Advances in Cancer Immunotherapy™ Webinar: Clinical Updates from ASCO 2021

Wednesday, October 6, 2021

2:00 p.m. – 3:00 p.m. ET

Webinar Agenda

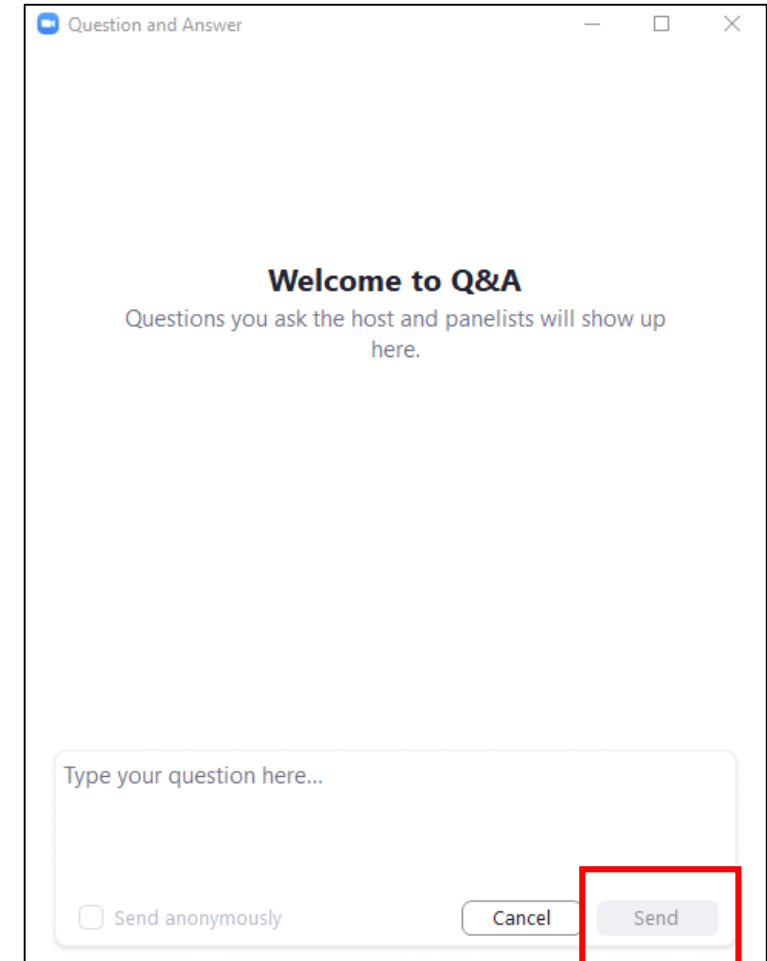2:00-2:05 p.m. ET Overview: Welcome and Introductions

2:05-2:45 p.m. ET Presentations

2:45-2:55 p.m. ET Question and Answer Session

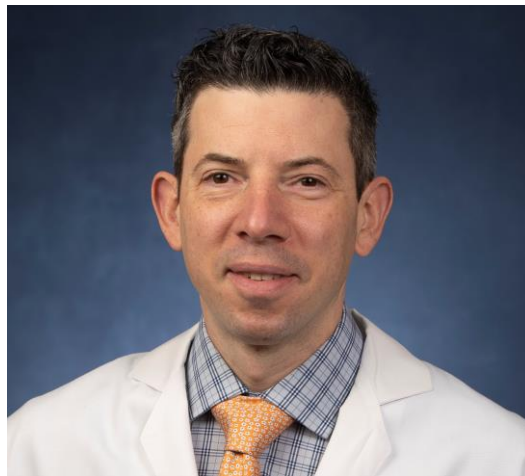2:55-3:00 p.m. ET Closing Remarks

How to Submit Questions

- Click the "Q&A" icon located on at the bottom of your Zoom control panel

- Type your question in the Q&A box, then click "Send"

- Questions will be answered in the Question & Answer session at the end of the webinar (as time permits)

Webinar Faculty

Matthew Frigault, MD, MSc – *Massachusetts General Hospital*

Evan J. Lipson, MD – *Johns Hopkins University*

Ulka Vaishampayan, MD - *University of Michigan*

Jarushka Naidoo, MBBCH, MHS - *Consultant Medical Oncologist Beaumont RCSI Cancer Centre Dublin*

Introduction to Advances in Cancer Immunotherapy™ Webinar: Clinical Updates from ASCO 2021

Learning Objectives

Upon completion of this program, participants will be able to:

- Summarize the most recent advances in cancer immunotherapy

- Analyze cutting-edge clinical trials to incorporate new research and techniques into clinical application for cancer immunotherapy

- Describe the role of clinical and investigational biomarkers in cancer immunotherapy

Webinar Outline

- Genitourinary– Dr. Vaishampayan

- Lung cancer– Dr. Naidoo

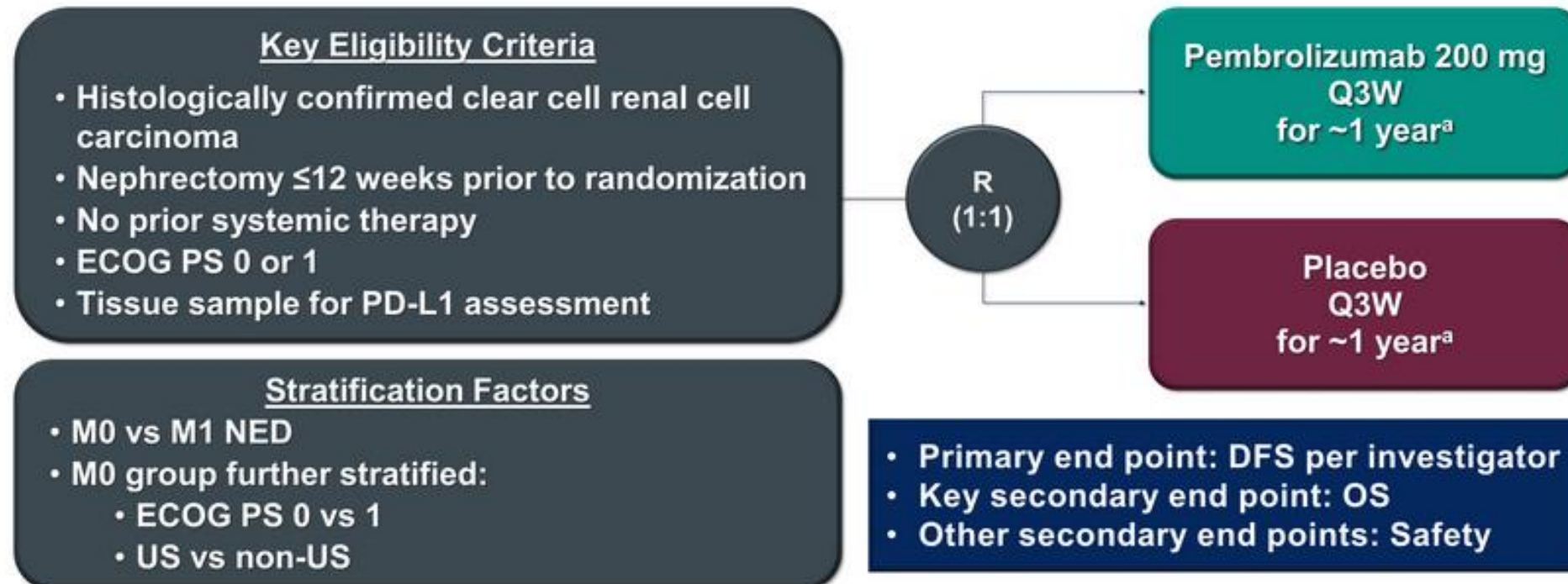- Cellular therapies – Dr. Frigault

Genitourinary

Ulka Vaishampayan MD

University of Michigan

Ann Arbor MI

Pembrolizumab versus placebo as post nephrectomy adjuvant therapy for renal cell carcinoma: Randomized, double-blind, phase 3 KEYNOTE-564 study

Toni K. Choueiri, *et al*

KEYNOTE-564 Study Design

Primary Endpoint: DFS per Investigator

DFS by Investigator, ITT Population

HR 0.68 (95% CI, 0.53–0.87)
$P = 0.0010^a$

12-month rate
85.7%
76.2%

24-month rate
77.3%
68.1%

	% Events	Median (95% CI)
Pembro	22.0%	NR (NR–NR)
Placebo	30.3%	NR (NR–NR)

Median follow-up: 24.1 (14.9–41.5) months.

No. at Risk

Pembro	496	457	414	371	233	151	61	21	1	0
Placebo	498	436	389	341	209	145	56	19	1	0

Choueiri, ASCO 2021

Interim Overall Survival

Choueiri, ASCO 2021
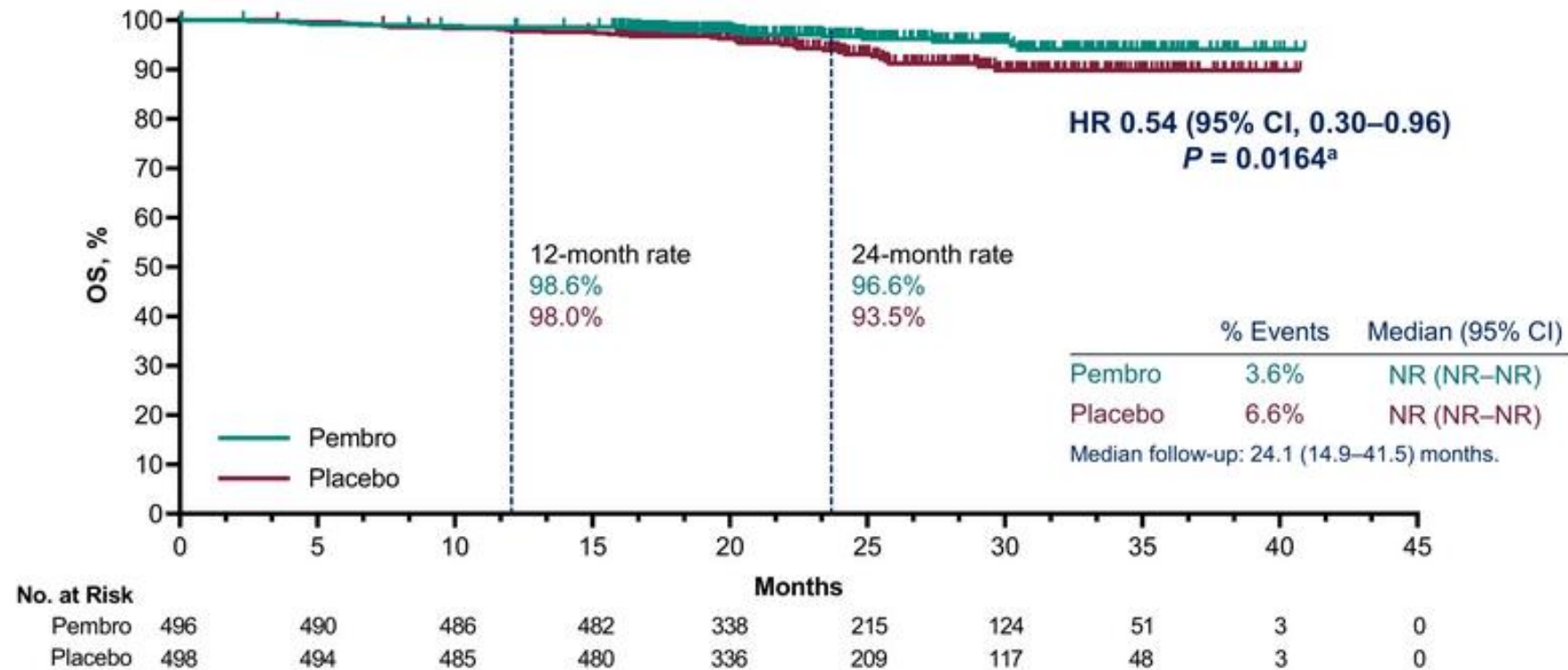
Safety

| Participants with ≥1 AE, n (%)	Pembro N = 488	Placebo N = 496
All-cause AEs	470 (96.3)	452 (91.1)
Grade 3–5	158 (32.4)	88 (17.7)
Led to treatment discontinuation	101 (20.7)	10 (2.0)
Led to death	2 (0.4)	1 (0.2)
Serious all-cause AEs[a]	100 (20.5)	56 (11.3)
Led to treatment discontinuation	49 (10.0)	5 (1.0)
Treatment-related AEs	386 (79.1)	265 (53.4)
Grade 3–5	92 (18.9)	6 (1.2)
Led to treatment discontinuation	86 (17.6)	3 (0.6)
Led to death	0	0

Pembrolizumab plus axitinib versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma: Results from 42-month follow-up of KEYNOTE-426

Brian I. Rini, *et al*

KEYNOTE-426 Study Design
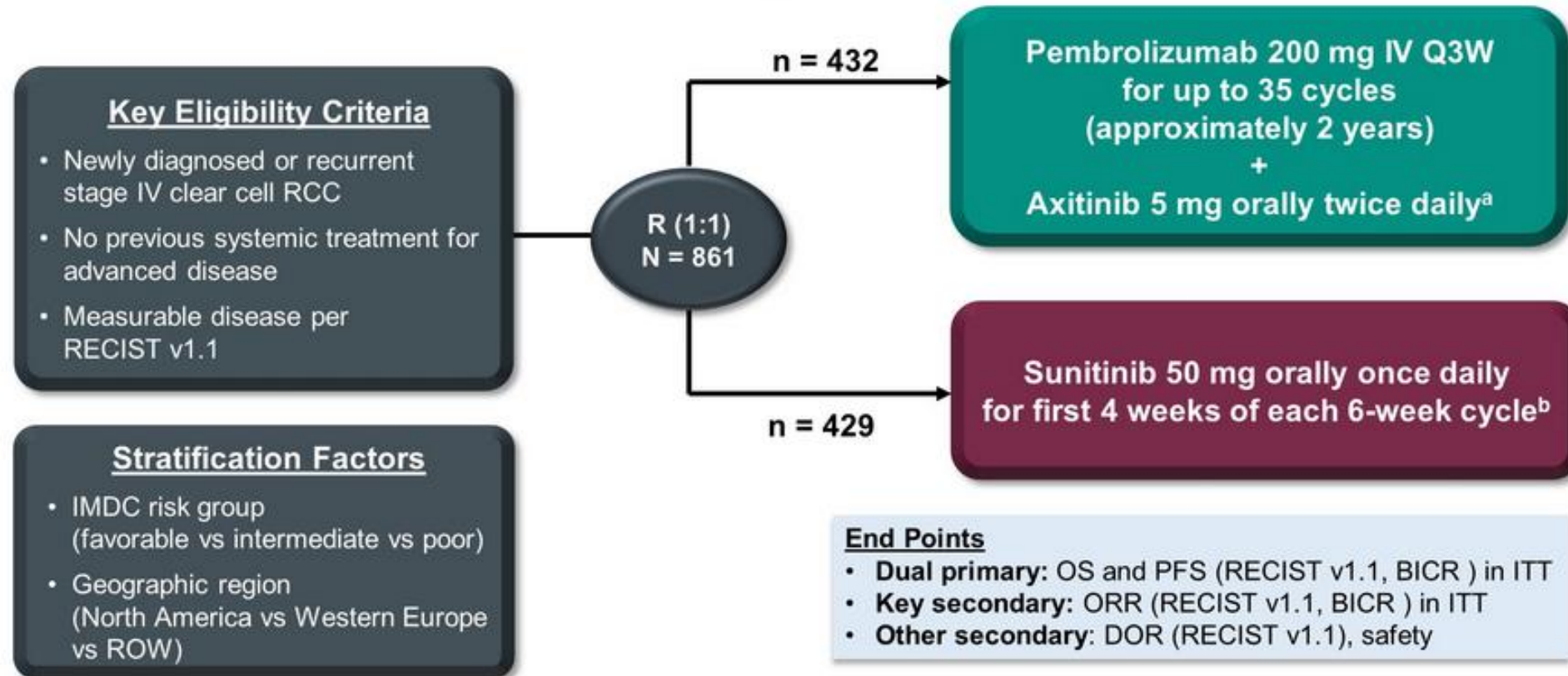
Primary Endpoint: OS
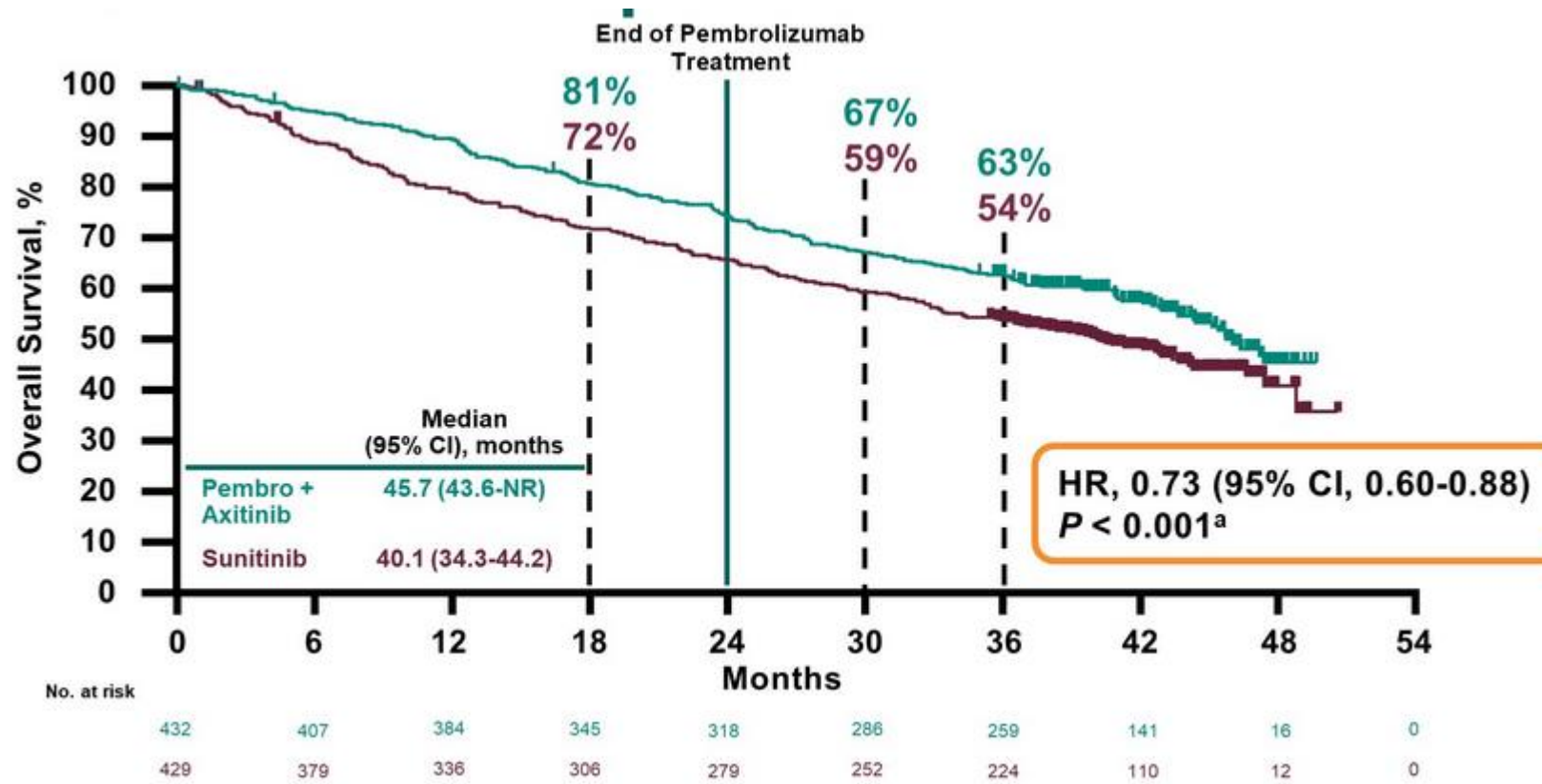
Primary Endpoint: PFS
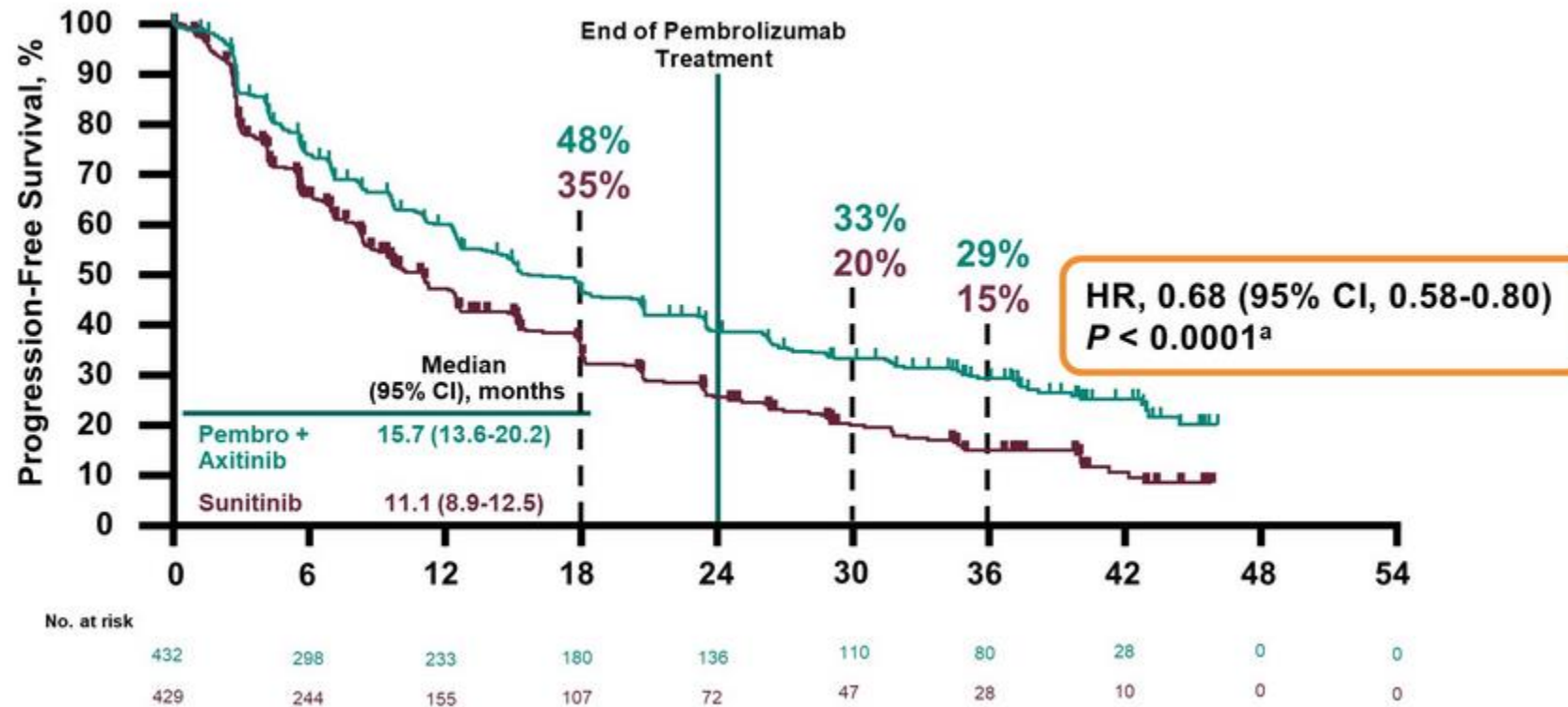
Duration of Response

	Pembro + Axitinib n = 261	Sunitinib n = 170
Time to response, median (range), months	2.8 (1.5-34.8)	3.0 (2.1-26.3)
DOR, median (range), months	23.6 (1.4+ to 43.4+)	15.3 (2.3 to 42.8+)
Response duration, n (%[a])		
≥6 months	215 (87.4)	126 (80.3)
≥12 months	171 (71.1)	92 (62.2)
≥18 months	138 (58.5)	60 (45.5)
≥24 months (end of pembrolizumab treatment)	102 (48.9)	42 (37.1)
≥30 months	87 (44.5)	29 (32.1)

Safety
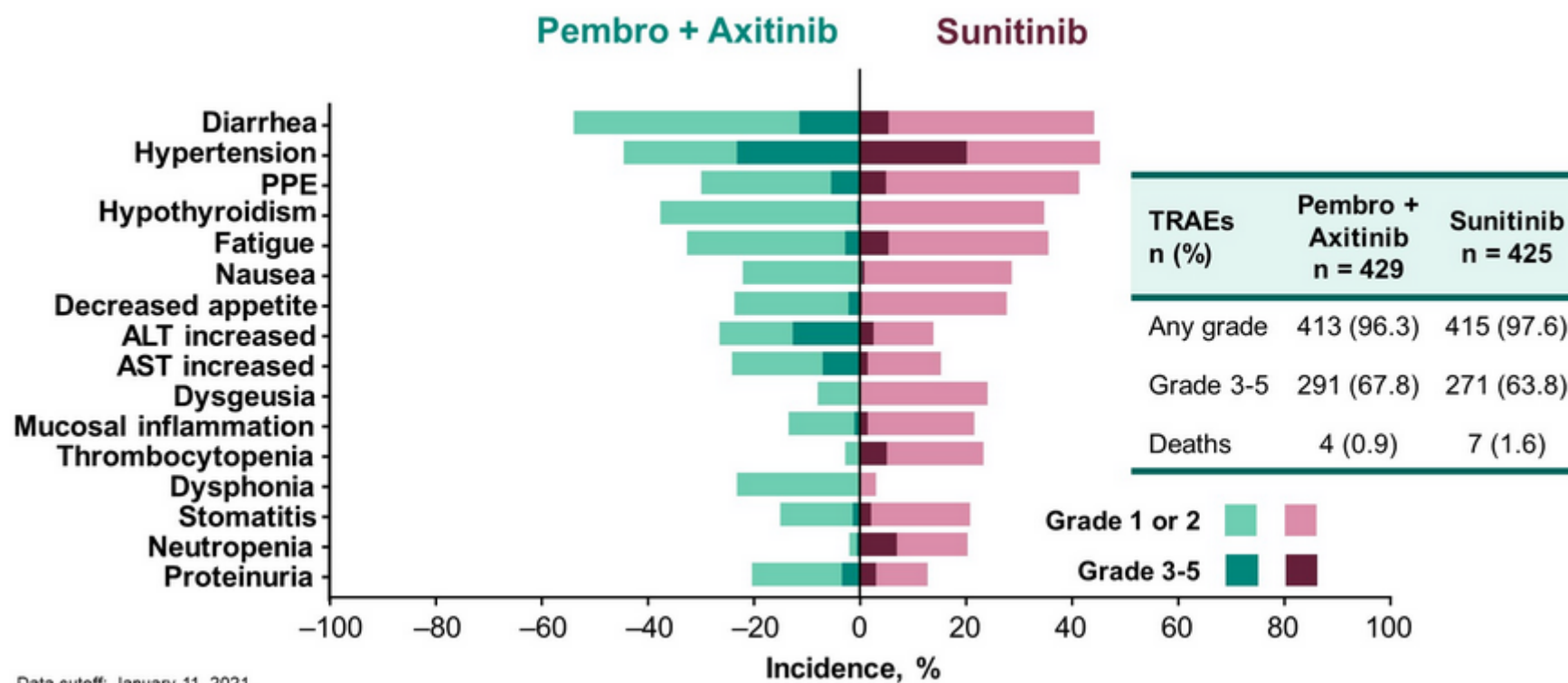
Data cutoff: January 11, 2021.

Rini, ASCO 2021

Pembrolizumab in combination with gemcitabine and concurrent hypofractionated radiation therapy as bladder sparing treatment for muscle-invasive urothelial cancer of the bladder: A multicenter phase 2 trial

Arjun V. Balar, *et al*

Study Design
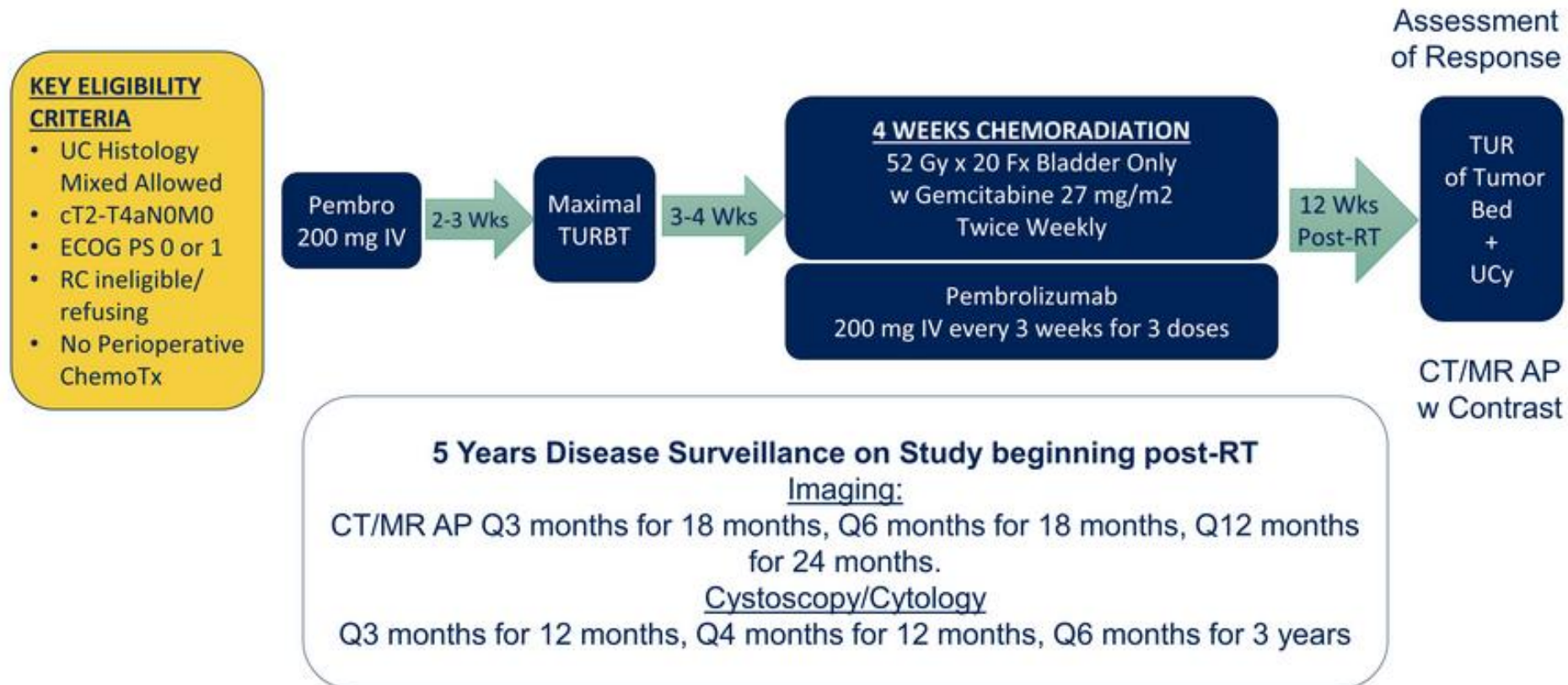
Primary Endpoint

Primary Endpoint: Bladder-Intact Disease-Free Survival - Efficacy Cohort (N=48)

Bladder Intact Disease Free Survival – Phase II Cohort
With Number of Subjects at Risk

1 year estimated BIDFS rate is 88% (95% CI 0.73 – 0.95)
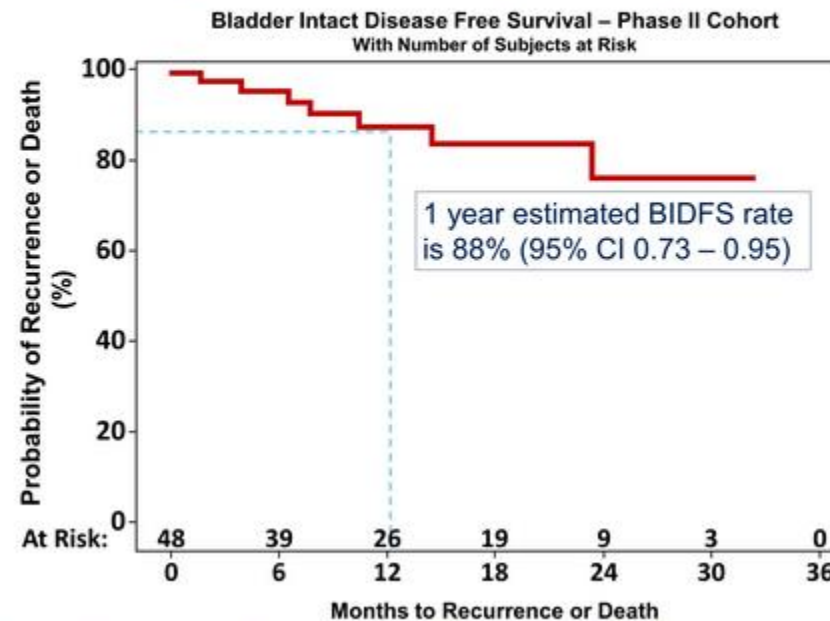
Median Follow up Efficacy Cohort: 14.6 months (1.6 months - 32.3 months)

Secondary Endpoint

Key Secondary Endpoint: Metastases-Free Survival- All Patients (N=54)

Metastases Free Survival With Number of Subjects at Risk

1 year estimated MFS rate: 85% (95% CI 0.71 – 0.93)
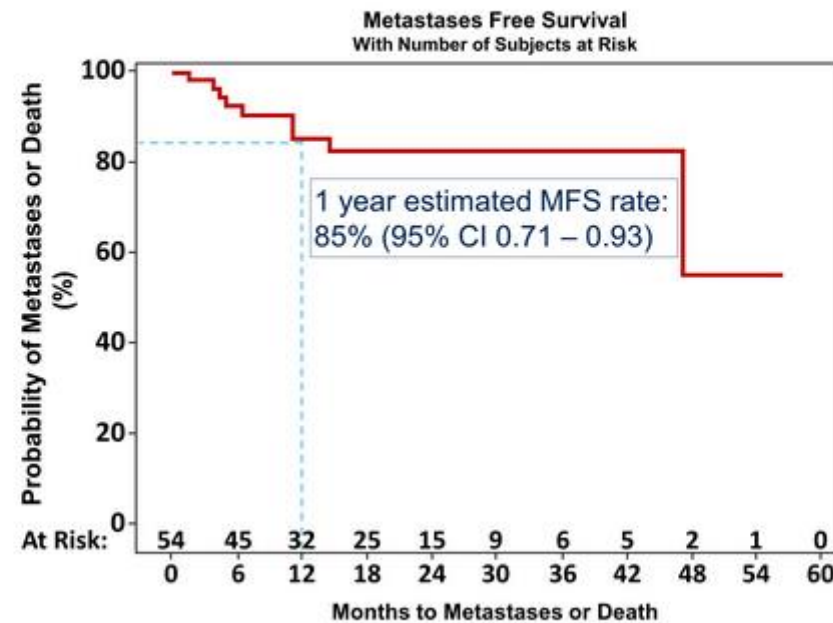
Median Follow up All Patients: 15.5 months (1.6 months – 56.5 months)

Safety

Safety
Treatment-Related Toxicities (N=48)
Efficacy Cohort

	Grade 1 & 2	%
Fatigue	20	41.7%
Nausea	17	35.4%
Diarrhea	16	33.3%
Urinary Urgency	14	29.2%
Rash Maculopapular	11	22.9%
Platelets Decreased	11	22.9%
Anorexia	10	20.8%
Anemia	8	16.7%
White Blood Cell Decreased	8	16.7%
Urinary Tract Pain	6	12.5%
Alanine Aminotransferase	6	12.5%
Aspartate Aminotransferase	6	12.5%
Vomiting	6	12.5%
Chills/Cold/Flu	5	10.4%
Pruritus	5	10.4%
Neutrophil Count Decreased	5	10.4%
Abdominal Pain	4	8.3%
Fever	4	8.3%
Urinary Incontinence	4	8.3%
GI Urgency	3	6.3%
Arthralgia/Arthritis	3	6.3%
Rectal Pain/Spasms	3	6.3%
Bladder Spasms	3	6.3%

	Grade 3 & 4	%
Diarrhea	2	4.2%
Lymphocyte Count Decreased	2	4.2%
Colitis	2	4.2%
Fatigue	1	2.1%
Anemia	1	2.1%
Urinary Tract Pain	1	2.1%
Abdominal Pain	1	2.1%
Hypokalemia	1	2.1%
Hyponatremia	1	2.1%
Urinary Tract Infection	1	2.1%
Neutropenia	1	2.1%
Febrile Neutropenia	1	2.1%
Protein Losing Enteropathy	1	2.1%
Immune-Related Polyneuropathy	1	2.1%
Colonic Perforation	1	2.1%

1 patient developed treatment-related Grade 4 colonic perforation which was treated, but subsequently developed multiple complications and died due to fungemia/sepsis

First-line pembrolizumab in cisplatin-ineligible patients with advanced urothelial cancer: Response and survival results up to 5 years from the KEYNOTE-052 Phase 2 study

Peter H. O'Donnell, *et al*

KEYNOTE-052 Study Design

Key Eligibility Criteria

- Histologically or cytologically confirmed locally advanced/metastatic UC of the renal pelvis, ureter, bladder, or urethra
- Measurable disease based on RECIST v1.1 per independent central review
- No prior systemic chemotherapy for UC[a]
- Ineligible for cisplatin-based chemotherapy
- ECOG PS 0-2

N = 370

Pembrolizumab 200 mg IV Q3W

Disease status and tumor response assessed by CT/MRI 9 weeks after first Pembrolizumab dose, then Q6W for 12 months and Q12W thereafter[b]

- Primary end point: confirmed ORR per RECIST v1.1 by independent radiology review
- Secondary end points: PFS and DOR per RECIST v1.1 by independent radiology review, OS, safety
- End points analyzed for the overall population, patients with PD-L1 CPS ≥10 and CPS <10[c]

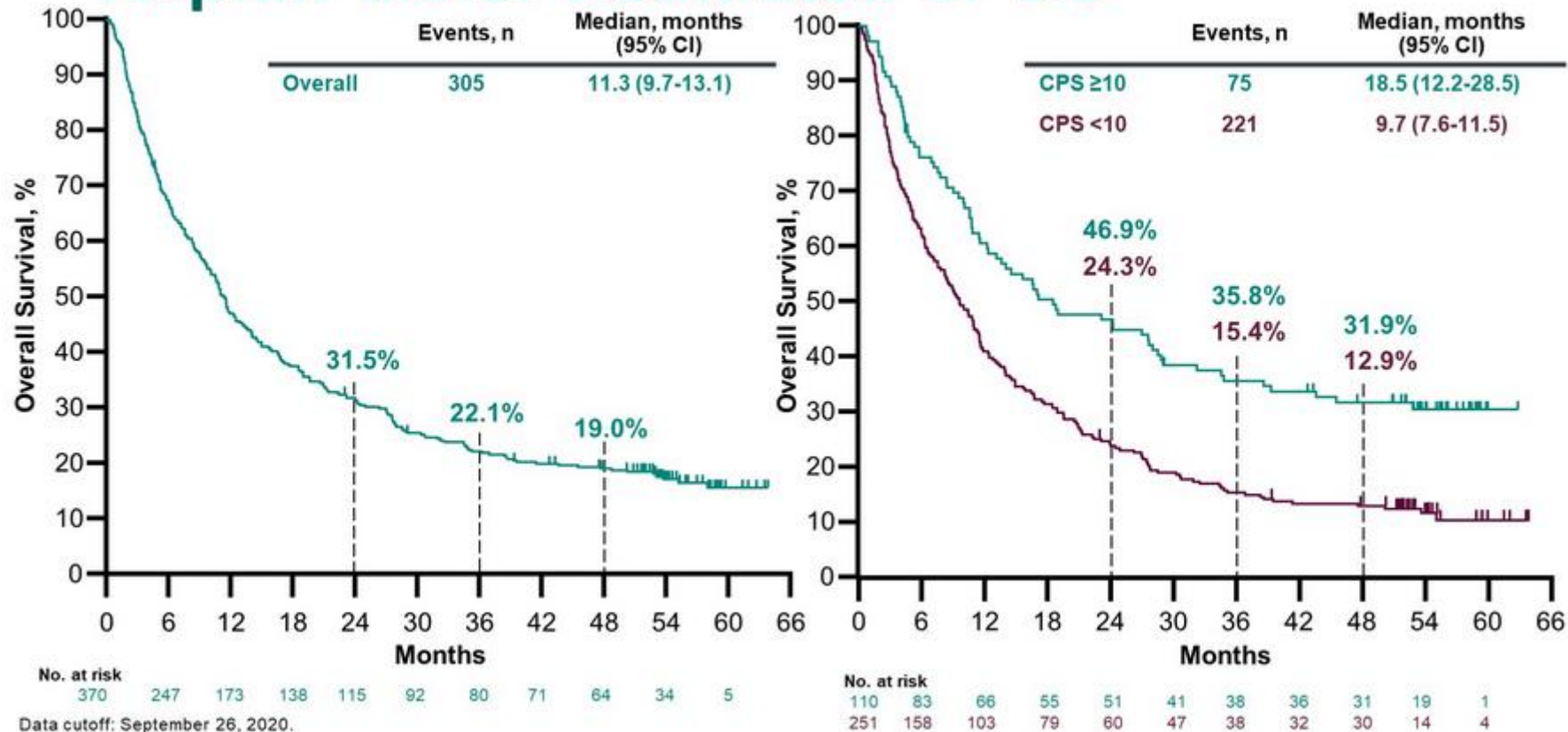# Duration of Response

Kaplan-Meier Estimates of DOR
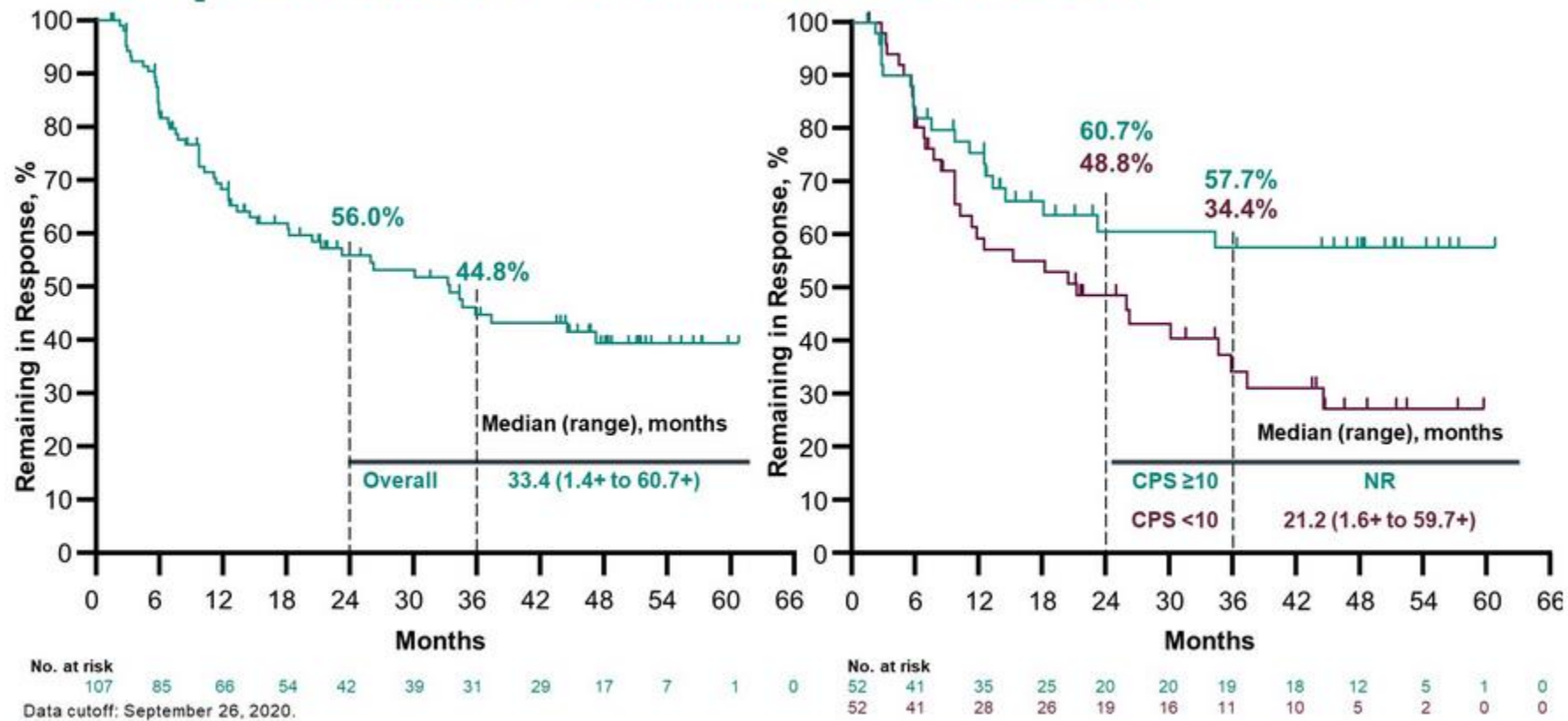
# Overall Survival

Kaplan-Meier Estimates of OS

O'Donnell, ASCO 2021

Safety

n (%)	Pembrolizumab N = 370
Any-grade AE	361 (97.6)
Any-grade TRAE[a]	249 (67.3)
Grade 3-5 TRAE	78 (21.1)
Serious TRAE	43 (11.6)
Death due to TRAE[b]	1 (0.3)
Discontinued[c] because of a TRAE	35 (9.5)
Discontinued because of a serious TRAE	16 (4.3)

TRAEs With ≥5% Incidence	Pembrolizumab N = 370	
	Any Grade	Grade 3-5
Pruritis	68 (18.4)	3 (0.8)
Fatigue	67 (18.1)	9 (2.4)
Rash	45 (12.2)	2 (0.5)
Decreased appetite	40 (10.8)	2 (0.5)
Hypothyroidism	37 (10.0)	0 (0)
Diarrhea	34 (9.2)	4 (1.1)
Nausea	32 (8.6)	1 (0.3)

O'Donnell, ASCO 2021

Primary Endpoint

Confirmed ORR per RECIST v1.1
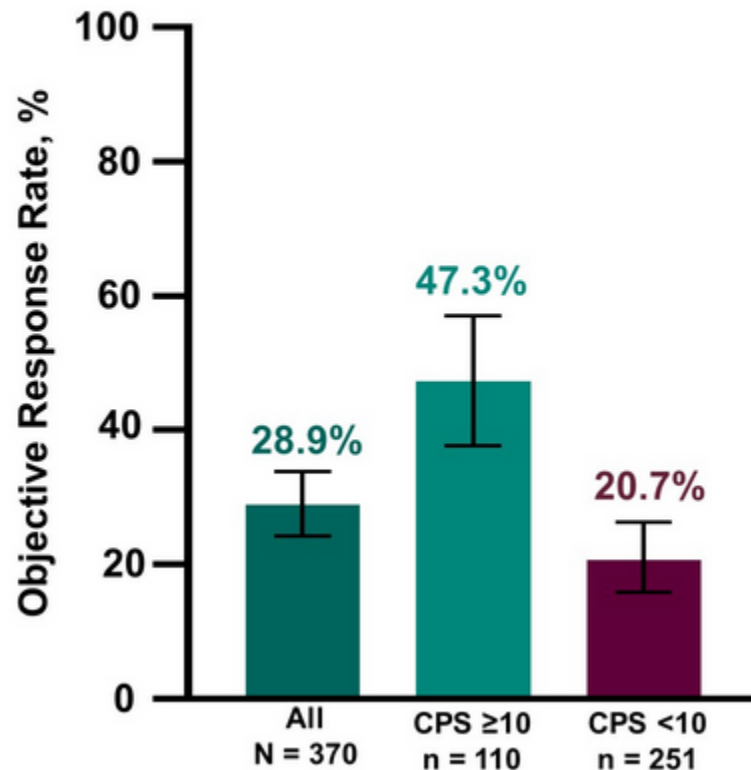
Best Response n (%)	All Patients N = 370	CPS ≥10 n = 110	CPS <10 n = 251
CR	35 (9.5)	23 (20.9)	10 (4.0)
PR	72 (19.5)	29 (26.4)	42 (16.7)
SD	67 (18.1)	22 (20.0)	44 (17.5)
PD	155 (41.9)	30 (27.3)	121 (48.2)
NA[a]	32 (8.6)	6 (5.5)	25 (10.0)
NE[b]	9 (2.4)	0 (0)	9 (3.6)

Take-aways for Genitourinary Cancers

- Adjuvant immunotherapy with pembrolizumab demonstrated benefit in RFS and OS post nephrectomy in high risk kidney cancer.

- Immune checkpoint inhibitor based therapy shows durable remissions in kidney cancer even after therapy is stopped.

- Cisplatin ineligible patients have promising duration of response and prolonged remission in advanced urothelial cancer.

- Low dose gemcitabine and hypofractionated RT and pembrolizumab show remarkable results of >80% patients free of metastases and local control at 12 months timepoint
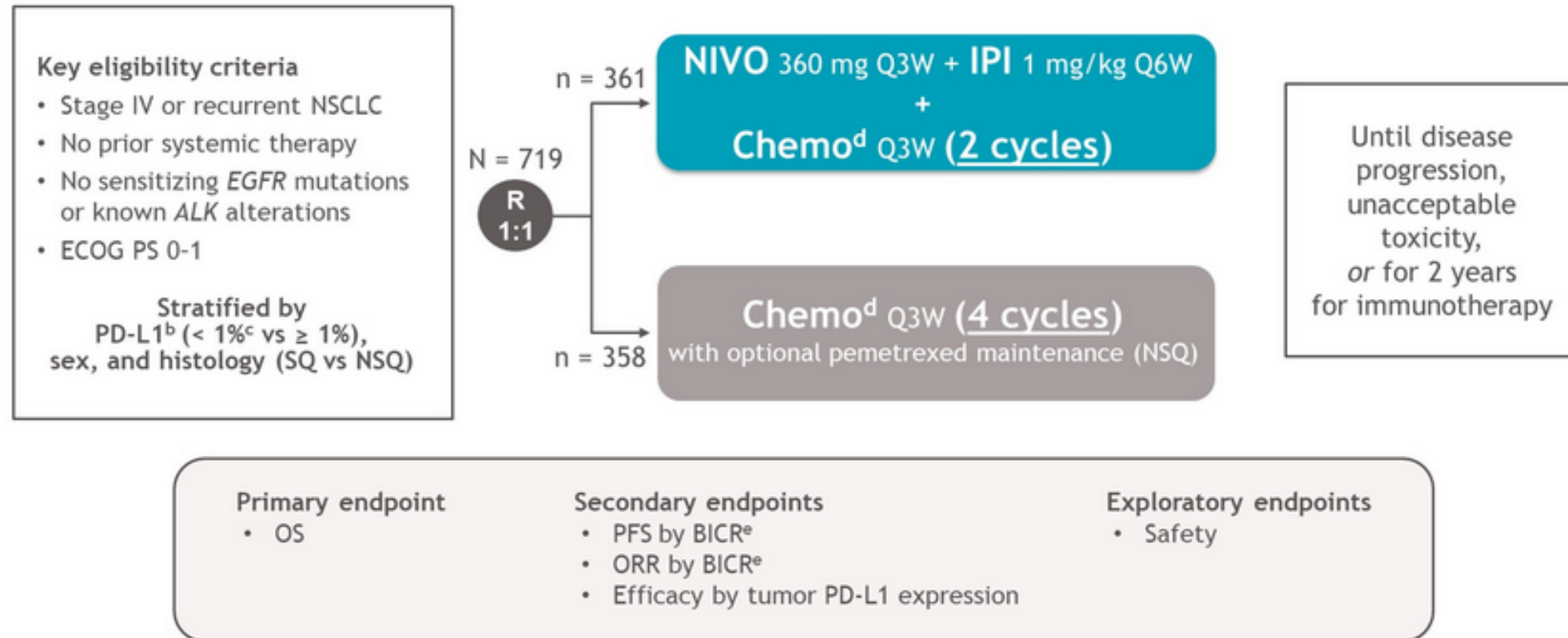
Lung cancer

Jarushka Naidoo

Beaumont RCSI Cancer Centre Dublin

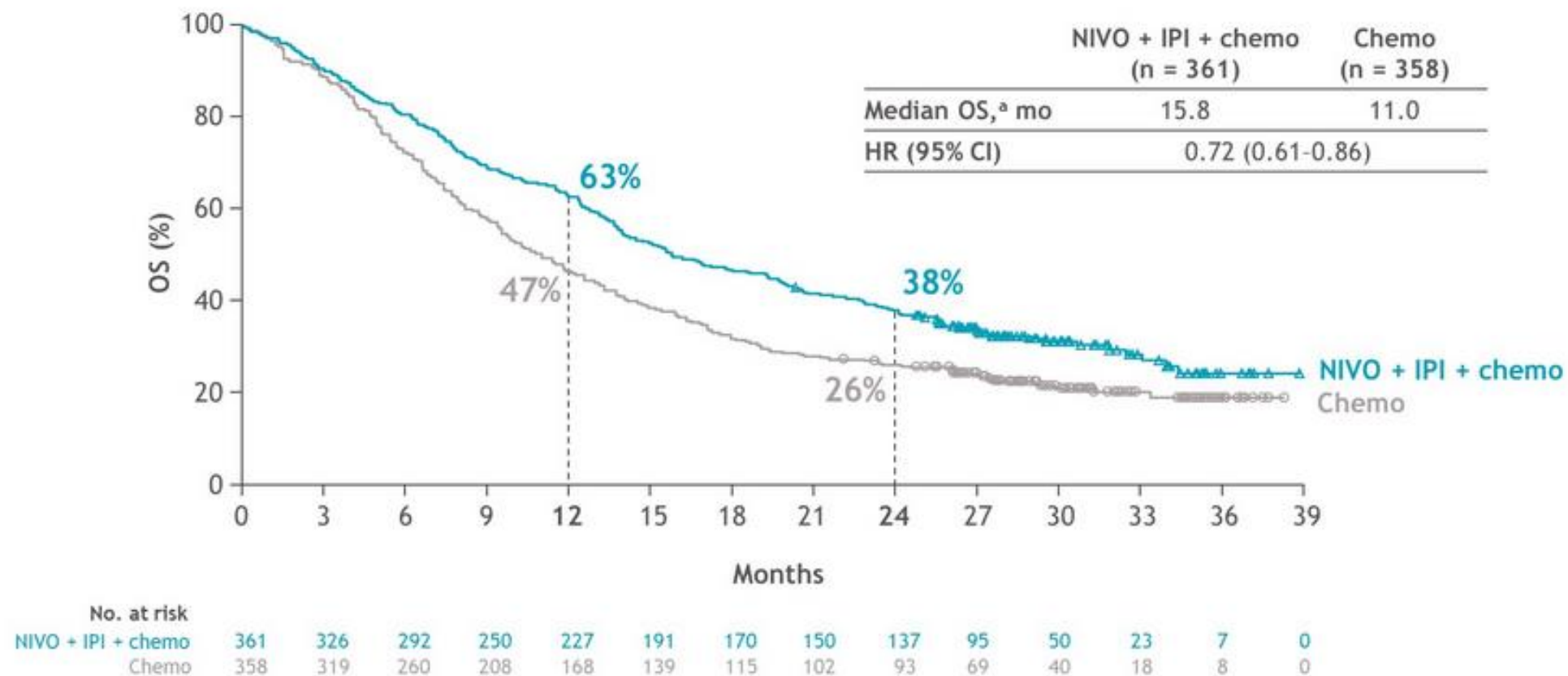Adjunct Assistant Professor, Johns Hopkins University

First-line nivolumab (NIVO) plus ipilimumab (IPI) plus two cycles of chemotherapy (chemo) versus chemo alone (4 cycles) in patients with advanced non-small cell lung cancer (NSCLC): Two-year update from CheckMate 9LA
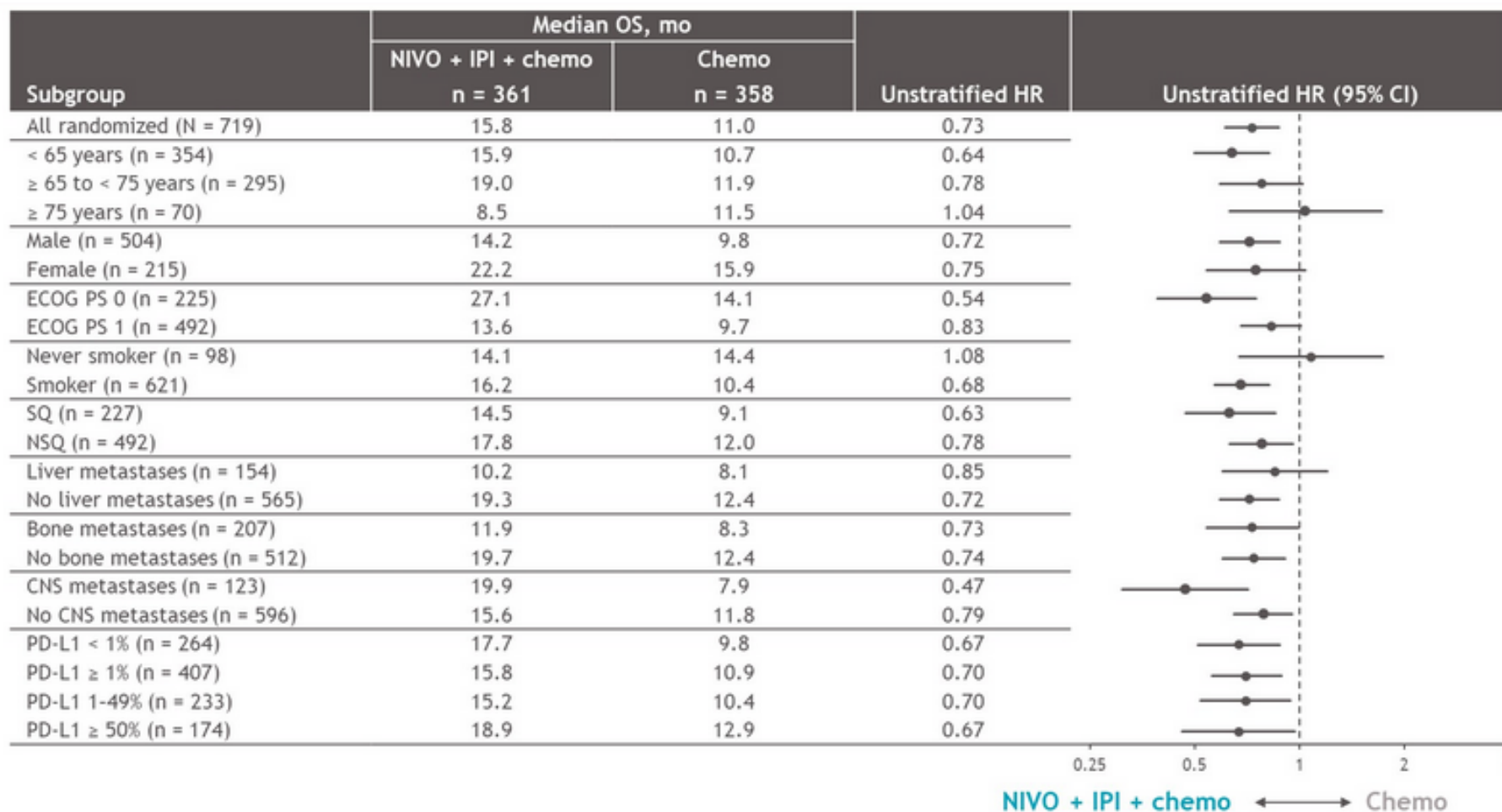
Martin Reck, *et al*

CheckMate 9LA Study Design

Key eligibility criteria
- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No sensitizing *EGFR* mutations or known *ALK* alterations
- ECOG PS 0-1

Stratified by PD-L1[b] (< 1%[c] vs ≥ 1%), sex, and histology (SQ vs NSQ)

N = 719

R 1:1

n = 361

NIVO 360 mg Q3W + **IPI** 1 mg/kg Q6W
+
Chemo[d] Q3W (**2 cycles**)

n = 358

Chemo[d] Q3W (**4 cycles**)
with optional pemetrexed maintenance (NSQ)

Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy

Primary endpoint
- OS

Secondary endpoints
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

Exploratory endpoints
- Safety

Primary Endpoint: Overall Survival

	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
Median OS,[a] mo	15.8	11.0
HR (95% CI)	0.72 (0.61-0.86)	

No. at risk

NIVO + IPI + chemo	361	326	292	250	227	191	170	150	137	95	50	23	7	0
Chemo	358	319	260	208	168	139	115	102	93	69	40	18	8	0

Reck, ASCO 2021

Subgroup Analysis

Subgroup	Median OS, mo		Unstratified HR	Unstratified HR (95% CI)
	NIVO + IPI + chemo n = 361	Chemo n = 358		
All randomized (N = 719)	15.8	11.0	0.73	
< 65 years (n = 354)	15.9	10.7	0.64	
≥ 65 to < 75 years (n = 295)	19.0	11.9	0.78	
≥ 75 years (n = 70)	8.5	11.5	1.04	
Male (n = 504)	14.2	9.8	0.72	
Female (n = 215)	22.2	15.9	0.75	
ECOG PS 0 (n = 225)	27.1	14.1	0.54	
ECOG PS 1 (n = 492)	13.6	9.7	0.83	
Never smoker (n = 98)	14.1	14.4	1.08	
Smoker (n = 621)	16.2	10.4	0.68	
SQ (n = 227)	14.5	9.1	0.63	
NSQ (n = 492)	17.8	12.0	0.78	
Liver metastases (n = 154)	10.2	8.1	0.85	
No liver metastases (n = 565)	19.3	12.4	0.72	
Bone metastases (n = 207)	11.9	8.3	0.73	
No bone metastases (n = 512)	19.7	12.4	0.74	
CNS metastases (n = 123)	19.9	7.9	0.47	
No CNS metastases (n = 596)	15.6	11.8	0.79	
PD-L1 < 1% (n = 264)	17.7	9.8	0.67	
PD-L1 ≥ 1% (n = 407)	15.8	10.9	0.70	
PD-L1 1-49% (n = 233)	15.2	10.4	0.70	
PD-L1 ≥ 50% (n = 174)	18.9	12.9	0.67	

0.25   0.5   1   2   4

NIVO + IPI + chemo ← → Chemo

Efficacy in Patients who Discontinued due to TRAEs
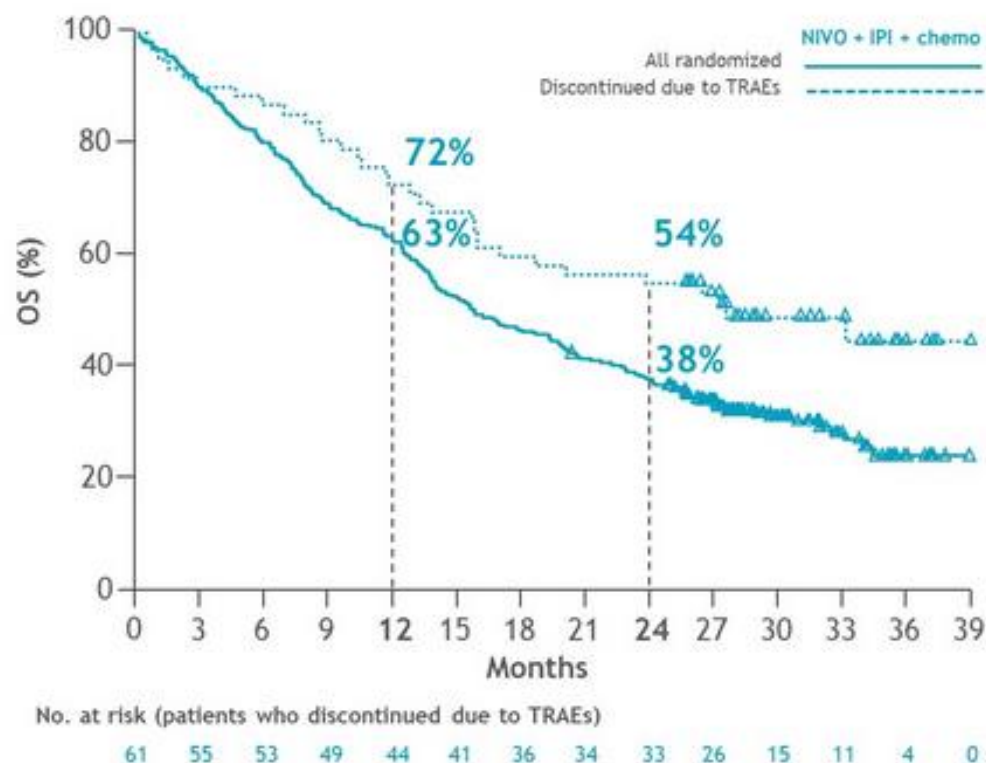
Patients who discontinued all components of NIVO + IPI + chemo due to TRAEs

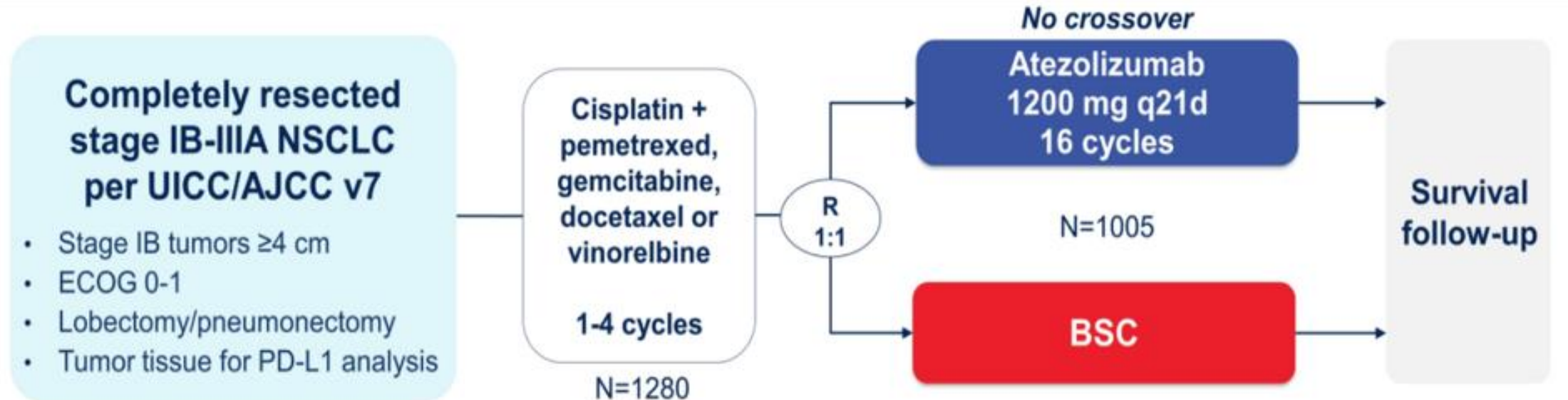|	NIVO + IPI + chemo (n = 61)
Median OS,[b] mo	27.5
2-year OS rate, %	54
ORR, n (%)	31 (51)
Median DOR after discontinuation,[c] mo	14.5
Ongoing response for ≥ 1 year after discontinuation,[c] %	56

Among patients who discontinued all components of NIVO + IPI + chemo due to TRAEs:
- Median (range) number of doses was 7 (1–33) for NIVO and 3 (1–17) for IPI
- Median (range) duration of treatment was 4.4 (0–23.3) months

IMpower010: Primary results of a phase III global study of atezolizumab versus best supportive care after adjuvant chemotherapy in resected stage IB-IIIA non-small cell lung cancer (NSCLC)

Heather A. Wakelee, *et al*

IMpower 010: Study Design

Completely resected stage IB-IIIA NSCLC per UICC/AJCC v7
- Stage IB tumors ≥4 cm
- ECOG 0-1
- Lobectomy/pneumonectomy
- Tumor tissue for PD-L1 analysis

Cisplatin + pemetrexed, gemcitabine, docetaxel or vinorelbine

1-4 cycles

N=1280

R 1:1

No crossover

Atezolizumab 1200 mg q21d 16 cycles

N=1005

BSC

Survival follow-up

Primary Endpoint: DFS
- PD-L1 >= 1%
- All comers stage IIA-III
- All comers stage IB-III
- OS

Baseline Characteristics
- N=1005
- 65.6% (659) non-squamous
- Stage: IB (12.2%); II (46.7%); III (41.1%)
- 54.6% PD-L1 >= 1% (SP263)

Wakelee, ASCO 2021

Primary Endpoint: Disease-free Survival

	PD-L1>=1%	All Stage II-IIIA	ITT, Stage IB-IIIA
DFS	0. 66 (0.5-0.88)	0.79 (0.64-0.96)	0.81 (0.67-0.99)
P-value	0.004	0.02	0.04

Wakelee, ASCO 2021

Overall Survival

PD-L1 TC ≥ 1% stage II-IIIA — HR,ᵃ 0.77 (95% CI 0.51, 1.17)

All-randomized stage II-IIIA — HR,ᵃ 0.99 (95% CI 0.73, 1.33)

ITT — HR,ᵃ 1.07 (95% CI 0.80, 1.42)
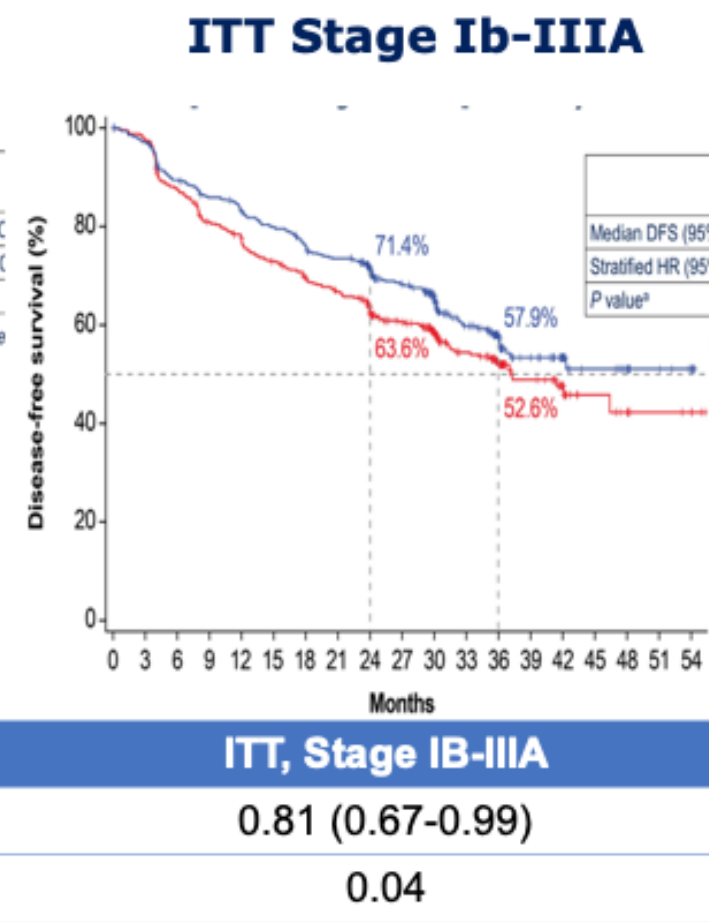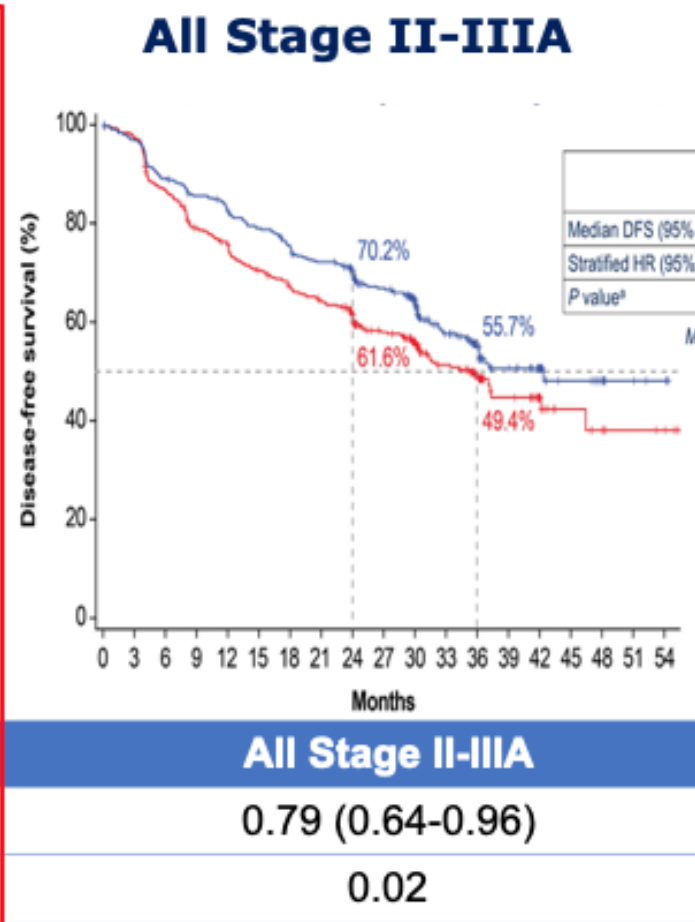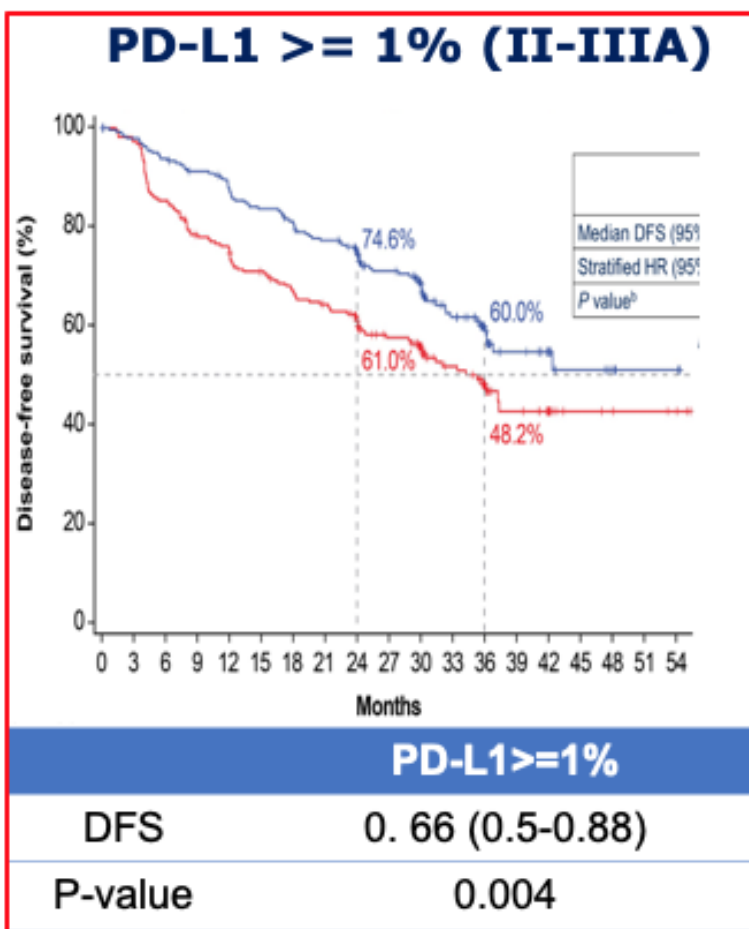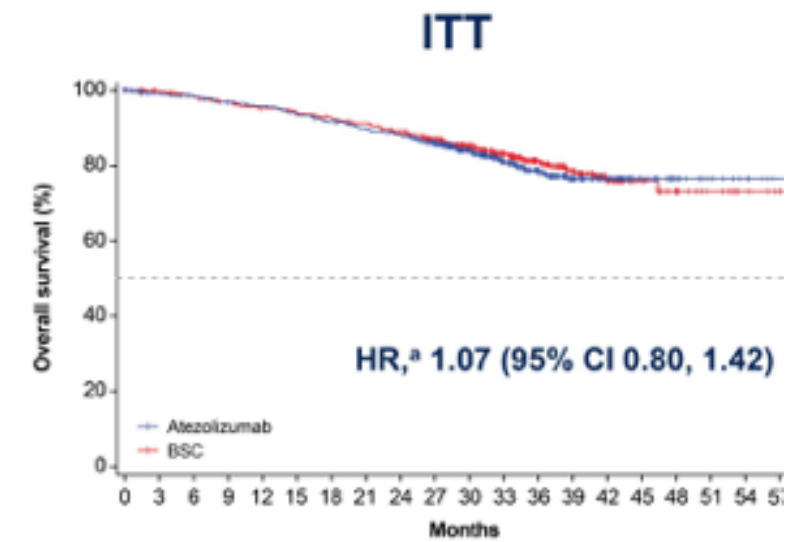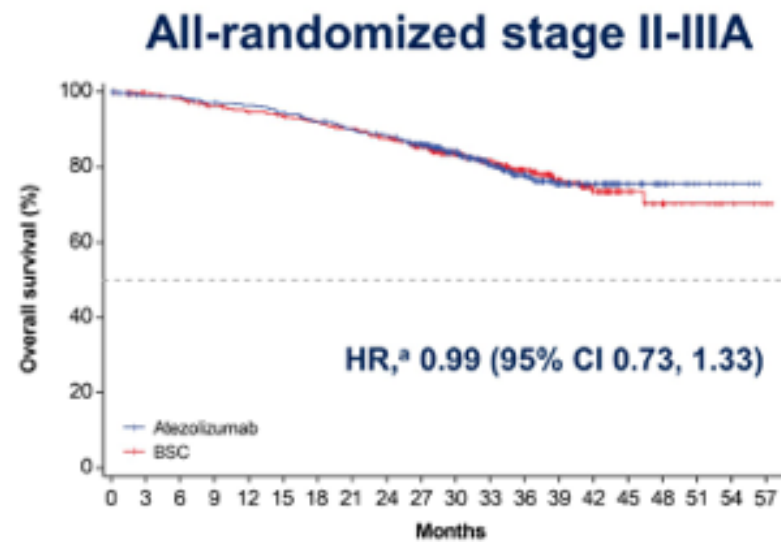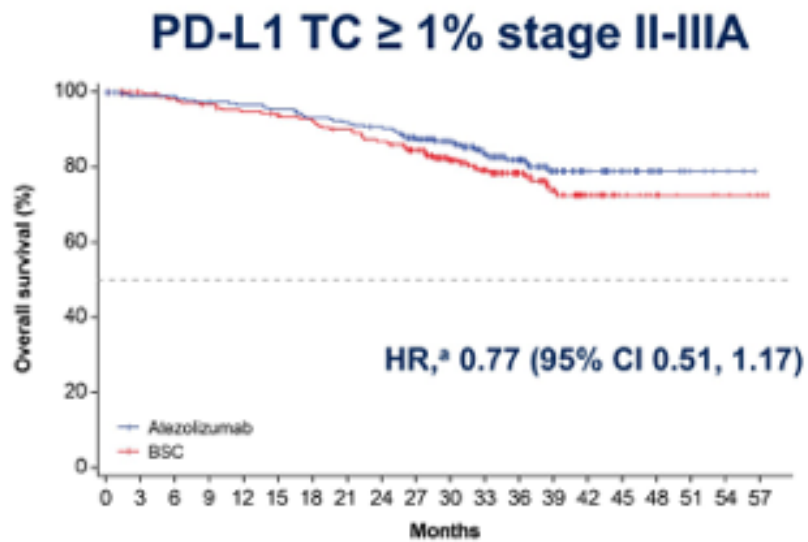
Adverse Events

	Atezolizumab (n=495)	BSC (n=495)
Treatment-related AE	335 (67.7)	
G3-4 Treatment-related AE	53 (10.7)	
Immune-related AE	256 (51.7)	47 (8.5)
G3-4 Immune-related AE	39 (7.9)	3 (0.6)
AE leading to atezolizumab discontinuation	90 (18.2)	

Surgical outcomes from the phase 3 CheckMate 816 trial: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer (NSCLC)

Jonathan Spicer, *et al*

CheckMate 816: Study Rationale

CM816: Nivo+Chemo vs. Chemo in Early Stage NSCLC

- Neoadjuvant immunotherapy have shown encouraging pCR, EFS, and OS in resectable NSCLC

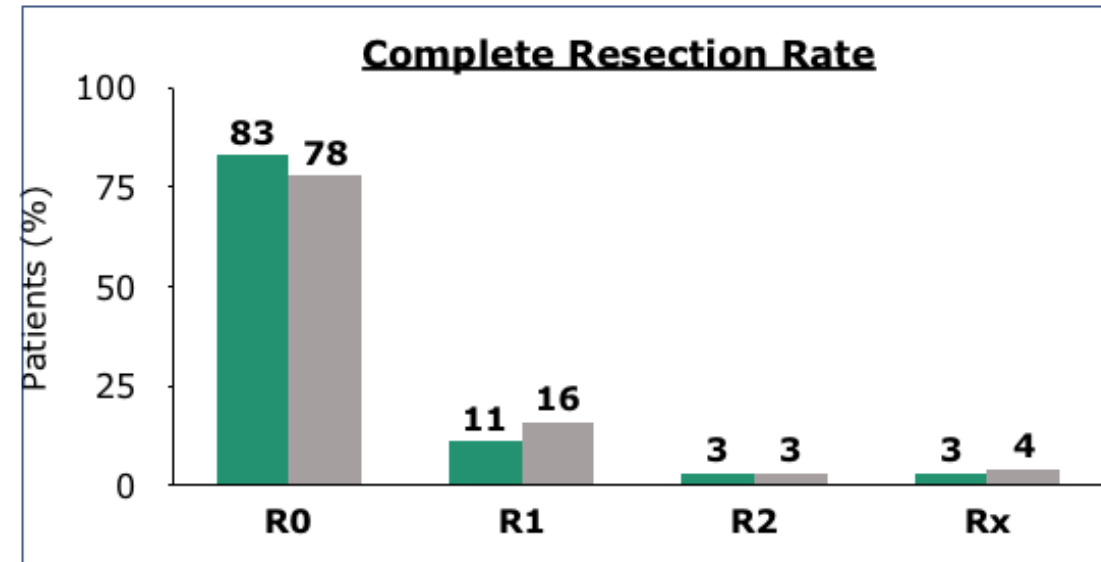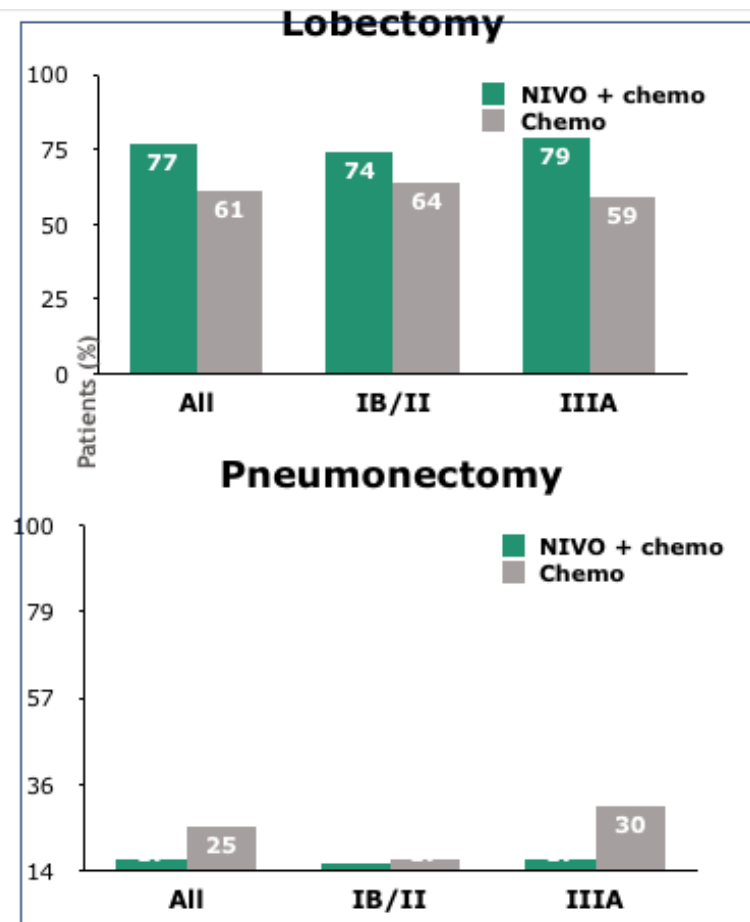- Neoadjuvant NIVO + chemo showed significant improvement in pCR vs chemo
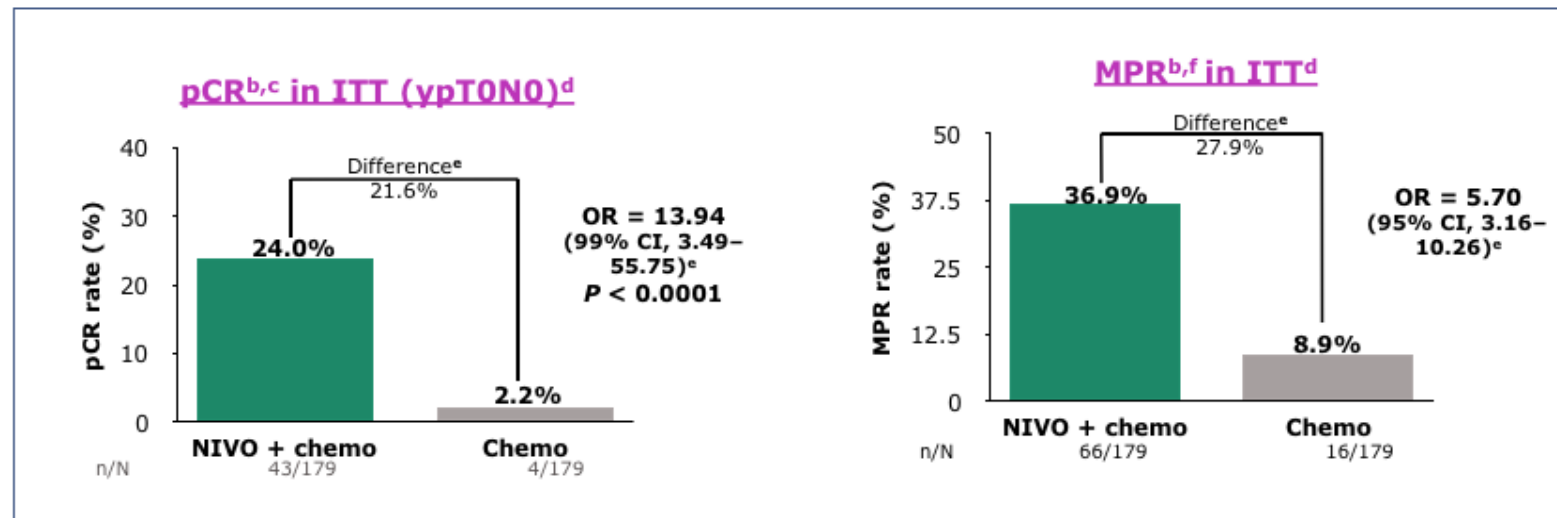
CheckMate 816: Study Design

Spicer, ASCO 2021
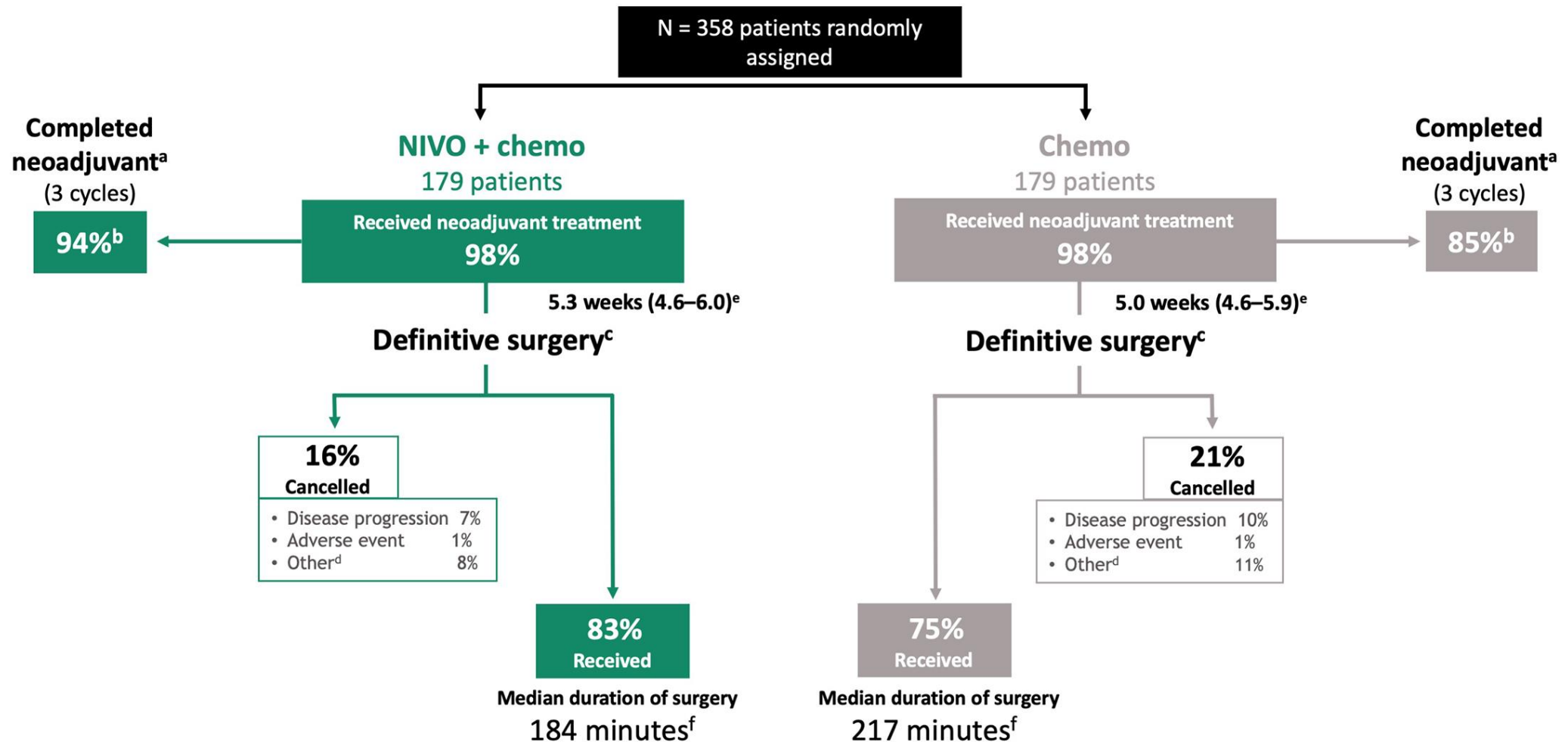
Primary Endpoint: pCR
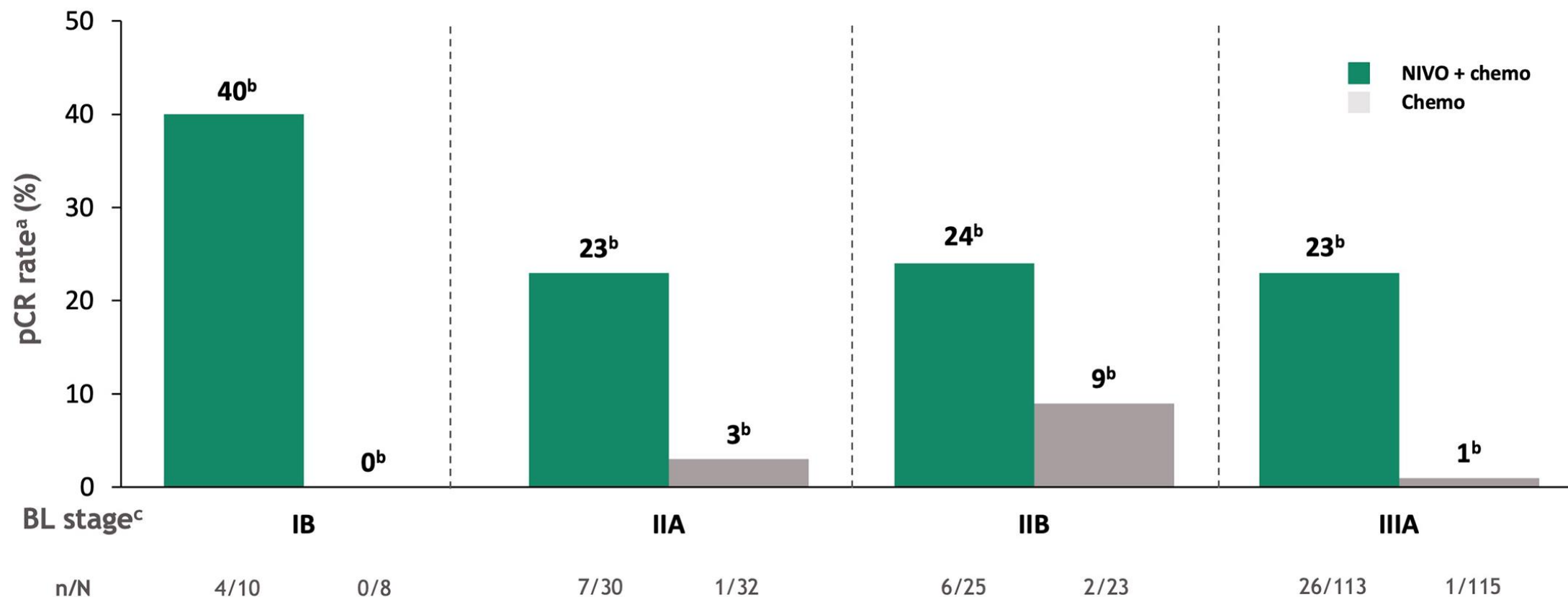
- pCR improvement with NIVO + chemo vs chemo was observed regardless of radiologic down-staging[d]

Spicer, ASCO 2021

Surgical Outcomes

Biomarker tissue journey among patients (pts) with untreated metastatic non-small cell lung cancer (mNSCLC) in the U.S. Oncology Network community practices

Nicholas J. Robert, *et al*

Study Design

Methods

- Retrospective, observational chart review

- Patients with mNSCLC initiating 1L systemic therapy between April 1, 2018 and March 31, 2020

- Data from practices within the US Oncology Network of community oncology practices that utilize a similar electronic health record
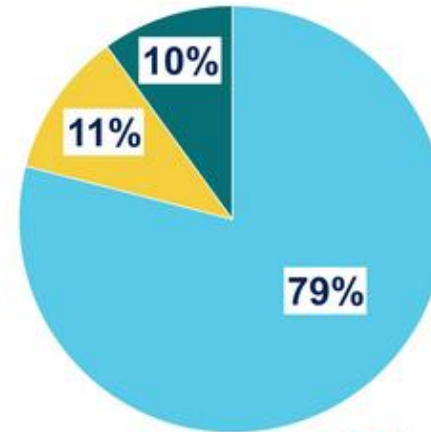
Objectives

- Testing rates for ALK, BRAF, EGFR, ROS1, PD-L1

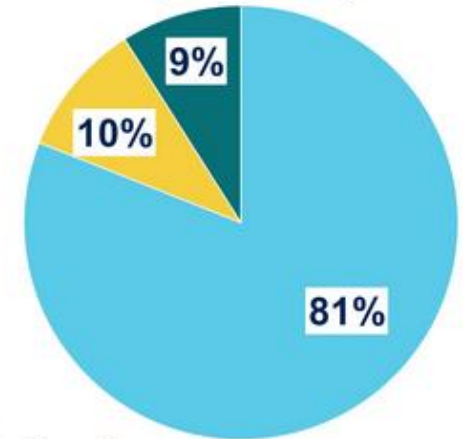- Timing of biomarker receipt of test results

- Turnaround times

Biomarker Testing Rates

| Test types	Overall N=3474	Nonsquamous N=2820
EGFR	70%	76%
ALK	70%	76%
ROS1	68%	73%
BRAF	55%	59%
PD-L1	83%	83%
Any biomarker	90%	91%
All 5 biomarker tests	46%	49%
NGS	37%	39%

Overall population (n=3474)

10%
11%
79%

Nonsquamous (N=2820)

9%
10%
81%

- ≥ 1 biomarker test result received before 1L
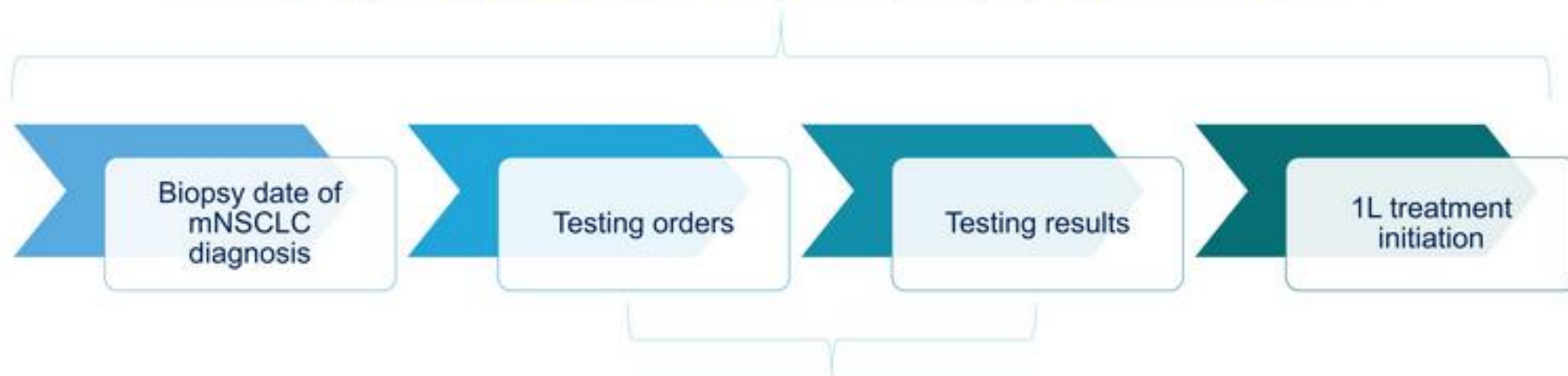- Biomarker test result received after 1L
- No biomarker test

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Biomarker Testing Over Time

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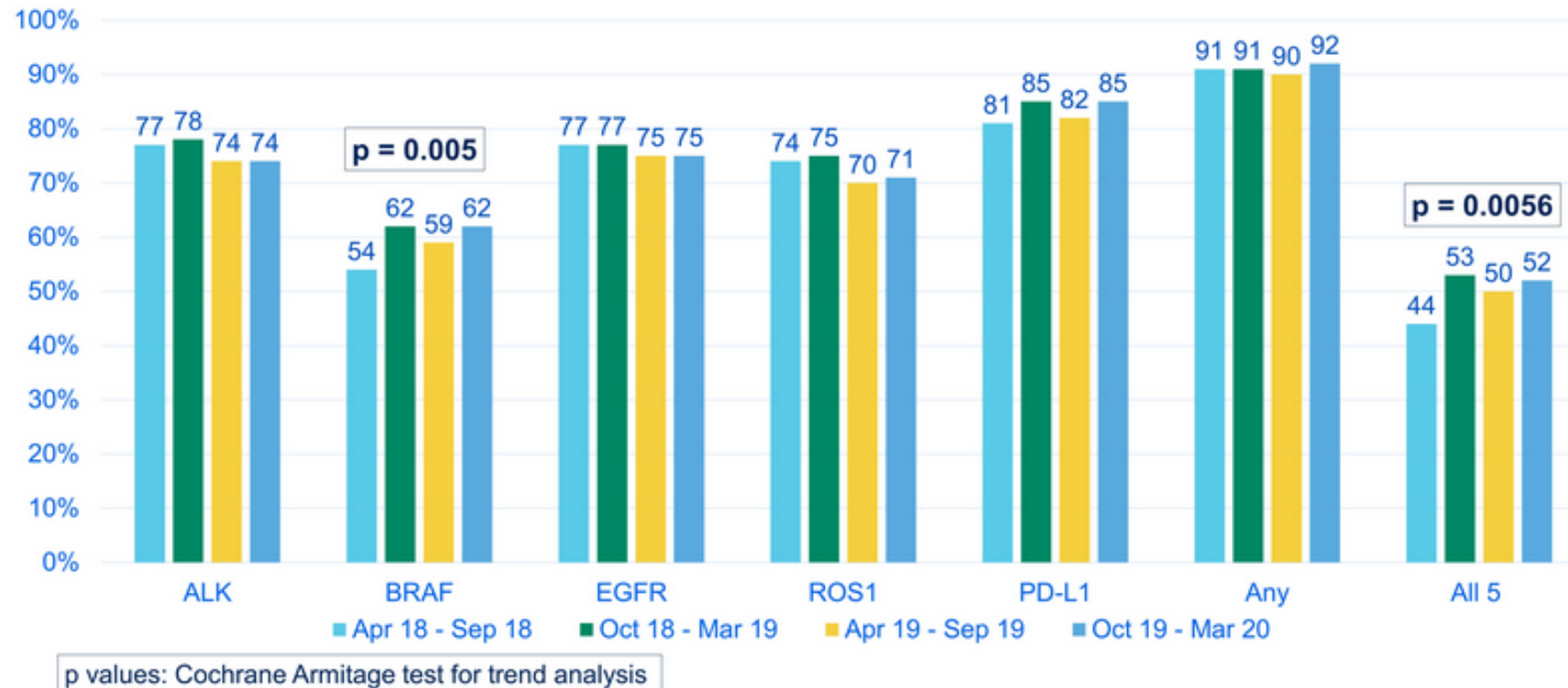
Turnaround Times

Overall time from mNSCLC diagnosis to 1L treatment

Median (IQR) = **35 (22, 55) days** for all patients; **36 (23, 57) for tested patients**

Biopsy date of mNSCLC diagnosis → Testing orders → Testing results → 1L treatment initiation

Time from Order to Results: Median (IQR) = **10 (6, 17)** to **15 (10, 22)** days by individual biomarker
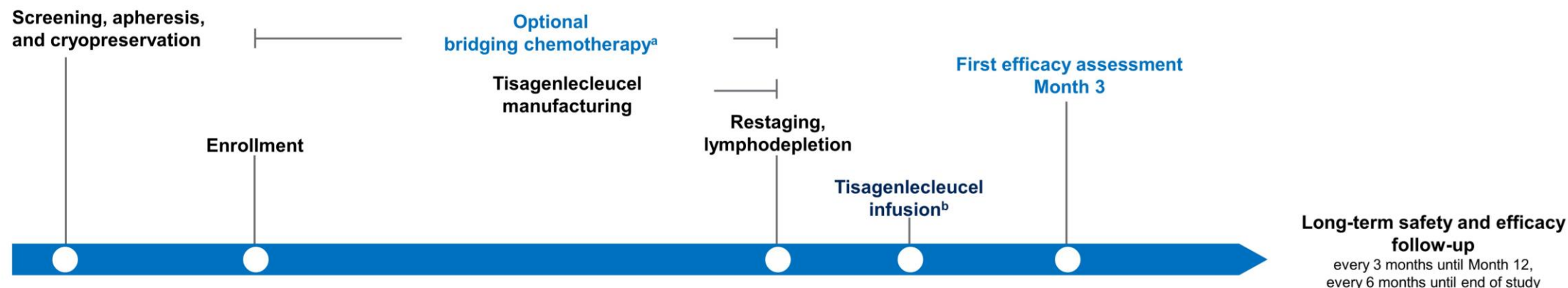
Take-aways for Lung Cancer

- **CM9LA**: Chemo-immunotherapy for Ipi/Nivo/Chemo demonstrates an ongoing tail-on-the-curve at 2 years, those who discontd. therapy for TRAEs continue to benefit from therapy

- **IMPOWER010**: Adjuvant atezolizumab confers a DFS benefit, driven by those with stage II-IIIA NSCLC with a PD-L1 >=1%

- **CM-816**: Neoadjuvant chemo-immunotherapy with nivolumab yields favorable pCR vs. chemotherapy alone, lower rates of pneumonectomy

- **Biomarker testing in NSCLC**: <50% of patients with advanced NSCLC had testing for all 5 biomarkers in community oncology practices across the US. There is room for improvement regarding biomarker testing in NSCLC

Cellular therapies

Efficacy and safety of tisagenlecleucel (Tisa-cel) in adult patients (Pts) with relapsed/refractory follicular lymphoma (r/r FL): Primary analysis of the phase 2 Elara trial

Stephen J. Schuster, *et al*

Study Design

Key eligibility criteria	Study treatment	End points

• ≥18 years of age
• FL grade 1, 2, or 3A
• Relapsed/refractory disease[c]
• No evidence of histological transformation/FL 3B
• No prior anti-CD19 therapy or allogeneic HSCT
	• Lymphodepleting chemotherapy options were
	  • Fludarabine (25 mg/m^2 IV daily for 3 days) + cyclophosphamide (250 mg/m^2 IV daily for 3 days)
	  • Bendamustine 90 mg/m^2 IV daily for 2 days
	• Tisagenlecleucel dose range (single IV infusion) was: 0.6-6×10^8 CAR-positive viable T cells
		Primary: CRR by IRC (Lugano classification 2014)
		
		Secondary: ORR, DOR, PFS, OS, safety, cellular kinetics

[a]Disease was reassessed prior to infusion for all patients requiring bridging therapy. [b]Infusion was conducted on an in- or outpatient basis at investigator discretion. [c]Refractory to ≥ 2nd line of systemic therapy (including an anti-CD20 antibody and alkylating agent) or relapsed within 6 months after ≥ 2nd line of therapy or after an autologous HSCT.
CAR, chimeric antigen receptor; CD, cluster of differentiation; CR, complete response rate; DOR, duration of response; FL, follicular lymphoma; HSCT, hematopoietic stem cell transplant; IRC, Independent Review Committee; IV, intravenous; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.
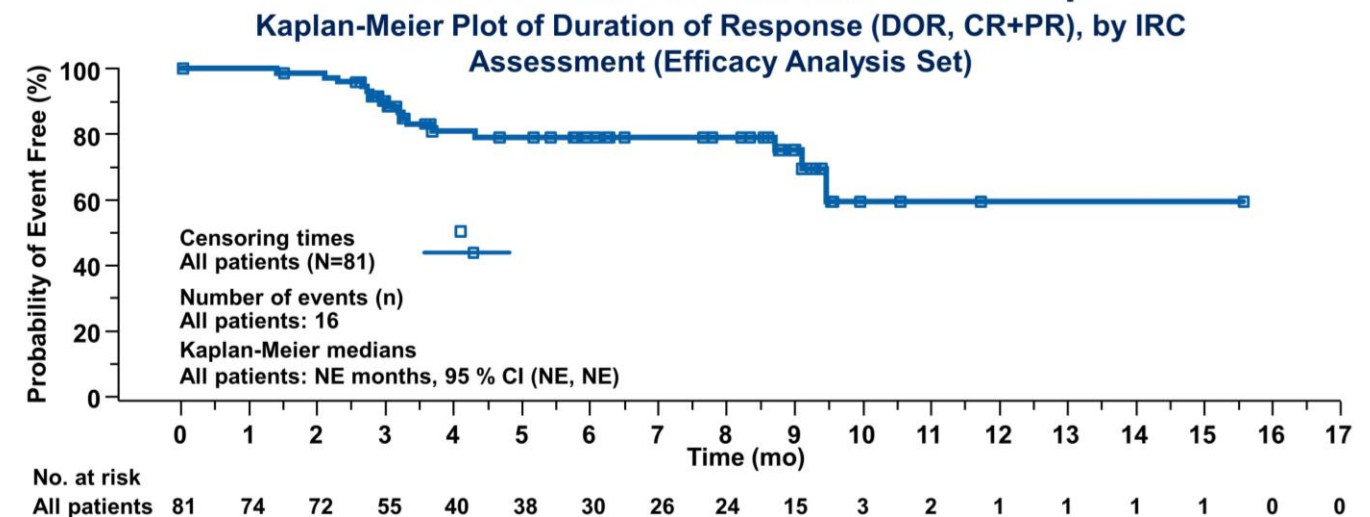
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Primary Endpoint: CRR

Best Overall Response Rate

Response Rate, %	Patients Evaluable for Efficacy[b] (n=94)
CR	66.0[b]
PR	20.2
ORR (CR+PR)	86.2

- Investigator-assessed CRR was 69.1%[c] (ORR 90.4%)
- CRRs/ORRs were comparable among key high-risk subgroups

Median DOR Was Not Reached at 11 Months Median Follow-Up

Kaplan-Meier Plot of Duration of Response (DOR, CR+PR), by IRC Assessment (Efficacy Analysis Set)

Censoring times
All patients (N=81)
Number of events (n)
All patients: 16
Kaplan-Meier medians
All patients: NE months, 95 % CI (NE, NE)

No. at risk
All patients 81 74 72 55 40 38 30 26 24 15 3 2 1 1 1 1 0 0

- Median follow-up for efficacy (n=94): 10.9 (4.3-19.7) months
- Probability for a responding patient to remain in response ≥6 months was 79% (95% CI, 66-87)
- 12 of 31 PRs (38.7%) converted to CRs; all but 1 occurred between Month 3 and Month 6
- Median time to next antilymphoma treatment was not reached

First efficacy assessment conducted at Month 3 (all but 1 responded at Month 3 assessment); probability of remaining in CR > Month 6.
[a]The primary end point was met at interim analysis. [b]P<0.0001; indicates statistical significance (1-sided) at the 0.0025 level so that the null hypothesis CRR ≤0.15 is rejected. [c]95% CI, 58.8-78.3.
CI, confidence interval; CR, complete response; CRR, complete response rate; DOR, duration of response; IRC, Independent Review Committee; NE, not estimable; PR, partial response; ORR, overall response rate.

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Safety

Adverse Events, n (%)	Treated Patients N=97
Any AE (all grade)	96 (99.0)
AEs suspected to be drug-related	75 (77.3)
Any SAE	40 (41.2)
Suspected to be drug-related	28 (28.9)
Any grade 3/4 AE	74 (76.3)
Suspected to be drug-related	44 (45.4)
Death	3 (3.1)
Deaths due to study indication	3 (3.1)
Deaths within 30 days post infusion	0
AE management, n (%)	
Tocilizumab[a]	16 (34)
Corticosteroids[a]	3 (6.4)

AESI (within 8 weeks of infusion)	Treated Patients N=97	
	All grades, %	Grade ≥3, %
Cytokine release syndrome[a,1]	48.5	0
Neurological adverse reactions	9.3	1.0
Infections	18.6	5.2
Tumor lysis syndrome	1.0	1.0
Prolonged depletion of B cells and/or agammaglobulinemia[b]	10.3	0
Hematologic disorders including cytopenias		
Neutropenia[c,d]	30.9	27.8
Anemia[c]	24.7	13.4
Thrombocytopenia[c]	16.5	9.3

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Study Design

Primary Objectives
- Phase 1b: Characterize cilta-cel safety and confirm the recommended phase 2 dose
- Phase 2: Evaluate cilta-cel efficacy

Key Eligibility Criteria
- Progressive MM per IMWG criteria
- ≥3 prior therapies or double refractory
- Prior PI, IMiD, anti-CD38 therapy
- Measurable disease
- ECOG PS ≤1

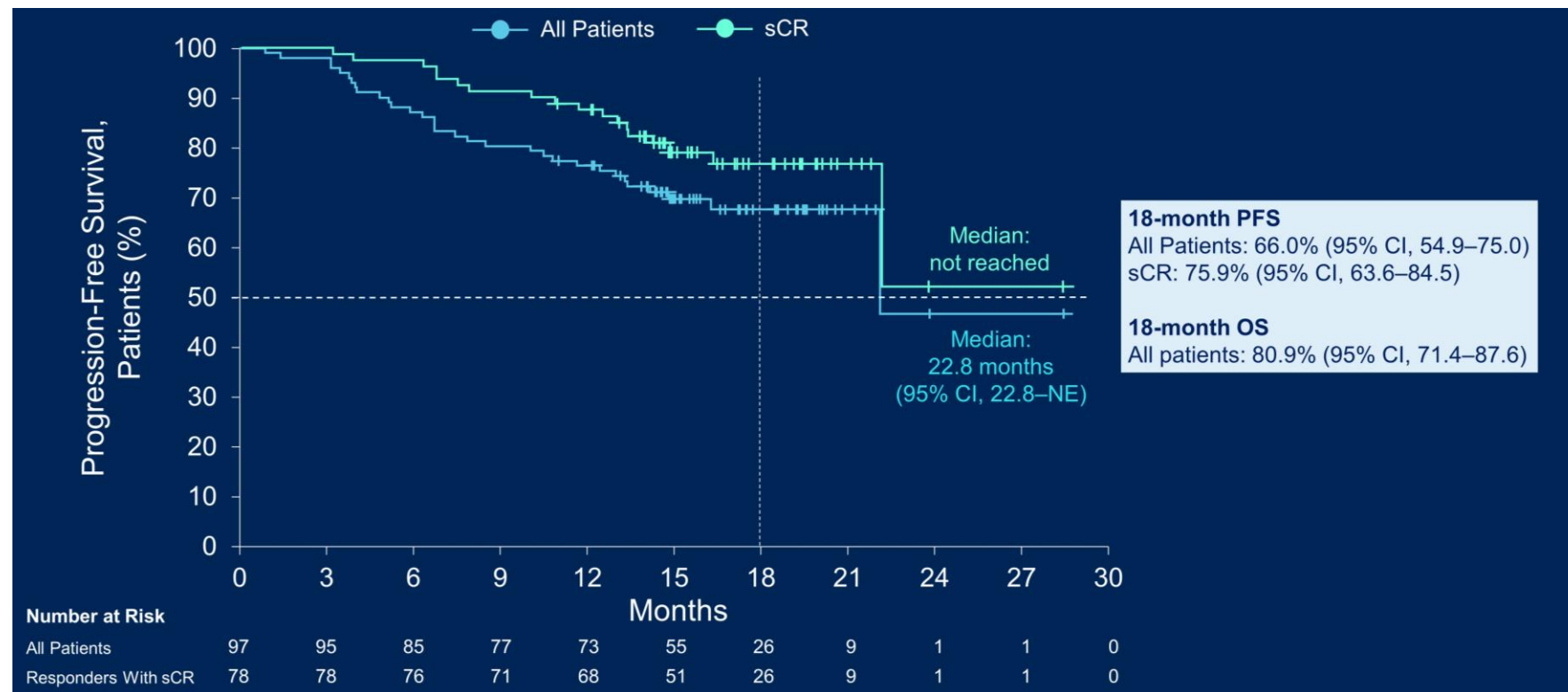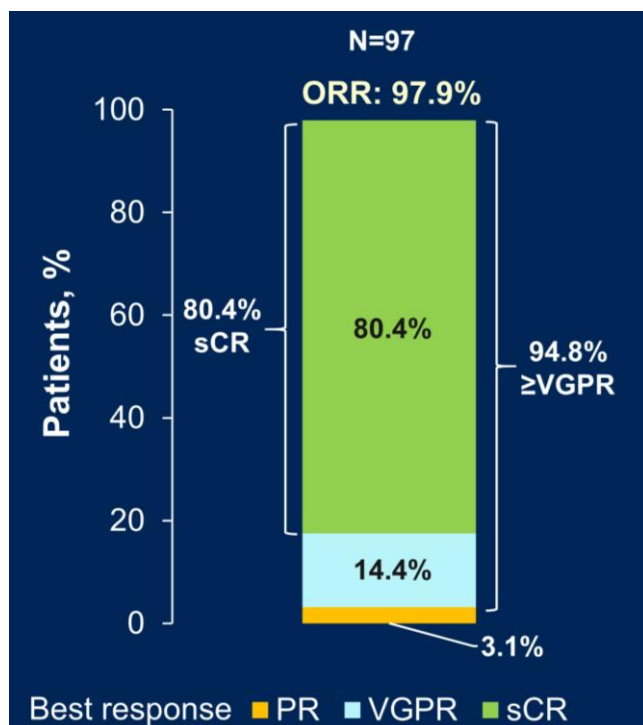Median administered dose: 0.71×10^6 $(0.51–0.95 \times 10^6)$ CAR+ viable T cells/kg

Screening (28 days)

Apheresis

Bridging therapy[a] (as needed)

Cy (300 mg/m^2) + Flu (30 mg/m^2) — Day -5 to -3

Cilta-cel infusion
Target: 0.75×10^6 $(0.5–1.0 \times 10^6)$ CAR+ viable T cells/kg — Day 1

Post-infusion assessments
Safety, efficacy, PK, PD, biomarker

Follow-up

Safety

No new safety signals with longer follow-up

	N=97	
	Any grade	**Grade 3/4**
Hematologic AEs ≥25%, n (%)		
Neutropenia	93 (95.9)	92 (94.8)
Anemia	79 (81.4)	66 (68.0)
Thrombocytopenia	77 (79.4)	58 (59.8)
Leukopenia	60 (61.9)	59 (60.8)
Lymphopenia	51 (52.6)	48 (49.5)
Nonhematologic AEs ≥25%, n (%)		
Metabolism and nutrition disorders		
Hypocalcemia	31 (32.0)	3 (3.1)
Hypophosphatemia	30 (30.9)	7 (7.2)
Decreased appetite	28 (28.9)	1 (1.0)
Hypoalbuminemia	27 (27.8)	1 (1.0)
Gastrointestinal		
Diarrhea	29 (29.9)	1 (1.0)
Nausea	27 (27.8)	1 (1.0)
Other		
Fatigue	36 (37.1)	5 (5.2)
Cough	34 (35.1)	0
AST increased	28 (28.9)	5 (5.2)
ALT increased	24 (24.7)	3 (3.1)

CRS	N=97
Patients with a CRS event,[a] n (%)	92 (94.8)
Time to onset, median (range) days	7 (1–12)
Duration, median (range) days	4 (1–97)[b]
Of 92 patients with CRS, majority (94.6%) were grades 1/2 **CRS resolved in 91 (98.9%) patients within 14 days of onset**	

	N=97
Total CAR T-cell neurotoxicities, n (%)	
Any Grade	20 (20.6)
Grade ≥3	10 (10.3)
ICANS, n (%)	
Any Grade	16 (16.5)
Grade ≥3	2 (2.1)
Other neurotoxicities,[c] n (%)	
Any Grade	12 (12.4)
Grade ≥3	9 (9.3)

Efficacy

Study Design

Patient Population

Unresectable or metastatic melanoma treated with ≥1 prior systemic therapy including a PD-1–blocking antibody and, if BRAF V600 mutation positive, a BRAFi ± MEKi

Cohort 1
Non-cryopreserved TIL product (Gen 1)
N=30
Closed to enrollment

Cohort 2
Cryopreserved TIL product (Gen 2)
N=60
Closed to enrollment

Cohort 3
TIL re-treatment
N=10

Cohort 4 (Pivotal)
Cryopreserved TIL product (Gen 2)
N=75
Closed to enrollment
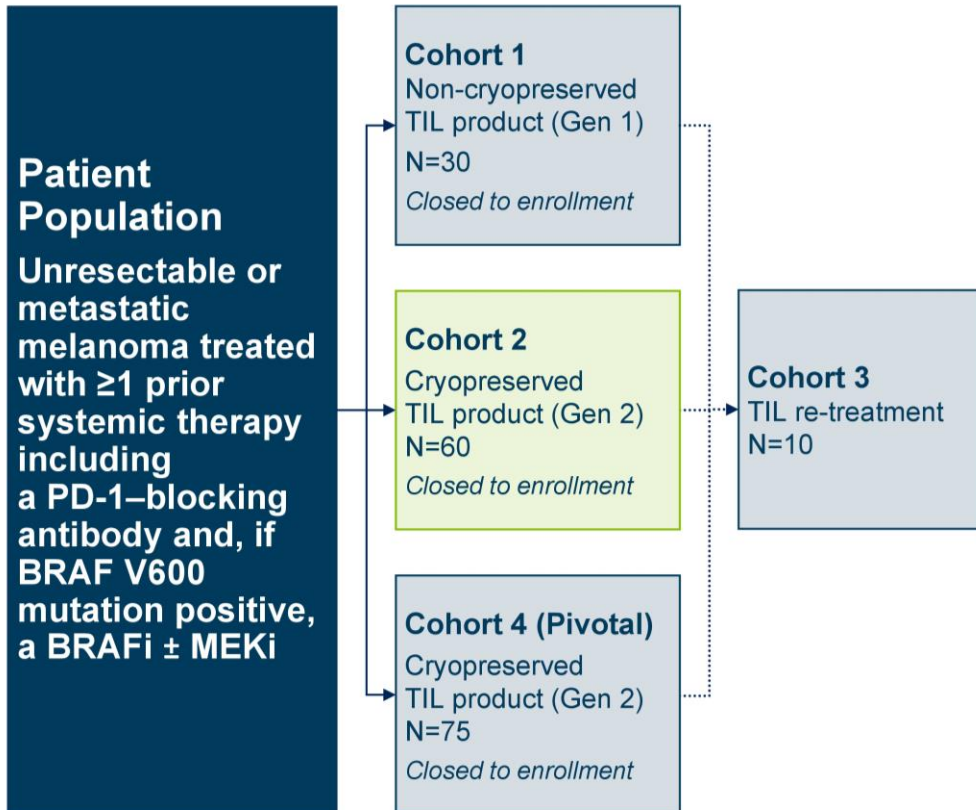
Cohort 2 Endpoints
- Primary: Efficacy per investigator-assessed ORR using RECIST 1.1 response criteria
- Secondary: Safety and additional parameters of efficacy

Key Eligibility Criteria
- Radiographic confirmation of progression
- One tumor lesion resectable for TIL generation (~1.5 cm in diameter) and ≥1 target tumor lesion for RECIST 1.1 response assessment
- Age ≥18 years at the time of consent
- ECOG performance status of 0–1

Methods
- Patients were enrolled from April 2017 to January 2019 at 26 sites across the US and EU
- Concomitant anticancer therapy was not permitted
- Imaging-evaluable disease was required
- All responses required confirmation
- Data cutoff: 22 April 2021

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Efficacy

Response, n (%)	N=66
Objective Response Rate	**24 (36.4)**
Complete response	3 (4.5)
Partial response	21 (31.8)
Stable disease	29 (43.9)
Progressive disease	9 (13.6)
Non-evaluable*	4 (6.1)
Disease control rate	53 (80.3)
Median Duration of Response	**Not Reached**
Min, max (months)	2.2, 38.5+
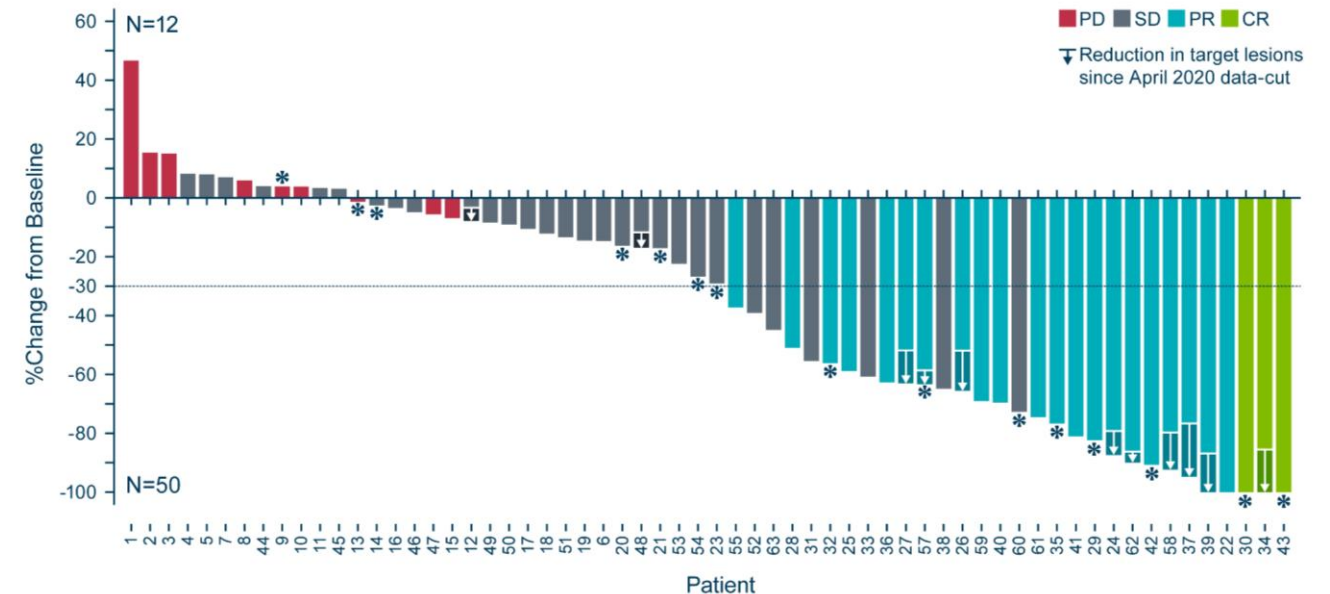
- After a median study follow-up of 33.1 months, median DOR was still not reached (range 2.2, 38.5+)

- 79% of responders received prior ipilimumab
  - 46% of responders received prior anti–PD-1 / anti–CTLA- 4 combination

- Responses continue to deepen over time
  - 17% of patients had deepening of response; 1 PR converted to CR after 24 months post-lifileucel

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Predictors of DOR

Parameter	Comparison	Responders (N=24)	
		HR (95% CI)	*P*-value
Baseline LDH	≤ULN vs >ULN	0.201 (0.040, 0.996)	0.049
Cumulative duration on prior anti–PD-1 / anti–PD-L1	For each 3-month decrease in exposure to prior anti–PD-1 / anti–PD-L1	0.715 (0.518, 0.987)	0.041
	For each 6-month decrease in exposure to prior anti–PD-1 / anti–PD-L1	0.511 (0.268, 0.974)	

> For each 6-month decrease in exposure to prior anti–PD-1 / anti–PD-L1, the median DOR to lifileucel will be nearly doubled[†]

Safety

AEs Over Time
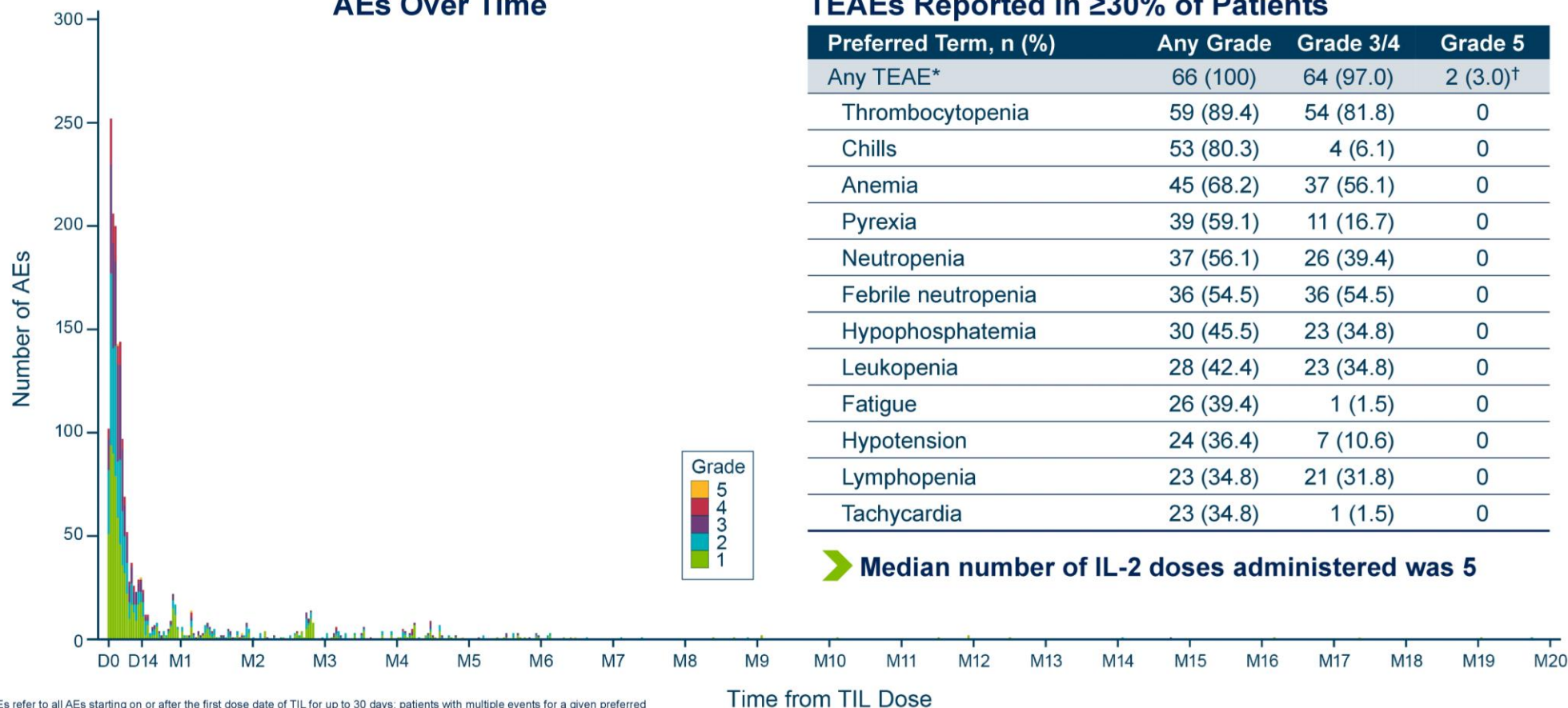
TEAEs Reported in ≥30% of Patients

Preferred Term, n (%)	Any Grade	Grade 3/4	Grade 5
Any TEAE*	66 (100)	64 (97.0)	2 (3.0)†
Thrombocytopenia	59 (89.4)	54 (81.8)	0
Chills	53 (80.3)	4 (6.1)	0
Anemia	45 (68.2)	37 (56.1)	0
Pyrexia	39 (59.1)	11 (16.7)	0
Neutropenia	37 (56.1)	26 (39.4)	0
Febrile neutropenia	36 (54.5)	36 (54.5)	0
Hypophosphatemia	30 (45.5)	23 (34.8)	0
Leukopenia	28 (42.4)	23 (34.8)	0
Fatigue	26 (39.4)	1 (1.5)	0
Hypotension	24 (36.4)	7 (10.6)	0
Lymphopenia	23 (34.8)	21 (31.8)	0
Tachycardia	23 (34.8)	1 (1.5)	0

> **Median number of IL-2 doses administered was 5**

Time from TIL Dose

*TEAEs refer to all AEs starting on or after the first dose date of TIL for up to 30 days; patients with multiple events for a given preferred term are counted only once using the maximum grade under each preferred term.
†Of 2 Grade 5 events, 1 was due to intra-abdominal hemorrhage considered possibly related to TIL, and 1 was due to acute respiratory failure assessed per investigator as not related to TIL.
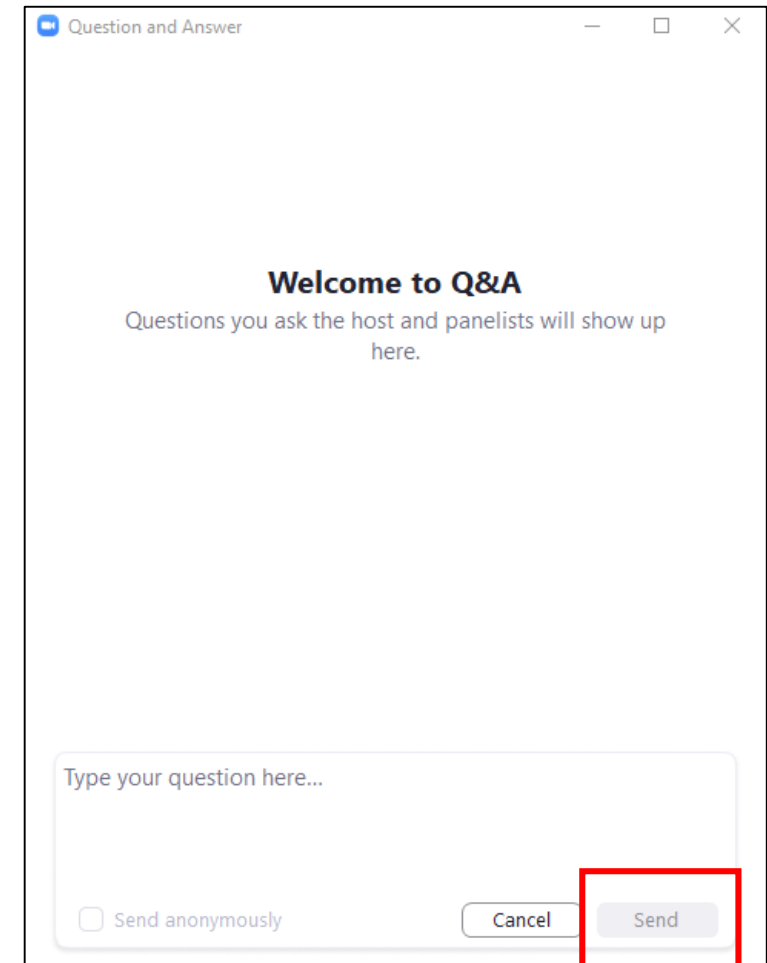AE, adverse event; D, day; IL-2, interleukin-2; M, month; TEAE, treatment-emergent adverse event; TIL, tumor infiltrating lymphocytes.

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Take-aways for Cellular Therapies

- Expanded access to new disease indications
    - Follicular lymphoma
    - Multiple myeloma
    - In addition to mantle cell lymphoma, diffuse large b-cell lymphoma, and adult and pediatric B-ALL

- Growth in the area of solid tumors
    - Expecting approvals of TIL therapies in the coming months

How to Submit Questions

- Click the "Q&A" icon located on at the bottom of your Zoom control panel

- Type your question in the Q&A box, then click "Send"

- Questions will be answered in the Question & Answer session at the end of the webinar (as time permits)

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