

UPDATE ON GCIG TRIALS FOR EPITHELIAL OVARIAN CANCER

Philipp Harter
Christian Marth

Published Trials

ICON7

Clinical

ICON7 –the manuscript
is under review at the
New England Journal of
Medicine – not yet
accepted however

ORIGINAL STUDY

Prospective Validation Study of a Predictive Score
for Operability of Recurrent Ovarian Cancer

*The Multicenter Intergroup Study DESKTOP II. A Project
of the AGO Kommission OVAR, AGO Study Group,
NOGGO, AGO-Austria, and MITO*

Philipp Harter, MD,† Jalid Sehouli, MD, PhD,‡ Alexander Reuss, MSc,§
Annette Hasenburg, MD, PhD,|| Giovanni Scambia, MD, PhD,¶ David Cibula, MD, PhD,#
Sven Mahner, MD,** Ignace Vergote, MD, PhD,†† Alexander Reinthaller, MD, PhD,‡‡
Alexander Burges, MD,§§ Lars Hanka, MD,|||| Martin Pölcher, MD,¶¶ Christian Kurzeder, MD,##
Ulrich Canzler, MD,*** Karl Ulrich Petry, MD, PhD,††† Andreas Obermair, MD, PhD,‡‡‡
Edgar Petru, MD, PhD,§§§ Barbara Schmalfeldt, MD, PhD,||||| Domenica Lorusso, MD,||
and Andreas du Bois, MD, PhD*†*

Phase III Trial of Carboplatin Plus Paclitaxel With or Without Gemcitabine in First-Line Treatment of Epithelial Ovarian Cancer

Andreas du Bois, Jørn Herrstedt, Anne-Claire Hardy-Bessard, Hans-Helge Müller, Philipp Harter, Gunnar Kristensen, Florence Joly, Jens Huober, Elisabeth Åvall-Lundqvist, Béatrice Weber, Christian Kurzeder, Svetislav Jelic, Eric Pujade-Lauraine, Alexander Burges, Jacobus Pfisterer, Martina Gropp, Anne Staehle, Pauline Wimberger, Christian Jackisch, and Jalid Sehouli

AGO-OVAR-9



CALYPSO PUBLISHED

Status	First author	Manuscript Title	Journal
Printed	E. Pujade-Lauraine	Pegylated Liposomal Doxorubicin and Carboplatin Compared With Paclitaxel and Carboplatin for Patients With Platinum-Sensitive Ovarian Cancer in Late Relapse	Journal of Clinical Oncology - Juillet 2010 (ref PubMed : J Clin Oncol. 2010 Jul 10;28(20):3323-9)
	J.E Kurtz	Ovarian cancer in elderly patients: carboplatin and pegylated liposomal doxorubicin versus carboplatin and paclitaxel in late relapse: a Gynecologic Cancer Intergroup (GCIg) CALYPSO sub-study	Annals of Oncology - 14 Mars 2011 (ref PubMed : Ann Oncol. 2011 Mar 14. [Epub ahead of print])
	F. Joly	Decreased hypersensitivity reactions with carboplatin–pegylated liposomal doxorubicin compared to carboplatin–paclitaxel combination: Analysis from the GCIg CALYPSO relapsing ovarian cancer trial	Gynecology Oncology 2011 Aug;122(2):226-32. Epub 2011 May 14.
	C. Lee	Early decline in cancer antigen 125 as a surrogate for progression-free survival in recurrent ovarian cancer	Journal of National Cancer Institute (short communication – Advance Access published August 11 2011

CALYPSO IN PRESS

First author	Manuscript Title	Journal
C. Lee	Carboplatin paclitaxel induced leukopenia and neuropathy predict progression-free survival in recurrent ovarian cancer	British Journal of Cancer (accepted with revisions on May 13 2011) and final acceptance on June 16 2011
C. Lee	Prognostic nomogram to predict progression-free survival in patients with platinum-sensitive recurrent ovarian cancer	British Journal of Cancer (submitted on April 13th 2011) – accepted with revisions in July 12...- definitive acceptance on August 18 th 2011
L. Gladiëff	Carboplatin and pegylated liposomal doxorubicin versus carboplatin and paclitaxel in partially platinum-sensitive ovarian cancer patients: results from a subset analysis of the CALYPSO phase III trial	Annals of Oncology (submitted on April 25th 2011 – accepted with revision on June 7 2011) – definitive acceptance on August 31th

First author	Manuscript Title	Journal
M. Brundage	Health related quality of life in recurrent platinum-sensitive ovarian cancer - results from the CALYPSO trial	Submitted in Annals of Oncology July 20st
J. Alexandre	Should CA-125 still be part of tumour evaluation criteria in ovarian cancer trials? Experience of the GCIG CALYPSO trial	To be submitted in British Journal of Cancer by Aug 26
U. Wagner	Pegylated liposomal doxorubicin and carboplatin (C-PLD) versus paclitaxel and carboplatin (C-P) in platinum-sensitive ovarian cancer (OC) patients (pts): treatment at recurrence and overall survival (OS) final analysis from CALYPSO phase III GCIG trial	To be submitted in Lancet Oncology , then Annals of Oncology as a second chance Review by Aug 26 by authors
S. Mahner	Carboplatin and pegylated liposomal doxorubicin versus carboplatin and paclitaxel in very platinum-sensitive ovarian cancer patients: results from a subset analysis of the CALYPSO phase III GCIG trial	To be submitted in Annals of Oncology
B. You	Mathematical modeling of CA125 kinetics in recurrent ovarian cancer (ROC) patients treated with chemotherapy and predictive value of early modeled kinetic parameters in CALYPSO trial (a GCIG study).	

Gynecologic Oncology 119 (2010) 5–6



Contents lists available at [ScienceDirect](#)

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno



Clinical Commentary

Progress in ovarian cancer trials: The GCIG consensus model – Is bigger, better?

M. Quinn

BRIEF REPORT

The Global Impact of the Gynecologic Cancer InterGroup in Enhancing Clinical Trials in Ovarian Cancer

Monica Bacon, RN, Henry Kitchener, MD,† Gavin C.E. Stuart, MD, FRCSC,‡ and Jan B. Vermorken, MD, PhD§ on behalf of the Gynecologic Cancer InterGroup and participants of the 4th Ovarian Cancer Consensus Conference*

REVIEW ARTICLE

First-Line Therapy in Ovarian Cancer Trials

Tate Thigpen, MD, PhD, Andreas duBois, MD, PhD,† Jessica McAlpine, MD,‡ Philip DiSaia, MD,* Keiichi Fujiwara, MD,§ William Hoskins, MD,|| Gunnar Kristensen, MD,¶ Robert Mannel, MD,* Maurie Markman, MD,# Jacobus Pfisterer, MD,† Michael Quinn, MD,** Nick Reed, MD,†† Ann Marie Swart, MD,‡‡ Jonathan Berek, MD,§§ Nicoletta Colombo, MD,|||| Gilles Freyer, MD PhD,¶¶ Dolores Gallardo, MD,### Marie Plante, MD,‡ Andres Poveda, MD,*** Lawrence Rubinstein, MD,|| Monica Bacon, RN,††† Henry Kitchener, MD,‡‡‡ and Gavin C.E. Stuart, MD FRCSC,‡ on behalf of the Gynecologic Cancer InterGroup*

REVIEW ARTICLE

Clinical Trials in Recurrent Ovarian Cancer

Michael Friedlander, MD, PhD, Edward Trimble, MD,† Anna Tinker, MD,‡ David Alberts, MD,§ Elisabeth Avall-Lundqvist, MD, PhD,|| Mark Brady, PhD,¶ Philipp Harter, MD,# Sandro Pignata, MD, PhD,** Eric Pujade-Lauraine, MD, PhD,†† Jalid Sehoul, MD,# Ignace Vergote, MD, PhD,‡‡ Philip Beale, MD,* Rudd Bekkers, MD,§§ Paula Calvert, MD,|||| Lawrence Copeland, MD,§ Ros Glasspool, MD,¶¶ Antonio Gonzalez-Martin, MD,### Dionysis Katsaros, MD,*** Jae Won Kim, MD,††† Brigitte Miller, MD,‡‡‡ Diane Provencher, MD,‡ Lawrence Rubinstein, MD,† Mostafa Atri, MD,§§§ Alain Zeimet, MD,||||| Monica Bacon, RN,¶¶¶ Henry Kitchener, MD,#### and Gavin C.E. Stuart, MD, FRCSC,‡ on behalf of the Gynecologic Cancer InterGroup*

REVIEW ARTICLE

2010 Gynecologic Cancer InterGroup (GCIG) Consensus Statement on Clinical Trials in Ovarian Cancer Report From the Fourth Ovarian Cancer Consensus Conference

Gavin C.E. Stuart, MD, FRCSC, Henry Kitchener, MD,† Monica Bacon, RN,‡ Andreas duBois, MD, PhD,§ Michael Friedlander, MD, PhD,|| Jonathan Ledermann, MD, FRCP,† Christian Marth, MD, PhD,¶ Tate Thigpen, MD, PhD,# Edward Trimble, MD,** and on behalf of the participants of the 4th Ovarian Cancer Consensus Conference (OCCC)*

ORIGINAL STUDY

Role of Molecular Agents and Targeted Therapy in Clinical Trials for Women With Ovarian Cancer

Jonathan A. Ledermann, BSc, MD, FRCP, Christian Marth, MD, PhD,† Mark S. Carey, MD,‡ Michael Birrer, MD, PhD,§ David D.L. Bowtell, PhD,|| Stan Kaye, MD, FRCP,¶¶ Iain McNeish, PhD, FRCP,* Amit Oza, MD,‡ Giovanni Scambia, MD,# Gordon Rustin, MD, FRCP,* Frederick B. Stehman, MD,§ David Gershenson, MD,** Gillian Thomas, MD,** Els Berns, MD,†† Antonio Casado, MD,†† Nelleke Ottewanger, MD,‡‡ Felix Hilpert, MD,§§ Byoung-Gie Kim, MD, PhD,|||| Aikou Okamoto, MD, PhD,¶¶ Monica Bacon, RN,### Henry Kitchener, MD,* and Gavin C.E. Stuart, MD, FRCSC,‡ and on behalf of the Gynecologic Cancer InterGroup*

REVIEW ARTICLE

Clinical Trials and Treatment of the Elderly Diagnosed With Ovarian Cancer

Gilles Freyer, MD, PhD, Anna V. Tinker, MD,† and on behalf of the Gynecologic Cancer InterGroup*

ORIGINAL STUDY

Patient-Reported Outcomes Clinical Trials in Ovarian Cancer

Mark S. Carey, MD and Carolyn Gotay, PhD† and on behalf of the Gynecologic Cancer InterGroup (GCIG)*

Closed Trials

Primary Chemotherapy — Tarceva

Patients

Leading

**Collection of data necessary —
missing events**

AUSTRIA, ANZGOG, GINECO,
EORTC/NCIC, MANGO

Carbo Topo vs Chemo (CT or CG) in recurrent Platinum-sensitive ovarian cancer

Patients	closed 550
Leading	NOGGO/AGO-OVAR
Participating	AGO-AUSTRIA, GEICO

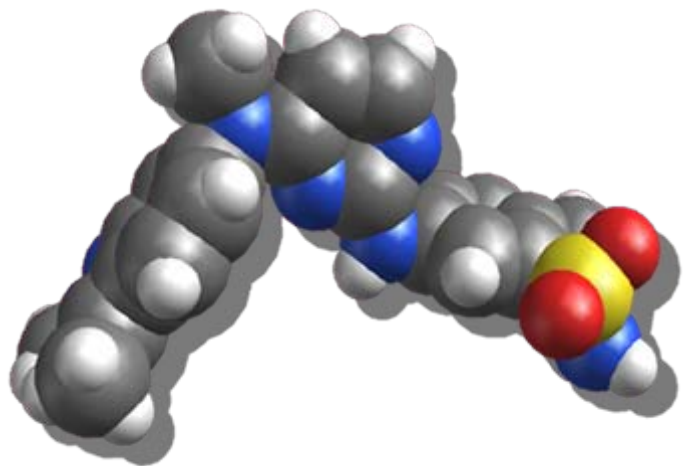
Carbo Paclitaxel +/- BIBF 1120 (Vargatef)

Patients 1366 / 1300 (2:1 random)

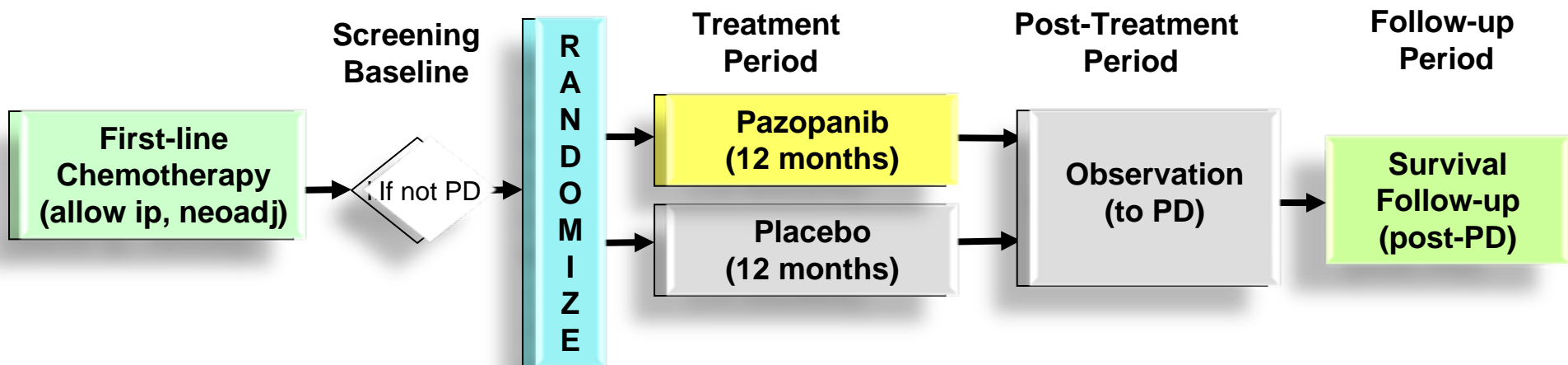
Leading AGO-OVAR

Participating AGO-Austria, BGOG, GINECO,
MANGO, MITO, NSGO, US Oncology

AGO-OVAR16



A Phase III Study to Evaluate the Efficacy and Safety of Pazopanib Monotherapy Versus Placebo in Women Who Have not Progressed after First Line Chemotherapy for Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer



AURELIA: Avastin Use in Resistant ovarian epithelial cancer

**A multi-centre, open-label, randomised,
two-arm phase III trial
of
bevacizumab plus chemotherapy
versus
chemotherapy alone
in patients with
platinum-resistant, epithelial ovarian, fallopian tube
or primary peritoneal cancer**

International Cooperative Phase III
Study for Clear Cell Carcinoma

-Clear Cell Ca
-Stage I~IV

RANDOMIZATION

TC
Paclitaxel 175 mg/m² (d1)
Carboplatin AUC 6 (d1)
Every 3 wk x 6

Irinotecan/CDDP
CPT-11 60 mg/m² (d1, 8, 15)
Cisplatin 60 mg/m² (d1)
Every 4 wk x 6

331 patients in each arm, 662 total for 4.25 years

Open Trials

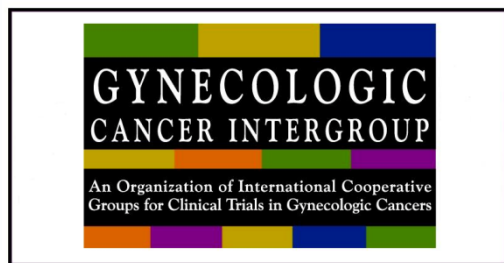
ICON 8

$C_{3w} P_{3w}$ vs $C_{3w} P_{1w}$ vs $C_{1w} P_{1w}$

Patients 11 / 1485

Leading MRC

Participating ANZGOG, GEICO, NSGO,
ICORG, EORTC, KGOG



mEOC

10 patients recruited. 30 sites are open. 17 are in set-up and 69 potential international sites

mEOC is an intergroup study with two identical protocols from GOG and NCRI with a single analysis





AGO – OVAR OP.3 (LION)

Lymphadenectomy In Ovarian Neoplasms

epithelial invasive
ovarian cancer

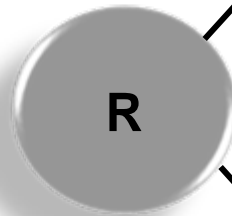
FIGO IIB - IV

ECOG 0/1 and
no CI against LNE

no visible extra-
and intra-abdominal
tumor residuals

no bulky lymph nodes

n = 520 / 640



System. Lymphadenectomy

- pelvic
- para-aortic

NO Lymphadenectomy

Endpoints: OS, PFS, QoL, toxicity/complications

Strata: centre, PS ,age

Cytoreductive surgery vs NO surgery in platinum-sensitive recurrent EOC

Patients 24 / 408

Leading AGO-OVAR

Participating AGO-A, GEICO, GINECO, KGOG,
MaNGO, MITO, NSGO, Shanghai-
GOG, Single Sites Leuven, and UK

A Randomized Phase II/III Trial of 3 Weekly Intraperitoneal versus Intravenous Carboplatin
in Combination with Intravenous Weekly Dose-Dense Paclitaxel
for Newly Diagnosed Epithelial Ovarian, Fallopian Tube and Primary Peritoneal Cancer

Epithelial ovarian, Fallopian tube or Primary peritoneal cancer
FIGO stage II–IV
Including Bulky Tumor

RANDOMIZATION

Paclitaxel 80 mg/m² IV **Day1,8,15**
Carboplatin AUC 6 IV
Q21, 6-8 Cycles

Paclitaxel 80 mg/m² IV **Day1,8,15**
Carboplatin AUC 6 IP
Q21, 6-8 Cycles

Primary Endpoint: PFS

Secondary Endpoint: OS, Toxicity, QOL

Accrual : **44** / 746 patients

A PHASE III/III STUDY OF INTRAPERITONEAL (IP) PLUS INTRAVENOUS (IV) CHEMOTHERAPY VERSUS IV CARBOPLATIN PLUS PACLITAXEL IN PATIENTS WITH EPITHELIAL OVARIAN CANCER OPTIMALLY DEBULKED AT SURGERY FOLLOWING NEOADJUVANT INTRAVENOUS CHEMOTHERAPY

A Gynecologic Cancer Intergroup (GCIg) Trial led by the NCIC CTG

NCIC CTG Protocol Number: OV.21

NCRI: UCL08/0379

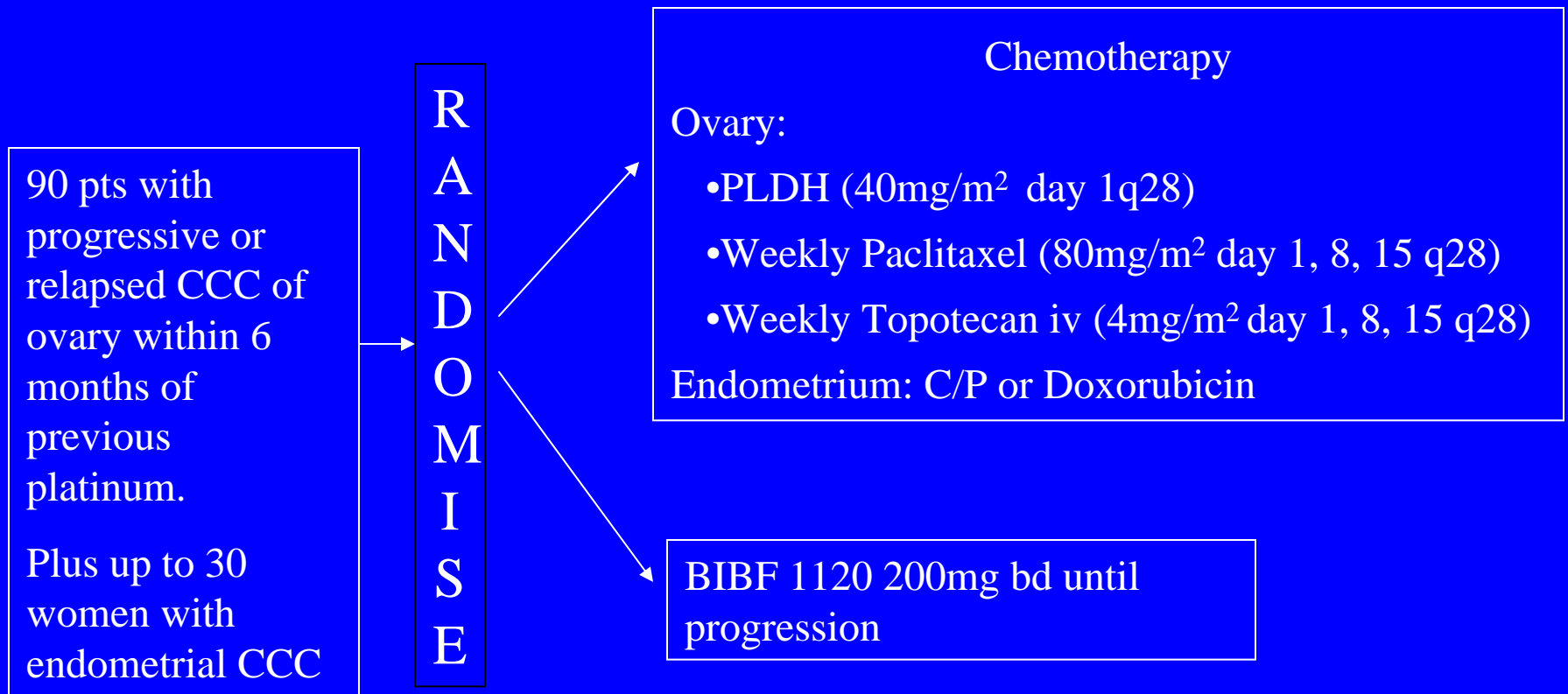
GEICO: 0902

SWOG: Pending

Phase III Trabectedin plus PLD versus Carboplatin plus PLD in relapsed ovarian cancer progressing within 6-12 months of last platinum

Patients	1/580
Leading	MaNGO
Participating	BGOG, DGOG, GEICO, SAKK, NOGGO, UK, NSGO, EORTC

Trial Design



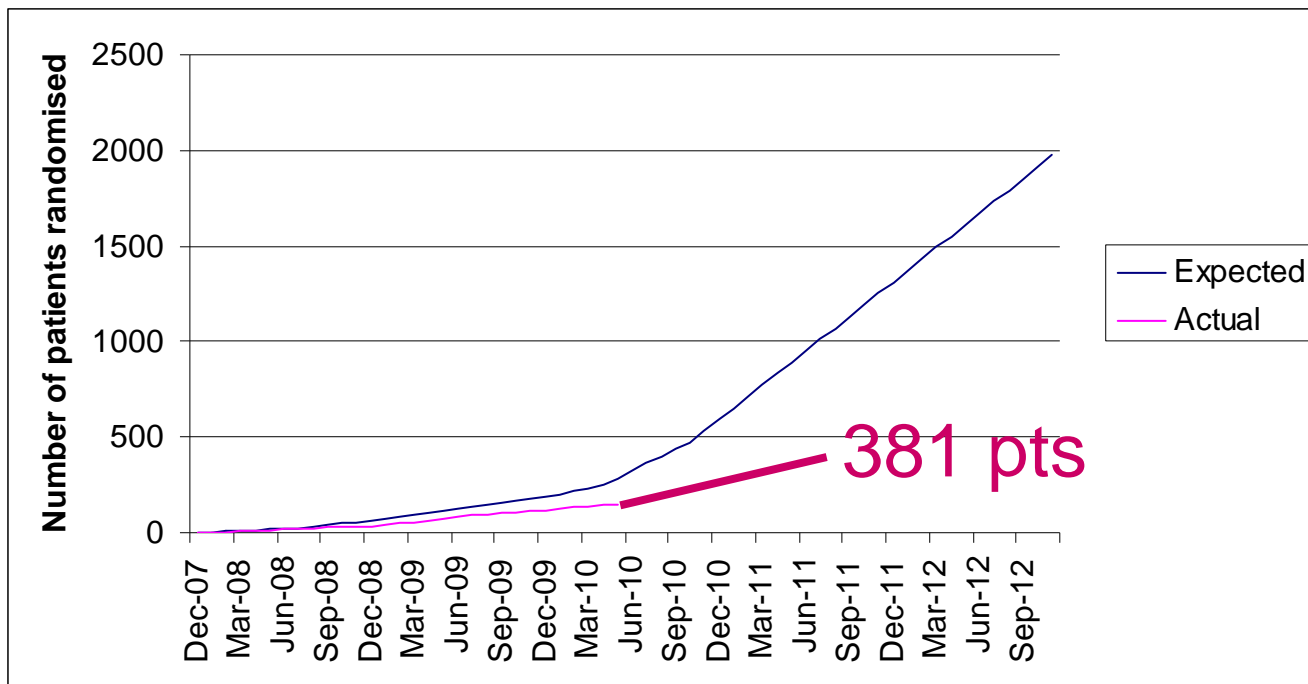
Primary Endpoint: PFS

Secondary Endpoints: OS, Toxicity, RR, QoL, Q-Twist

ICON6

A Randomised Trial of Concurrent Cediranib
(with Platinum-based Chemotherapy) and
Maintenance Cediranib in Women with
Platinum-Sensitive Relapsed Ovarian
Cancer

Expected vs Actual Accrual





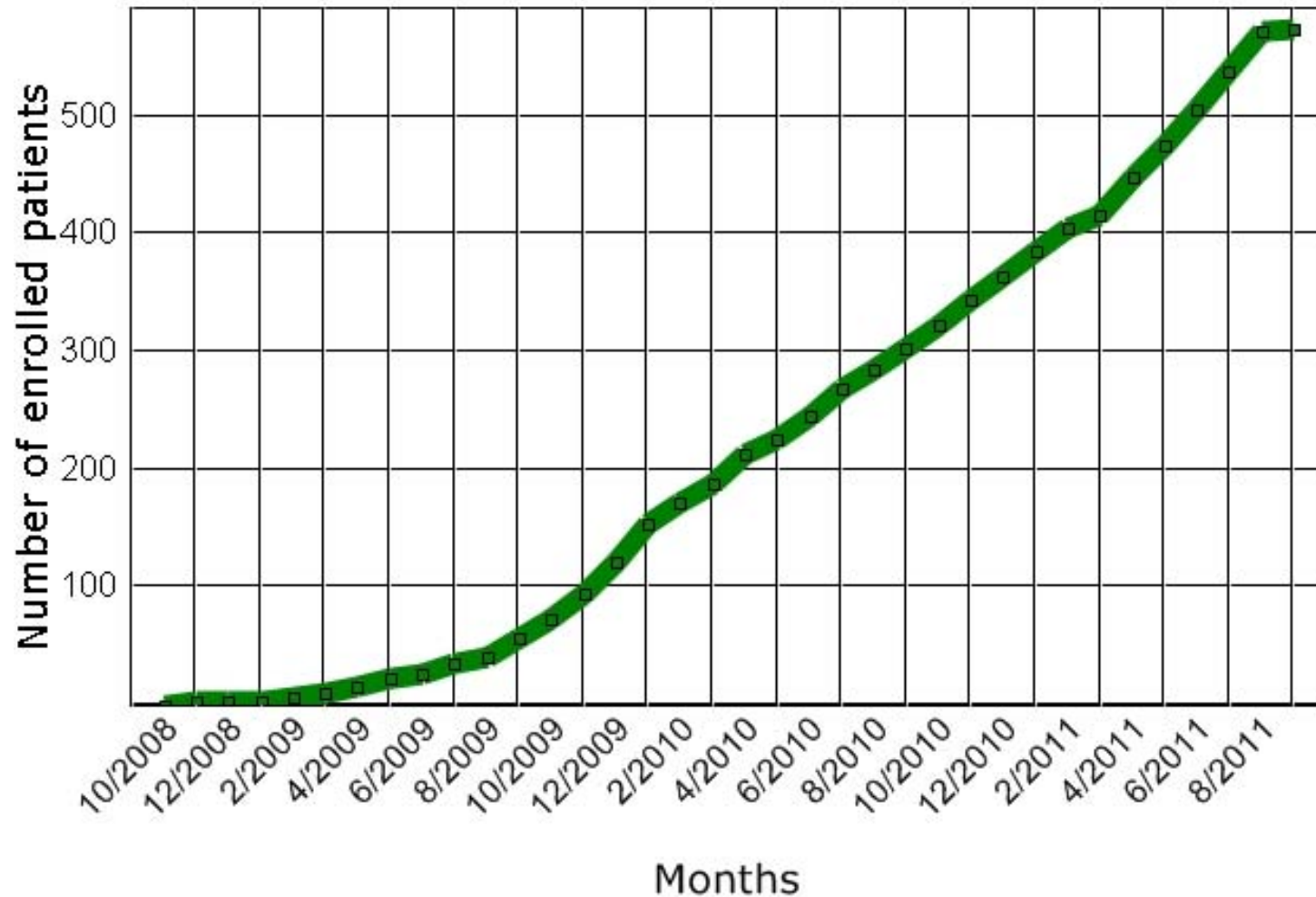
First line weekly carboplatin and
paclitaxel vs every 3 weeks
carboplatin/paclitaxel in patients with
ovarian cancer:

Phase III multicenter trial

MITO – 7 ENGOT OV10



MITO-7 study cumulative enrollment





**Liposomal doxorubicin vs
carboplatin/paclitaxel in recurrent
ovarian cancer patients with
platinum-free interval between 6-12
months**

MITO-8, ENGOT OV-1, AGO-OVAR 2.16



MITO-8 study cumulative enrollment





Weekly Paclitaxel vs weekly Paclitaxel
and Pazopanib in patients with
resistant/refractory ovarian cancer:
Phase II randomized multicenter trial

MITO - 11





A multicenter randomized study in patients with epithelial ovarian cancer with bevacizumab plus chemo vs chemo at progression after first line chemo + bevacizumab

**MITO – 16
Mango OV2**



MITO/MaNGO Phase III trial

Front line treatment

Second line treatment

**Chemonaive
Stage III - IV
OC, PP or FT
cancer**

Bevacizumab 15 mg/kg q3w with
CBDCA+Paclitaxel 6 cycles + followed by
Bevacizumab (GOG 218)

II line SOC*
Caelyx (plt res) or
CBDCA+Doxo, CBDCA+Gem,
CBDCA+Pacl (plat sens)

II line SOC
Caelyx (plt res) or
CBDCA+Doxo, CBDCA+Gem,
CBDCA+Pacl (plat sens)
+
Bevacizumab 15 mg/kg q3w

- Studies on BRCA-mutated ovarian cancer patients
- Evaluation of IL-6 in clear cell carcinoma
- Primary refractory ovarian cancer patients
- Consolidation
- Early detection
- *.....and what is your proposal?*