

# ADVANCES IN IMMUNOTHERAPY FOR CERVICAL CANCER

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Survive and Thrive  
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# CHEMOTHERAPY REGIMENS

Phase 2 studies (1998-2010)

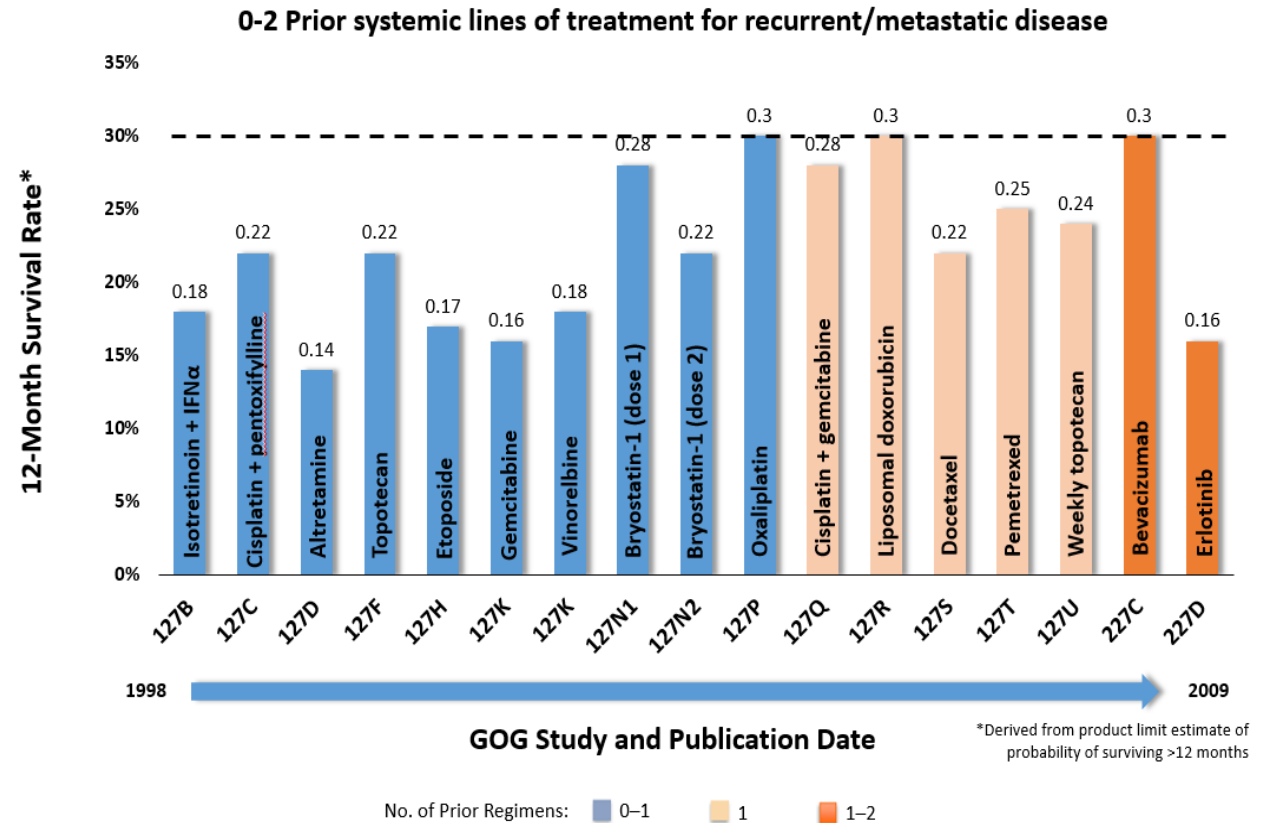
- 12-month OS rate: ~30% (at best)

Chemotherapy + bevacizumab (2014)

- Median OS: 16.8 months
- 12-month OS rate: ~60%

Second-line therapies with minimal efficacy

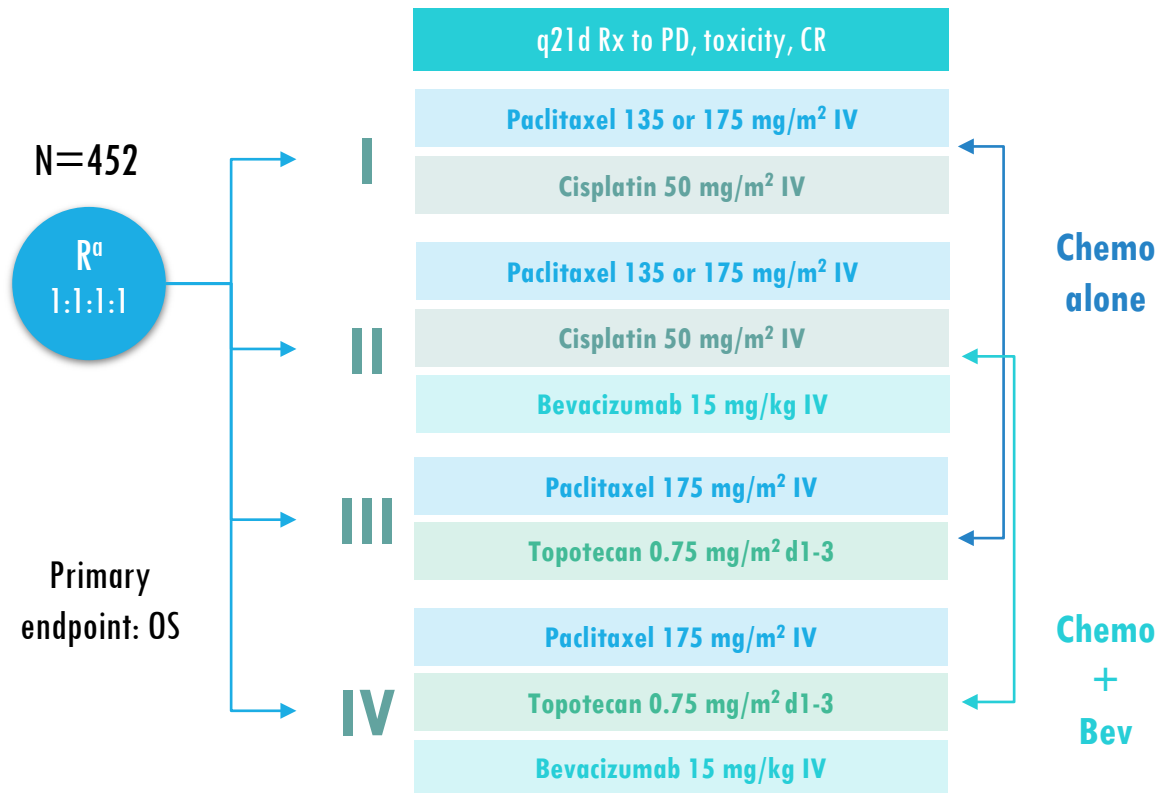
Highlights the need for new therapeutics



# GOG 240: PHASE 3 TRIAL DESIGN AND PATIENTS

## Carcinoma of the cervix

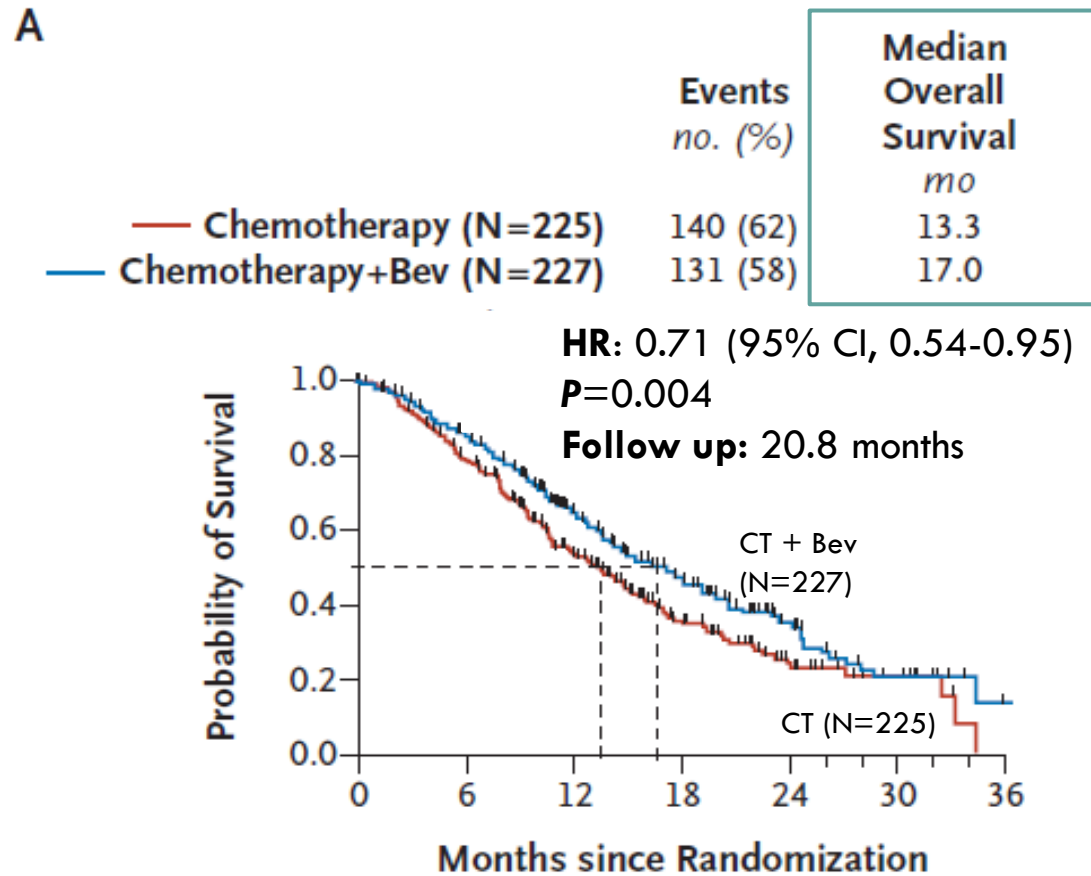
- Primary stage IVB
- Recurrent/persistent
- Measurable disease
- GOG PS 0-1
- No prior chemotherapy for recurrence



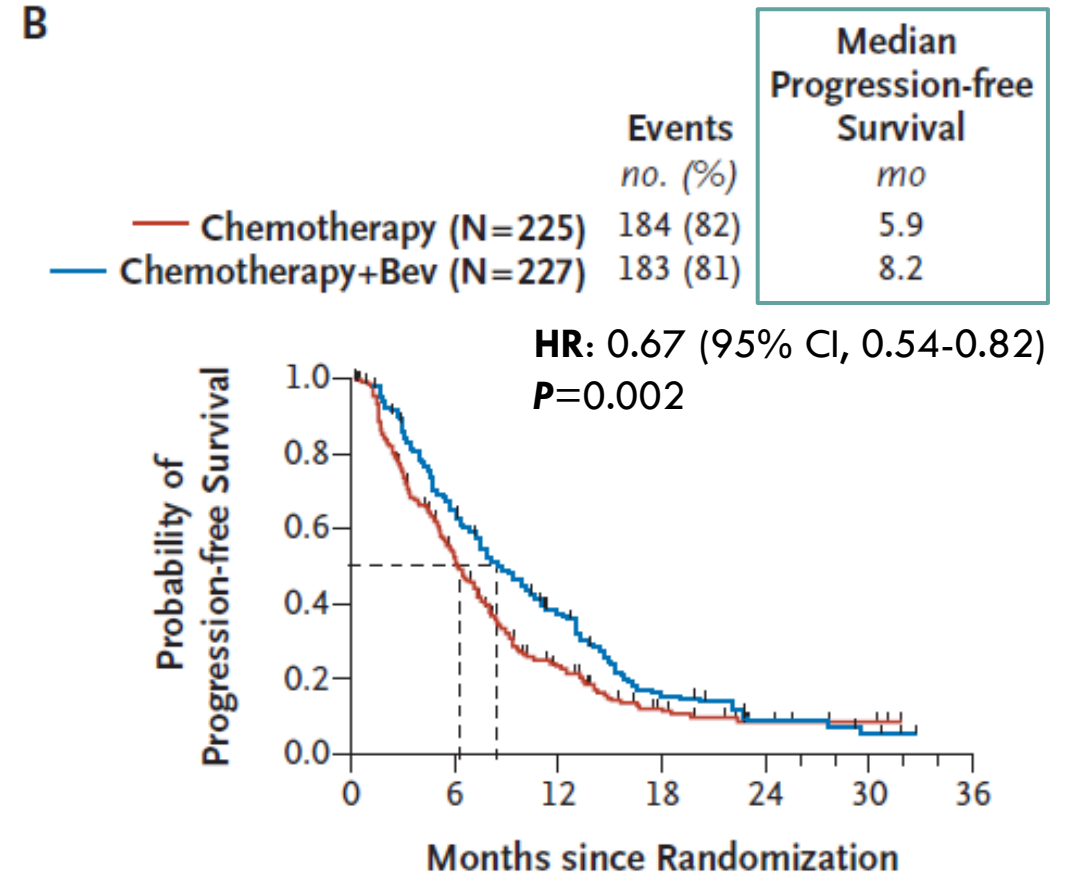
Characteristic	Chemo (n=225)	Chemo + bevacizumab (n=227)
Age, median (range), y	46 (20-83)	48 (22-85)
Histology, %	Squamous	68
	Adenocarcinoma, unspecified	20
Disease stage, %	Recurrent	73
	Persistent	10
	Advanced	16
GOG PS 1, %	42	42
Prior platinum, %	74	75
Pelvic disease, %	53	54

<sup>a</sup> Stratification factors: stage IVB vs recurrent/persistent disease; performance status; prior cisplatin treatment as radiation sensitizer. Tewari KS, et al. *N Engl J Med.* 2014;370(8):734-743.

# GOG 240: FINAL OS/PFS



No. at Risk						
Chemotherapy	225	167	94	45	17	8
Chemotherapy +bev	227	184	121	69	30	10

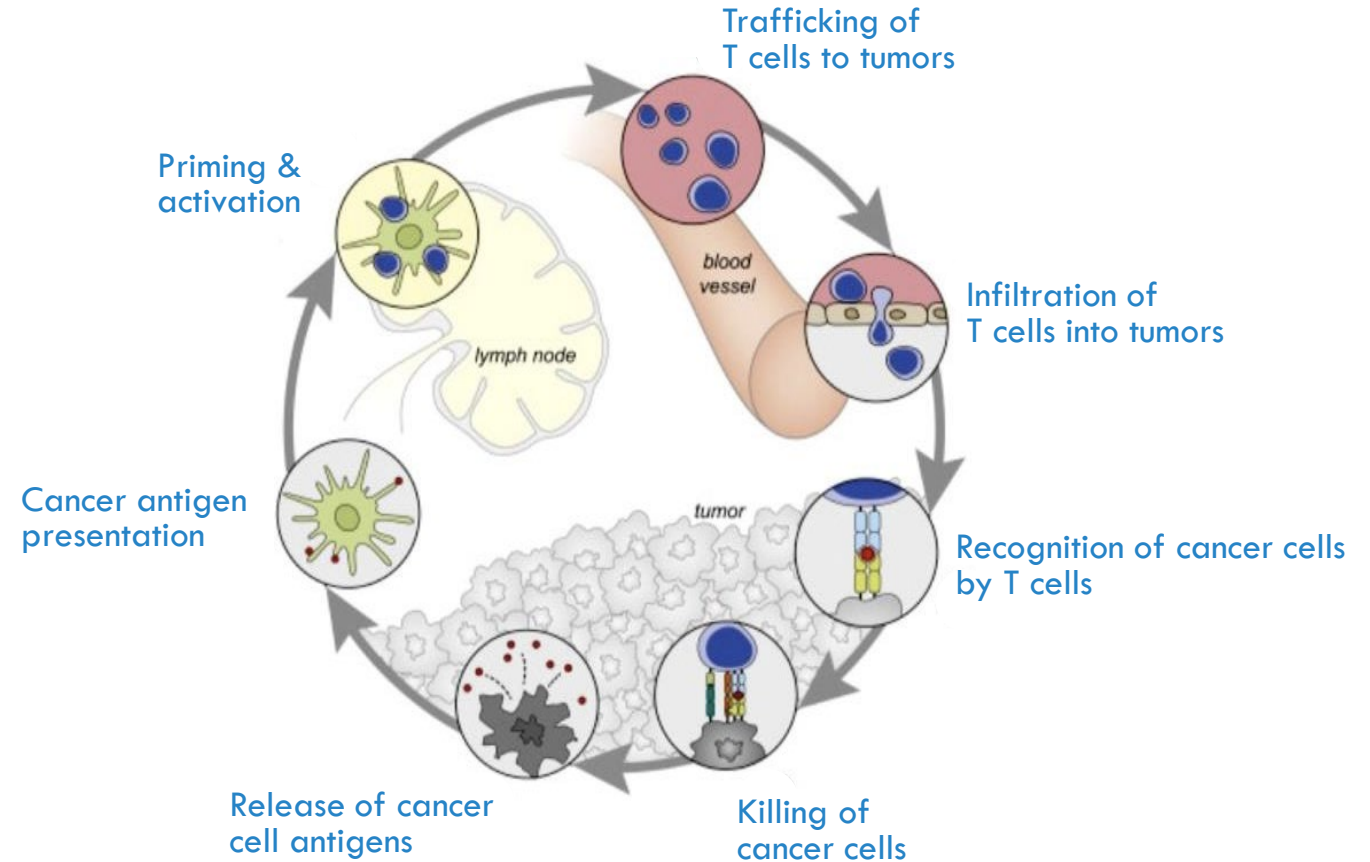


No. at Risk						
Chemotherapy	225	103	40	14	6	3
Chemotherapy +bev	227	132	70	22	6	3

# RATIONALE FOR IMMUNOTHERAPY

## Immunotherapy

- PD-1/L1 inhibition
  - Promotes T-cell activation against tumors
- CTLA-4 inhibition
  - Enhances tumor-specific CD8+ T-cell responses



# IMMUNOTHERAPY BIOMARKERS

## PD-L1 expression

- ~60% in cervical cancer

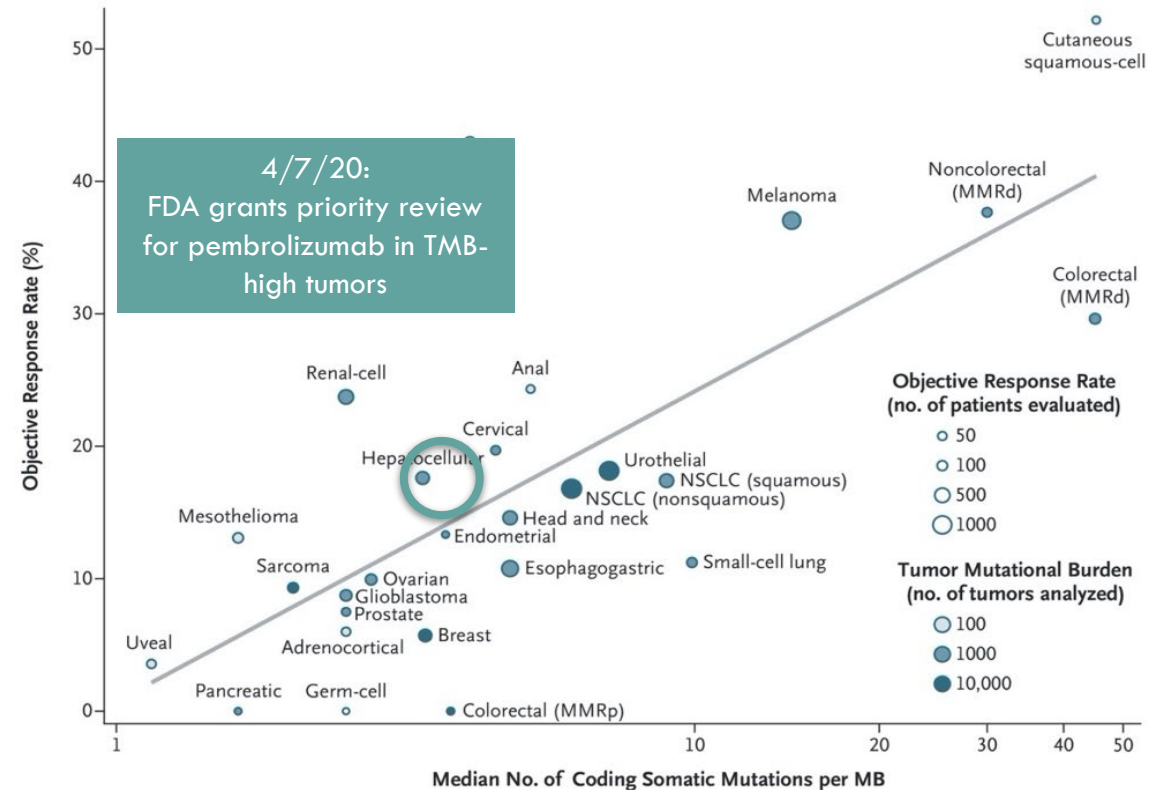
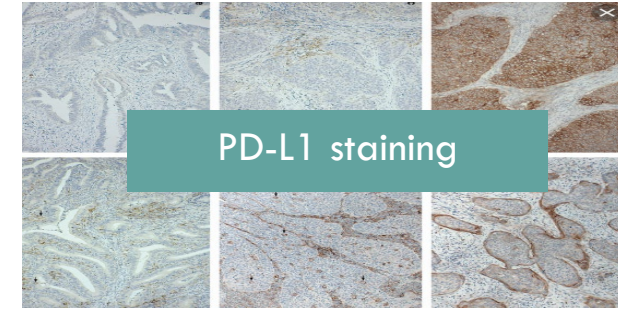
## CPS

- Ratio of the number of PD-L1+ cells (tumor cells, lymphocytes, macrophages) to all tumor cells
- $\geq 1$  used for cervical cancer

## TMB high status = ~6%

## MSI

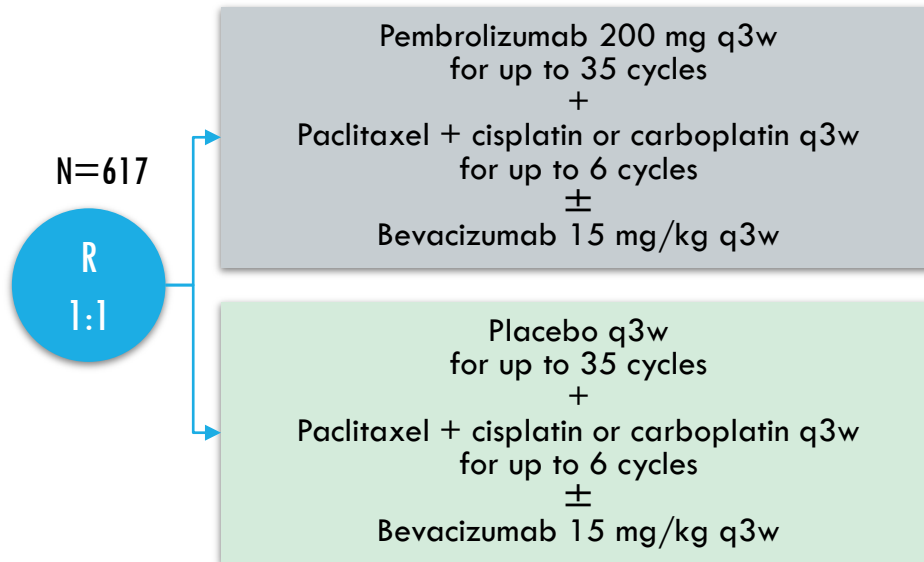
- Ranges from 2.6% to 14%



1. Meng Y, et al. *J Cancer*. 2018;9(16):2938-2945. 2. Enwere EK, et al. *Mod Pathol*. 2017;30(4):577-586. 3. Zhang L, et al. *N Engl J Med*. 2003;348(3):203-213. 4. Yarchoan M, et al. *N Engl J Med*. 2017;377(25):2500-2501. 5. Kulangara K, et al. *Arch Pathol Lab Med*. 2019;143(3):330-337. 6. Chung TK, et al. *Gynecol Obstet Invest*. 2001;52(2):98-103. 7. Bonneville R. *JCO Precis Oncol*. 2017;PO.17.00073.

# KEYNOTE 826: PHASE 3 TRIAL DESIGN AND PATIENTS

- Persistent, recurrent, or metastatic cervical cancer not amenable to curative treatment
- No prior systemic chemotherapy
- ECOG PS 0-1



## Endpoints

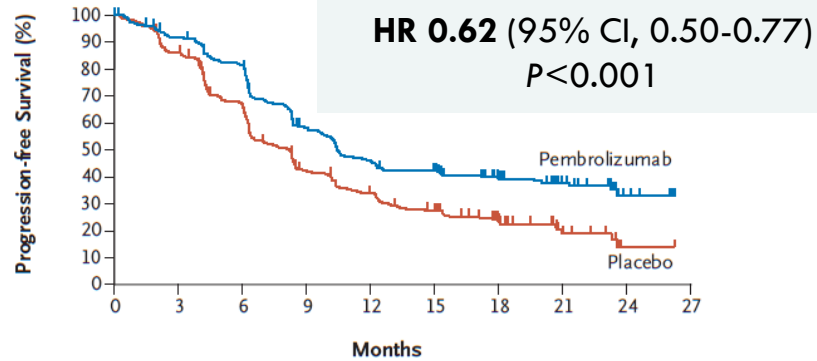
- Dual primary: OS and PFS
- Secondary: ORR, DOR, 12-mo PFS, and safety

	Pembrolizumab group (n=308)	Placebo group (n=309)
Age, median (range), y	51 (25-82)	50 (22-79)
ECOG PS 1, no. (%)	128 (42)	139 (45)
SCC, no. (%)	235 (76)	211 (68)
PD-L1 CPS, no. (%)		
<1	35 (11)	34 (11)
1 to <10	115 (37)	116 (38)
≥10	158 (51)	159 (51)
Bevacizumab use during trial, no. (%)	196 (64)	193 (62)

FDA approved October 2021 in combination with chemotherapy, with or without bevacizumab, for patients with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1)

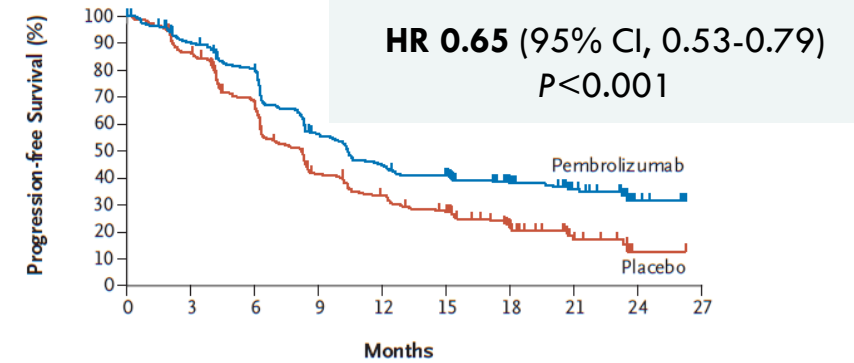
# KEYNOTE 826: PFS

## PD-L1 CPS $\geq 1$ Population



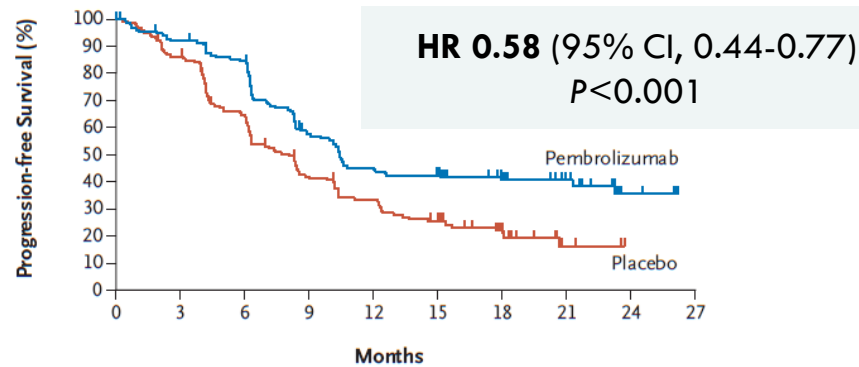
No. at Risk	0	3	6	9	12	15	18	21	24	27
Pembrolizumab	273	238	208	143	112	101	66	34	10	0
Placebo	275	229	170	103	81	63	38	13	1	0

## ITT Population



No. at Risk	0	3	6	9	12	15	18	21	24	27
Pembrolizumab	308	263	229	155	123	110	70	35	10	0
Placebo	309	259	195	113	89	71	39	13	1	0

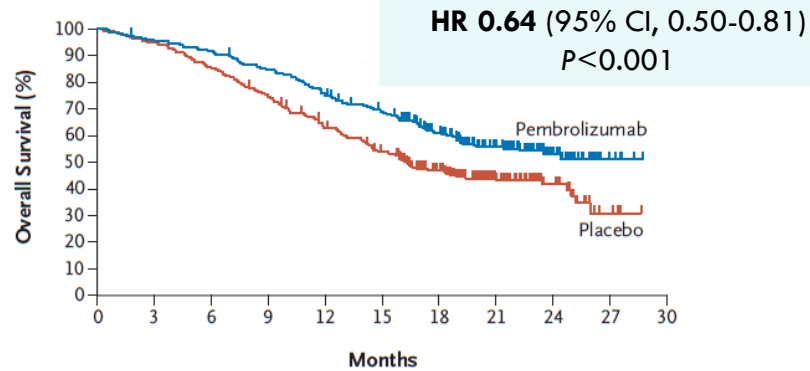
## PD-L1 CPS $\geq 10$ Population



No. at Risk	0	3	6	9	12	15	18	21	24	27
Pembrolizumab	158	138	124	80	62	58	35	21	7	0
Placebo	159	131	95	60	47	35	19	3	0	0

# KEYNOTE 826: OS

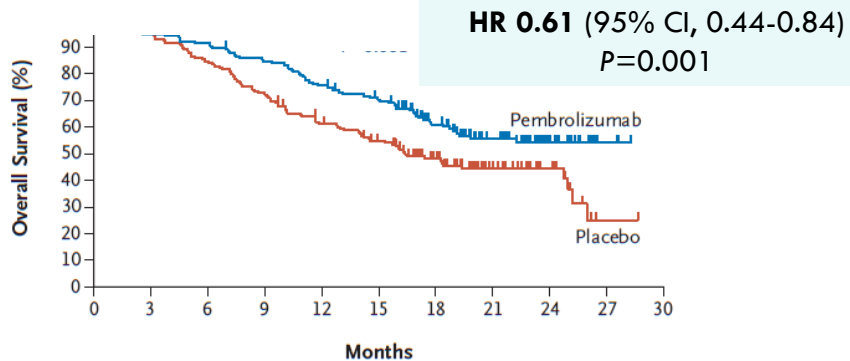
## PD-L1 CPS $\geq 1$ Population



### No. at Risk

Pembrolizumab	273	260	250	229	204	181	132	82	34	6	0
Placebo	275	261	235	206	168	140	100	55	25	4	0

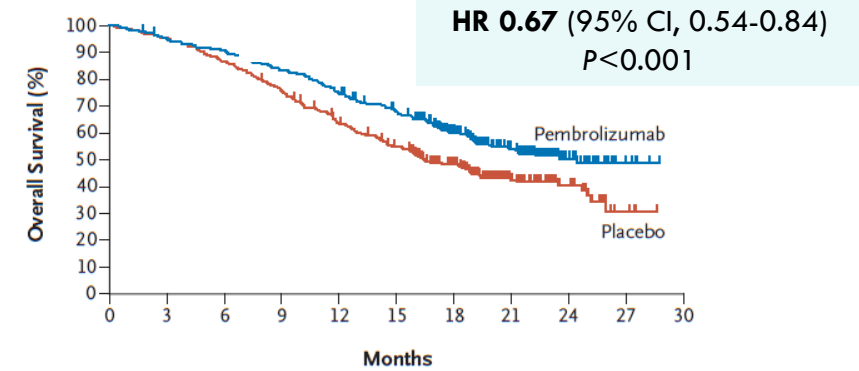
## PD-L1 CPS $\geq 10$ Population



### No. at Risk

Pembrolizumab	158	149	144	132	118	106	76	46	21	3	0
Placebo	159	151	135	116	95	81	56	31	15	1	0

## ITT Population

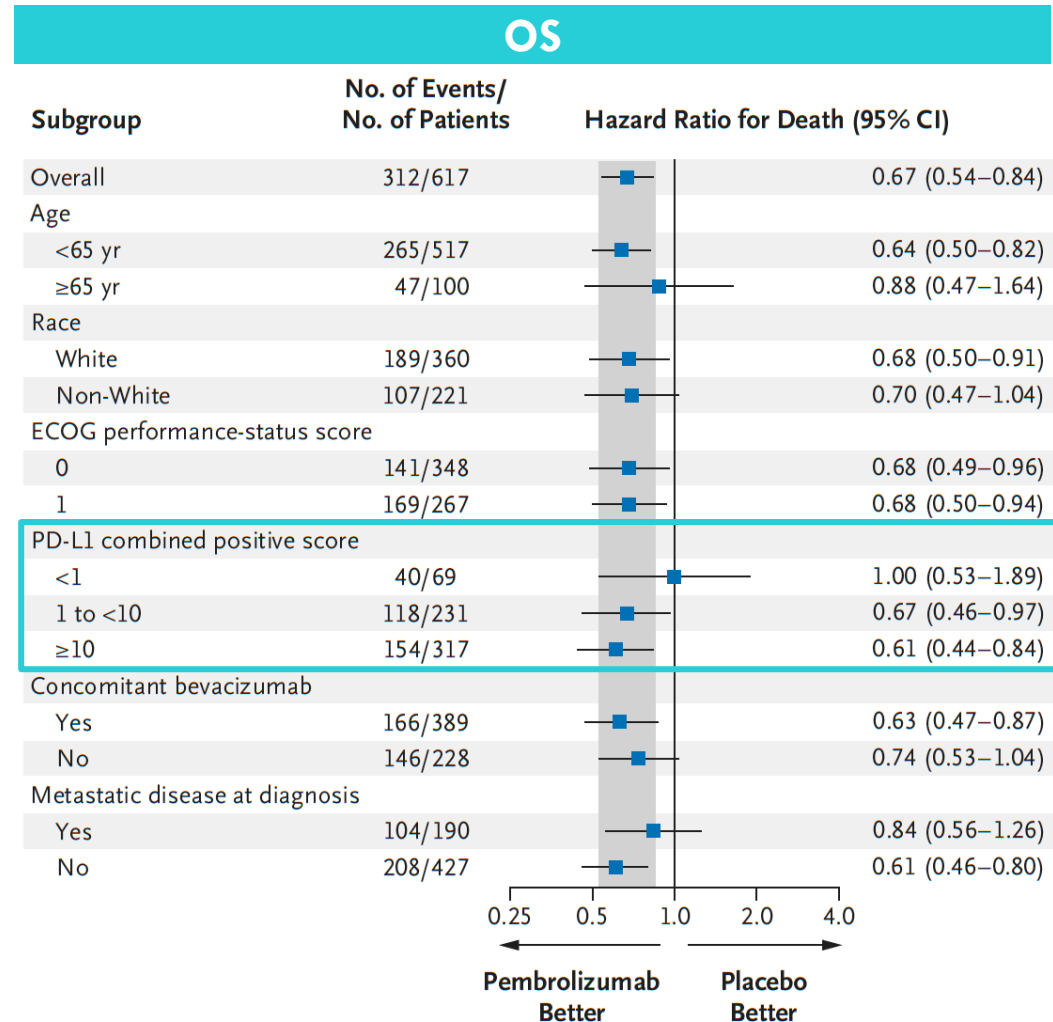
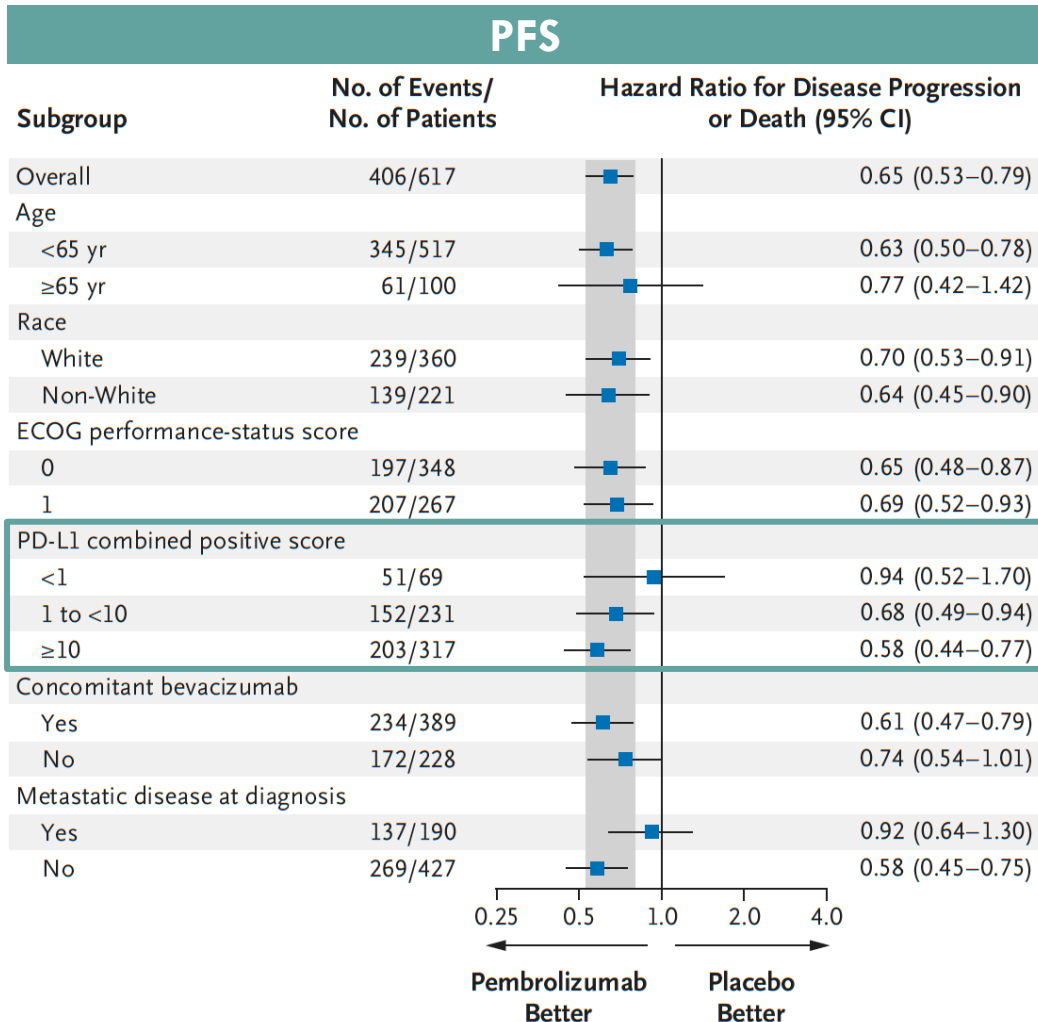


### No. at Risk

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

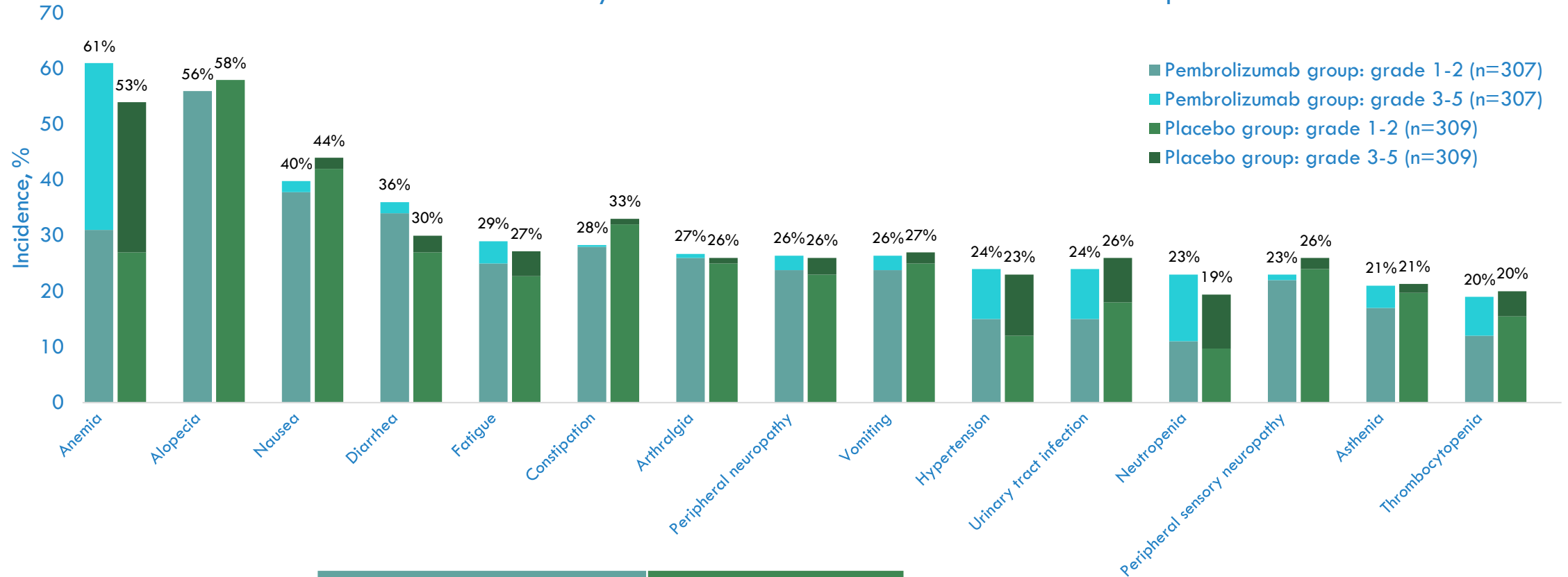
**Pembrolizumab group mOS (ITT):**  
**24.4 months**

# KEYNOTE 826: ITT POPULATION SUBGROUP ANALYSIS



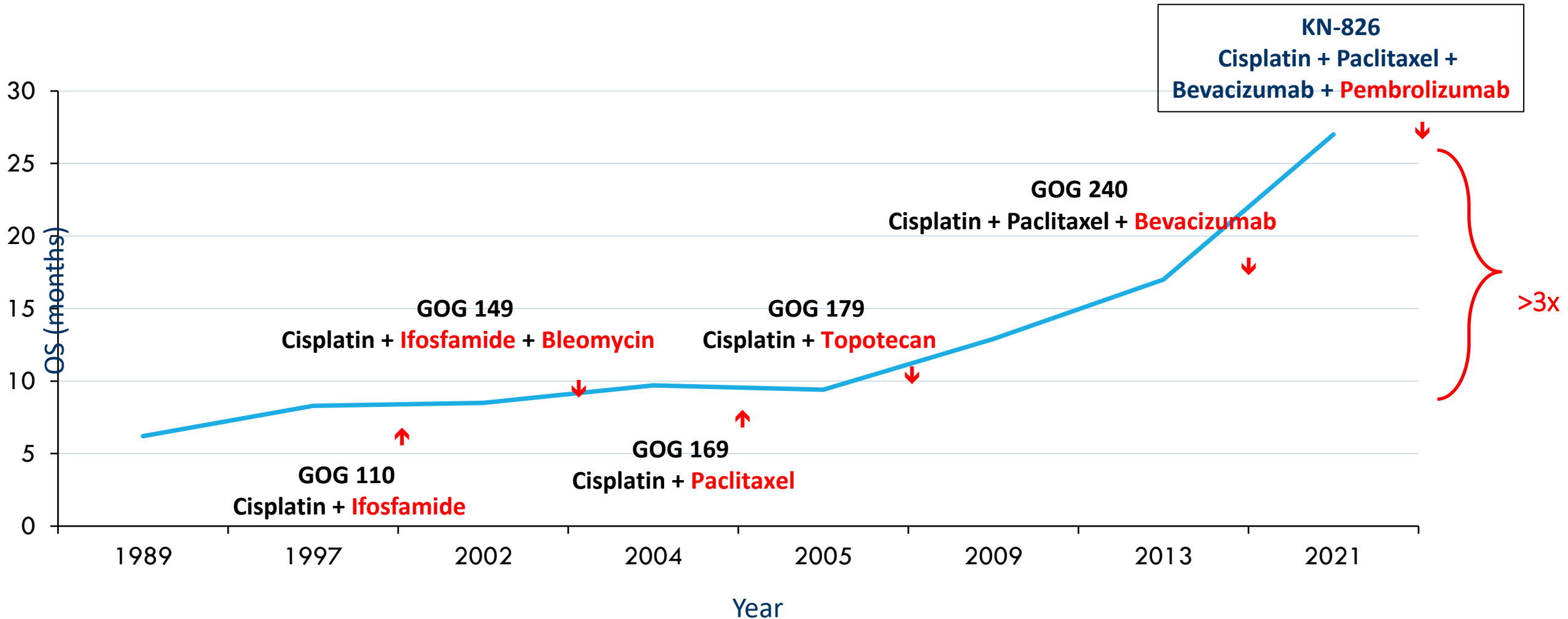
# KEYNOTE 826: ADVERSE EVENTS

Adverse Events of Any Cause With an Incidence  $\geq 20\%$  in Either Group



	Pembrolizumab group (n=307)		Placebo group (n=309)	
	Any grade	Grade 3-5	Any grade	Grade 3-5
Potentially immune-mediated AEs, %	33.9	11.4	15.2	2.9

# IMPROVING OVERALL SURVIVAL IN RECURRENT OR METASTATIC CERVICAL CANCER



# NCCN GUIDELINES<sup>®</sup>: RECURRENT OR METASTATIC CERVICAL CANCER

Setting	Preferred Regimens	Category of Evidence
<b>First Line Combination Therapy</b>	Pembrolizumab + cisplatin/paclitaxel ± bevacizumab (for PD-L1 positive tumors)	Category 1
	Pembrolizumab + carboplatin/paclitaxel ± bevacizumab (for PD-L1 positive tumors)	Category 1
	Cisplatin/paclitaxel/bevacizumab	Category 1
	Carboplatin/paclitaxel/bevacizumab	Category 2A
	Other: chemotherapy <sup>ab</sup>	Category 1/2A
<b>First Line Single-Agent Therapy</b>	Cisplatin	Category 2A
	Other: chemotherapy <sup>ac</sup>	Category 2A
<b>Second Line or Subsequent Therapy</b>	Pembrolizumab (for PD-L1 positive or MSI-H/dMMR tumors)	Category 2A
	Nivolumab (for PD-L1 positive tumors)	Category 2A
	Other: tisotumab vedotin-tftv <sup>a</sup>	Category 2A
	Other: bevacizumab <sup>a</sup>	Category 2B
	Other: chemotherapy <sup>ad</sup>	Category 2B

<sup>a</sup> Other recommended regimen; not a preferred regimen.

<sup>b</sup> Cisplatin/paclitaxel (Category 1); carboplatin/paclitaxel (Category 1 if received prior cisplatin); topotecan/paclitaxel/bevacizumab (Category 1); topotecan/paclitaxel (Category 2A); cisplatin/topotecan (Category 2A).

<sup>c</sup> Carboplatin or paclitaxel.

<sup>d</sup> Albumin-bound paclitaxel, docetaxel, fluorouracil, gemcitabine, ifosfamide, irinotecan, mitomycin, pemetrexed, topotecan, or vinorelbine.