



**2024 Breast Cancer Congress**

with Updates from the 2023 SABCS

**Friday, February 2, 2024**

11:05 AM – 11:30 AM CST

# Updates to the Management of Triple Negative Breast Cancer with SABCS Updates

**Cesar A. Santa-Maria, MD, MSCI**

*The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins*

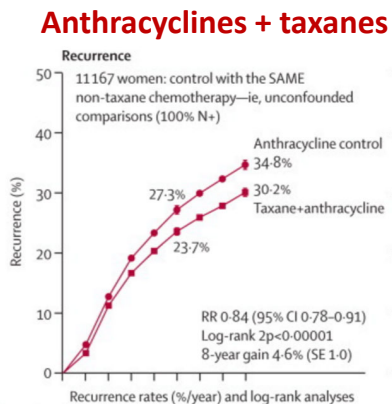
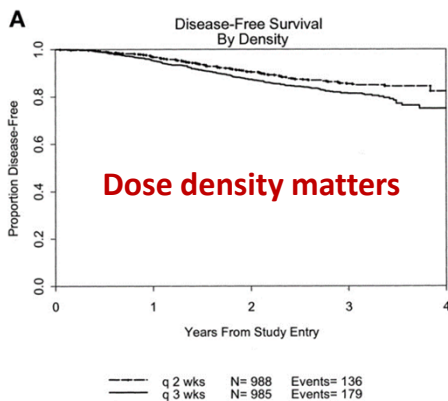
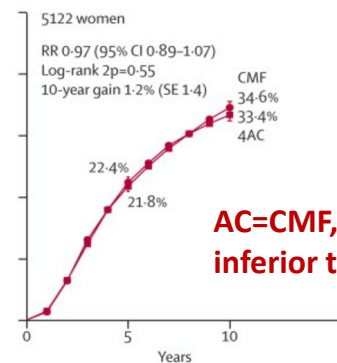
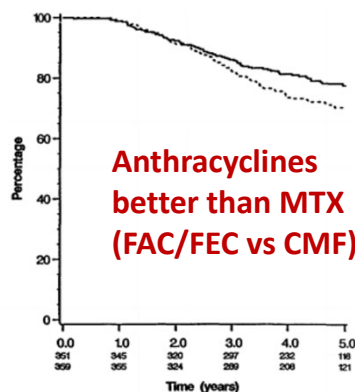
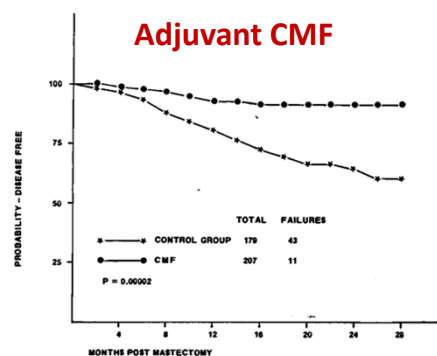
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# Outline

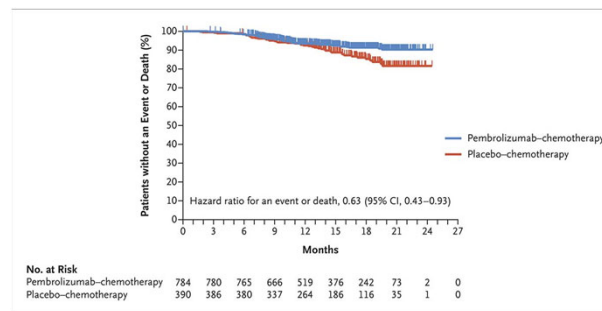
- Review the development of immunotherapy (IO) in early-stage TNBC
- Review and summarize the most impactful IO studies in early-stage TNBC
- Discuss the evolving relationship between pCR and EFS in the context of IO in early-stage TNBC
- Discuss some of the updates from SABCS 2023 related to IO in early-stage TNBC
- Review anticipated studies that will further enhance our understanding of IO in early-stage TNBC
- Review updates in practice algorithm for patients with early-stage TNBC

# Road to KN522

Bonadonna NEJM 1976  
 Levine JCO 1998  
 Martin Ann Oncol 2003  
 EBCTCG Lancet 2012  
 NSABP B-34  
 Citron JCO 2003  
 Schmid NEJM 2020



## Adding carboplatin and pembrolizumab to AC/T



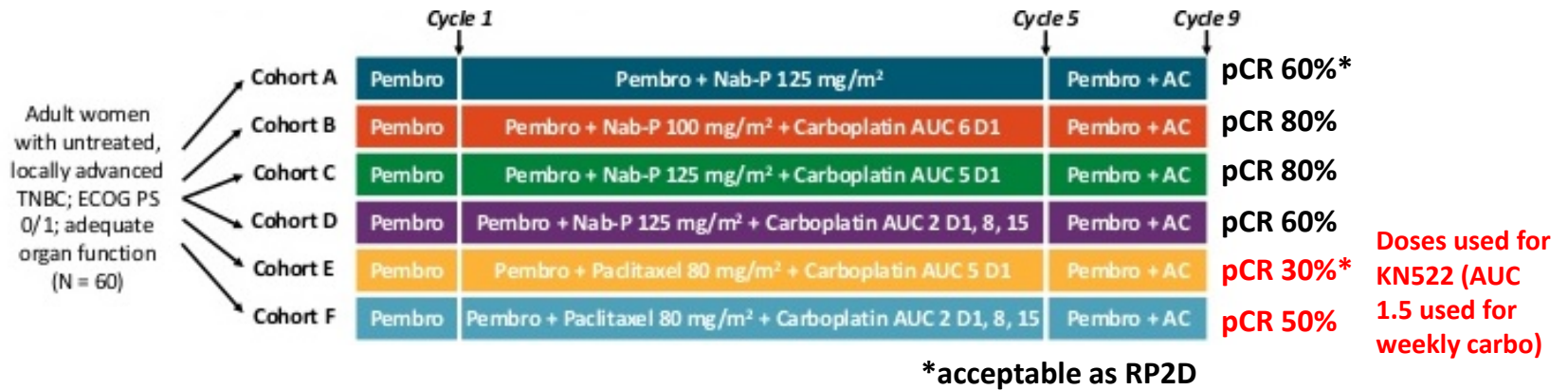
# Adding pembrolizumab to chemo

- iSPY2 study showed higher pCR rates with adding pembro to AC/T
- KEYNOTE-173 designed to determine safety and RP2D of chemo/pembro combos
  - pCR rate same with or without platinum (60%)

**ISPY2 (HER2-)**

Estimated pCR rate

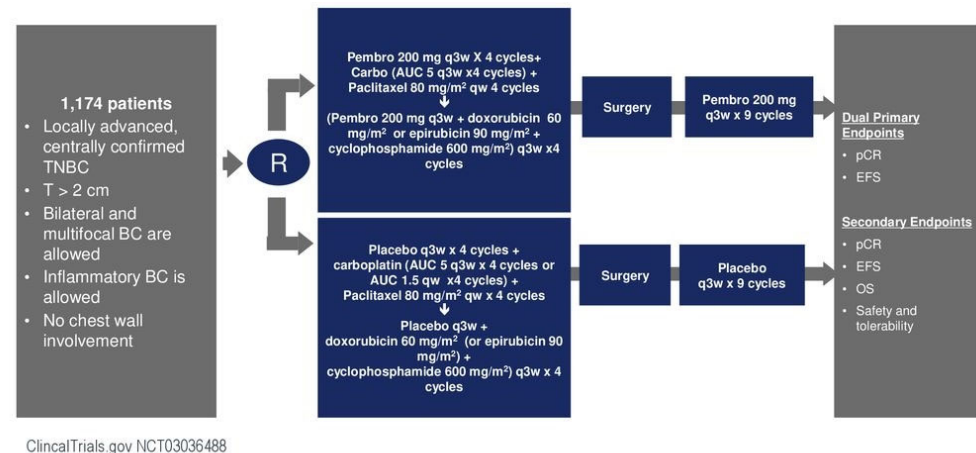
Paclitaxel → AC	13% in ER+ 20% in TNBC
Paclitaxel → AC Pembro	34% in ER+ 60% in TNBC



Nanda et al ASCO 2017  
Schmid et al SABCS 2018, Ann Oncol 2020

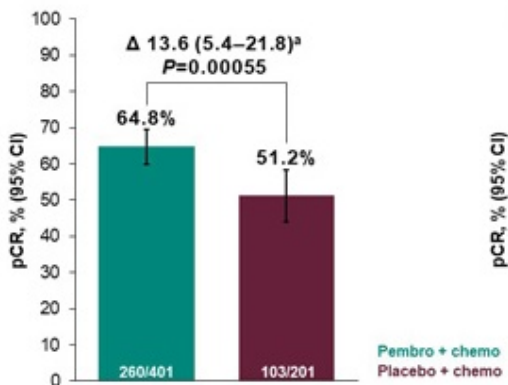
# Revisiting KEYNOTE-522: Challenges and controversies in design

- AC given q3 weeks (not dose dense) → dd known EFS/OS benefit
- Carboplatin used → very little EFS data, no OS data
- In pembrolizumab arm, pembro given irrespective of response
- Adjuvant capecitabine not allowed → known EFS/OS benefit



# pCR results

Primary Endpoint: ypT0/Tis ypN0

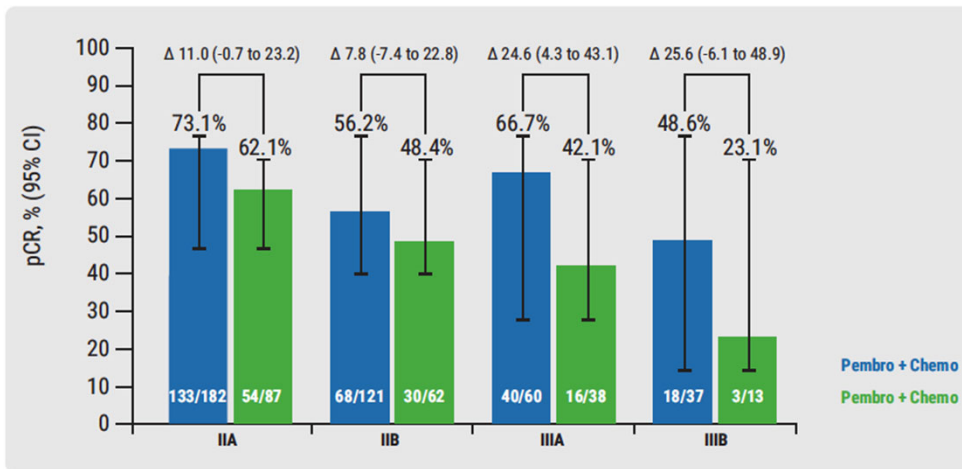
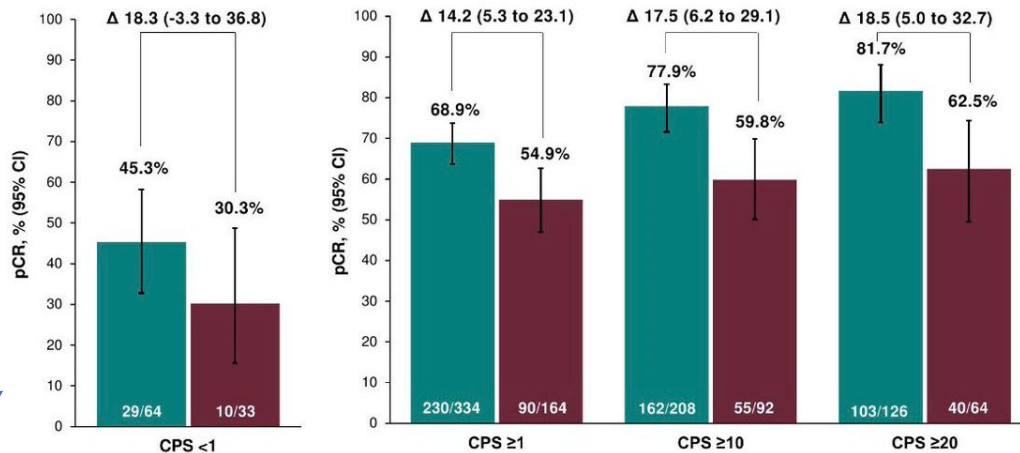


**63%** **55.6%**

Updated pCR analysis

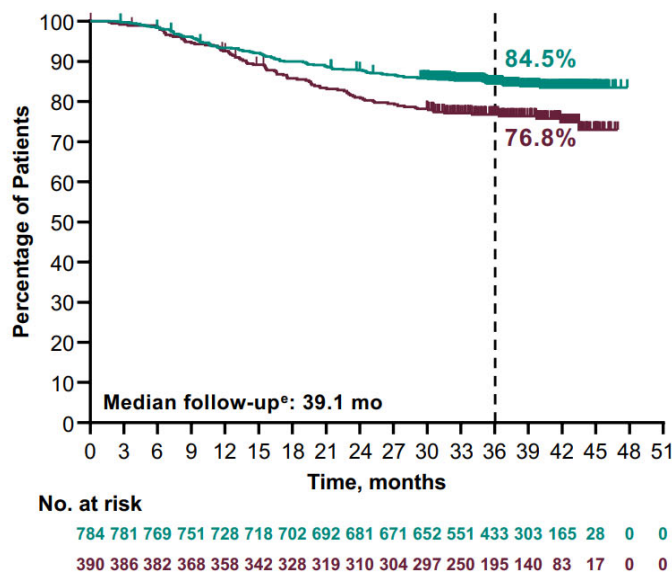
PDL1 status

Stage 2 vs 3

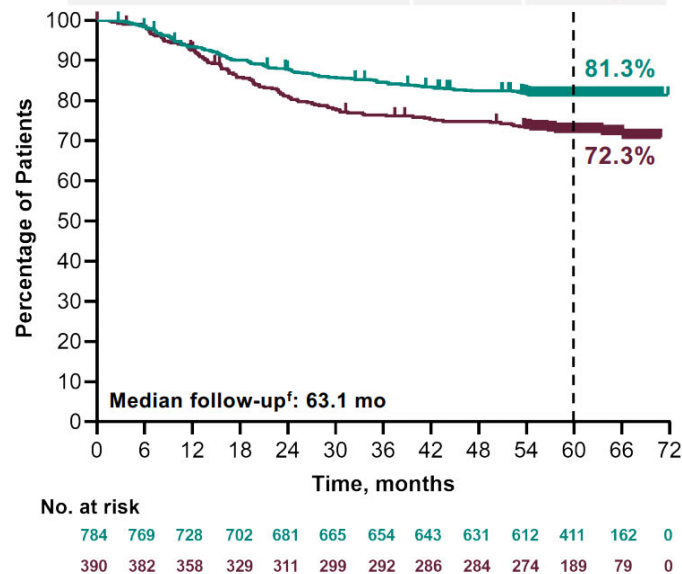


# EFS at IA4 and IA6

IA4 <sup>a</sup>	Events	HR (95% CI)	P value
Pembro + Chemo/Pembro	15.7%	0.63 <sup>c</sup> (0.48–0.82)	0.00031 <sup>d</sup>
Placebo + Chemo/Placebo	23.8%		

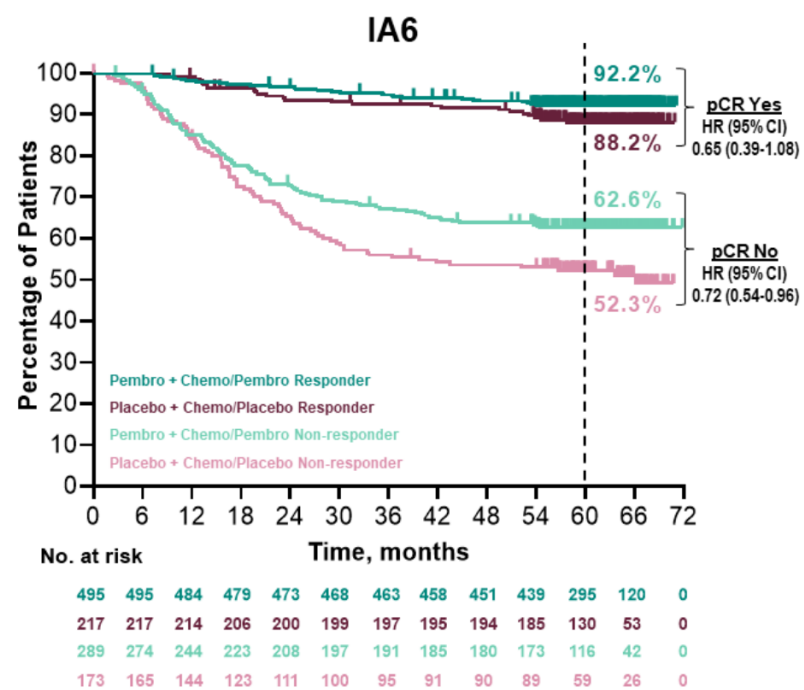
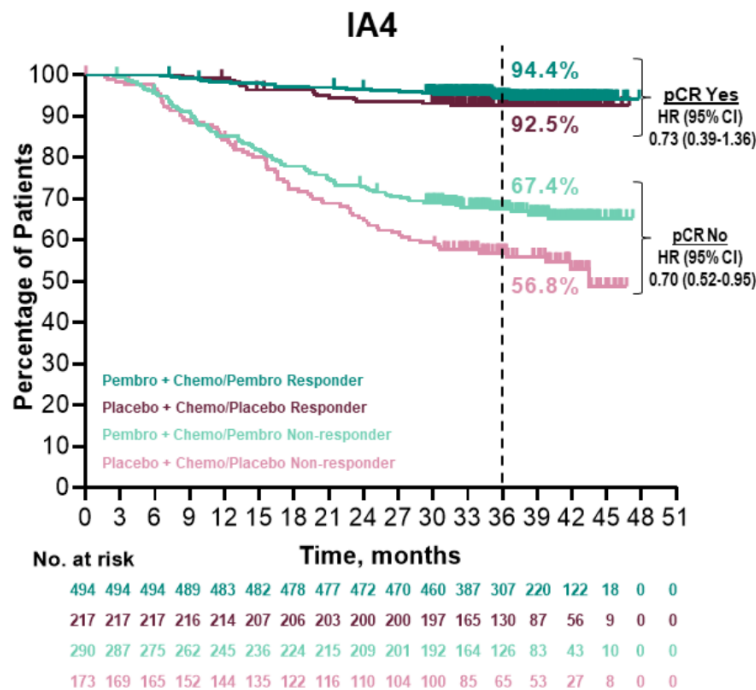


IA6 <sup>b</sup>	Events	HR (95% CI)
Pembro + Chemo/Pembro	18.5%	0.63 <sup>c</sup> (0.49–0.81)
Placebo + Chemo/Placebo	27.7%	



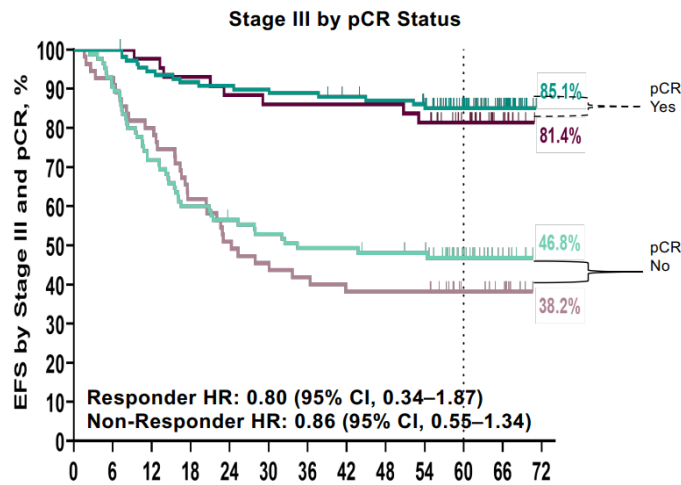
Schmid et al SABCS 2023

# Pembrolizumab adds EFS benefit irrespective of pCR: road to pCR matters?



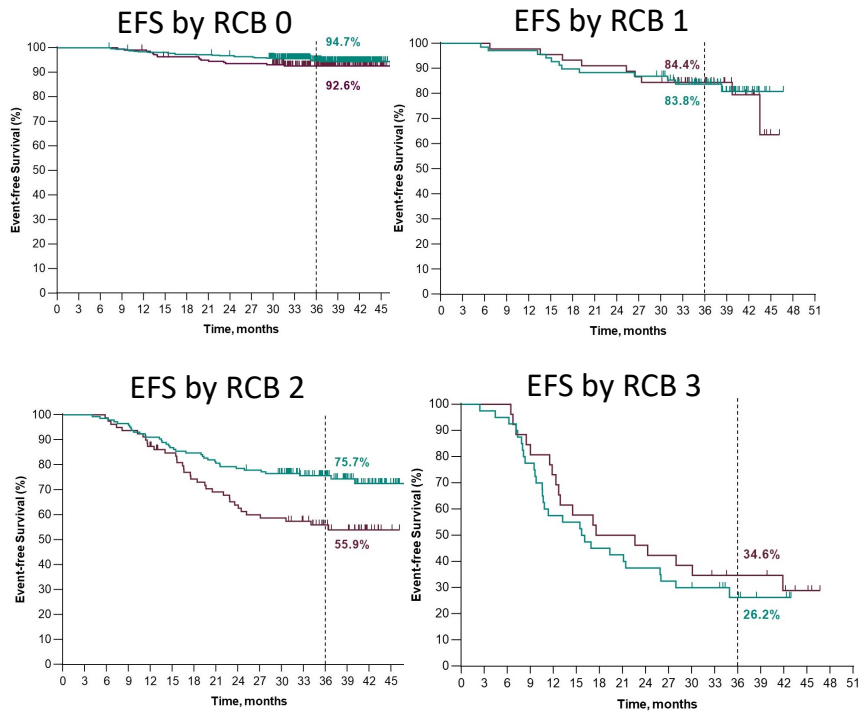
Schmid et al ESMO 2023

# Patients with residual disease have high rates of recurrence, mostly RCB-2/3, pembro benefit most evident in RCB-2



No. at risk	0	6	12	18	24	30	36	42	48	54	60	66	72
Pembro + Chemo/Pembro Responder	109	109	102	99	98	97	96	93	91	88	59	30	0
Pbo + Chemo/Pbo Responder	43	43	42	40	38	37	37	37	35	24	11	0	0
Pembro + Chemo/Pembro Non-Responder	85	77	61	51	47	44	41	41	39	38	21	7	0
Pbo + Chemo/Pbo Non-Responder	55	51	44	34	28	25	23	21	21	21	12	8	0

Schmid et al SABCS 2023

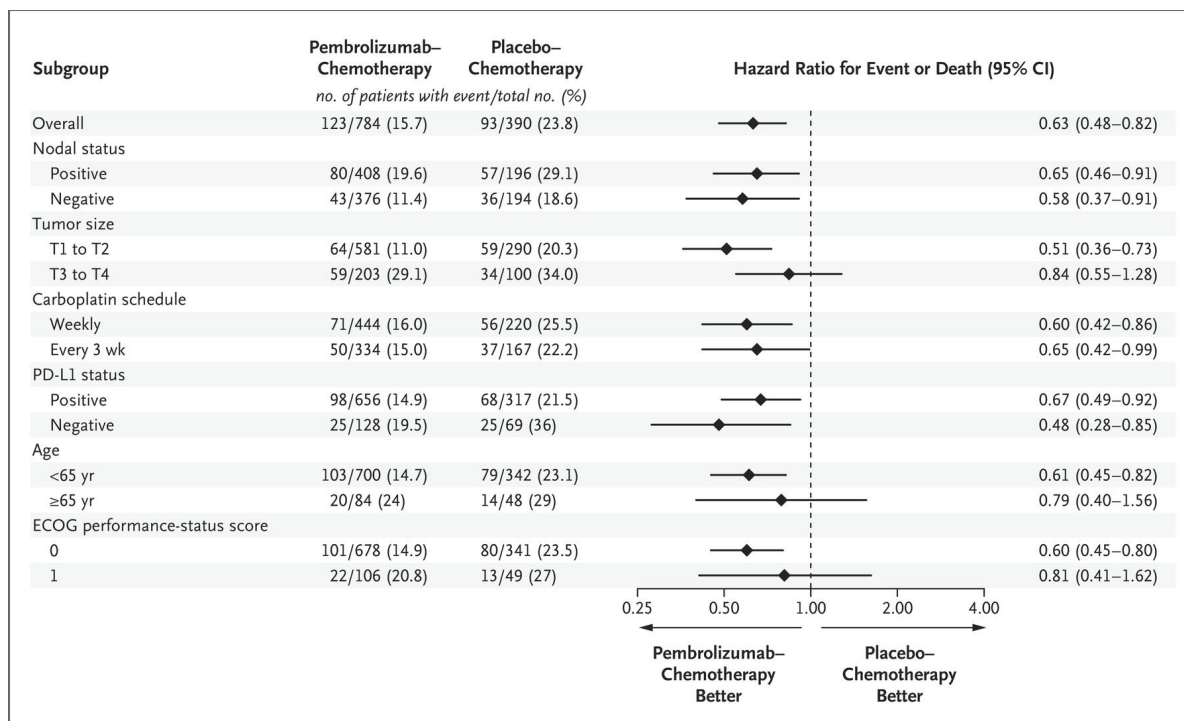
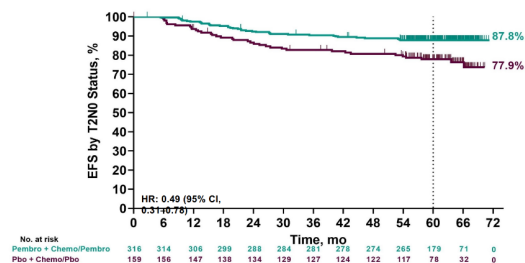


Pusztai et al ASCO 2022

# Are there any patients who can avoid pembrolizumab?

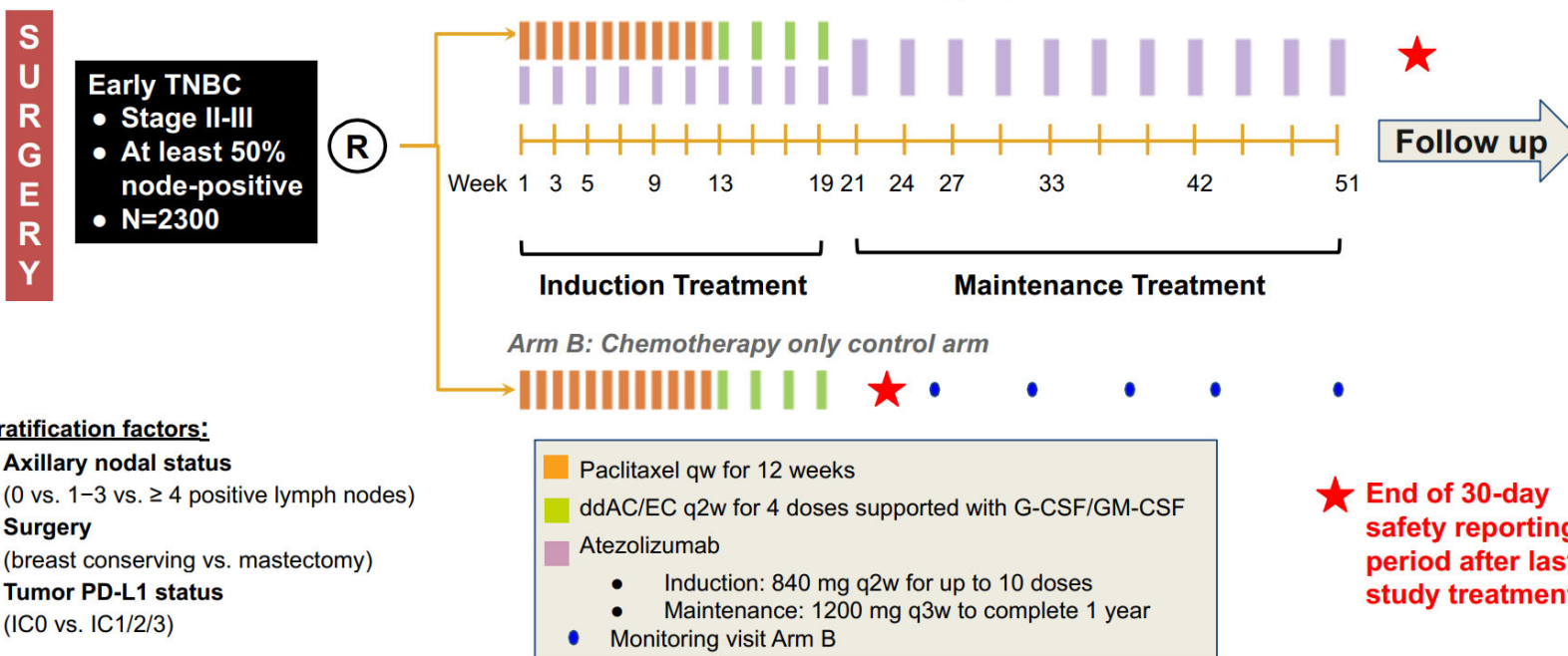
- Benefit irrespective of nodal status (including T2N0) and PDL1 status
- Benefit less clear in  $\geq 65$ yr and ECOG 1

EFS at IA6 by T2N0 Status



Schmid et al NEJM 2022  
Schmid et al SABCS 2023

# ALEXANDRA/IMpassion030: initial experience with adjuvant-only IO



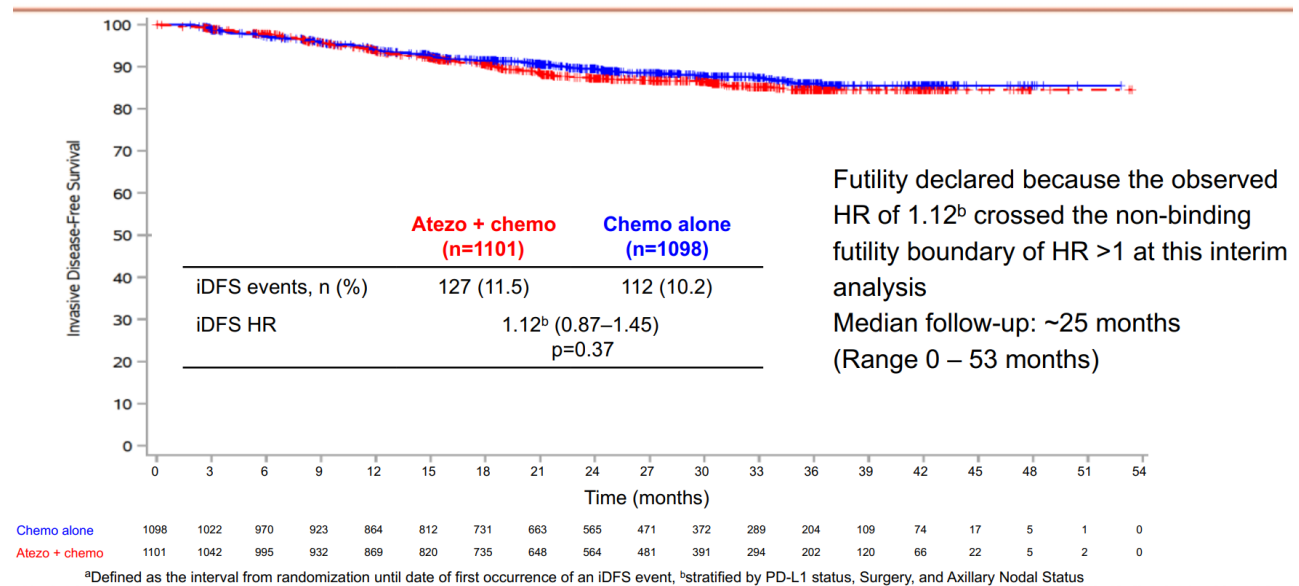
Ignatiadis et al SABCS 2023

# IMpassion030 Results

- No difference by PDL1 status or other subgroup
- No OS benefit
- Grade 3+ TRAEs 53.7% (77% in KN522)

Primary efficacy endpoint: iDFS<sup>a</sup> (ITT population)

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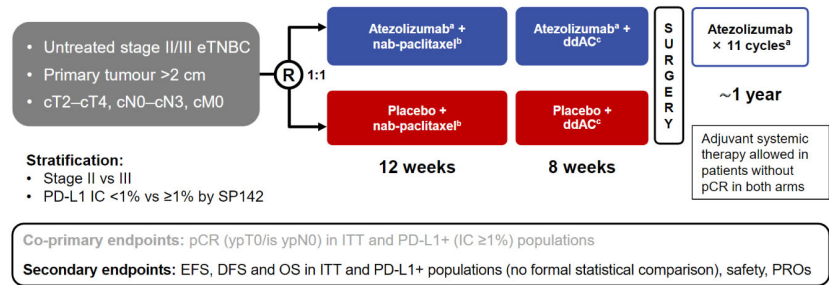


Ignatiadis et al SABCS 2023

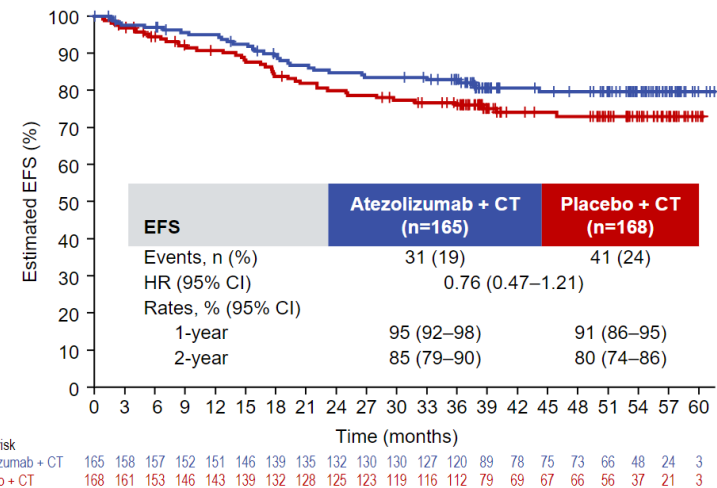
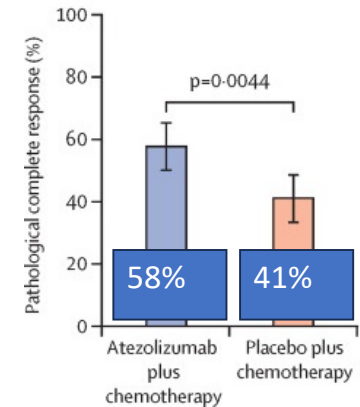
# Contrast with IMpassion031

- Improvement in pCR
- G3+ TRAE 59% in atezo arm (no carbo)  
→ 77% in KN522
- No statistically significant EFS benefit

Randomised international phase 3 trial



Mittendorf et al Lancet 2020  
Barrios et al ESMO 2023

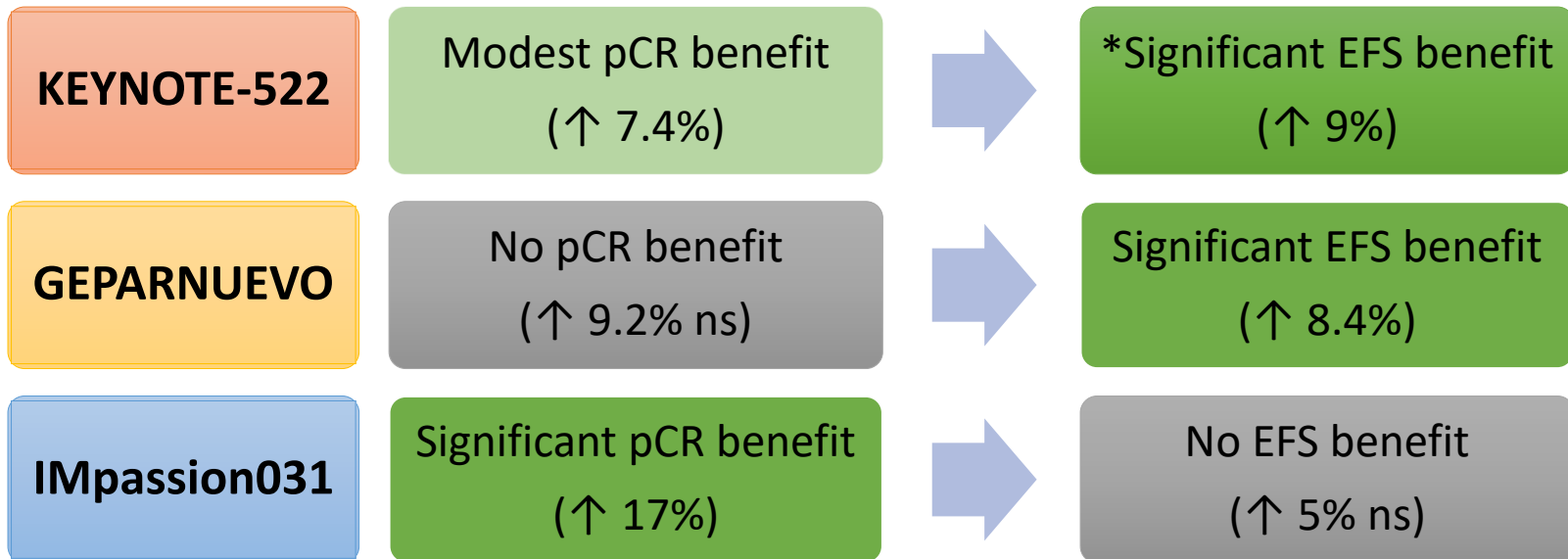


## Summary experience of IO in early-TNBC

Study	Regimens	Phase (n)	pCR control	pCR exp	EFS control	EFS exp
KEYNOTE-522	Tcarbo/AC +/- pembro	3 (n=602)	55.6%	63%	72.3% (5y)	81.3% (5y)
IMpassion031	ddAC/nab-paclitaxel +/- atezo	3 (n=455)	41%	58%	*80% (2y)	*85% (2y)
GeparNuevo	nab-paclitaxel/EC +/- durva	2 (n=174)	*44.2%	*53.4%	77.2% (3yr)	85.6% (3yr)
IMpassion030	Adj. ddAC/T +/- atezo	3 (n=2300)	n/a	n/a	89.8% (2y)	88.5% (2y)
NeoPACT	Docetaxel/carbo/pembro	2 (n=115)	n/a	58%	86% (3yr)	
NeoTRIPaPD1	Abraxane/carbo +/- atezo	3 (n=280)	*40.8%	*43.5%	Not reported	
ETCTN013	Tcarbo +/- atezo	2 (n=67)	18.8%	55.6%	Not reported	
Neo-N	N → Tcarbo/nivo vs Tcarbo/nivo → N	2 (n=108)	*51%	*55%	Not reported	
iSPY2	T-/ddAC +/- pembro	2 (n=108)	20%	60%	Not reported	

\* Not statistically significant

## pCR/EFS relationship in chemo IO



\*powered for EFS

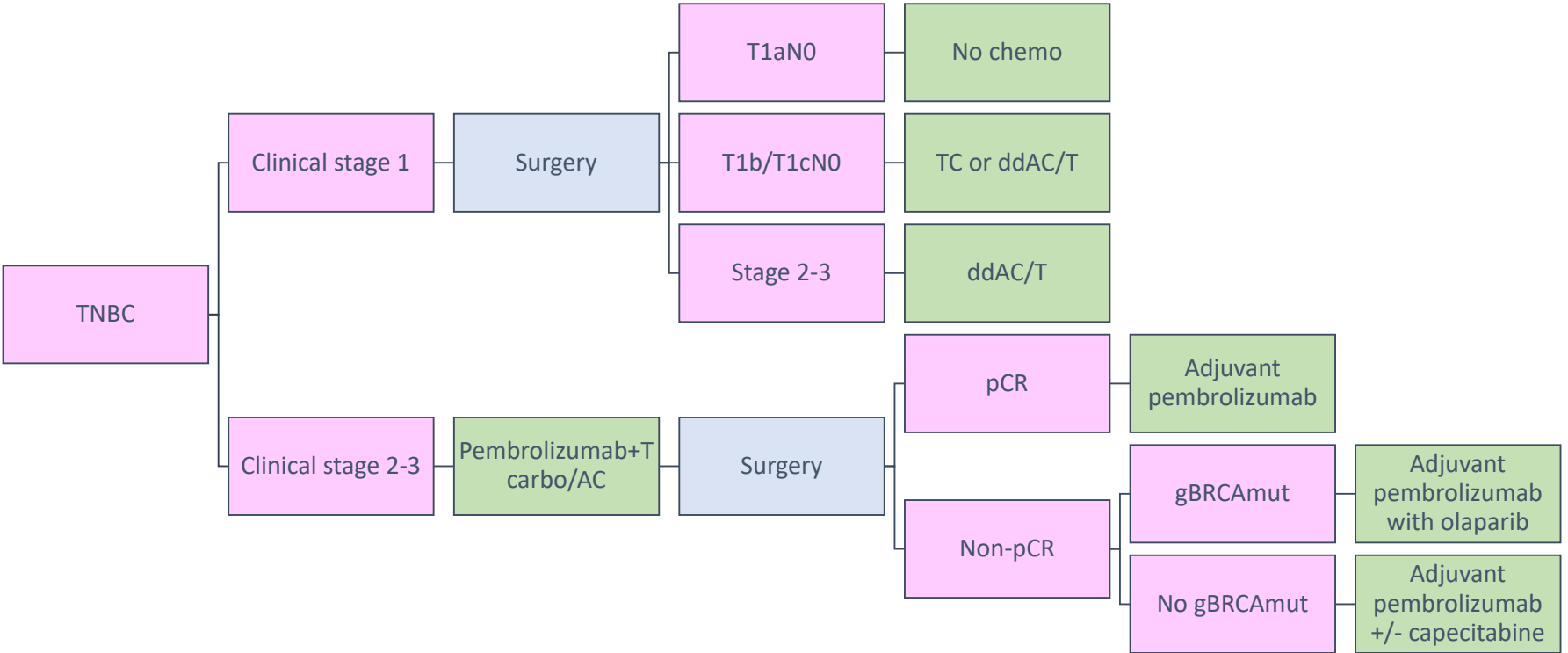
# What we learned/re-enforced at SABCS 2023

- Probably important to give chemo/IO neoadjuvantly
  - IMpassion030 does not support the role of adjuvant atezolizumab → we don't know for sure if the same would apply to pembrolizumab (diff drug)
  - SWOG-1801 in melanoma supports benefit to neoadjuvant vs adjuvant approach
  - Adjuvant pembro will be further studied in S1418 (IO-naïve), OPTIMICE-pCR (after chemo-IO pCR)
  - Clinical implication: stage 1 pts who get upstaged at surgery may omit pembrolizumab
- Pembro adds EFS benefit in pts achieving pCR (diff at 3yrs was 1.9%, at 5 years now 4%) → road to pCR may matter?
  - Adds to the importance that IO needs to be given neoadjuvantly
  - Does not mean adjuvant pembro necessarily provides benefit (IMP030 suggests probably does not)
  - Until more data emerges, need to continue adjuvant pembro irrespective of response as long as no clinically significant irAEs

# What we learned/re-enforced at SABCS 2023

- RD is a very high-risk situation (especially RCB 2/3)
  - Trop2 RD studies underway (ASCENT-05, TROPION-Br03, MK2870-012)
- Taxane/platinum IO combos can have high pCR rates (Neo-N, ETCTN10013)
  - Unknown if IO adds benefit (NeoTRIP) → SWOG-2212 (SCARLET) will formally evaluate (Doce/carbo/pembro x6 vs KN522)
- While patients who achieve pCR have a better EFS, the relationship between pCR and EFS in a trial is dynamic → important to have studies powered for EFS

# Guidance in integrating chemo-immunotherapy in early-stage TNBC



# Thank you!



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## Who We Are

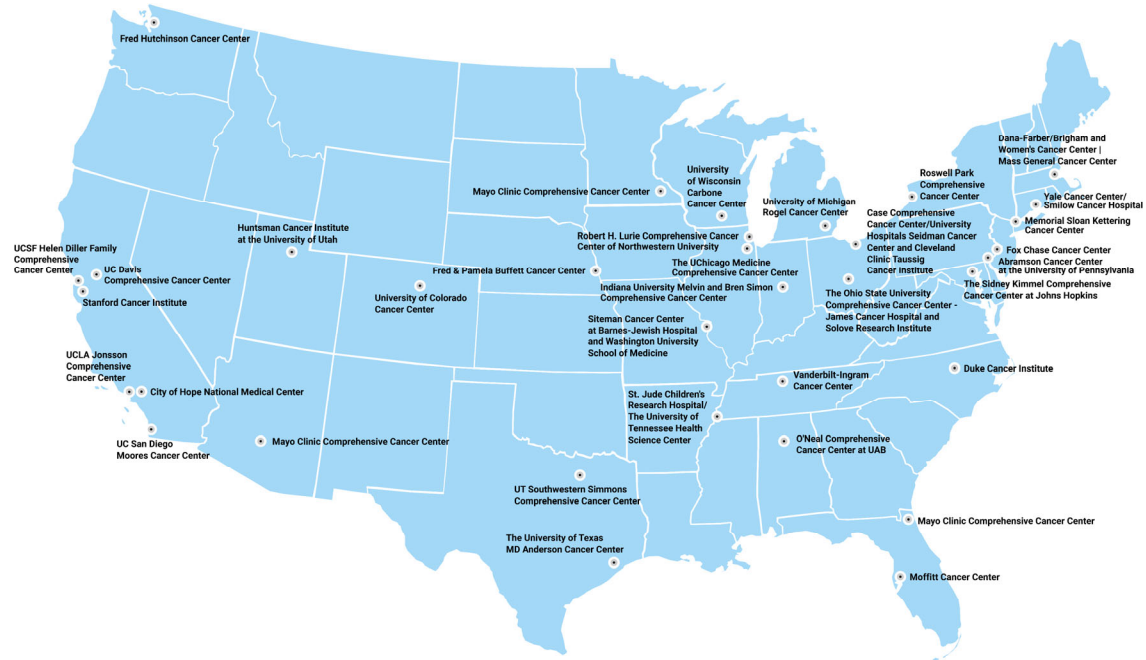
An alliance of leading cancer centers devoted to patient care, research, and education

## Our Mission

To improve and facilitate quality, effective, equitable, and accessible cancer care so all patients can live better lives

## Our Vision

To define and advance high-quality, high-value, patient-centered cancer care globally



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