Current Systemic Treatment of Advanced Cervical Cancer and Endometrial Cancer

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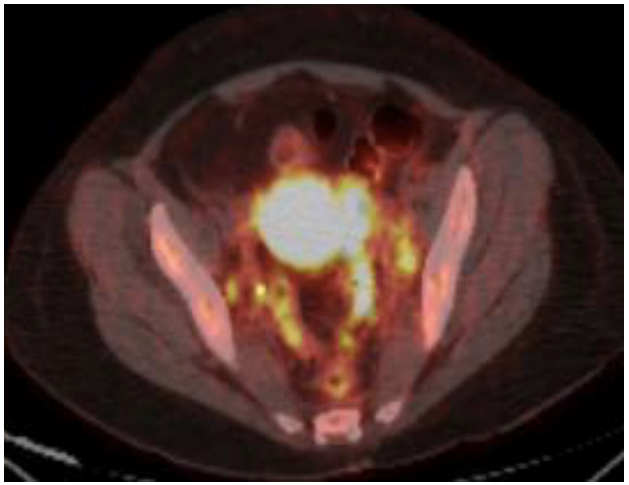
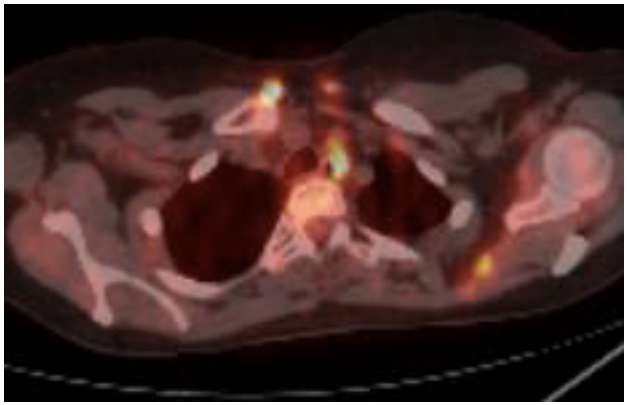
Advanced Cervical Cancer

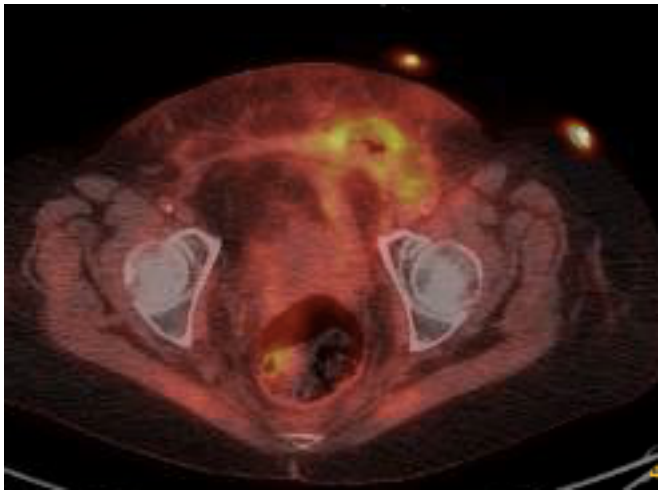
- 50 y.o. female with stage IVB SCC of the cervix who presented with profuse vaginal bleeding and pelvic pain. Initial PET/CT demonstrated widely metastatic disease. She was otherwise healthy.
- She was treated with concurrent chemoradiation for local control.
- Additional therapy options?

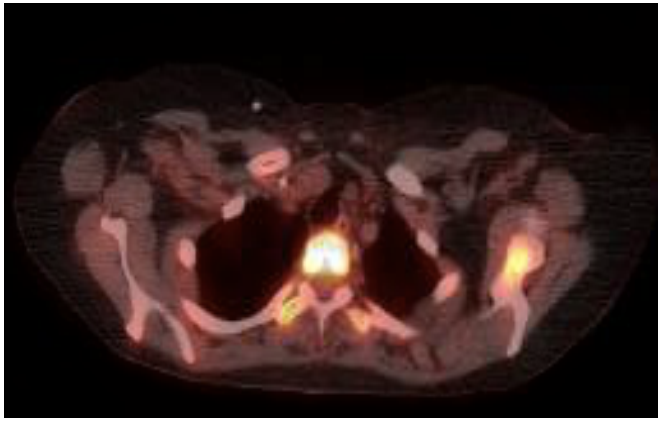




Advanced Cervical Cancer
Follow up

- She was treated with cisplatin, paclitaxel and bevacizumab x 9 cycles with excellent response to therapy but bone marrow toxicity.
- Next steps
  - Dosing strategies
  - Maintenance bevacizumab
  - Observation





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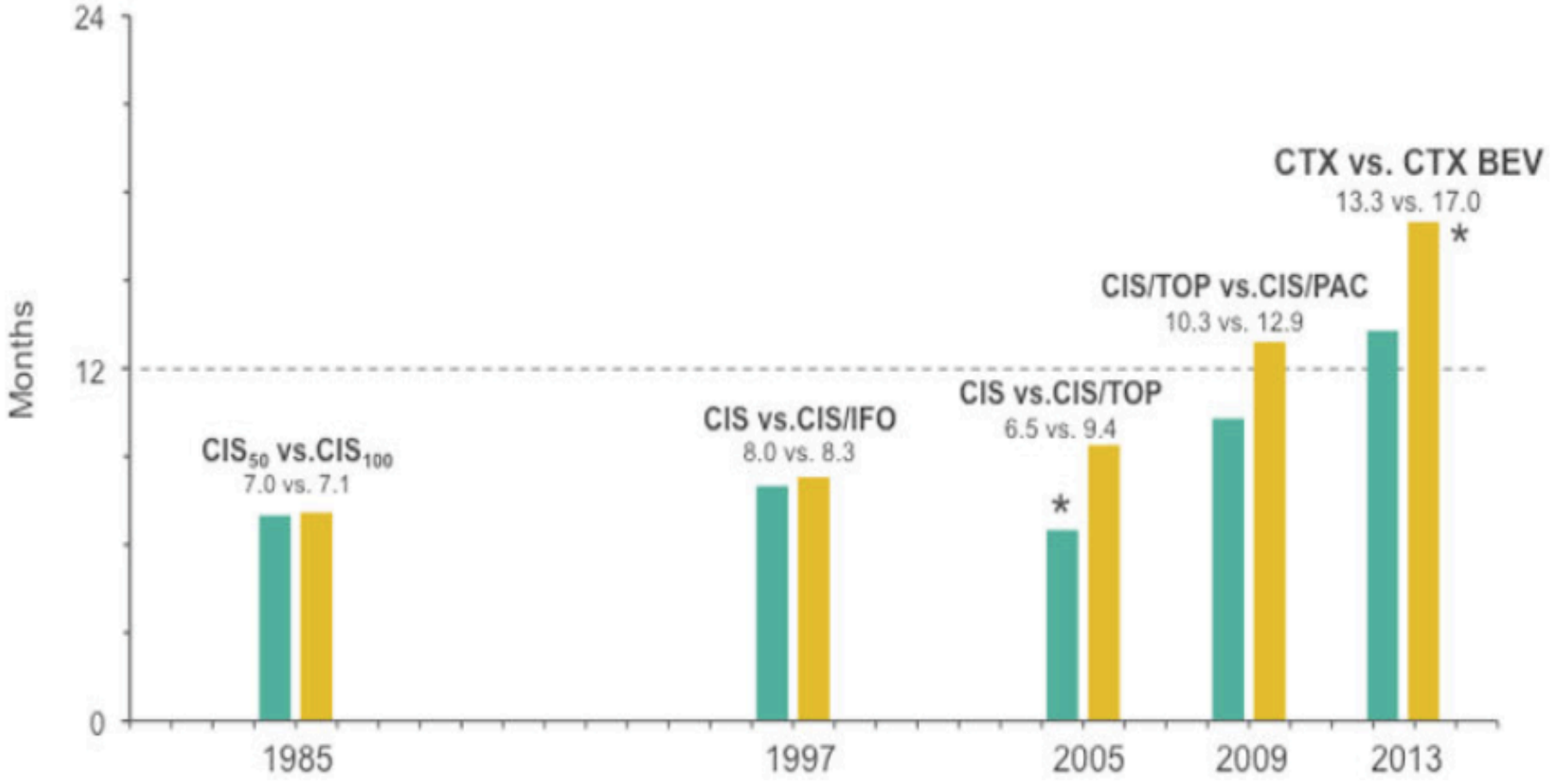
Disclosures

Advisory Committee	AstraZeneca Pharmaceuticals LP, Genentech BioOncology, Janssen Biotech Inc, Tesaro Inc
Contracted Research	AbbVie Inc, Amgen Inc, Astellas Pharma Global Development Inc, Astex Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Eisai Inc, Endocyte Inc, Exelixis Inc, Genentech BioOncology, GlaxoSmithKline, Incyte Corporation, Merck, Morphotek Inc, Tesaro Inc

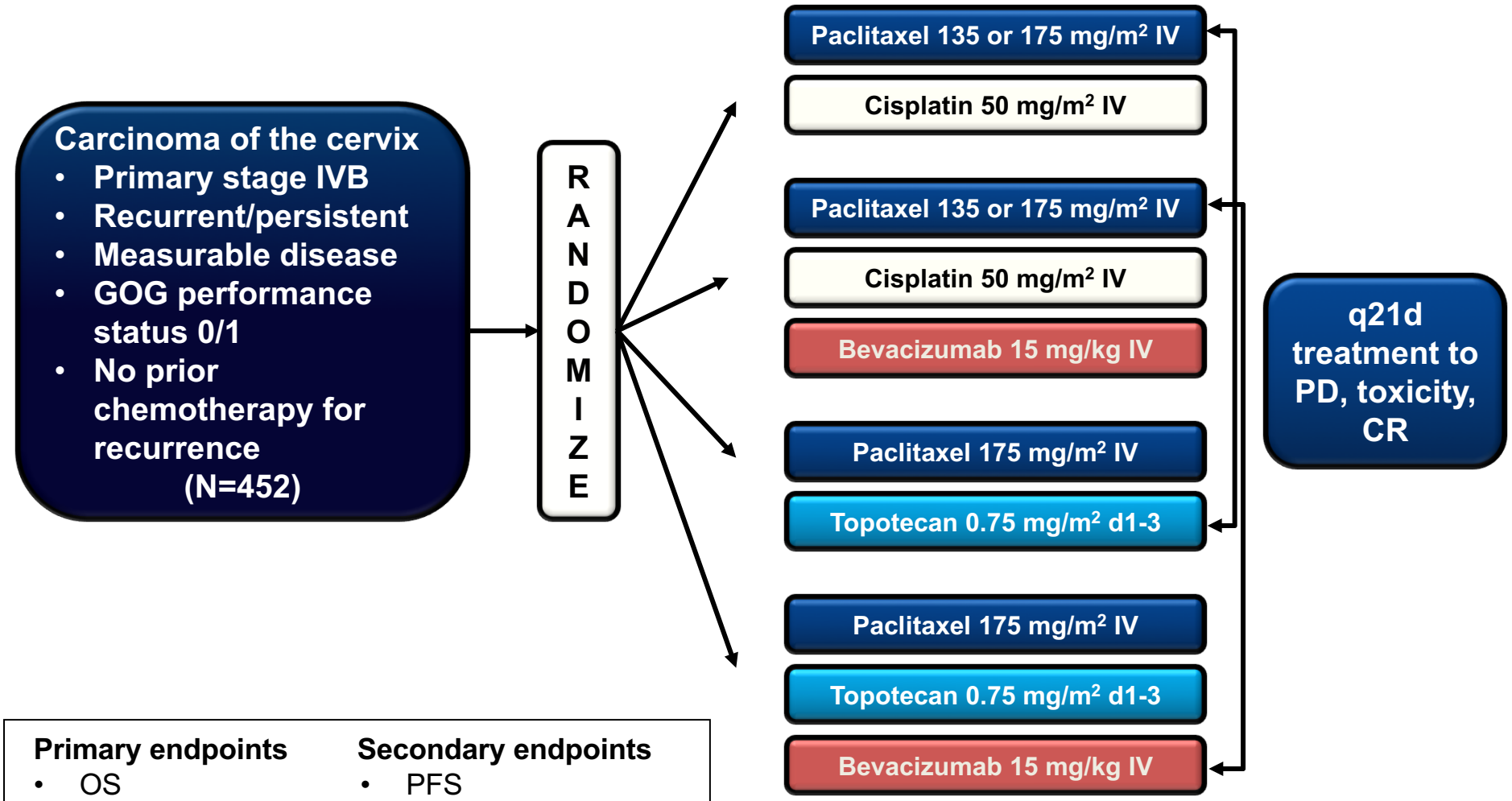
Cervical Cancer
Historical Perspective Overall Survival



Tewari KS, et al. Clin Cancer Res. 2015 Dec 15; 21(24): 5480–7

* $p<0.05$

GOG-0240: Schema



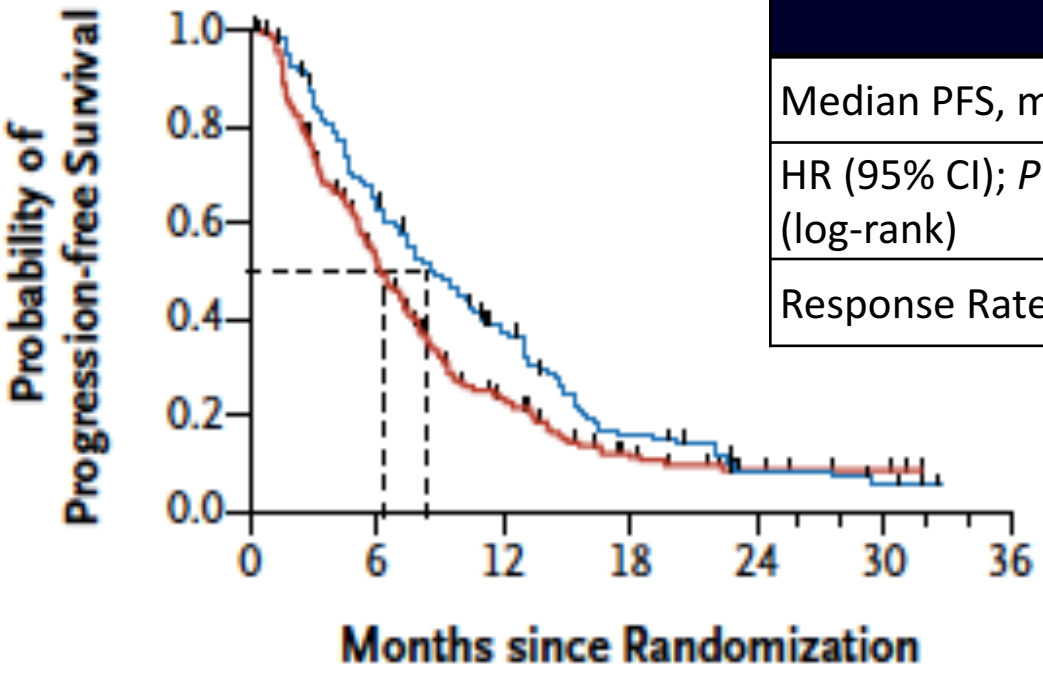
Primary endpoints	Secondary endpoints
• OS	• PFS
• Safety	• ORR

Tewari KS, et al. NEJM 2014; 370(8):734-43

NCT00803062

GOG-0240: PFS for Chemotherapy vs Chemotherapy + Bevacizumab (ITT)

	CT (n = 225)	Bev + CT (n = 227)
Median PFS, months	5.9	**8.2**
HR (95% CI); *P* value (log-rank)	0.67 (0.54-0.82); 0.002	
Response Rate	36%	48%

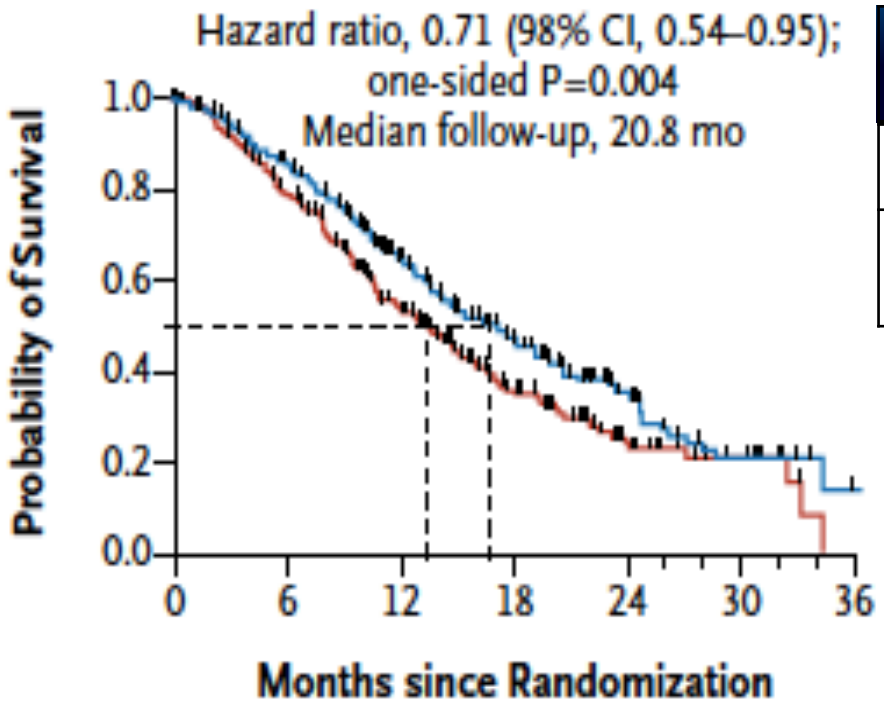


No. at Risk

Chemotherapy	225	103	40	14	6	3
Chemotherapy +bev	227	132	70	22	6	3

Tewari KS, et al. NEJM 2014; 370(8):734-43

GOG-0240: OS for Chemotherapy vs Chemotherapy + Bevacizumab (ITT)



	CT (n = 225)	Bev + CT (n = 227)
Median OS, months	**13.3**	**17.0**
HR (95% CI); *P* value	0.71 (0.54-0.95); 0.004	

No. at Risk

Chemotherapy	225	167	94	45	17	8
Chemotherapy +bev	227	184	121	69	30	10

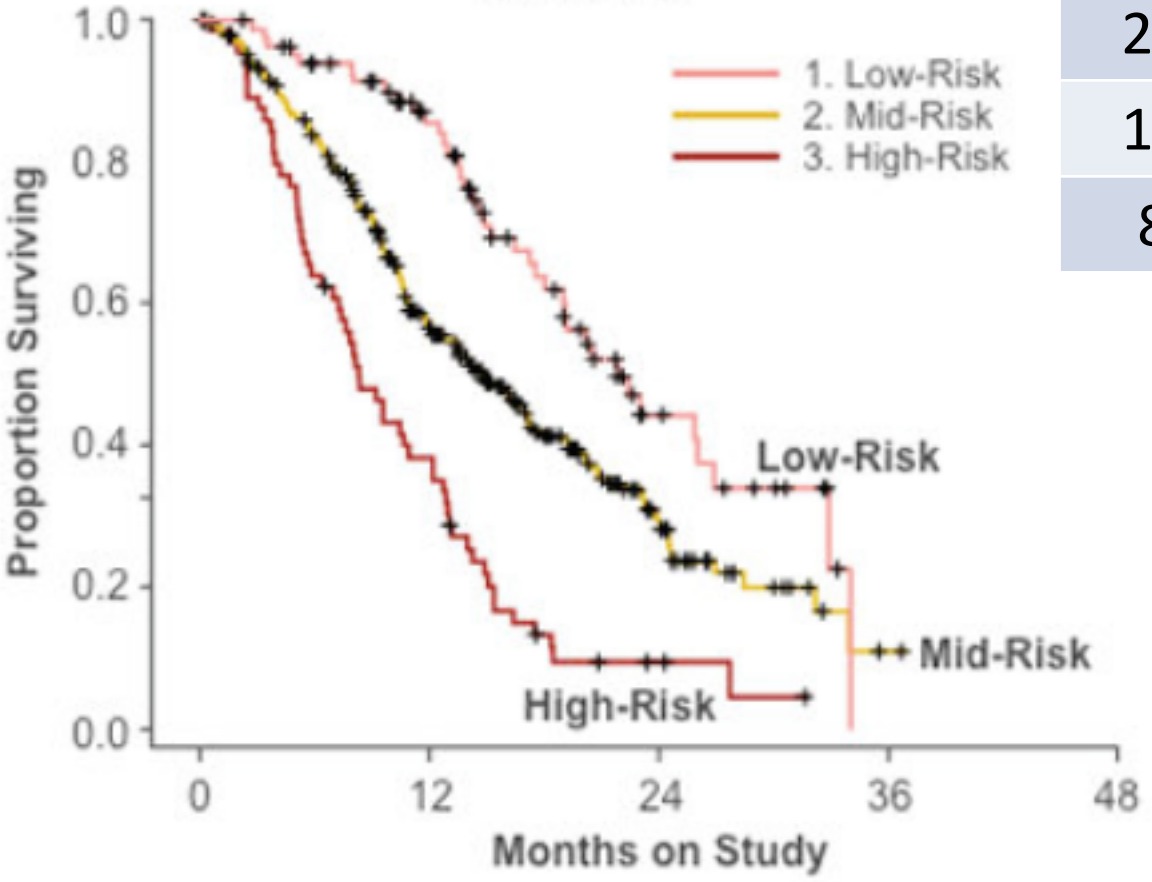
Tewari KS, et al. NEJM 2014; 370(8):734-43

GOG-0240: AEs of Special Interest

Event	Chemotherapy Alone (N=219)	Chemotherapy plus Bevacizumab (N=220)	
	no. of patients (%)		
Gastrointestinal events, excluding fistulas (grade ≥2)	96 (44)	114 (52)	
Fistula (grade ≥3)			
Gastrointestinal	0	7 (3)	*
Genitourinary	1 (<1)	6 (3)	
Total†	1 (<1)	13 (6)	*
Hypertension (grade ≥2)‡	4 (2)	54 (25)	*
Proteinuria (grade ≥3)	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)	*
CNS bleeding (grade ≥3)	0	0	
Gastrointestinal bleeding (grade ≥3)§	1 (<1)	4 (2)	
Genitourinary bleeding (grade ≥3)§	1 (<1)	6 (3)	

Tewari KS, et al. NEJM 2014; 370(8):734-43

GOG-0240: Overall Survival by Risk Group



mOS	mPFS	RR (%)
21.8	9.2	57.1
14.7	6.9	43.2
8.2	4.7	18.5

Risk factors:

black race

PS

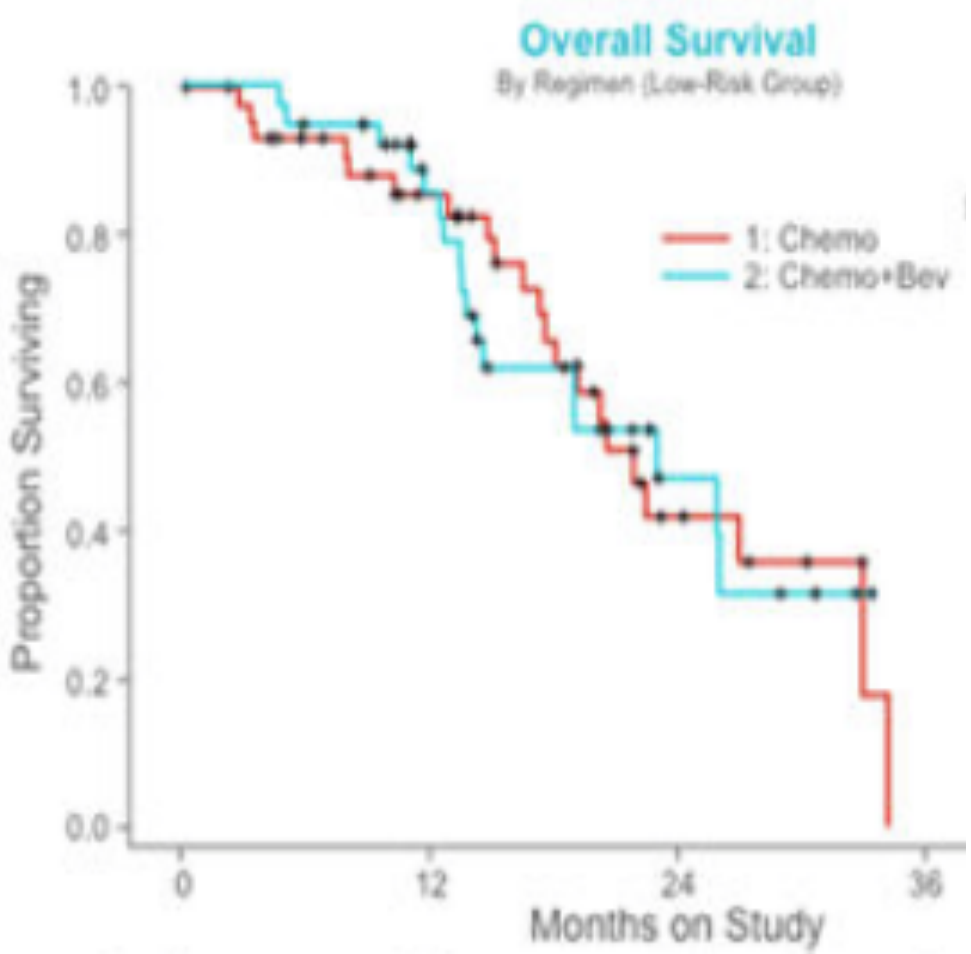
pelvic disease

prior cisplatin

PFI<365 days

Tewari KS, et al. Clin Cancer Res. 2015; 21(24): 5480–7

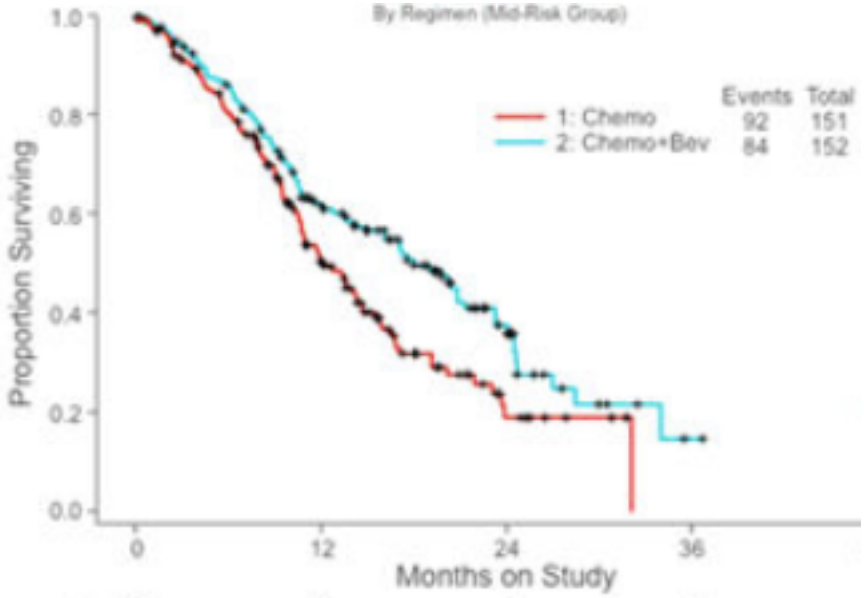
GOG-0240: Bevacizumab Efficacy in the Low Risk Subset



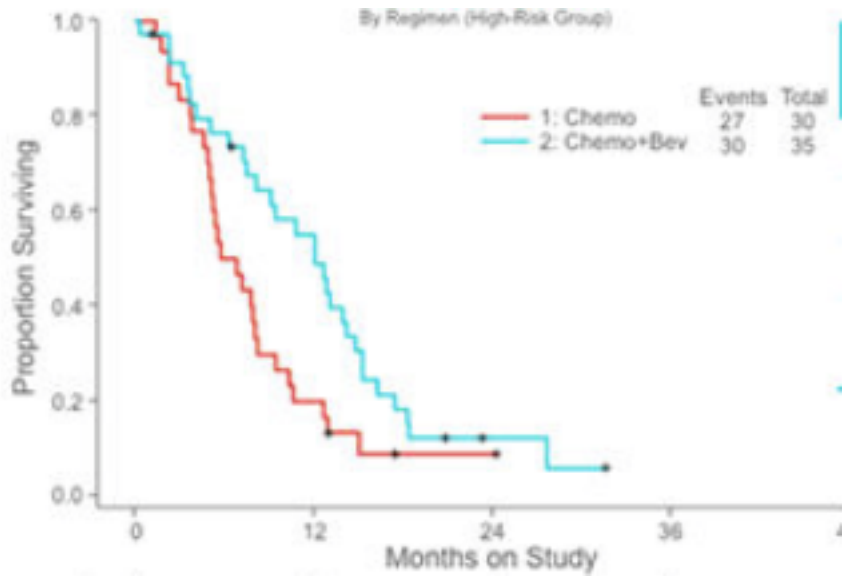
	mOS	mPFS	RR (%)
Chemo	21.8	8.0	52
Chemo + Bev	22.9	10.9	62.5
HR	1.119	0.755	1.522

Tewari KS, et al. Clin Cancer Res. 2015; 21(24): 5480–7

GOG-0240: Bevacizumab Efficacy in Medium and High Subsets



Medium	mOS	mPFS	RR (%)
Chemo	12.1	5.8	36
Chemo + Bev	17.9	7.9	50.7
HR	0.695	0.629	1.844

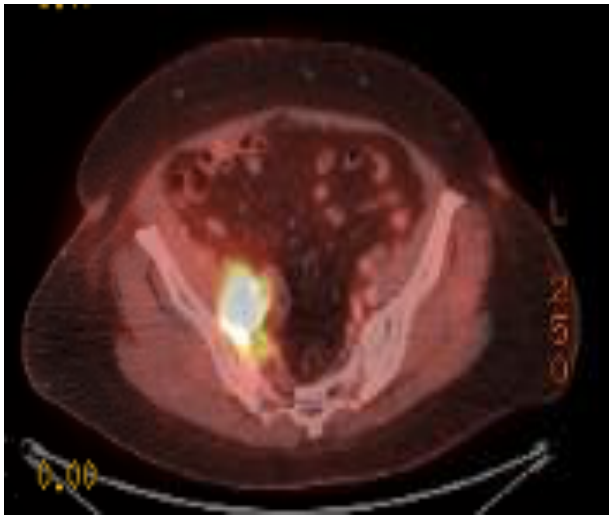


High	mOS	mPFS	RR (%)
Chemo	6.3	3.0	13
Chemo + Bev	12.1	6.0	22.9
HR	0.377	0.506	1.926

Tewari KS, et al. Clin Cancer Res. 2015

Advanced Endometrial Cancer

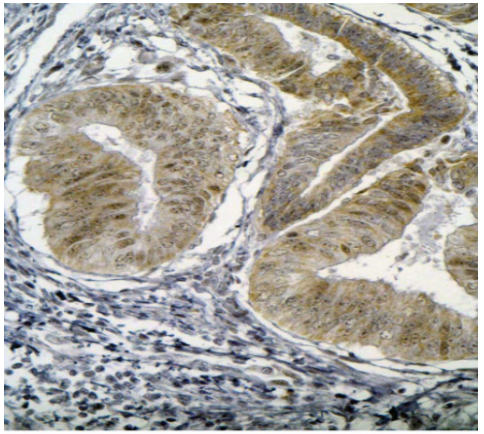
- 65 y.o. female with history of stage IIIC2 grade 2 endometrioid endometrial cancer s/p RA TLH BSO SLN and PALND followed by adjuvant WPRT with extended field who presented with right pelvic pain.
- CT/PET demonstrated pulmonary nodules and right pelvic adenopathy with ureteral and sidewall involvement.

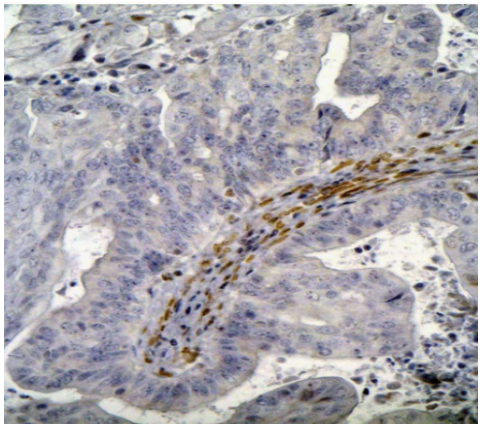


Advanced Endometrial Cancer

- Initial IHC testing revealed retained expression of mismatch repair proteins; and ER +/PR – hormone status.
- She has mild hypertension and is currently on low dose HCTZ.

MLH1 positive



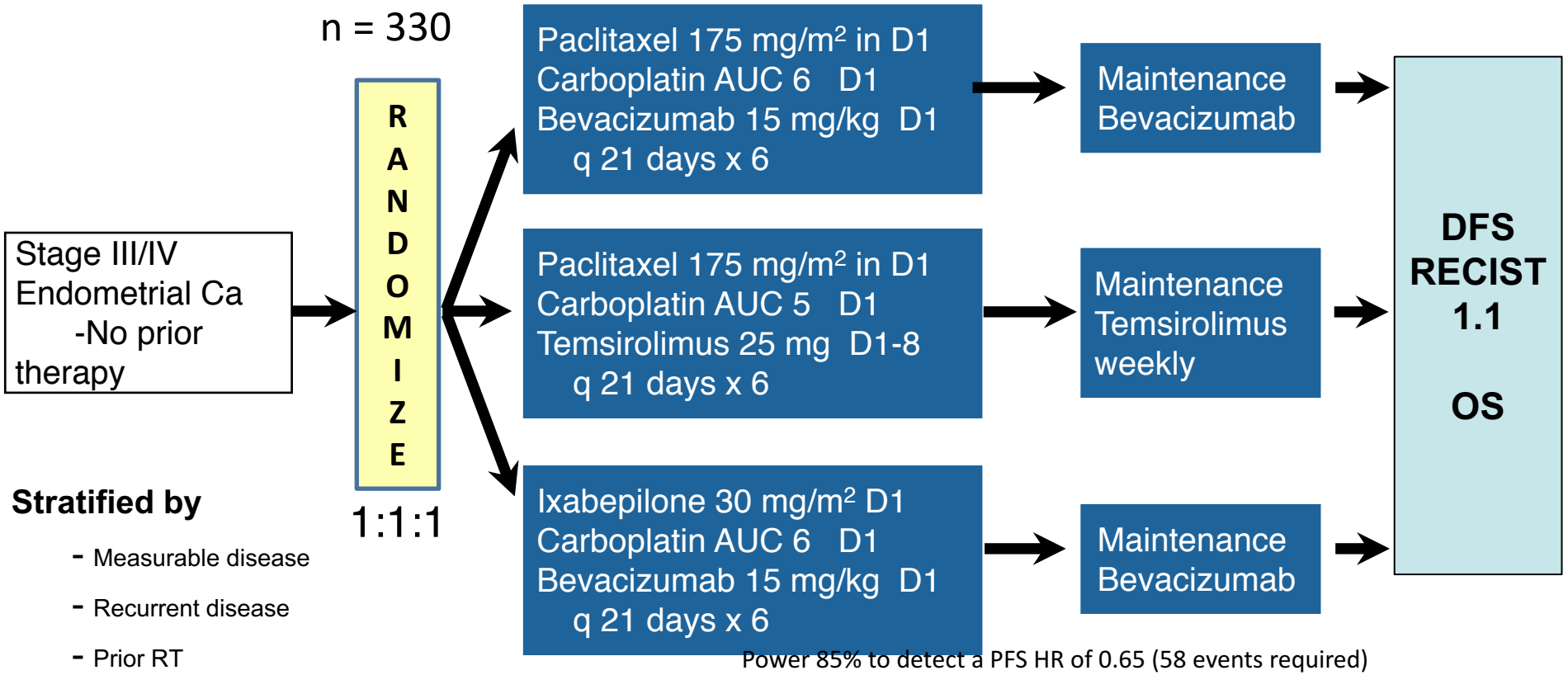


MLH1 negative

Masuda K. et al; Oncology Reports 2012

GOG-86P: A Randomized Phase II Trial in Endometrial Cancer

GOG 209 used for historic control



Power 85% to detect a PFS HR of 0.65 (58 events required)

Time: 9/09 - 1/12

NCT00977574

Aghajanian C, et al. J Clin Oncol 33(suppl abstr 5500), 2015

GOG-86P: Toxicity and Efficacy

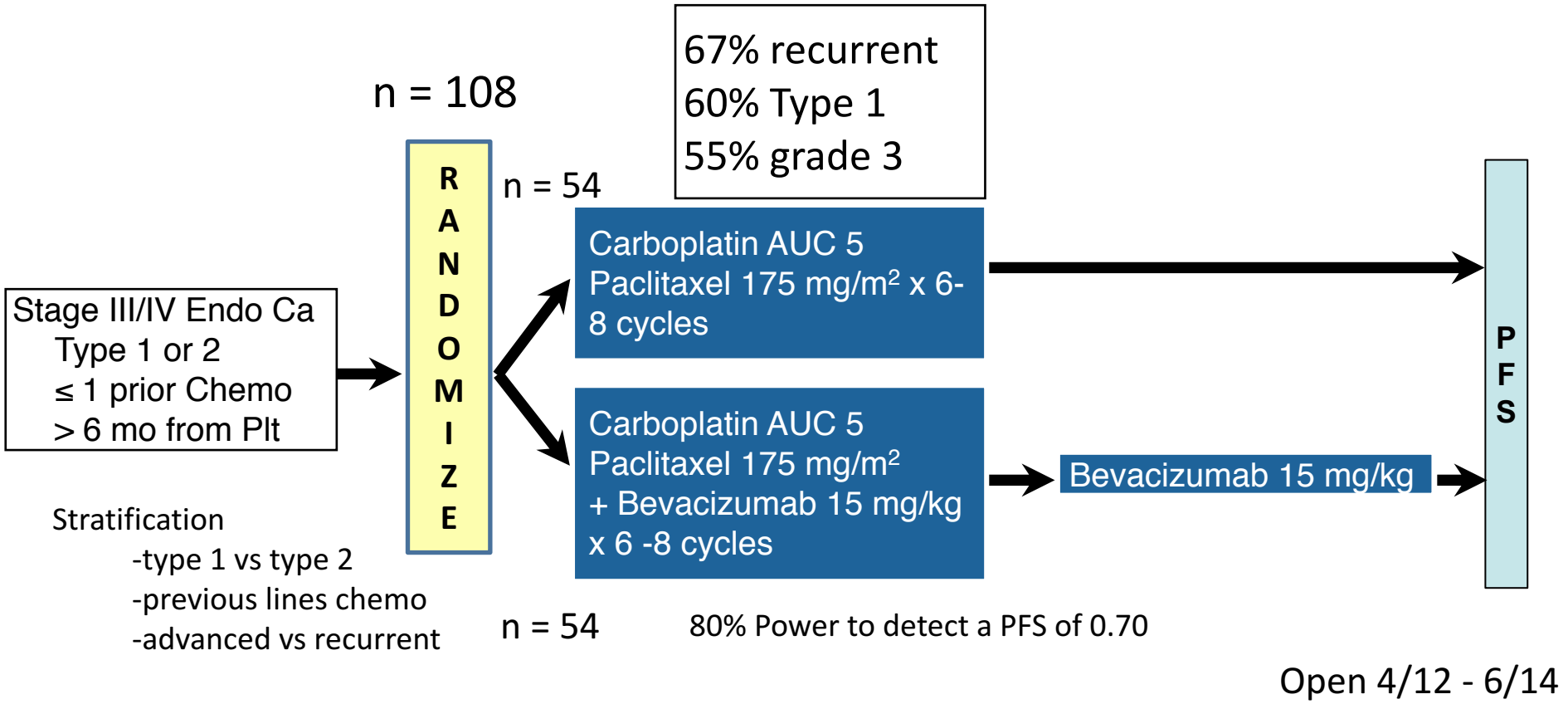
	Paclitaxel Carboplatin Bevacizumab	Paclitaxel Carboplatin Temsirolimus	Ixabepilone Carboplatin Bevacizumab
Cycles Bev/Tem	12	8	9
Response Rate % (CR/PR)	59.5 (24.7 + 34.8)	55.3 (16.5 + 38.8)	51.2 (10.8 + 40.4)
PFS*	0.81 (0.63 - 1.02)	1.22 (0.96 - 1.55)	0.87 (0.68 - 1.11)
OS*	0.71 (0.55 - 0.91)	0.99 (0.78 - 1.26)	0.97 (0.77 - 1.23)
Toxicities	HTN	Pneumonitis Mucocitis	HTN

*Compared to GOG 209

Aghajanian C, et al. J Clin Oncol 33(suppl abstr 5500), 2015

NCT00977574

MITO END-2 trial: Randomized phase II trial carboplatin-paclitaxel +/- bevacizumab in advanced or recurrent endometrial cancer



Lorusso D et al. J Clin Oncol 33, 2015 (suppl; abstr 5502)

MITO END-2 Trial: Summary of Efficacy

	CP (N = 48)	CP-B (N = 48)	
PFS (IRC*)			
Events, n (%)	31 (35.4)	27 (43.8)	
HR (95% CI)	0.57 (0.34, 0.96) Log-rank p = 0.036		
Median, mo (95% CI)	8.7 (6.3-11.2)	13.0 (9.2-16.8)	↑ 4.3 mo
ORR (IRC), %	(54.3)§ (39.9-68.7)	(72.7)° (59.5-85.9)	↑ 18%

§Calculated on 46 cases; ° calculated on 44 cases.

Lorusso D. et al. J Clin Oncol 33, 2015 (suppl; abstr 5502)

GOG-86P and MITO END-2: AEs of Special Interest

	PC Bev n = 112	PC Tem n = 113	IxC Bev n = 114	PC n = 53	PC Bev n = 52
ATE, ≥ G3	0.9	0	0.9	0	11.5
VTE, ≥ G3	8	9.7	7.9		
Non-CNS Bleeding, > G3	2.7	0.9	4.4		
GIP, Leak, Fistula, any G	2.7	1.8	4.4	0	1.9
HTN, ≥ G3/G2	16.1	2.7	16.7	0	21.1
Proteinuria, ≥ G3/Renal Toxicity	5.4	0	4.4	0	1
Cardiac disorders, ≥ G2					
Pneumonitis, any G	0	6.2	0.9		
Mucositis, oral, ≥ G2	4.5	15.9	2.6		
Rash, ≥ G2	2.7	16.8	3.5		
Febrile Neutropenia				0	5.7

Aghajanian C, et al. J Clin Oncol, 2015. Lorusso D. et al, J Clin Oncol 2015

Conclusions

- Results from GOG-86P and MITO END-2 suggest paclitaxel/carboplatin and bevacizumab improve disease control and survival
  - GOG-86P
    - $OS_{36\ months}$,: HR = 0.71 (0.55-0.91) p < 0.039
  - MITO END-2
    - PFS: HR = 0.57 (0.34-0.96) p=0.036
    - Median PFS 7 vs 13 months
    - ORR 54.3 vs 71.7%
    - 6 months disease control 69 vs 83%
- Toxicity:
  - Monitor for cardiovascular toxicity in older population when using bevacizumab
  - Otherwise no new safety signals
- Further exploration warranted in randomized phase III tiral

Aghajanian C, et al. J Clin Oncol, 2015. Lorusso D. et al, J Clin Oncol 2015