling at least 342 eligible and evaluable patients will result in the required number of recurrences without any changes to the study operating characteristics.

Assuming uniform accrual with 5% ineligible proportion estimated from this study, the targeted accrual is 360 patients expected to be met in 2020.

GOG263: RANDOMIZED CLINICAL TRIAL OF ADJUVANT RADIATION VERSUS CHEMORADIATION IN INTERMEDIATE RISK, STAGE I/IIA CERVICAL CANCER TREATED WITH INITIAL RADICAL HYSTERECTOMY AND PELVIC LYMPHADENECTOMY



GOG263: RANDOMIZED CLINICAL TRIAL OF ADJUVANT RADIATION VERSUS CHEMORADIATION IN INTERMEDIATE RISK, STAGE I/IIA CERVICAL CANCER TREATED WITH INITIAL RADICAL HYSTERECTOMY AND PELVIC LYMPHADENECTOMY