Gastric and Gastroesophageal Junction Adenocarcinoma

US Food & Drug Administration
Oncologic Drugs Advisory Committee
September 26, 2024

Bristol Myers Squibb®

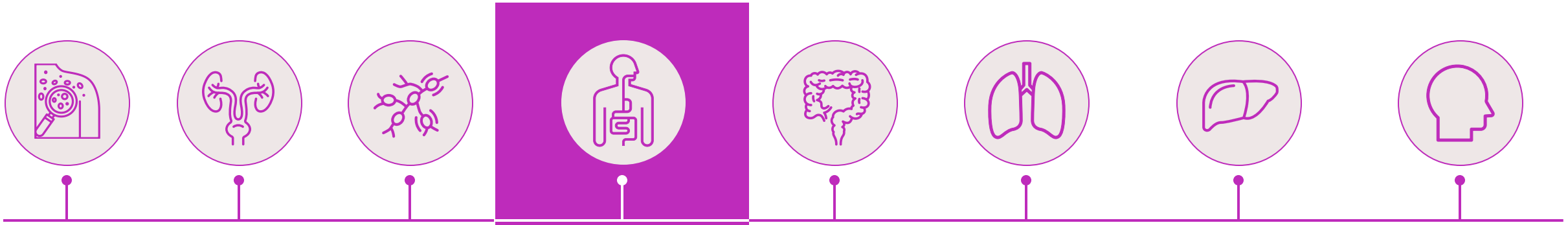
Ian Waxman, MD

Vice President,
Late Development Oncology

BMS

Introduction

Opdivo Approved for 11 Cancer Types in United States



- Melanoma
- Renal Cell Carcinoma
- Urothelial Carcinoma
- Classic Hodgkin Lymphoma
- **Gastric, GEJ, and Esophageal Adenocarcinoma**
- **Esophageal Squamous Cell Carcinoma**
- Colorectal Cancer
- Non-small Cell Lung Cancer
- Mesothelioma
- Hepatocellular Carcinoma
- Squamous Cell Carcinoma of the Head & Neck

First approved in 2014

Opdivo USPI.

Opdivo® (nivolumab) Fully Approved for Gastric Cancer on April 16, 2021

Treatment of adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma in combination with fluoropyrimidine and platinum-containing chemotherapy.

No restriction based on PD-L1 status

Opdivo USPI.

Current US Prescribing Information Includes Data by PD-L1 Expression Level in Section 14.13

Table 76: Efficacy Results - CHECKMATE-649

	OPDIVO and mFOLFOX6 or CapeOX (n=789)	mFOLFOX6 or CapeOX (n=792)	OPDIVO and mFOLFOX6 or CapeOX (n=641)	mFOLFOX6 or CapeOX (n=655)	OPDIVO and mFOLFOX6 or CapeOX (n=473)	mFOLFOX6 or CapeOX (n=482)
	All Patients		PD-L1 CPS ≥1		PD-L1 CPS ≥5	
Overall Survival						
Deaths (%)	544 (69)	591 (75)	434 (68)	492 (75)	309 (65)	362 (75)
Median (months) (95% CI)	13.8 (12.6, 14.6)	11.6 (10.9, 12.5)	14.0 (12.6, 15.0)	11.3 (10.6, 12.3)	14.4 (13.1, 16.2)	11.1 (10.0, 12.1)
Hazard ratio (95% CI)[a]	0.80 (0.71, 0.90)		0.77 (0.68, 0.88)		0.71 (0.61, 0.83)	
p-value[b]	0.0002		<0.0001		<0.0001	

In an exploratory analysis in patients with PD-L1 CPS <1 (n = 265), the median OS was 13.1 months (95% CI: 9.8, 16.7) for the OPDIVO and chemotherapy arm and 12.5 months (95% CI: 10.1, 13.8) for the chemotherapy arm, with a stratified HR of 0.85 (95% CI: 0.63, 1.15).

In an exploratory analysis in patients with PD-L1 CPS <5 (n = 606), the median OS was 12.4 months (95% CI: 10.6, 14.3) for the OPDIVO and chemotherapy arm and 12.3 months (95% CI: 11.0, 13.2) for the chemotherapy arm, with a stratified HR of 0.94 (95% CI: 0.78, 1.14).

CPS subgroup data, based on Agilent/Dako PD-L1 IHC 28-8 pharmDx test, provided in the clinical trial section.

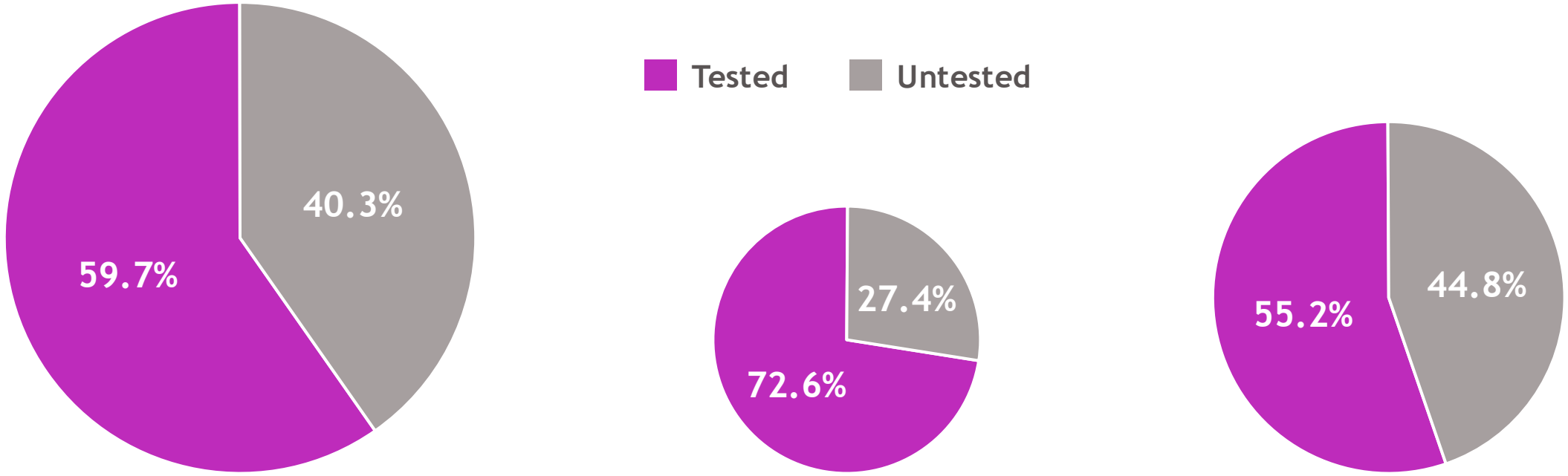
NCCN Guidelines Complement Information Included in Opdivo Label

		Recommended Population to Treat	
Tumor Type	**Recommended First-line Regimen**	**USPI[1]**	**NCCN[2]**
Gastric, GEJ, and Esophageal Adenocarcinoma	**Nivolumab** + fluoropyrimidine, and platinum-containing chemotherapy	No restriction	CPS ≥5[Cat 1] CPS <5[Cat 2B]
	Pembrolizumab + fluoropyrimidine, and platinum-containing chemotherapy	No restriction	CPS ≥10[Cat 1] CPS 1 - <10[Cat 2B]
	Tislelizumab + chemotherapy	TBD	TBD

[1]Opdivo USPI.
[2]NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Gastric Cancer. Version 4.2024 — August 12, 2024.

PD-L1 CPS Testing Patterns — US Flatiron Analysis

Gastric, GEJ, and Esophageal Adenocarcinoma



All treated patients
N=698

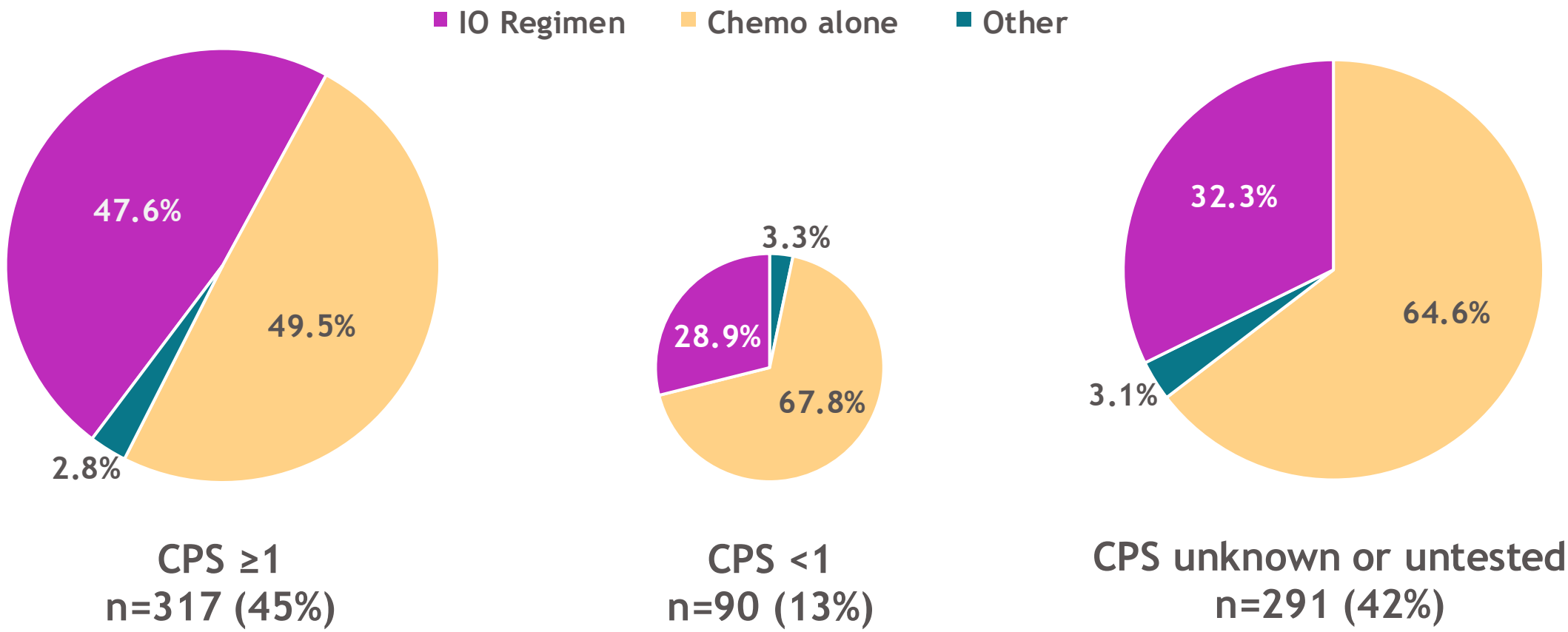
Nivo + Chemo[a]
n=208 (30%)

Chemo only regimens[b]
n=406 (58%)

Testing patterns among patients diagnosed with advanced/metastatic GC/GEJC/EAC from January 2023 to March 2024 using the Flatiron database. PubD 00065829. Princeton, NJ: Bristol-Myers Squibb Company; 2024.
[a]Chemo regimens in this group included FOLFOX/CAPEOX/FP/XP; [b]Chemo only regimens included FOLFOX/CAPEOX/FP/XP and other chemo groups.

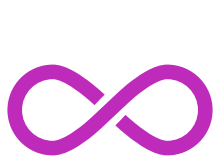
First-Line Treatment Patterns — US Flatiron Analysis (N=698)

Gastric, GEJ, and Esophageal Adenocarcinoma



1L treatment patterns among advanced GC/GEJC/EAC patients diagnosed from January 2023 to March 2024 by PD-L1 CPS cutoff 1 using the Flatiron database.
PubD 00065829. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

What We're Here to Discuss

1 

Potential changes to the product label based on PD-L1 expression

2 

We desire to do what's right for patients and ensure that information provided to physicians and patients is clear

3 

Important challenges in seeking harmonization

Potential Labeling Options

Modify the indication to PD-L1 positive (PD-L1 CPS ≥1)

Benefit:

- Limits treatment to patients most likely to benefit based on clinical trial data

Considerations:

- PD-L1 is a dynamic biomarker and expression is heterogeneous; therefore, some patients may be incorrectly identified as PD-L1 negative
- Some patients may have inadequate tumor tissue for biomarker testing
- Choice of a cut-off higher than CPS 1 is challenging given variability in CPS scoring in clinical practice

Keep current indication

Benefit:

- Provides physicians/patients an opportunity to make informed decisions on an individual patient basis based on USPI and NCCN guidelines

Considerations:

- Raises concerns about exposing patients who are less likely to benefit to additional toxicity

Agenda

Benefit Risk Profile in PD-L1 Subgroups

Dana Walker, MD, MSCE
Vice President,
Global Program Lead,
Opdivo/Yervoy, GI and GU
BMS

PD-L1 Testing in Clinical Practice

Robert A. Anders, MD, PhD
Division of GI and
Liver Pathology
The Johns Hopkins University

Conclusion

Ian Waxman, MD
Vice President,
Late Development Oncology
BMS

Dana Walker, MD, MSCE

Vice President, Global Program Lead, Opdivo/Yervoy, GI and GU

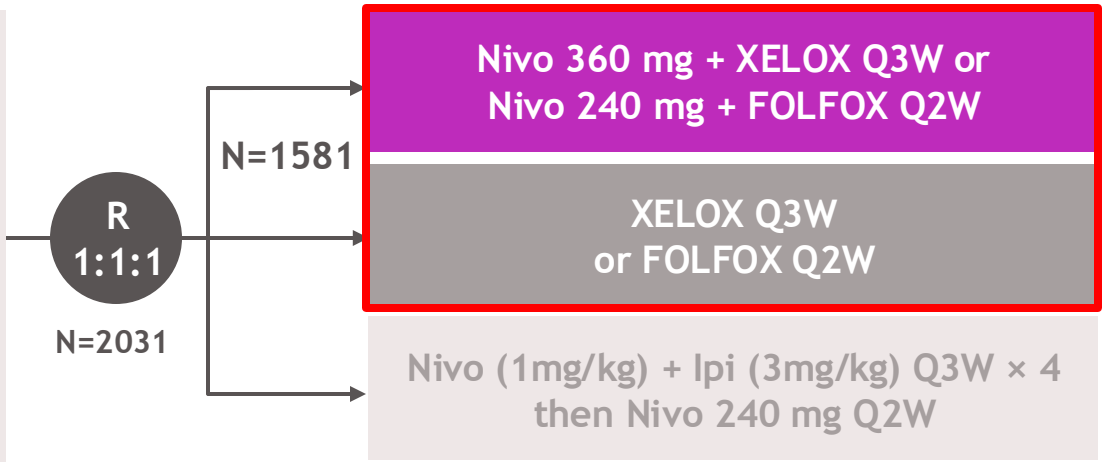
BMS

Benefit Risk Profile in PD-L1 Subgroups

CheckMate 649 Study Design

Key eligibility criteria

- Previously untreated, unresectable, advanced or metastatic gastric/GEJ/ esophageal adenocarcinoma
- No known HER2-positive status
- ECOG PS 0–1



Primary endpoints:
- OS and PFS (CPS ≥5)

Secondary endpoints:
- OS (CPS ≥10, 1, all randomized)[a]
- PFS (CPS ≥10, 1, all randomized)
- ORR

Exploratory endpoints:
- Safety
- QoL

Stratification factors
- Tumor cell PD-L1 expression (≥1% vs <1%)
- Region (Asia vs United States/Canada vs ROW)
- ECOG PS (0 vs 1)
- Chemo (XELOX vs FOLFOX)

28-8 Agilent/Dako IHC Assay
- PD-L1 TPS used for stratification
- PD-L1 CPS used for analysis

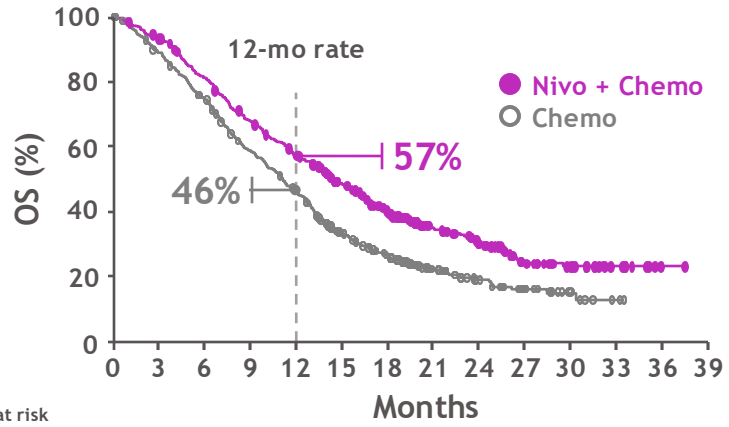
[a]OS in CPS ≥1 and all randomized populations were formally tested. Janjigian YY, et al. *Lancet*. 2021;398:27-40.

Statistically Significant and Clinically Meaningful OS Benefit in Primary and Secondary Analysis Populations

CheckMate 649

Primary Endpoint PD-L1 CPS ≥5[a]

	Nivo + Chemo (n=473)	Chemo (n=482)
Median OS, mo	14.4	11.1
(95% CI)	(13.1-16.2)	(10.0-12.1)
HR (98.4% CI)	0.71 (0.59-0.86)	
P value	<0.0001	

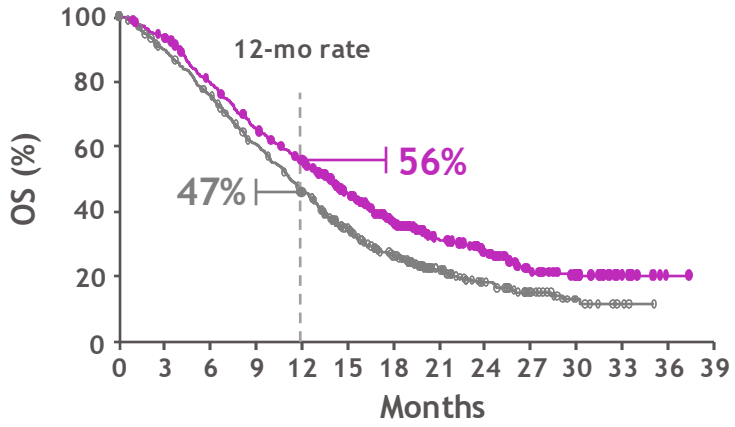


No. at risk

Nivo + Chemo	473	438	377	313	261	198	149	96	65	33	22	9	1	0
Chemo	482	421	350	271	211	138	98	56	34	19	8	2	0	0

PD-L1 CPS ≥1[a]

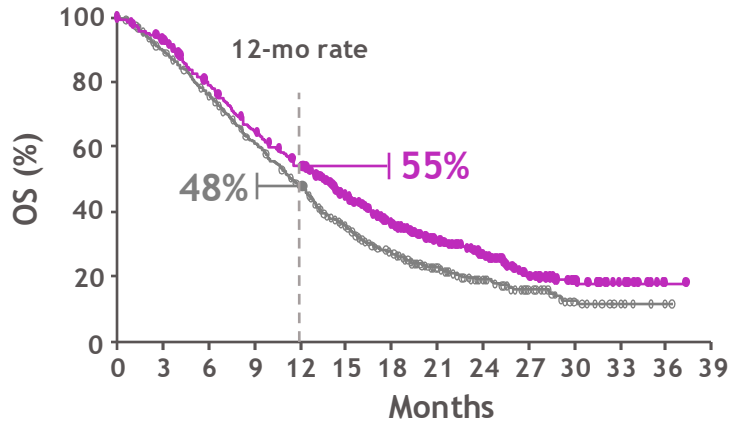
	Nivo + Chemo (n=641)	Chemo (n=655)
Median OS, mo	14.0	11.3
(95% CI)	(12.6-15.0)	(10.6-12.3)
HR (99.3% CI)	0.77 (0.64-0.92)	
P value	<0.0001	



Nivo + Chemo	641	595	502	412	344	254	183	118	80	40	28	11	1	0
Chemo	655	575	483	383	292	194	131	77	45	25	10	3	0	0

All randomized[a]

	Nivo + Chemo (n=789)	Chemo (n=792)
Median OS, mo	13.8	11.6
(95% CI)	(12.6-14.6)	(10.9-12.5)
HR (99.3% CI)	0.80 (0.68-0.94)	
P value	0.0002	



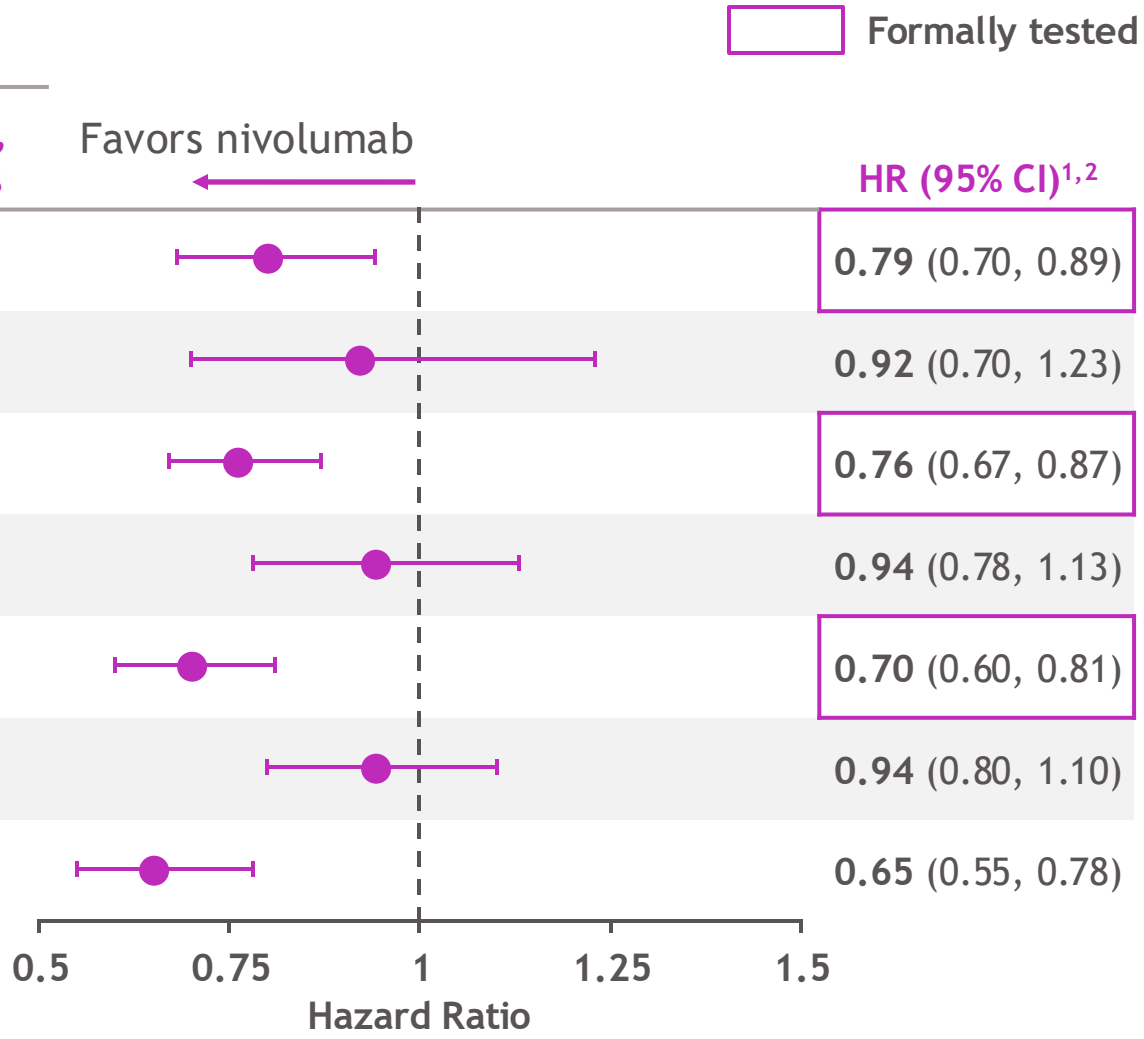
Nivo + Chemo	789	731	621	506	420	308	226	147	100	49	34	14	2	0
Chemo	792	697	586	469	359	239	160	94	59	35	15	7	2	0

[a]Minimum follow-up 12.1 months. Stratified hazard ratio. Janjigian YY, et al. *Lancet*. 2021;398:27-40.

Overall Survival Benefit in PD-L1 Subgroups

CheckMate 649

	Nivo + Chemo			Chemo			
PD-L1	N	Events	Median, months	N	Events	Median, months	HR (95% CI)[1,2]
All randomized	789	544	13.83	792	591	11.56	**0.79** (0.70, 0.89)
CPS <1	140	103	13.08	125	91	12.48	**0.92** (0.70, 1.23)
CPS ≥1	641	434	13.96	655	492	11.33	**0.76** (0.67, 0.87)
CPS <5	308	228	12.42	298	221	12.25	**0.94** (0.78, 1.13)
CPS ≥5	473	309	14.39	482	362	11.10	**0.70** (0.60, 0.81)
CPS <10	406	302	12.55	387	288	12.52	**0.94** (0.80, 1.10)
CPS ≥10	375	235	15.01	393	295	10.87	**0.65** (0.55, 0.78)



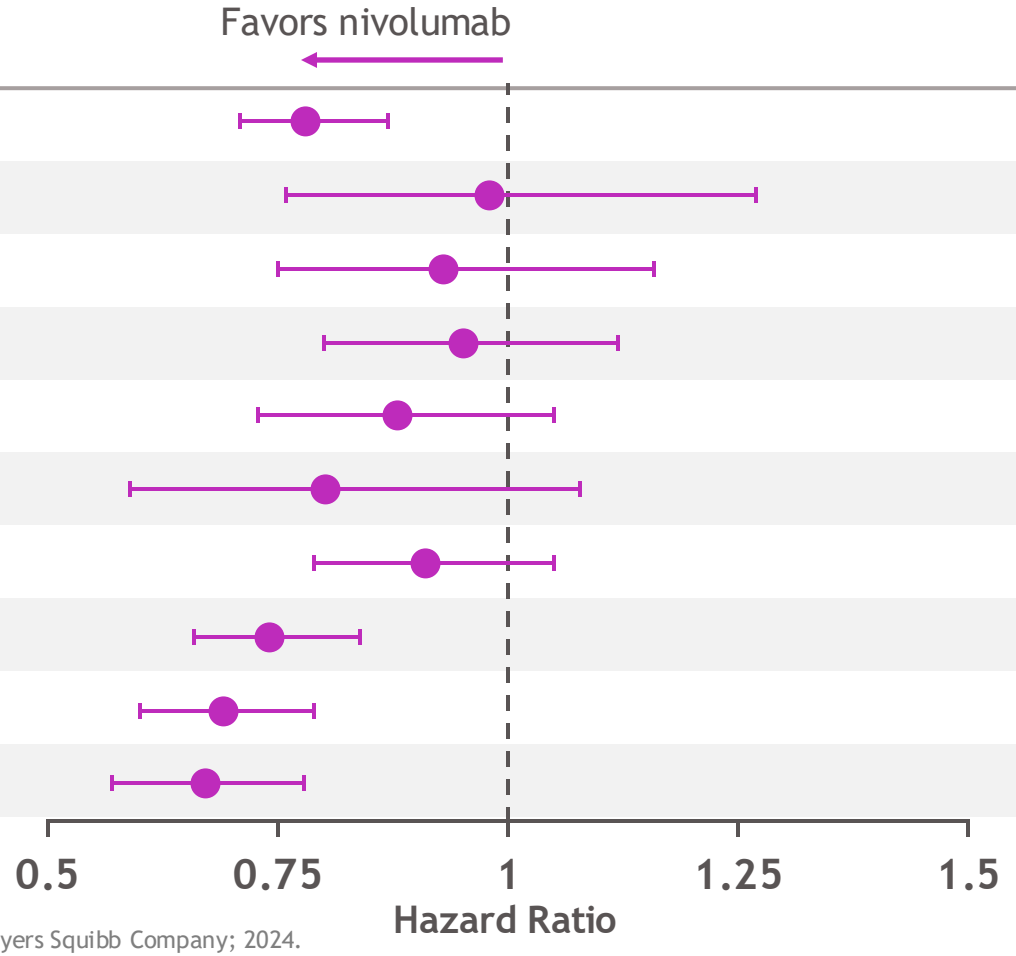
[1]Unstratified hazard ratio. Janjigian YY, et al. *Lancet*. 2021;398:27-40.
[2]Data on file. BMS-REF-NIVO-0302. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

Summary of OS Benefit by PD-L1 CPS in 1L Gastric Cancer

CheckMate 649, 4-year follow-up

CM649 formally tested endpoint at primary analysis

PD-L1	N	Events	OS HR (95% CI)
All randomized	1581	1398	**0.78** (0.71, 0.87)
CPS <1	265	237	**0.98** (0.76, 1.27)
CPS ≥1- <5	342	319	**0.93** (0.75, 1.16)
CPS <5	607	556	**0.95** (0.80, 1.12)
CPS ≥1- <10	529	491	**0.88** (0.73, 1.05)
CPS ≥5- <10	187	172	**0.80** (0.59, 1.08)
CPS <10	794	728	**0.91** (0.79, 1.05)
CPS ≥1	1297	1143	**0.74** (0.66, 0.84)
CPS ≥5	955	824	**0.69** (0.60, 0.79)
CPS ≥10	768	652	**0.67** (0.57, 0.78)



Unstratified hazard ratio. Data on file. BMS-REF-NIVO-0302. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

Safety Profile of Nivo + Chemo Versus Chemo

CheckMate 649

	Patients, n (%)[1]	
	Nivo + Chemo N=782	Chemo N=767
All grade, all causality AEs	776 (99.2)	752 (98.0)
All grade, TRAEs	738 (94.4)	679 (88.5)
Grade 3/4	462 (59.1)	341 (44.5)
All grade, TRAEs leading to DC[a]	284 (36.3)	181 (23.6)
Grade 3/4	132 (16.9)	67 (8.7)
Treatment-related deaths	12 (1.5)	4 (0.5)

No difference in safety profile based on PD-L1 status

[1]Data on file. BMS-REF-NIVO-0302. Princeton, NJ: Bristol-Myers Squibb Company; 2024. [a]Reflects discontinuation (DC) of any component of a regimen.

Summary — First-Line Treatment of Advanced/Metastatic Gastric, GEJ, and Esophageal Adenocarcinoma

- CM-649 demonstrated statistically significant and clinically meaningful OS benefit in the CPS ≥5, CPS ≥1, and all randomized populations
  - Exploratory analyses showed greater OS benefit in all PD-L1 positive subgroups by CPS
  - Long-term follow-up data are consistent with the data available at the time of approval
- The safety profile of Nivo + Chemo was consistent with the known safety profile of the individual drug components
  - Similar safety profile regardless of PD-L1 status
- Positive benefit risk profile in all PD-L1 positive subgroups by CPS

Robert A. Anders, MD, PhD
Division of GI and Liver Pathology
The Johns Hopkins University

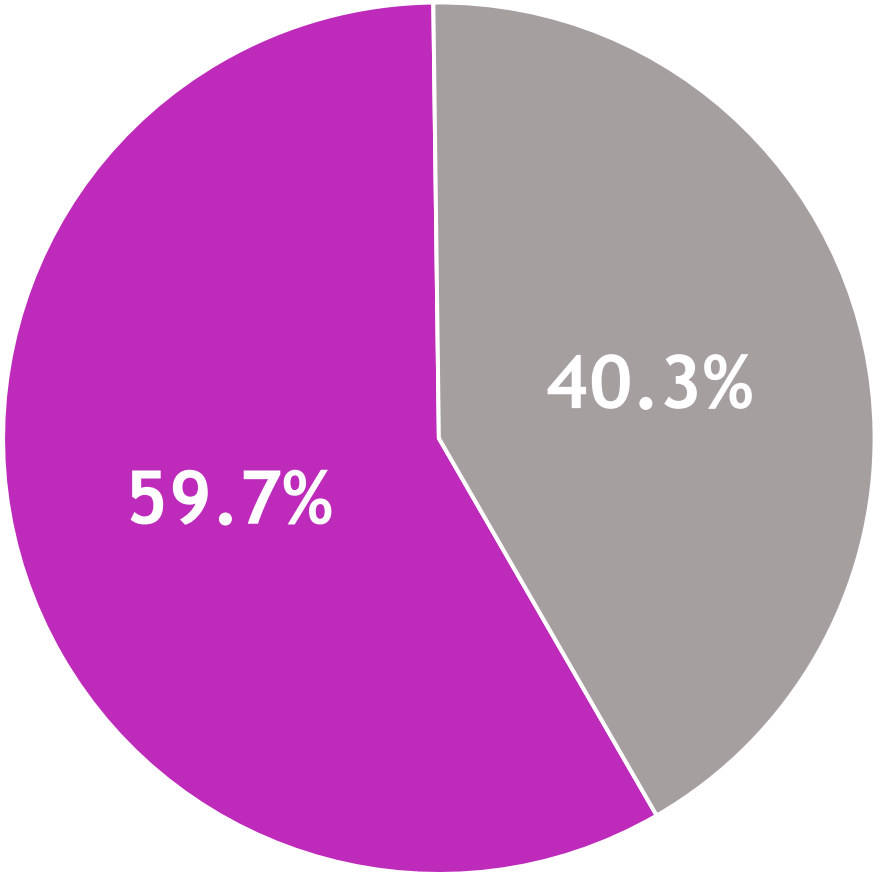
PD-L1 Testing in Clinical Practice

Bristol Myers Squibb®

Real-World PD-L1 CPS Testing Patterns — US Flatiron Analysis

Gastric, GEJ, and Esophageal Adenocarcinoma

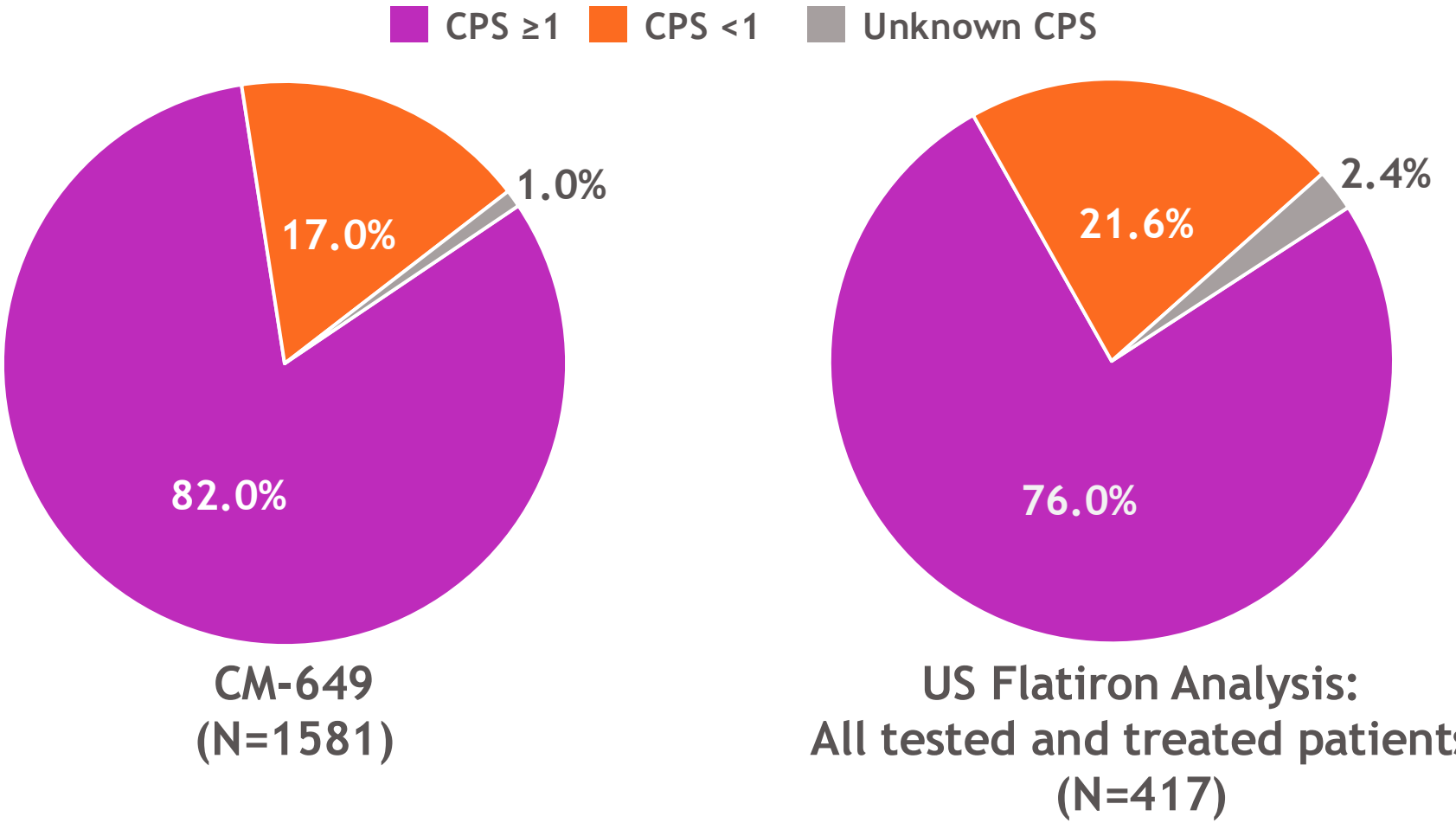
All treated patients (N=698)



Testing patterns among patients diagnosed with advanced/metastatic GC/GEJC/EAC from January 2023 to March 2024 using the Flatiron database. PubD 00065829. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

PD-L1 Expression by CPS

Gastric, GEJ, and Esophageal Adenocarcinoma



US Flatiron Analysis: PD-L1 CPS Expression among patients diagnosed with advanced/metastatic GC/GEJC/EAC from January 2023 to March 2024. PubD 00065829. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

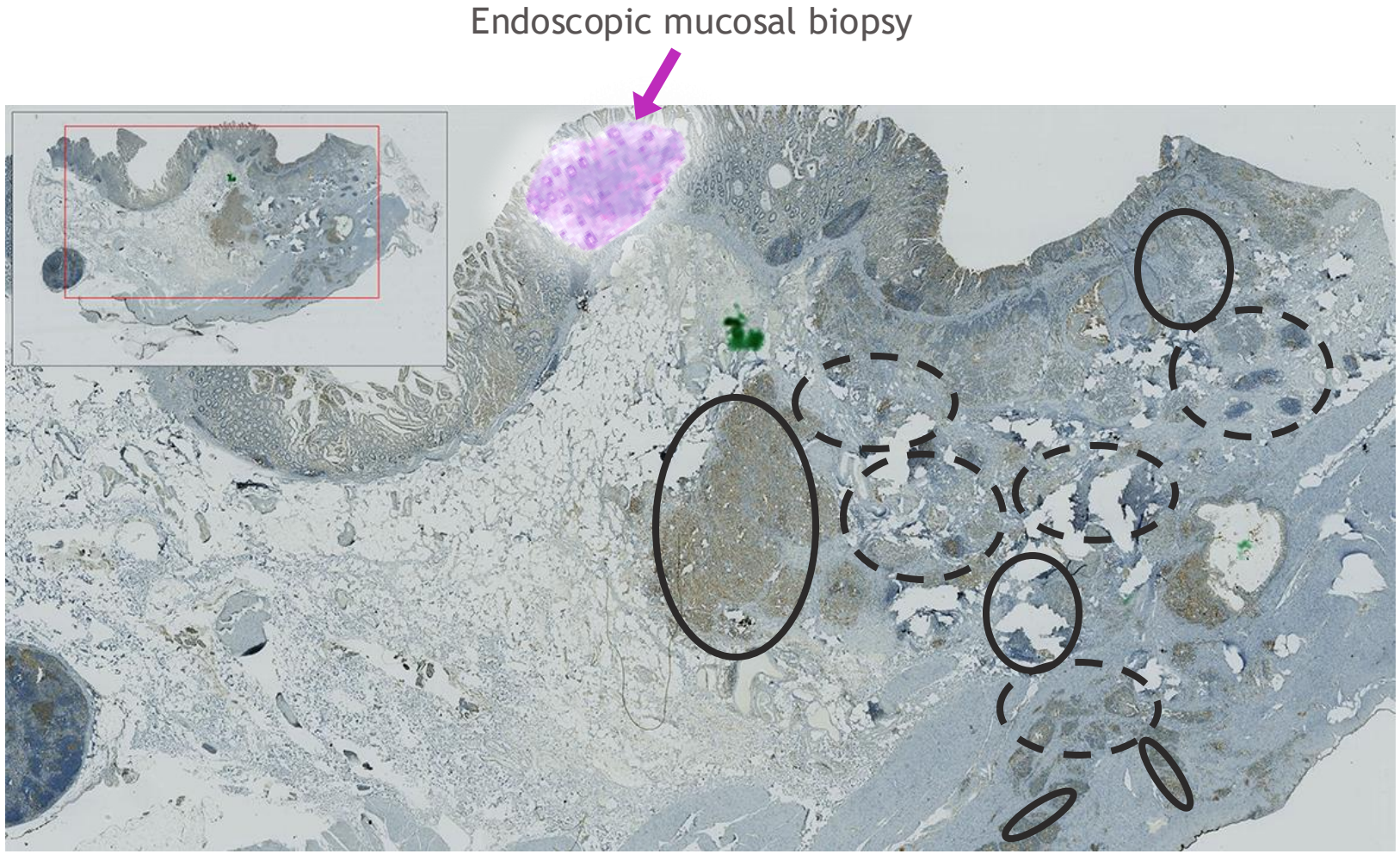
Pre-analytic Variables Can Affect Results

Type of tissue sample

- Full thickness resection
- Biopsy

Spatial heterogeneity of PD-L1 expression

Temporal heterogeneity



Courtesy of Dr. Robert Anders, The Johns Hopkins University, 2024.

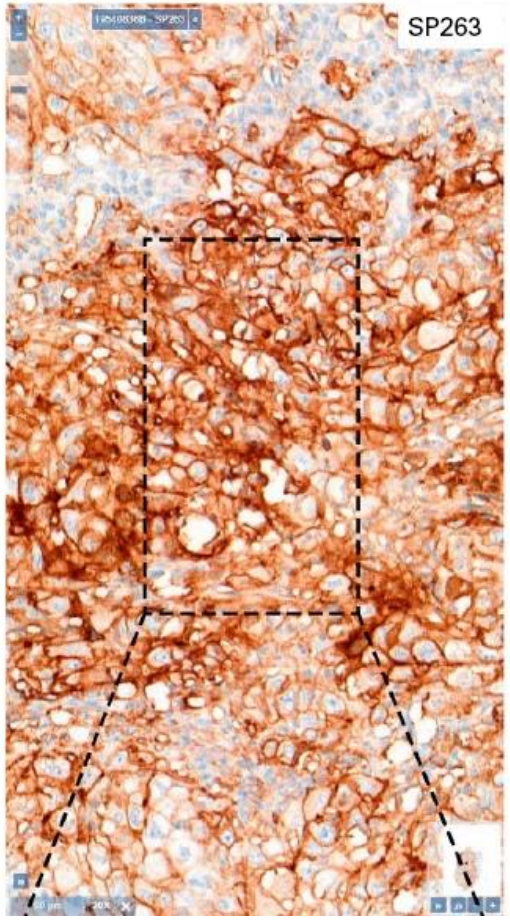
Analytic Variables Make Harmonization Challenging

Antibody performance

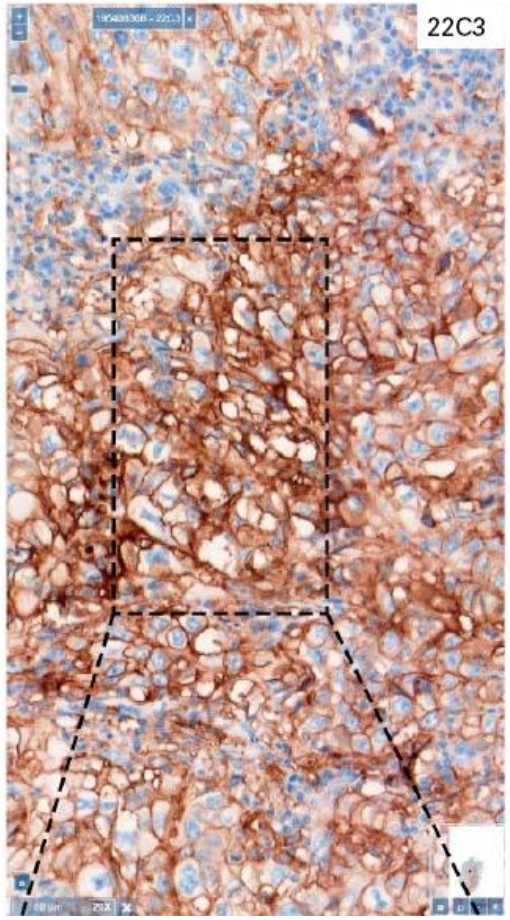
≈ Similar

≠ Not identical

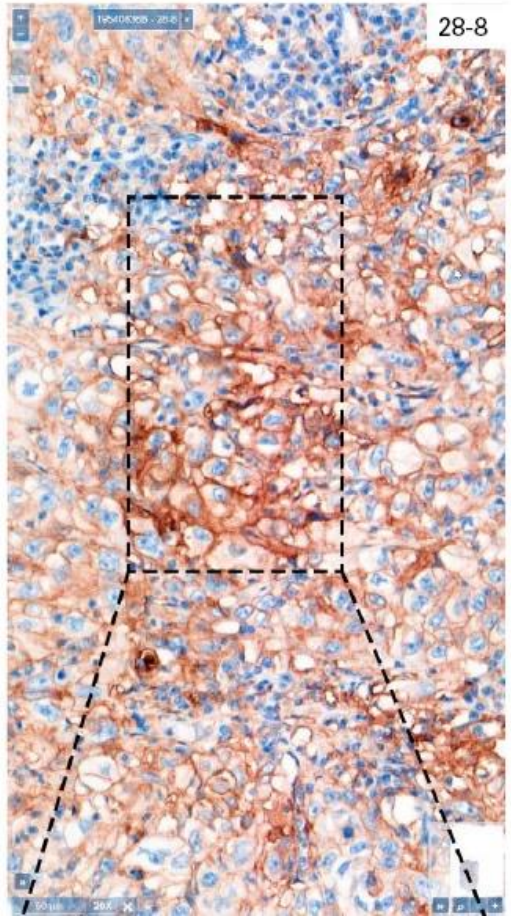
SP263



22C3



28-8



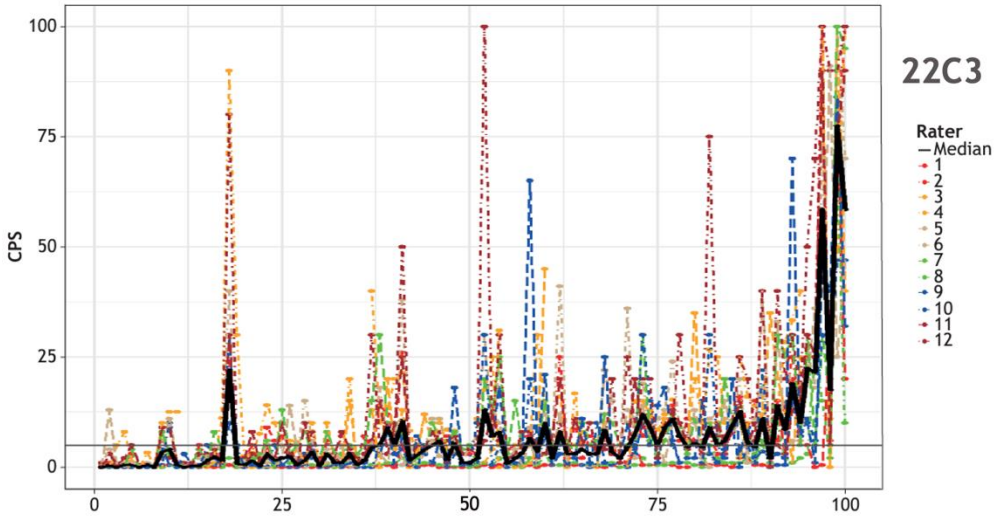
Klempner SJ, et al. *JCO Precis Oncol*. 2024;8:e2400230. https://ascopubs.org/doi/full/10.1200/PO.24.00230. Reprinted with permission.

High Interobserver Variability

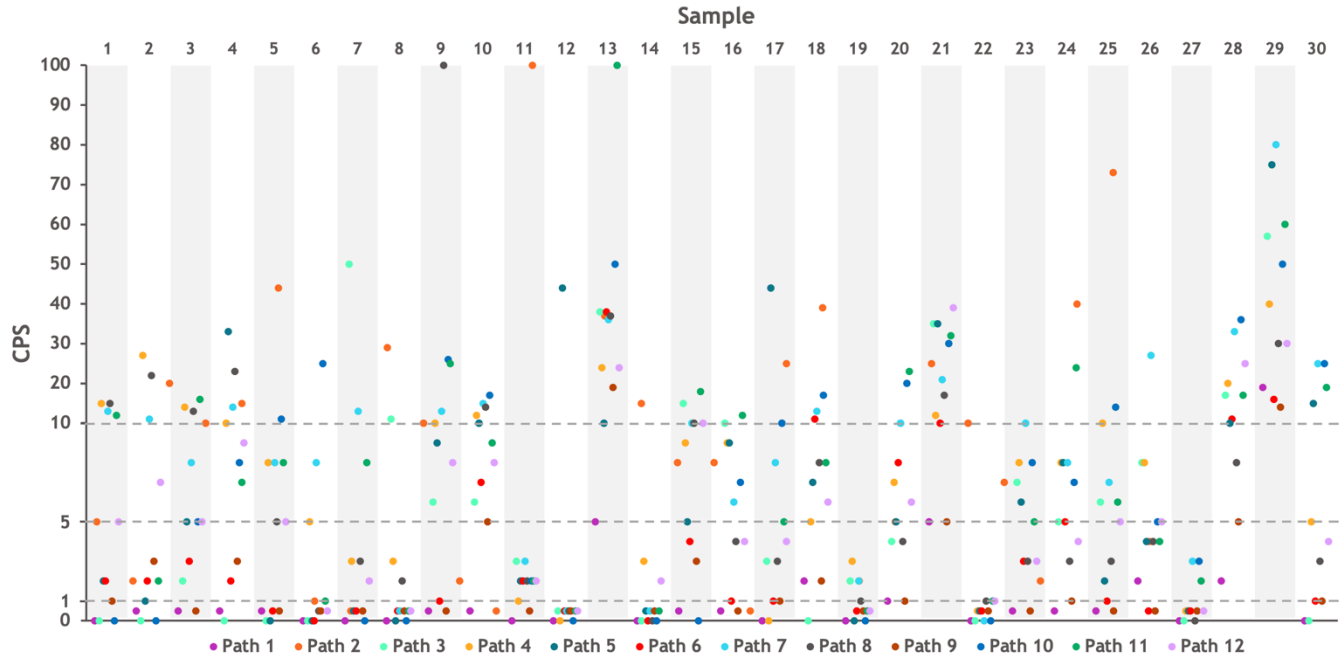
High interobserver variability among pathologists evaluating PD-L1 expression by CPS on gastric cancer biopsies

PD-L1 Expression Scoring

- Subjective
- Immune cells vs tumor cells
- Poor concordance irrespective of CPS cutoff

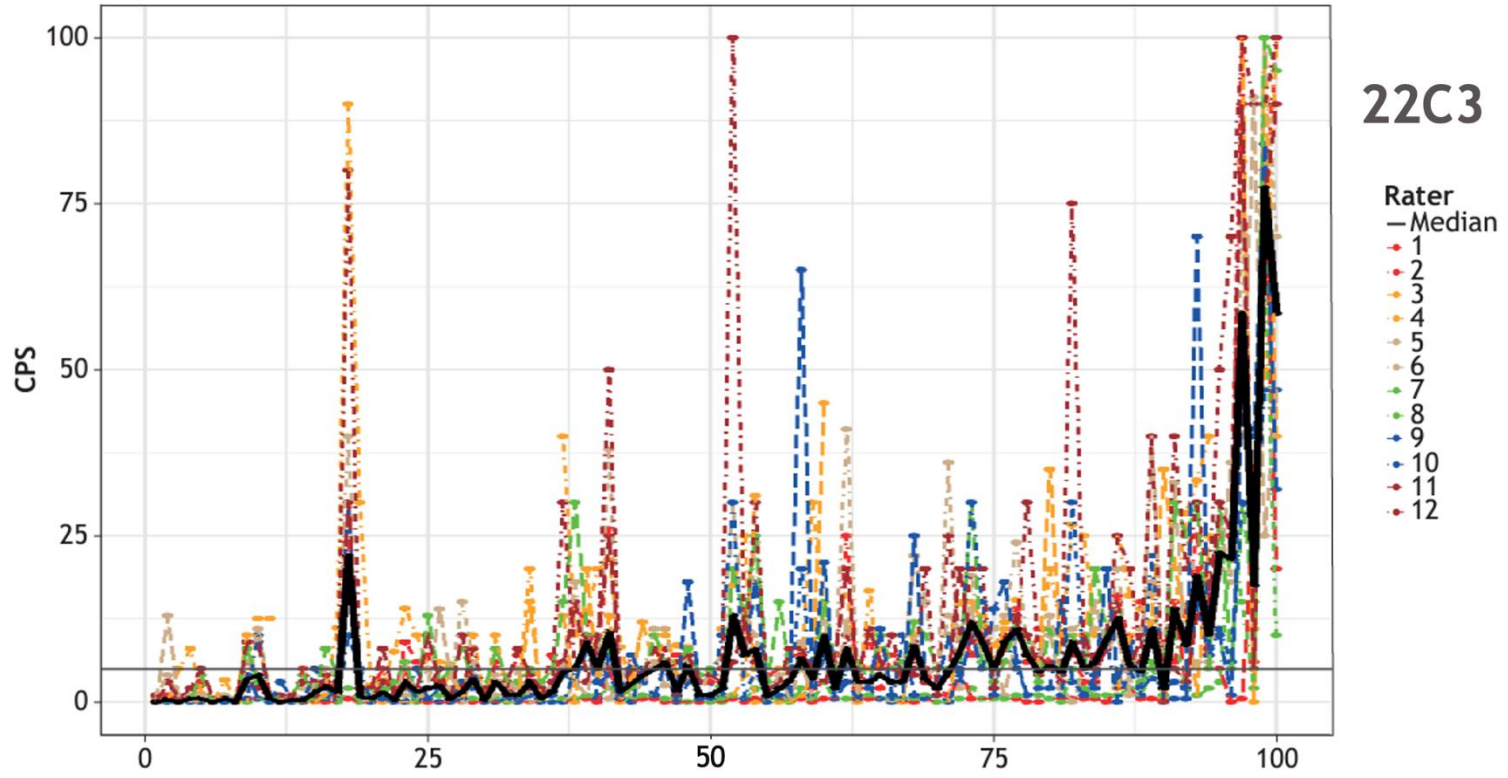


	Pre-training	Post-training
No. of samples, n	100	100
ICC (95% CI)	0.55 (0.47, 0.63)	0.56 (0.49, 0.64)



ICC, intraclass correlation coefficient. Robert ME, et al. *Mod Pathol*. 2023;36:100154. https://creativecommons.org/licenses/by/4.0/.
Robert M, et al. Presented at the USCAP 112th Annual Meeting, March 11-16, 2023, New Orleans, LA, USA.
PubD 00066171. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

High Interobserver Variability



	Pre-training	Post-training
No. of samples, n	100	100
ICC (95% CI)	0.55 (0.47, 0.63)	0.56 (0.49, 0.64)

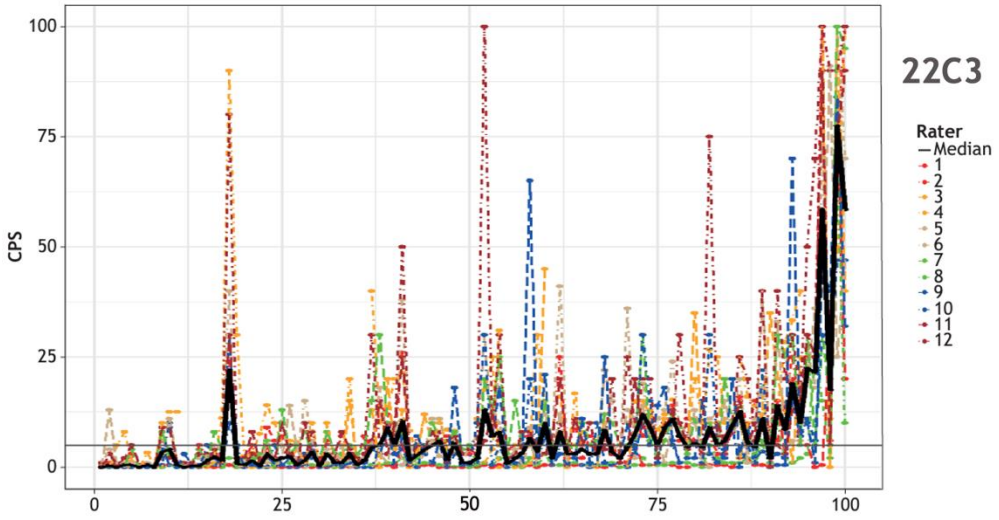
ICC, intraclass correlation coefficient. Robert ME, et al. *Mod Pathol*. 2023;36:100154. https://creativecommons.org/licenses/by/4.0/.
Robert M, et al. Presented at the USCAP 112th Annual Meeting, March 11-16, 2023, New Orleans, LA, USA.
PubD 00066171. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

High Interobserver Variability

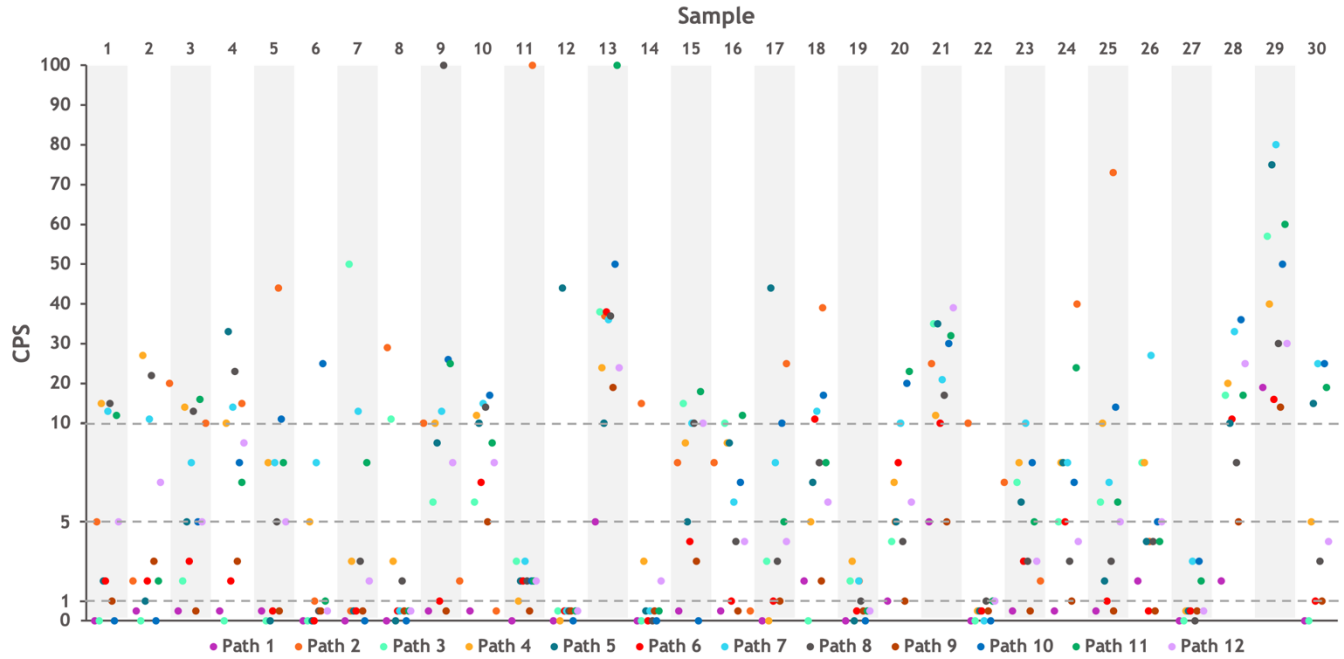
High interobserver variability among pathologists evaluating PD-L1 expression by CPS on gastric cancer biopsies

PD-L1 Expression Scoring

- Subjective
- Immune cells vs tumor cells
- Poor concordance irrespective of CPS cutoff

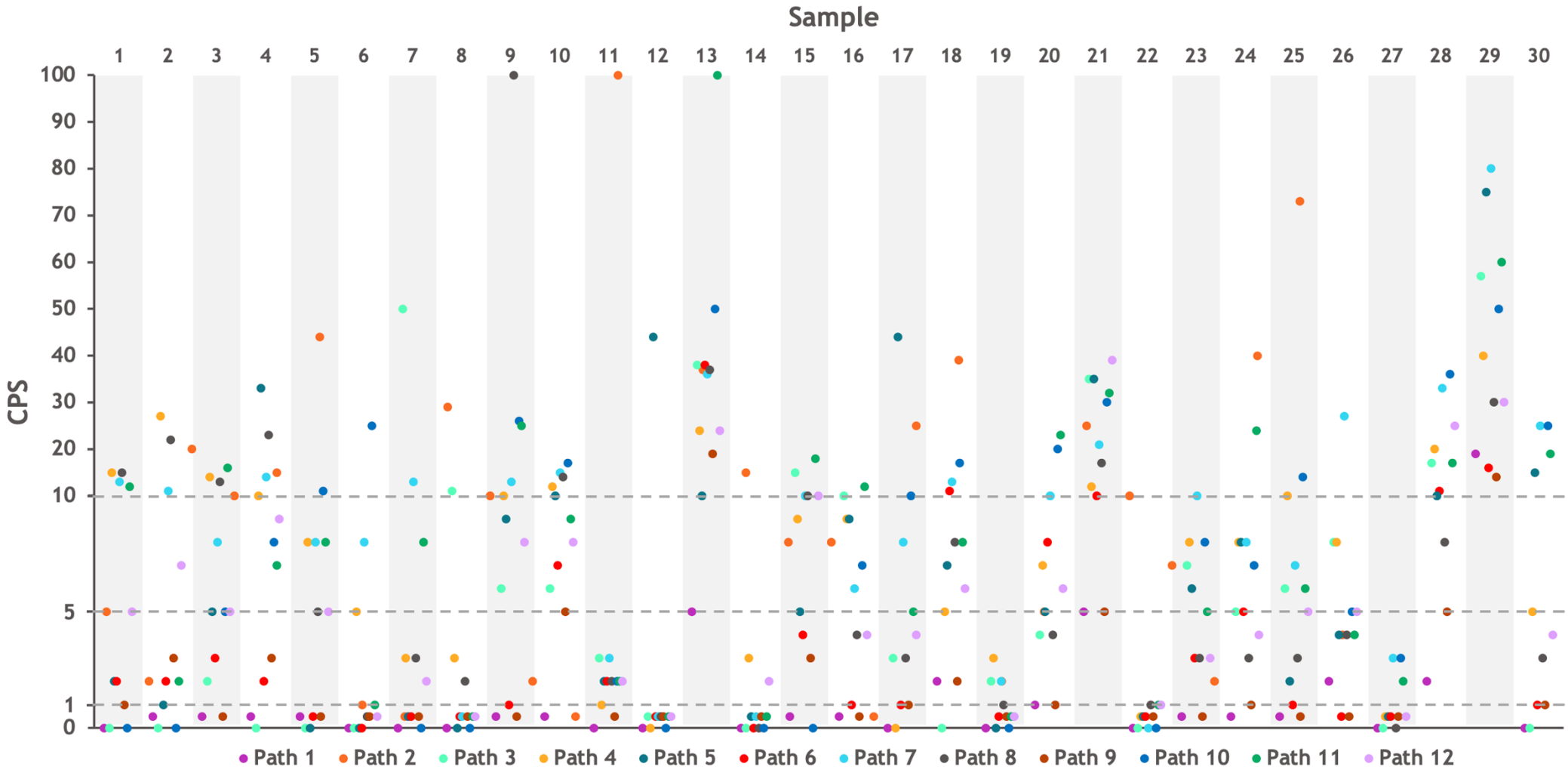


	Pre-training	Post-training
No. of samples, n	100	100
ICC (95% CI)	0.55 (0.47, 0.63)	0.56 (0.49, 0.64)



ICC, intraclass correlation coefficient. Robert ME, et al. *Mod Pathol*. 2023;36:100154. https://creativecommons.org/licenses/by/4.0/.
Robert M, et al. Presented at the USCAP 112th Annual Meeting, March 11-16, 2023, New Orleans, LA, USA.
PubD 00066171. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

High Interobserver Variability



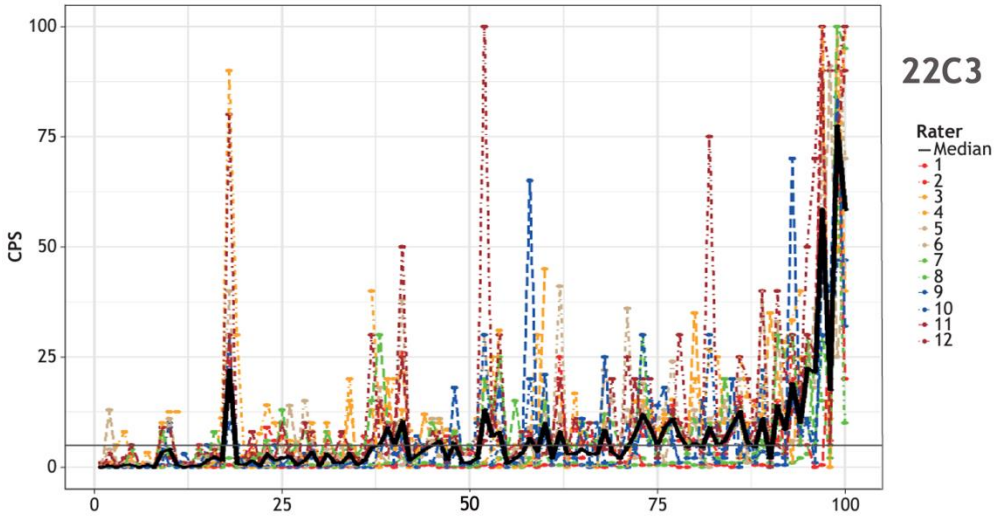
ICC, intraclass correlation coefficient. Robert ME, et al. *Mod Pathol*. 2023;36:100154. https://creativecommons.org/licenses/by/4.0/.
Robert M, et al. Presented at the USCAP 112th Annual Meeting, March 11-16, 2023, New Orleans, LA, USA.
PubD 00066171. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

High Interobserver Variability

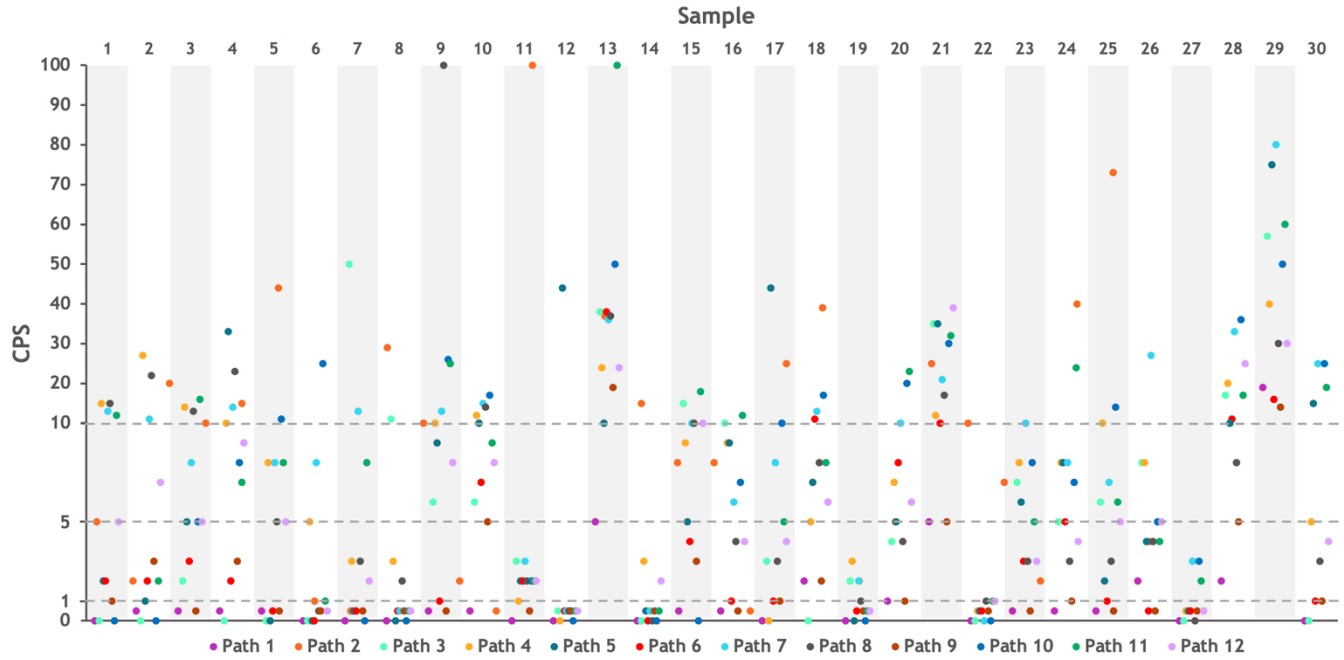
High interobserver variability among pathologists evaluating PD-L1 expression by CPS on gastric cancer biopsies

PD-L1 Expression Scoring

- Subjective
- Immune cells vs tumor cells
- Poor concordance irrespective of CPS cutoff

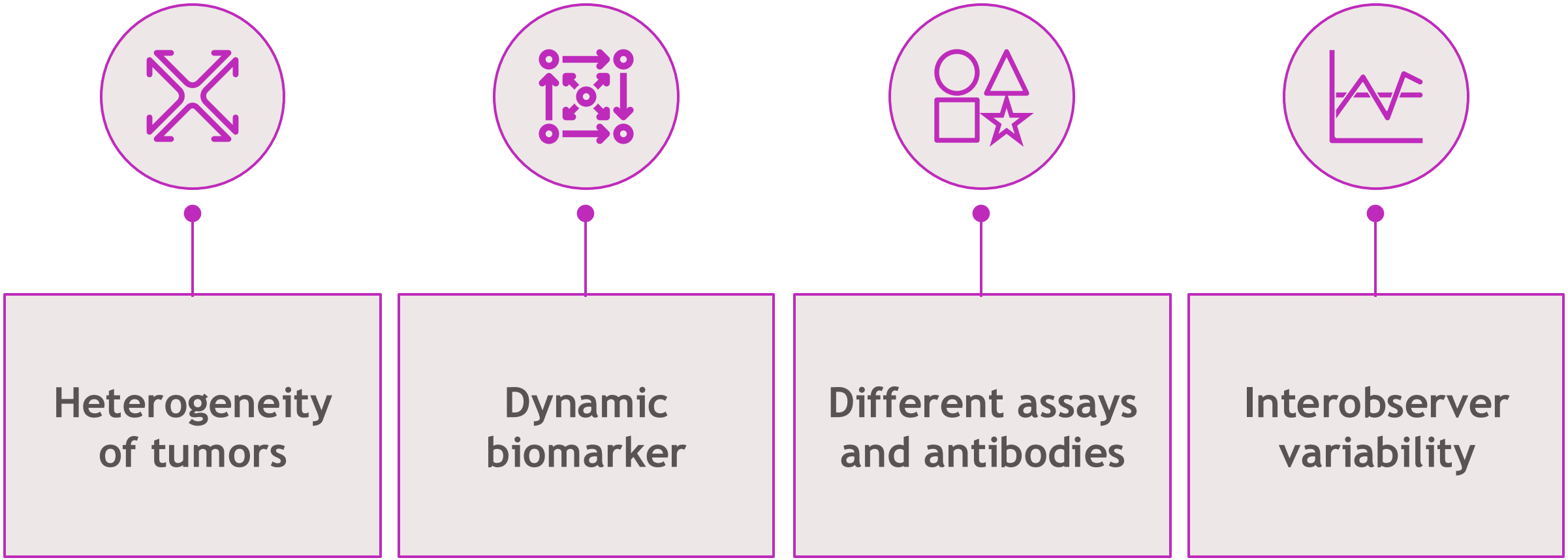


	Pre-training	Post-training
No. of samples, n	100	100
ICC (95% CI)	0.55 (0.47, 0.63)	0.56 (0.49, 0.64)



ICC, intraclass correlation coefficient. Robert ME, et al. *Mod Pathol*. 2023;36:100154. https://creativecommons.org/licenses/by/4.0/.
Robert M, et al. Presented at the USCAP 112th Annual Meeting, March 11-16, 2023, New Orleans, LA, USA.
PubD 00066171. Princeton, NJ: Bristol-Myers Squibb Company; 2024.

Reality of PD-L1 Testing in Clinical Practice



Ian Waxman, MD

Vice President,
Late Development Oncology

BMS

Conclusion

Summary of Trial Data and Testing Considerations

- Clinical trial data show OS benefit at CPS ≥1
- Multiple considerations impact the ability to measure PD-L1
  - PD-L1 is a dynamic biomarker
  - Tumor heterogeneity leads to variability in scores
  - Quality/adequacy of tissue may be a barrier to testing
- Despite these challenges, patients should be tested when possible, to best inform benefit risk
- If PD-L1 positivity is deemed necessary for treatment, a cut-off based on CPS ≥1 is the most reasonable choice based on the data from CheckMate 649 and testing considerations

Multiple Solutions Warrant Consideration

Modify the indication based on CPS ≥1

- Rational approach that would ensure only patients most likely to benefit receive treatment
- However, this would also leave some patients without a potentially important treatment option
  - Risk could be minimized by choosing a cut-off of CPS ≥1 rather than a higher cut-off

Keep current indication

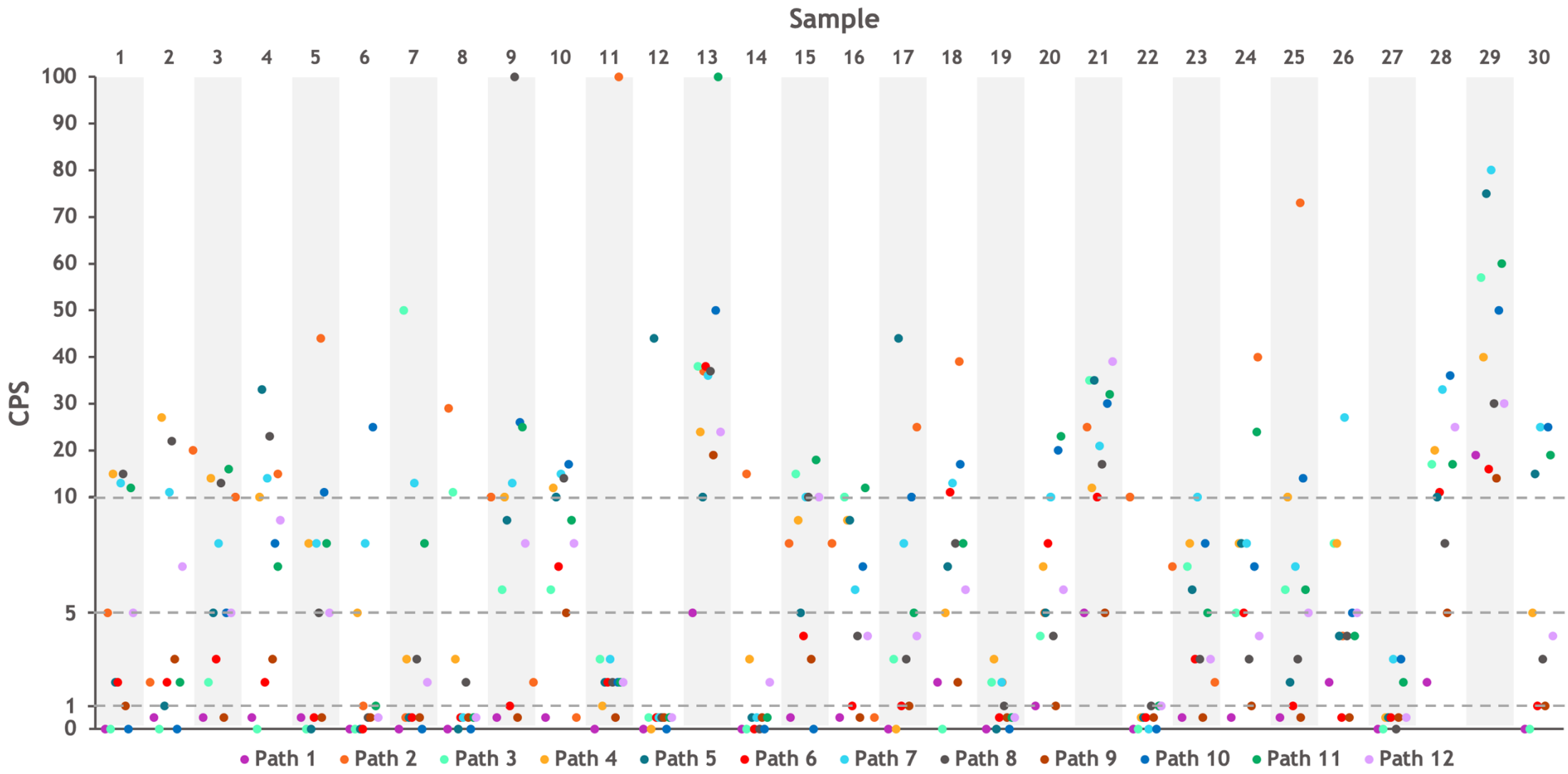
- Leaves decision-making in the hands of the treating physician and maximizes the chance for patients to benefit, given the shortcomings of available testing in gastric cancer

Back Up Slides Shown

US Food & Drug Administration
Oncologic Drugs Advisory Committee
September 26, 2024

Bristol Myers Squibb®

High Interobserver Variability (Robert et al. *Mod Pathol*. 2023)



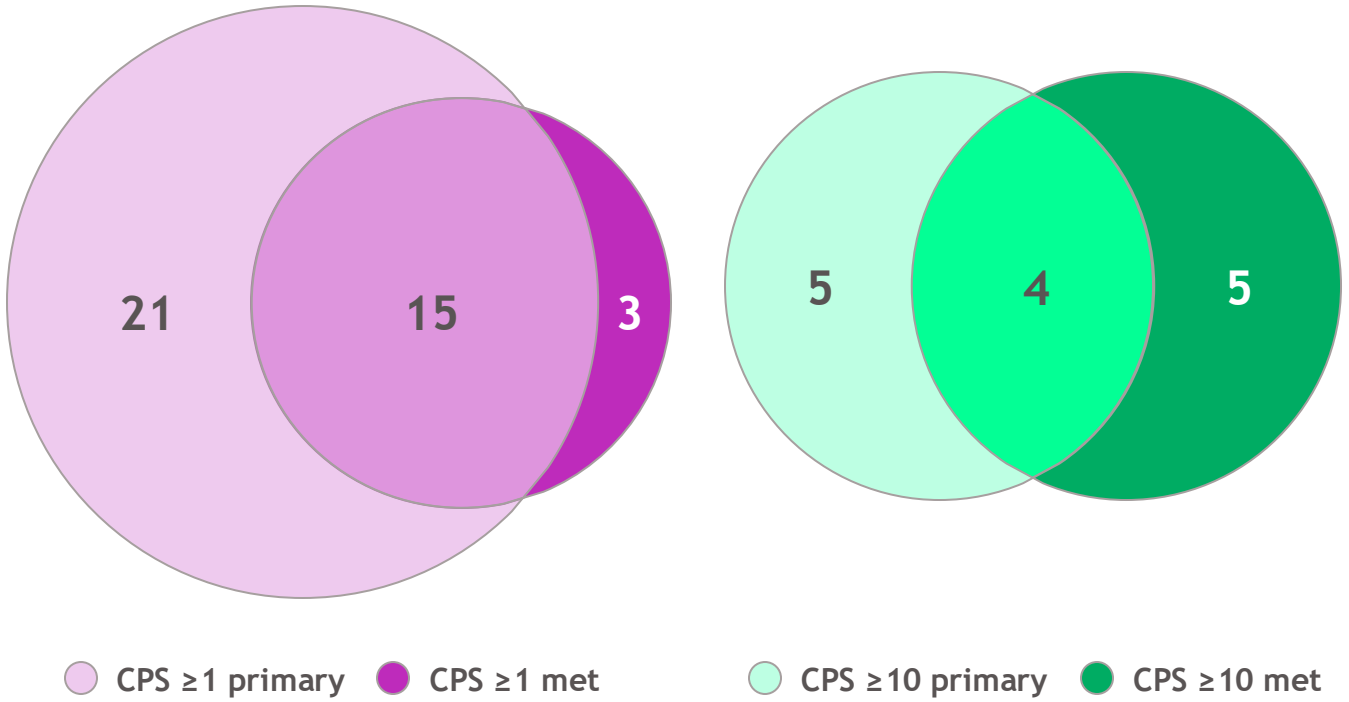
PubD 00066171. Princeton, NJ Bristol Myers Squibb Company; 2024

PD-L1 Expression is Dynamic

Spatiotemporal Heterogeneity

Primary vs Metastatic

61% intra-patient agreement



		Baseline met PD-L1		
		Negative	Positive	Total
Baseline 1° PD-L1	Negative	23 (88%)	3 (12%)	26
	Positive	21 (58%)	15 (42%)	36
	Total	44 (71%)	18 (29%)	62

$P = 2.4 \times 10^{-4}$ by McNemar test

		Baseline met PD-L1		
		CPS <10	CPS ≥10	Total
Baseline 1° PD-L1	CPS <10	48 (91%)	5 (9%)	53
	CPS ≥10	5 (56%)	4 (44%)	9
	Total	53 (85%)	9 (15%)	62

$P = 1$ by McNemar test

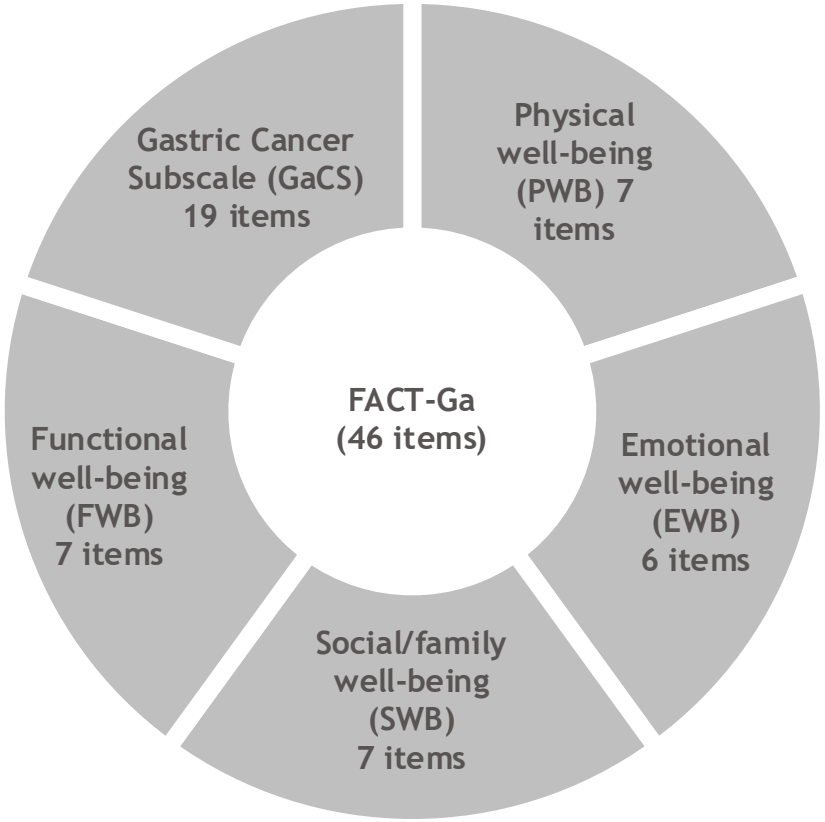
Gastroesophageal adenocarcinoma; Zhou KI, et al. *Clin Cancer Res*. 2020 Dec 15;26(24):6453-6463.

Method - FACT-Ga

The Functional Assessment of Cancer Therapy - General (FACT-Ga) is a 46-item questionnaire designed to measure five domains of HRQOL in cancer patients: Physical, social/family, emotional, functional well-being and Gastric Cancer Subscale (GaCS)

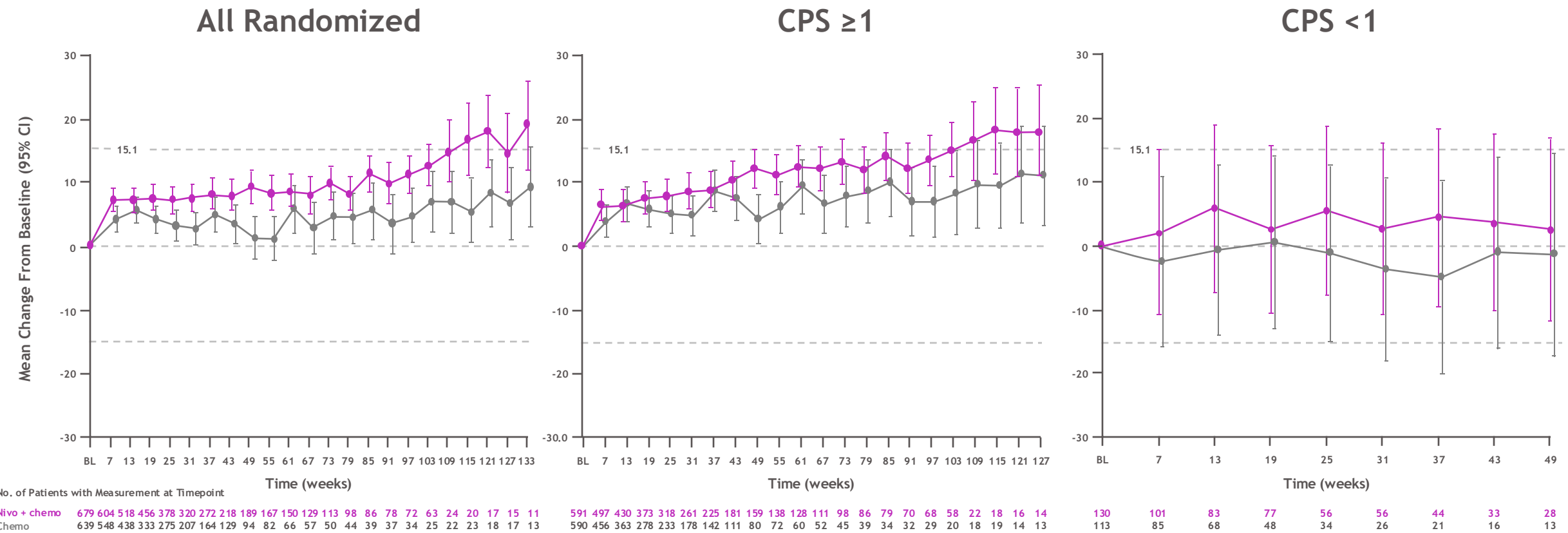
Higher scores indicated better health/HRQoL

PRO measure	Range	Meaningful Change Threshold (MCT)
PWB subscale	0-28	3
SWB subscale	0-28	3
EWB subscale	0-24	3
FWB subscale	0-28	3
GaCS	0-76	8.2
FACT-Ga total score	0-184	15.1



Cella D, et al. *Qual Life Res*. 2002 May;11(3):207-21.; Yost KJ, et al. *Value Health*. 2005 Mar-Apr;8(2):117-27.; Garland SN, et al. *Cancer*. 2011 Mar 15;117(6):1302-12.

Mean Change in FACT-Ga from Baseline – Physical, Emotional, Social, Functional Well Being and Gastric Cancer Subscale (46 Questions)



When there were less than 5 patients with assessments at a timepoint in either treatment arm, no further data was reported.

Moehler et al. J Clin Oncol 2023 41:5388-5399, BMS Data on File

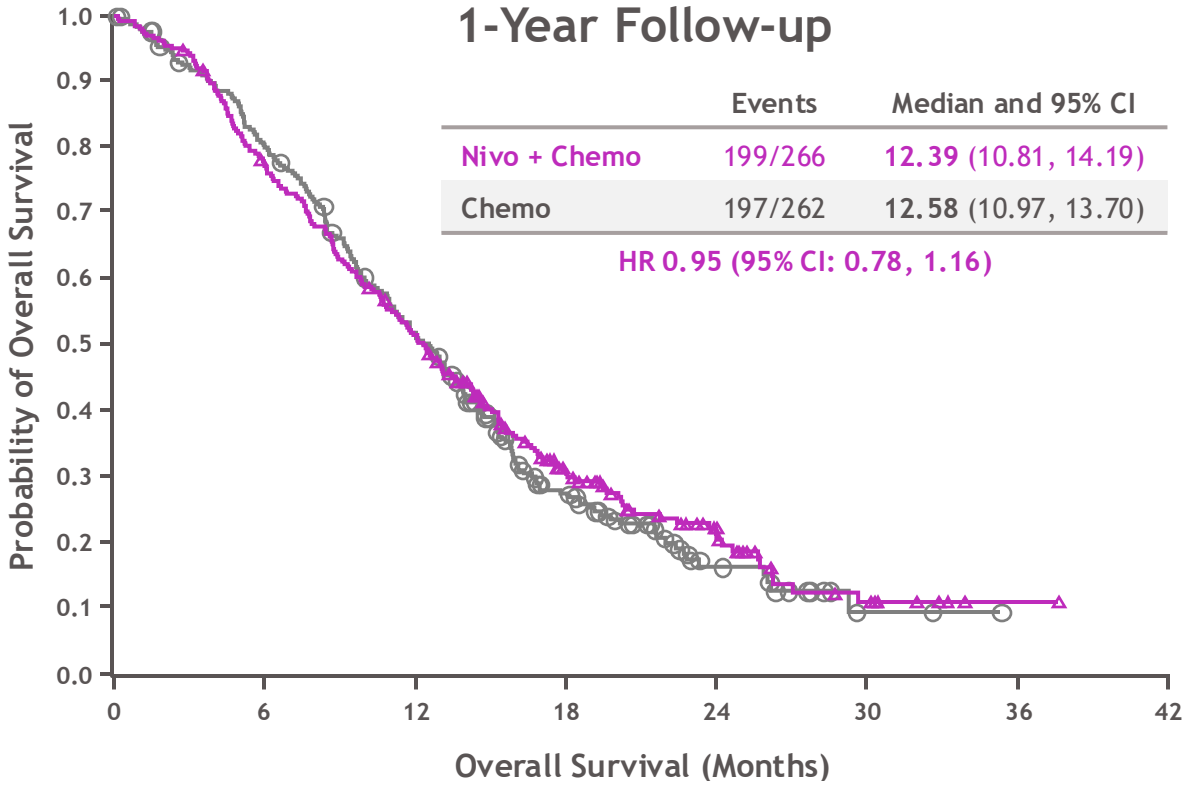
Overall Survival in CPS ≥1 to <10 Subgroup (Exploratory)

CheckMate-649

1-Year Follow-up

	Events	Median and 95% CI
Nivo + Chemo	199/266	12.39 (10.81, 14.19)
Chemo	197/262	12.58 (10.97, 13.70)

HR 0.95 (95% CI: 0.78, 1.16)

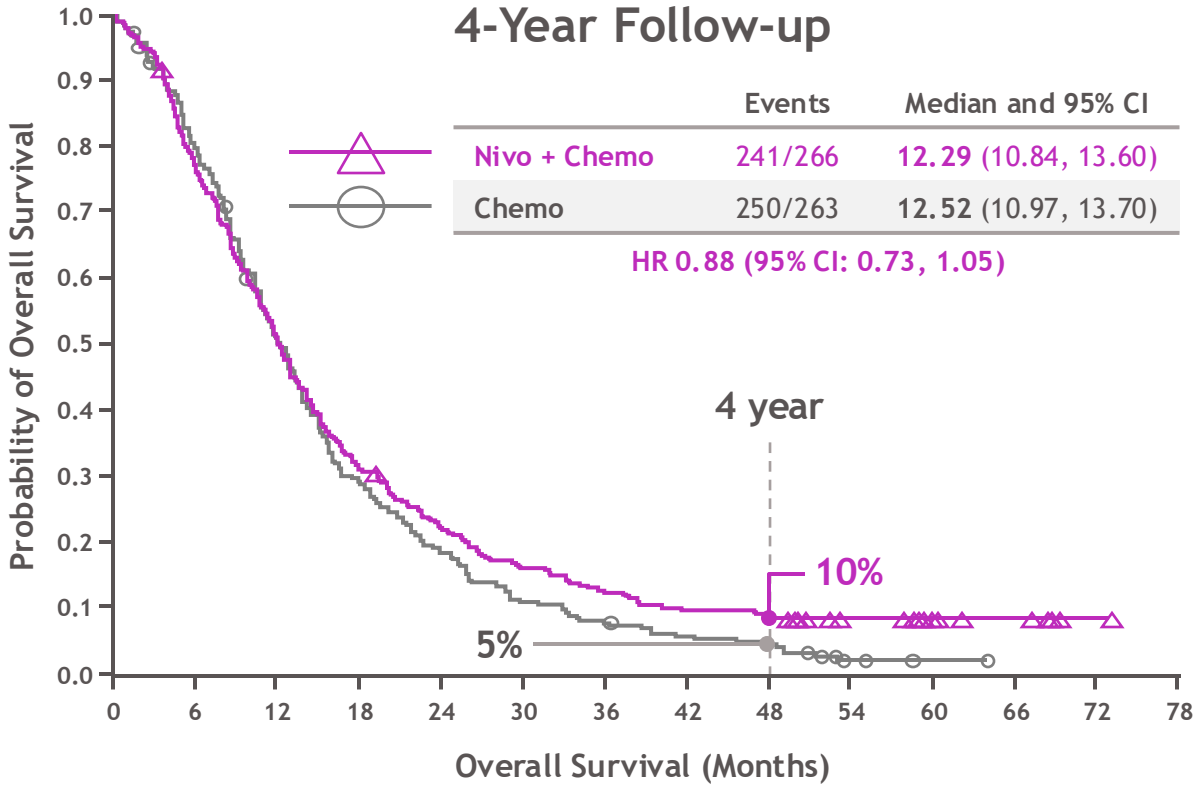


Number of Subjects							
Nivo + Chemo							
266	203	134	58	23	7	1	0
Chemo							
262	205	128	53	15	2	0	0

4-Year Follow-up

	Events	Median and 95% CI
Nivo + Chemo	241/266	12.29 (10.84, 13.60)
Chemo	250/263	12.52 (10.97, 13.70)

HR 0.88 (95% CI: 0.73, 1.05)



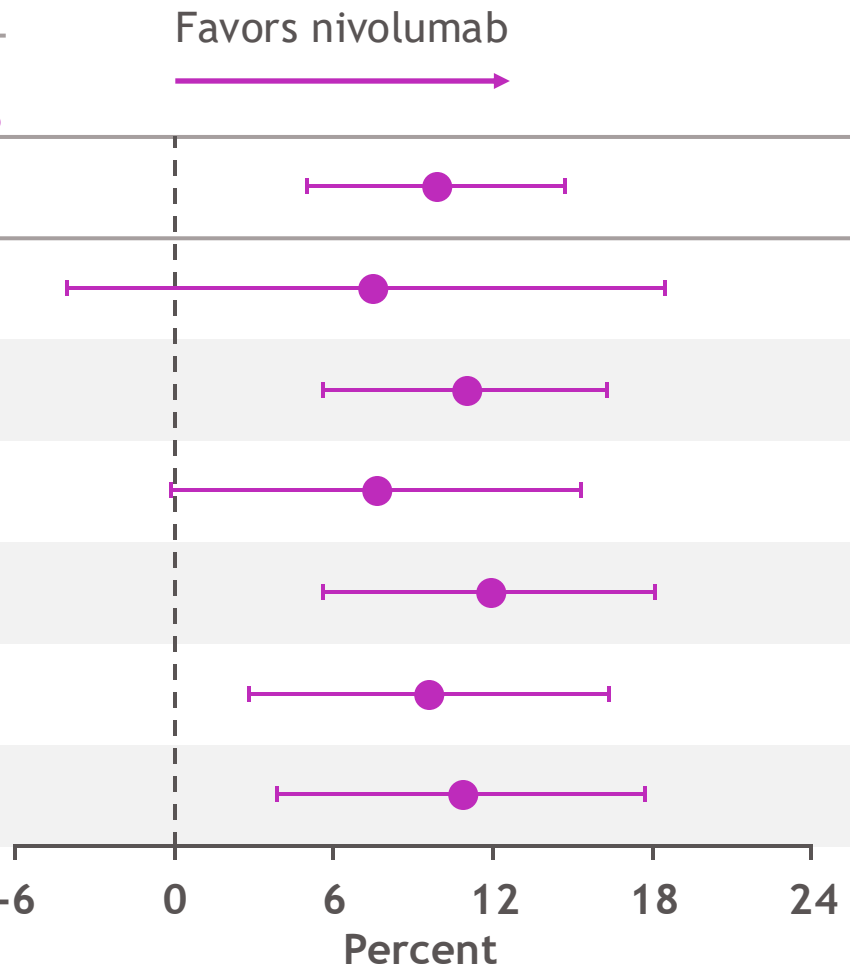
Number of Subjects													
Nivo + Chemo													
266	205	136	84	59	43	34	26	25	16	11	5	1	0
Chemo													
263	208	131	76	49	29	22	15	13	3	1	0	0	0

BMS Data on File

Improvement in ORR Across PD-L1 Subgroups

CheckMate 649 All Randomized Patients

Population	Nivo + Chemo N	Nivo + Chemo Response, n	Nivo + Chemo ORR[a], %	Chemo N	Chemo Response, n	Chemo ORR[a], %	ORR Difference, % (95% CI)
All randomized	789	370	46.9	792	280	37.0	**9.9** (5.0,14.7)
PD-L1 CPS <1	140	53	37.9	125	38	30.4	**7.5** (-4.0, 18.5)
PD-L1 CPS ≥1	641	314	49.0	655	249	38.0	**11.0** (5.6, 16.3)
PD-L1 CPS <5	308	130	42.2	298	103	34.6	**7.6** (-0.1, 15.3)
PD-L1 CPS ≥5	473	237	50.1	482	184	38.2	**11.9** (5.6, 18.1)
PD-L1 CPS <10	406	186	45.8	387	140	36.2	**9.6** (2.8, 16.4)
PD-L1 CPS ≥10	375	181	48.3	393	147	37.4	**10.9** (3.9, 17.7)

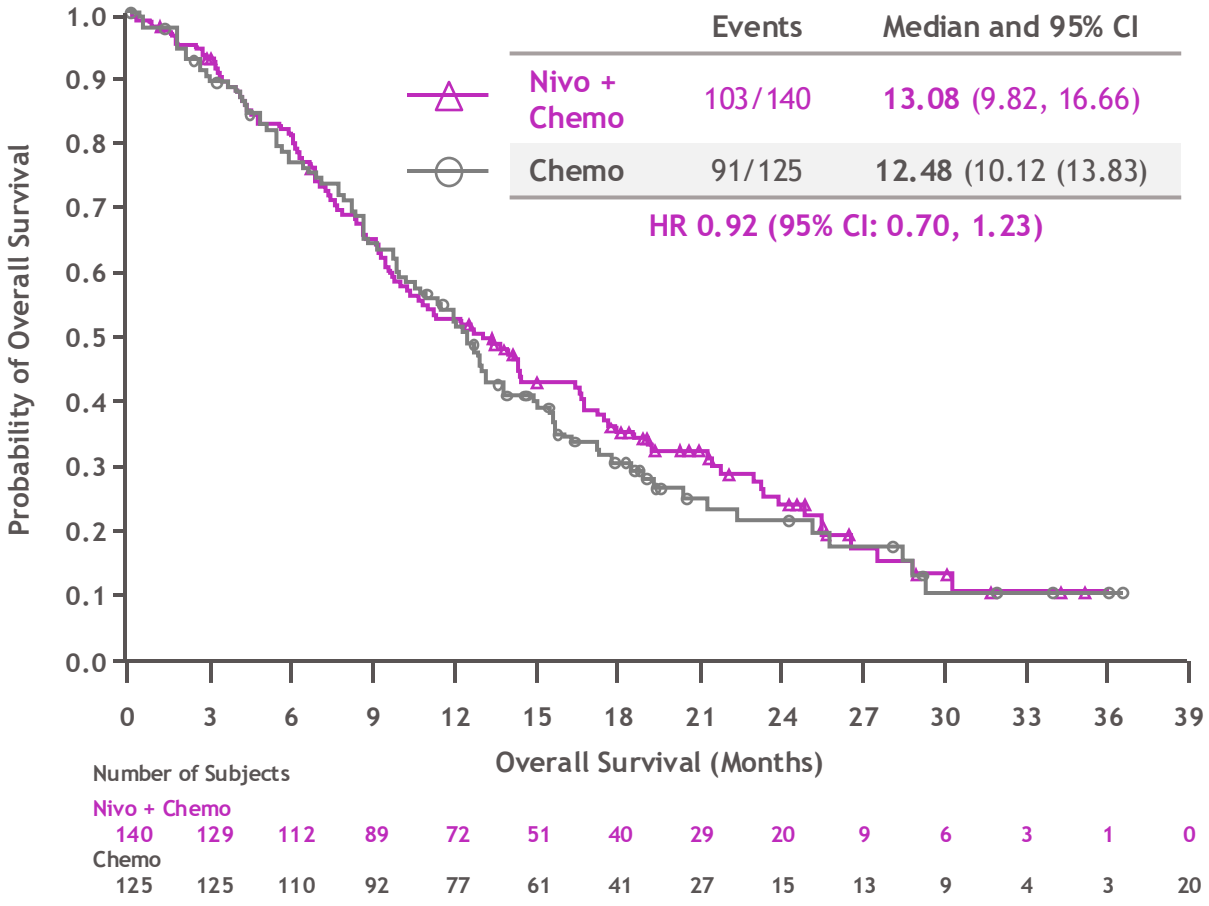


BMS Data on File

Overall Survival in CPS <1 Subgroup (Exploratory)

CheckMate-649

1-year follow-up



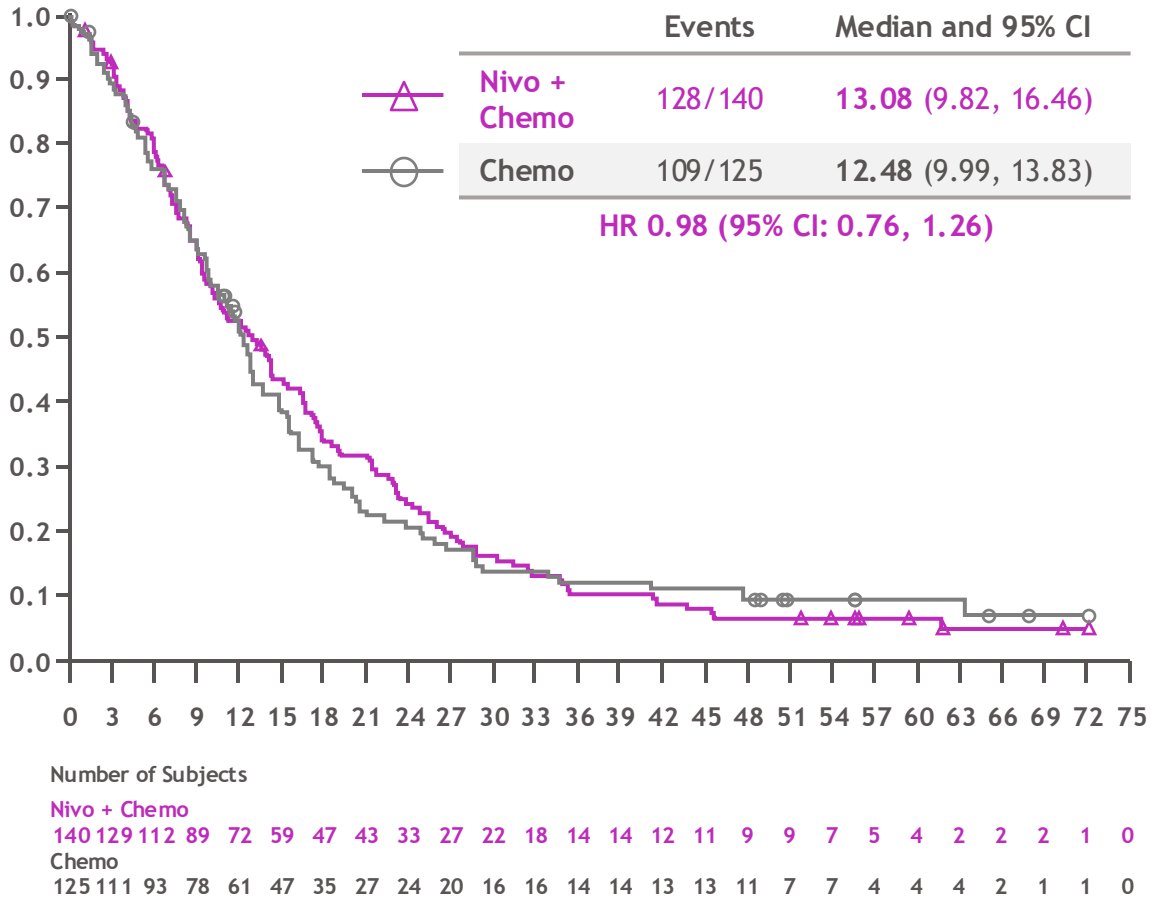
	Events	Median and 95% CI
Nivo + Chemo	103/140	**13.08** (9.82, 16.66)
Chemo	91/125	**12.48** (10.12 (13.83)

HR 0.92 (95% CI: 0.70, 1.23)

Number of Subjects

Nivo + Chemo	140	129	112	89	72	51	40	29	20	9	6	3	1	0
Chemo	125	125	110	92	77	61	41	27	15	13	9	4	3	20

4-year follow-up



	Events	Median and 95% CI
Nivo + Chemo	128/140	**13.08** (9.82, 16.46)
Chemo	109/125	**12.48** (9.99, 13.83)

HR 0.98 (95% CI: 0.76, 1.26)

Number of Subjects

Nivo + Chemo	140	129	112	89	72	59	47	43	33	27	22	18	14	14	12	11	9	9	7	5	4	2	2	2	1	0
Chemo	125	111	93	78	61	47	35	27	24	20	16	16	14	14	13	13	11	7	7	4	4	4	2	1	1	0

BMS Data on File