MADRID 2014 ESMO congress

VHIO VALL D'HEBRON Institute of Oncology

Vall d'Hebron Hospital

Targeted Therapy in Gyneacological Cancer

The impact of Targeted Therapy in Endometrial and Cervical Cancer

Ana Oaknin, MD
Gyneacological Cancer and Developmental Therapeutics Program
Vall d'Hebron Institute of Oncology
Barcelona, Spain
aoaknin@vhio.net

26-30 September 2014, Madrid, Spain

MADRID 2014 ESMO congress

I have nothing to disclose

OUTLINE

- Endometrial Cancer
  - PI3K Pathway
  - Metformin
  - Angiogenesis
- Cervical Cancer
  - Angiogenesis

Endometrial Cancer (EC): Introduction

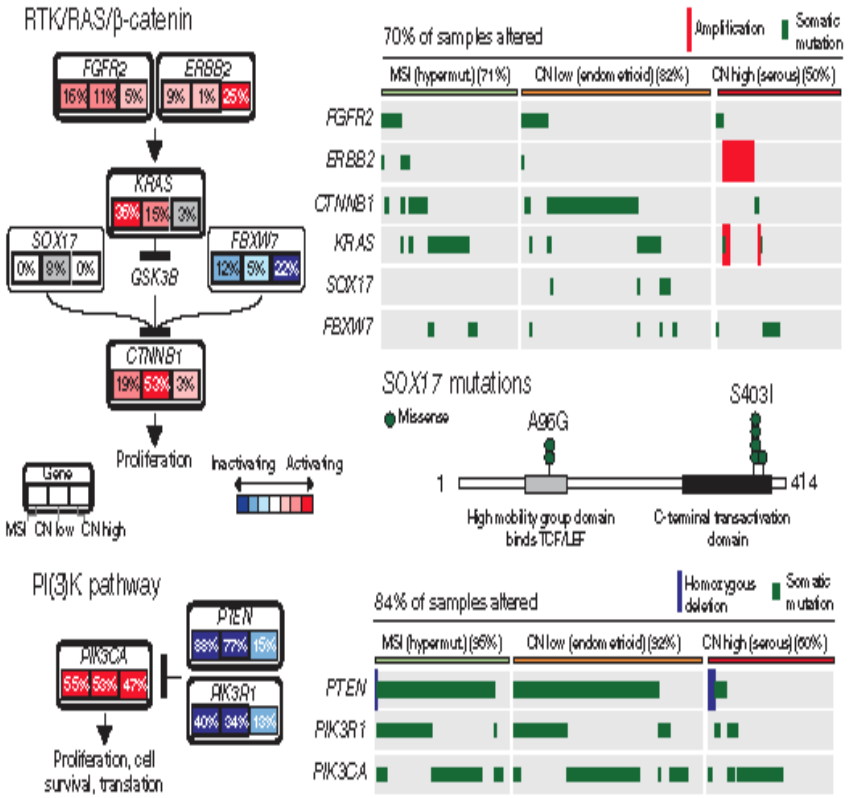
- EC is the most common gynecological cancer in developed countries.
- **52,630** estimated new cases and **8590** deaths in 2014 in the USA .
- The majority of EC (72%) are diagnosed in the early stages with a good prognosis, however 15-20% of these carcinoma will recur.
- For women with advanced or recurrent disease, survival has remained unchanged over the last 20 years(median survival:7-15months), highlighting the need for better therapies.
- The improved understanding of deregulated pathways in EC have led to clinical trials testing approaches with the key drivers of these pathways.

Pathways alterations in EC

Table 1 | Molecular alterations in endometrial cancer

Alteration	Prevalence in type I (%)	Prevalence in type II (%)
PIK3CA mutation[33–37]	~30	~20
Exon 9	7–15.5	0
Exon 20	10–34	21
PIK3CA amplification[14,36]	2–14	46
KRAS mutation[27,42,43]	11–26	2
AKT mutation[40]	3	0
PTEN loss of function[38,39]	83	5
Microsatellite instability[53,54]	20–45	0–5
Nuclear accumulation of β-catenin[56–59]	18–47	0
E-cadherin loss[29,30]	5–50	62–87
TP53 mutation[34,43,51]	~20	~90
Loss of function of p16[54]	8	45
HER2 overexpression[31,32]	3–10	32
HER2 amplification[13]	1	17
FGFR2 mutations[12,42,47]	12–16	1

Dedes KJ et al. Nature Reviews; Vol 8, May 2011

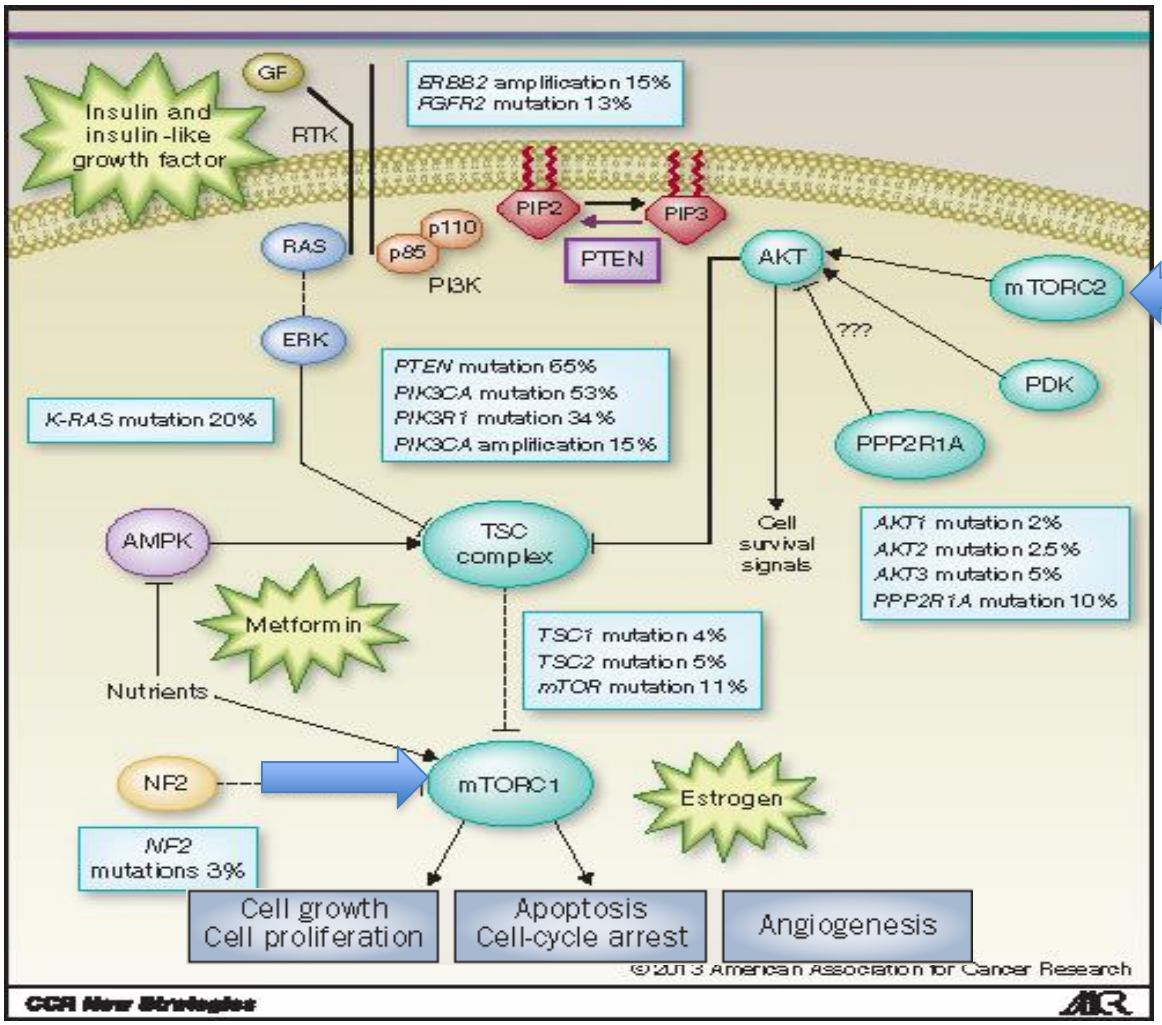


Endometrioid: 93% PI3KCA Mutations
Serous- Papillary: 42% PI3KCA Mutations

nature

G Getz *et al.* Nature 497, 67-73 ;2013

Targeting the PI3K/mTOR Pathway



Myers AP; Clin Cancer Res 2013;19:5264-5274

PI3K/mTOR Pathway Inhibitors: Rapalogs as Single Agents

Investigational agent	Target	Treatment population	NCT # (date registered)	Clinical results (n)	Toxicities
Temsirolimus	mTORC1	Chemo naïve	NCT00072176 (11/2003)	CR (0/33)[b] PR (4/33)[b] SD ≥ 8 weeks[c] (20/33)	Most common ≥ grade 3 AEs: fatigue, diarrhea, pneumonitis
Temsirolimus	mTORC1	1 prior line	NCT00072176 (11/2003)	CR (0/27) PR (1/27) SD ≥ 8 weeks[c] (12/27)	Most common ≥ grade 3 AEs: fatigue, diarrhea, pneumonitis, dyspnea, hypokalemia
Everolimus	mTORC1	1 2 prior lines[d]	NCT00087685 (7/2004)	CR (0/35) PR (0/35) SD ≥ 8 weeks (12/35)	Most common ≥ grade 3 AEs: fatigue, nausea lymphopenia, anemia, hyperglycemia
Ridaforolimus[e]	mTORC1	1 2 prior lines	NCT00122343 (7/2005)	CR (0/45) PR (5/45) SD ≥ 16 weeks (8/45)	Most common ≥ grade 3 AEs: anemia, hyperglycemia, mouth sores
Ridaforolimus	mTORC1	Adjuvant only	NCT00770185 (10/2008)	CR (0/35) PR (2/35) SD ≥ 8 weeks[c] (15/35)	Most common ≥ grade 3 AEs: lymphopenia, anemia
Ridaforolimus (vs. progestins)	mTORC1	1 2 lines	NCT00739830 (8/2010)	CR (0/64)[b] PR (0/64)[b] SD ≥ 8 weeks[c] (22/64) median PFS 3.6 vs. 1.9 months (ridaforolimus vs. progestins)	Most common ≥ grade 3 AEs: anemia, hyperglycemia, back pain, asthenia
Everolimus	mTORC1	1 2 prior lines	NCT00870337 (3/2009)	CR (0/44) PR (4/44) SD ≥ 12 weeks (14/44)	Most Common ≥ grade 3 AEs: fatigue, anorexia, infection, diarrhea, lymphopenia, anemia, thromboembolic event, hyperglycemia

- ✓ **ORR: 0%-25%**
- ✓ **Higher in chemo-naïve patients.**
- ✓ **Across histological types**

Myers AP; Clin Cancer Res 2013;19:5264-5274

Molecular Determinants of Outcome With Mammalian Target of Rapamycin Inhibition in Endometrial Cancer

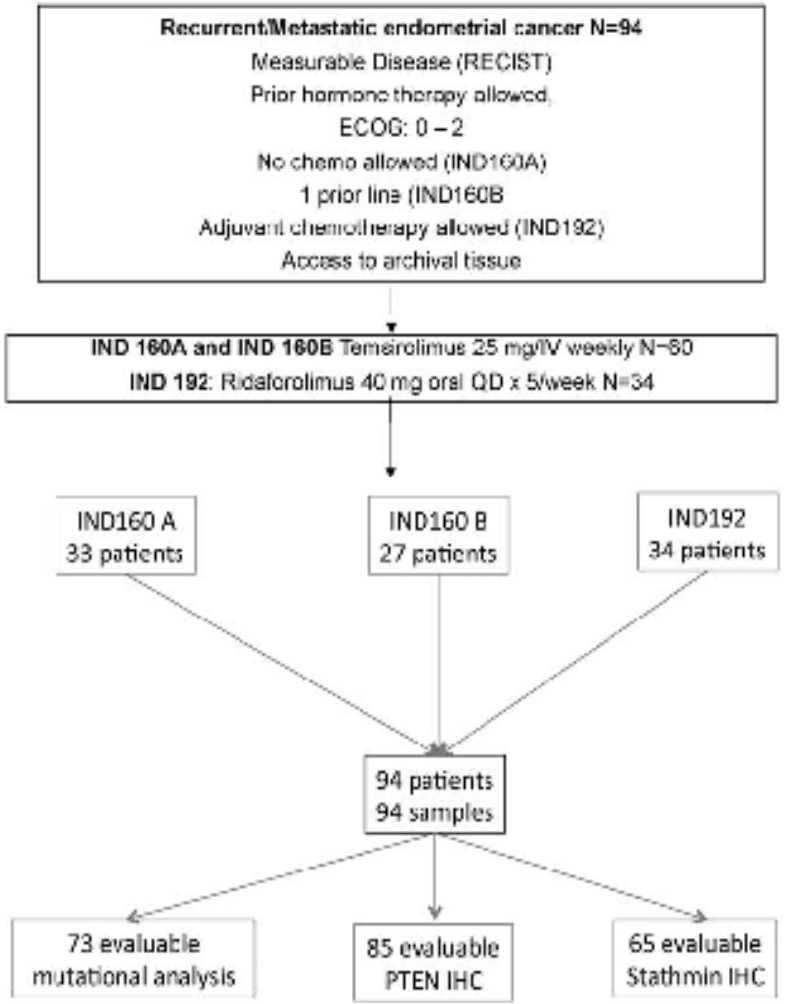


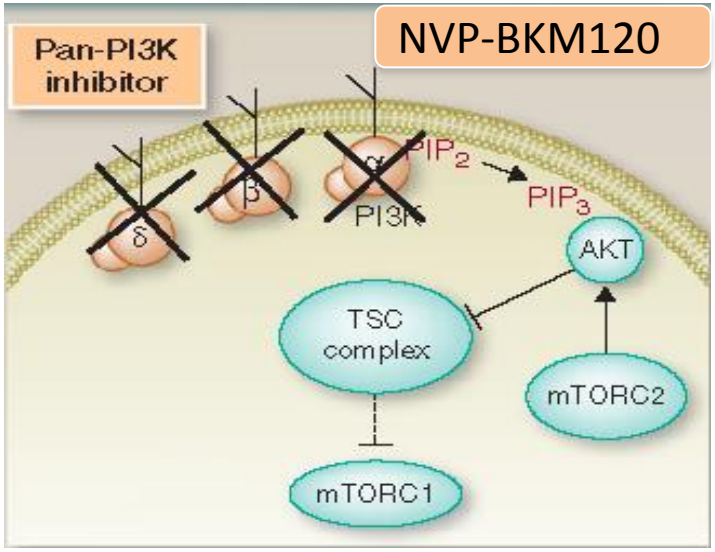
TABLE 2. Mutational Analysis and Association With Outcomes Among 73 Evaluable Patients

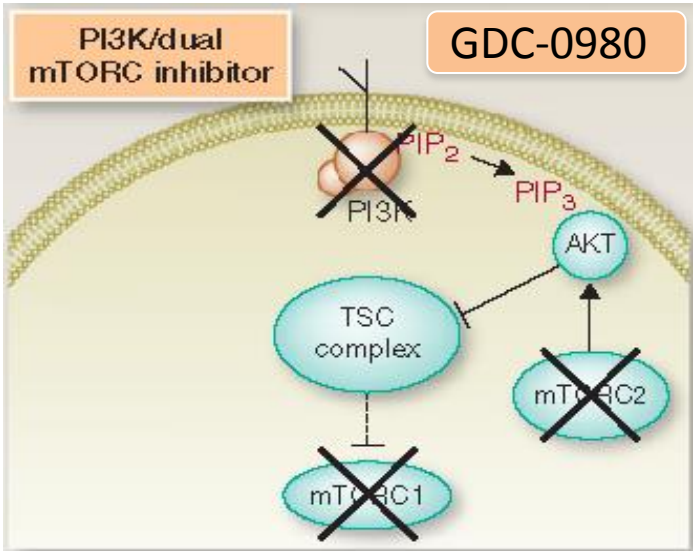
Mutation Group	No. (%[a])	Response (%[b])	P	Progression (%[b])	P
Any mutation			1.00		1.00
Yes	32 (43.8)	3 (9.4)		10 (31.3)	
No	41 (56.2)	4 (9.8)		13 (31.7)	
PIK3CA mutation			.40		.79
Yes	21 (28.8)	3 (14.3)		6 (28.6)	
No	52 (71.2)	4 (7.7)		17 (32.7)	
Type of PIK3CA mutation					
R88Q	7 (9.6)				
H104R	6 (8.2)				
E545K	4 (5.5)				
C420R	2 (2.7)				
H1047L	1 (1.4)				
P539R	1 (1.4)				
E542K	1 (1.4)				
KRAS mutation			.58		.49
Yes	10 (13.7)	0 (0.0)		2 (20.0)	
No	63 (86.3)	7 (11.1)		21 (33.3)	

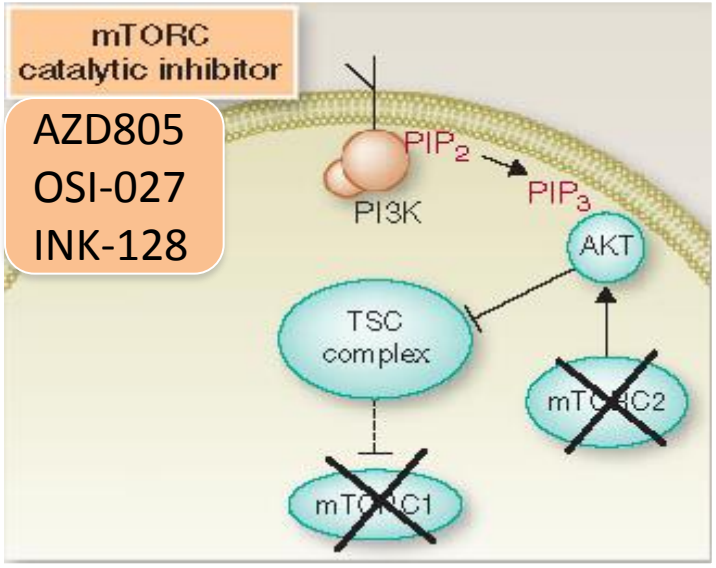
Group	No.	Response (%[a])	P	Progression (%[a])	P
PTEN expression			0.46		.35
Negative	46	3 (6.5)		12 (26.1)	
Positive	39	5 (12.8)		14 (35.9)	
Stathmin expression			0.89		.34
Negative	2	0 (0.0)		1 (50.0)	
Weak	21	2 (9.5)		5 (23.8)	
Moderate	27	2 (7.4)		7 (25.9)	
Strong	15	2 (13.3)		7 (46.7)	
Histologic subtype			0.74		.69
Endometrioid	66	6 (9.1)		19 (28.8)	
Clear cell	4	0 (0.0)		0 (0.0)	
Serous	12	2 (16.7)		3 (25.0)	

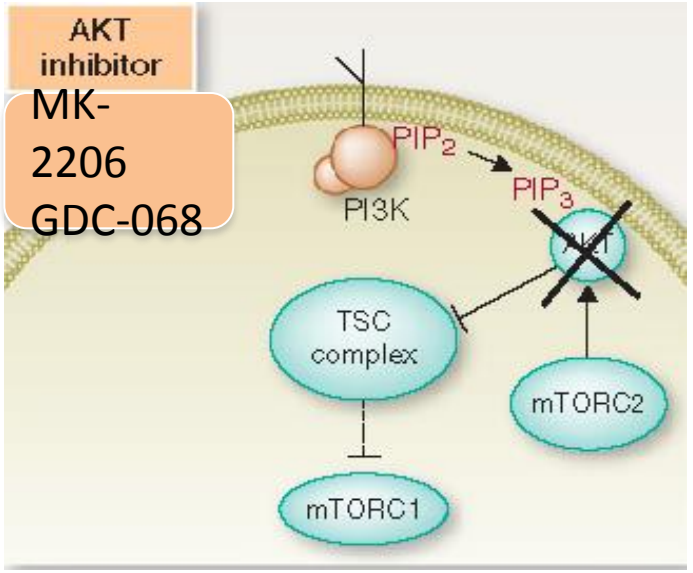
H. Mackay et al; Cancer .February 15;2014

Other Classes of PI3K/mTOR Pathway Inhibitors









Slomovitz and Coleman,Clin Cancer Res; 18(21) Nov 1, 2012;
Myers AP; Clin Cancer Res 2013;19:5264-5274; Myers AP; J Clin Oncol 31, 2013(suppl; abstr 5524)

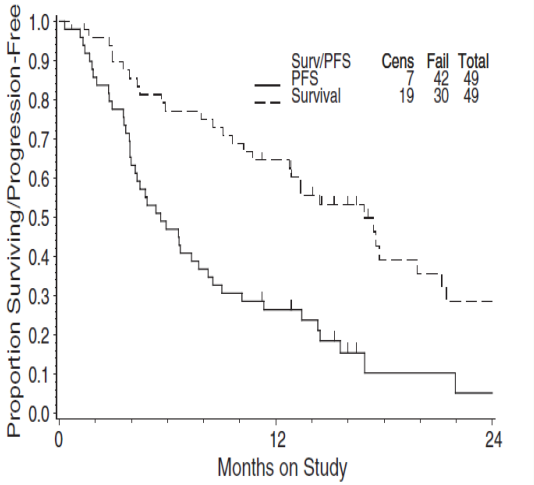
MADRID 2014 ESMO congress

Rapalogs in combination

Temsirolimus with or without megestrol acetate and tamoxifen for endometrial cancer: A gynecologic oncology group study

- **The combination therapy resulted in an unacceptable rate of Thrombotic Events (33%) which led to an early closure of the study.**
- **The combination arm did not improved response rates compared to Temsirolimus (14% vs 22%).**

Phase II trial of combination bevacizumab and temsirolimus in the treatment of recurrent or persistent endometrial carcinoma: A Gynecologic Oncology Group study ☆



Promising Activity:

- ORR:24.5%
- PFS>6mths:46%
- mPFS:5.6mths
- mOS:16.9mths

Significant Toxicity:

- **38.8% stopped due to Toxicity.**
- 2 G.I-Vaginal fistulas,
- 2 intestinal perforations
- 1 Gr4 thrombosis

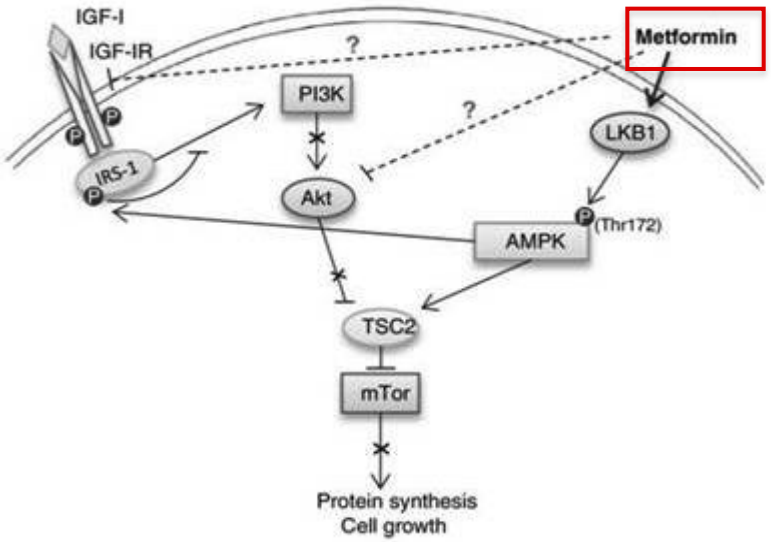
Fleming. G et al; Gyn Oncol 132 (2014) 585–592; Alvarez E et al; Gyn Oncol 129 (2013) 22–27

Metformin:
Our old friend returns

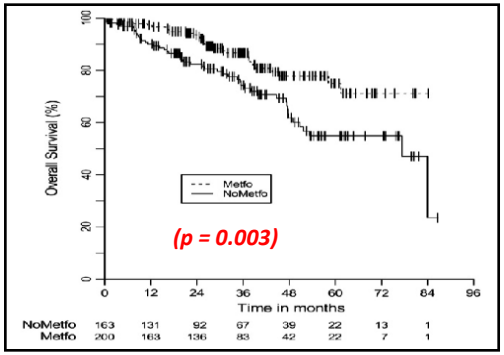
Metformin

Mechanism of Action:

- **Direct:**
  - Activates AMPK- Inhibition of mTOR
- **Indirect:**
  - Increases Insulin Sensitivity
  - Decrease gluconeogenesis
  - Decreases circulating Insulin levels



- Metformin is currently used as the first line treatment for type II diabetes mellitus .
- Population based studies have suggested a protective role for metformin in the prevention of solid tumor malignancies in diabetic patients.
- Metformin is a potent inhibitor of cell proliferation in EC cell lines. This effect is partially mediated through inhibition of the mTOR Pathway[2].
- Metformin in combination with paclitaxel resulted in a synergistic anti-proliferative effect in these cell lines[3].
- Metformin is associated with improved survival in endometrial cancer[4]



1. Adapted from J Pancreas 2013;14(4); 2.Cantrell LA et al; Gyn Oncol 2010;116(1).
3. Hanna RK et al. Gynecol Oncol 2012;125(2);4.Emily M. Ko et al; Gynecol Oncol 2014; 132: 438-442

MADRID 2014 ESMO congress

- Phase II/III
- N= 240/300 pts (500pts)
- 1º End- Point: PFS/OS

GOG#0286B

- **Eligibility:**
- Stage III or IVA EC measurable disease
- Stage IVB or Recurrent EC (whether there is measurable disease or not)
- No prior chemotherapy

Arm 1:

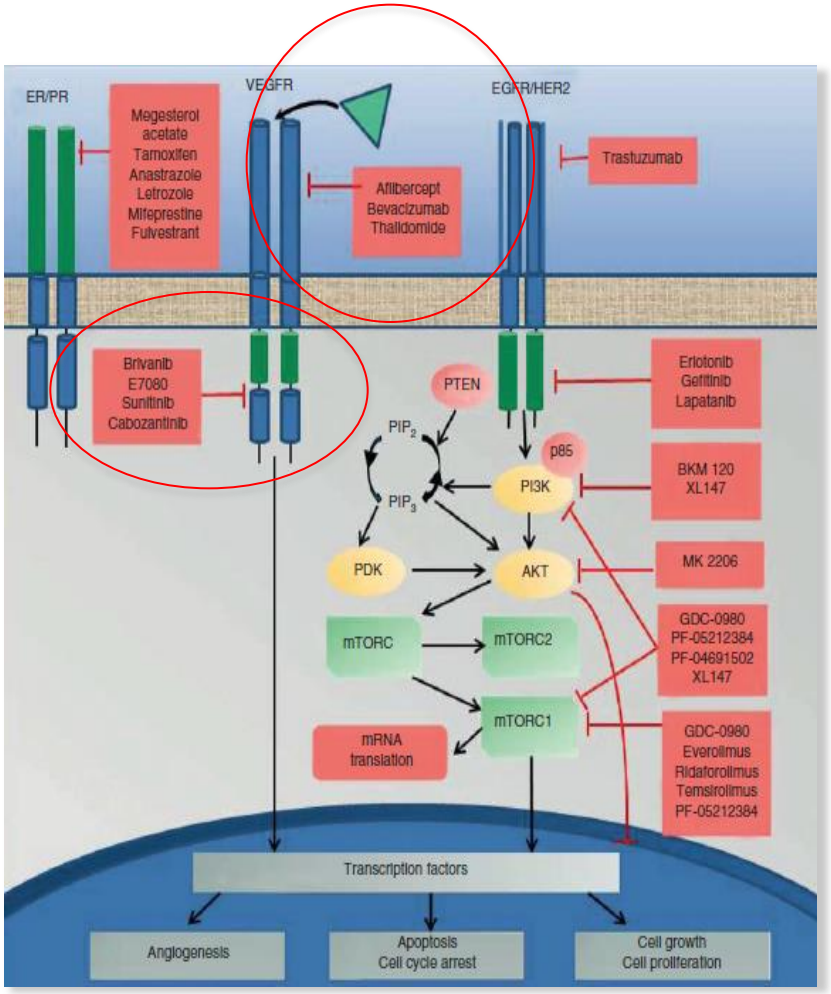
Paclitaxel 175 mg/m2 IV over 3 hours day 1
Carboplatin AUC = 5 IV day 1
Metformin 850 mg oral QD, beginning on day 1. If tolerated for 4 weeks, the dose will be increased to Metformin 850 mg BID.
Maintenance regimen: Metformin 850 mg oral BID until disease progression or prohibition of further therapy.

Arm 2:

Paclitaxel 175 mg/m2 IV over 3 hours day 1
Carboplatin AUC = 5 IV day 1
Placebo for Metformin 850 mg oral QD, beginning on day 1. If tolerated for 4 weeks, the dose will be increased to placebo for Metformin 850 mg BID.
Maintenance regimen: Matched Placebo oral until disease progression or prohibition of further therapy.

PI: Victoria Bae-Jump, M.D. PhD
Open: 17/March/2014
ClinicalTrials.gov Identifier:NCT02065687

Angiogenesis



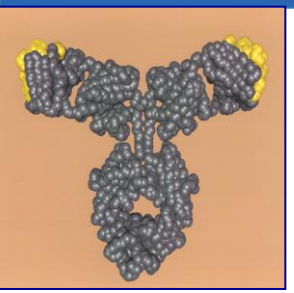
- VEGF is a key driver of angiogenesis and has been recognized as a potentially important mechanism of tumor growth, survival and metastasis in EC.
- In many reports, increased levels of VEGF and angiogenic markers are associated with poor outcome.
- Angiogenesis is an attractive target but VEGF inhibition has not been extensively studied in EC

Lheureux et al 2014 Exp Opin Investig Drugs

Kamat A. et al; Clin Cancer Res 2007;13(24); McMeekin DS;Gynecol Oncol 2007;105(2)

GOG 229-E

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT



Phase II Trial of Bevacizumab in Recurrent or Persistent Endometrial Cancer: A Gynecologic Oncology Group Study

Carol Aghajanian, Michael W. Sill, Kathleen M. Darcy, Benjamin Greer, D. Scott McMeekin, Peter G. Rose, Jacob Rotmensch, Mack N. Barnes, Parviz Hanjani, and Kimberly K. Leslie

- Persistent or recurrent EMC.
- **N=52 assessable pts**
- 1-2 prior cytotoxic regimens
  - **36.5% 2 prior lines**
- **Prior RDT: 55.8%**
- Measurable disease
- PS ≤ 2

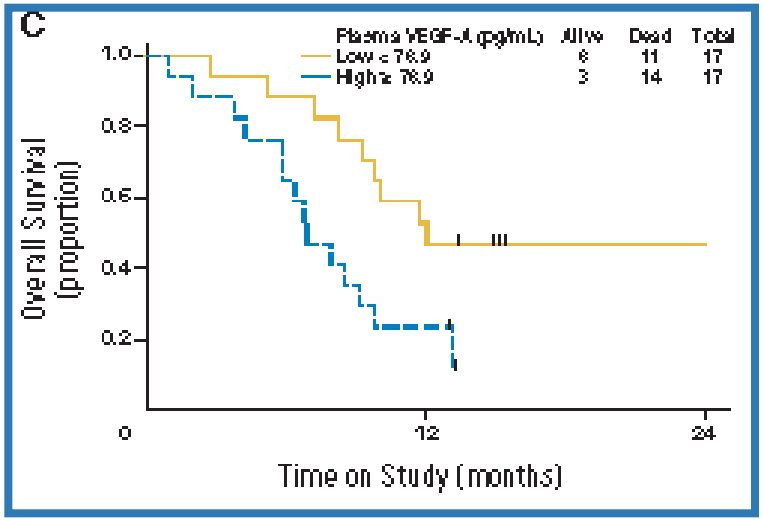
BEV 15mg /kg/21 days IV

- 7 pts (13.5%): ORR
- 21 pts (40.4 %)≥6 mths PFS
- Median PFS: 4 .17mths
- Median OS: 10.55 mths

Responses across histologic types

Toxicity Profile:

✓No fistulas or perforations seen
✓1Gr4 gastric hemorrhage
✓1Gr3 rectal hemorrhage
✓2Gr3 thrombotic events



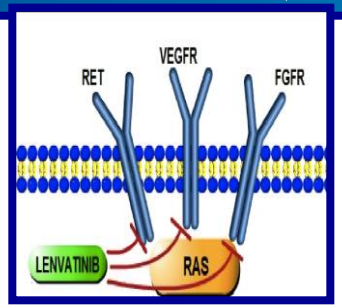
Aghajanian C, et al. J Clin Oncol. 2011;16):2259-2265.

A PHASE 2 TRIAL OF LENVATINIB IN PATIENTS WITH ADVANCED OR RECURRENT ENDOMETRIAL CANCER: ANGIOPOIETIN-2 AS A PREDICTIVE MARKER FOR CLINICAL OUTCOMES

I. Vergote,[1] M. Teneriello,[2] M.A. Powell,[3] D.S. Miller,[4] A.A. Garcia,[5] O.N. Mikheeva,[6] T. Pinter,[7] M. Bidzinski,[8] C.L. Cebotaru,[9] J. Fan,[10] M. Ren,[10] N. Meneses,[10] Y. Funahashi,[11] T. Kadowaki,[11] J.P. O'Brien,[10] and R.T. Penson[12]

[1]University Hospitals Leuven, Leuven, Belgium, European Union; [2]US Oncology, The Woodlands, Texas; [3]Washington University School of Medicine, St. Louis, Missouri; [4]University of Texas Southwestern Medical Center, Dallas, Texas; [5]University of Southern California, Los Angeles, California; [6]State Healthcare Institution Leningrad Regional Oncology Center, St. Petersburg, Russia; [7]Aladar Petz Teaching County Hospital, Gyor, Hungary; [8]Maria Sklodowska-Curie Memorial Institute, Warsaw, Poland; [9]Institute of Oncology "Prof. Dr. Ion Chincuta," Cluj-Napoca, Romania; [10]Eisai Inc., Woodcliff Lake, New Jersey; [11]Eisai Inc., Andover, Massachusetts; [12]Massachusetts General Hospital Cancer Center and DFHCC, Boston, Massachusetts

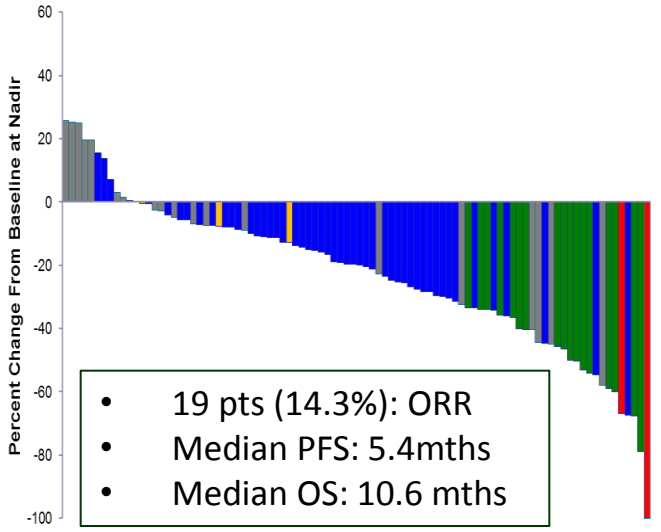
- **Lenvatinib: TKI** of **VEGFR1-3; FGFR1-4,PDGFRβ RET,KIT**
- N=133 pts advanced or recurrent EC
- All 1 prior Platinum QT
- Prior RDT:82%
- **Lenvatinib:** 24mg qd in a 28-day cycle



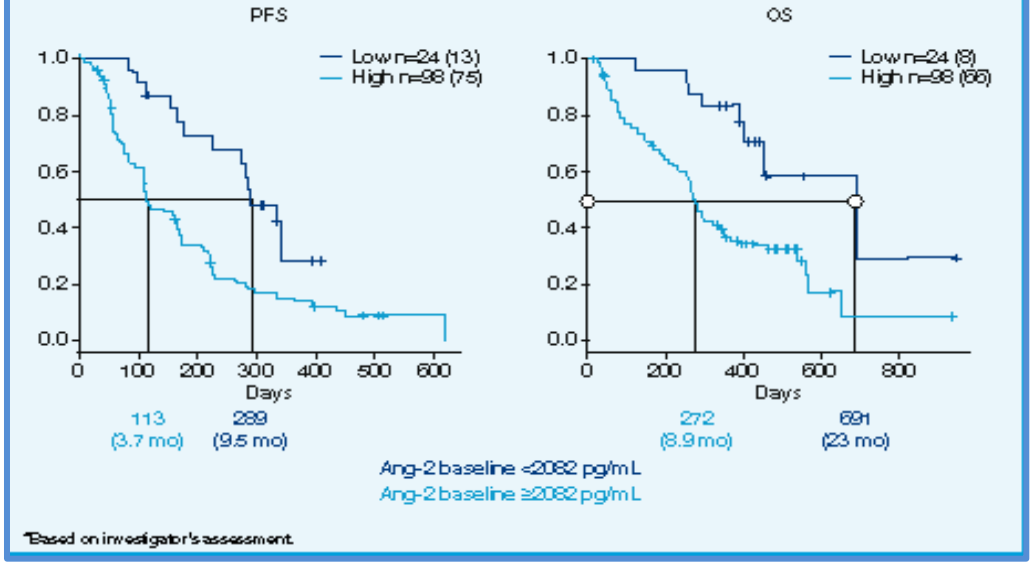
Phase II Single-Arm Objectives:

- Safety and efficacy of lenvatinib
- Identify predictive markers for lenvatinib response

Maximum % Change in Sum of Diameter From Baseline



Observed Progression Free Survival and Overall Survival in low and High Ang-2 Subgroups



Vergote I et al; J Clin Oncol 31, 2013 (suppl; abstr 5520)

MADRID 2014 ESMO congress

Other AntiAngiogenic Agents: Toxicity was an issue

AGENT	SETTING	RR%	PFS@ 6 Mths	PFS/OS (Mths)	Toxicity:
SORAFENIB[1]	EC: 1st or 2nd line (including Carcinosarcomas)	5%	29%	NR/11.4	**Gr3/4:** HTA:13% HFS:13% Diarrhea:5% Fatigue:5%
SUNITINIB[2]	EC 1st or 2nd line (including Carcinosarcomas)	18.2%	30%	3.0/19.4	**50% dose reduction. Gr3/4:** Fatigue:50% HTA:23% HFS:17%
AFLIBERCEPT GOG#229F[3]	EC :1 or 2 prior lines	7%	23%	2.9/14.5	**32% removed from study for Toxicity .** 2 Gr 5: g.i perforation/ ruptured artery Leukoencephalopaty (2 events)

1. Nimeiri HS, Gynecol Oncol. 2010;111(1):37-40
2. Castonguay V, Gynecol Oncol 134 (2014) 274–280
3. Coleman R, Gynecol Oncol 127 (2012) 538–543

MADRID 2014 ESMO congress

- Phase II Randomized
- 1º End-Point: PFS
- N= 349

GOG#0086P

- Eligibility:
- Stage III or IVA EC measurable disease
- Stage IVB or Recurrent EC (whether there is measurable disease or not)
- No prior Chemotherapy

Arm 1:
Paclitaxel 175 mg/m2 IV over 3 hours day 1
Carboplatin AUC = 6 IV day 1
Bevacizumab 15mg/kg IV day 1
Maintenance regimen - Bevacizumab 15mg/kg IV every 21 days until disease progression or prohibition of further therapy.

Arm 2:
Paclitaxel 175 mg/m2 IV over 3 hours day 1
Carboplatin AUC = 5 IV day 1
Temsirolimus 25 mg IV days 1 and 8
Maintenance regimen – Temsirolimus 25 mg IV weekly. Days 1,8 and 15 until disease progression or prohibition of further therapy.

Arm 3:
Ixabepilone 30 mg/m2 IV over 1 hour day 1
Carboplatin AUC = 6 IV day 1
Bevacizumab 15mg/kg IV day
Maintenance regimen - Bevacizumab 15mg/kg IV every 21 days until disease progression or until prohibition further therapy.

PI: Carol Aghajanian, M.D.
From: 9/14/2009 to 9/9/2014
ClinicalTrials.gov Identifier:NCT00977574

Cervical Cancer: Introduction

- CC is still the second leading cause of cancer death in women worldwide.
- Risk of recurrent disease is 10–20% FIGO stages Ib–IIa and 50–70% in locally advanced cases (stages IIb–IVa).
- Patients with recurrent disease not amenable to local control or distant metastases, having a very poor prognosis: **1 Year Survival< 20%**
- Cervical carcinogenesis is driven in the majority of cases, by HPV infection.
- Oncoproteins, HPV-E6 and HPV-E7 led a biological events that affect different molecular pathways: DNA Repair, cell cycle and angiogenesis.

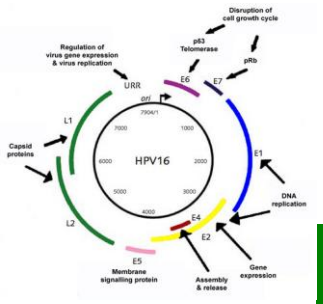
Main molecular targets (and agents in development) in cervical cancer.

Biological pathway	Molecular target(s)	Therapeutic agent
Angiogenesis	VEGF	Bevacizumab
	VEGFR-1,-2,-3,PDGFR,c-kit	Sunitinib
	VEGFR-1,-2,-3,PDGFR,c-kit	Pazopanib
	VEGFR-2, FGFR	Brivanib
	ANGPT-1, ANGPT-2	AMG386
EGF	EGFR-TK	Gefitinib
		Erlotinib
	EGFR	Cetuximab
mTOR/PI3K/Akt	mTOR C1	Temsirolimus
DNA repair	PARP	Veliparib
		Olaparib
Cell cycle	Wee1	MK-1775
Apoptosis	TRAIL-R1	Mapatumumab

Woodman et al. Nature Reviews Cancer 7, 11-22;2007
Diaz-Padilla et al. Critical Reviews in Oncology 85(2013): 303-314

Angiogenesis in Cervical Cancer:

- **Bevacizumab** activity in cervical cancer was demonstrated in a phase 2 single-agent study **(GOG 227C)**



HPV E6 → p53 degradation → TSP-1 → ↑ VEGF → ↑ angiogenesis

Anti-VEGF therapy

HPV E7 → Displacement of HDAC1, HDAC4, HDAC7 → ↑ HIF1α → ↑ VEGF → ↑ angiogenesis

HPV E7 → pRb inactivation → p21-RB pathway dysregulation

Tewari KS, et al. Gynecol Oncol 2000;77:137-48.
Monk BJ, et al. J Clin Oncol. 2009;27(7):1069-74.
http://www.microbiologybytes.com/virology/Papillomaviruses.html

GOG#240: Incorporation of Bevacizumab in the treatment of Recurrent and Metastatic Cervical Cancer

Activated: 4/6/09
Closed to accrual: 1/3/12

Carcinoma of the cervix
- Primary stage IVB
- Recurrent/persistent
- Measurable disease
- GOG PS 0–1
- No prior chemotherapy for recurrence

(N=452)

RANDOMIZE

I	Paclitaxel 135 or 175 mg/m² IV Cisplatin 50 mg/m² IV	Chemo alone
II	Paclitaxel 135 or 175 mg/m² IV Cisplatin 50 mg/m² IV Bevacizumab 15 mg/kg IV	Q21d Rx to PD, toxicity, CR
III	Paclitaxel 175 mg/m² IV Topotecan 0.75 mg/m² d1-3	Chemo + Bev
IV	Paclitaxel 175 mg/m² IV Topotecan 0.75 mg/m² d1-3 Bevacizumab 15 mg/kg IV	Chemo + Bev

1º END-POINTS:
If adding BEV to Chemo improves OS
If a non-platinum doublet improves OS

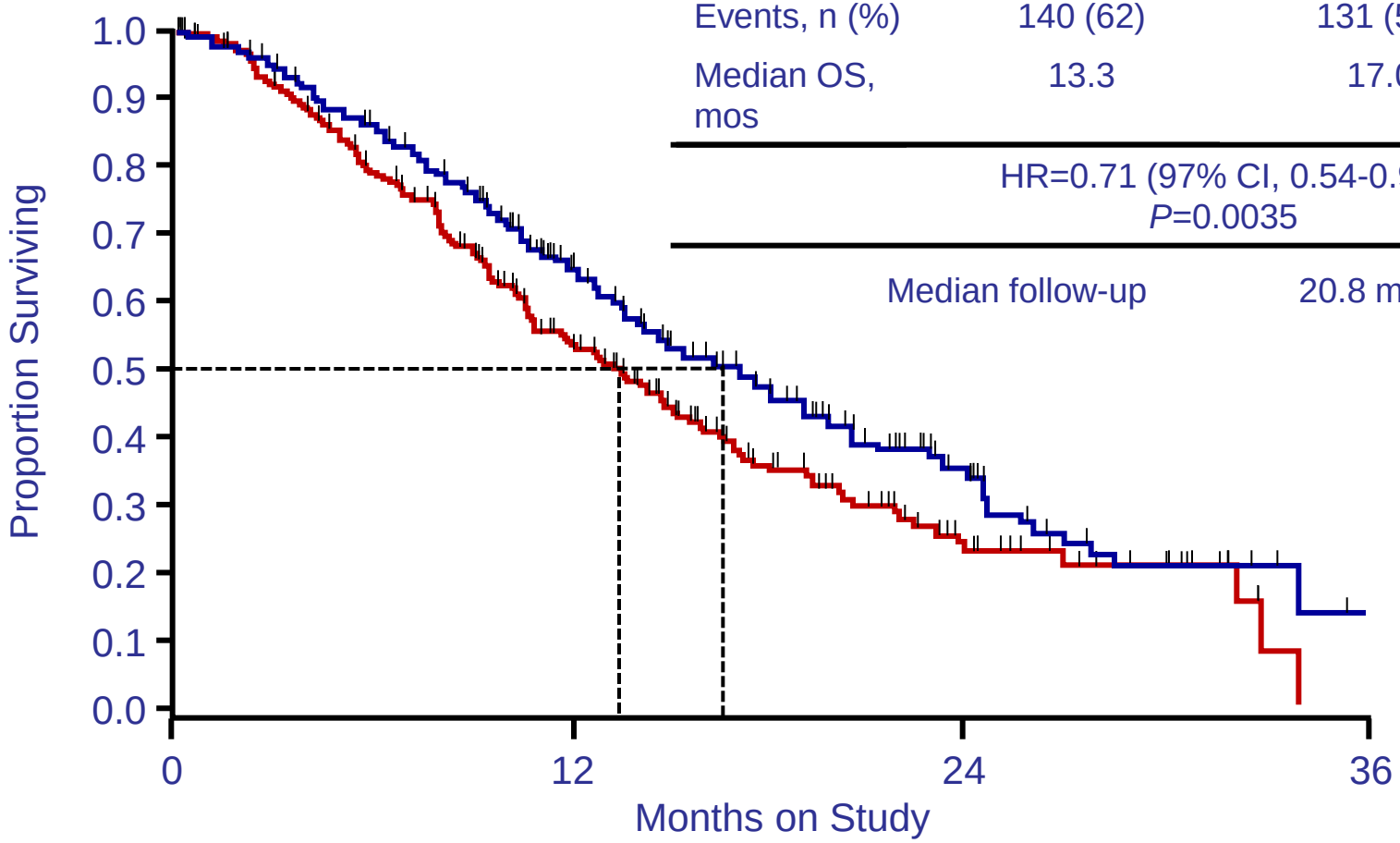
Stratification factors:
- Stage IVB vs. recurrent/persistent disease
- Performance status
- Prior cisplatin Rx as radiation-sensitizer

KS Tewari (study chair). www.ClinicalTrials.gov Identifier: NCT00803062.

GOG #240:

OS for Chemo vs Chemo + Bev

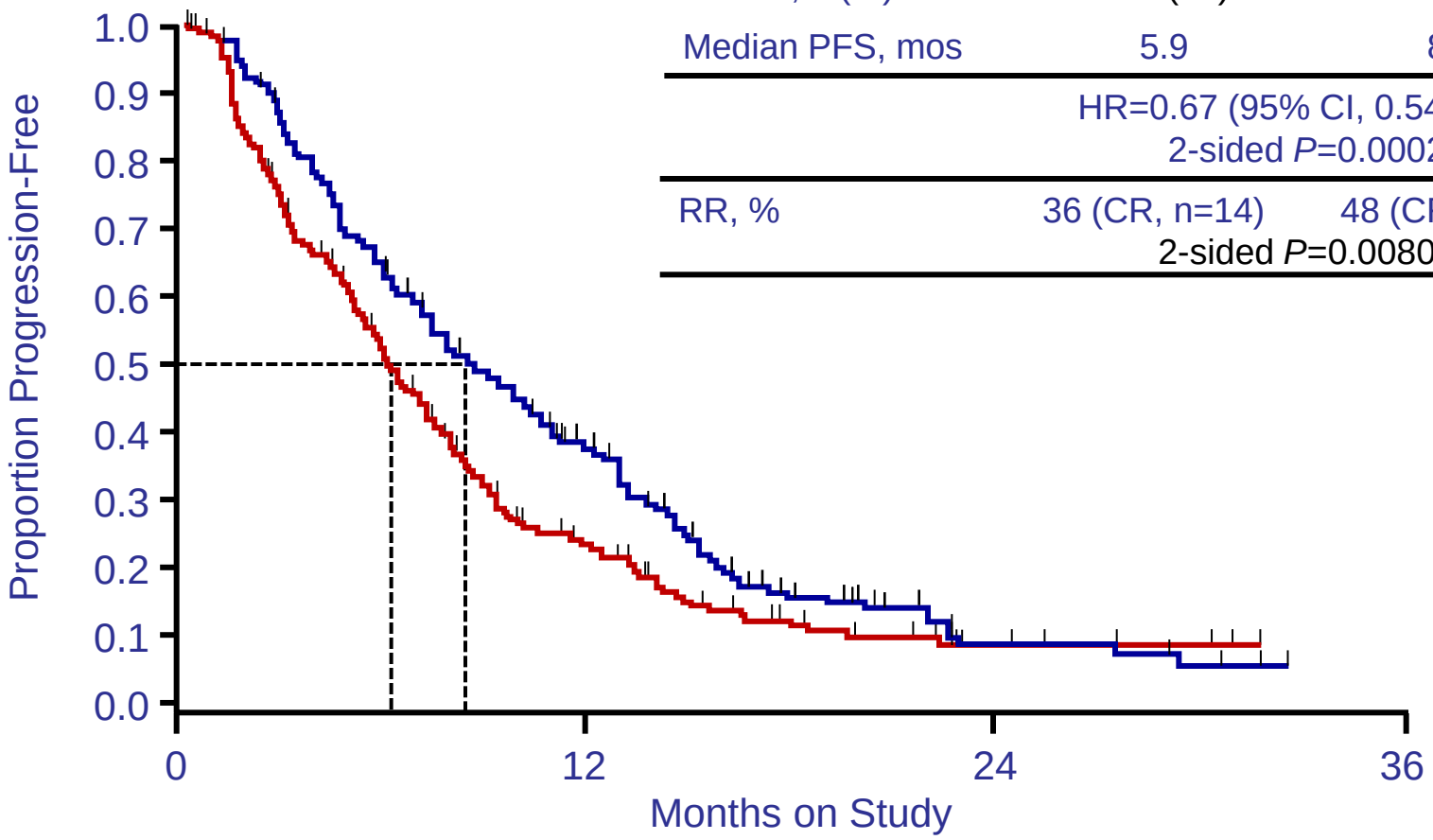
	Chemotherapy (n=225)	Chemotherapy + Bev (n=227)
Events, n (%)	140 (62)	131 (58)
Median OS, mos	13.3	17.0
	HR=0.71 (97% CI, 0.54-0.94) *P*=0.0035	
Median follow-up		20.8 mos



N ENGL J MED 370;8 NEJM.ORG FEBRUARY 20, 2014

GOG #240:
PFS for Chemo vs Chemo + Bev

	Chemotherapy (n=225)	Chemotherapy + Bev (n=227)
Events, n (%)	184 (82)	183 (81)
Median PFS, mos	5.9	8.2
	HR=0.67 (95% CI, 0.54-0.82) 2-sided *P*=0.0002	
RR, %	36 (CR, n=14)	48 (CR, n=28) 2-sided *P*=0.00807



N ENGL J MED 370;8 NEJM.ORG FEBRUARY 20, 2014

GOG #240:

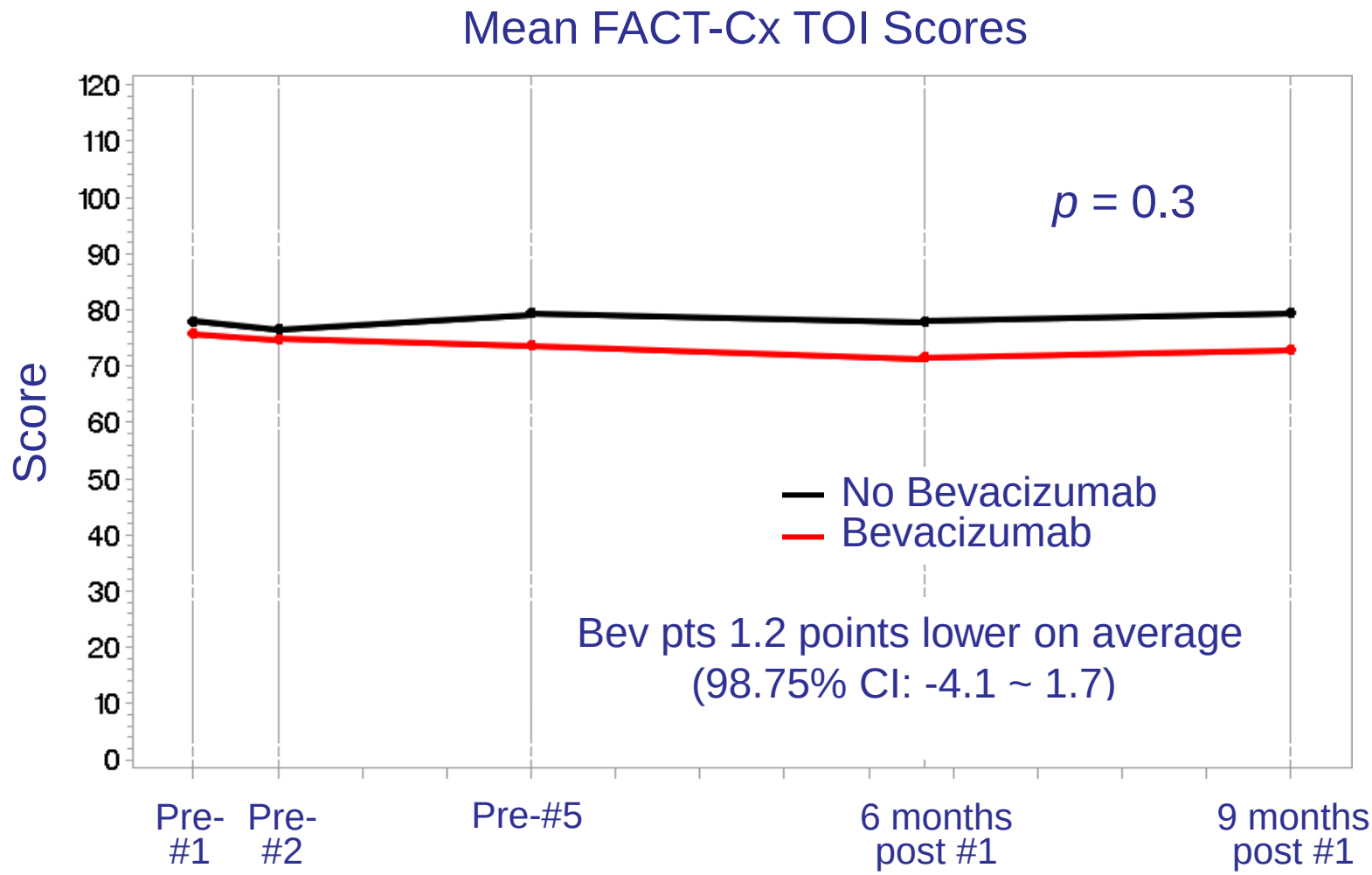
Treatment Exposure and Specific Adverse Events

Adverse Event, n (%)	Chemo Alone (n=219)	Chemo + Bev (n=220)
Treatment cycles, median (range)	6 (0-30)	7 (0-36)
Grade 5 AE(s)	4 (1.8)	4 (1.8)
GI events, non-fistula (grade ≥2)	96 (44)	114 (52)
GI fistula (grade ≥3)*	0 (0)	7 (3)
GI perforation (grade ≥3)	0 (0)	5 (2)
GU fistula (grade ≥3)*	1 (0)	6 (2)
Hypertension (grade ≥2)*	4 (2)	54 (25)
Proteinuria (grade ≥3)	0 (0)	4 (2)
Pain (grade ≥2)	62 (28)	71 (32)
Neutropenia (grade ≥4)*	57 (26)	78 (35)
Febrile neutropenia (grade ≥3)	12 (5)	12 (5)
Thromboembolism (grade ≥3)*	3 (1)	18 (8)
Bleeding CNS (any grade)	0 (0)	0 (0)
GI (grade ≥3)	1 (0)	4 (1)
GU (grade ≥3)	1 (0)	6 (3)

*$p<0.05$

N ENGL J MED 370;8 NEJM.ORG FEBRUARY 20, 2014

GOG #240:
HRQoL Mean FACT-Cx TOI



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Improved Survival with Bevacizumab in Advanced Cervical Cancer

Krishnansu S. Tewari, M.D., Michael W. Sill, Ph.D., Harry J. Long III, M.D., Richard T. Penson, M.D., Helen Huang, M.S., Lois M. Ramondetta, M.D., Lisa M. Landrum, M.D., Ana Oaknin, M.D., Thomas J. Reid, M.D., Mario M. Leitao, M.D., Helen E. Michael, M.D., and Bradley J. Monk, M.D.

FDA News : For Immediate Release

August 14, 2014

FDA approves Bevacizumab to treat patients with aggressive and late-stage cervical cancer

First targeted agent licensed for gynecologic malignancy in the USA

Targeted Therapies underway

❑ Targeting the PI3K/PTEN/AKT Pathway

- Link between mTOR and HPV (E6 interacts TSC2, 4E-BP1 and E7)
- 36% (5/14) PIK3CA mutations squamous cell cervix. Response rate PIK3CA mutant 40% (2/5) (Janku JCO 2012)
- **Phase II temsirolimus (mTOR) (Tinker Gyn Onc 2013)**
  - 3% PR; 58% stable (duration 6.5 m); 6m PFS 28% median PFS 3.5 months
  - No molecular markers for benefit identified

❑ PARP inhibitors

- FANCF inactivated in cervical cancer (Narayan Can Res 2004)
- **GOG#0076[1]:** Paclitaxel, Cisplatin, and Veliparib; **GOG#0127[2]** Topotecan+Veliparib

❑ Immunotherapy

- **GOG phase II live-attenuated *L. monocytogenes* cancer vaccine** (against viral oncoprotein E7) (ADXS-001) in persistent/recurrent cervical cancer
- **NCI phase II ipilimiumab[3]** (HPV-related)

1.ClinicalTrials.gov Identifier:NCT01281852
2.ClinicalTrials.gov Identifier: NCT01266447
3.ClinicalTrials.gov Identifier:NCT01711515

CONCLUSIONS

Endometrial Cancer

- Targeting the PI3KCA Pathways needs further investigation and clarification of relevant biomarkers.
- Metformin is an interesting drug, which is likely to be the subject to a number of upcoming trials.
- Antiangiogenesis agents seem to be an useful strategy.

Cervical Cancer

- Bevacizumab improved overall survival in recurrent/ metastatic disease.
- New agents including immunotherapy are under investigation.

MADRID 2014 ESMO congress

VHIO VALL D'HEBRON Institute of Oncology

Vall d'Hebron Hospital

THANK YOU FOR YOUR ATTENTION

GRACIAS POR SU ATENCION