Cervical Cancer – SGO and ASCO updates Relevant ongoing studies

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Friday, June 9, 2022

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Transforming the standard of care™

Open vs Minimally Invasive Radical Hysterectomy in Patients with Early-Stage Cervical Cancer (LACC Trial): Final Analysis

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Professor
Department of Gynecologic Oncology & Reproductive Medicine
The University of Texas MD Anderson Cancer Center

ANNUAL MEETING ON WOMENS' CANCER
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 19 - 21, 2021

SGO Society of Gynecologic Oncology

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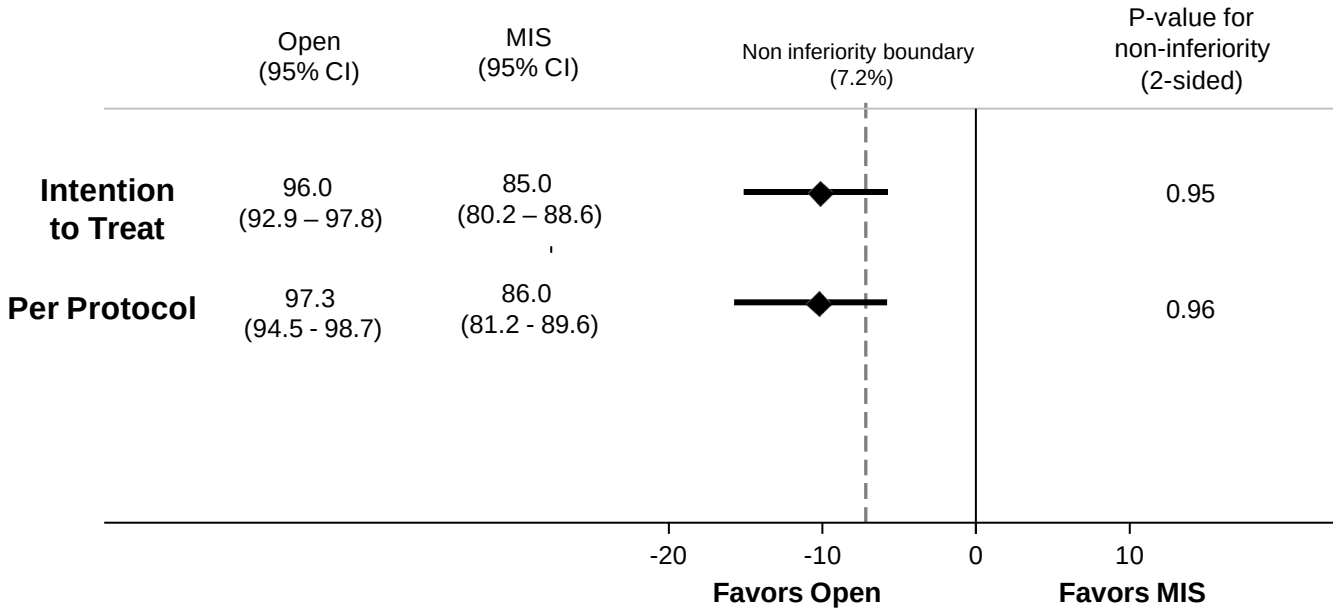
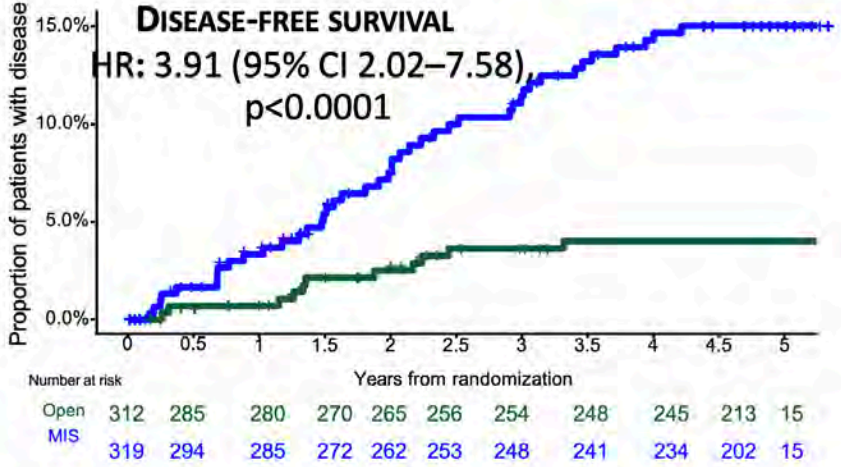
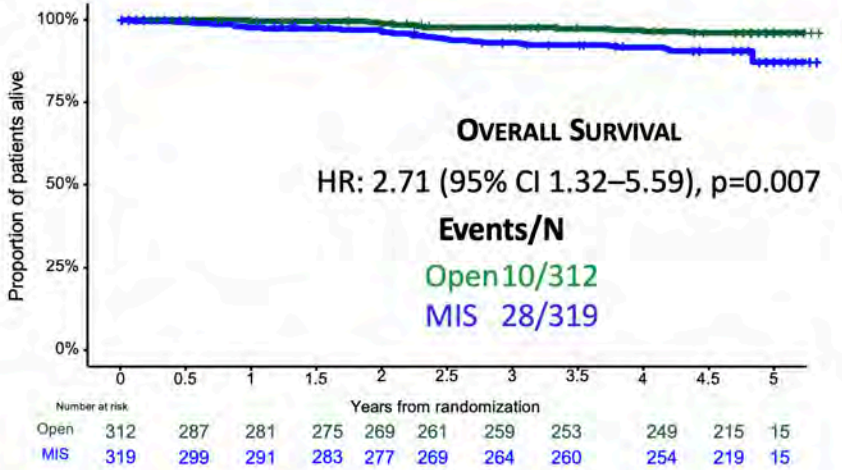
PRIMARY OUTCOME: DISEASE-FREE SURVIVAL AT 4.5 YEARS



LACC: Updated DFS and OS





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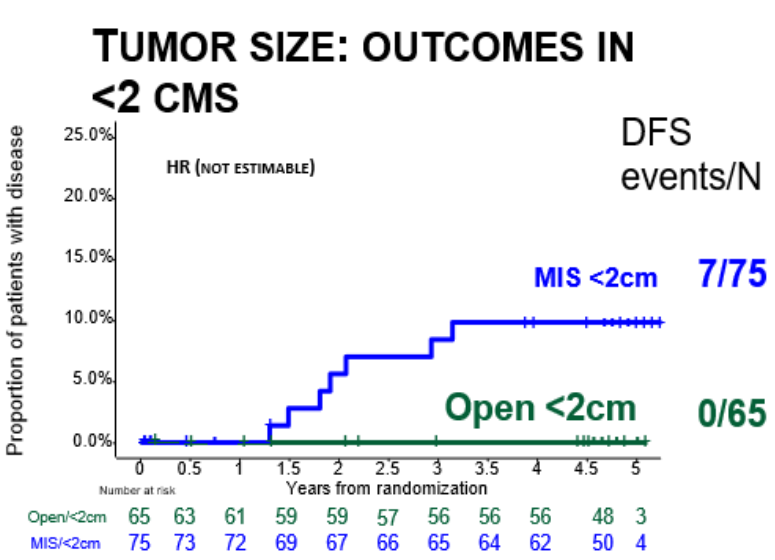
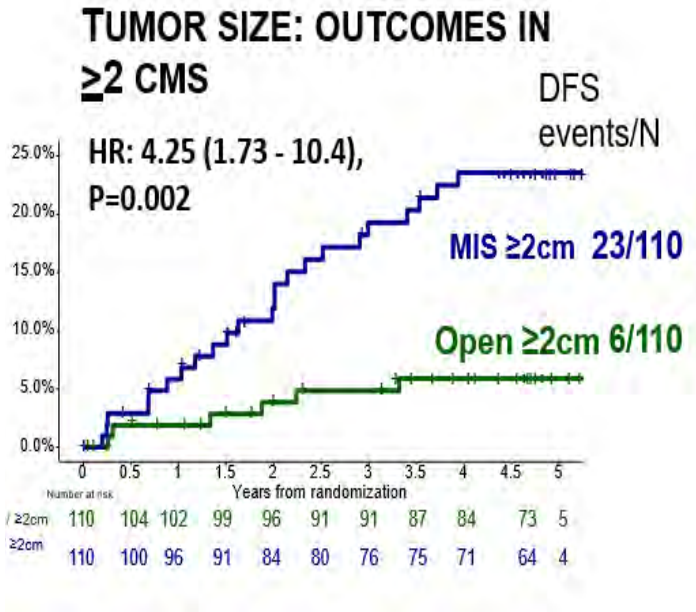
DFS by tumor size (2 cm cutoff)





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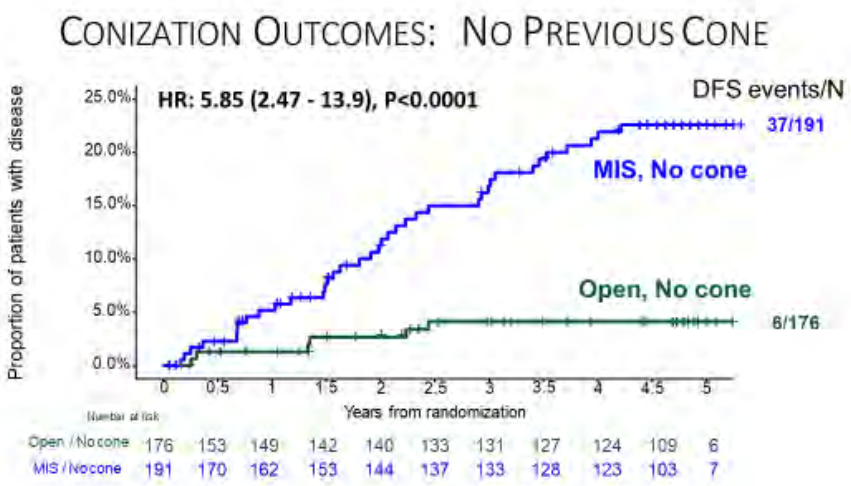
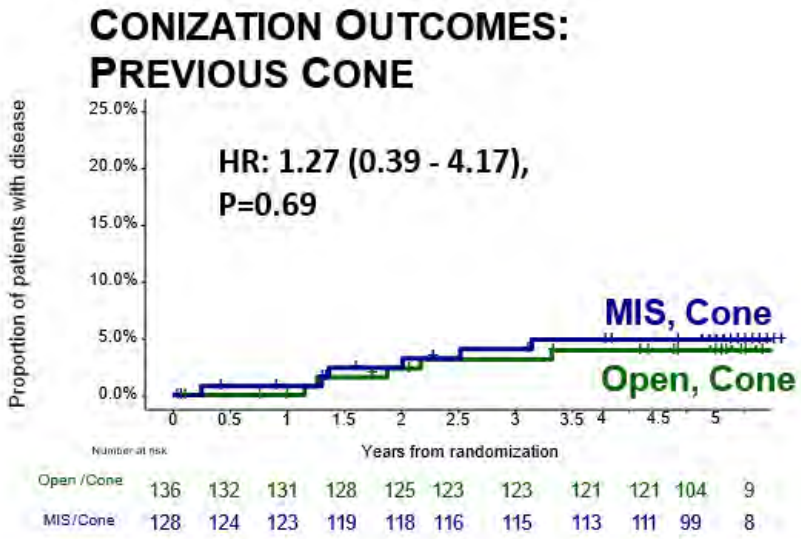
DFS with or without prior cone biopsy





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CHARACTERISTICS OF RECURRENCE: CARCINOMATOSIS

	Open	MIS
Total recurrences	11	37
Carcinomatosis (randomized)	1 (9%)	8 (22%)
Carcinomatosis (received)	0	9 (24%)
Site of recurrence		
Vault	3 (27%)	6 (16%)
Pelvis	0 (0%)	10 (27%)
Abdomen	0 (0%)	2 (5%)
Distant	3 (27%)	2 (5%)
Multiple	3 (27%)	14 (38%)
Other	2 (18%)	3 (8%)

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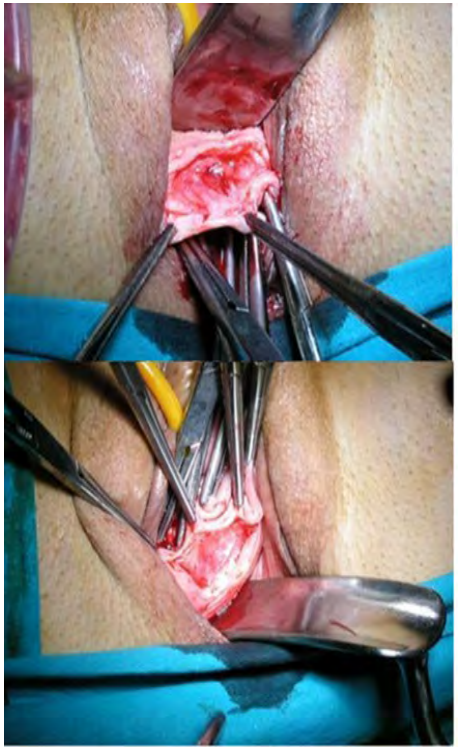
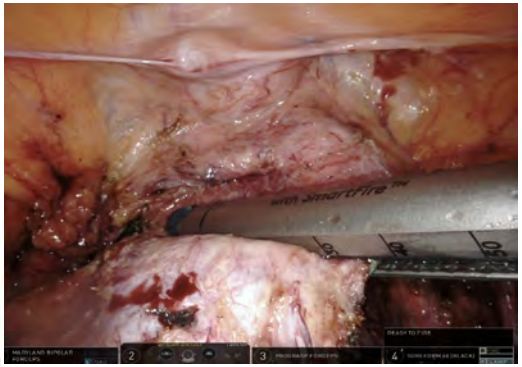
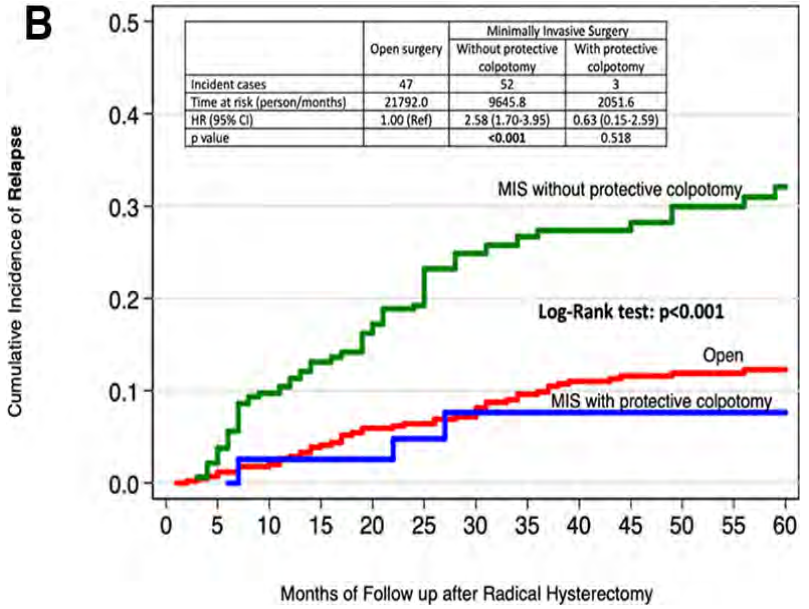
Tumor containment: SUCCOR study





From video courtesy of Dr. Mario Leitao



	Open surgery	Minimally Invasive Surgery	
		Without protective colpotomy	With protective colpotomy
Incident cases	47	52	3
Time at risk (person/months)	21792.0	9645.8	2051.6
HR (95% CI)	1.00 (Ref)	2.58 (1.70-3.95)	0.63 (0.15-2.59)
p value		<0.001	0.518

Chiva L, Zanagnolo V, Querleu D, et al. Int J Gynecol Cancer 2020;30:1269–1277.

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GOG-3043 (ROCC Trial)

A Randomized Controlled Trial of Robotic versus Open Radical Hysterectomy for Cervical Cancer

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GOG PARTNERS

#GOGROCC

PI: Kristin Bixel
Mario Leitao

IA2-IB2 (FIGO 2018) (4cm cutoff)
- Histology: SCC, adeno, adenosquamous
- MRI required
- Uterus <12 cm

Randomized 1:1

Robotic radical hysterectomy* + LN assessment (N=420)	Open radical hysterectomy* + LN assessment (N=420)

*Tumor containment

Primary Outcome: 3 year DFS
Secondary outcomes: DSS/OS, patterns of recurrence, complications, lymphedema, PRO's

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NCCN Guidelines Version 1.2022
Cervical Cancer

NCCN Guidelines Index
Table of Contents
Discussion

SYSTEMIC THERAPY FOR CERVICAL CANCER[a]

Squamous Cell Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma

Chemoradiation	Recurrent or Metastatic Disease		
	First-line Combination Therapy[b,c]	Possible First-line Single-agent therapy[c]	Second-line or Subsequent Therapy[g]
Preferred Regimens • Cisplatin • Carboplatin if patient is cisplatin intolerant	**Preferred Regimens** • Pembrolizumab + cisplatin/paclitaxel ± bevacizumab for PD-L1–positive tumors (category 1)[d,e,f,1] • Pembrolizumab + carboplatin/paclitaxel ± bevacizumab for PD-L1–positive tumors (category 1)[d,e,f,1] • Cisplatin/paclitaxel/bevacizumab[d,2] (category 1) • Carboplatin/paclitaxel/bevacizumab[d] **Other Recommended Regimens** • Cisplatin/paclitaxel (category 1)[3,4] • Carboplatin/paclitaxel[5,6] (category 1 for patients who have received prior cisplatin therapy) • Topotecan/paclitaxel/bevacizumab[d,2] (category 1) • Topotecan/paclitaxel[2] • Cisplatin/topotecan[7]	**Preferred Regimens** • Cisplatin[4] **Other Recommended Regimens** • Carboplatin[8] • Paclitaxel[9,10]	**Preferred Regimens** • Pembrolizumab for PD-L1–positive or MSI-H/dMMR tumors[e,f,11] • Nivolumab for PD-L1–positive tumors[e,f,12] **Other Recommended Regimens** (All agents listed here are category 2B unless otherwise noted) • Bevacizumab[d] • Albumin-bound paclitaxel • Docetaxel • Fluorouracil • Gemcitabine • Ifosfamide • Irinotecan • Mitomycin • Pemetrexed • Topotecan • Vinorelbine • Tisotumab vedotin-tftv (category 2A)[13] **Useful in Certain Circumstances** • Pembrolizumab for TMB-H tumors[e,h] • Larotrectinib or entrectinib for *NTRK* gene fusion-positive tumors (category 2B)

KEYNOTE-826: Randomized, Double-Blind, Phase 3 Study

Key Eligibility Criteria

- Persistent, recurrent, or metastatic cervical cancer not amenable to curative treatment
- No prior systemic chemotherapy (prior radiotherapy and chemoradiotherapy permitted)
- ECOG PS 0 or 1

R 1:1

Pembrolizumab 200 mg IV Q3W
for up to 35 cycles
+
Paclitaxel + Cisplatin or Carboplatin IV Q3W
for up to 6 cycles[a]
±
Bevacizumab 15 mg/kg IV Q3W

Placebo IV Q3W
for up to 35 cycles
+
Paclitaxel + Cisplatin or Carboplatin IV Q3W
for up to 6 cycles[a]
±
Bevacizumab 15 mg/kg IV Q3W

Stratification Factors

- Metastatic disease at diagnosis (yes vs no)
- PD-L1 CPS (<1 vs 1 to <10 vs ≥10)
- Planned bevacizumab use (yes vs no)

End Points

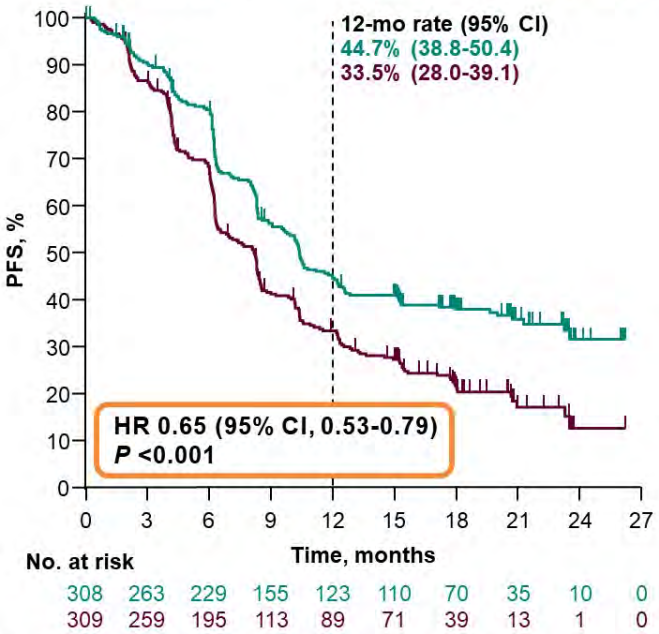
- **Dual primary:** OS and PFS per RECIST v1.1 by investigator
- **Secondary:** ORR, DOR, 12-mo PFS, and safety
- **Exploratory:** PROs assessed per EuroQol EQ-5D-5L VAS

[a]Paclitaxel: 175 mg/m^2. Cisplatin: cisplatin 50 mg/m^2. Carboplatin: AUC 5 mg/mL/min. The 6-cycle limit was introduced with protocol amendment 2, although participants with ongoing clinical benefit who were tolerating chemotherapy could continue beyond 6 cycles after sponsor consultation.
CPS, combined positive score (number of PD-L1–staining cells [tumor cells, lymphocytes, macrophages] divided by the total number of viable tumor cells, multiplied by 100); PROs, patient-reported outcomes; VAS, visual analog scale. KEYNOTE-826 ClinicalTrials.gov identifier, NCT03635567.

Dual Primary Endpoints: All-Comer Population

PFS[a]

	Pts w/Event	Median, mo (95% CI)
Pembro + Chemo ± Bev	58.4%	10.4 (9.1-12.1)
Pbo + Chemo ± Bev	73.1%	8.2 (6.4-8.4)

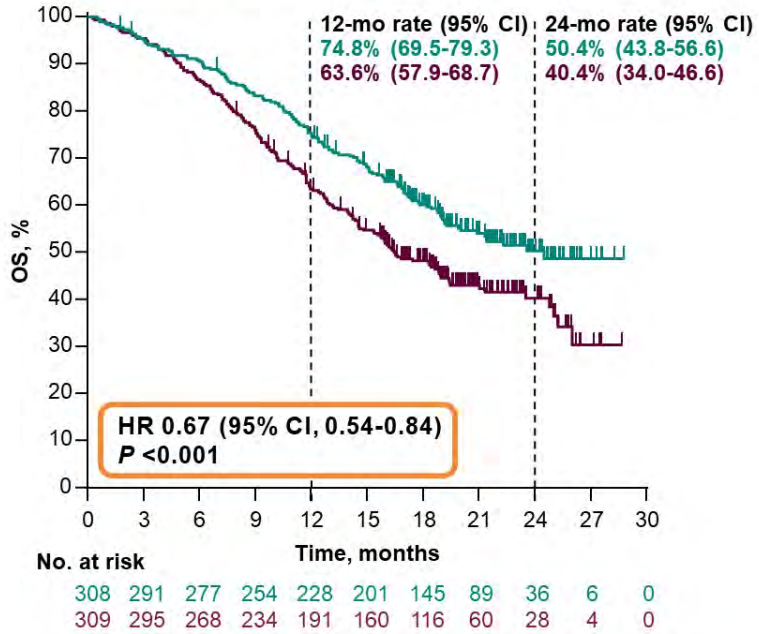


No. at risk

308	263	229	155	123	110	70	35	10	0
309	259	195	113	89	71	39	13	1	0

OS

	Pts w/Event	Median, mo (95% CI)
Pembro + Chemo ± Bev	44.8%	24.4 (19.2-NR))
Pbo + Chemo ± Bev	56.3%	16.5 (14.5-19.4)

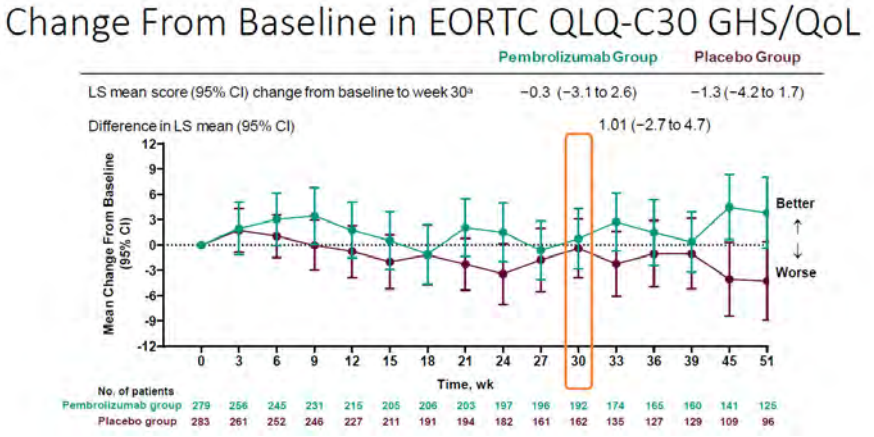


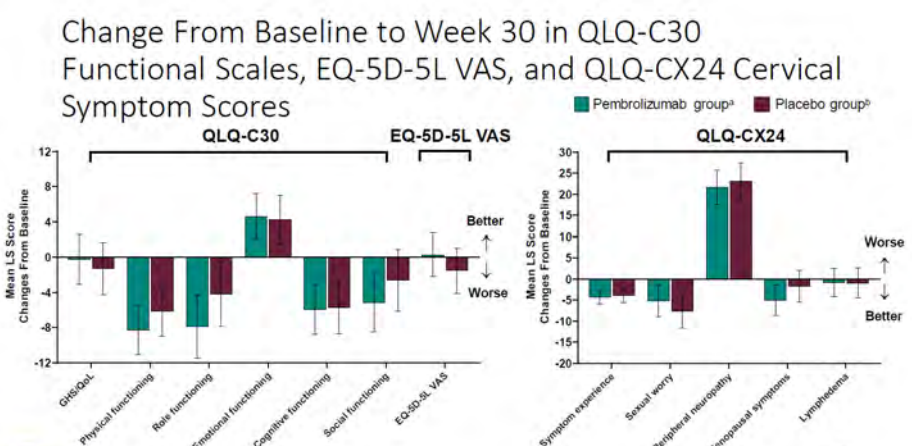
No. at risk

308	291	277	254	228	201	145	89	36	6	0
309	295	268	234	191	160	116	60	28	4	0

Colombo N et al. *N Engl J Med* 2021;385:1856-67.
[a]Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: May 3, 2021.

IMPROVED QoL/PROs with pembrolizumab





Monk B et al. SGO 2022 Abstract 23

PFS: Subgroups, All-Comer and CPS ≥1 Populations

All-Comer

	No. of Events/ No. of Participants	Hazard Ratio (95% CI)
Overall	406/617	0.65 (0.53-0.79)
Histology		
Squamous	297/447	0.63 (0.50-0.80)
Non-squamous	108/169	0.66 (0.43-1.00)
Platinum use		
Carboplatin	330/495	0.69 (0.55-0.86)
Cisplatin	75/120	0.47 (0.28-0.77)
Concomitant bevacizumab		
Yes	234/389	0.61 (0.47-0.79)
No	172/228	0.74 (0.54-1.01)
Prior CRT only		
Yes	165/243	0.62 (0.45-0.86)
No	241/374	0.69 (0.53-0.90)

CPS ≥1

	No. of Events/ No. of Participants	Hazard Ratio (95% CI)
Overall	355/548	0.62 (0.50-0.77)
Histology		
Squamous	269/409	0.61 (0.48-0.78)
Non-squamous	85/138	0.59 (0.37-0.93)
Platinum use		
Carboplatin	293/447	0.68 (0.53-0.85)
Cisplatin	61/99	0.39 (0.22-0.68)
Concomitant bevacizumab		
Yes	203/346	0.61 (0.46-0.80)
No	152/202	0.66 (0.47-0.92)
Prior CRT only		
Yes	142/215	0.55 (0.39-0.78)
No	213/333	0.68 (0.52-0.90)

Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: May 3, 2021.

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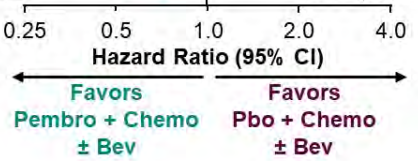
OS: Subgroups, All-Comer and CPS ≥1 Populations

All-Comer

	No. of Events/ No. of Participants	Hazard Ratio (95% CI)
Overall	312/617	0.67 (0.54-0.84)
Histology		
Squamous	237/447	0.61 (0.47-0.80)
Non-squamous	75/169	0.76 (0.47-1.23)
Platinum use		
Carboplatin	259/495	0.69 (0.54-0.89)
Cisplatin	51/120	0.59 (0.32-1.09)
Concomitant bevacizumab		
Yes	166/389	0.63 (0.47-0.87)
No	146/228	0.74 (0.53-1.04)
Prior CRT only		
Yes	136/243	0.64 (0.45-0.91)
No	176/374	0.71 (0.53-0.97)

CPS ≥1

	No. of Events/ No. of Participants	Hazard Ratio (95% CI)
Overall	272/548	0.64 (0.50-0.81)
Histology		
Squamous	213/409	0.60 (0.46-0.79)
Non-squamous	59/138	0.70 (0.41-1.20)
Platinum use		
Carboplatin	231/447	0.65 (0.50-0.85)
Cisplatin	39/99	0.53 (0.27-1.04)
Concomitant bevacizumab		
Yes	143/346	0.62 (0.45-0.87)
No	129/202	0.67 (0.47-0.96)
Prior CRT only		
Yes	118/215	0.56 (0.39-0.81)
No	154/333	0.72 (0.52-1.00)

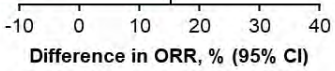


Data cutoff date: May 3, 2021.

ORR: All-Comer and CPS ≥1 Populations

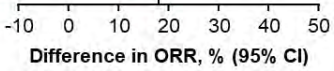
All-Comer

	ORR, % Pembro[a]	ORR, % Placebo[a]	Difference in ORR, % (95% CI)
Overall	65.9%	50.8%	15.3 (7.8-22.6)
Histology			
Squamous	65.3%	45.5%	20.3 (11.4-29.0)
Non-squamous	67.6%	62.2%	8.1 (-6.8-21.7)
Platinum use			
Carboplatin	62.2%	48.6%	14.0 (5.4-22.3)
Cisplatin	82.0%	61.0%	19.6 (3.5-35.2)
Concomitant bevacizumab			
Yes	75.5%	60.6%	15.1 (5.8-24.3)
No	49.1%	34.5%	14.6 (1.8-27.0)
Prior CRT only			
Yes	61.6%	43.2%	18.7 (6.4-30.5)
No	68.9%	55.5%	13.5 (3.9-22.9)



CPS ≥1

	ORR, % Pembro[a]	ORR, % Placebo[a]	Difference in ORR, % (95% CI)
Overall	68.1%	50.2%	18.0 (10.1-25.7)
Histology			
Squamous	67.0%	46.2%	20.4 (11.1-29.4)
Non-squamous	71.7%	60.3%	13.8 (-2.2-28.1)
Platinum use			
Carboplatin	64.5%	48.5%	16.1 (7.2-24.8)
Cisplatin	84.6%	59.6%	26.1 (9.4-42.6)
Concomitant bevacizumab			
Yes	77.1%	60.2%	17.3 (7.5-26.9)
No	52.0%	33.7%	18.3 (4.7-31.3)
Prior CRT only			
Yes	64.3%	40.8%	23.8 (10.8-36.1)
No	70.8%	55.8%	15.0 (4.9-24.7)



Response assessed per RECIST v1.1 by investigator review.
[a]The treatment regimen in both arms included chemo ± bev.
Data cutoff date: May 3, 2021.

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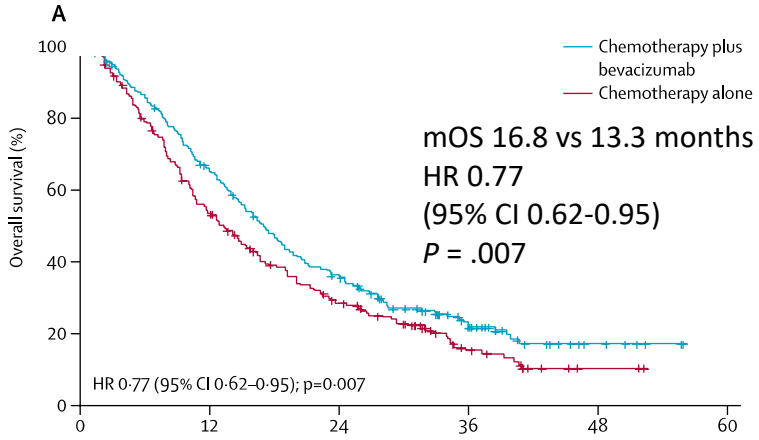
GOG 240 : SOC for PDL1- and PDL1+

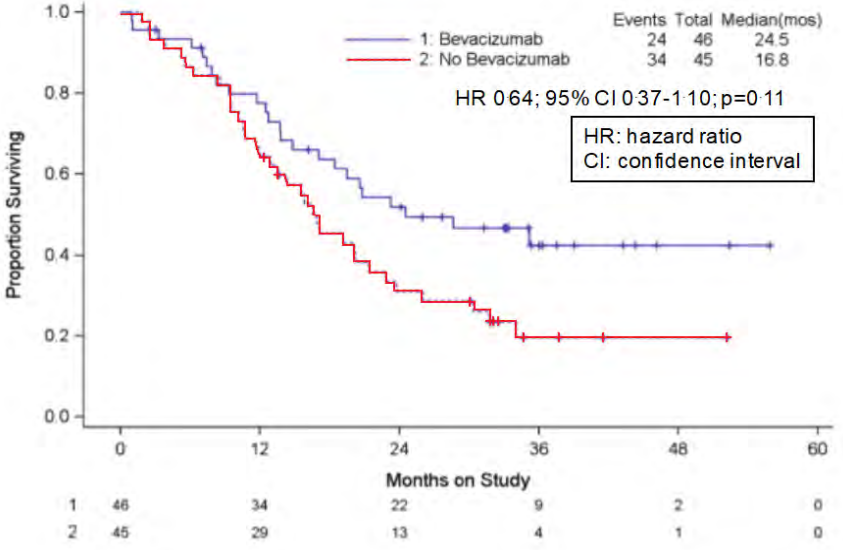
Intent to Treat



mOS 16.8 vs 13.3 months
HR 0.77
(95% CI 0.62-0.95)
P = .007

Number at risk (number censored)						
Chemotherapy plus bevacizumab	227 (0)	142 (9)	75 (12)	30 (31)	6 (51)	0 (57)
Chemotherapy alone	225 (0)	114 (9)	54 (18)	17 (35)	2 (45)	0 (47)

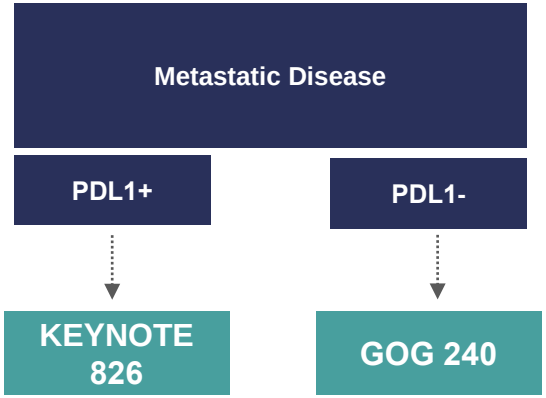
*Not Previouslv Irradiated

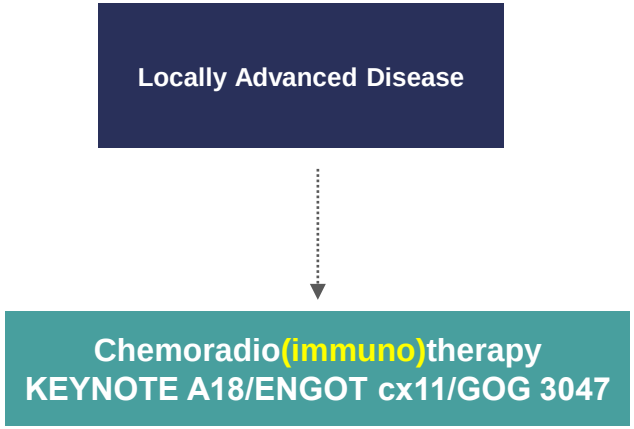


*Not analytical

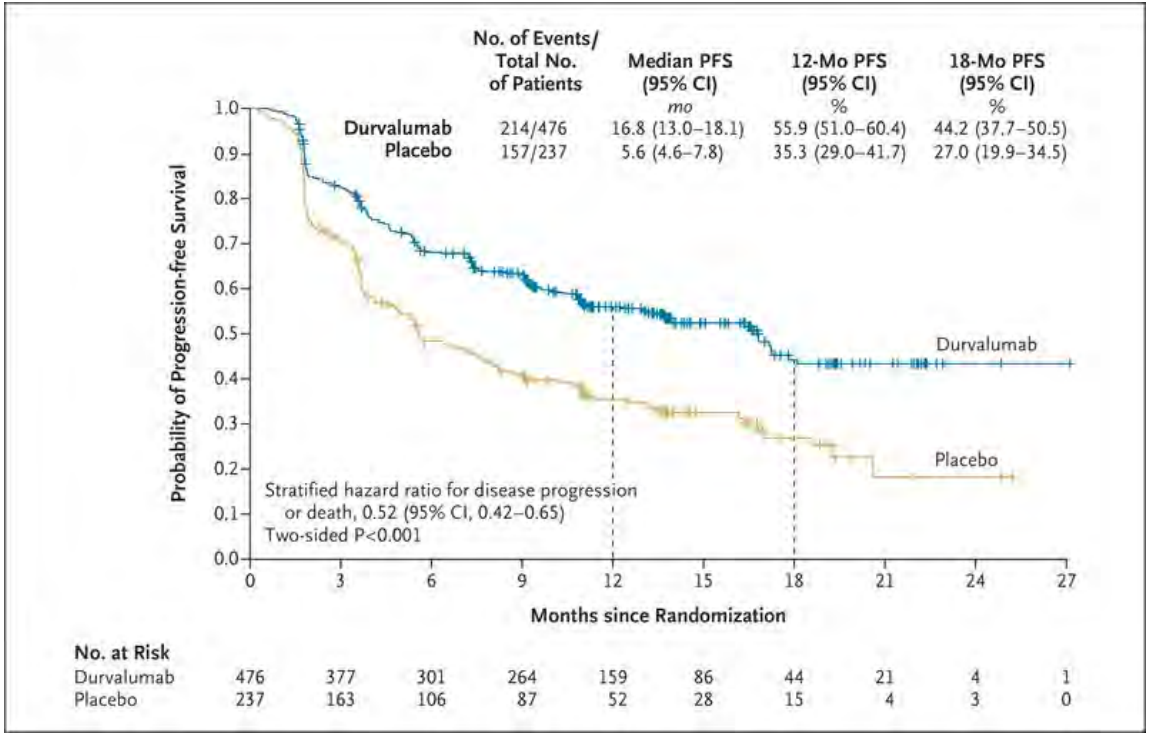
Tewari KS, et al. *Lancet*. 2017;390(10103):1654-1663.

From last Highlight Reel….





PACIFIC: Anti-PD-L1 therapy post-CRT for locally-advanced lung cancer



Antonia SJ et al. Engl J Med. 2017 Nov 16;377(20):1919-1929.

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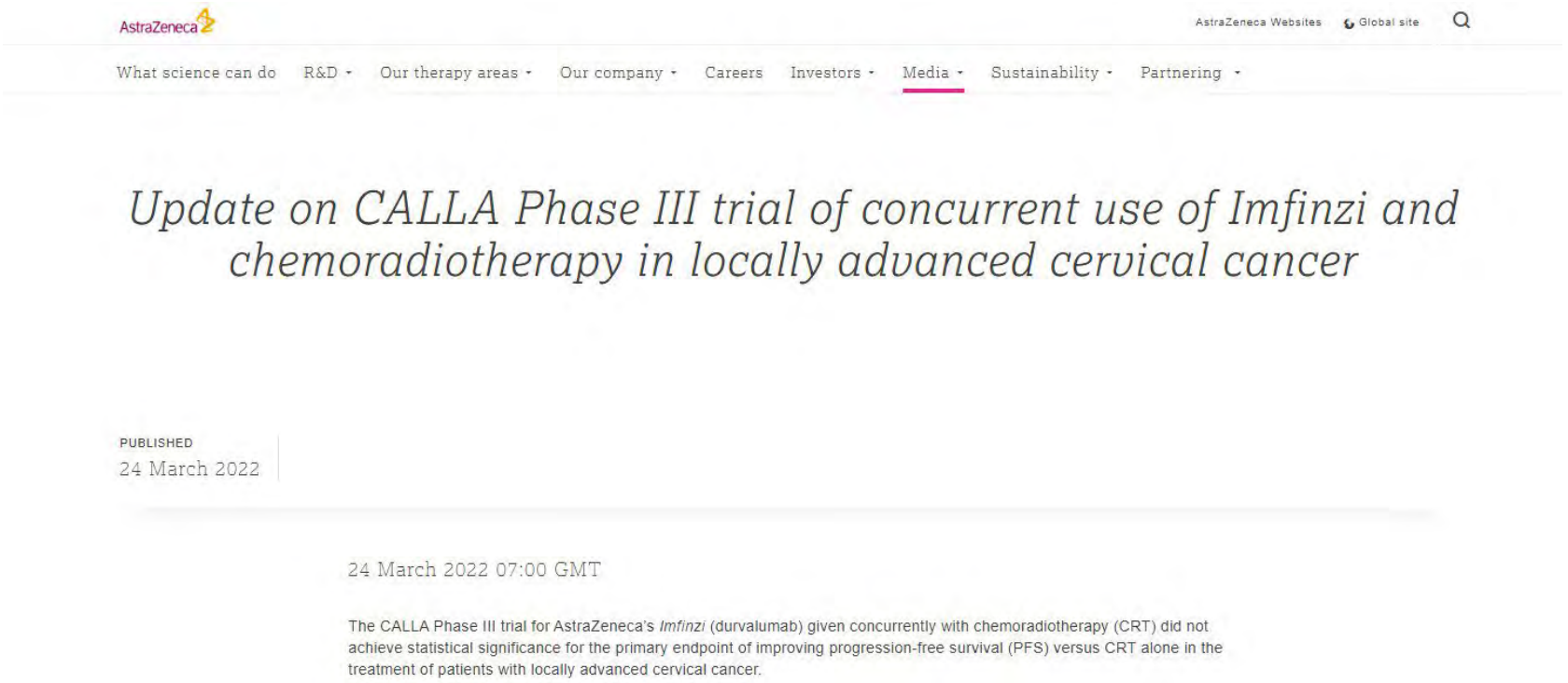
Press Release March 24, 2022



https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2022

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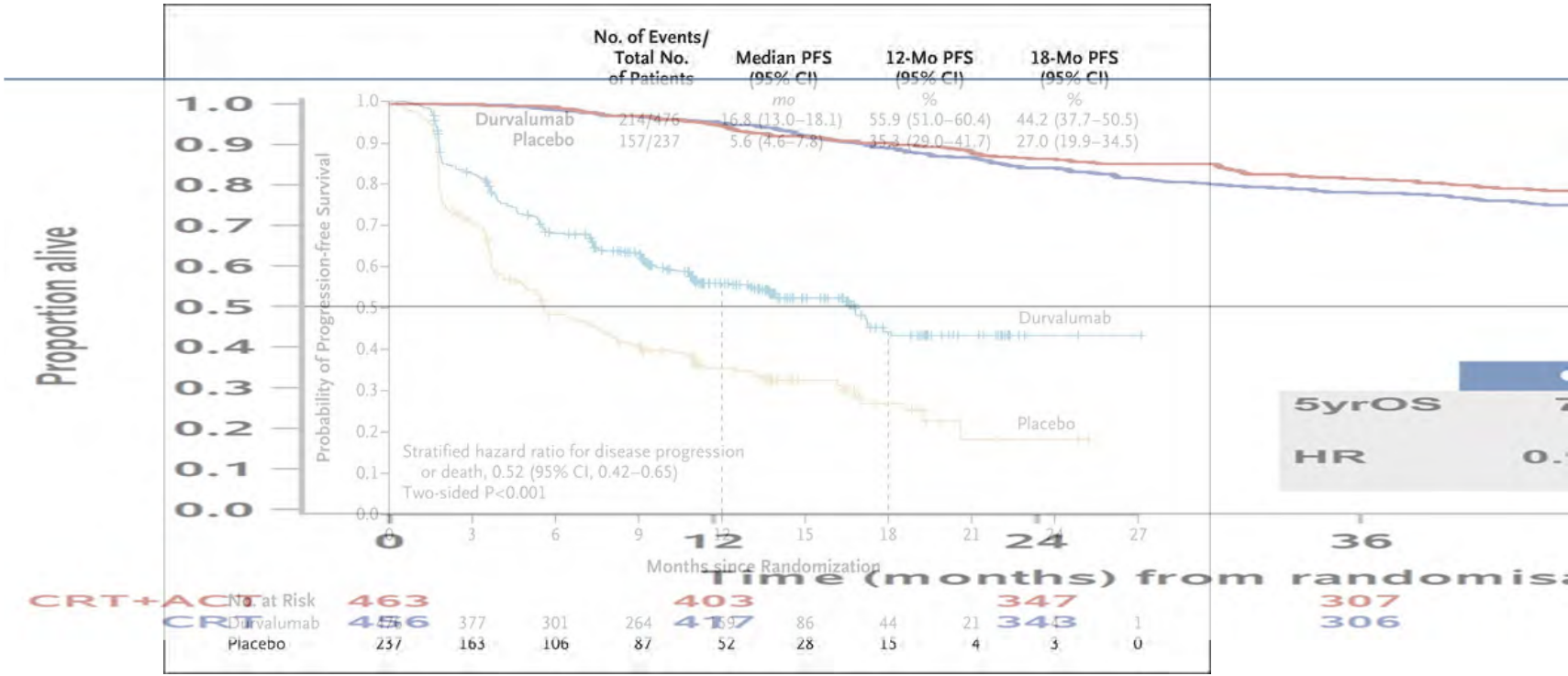
PACIFIC[1] vs OUTBACK[2]



1. Antonia SJ et al. Engl J Med. 2017 Nov 16;377(20):1919-1929.
2. Mileshkin L et al. ASCO 2021

GOG FOUNDATION

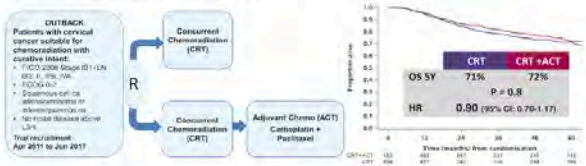
#5531 Staging locally advanced cervical cancer with FIGO 2018 versus FIGO 2008 impact on overall survival and progression-free survival in the OUTBACK trial (ANZGOG 0902, RTOG 1174, NRG 0274)

Linda R. Mileshkin, Kathleen N. Moore, Elizabeth H. Barnes, Yeh Chen Lee, Val Gebski, Kailash Narayan, Nathan Bradshaw, Katrina Diamante, Anthony W. Fyles, William Small Jr., David K. Gaffney, Pearly Khaw, Susan Brooks, Spencer Thompson, Warner King Huh, Matthew Carlson, Katina Robison, Danny Rischin, Martin R. Stockler, Bradley J. Monk

Background & Methods

The International Federation of Obstetrics and Gynecology staging system for cervical cancer (FIGO 2008) was revised in 2018 to incorporate lymph node involvement (FIGO 2018). We evaluated the effects of classifying participants (pts) with these 2 staging systems in the OUTBACK trial population.

OUTBACK is an international, randomized phase 3 trial of adjuvant chemotherapy versus observation after standard of care treatment with chemoradiation for women with locally advanced cervical cancer. OUTBACK found no benefit from the addition of adjuvant chemotherapy.



We assessed the effects of stage grouping into stage I, II, and III/IVa with FIGO 2008 versus FIGO 2018, on progression-free survival (PFS) and overall survival (OS) at 5 years using Kaplan-Meier estimates

We used Cox proportional hazard regression to perform univariable analyses, and multivariable analyses adjusting for important prognostic factors and randomly allocated treatment.

Results

All 919 pts had complete data for staging according to the 2 staging systems and most prognostic factors for adjustment.

Among all participants, the 5-year outcomes were PFS = 62% and OS = 72%.

Classification according to FIGO 2018 rather than FIGO 2008 yielded higher 5-year PFS and OS in each stage group

	Number (%)		5-year PFS %		5-year OS %	
Stage	FIGO 2008	FIGO 2018	FIGO 2008	FIGO 2018	FIGO 2008	FIGO 2018
I	242 (26)	105 (11)	71	81	78	89
II	457 (50)	261 (28)	65	68	75	78
III/IVa	220 (24)	553 (60)	48	56	58	66

Both staging systems were the only independently significant prognostic factors in both univariable and multivariable analyses (all p<0.0001) for both PFS and OS.

Conclusions

Staging locally advanced cervical cancer using FIGO 2018 rather than FIGO 2008 resulted in higher PFS and OS in each stage grouping that **reflected stage migration, rather than a true improvement in outcomes**.

Compared with staging using FIGO 2008, reclassifying using FIGO 2018 resulted in more pts being classified as stage 3 due to the incorporation of nodal status.

FIGO stage remains the strongest predictor of OS after CRT but survival outcomes by stage in trials using the old vs new staging system are not comparable.

Predictor of **OVERALL SURVIVAL**		Univariable analysis		Multivariable analysis			
				FIGO 2008		FIGO 2018	
	Value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
FIGO 2008 (Ref=Stage I)	Stage II (2008)	1.15 (0.81 - 1.64)	0.43	1.20 (0.85 - 1.70)	0.31		
	Stage III-IV (2008)	2.37 (1.86 - 3.04)	<.01	2.42 (1.88 - 3.09)	<.01		
FIGO 2018 (Ref=Stage I)	Stage II (2018)	1.86 (0.97 - 3.67)	0.06			1.78 (0.93 - 3.45)	0.08
	Stage III-IV (2018)	3.23 (1.79 - 5.94)	<.01			3.14 (1.70 - 5.78)	<.01
Age (Ref=<60)	≥60	1.10 (0.77 - 1.56)	0.60	1.07 (0.75 - 1.53)	0.71	1.15 (0.81 - 1.65)	0.43
Histology (Ref=Non-squamous)	Squamous cell ca	1.14 (0.82 - 1.59)	0.44	1.01 (0.72 - 1.41)	0.97	1.05 (0.75 - 1.46)	0.78
Smoking status (Ref=Never smoked)	Current/ex-smoker/unknown	1.18 (0.91 - 1.53)	0.21	1.15 (0.88 - 1.50)	0.30	1.15 (0.88 - 1.49)	0.31
Race (Ref=White/Caucasian)	All other/unknown	0.90 (0.67 - 1.21)	0.49	0.94 (0.69 - 1.27)	0.68	0.92 (0.68 - 1.25)	0.60
Pelvic/common iliac node (Ref=No/unknown)	Yes	1.58 (1.23 - 2.05)	<.01	1.59 (1.22 - 2.07)	<.01		
Randomised treatment (Ref=CRT)	CRT + Adjuvant	0.90 (0.70 - 1.17)	0.43	0.86 (0.66 - 1.11)	0.25	0.88 (0.68 - 1.14)	0.34

Predictor of **PROGRESSION FREE SURVIVAL**		Univariable analysis		Multivariable analysis			
				FIGO 2008		FIGO 2018	
	Value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
FIGO 2008 (Ref=Stage I)	Stage II (2008)	1.26 (0.93 - 1.68)	0.13	1.34 (0.99 - 1.80)	0.05		
	Stage III-IV (2008)	2.18 (1.60 - 2.97)	<.01	2.35 (1.71 - 3.22)	<.01		
FIGO 2018 (Ref=Stage I)	Stage II (2018)	1.82 (1.09 - 3.04)	0.02			1.80 (1.07 - 3.03)	0.03
	Stage III-IV (2018)	2.72 (1.69 - 4.40)	<.01			2.80 (1.73 - 4.53)	<.01
Age (Ref=<60)	≥60	1.04 (0.77 - 1.41)	0.79	1.03 (0.76 - 1.41)	0.83	1.09 (0.80 - 1.48)	0.58
Histology (Ref=Non-squamous)	Squamous cell ca	0.80 (0.62 - 1.04)	0.10	0.71 (0.54 - 0.93)	0.01	0.74 (0.56 - 0.98)	0.02
Smoking status (Ref=Never smoked)	Current/ex-smoker/unknown	1.10 (0.89 - 1.37)	0.38	1.11 (0.89 - 1.39)	0.35	1.12 (0.89 - 1.40)	0.33
Race (Ref=White/Caucasian)	All other/unknown	1.09 (0.85 - 1.39)	0.49	1.16 (0.90 - 1.49)	0.24	1.13 (0.88 - 1.45)	0.33
Pelvic/common iliac node (Ref=No/unknown)	Yes	1.44 (1.15 - 1.80)	<.01	1.50 (1.20 - 1.88)	<.01		
Randomised treatment (Ref=CRT)	CRT + Adjuvant	0.86 (0.69 - 1.08)	0.19	0.86 (0.68 - 1.07)	0.19	0.87 (0.70 - 1.08)	0.22

Contact: Linda.Mileshkin@petermac.org

We acknowledge and thank women participating and their families; Staff at sites in the USA, Australia, New Zealand, Canada, China, Singapore, Saudi Arabia; Staff at the NHMRC Clinical Trials Centre, Australia New Zealand Gynaecological Oncology Group (ANZGOG), and NRG Oncology; NHMRC Project Grant (APP1044349) and US NCI for financial support; Hospira for providing paclitaxel in Australia and New Zealand; and IDSMC members

Predictor of **OVERALL SURVIVAL**		Univariable analysis		Multivariable analysis			
				FIGO 2008		FIGO 2018	
	Value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
FIGO 2008 (Ref=Stage I)	Stage II (2008)	1.15 (0.81 - 1.63)	0.43	1.20 (0.85 - 1.70)	0.31		
	Stage III-IV (2008)	2.37 (1.65 - 3.38)	<.01	2.42 (1.68 - 3.49)	<.01		
FIGO 2018 (Ref=Stage I)	Stage II (2018)	1.86 (0.97 - 3.57)	0.06			1.78 (0.93 - 3.43)	0.08
	Stage III-IV (2018)	3.23 (1.75 - 5.94)	<.01			3.14 (1.70 - 5.78)	<.01
Age (Ref=<60)	≥60	1.10 (0.77 - 1.56)	0.60	1.07 (0.75 - 1.53)	0.71	1.15 (0.81 - 1.65)	0.43
Histology (Ref=Non-squamous)	Squamous cell ca	1.14 (0.82 - 1.59)	0.44	1.01 (0.72 - 1.41)	0.97	1.05 (0.75 - 1.46)	0.78
Smoking status (Ref=Never smoked)	Current/ex-smoker/unknown	1.18 (0.91 - 1.53)	0.21	1.15 (0.88 - 1.50)	0.30	1.15 (0.88 - 1.49)	0.31
Race (Ref=White/Caucasian)	All other/unknown	0.90 (0.67 - 1.21)	0.49	0.94 (0.69 - 1.27)	0.68	0.92 (0.68 - 1.25)	0.60
Pelvic/common iliac node (Ref=No/unknown)	Yes	1.58 (1.21 - 2.05)	<.01	1.59 (1.22 - 2.07)	<.01		
Randomised treatment (Ref=CRT)	CRT + Adjuvant	0.90 (0.70 - 1.17)	0.43	0.86 (0.66 - 1.11)	0.25	0.88 (0.68 - 1.14)	0.34

Benchmarks in higher risk population (PA node +)

Study	Design	PA nodal status Histology (H), Imaging (I), either (E)	PF at 30 months (%)*
Berman et al.	Retrospective/obs	Positive (H)	25 (36 mos)
Perry et al	Retrospective/obs	Positive (H)	28
Varia et al GOG 125	Prospective/CRT with extended field	Positive (H)	42(FIGO II) 24 (FIGO III/IV)
Walker et al. GOG 9804	Prospective/CRT with paclitaxel	Positive (H)	71 (OS)
Boardman et al. GOG 98	Prospective/CRT with OUTBACK cis/paclitaxel	Positive (E)	60 (projected)

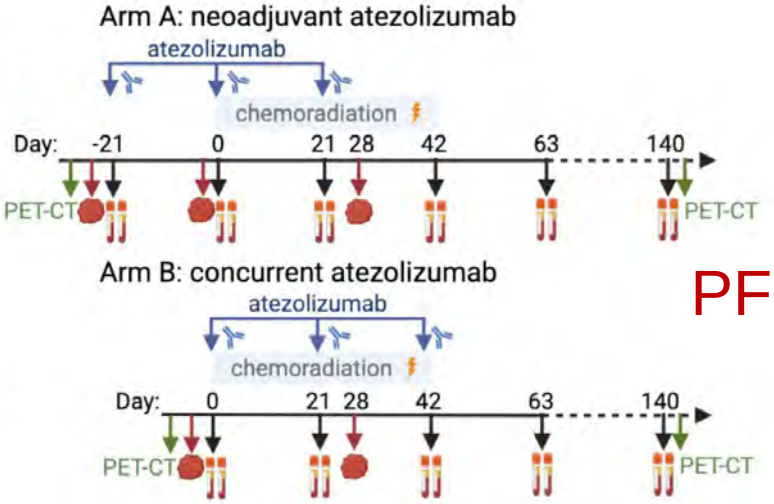
Berman ML et al. Gynecol Oncol. 1984 Sep;19(1):8-16. Perry LJ et al. Int J Gynecol Cancer. 2014 Mar;24(3):564-9. **Varia MA et al. Int J Radiat Oncol Biol Phys. 1998 Dec 1;42(5):1015-23. Walker J et al. Gynecol Oncol. 2009 Jan;112(1):78-84. Boardman CH et al. Gynecol Oncol. 2018 Nov;151(2):202-207. Rose PG et al. J Clin Oncol. 2007 Jul 1;25(19):2804-10. Mileshkin and Moore KN et al. ASCO 2021 LBA 3.**

PA node + focus-highest risk

Cervical cancer:
Stage IB-IVA, +PALN
Stage IIB-IVA, + PLN, +/-PALN

Biopsy

Blood



PFS at 30 months
62-78%

ANNUAL MEETING ON WOMENS' CANCER
BUILDING BRIDGES // BREAKING BARRIERS

Mayadev J et al. SGO 2022 Abstract 24

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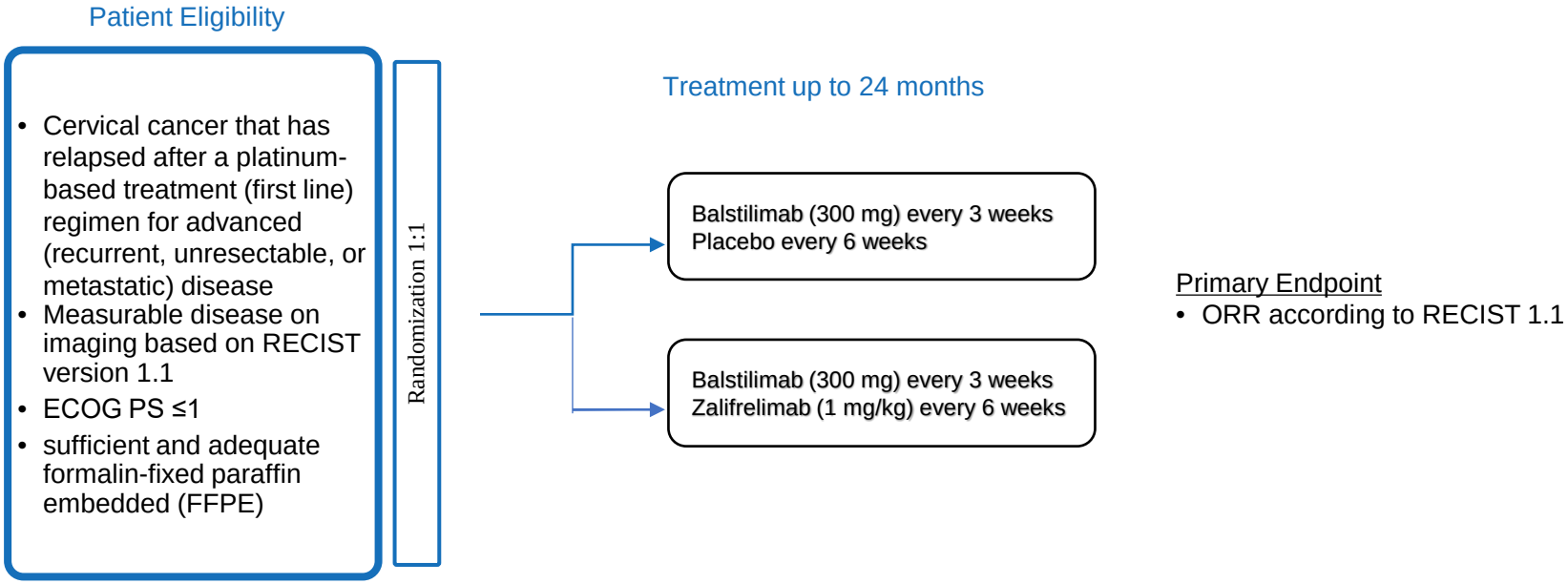
Frontline ICI trial	Population	Investigational Agent Duration	Design (n)	Primary endpoint(s)
CALLA (NCT03830866) PI Brad Monk	FIGO 2009 IB2-IIB node + IIIA-IVA node +/-	Durvalumab During CRT + 24 months	Phase 3 2 arm 1:1 CRT control (714)	PFS
ENGOT cx11/GOG 3047/ KEYNOTE-A18 (NCT04221945) PI Ketta LoRusso		Pembrolizumab During CRT + 24 months	Phase 3 2 arm 1:1 CRT control (980)	PFS/OS
ATEZOLACC (NCT03612791) PI Cyrus Chargari		Atezolizumab During CRT + 14 months	Phase 2 2 arm 1:1 CRT control (189)	PFS
GEICO 78-C/ATOMICC (NCT03833479) PI Ana Oaknin		Dostarlimab Following CRT 24 months	Phase 2 2 arm 1:2 CRT control (132)	PFS

GOG-3028 - A Two Arm, Randomized, Non Comparative Blinded Phase 2 Trial of Balstilimab +/- Zalifrelimab in Second Line Cervical Cancer

RaPiDS



PI: Dave O'Malley

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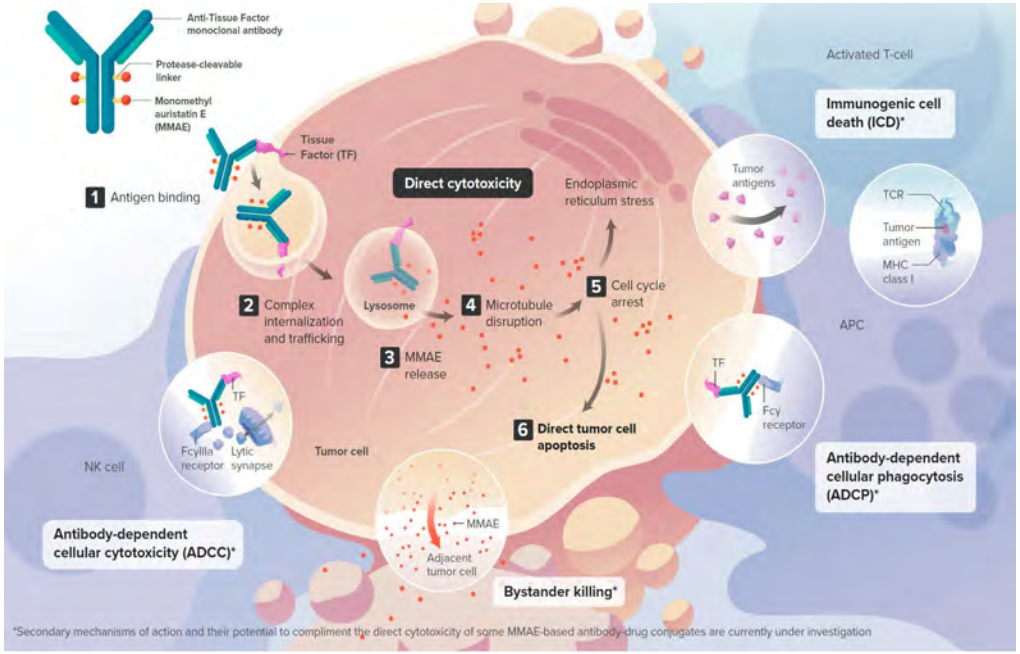
Tisotumab Vedotin (TV)

- Tisotumab vedotin is an investigational antibody–drug conjugate directed to TF and covalently linked to the microtubule-disrupting agent, MMAE, via a protease-cleavable linker[1,2]
  - TF is a protein highly expressed in cervical cancer and other solid tumors[3-6]
- Multimodal MOA of tisotumab vedotin[1,2,7]
  - Direct cytotoxicity
  - Bystander killing
  - Immunogenic cell death
  - ADCC
  - ADCP



.ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; MMAE, monomethyl auristatin E; MOA, mechanism of action; TF, tissue factor

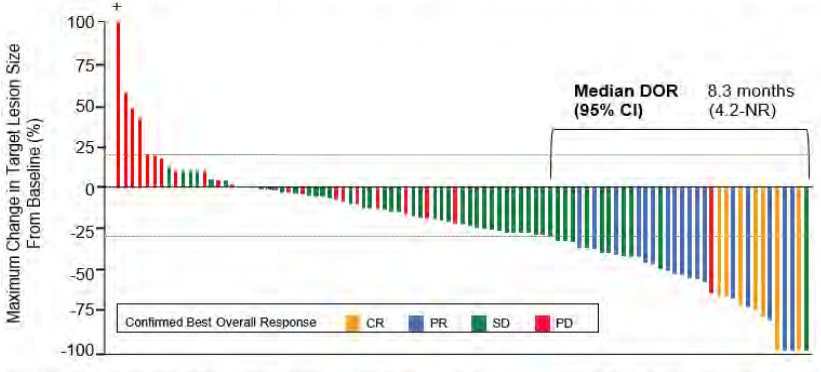
1. Breij EC et al. *Cancer Res*. 2014;74(4):1214-1226. 2. De Goeij BE et al. *Mol Cancer Ther*. 2015;14(5):1130-1140. 3. Forster Y et al. *Clin Chim Acta.* 2006;364:12-21. 4. Pan L et al. *Mol Med Rep*. 2019;19:2077-2086. 5. Cocco E et al. *BMC Cancer.* 2011;11:263. 6. Zhao X et al. *Exp Ther Med.* 2018;16:4075-4081. 7. Alley SC et al. AACR 2019; Abstract 221.

Genmab

Genmab and Seagen Announce FDA Accelerated Approval for TIVDAK™ (tisotumab vedotin-tftv) in Previously Treated Recurrent or Metastatic Cervical Cancer

September 20, 2021 17:00 ET | Source: Genmab A/S

ENGOT cx6/GOG 3023/innovaTV204



	N=101
Confirmed ORR (95% CI), %	24 (15.9–33.3)
CR, n (%)	7 (7)
PR, n (%)	17 (17)
SD, n (%)	49 (49)
PD, n (%)	24 (24)
Not evaluable, n (%)	4 (4)

Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months. + indicates a change greater than 100%. Horizontal dashed lines indicate 20% increase and 30% decrease in target lesion diameters from baseline for RECIST v1.1 assessment. Colored bars represent the best overall confirmed response. CR, PR, SD, and PD were based on RECIST v1.1 as evaluated by IRC.
CR, complete response; IRC, independent review committee; PD, disease progression; PR, partial response; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; SD, stable disease.

Coleman RL et al. ESMO 2020. Abstract LBA32.
Coleman RL. *Lancet Oncol.* 2021:S1470-2045(21)00056-5.

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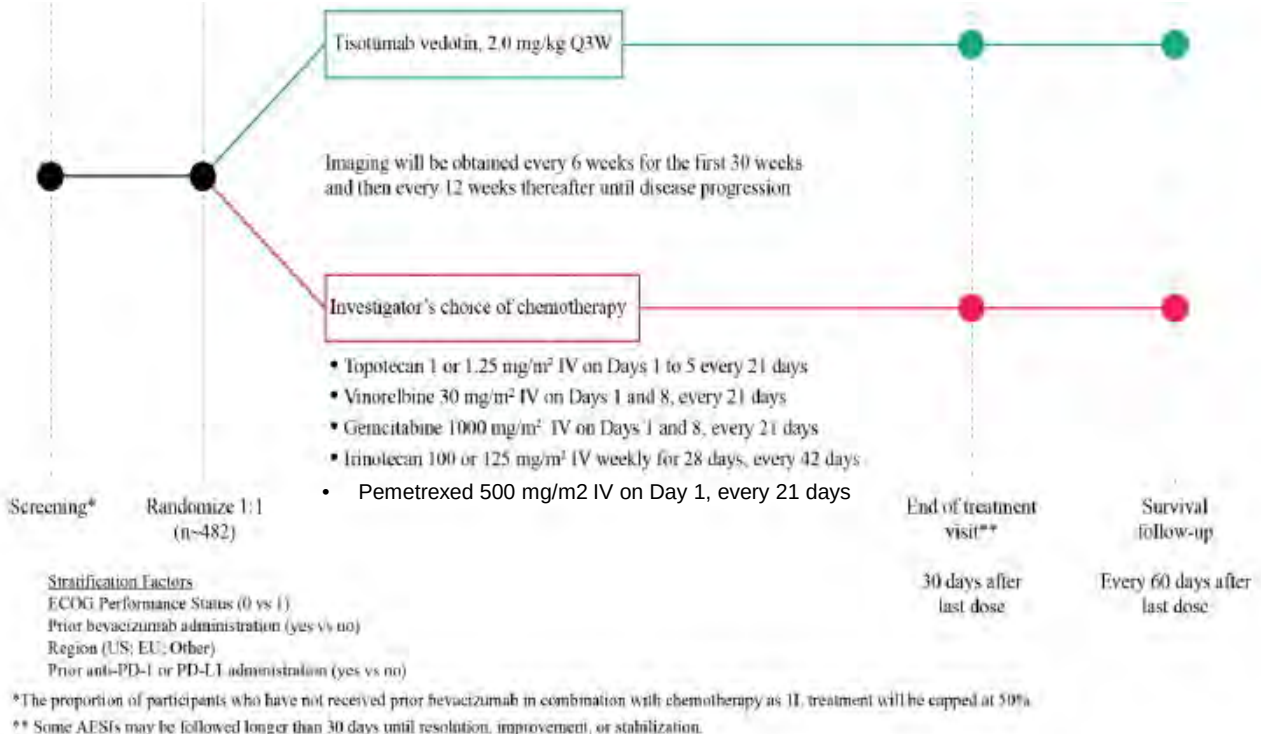
ENGOT cx12/GOG-3057/innovaTV 301: Schema



Primary Endpoint = OS

US PI: Brian Slomovitz

innovaTV 301. Updated April 28, 2021. Accessed April 30, 2021. https://www.clinicaltrials.gov/ct2/show/NCT04697628

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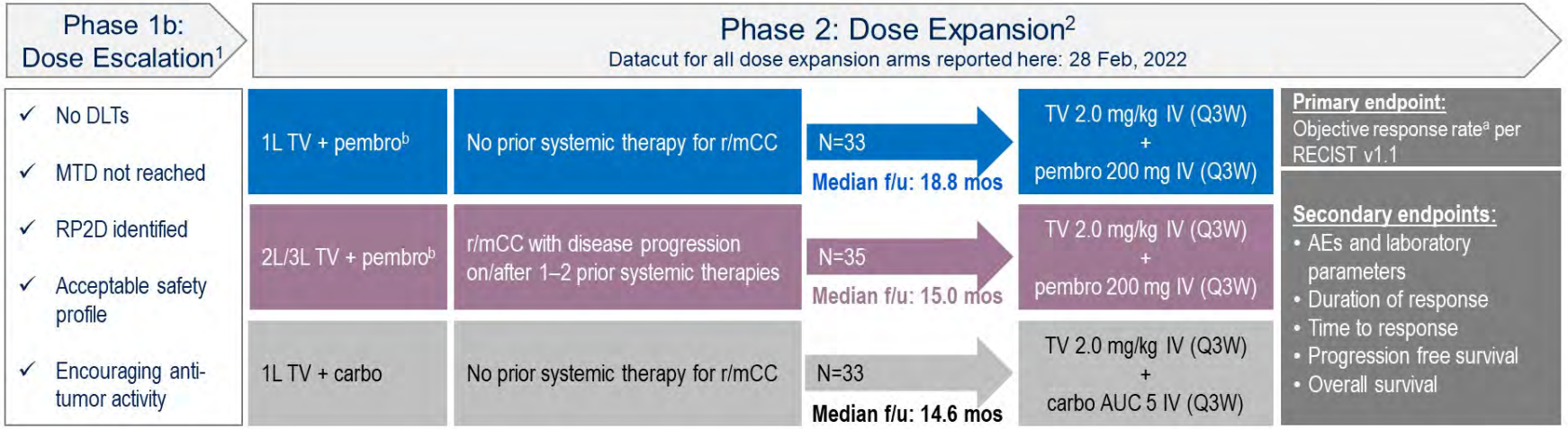
ENGOT-cx8/GOG-3024 /innovaTV 205: Dose-expansion phase



1L TV + pembro in patients with r/mCC: First disclosure

2L/3L TV + pembro & 1L TV + carbo: Updated with longer follow-up

[a]Tumor response assessed every 6 weeks; [b]Pembro will be administered up to 35 cycles, approximately 2 years.
f/u, follow-up; r/mCC, recurrent or metastatic cervical cancer; TV, tisotumab vedotin.
1. Monk B, et al. International Gynecologic Cancer Society: 2021; 2. Vergote I, et al. European Society for Medical Oncology 2021. (initial disclosure of 1L TV + carbo and 2L/3L TV + pembro)

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Baseline demographics and clinical characteristics

Demographics and characteristics	1L TV + Pembro (N = 33)	2L/3L TV + Pembro (N = 35)	1L TV + Carbo (N = 33)
Age, median (range), years	47 (29 - 76)	47 (31 - 73)	51 (25 - 78)
Race (White), n (%)	31 (93.9)	27 (77.1)	28 (84.8)
Ethnicity (Not Hispanic/Latino), n (%)	32 (97.0)	29 (82.9)	29 (87.9)
ECOG performance status, n (%)			
0	25 (75.8)	22 (62.9)	21 (63.6)
1	8 (24.2)	13 (37.1)	12 (36.4)
Cancer recurrence at the time of screening, n (%)	26 (78.8)	31 (88.6)	30 (90.9)
Histology, n (%)			
Squamous	22 (66.7)	19 (54.3)	24 (72.7)
Adenocarcinoma	11 (33.3)	15 (42.9)	8 (24.2)
Adenosquamous	0	0	1 (3.0)
Other	0	1 (2.9)	0
PD-L1 positive,[a] n (%)	28 (96.6)[b]	22 (81.5)[b]	NA
Prior radiotherapy, n (%)	25 (75.8)	30 (85.7)	27 (81.8)
Prior chemoradiation, n (%)	24 (72.7)	19 (54.3)	23 (69.7)
Prior lines of systemic regimen,[c] n (%)			
0	33 (100)	0	33 (100)
1	0	25 (71.4)	0
2	0	10 (28.6)[d,e]	0
Prior bevacizumab,[f] n (%)	NA	19 (54.3)	NA

[a]Prevalence of CPS PD-L1 ≥ 1. [b]Based on evaluable biopsies, n=29 and 27 for 1L and 2L/3L TV + pembro respectively. [c]Systemic regimen administered in the metastatic or recurrent setting, excludes chemoradiation. [d]Includes 1 patient receiving prior 1L treatment with nivolumab + ipilimumab. [e]Includes 1 patient receiving prior 2L treatment with pembro. [f]Adjuvant and neoadjuvant settings are excluded.
There were 2 Asian patients each in the 1L and 2L TV+pembro arms, and 1 in the 1L TV + carbo arm. The number of Hispanic/Latino patients was 1, 0, and 0, respectively; ethnicity is missing for 0, 6, and 4 patients; respectively.
TV, tisotumab vedotin.

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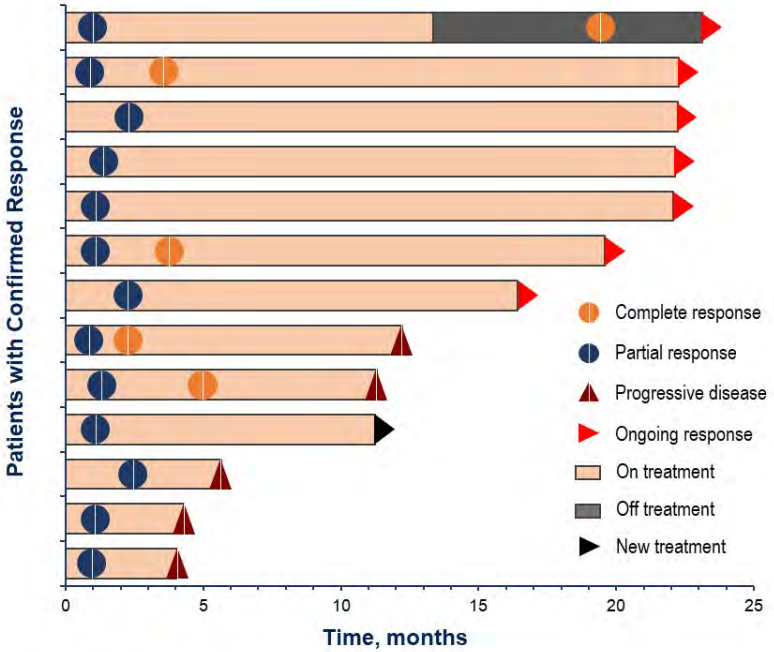
Anti-tumor activity – 1L TV + Pembro

Efficacy parameter	1L TV + Pembro (N = 32*) Median f/u: 18.8 months
Confirmed ORR, % [95% CI]	40.6 [23.7 – 59.4]
Complete response	5 (15.6)
Partial response	8 (25.0)
Stable disease	14 (43.8)
Progressive disease	1 (3.1)
Not evaluable	4 (12.5)
DCR[a], % [95% CI]	84.4 [67.2 – 94.7]
Median DOR[b], months (range)	NR (2.8 – 21.9+)
Median time to response, months (range)	1.4 (1.2 – 2.8)
Median PFS[c], months [95% CI]	5.3 [4.0 – 12.2]
Median OS[d], months (range)	NR (0.5 – 24.9+)

+, censored; NR, not reached.
*1 patient was excluded from the full-analysis set due to receiving incorrect study drug.
[a]Defined as SD (at least 5 weeks after the first dose of study treatment) or confirmed CR or PR.
[b]8 patients are censored; [c]12 patients are censored;[d]19 patients are censored.



With 18.8 months median follow-up, compelling, durable preliminary efficacy was observed in 1L with >50% of responders with ongoing response

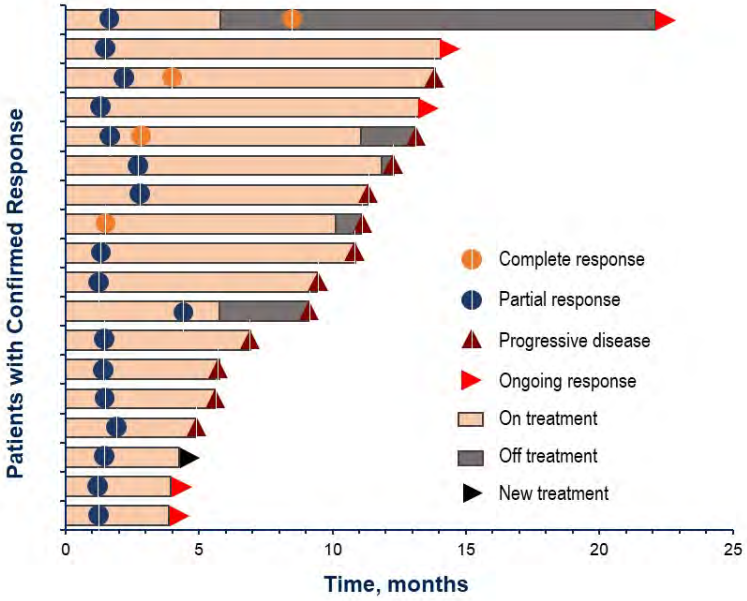
DCR, disease control rate; f/u, follow-up; TV, tisotumab vedotin.

Anti-tumor activity – 1L TV + Carbo

ORR plt/tax/Pembro +/-bev 68/77/52
cis/tax/bev GOG 240 50%

Efficacy parameter	1L TV + Carbo (N = 33) Median f/u: 14.6 months
Confirmed ORR, % [95% CI]	54.5 [36.4 – 71.9]
Complete response	4 (12.1)
Partial response	14 (42.4)
Stable disease	12 (36.4)
Progressive disease	2 (6.1)
Not evaluable	1 (3.0)
DCR[a], % [95% CI]	90.9 [75.7 – 98.1]
Median DOR[b], months [95% CI]	8.6 [4.2; 11.5]
Median time to response, months (range)	1.4 (1.1 – 4.4)
Median PFS[c], months [95% CI]	6.9 [4.0 – 11.1]
Median OS[d], months (range)	NR (0.8+ – 22.1+)

+, censored; NR, not reached.
[a]Defined as SD (at least 5 weeks after the first dose of study treatment) or confirmed CR or PR.
[b]4 patients are censored; [c]9 patients are censored; [d]22 patients are censored.



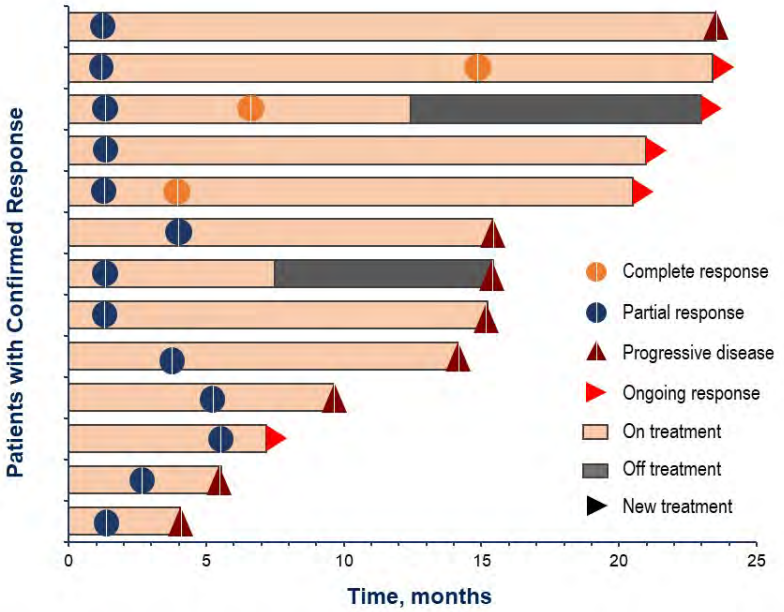
Compelling antitumor activity was observed in 1L patients with >50% experiencing a response and >90% with disease control

DCR, disease control rate; f/u, follow-up; TV, tisotumab vedotin.

Anti-tumor activity – 2L/3L TV + Pembro

Efficacy parameter	2L/3L TV + Pembro (N = 34*) Median f/u: 15.0 months
Confirmed ORR, % [95% CI]	38.2 [22.2 – 56.4]
Complete response	3 (8.8)
Partial response	10 (29.4)
Stable disease	12 (35.3)
Progressive disease	7 (20.6)
Not evaluable	2 (5.9)
DCR[a], % [95% CI]	73.5 [55.6 – 87.1]
Median DOR[b], months [95% CI]	14.0 [2.8 – NR]
Median time to response, months (range)	1.4 (1.3 – 5.8)
Median PFS[c], months [95% CI]	5.6 [2.7 – 14.2]
Median OS[d], months [95% CI]	15.3 [9.9 – NR]

+, censored; NR, not reached
*1 patient was excluded from the full analysis set as they had no target lesions at baseline.
[a]Defined as SD (at least 5 weeks after the first dose of study treatment) or confirmed CR or PR.
[b]5 patients are censored; [c]10 patients are censored; [d]14 patients are censored



With 15 months median follow-up, compelling, durable preliminary efficacy was observed in 2L/3L with ~40% of responders ongoing in response

DCR, disease control rate; f/u, follow-up; TV, tisotumab vedotin.

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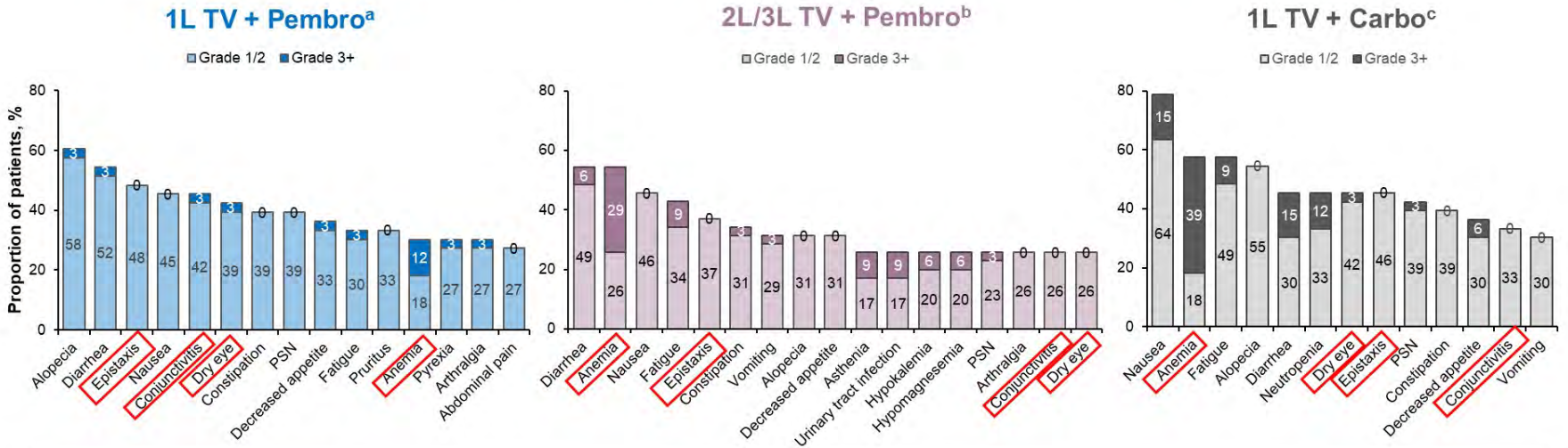
Safety summary of common AEs reported >25% of patients



- Most TEAEs were grade 1 or 2
- Observed safety profile was generally consistent with those known for each individual agent
- There was a single grade 5 event with 1L TV + pembro considered by the investigator to be related to trial treatment (due to disseminated intravascular coagulation)
- Immune-mediated AEs observed with TV + pembro were consistent with known safety profile of checkpoint inhibitors

[a]8 (24.2%) patients discontinued TV due to AEs; [b]12 (34.3%) patients discontinued TV due to AEs; [c]7 (21.2%) patients discontinued TV due to AEs; AEs leading to discontinuation of TV were mostly related to ocular or neuropathic events. PSN, peripheral sensory neuropathy; TV, tisotumab vedotin.

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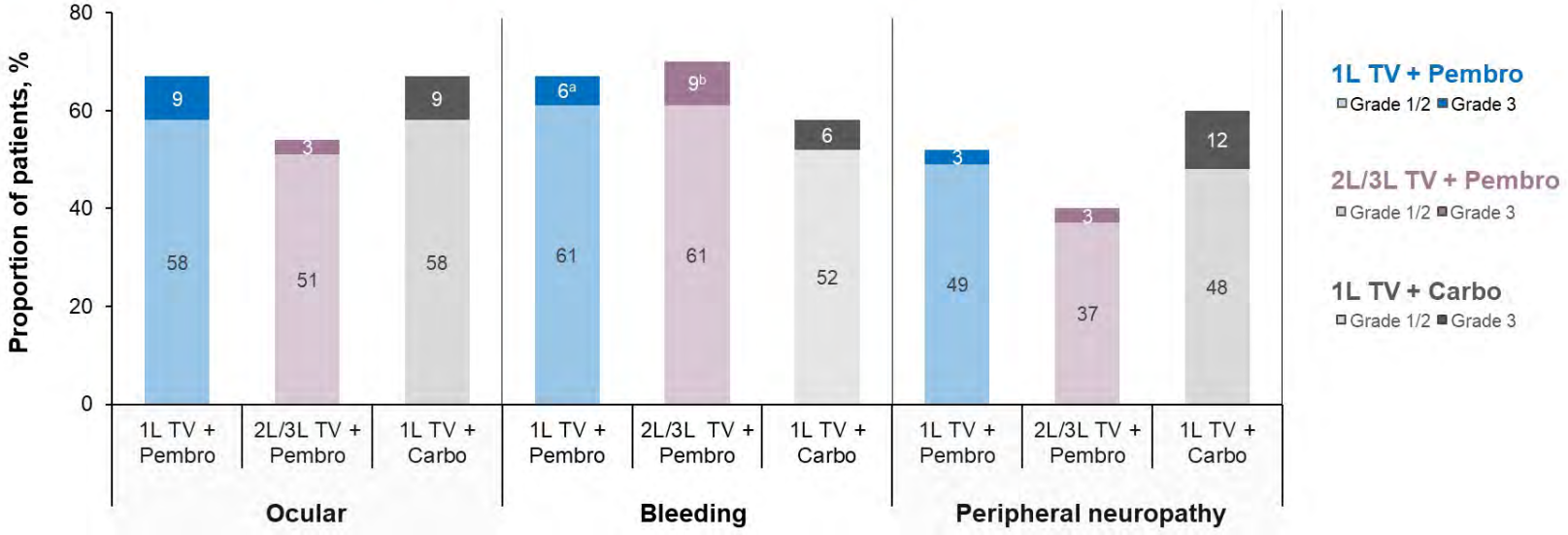
Adverse events of special interest with TV



[a]Includes one patient with grade 5 disseminated intravascular coagulation; [b]Includes one patient with grade 4 hematuria

AEs of special interest with TV were generally consistent across cohorts and were mostly grade 1-2

TV, tisotumab vedotin.

With Novel Therapies, Disparities Emerge or Widen

- Cancer care disparities emerge or worsen with discoveries of new, more effective approaches to cancer treatment.
- Rapidly expanding use of immunotherapy for many different cancers across the spectrum from late to early stages has, predictably, been followed by emerging evidence of disparities in access to these highly effective but expensive treatments.
- The danger that these new treatments will further widen preexisting cancer care and outcome disparities requires urgent corrective intervention.

Karjalainen, 1990; Erikson et al., 2007

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Geographic Disparities in Gynecologic Cancer Survival Observed in Several Studies

- Knowing whether cancer incidence and survival vary geographically is important because health care is most often delivered locally
- Identification of areas with high cancer incidence and better or worse survival may reflect access to, and quality of, care
- Accordingly, understanding how location of cancer specialists influences survival outcomes for those with cancer is critical.

(Karjalainen, 1990; Erikson et al., 2007; Gunderson et al., 2013; Ward et al., 2004).

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Cervical Cancer Geographic Analyzer

- Novel, innovative public access tool to assess incidence of cervical cancer as well as recurrent and metastatic cervical cancer cases for potential policy intervention purposes
- Retrospective claims analysis was conducted using the MarketScan® Commercial and Medicare Supplemental Database for adult cervical cancer (CC) and r/mCC patients diagnosed between 1/1/15-12/31/20.
- Metropolitan Statistical Areas assessed: a core area containing a substantial population nucleus, together with adjacent communities having a high degree of economic and social integration with that core.

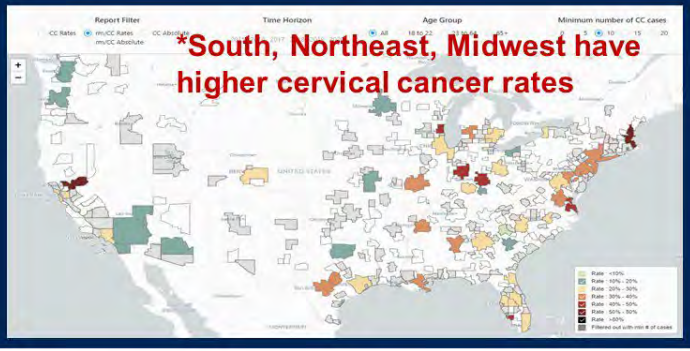

Table 1: *Top 5 MSAs with highest burden and point prevalence of r/mCC in the US*

MSA	2020	2019	2018	Average
Cape Coral-Fort Myers, FL	40%	31%	64%	45%
Sacramento-Roseville-Arden-Arcade, CA	50%	46%	33%	45%
Grand Rapids, MI	31%	36%	55%	42%
Boston-Cambridge-Newton, MA	50%	45%	41%	40%
Baltimore-Columbia-Towson, MD	38%	33%	39%	36%

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