2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
• OlympiA* • MONALEESA-3 • PALOMA-3 • ASCENT • DESTINY-Breast01 • OUTBACK*	• IMpower010 • CodeBreaK100 • CheckMate -9LA • CheckMate -227	• VISION* • KEYNOTE-564*	• DESTINY-Gastric01 • CheckMate -648

*2021 ASCO Annual Meeting Plenary Session

CLINICAL QUESTION

OlympiA Clinical Trial

Does 1 year of oral olaparib (Lynparza®) treatment, after surgery and chemotherapy, reduce the risk of breast cancer returning in persons who had an inherited mutation in their BRCA1 or BRCA2 genes?

KEY DATA

OlympiA Clinical Trial

Study Design: Phase 3

Stratified by Hormone receptor status (ER and/or PR+/HER2 negative vs TNBC), prior neoadjuvant vs adjuvant chemotherapy, and prior platinum use for breast cancer.

- Local genetic testing or on-study central screening
- Germline pathogenic or likely pathogenic BRCA1/2 mutation
- HER2-negative (HR+ or TNBC)
- Stage II-III breast cancer or lack of PathCR to NACT

Neoadjuvant group
TNBC: non pCR
HR+: non pCR and CPS+EG score ≥ 3

≥6 cycles Neoadj Chemotherapy → surgery → +/-radiotherapy

Adjuvant group
TNBC: ≥ pT2 or ≥ pN1
HR+: ≥ 4 positive lymph nodes

Surgery → ≥6 cycles adj Chemotherapy → +/- radiotherapy

Randomized 1:1
N=1836

Olaparib
orally twice daily (b.i.d.)
at 300 mg
(n=921)

Placebo
orally twice daily (b.i.d.)
(n=915)

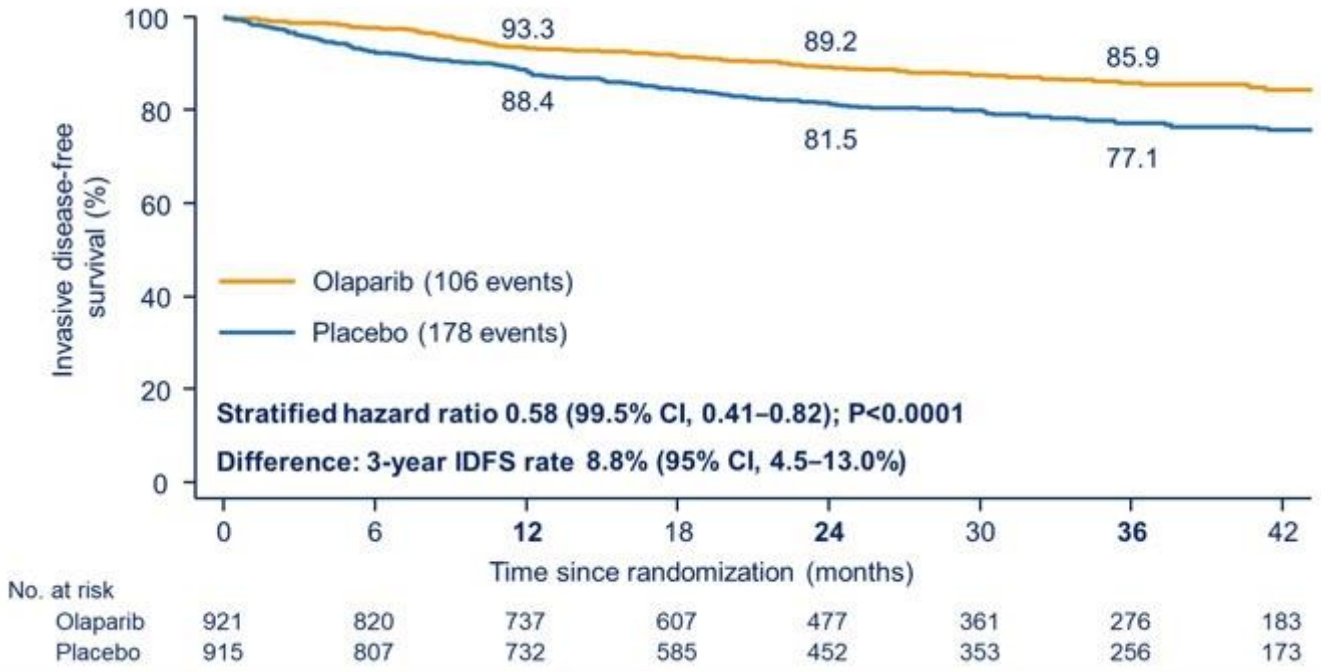
- **Primary End Point:** Invasive disease free survival
- **Secondary Endpoints:** Distant disease free survival, Overall survival, BRCA1 or BRCA2 associated cancers, Symptom/health related QoL, Safety

ASCO 2021: J Clin Oncol 39, 2021 (suppl 15; abstr LBA1); ClinicalTrials.gov Identifier: NCT02032823

KEY DATA

OlympiA Clinical Trial

Invasive disease-free survival (ITT)



Type of first IDFS Event

	Olaparib (N = 921)	Placebo (N = 915)
Number of patients with a first IDFS event	**106 (11.5%)**	**178 (19.5%)**
Distant recurrence	**72 (7.8%)**	**120 (13.1%)**
Distant CNS Recurrence	22 (2.4%)	36 (3.9%)
Distant excluding CNS Recurrence	50 (5.4%)	84 (9.2%)
Regional (Ipsilateral) Recurrence	6 (0.7%)	14 (1.5%)
Local (Ipsilateral) Recurrence	7 (0.8%)	11 (1.2%)
Contralateral invasive breast cancer	8 (0.9%)	12 (1.3%)
Second primary non-breast malignancies	11 (1.2%)	21 (2.3%)
Ovarian	1 (0.1%)	4 (0.4%)
Peritoneal	0 (0.0%)	0 (0.0%)
Fallopian tube	1 (0.1%)	4 (0.4%)
Other	9 (1.0%)	13 (1.4%)
Deaths without a prior IDFS event*	2 (0.2%)	0 (0.0%)

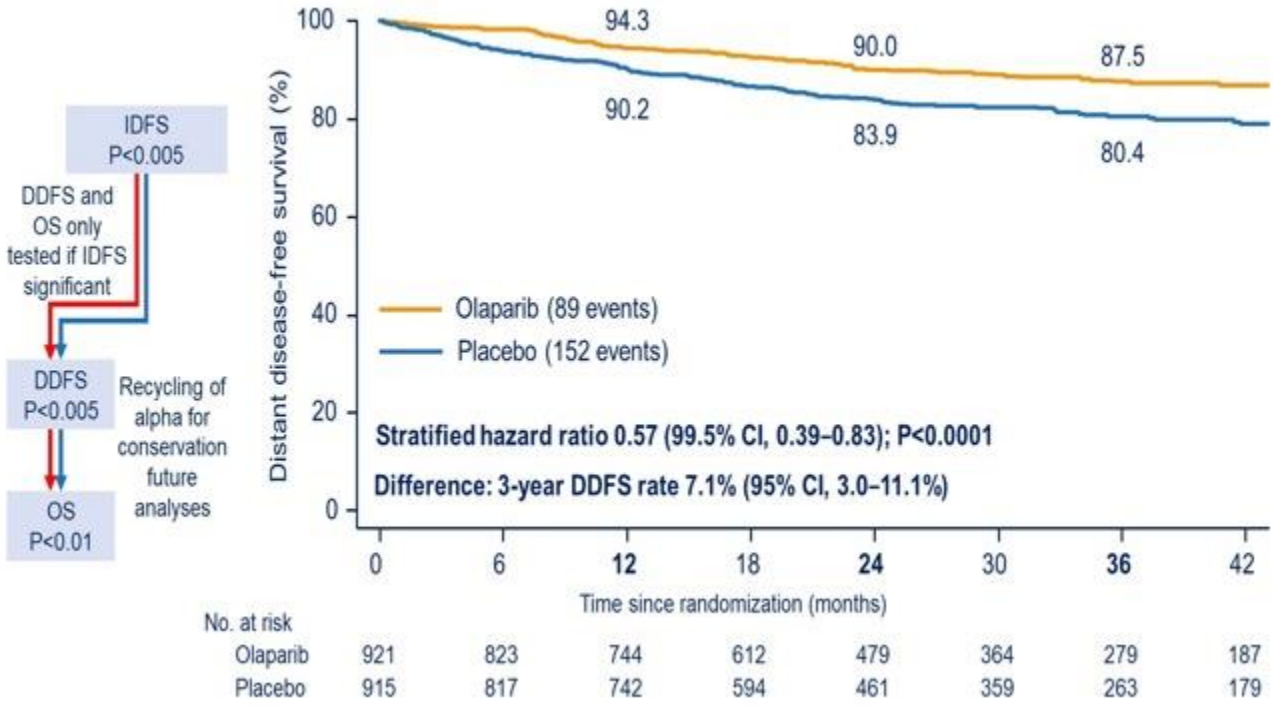
Only one first IDFS event per patient listed
*1 death due to cardiac arrest; 1 unknown

ASCO 2021: J Clin Oncol 39, 2021 (suppl 15; abstr LBA1); ClinicalTrials.gov Identifier: NCT02032823

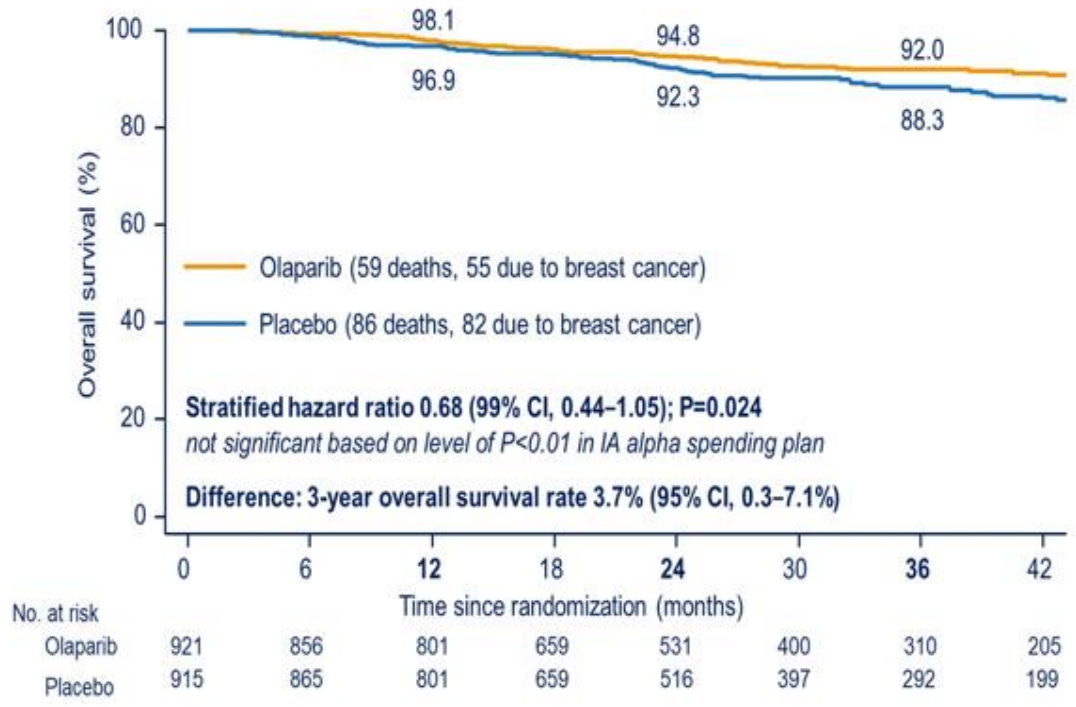
KEY DATA

OlympiA Clinical Trial

Distant disease-free survival



Overall Survival



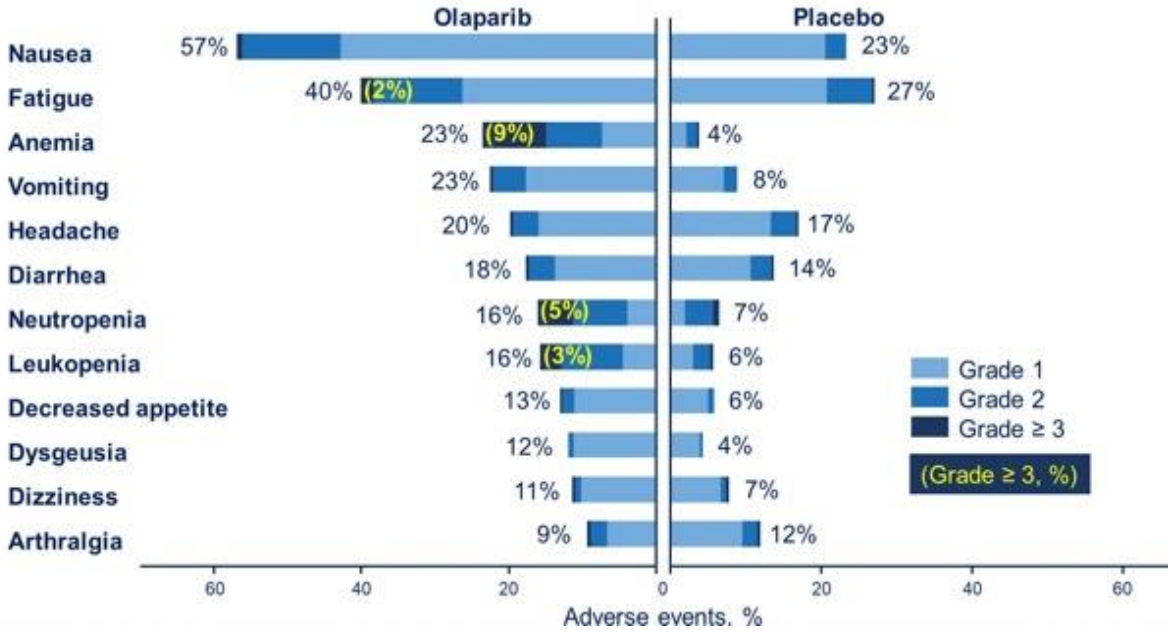
Only one first IDFS event per patient; *1 death due to cardiac arrest; 1 unknown

ASCO 2021: J Clin Oncol 39, 2021 (suppl 15; abstr LBA1); ClinicalTrials.gov Identifier: NCT02032823

OlympiA Clinical Trial

Summary of Adverse Events

	Olaparib (N = 911)	Placebo (N = 904)
Any adverse event	835 (91.7%)	753 (83.3%)
Serious adverse event (SAE)	**79 (8.7%)**	**76 (8.4%)**
Adverse event of special interest	**30 (3.3%)**	**46 (5.1%)**
MDS/AML	**2 (0.2%)**	**3 (0.3%)**
Pneumonitis	9 (1.0%)	11 (1.2%)
New primary malignancy	**20 (2.2%)**	**32 (3.5%)**
Grade ≥ 3 adverse event	221 (24.3%)	102 (11.3%)
Grade 4 adverse event	**17 (1.9%)**	**4 (0.4%)**
Adverse event leading to permanent discontinuation of treatment*	**90 (9.9%)**	**38 (4.2%)**
Adverse event leading to death†	1 (0.1%)	2 (0.2%)



Includes adverse events with an onset date on or after the first dose date and up to and including 30 days following date of last dose of study medication.
AML (acute myeloid leukemia); MDS (myelodysplastic syndrome)
*Adverse events leading to permanent discontinuation of treatment in the olaparib group occurring in >1% were nausea, anemia and fatigue
†Adverse events leading to death are cardiac arrest (Olaparib, n=1), AML (placebo, n=1), and ovarian cancer (placebo, n=1)

ASCO 2021: J Clin Oncol 39, 2021 (suppl 15; abstr LBA1); ClinicalTrials.gov Identifier: NCT02032823

SUMMARY

OlympiA Clinical Trial

- Adjuvant olaparib for 1 year significantly improves IDFS and DDFS
  - Reduced the risk of recurrence or death by approximately **42%** when compared with placebo
    - At 3 years, 85.9% of patients in the olaparib group and 77.1% in the placebo group were alive and free from invasive disease, for a difference of 8.8% (HR 0.58)
  - Reduced the risk of mBC, new cancer, and death due to any cause by **43%** when compared to placebo
    - At 3-year, DDFS was 87.5% and 80.4%, for a 7.1% difference between the olaparib treatment and placebo group respectively (HR 0.57)
- OS data are immature
  - At 3 years, OS was 92% vs 88.3% (HR 0.68) for olaparib vs placebo

ASCO 2021: J Clin Oncol 39, 2021 (suppl 15; abstr LBA1); ClinicalTrials.gov Identifier: NCT02032823

OlympiA Clinical Trial

Adjuvant use of the PARP inhibitor olaparib (Lynparza®) is expected to become standard of care for patients with inherited BRCA1 and BRCA2 mutations

Highlights the importance of germline genetic testing for all patients with invasive BC

OlympiA Clinical Trial

June 15, 2021: ASCO Releases Rapid Guideline Recommendation Update for Certain Patients With Hereditary Breast Cancer

For patients with early-stage, HER2–negative breast cancer with high risk of recurrence and germline *BRCA1* or *BRCA2* pathogenic or likely pathogenic variants, one year of adjuvant olaparib should be offered after completion of (neo)adjuvant chemotherapy and local treatment, including radiation. For those who had surgery first, adjuvant olaparib is recommended for patients with TNBC and tumor size > 2 cm or any involved axillary nodes.

For patients with hormone receptor-positive disease, adjuvant olaparib is recommended for those with at least four involved axillary lymph nodes. For patients who had neoadjuvant chemotherapy, adjuvant olaparib is recommended for patients with TNBC and any residual cancer. Adjuvant olaparib is recommended for patients with residual disease and an estrogen receptor status and tumor grade (CSP+EG) score ≥3.

Olaparib is already approved for use in the metastatic setting for gBRCAm HER2-negative breast cancer on the basis of data from the pivotal OlympiAD trial (2018).
Adjuvant use has not yet been approved by the FDA.

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Several societies have provided recommendations for germline BRCA1 and BRCA2 testing for new pts diagnosed with breast cancer

- *The American Society of Breast Surgeons (2019)*

"Genetic testing should be made available to all patients with a personal history of breast cancer. Recent data support that genetic testing should be offered to each patient with breast cancer (newly diagnosed or with a personal history). If genetic testing is performed, such testing should include BRCA1/BRCA2 and PALB2, with other genes as appropriate for the clinical scenario and family history. For patients with newly diagnosed breast cancer, identification of a mutation may impact local treatment recommendations (surgery and potentially radiation) and systemic therapy. Additionally, family members may subsequently be offered testing and tailored risk reduction strategies."

- *US Preventive Services Task Force (2013, updated 2019)*

"The USPSTF recommends that primary care clinicians assess women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or who have an ancestry associated with BRCA1/2 gene mutations with an appropriate brief familial risk assessment tool. Women with a positive result on the risk assessment tool should receive genetic counseling and, if indicated after counseling, genetic testing. (B recommendation) The USPSTF recommends against routine risk assessment, genetic counseling, or genetic testing for women whose personal or family history or ancestry is not associated with potentially harmful BRCA1/2 gene mutations. (D recommendation)"

Guidelines for testing should be updated by all relevant societies and groups, such as NCCN and ASCO, as well as insurance companies

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KEY DATA

monarchE and OlympiA Clinical Trial

Study Design	monarchE: CDK4/6 Inhibitor		OlympiA: PARP Inhibitor	
Inhibitor	**Abemaciclib** ± Endocrine Therapy High-Risk, Node-Positive, HR+/HER2- EBC		**Olaparib** BRCA1/2 mutation; high-risk HR+/HER2- or TNBC early BC	
Trial	Phase III trial		Phase III trial	
Inclusion Criteria	Prior (neo)adjuvant CT permitted; pre- or postmenopausal no distant metastasis; ≤ 16 months from surgery to randomization; ≤ 12 weeks of ET after last non-ET		BRCA1/2 mutation, (neo)adjuvant chemotherapy, surgery ± RT	
Total # Participants	N = 5637 **Of which, 2056 (36.5%) received neoadjuvant chemotherapy**		**N=1836**	
Trial Design	**Abemaciclib** 150 mg BID up to 2 years + ET per standard of care of physician's choice for 5-10 years as clinically indicated (ITT, n=2808)	ET per standard of care of physician's choice for 5-10 years as clinically indicated (ITT, n=2829)	**Olaparib** 300 mg BID (n=921)	**Placebo** (n=915)
IDFS, 2 year rate % (95% CI)	87.2 (**NAC, n=1025**)	80.6 (**NAC, n=1031**)	89.2	81.5
HR	0.614 (0.473, 0.797)		0.58 (0.41, 0.82)	

J Clin Oncol 39, 2021 (suppl 15; ASCO abstr 517)

J Clin Oncol 39, 2021 (suppl 15; ASCO abstr LBA1)

2021 ASCO Key Studies

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*2021 ASCO Annual Meeting Plenary Session

CLINICAL QUESTION

MONALEESA-3 and PALOMA-3 Clinical Trial

Does the use of a CDK4/6 inhibitor with fulvestrant (Faslodex®) benefit patients with HR+/HER2- *advanced* breast cancer?

Ribociclib (Kisqali®) and Palbociclib (Ibrance®)

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KEY DATA

MONALEESA-3 and PALOMA-3 Clinical Trial

Study Design	MONALEESA-3		PALOMA-3	
CDK4/6 Inhibitor	**Ribociclib ± Fulvestrant** in HR+/HER2- advanced breast cancer		**Palbociclib ± Fulvestrant** in HR+/HER2- advanced breast cancer	
Trial	Phase III trial, randomized double blind, placebo controlled (NCT02422615)		Phase III trial, randomized double blind, placebo controlled (NCT01942135)	
Inclusion Criteria	**Postmenopausal** patients with HR+ HER2- advanced breast cancer**, no prior chemotherapy for advanced cancer**, **≤ 1 line of prior ET** for advanced disease Median follow-up of **56.3** months		Women with HR+, HER2- advanced breast cancer, pre-/peri or postmenopausal, **progression on or after ET in the adjuvant or metastatic setting**, **≤ 1 prior chemotherapy regimen for advanced cancer** Median follow-up of **73.3** months	
Total # of Trial Participants	**N = 726**		**N = 521**	
Trial Design	2: 1 randomization Primary endpoint: PFS Secondary endpoints: OS, ORR, CBR, TTR, DOR, safety and tolerability, HRQoL		2: 1 randomization Primary endpoint: PFS Secondary endpoints: ORR, OS, DOR, and safety	
	Ribociclib 600 mg/day (3 weeks on, 1 week off) + **Fulvestrant 500 mg**/28 days (1 additional dose on cycle 1 day 15) (n = 484)	**Placebo** + **Fulvestrant 500 mg**/28 days (1 additional dose on cycle 1 day 15) (n = 242)	**Palbociclib 125 mg** PO (once daily, 3 weeks on, 1 week off) + **Fulvestrant 500 mg** IM on Days 1, 15, and 29, monthly thereafter (n = 347)	**Placebo** PO (once daily, 3 weeks on, 1 week off) + **Fulvestrant 500 mg** IM on Days 1, 15, and 29, monthly thereafter (n = 174)

J Clin Oncol 39, 2021 (suppl 15; abstr 1001)

J Clin Oncol 39, 2021 (suppl 15; abstr 1000)

KEY DATA

MONALEESA-3 and PALOMA-3 Clinical Trial

	MONALEESA-3 Median follow-up **56.3** months		**PALOMA-3** Median follow-up **73.3** months	
Treatment Arms	**Ribociclib + Fulvestrant** (n=484)	**Placebo + Fulvestrant** (n = 242)	**Palbociclib + Fulvestrant** (n = 347)	**Placebo + Fulvestrant** (n=174)
Median Overall Survival (ITT)	53.7 months	41.5 months	34.8 months	28.0 months
HR	0.73 (95% CI, 0.59-0.90)		0.81 (95% CI, 0.65-0.99)	
	1L setting (n=365)		**Without prior chemotherapy (n=344)**	
Median Overall Survival	NR n=237	51.8 months n=128	39.3 months	29.7 months
HR	0.64 (95% CI, 046-0.88)		0.72 (95% CI, 0.55-0.94)	

J Clin Oncol 39, 2021 (suppl 15; abstr 1001)

J Clin Oncol 39, 2021 (suppl 15; abstr 1000)

MONALESSA-3 and PALOMA-3 Clinical Trial

Use of either palbociclib (Ibrance®) or ribociclib (Kisqali®) when combined with fulvestrant (Faslodex®), demonstrate a durable clinically relevant OS benefit of greater than 1 year in HR+, HER2- advanced breast cancer patients

2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
• OlympiA* • MONALEESA-3 • PALOMA-3 • ASCENT • DESTINY-Breast01 • OUTBACK*	• IMpower010 • CodeBreaK100 • CheckMate -9LA • CheckMate -227	• VISION* • KEYNOTE-564*	• DESTINY-Gastric01 • CheckMate -648

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CLINICAL QUESTION

ASCENT Clinical Trial

Does sacituzumab govitecan-hziy (Trodelvy®) benefit patients with advanced TNBC ≥ 65 years, or those who develop recurrence ≤ 12 months of (neo)adjuvant therapy, and when compared to various chemotherapy agents?

Subgroup analyses

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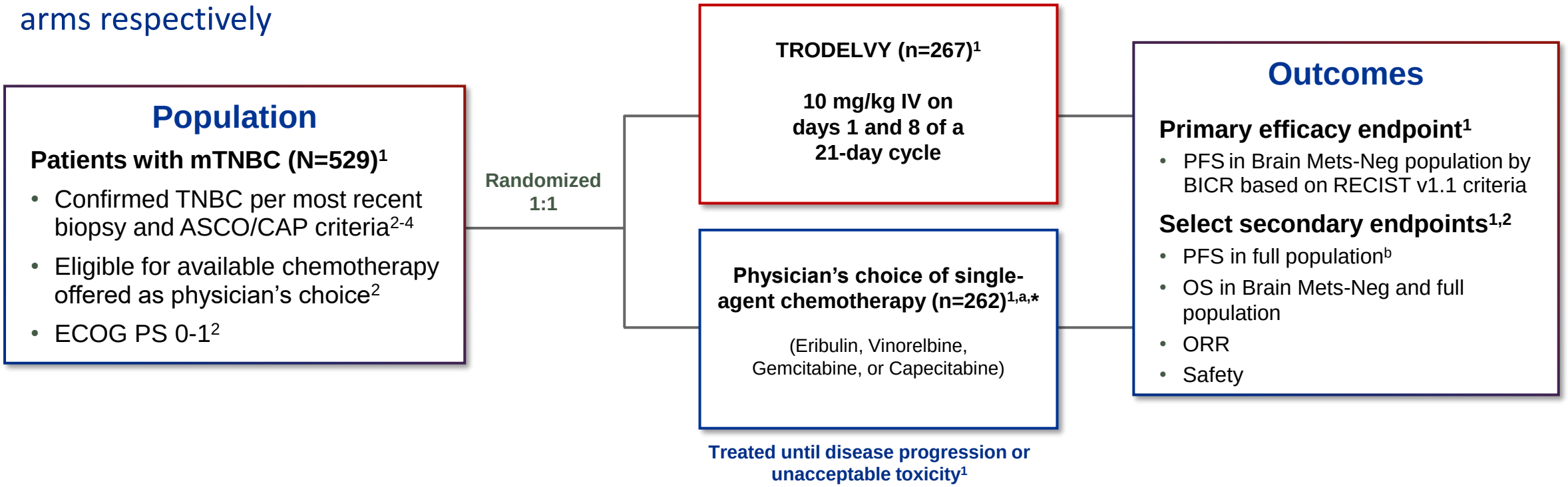
KEY DATA

ASCENT Clinical Trial

An international phase 3, multicenter, open-label, randomized trial of patients (n = 529) with unresectable locally advanced TNBC or mTNBC who had tumor relapse after at least 2 prior chemotherapies for breast cancer (one of which could be in the neoadjuvant or adjuvant setting provided progression occurred within a 12-month period)[1,2]

- Of the 529 total patients, there were 235 and 233 brain mets negative patients in the SacGovi and TPC arms respectively



J Clin Oncol 39, 2021 (suppl 15; abstr 1011; abstr 1080; abstr 1077)

KEY DATA

ASCENT Clinical Trial

	SaciGovi	Physician Choice treatment	SaciGovi	Physician Choice treatment
	Median PFS months (95% CI)		**Median OS months (95% CI)**	
Aged < 65 years	4.6 (3.7 – 5.7) (n=191)	1.7 (1.5 – 2.5) (n=187)	11.2 (9.9 – 13.4) (n=133)	6.6 (5.3 – 7.4) (n=150)
HR (95% CI), *P* value	**0.46** (0.35 – 0.59), ***P*<0.0001**		**0.50** (0.40 – 0.64), ***P*<0.0001**	
Aged ≥ 65 years	7.1 (5.8 – 8.9) (n=44)	2.4 (1.4 – 2.9) (n=46)	15.3 (12.4 – NE) (n=22)	8.2 (5.6 – 9.8) (n=35)
HR (95% CI), *P* value	**0.22** (0.12 – 0.40), ***P*<0.0001**		**0.37** (0.22 – 0.64), ***P*=0.0003**	
In patients without brain mets, recurred ≤12 months	5.7 (2.6 – 8.1) (n=33)	1.5 (1.4 – 2.6) (n=32)	10.9 (6.9 – 19.5) (n=33)	4.9 (3.1 – 7.1) (n=32)
HR (95% CI), *P* value	**0.41** (0.22 – 0.76)		**0.51** (0.28 – 0.91)	

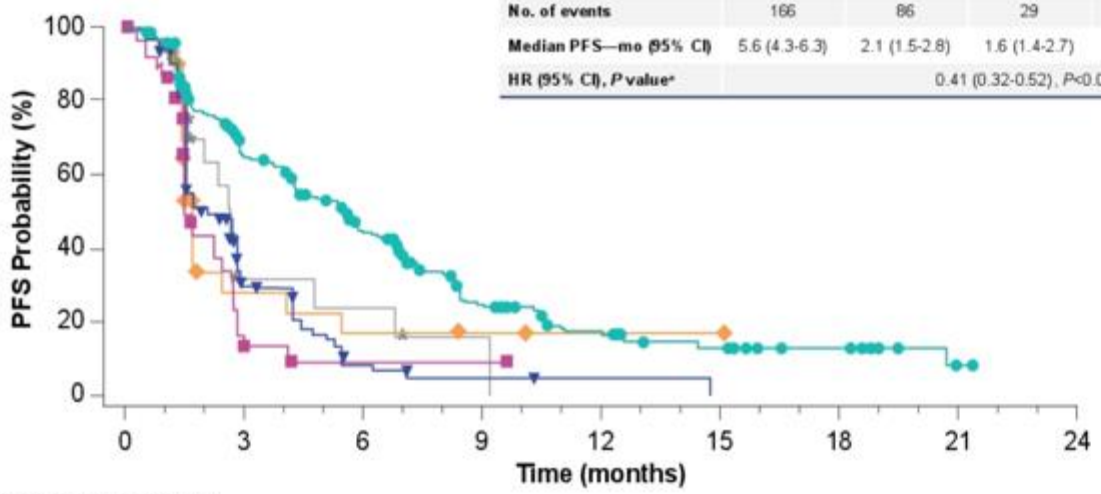
J Clin Oncol 39, 2021 (suppl 15; abstr 1011; abstr 1080; abstr 1077)

KEY DATA

ASCENT Clinical Trial

PFS and OS benefit was observed in SaciGovi treated patients when compared to each individual physician's choice chemotherapy

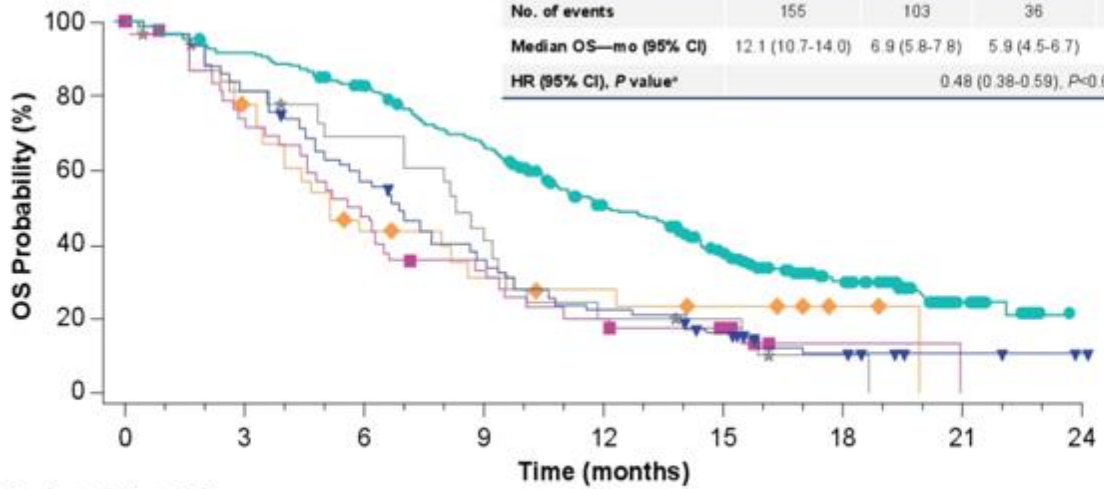
PFS BICR Analysis	SG (n=235)	TPC (n=233)			
		Eribulin (n=126)	Vinorelbine (n=47)	Capecitabine (n=31)	Gemcitabine (n=29)
No. of events	166	86	29	20	15
Median PFS—mo (95% CI)	5.6 (4.3-6.3)	2.1 (1.5-2.8)	1.6 (1.4-2.7)	1.6 (1.4-2.4)	2.7 (1.6-4.8)
HR (95% CI), *P* value[a]	0.41 (0.32-0.52), *P*<0.001				



No. of Patients Still at Risk

SG	235	222	166	134	127	104	81	63	54	37	33	24	22	16	15	13	9	8	8	5	3	1	0
Eribulin	126	98	49	23	20	11	5	4	2	2	2	1	1	1	1	0	0	0	0	0	0	0	0
Vinorelbine	47	32	13	3	3	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Capecitabine	31	28	6	5	5	4	3	3	3	2	2	1	1	1	1	1	0	0	0	0	0	0	0
Gemcitabine	29	21	10	4	4	3	3	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0

Overall Survival	SG (n=235)	TPC (n=233)			
		Eribulin (n=126)	Vinorelbine (n=47)	Capecitabine (n=31)	Gemcitabine (n=29)
No. of events	155	103	36	23	23
Median OS—mo (95% CI)	12.1 (10.7-14.0)	6.9 (5.8-7.8)	5.9 (4.5-6.7)	5.2 (3.5-8.6)	8.4 (5.0-9.6)
HR (95% CI), *P* value[a]	0.48 (0.38-0.59), *P*<0.001				



No. of Patients Still at Risk

SG	235	228	220	214	206	197	190	174	161	153	135	118	107	101	90	70	52	43	37	30	21	13	8	1	0	0
Eribulin	126	117	111	98	89	77	68	57	48	42	32	28	25	24	21	16	11	8	7	5	3	3	3	2	1	0
Vinorelbine	47	41	39	31	28	24	20	15	14	13	10	9	8	6	6	5	2	1	1	1	1	0	0	0	0	0
Capecitabine	31	30	27	23	20	16	12	11	10	8	7	7	7	6	6	5	5	4	2	1	0	0	0	0	0	0
Gemcitabine	29	26	23	21	19	17	17	16	15	11	7	6	5	5	4	4	2	1	1	0	0	0	0	0	0	0

J Clin Oncol 39, 2021 (suppl 15; abstr 1011; abstr 1080; abstr 1077)

ASCENT Clinical Trial

The benefit of sacituzumab govitecan (Trodelvy®) for mTNBC is irrespective of age, timing of tumor relapse, or individual chemotherapy comparison

2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
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*2021 ASCO Annual Meeting Plenary Session

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CLINICAL QUESTION

DESTINY-Breast01 Clinical Trial

Does fam-trastuzumab deruxtecan-nxki (T-DXd, ENHERTU®) benefit patients with HER2+ brain metastases?

KEY DATA

DESTINY-Breast01 Clinical Trial

Subgroup analysis of T-DXd patients with a history of brain metastases

184 patients received T-DXd at the recommended dose of 5.4 mg/kg; 24 had a history of brain metastases

Study Design and Population:

- A phase 2, open-label, multicenter study (NCT03248492)
- Adults with unresectable locally advanced or metastatic HER2+ BC; Prior T-DM1; pretreated and stable brain mets allowed; received T-DXd recommended dose (5.4 mg/kg) q3w
- Primary endpoint – Confirmed ORR by ICR per RECIST version 1.1
- Secondary endpoints - Investigator-assessed ORR, DCR, DOR, CBR, PFS, OS, Pharmacokinetics and safety

Median lines of therapy = 5 (range: 2-27)

- 100% received prior trastuzumab & TDM1
- 66% received prior pertuzumab
- 54% received other HER2 therapies

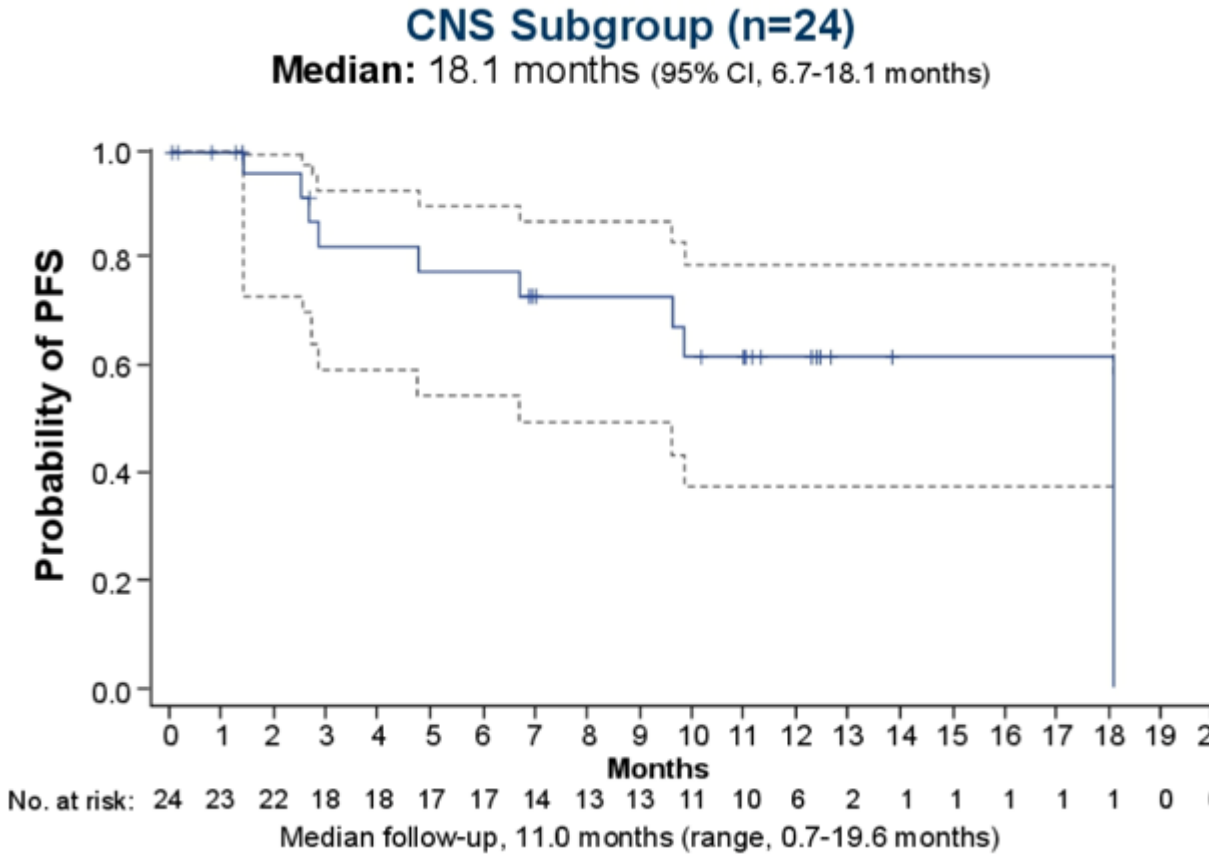
Table 1. Baseline Characteristics[10]

	CNS subgroup (n=24)	All patients (N=184)
Age, median (range), years	58.0 (33-85)	55.0 (28-96)
Female, %	100	100
Region, %		
Asia	37.5	34.2
Europe	37.5	37.0
North America	25.0	28.8
ECOG performance status, %		
0	62.5	55.4
1	37.5	44.0
2	0	0.5
HR status, %		
Positive	37.5	52.7
Negative	58.3	45.1
Unknown	4.2	2.2
HER2 expression, %[a]		
IHC 3+	79.2	83.7
IHC 2+; ISH+	20.8	15.2
IHC 1+; ISH+	0	1.1
Presence of visceral disease, %	100	91.8
Prior CNS treatment, %[b]		
Radiotherapy only	54.2	
Surgery only	4.2	
Radiotherapy + surgery	20.8	
None reported	20.8	

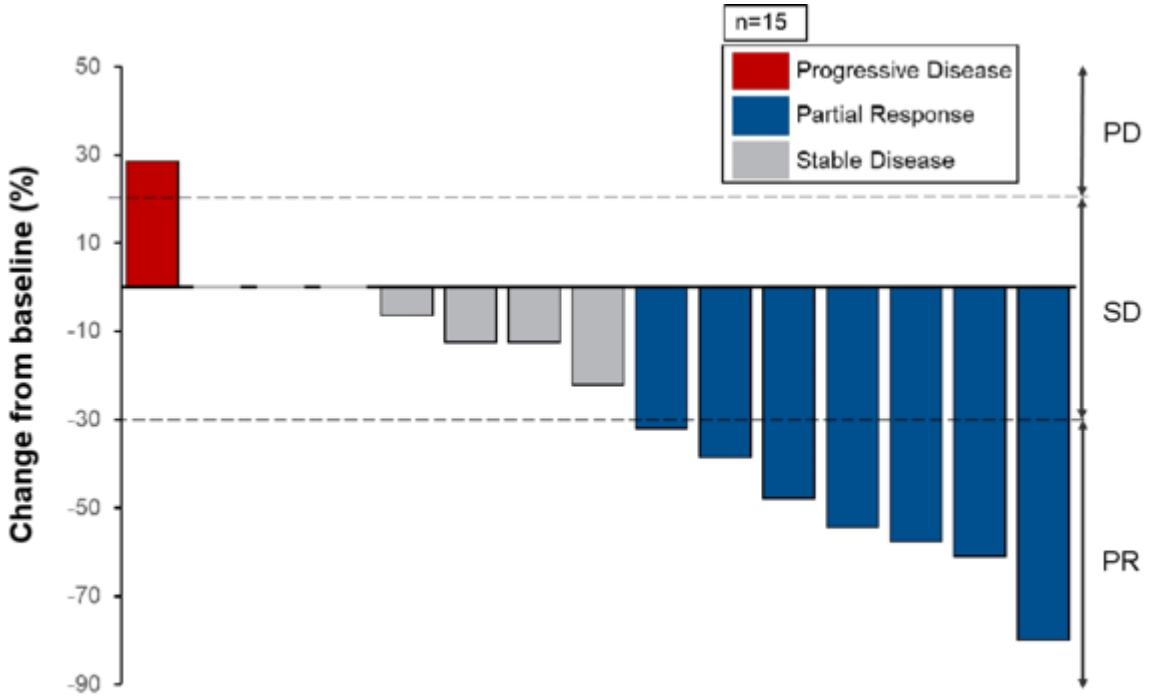
ASCO 2021 Abst 526

KEY DATA

DESTINY-Breast01 Clinical Trial



Best response in brain lesions in the CNS subgroup



3 patients with reported baseline measurements had no change over time.
2 patients with brain metastases at baseline did not have sufficient data to evaluate response in the brain and are not shown.

Note: All patients (N=184), Median 16.4 months (95% CI, 12.7 months – NE)

ASCO 2021 Abst 526

SUMMARY

DESTINY-Breast01 Clinical Trial

- Efficacy of T-DXd in the CNS subgroup was comparable to the overall population
- Of the 17 patients with brain lesions at baseline:
  - 41.2% (n=7) experienced a PR
  - 41.2% (n=7) experienced SD
- Interpretation is limited by the small patient number and post hoc analysis of CNS response
- Ongoing trials will continue to assess the potential of T-DXd in patients with breast cancer and active brain metastases

ASCO 2021 Abst 526

DESTINY-Breast01 Clinical Trial

In addition to the data for "all comers", Fam-trastuzumab deruxtecan-nxki (T-DXd, ENHERTU®) demonstrated disease control in the subgroup of patients with HER2+ MBC with stable, treated brain metastases at baseline

2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
• OlympiA* • MONALEESA-3 • PALOMA-3 • ASCENT • DESTINY-Breast01 • OUTBACK*	• IMpower010 • CodeBreaK100 • CheckMate -9LA • CheckMate -227	• VISION* • KEYNOTE-564*	• DESTINY-Gastric01 • CheckMate -648

*2021 ASCO Annual Meeting Plenary Session

OUTBACK Clinical Trial

Does adjuvant chemotherapy following chemoradiation improve outcome for patients with locally advanced cervical cancer?

Initial concurrent cisplatin and radiation with brachytherapy has been the standard of care since 1999
Individual pt data meta-analysis of 18 trials confirmed benefit of concurrent chemo, with 5-year OS improved from 60% to 66%

KEY DATA

OUTBACK Clinical Trial

Study Design: Phase 3 Adjuvant Study

Patients with cervical cancer suitable for chemoradiation with curative intent:

- FIGO 2008 Stage IB1+LN, IB2, II, IIIB, IVA
- ECOG 0-2
- Squamous cell ca adenocarcinoma or adenosquamous ca
- No nodal disease above L3/4

Stratification factors
Pelvic or common iliac nodal involvement, requirement for extended-field radiotherapy, FIGO 2008 stage: IB/IIA or IIB or IIIB/IVA
Age <60 or ≥ 60 years
Hospital/site

Randomized 1:1

Concurrent chemoradiation (CRT) (n=461)

Concurrent chemoradiation (CRT) (n=465)

Adjuvant chemo (ACT) Carboplatin + Paclitaxel

Median follow-up 5 years

CRT: 40-45 Gy of external beam XRT in 20 to 25 fractions including a nodal boost plus brachytherapy; cisplatin 40 mg/m^2 weekly during XRT
ACT: Carboplatin AUC5 and paclitaxel 155 mg/m^2, 3 weekly x 4 cycles

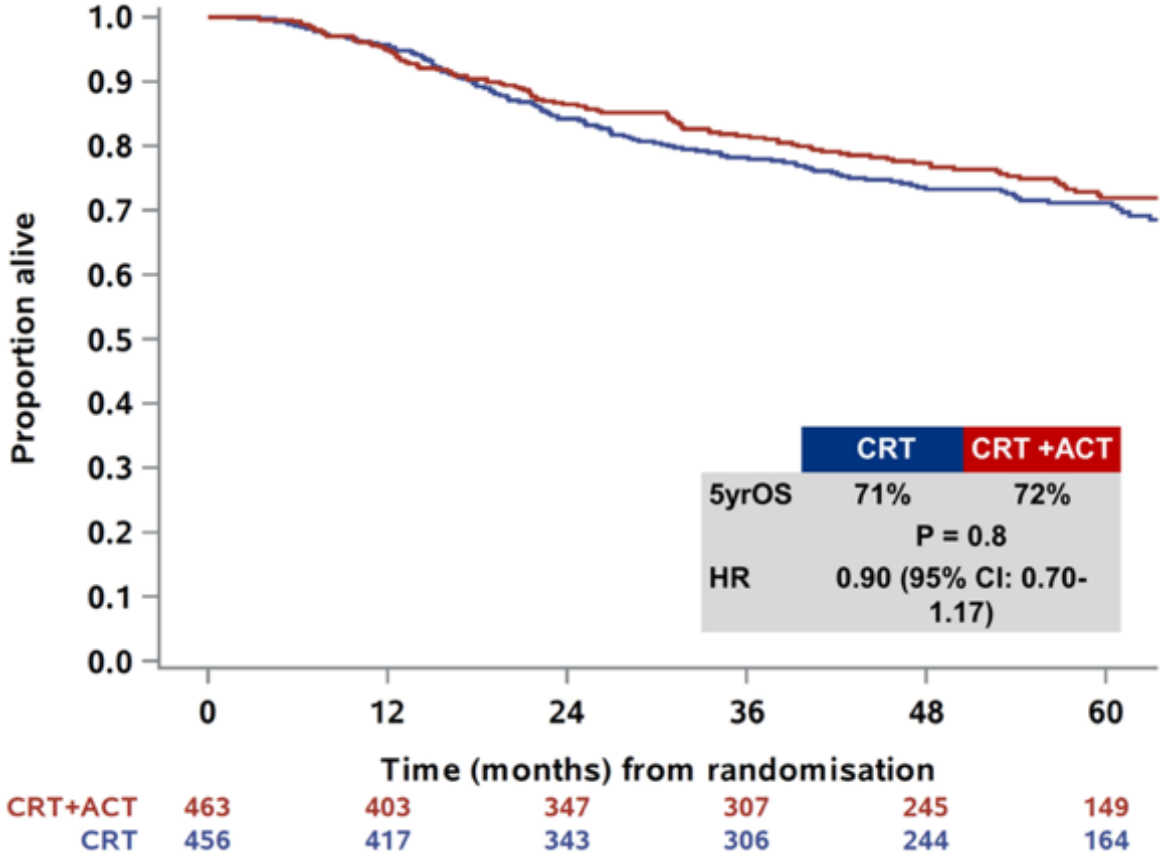
Primary Endpoint: Overall survival
Secondary Endpoints: Progression free survival, Adverse events, Sites of recurrence, Radiation protocol compliance
Patient reported outcomes

J Clin Oncol 39, 2021 (suppl 15; abstr LBA3)

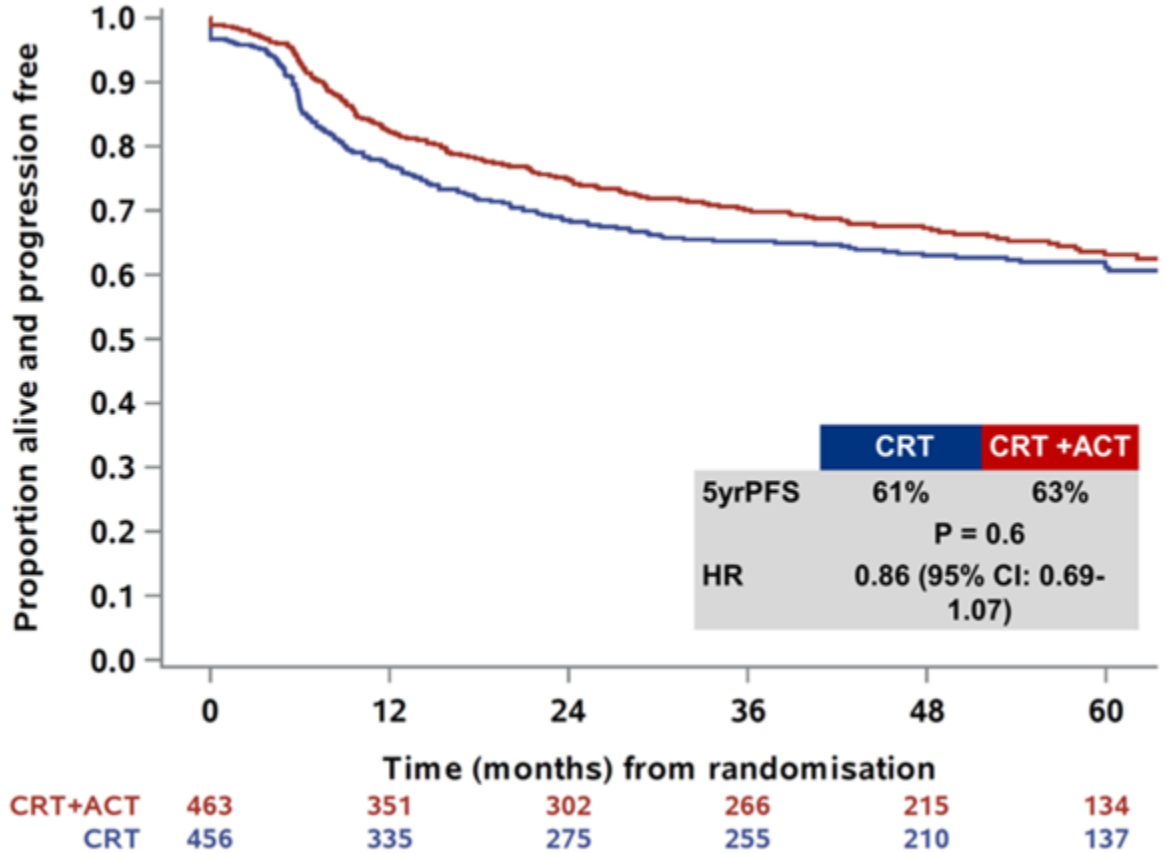
KEY DATA

OUTBACK Clinical Trial

Overall Survival



Progression-Free Survival



J Clin Oncol 39, 2021 (suppl 15; abstr LBA3)

OUTBACK Clinical Trial

The use of adjuvant chemotherapy with carboplatin and paclitaxel after chemoradiation with weekly cisplatin does not provide additional benefit for patients with locally advanced cervical cancer

2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
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CLINICAL QUESTION

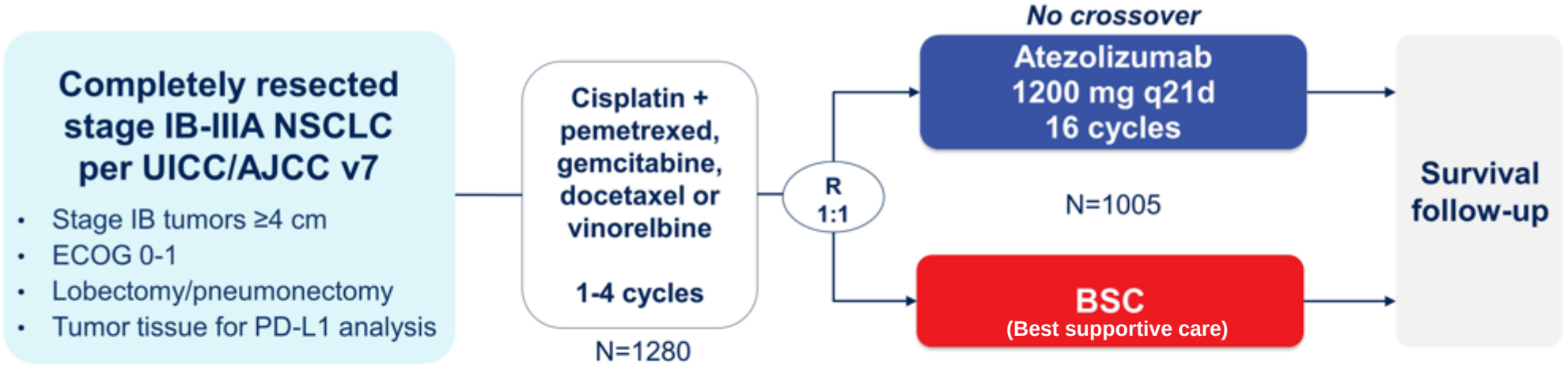
IMpower010 Clinical Trial

Does adjuvant atezolizumab (TECENTRIQ®), compared to SoC, provide benefit for patients with PD-L1-positive stage II-IIIA, fully resected NSCLC after adjuvant chemotherapy?

KEY DATA

IMpower010 Clinical Trial

Study Design: Phase 3



Stratification factors
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints
- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Key secondary endpoints
- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

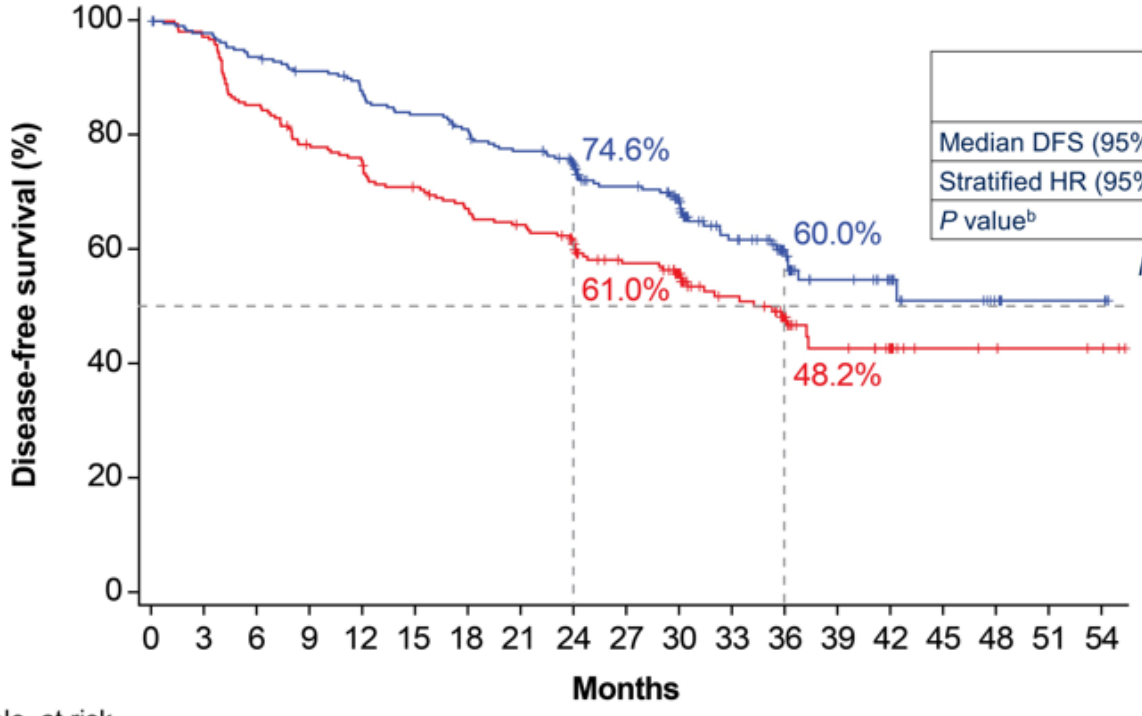
Both arms included observation and regular scans for disease recurrence on the same schedule.
ECOG, Eastern Cooperative Oncology Group; IC, tumor-infiltrating immune cells; ITT, intent to treat; TC, tumor cells. [a] Per SP142 assay.

J Clin Oncol 39, 2021 (suppl 15; abstr 8500)

KEY DATA

IMpower010 Clinical Trial

Primary endpoint: Median DFS in PD-L1 TC ≥ 1%, stage II-IIIA population



	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	

Median follow-up: 32.8 mo (range, 0.1-57.5)

No. at risk

Atezolizumab	248	235	225	217	206	198	190	181	159	134	111	76	54	31	22	12	8	3	3
BSC	228	212	186	169	160	151	142	135	117	97	80	59	38	21	14	7	6	4	3

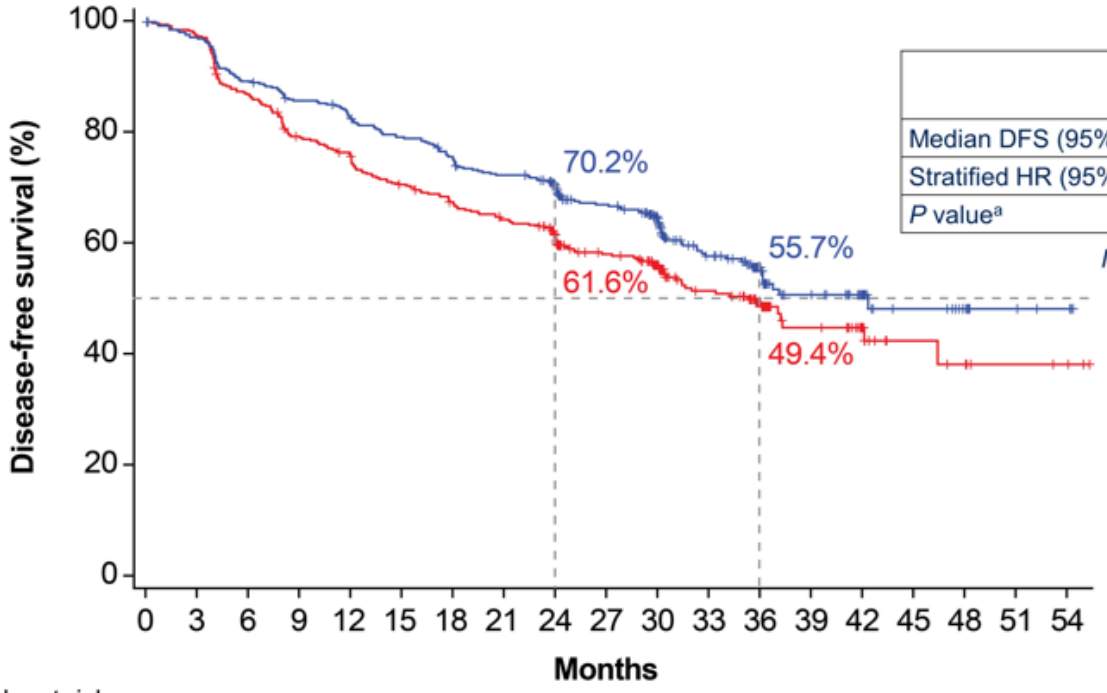
Clinical cutoff: January 21, 2021. CI, confidence interval; HR, hazard ratio; NE, not evaluable. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS.

J Clin Oncol 39, 2021 (suppl 15; abstr 8500)

KEY DATA

IMpower010 Clinical Trial

Primary endpoint: Median DFS in the all-randomized, stage II-IIIA population



	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[a]	0.02[b]	

Median follow-up: 32.2 mo (range, 0-57.5)

No. at risk

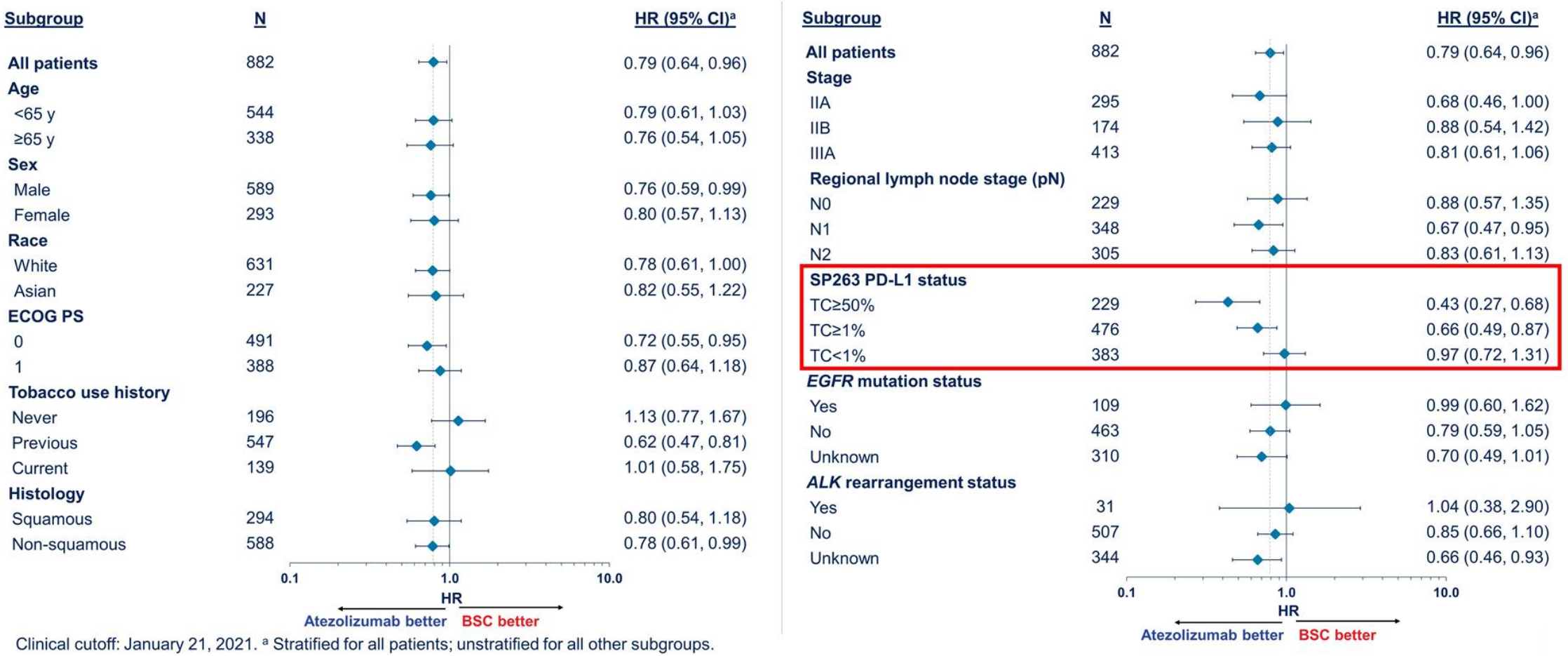
Atezolizumab	442	418	384	367	352	337	319	305	269	225	185	120	84	48	34	16	11	5	3
BSC	440	412	366	331	314	292	277	263	230	182	146	102	71	35	22	10	8	4	3

Clinical cutoff: January 21, 2021. [a] Stratified log-rank. [b] Crossed the significance boundary for DFS.

J Clin Oncol 39, 2021 (suppl 15; abstr 8500)

IMpower010 Clinical Trial

DFS in key subgroups of the all-randomized stage II-IIIA population



Clinical cutoff: January 21, 2021. [a] Stratified for all patients; unstratified for all other subgroups.

J Clin Oncol 39, 2021 (suppl 15; abstr 8500)

SUMMARY

IMpower010 Clinical Trial

- IMpower010 is the first Phase III study of cancer immunotherapy to demonstrate DFS improvement in the adjuvant NSCLC setting after platinum-based chemotherapy
  - Adjuvant atezolizumab, following complete resection and adjuvant chemotherapy, showed statistically significant DFS benefit in the PD-L1 TC≥1% stage II-IIIA (HR 0.66; 95% CI: 0.50-0.88) and all-randomized stage II-IIIA (HR 0.79; 85%CI: 0.64 -0.96) populations, with enriched clinical benefit in patients whose tumors express PD-L1

- DFS and OS analyses in the ITT population ongoing
  - DFS in the ITT population, including patients with Stage1B disease did not cross the significance boundary at this interim analysis
  - OS is immature and not formally tested

- The safety profile of atezolizumab was consistent with prior experience across indications and lines of therapy

J Clin Oncol 39, 2021 (suppl 15; abstr 8500)

IMpower010 Clinical Trial

Atezolizumab (TENCENTRIQ®) may be considered a practice changing adjuvant treatment option for patients with PD-L1 TC ≥1%, stage II-IIIA NSCLC

More to come…

cornerstone specialty network™

Is DFS enough?

- PACIFIC
  - Durvalumab
- ADAURA
  - Osimertinib

- IMPower010: DFS
- ANVIL: DFS, OS
- KEYNOTE-091: DFS
- BR. 31: DFS

2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
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CLINICAL QUESTION

CodeBreaK100 Clinical Trial

Does sotorasib (LUMAKRAS™) provide clinical benefit for patients with *KRAS*-mutated non-small cell lung cancer (NSCLC) after progression on 1L treatment?

KEY DATA

CodeBreaK100 Clinical Trial

Study Design: Phase 2

Screening enrollment
Key Eligibility:

- Local advanced or metastatic NSCLC
- KRAS p.G12C mutation as assessed by central testing of tumor biopsies
- Progressed on prior standard therapies
- Stable brain mets were allowed

→

Sotorasib orally administered at 960 mg once daily until disease progression

Radiographic scan every 6 weeks up to week 48 and once every 12 weeks thereafter

Safety
and
Long-term follow-up

Primary Endpoint: ORR (RECIST1.1)
Secondary Endpoints: DoR, Disease control rate, TTR, PFS, OS, safety
Evaluation of biomarkers

J Clin Oncol 39, 2021 (suppl 15; abstr 9003)

KEY DATA

CodeBreaK100 Clinical Trial

Baseline Characteristics	Sotorasib 960mg, QD N = 126
Median age – years (range)	63.5 (37–80)
ECOG performance status – n (%)	
0	38 (30.2)
1	88 (69.8)
Smoking history – n (%)	
Never	6 (4.8)
Current or former	117 (92.9)
Prior lines of systemic anticancer therapy – n (%)	
1	54 (42.9)
2	44 (34.9)
3	28 (22.2)
Types of prior anticancer therapy – n (%)	
Platinum-based chemotherapy	113 (89.7)
PD-1 or PD-L1 inhibitors	115 (91.3)
Platinum-based chemotherapy and PD-1/PD-L1 inhibitors	102 (81.0)

J Clin Oncol 39, 2021 (suppl 15; abstr 9003)

KEY DATA

CodeBreaK100 Clinical Trial

	Sotorasib 960mg, QD N = 124[a]
Objective Response Rate – % (95% CI)	37.1 (28.6, 46.2)
Best Overall Response – n (%)	
Complete response	4 (3.2)
Partial response	42 (33.9)
Stable disease	54 (43.5)
Progressive disease	20 (16.1)
Not evaluable or missing scan[b]	4 (3.2)
Disease Control Rate – % (95% CI)	80.6 (72.6, 87.2)
Duration of Response – months	
Median (95% CI)	11.1 (6.9, NE)
Time to Response – months	
Median (min, max)	1.35 (1.2, 10.1)

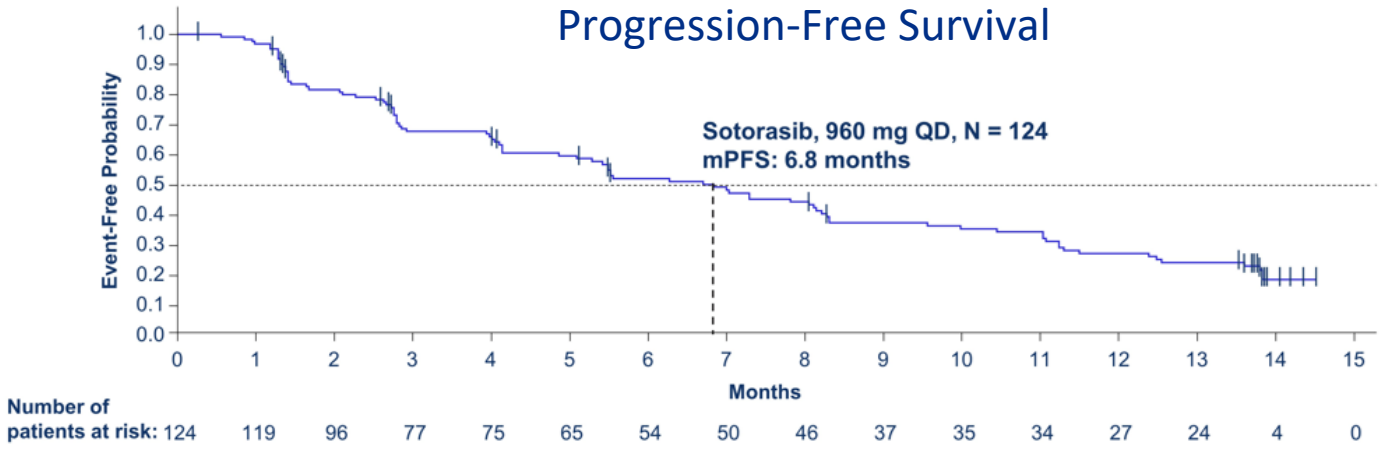
a: according to central review, 2 patients did not have measurable lesions at baseline per RECIST 1.1 and were excluded from response assessment; b: 2 patients stopped treatment without postbaseline scans and were deemed as "missing scan"; 2 patients had 1 postbaseline scan and were assessed as "not evaluable" by central review.
CI: confidence interval; NE: not evaluable; QD: once a day; RECIST: Response Evaluation Criteria in Solid Tumors.

J Clin Oncol 39, 2021 (suppl 15; abstr 9003)

KEY DATA

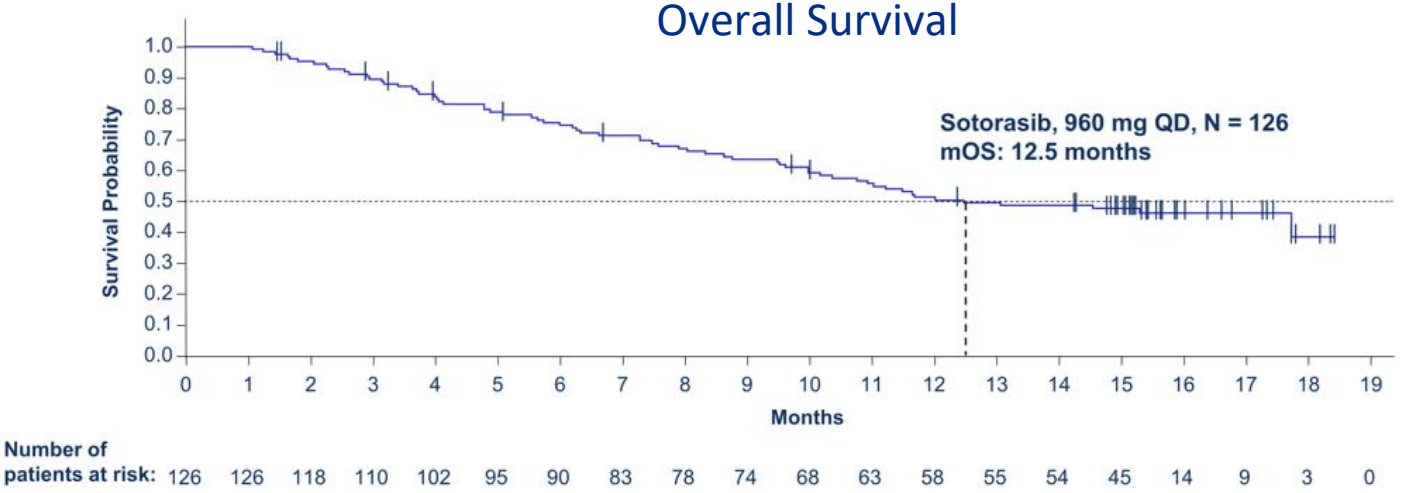
CodeBreaK100 Clinical Trial

Progression-Free Survival



Median PFS was 6.8 months
(95% CI: 5.1, 8.2)

Overall Survival



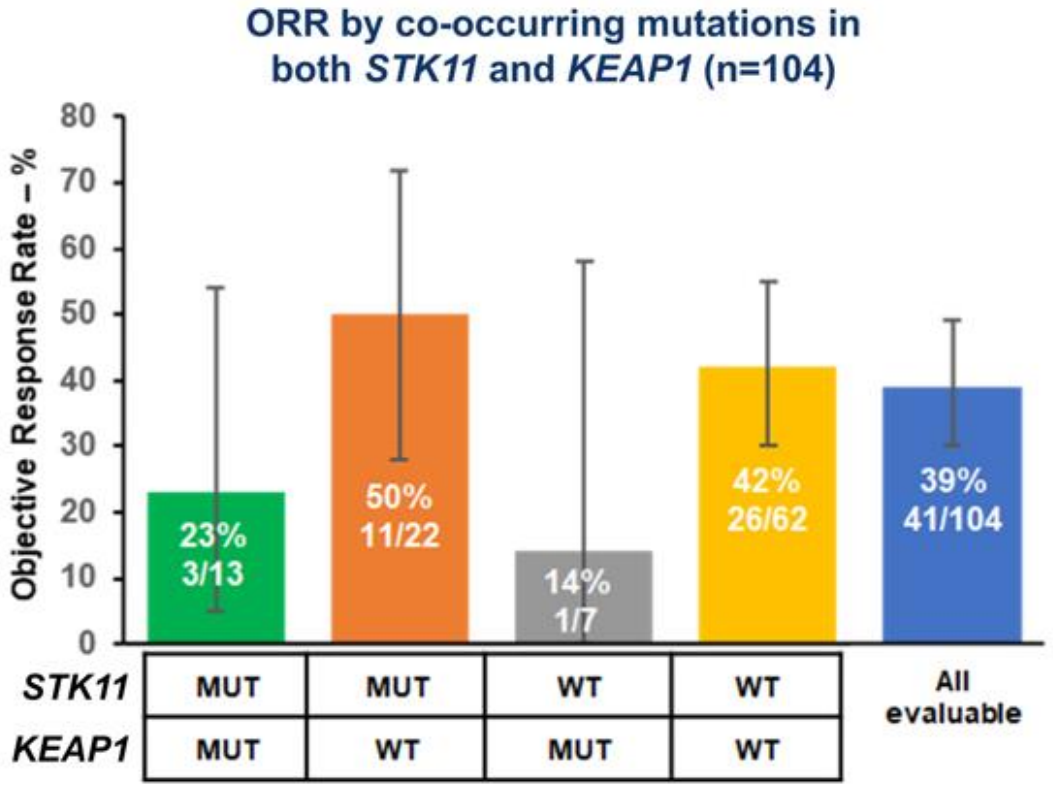
Median overall survival was 12.5 months
(95% CI: 10.0, not evaluable)

J Clin Oncol 39, 2021 (suppl 15; abstr 9003)

KEY DATA

CodeBreaK100 Clinical Trial

Efficacy in molecularly defined subgroups: Exploratory analyses



PFS and OS by co-occurring mutations in both *STK11* and *KEAP1* (n=104)

STK11 status	*KEAP1* status	n	mPFS month (95% CI)	mOS month (95% CI)
MUT	MUT	13	2.6 (1.4, 11.1)	4.8 (2.1, 10.8)
MUT	WT	22	11.0 (2.8, NE)	15.3 (4.8, NE)
WT	MUT	7	5.5 (0, 7.0)	7.5 (0, NE)
WT	WT	62	6.8 (4.0, 11.0)	NE (NE, NE)
All evaluable	All evaluable	104	6.3 (4.1, 8.3)	13.1 (9.5, NE)

- Improved efficacy with sotorasib in *STK11*-mutant group with concurrent wild-type *KEAP1*, whereas *KEAP1*-mutant groups appeared to derive less benefit with limitation of small sample size and exploratory nature

J Clin Oncol 39, 2021 (suppl 15; abstr 9003)

KEY DATA

CodeBreaK100 Clinical Trial

Treatment-Related Adverse Events (TRAEs) Occurring in > 5%	Any Grade N = 126 n (%)	Grade 3 N = 126 n (%)
Any TRAEs	88 (69.8)	25 (19.8)
Diarrhea	40 (31.7)	5 (4.0)
Nausea	24 (19.0)	0
ALT increase	19 (15.1)	8 (6.3)
AST increase	19 (15.1)	7 (5.6)
Fatigue	14 (11.1)	0
Vomiting	10 (7.9)	0
Blood alkaline phosphatase increase	9 (7.1)	1 (0.8)
Maculopapular rash	7 (5.6)	0

One patient (0.8%) reported grade 4 TRAEs (pneumonitis and dyspnea)

- **No fatal TRAEs occurred**
- **TRAEs led to dose modifications in 28 patients (22.2%)**
- **TRAEs led to treatment discontinuation in 9 patients (7.1%)**
  - Drug-induced liver injury (n=3, 2.4%)
  - LFT increase (n=1, 0.8%)
  - ALT increase (n= 2, 1.6%)
  - AST increase (n=2, 1.6%)
  - Blood alkaline phosphatase increase (n=1, 0.8%)
  - Transaminases increase (n=1, 0.8%)
  - Pneumonitis (n=2, 1.6%)
  - Dyspnea (n=1, 0.8%)

J Clin Oncol 39, 2021 (suppl 15; abstr 9003)

SUMMARY

CodeBreaK100 Clinical Trial

- This is the first approved targeted therapy for tumors with any *KRAS* mutation, which accounts for approximately 25% of mutations in non-small cell lung cancers
    - *KRAS G12C* mutations represent about 13% of mutations in non-small cell lung cancers

J Clin Oncol 39, 2021 (suppl 15; abstr 9003)

IMPACT

CodeBreaK100 Clinical Trial

Sotorasib (LUMAKRAS™) provides clinical benefit in patients pretreated for KRAS G12C mutated NSCLC and is the first approved targeted therapy for tumors with any KRAS mutation

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INDICATION

FDA recent approval based on CodeBreaK100

MAY 28, 2021: FDA granted accelerated approval for Lumakras™ (sotorasib) as the first treatment for adult patients with *KRAS* G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.

Partnered with Guardant Health and QIAGEN to develop blood- and tissue-based companion diagnostics (CDx), respectively, for LUMAKRAS™

The FDA approval of LUMAKRAS™ is based on results from a subset of patients in CodeBreaK 100, the largest clinical trial conducted to date exclusively for patients with the *KRAS* G12C mutation. This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Future!

✓ Molecularly enriched population: front line!

✓ Refining the dose selection

✓ Combination

✓ More agents

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CLINICAL QUESTION

CheckMate -9LA and CheckMate -227 Clinical Trials

Does first-line combination immunotherapy provide benefit for patients with advanced NSCLC?

Nivolumab (Opdivo®) Plus ipilimumab (Yervoy®)

A 2-year update of CheckMate -9LA evaluating nivolumab/ipilimumab plus chemotherapy vs chemotherapy alone

&

A 4-year update of CheckMate -227 evaluating nivolumab/ipilimumab vs chemotherapy

ASCO 2021 Abstract #: 9000 and 9016

KEY DATA

CheckMate -9LA and CheckMate -227 Clinical Trials

	CheckMate -9LA 2 year update	CheckMate -227 4 year update	
1L combination immunotherapy	NIVO + IPI + 2 cycles of chemotherapy vs chemotherapy	NIVO + IPI vs chemotherapy	
Trial	Phase 3; open-label multi-center, randomized trial	Phase 3; multi-part open-label	
Inclusion Criteria	Stage IV or recurrent NSCLC; no prior systemic therapy; no sensitizing EGFR mutations or known ALK alternations; ECOG PS 0-1 Stratified by PD-L1 (<1% or ≥1%), sex, and histology (SQ vs NSQ)	Stage IV or recurrent NSCLC; no prior systemic therapy; no sensitizing EGFR mutations or known ALK alternations; no untreated CNS metastases; ECOG PS 0-1 Stratified by SQ vs NSQ	
Total # of Trial Participants	N=719 R 1:1	PD-L1 expression ≥ 1% N=1189 (Part 1a) PD-L1 expression < 1% N=550 (Part 1b)	
Trial Design	Primary endpoint: OS Secondary endpoints: PFS by BICR, ORR by BICR, Efficacy by tumor PD-L1 expression; safety	Primary endpoints: OS in PD-L1 ≥ 1% population PFS in high TMB (≥ 10 mut/Mb) population	
	NIVO 360 mg Q3W + IPI 1mg/kg Q6W + Chemo Q3W (2 cycles) n=361 (356 received treatment)	Chemo Q3W (4 cycles) n=358 (349 received treatment)	Part 1a NIVO (3 mg/kg Q2W) +IPI (1 mg/kg Q6W) (n=396) vs Chemo Q3W (4 cycles) (n=397) vs NIVO (240 mg every 2 weeks) (n=396)	Part 1b NIVO (360 mg Q3W) + IPI (n=187) vs Chemo (n=186) vs NIVO (360 mg Q3W) + chemo (n=177)

ASCO 2021 Abstract #: 9000 and 9016

KEY DATA

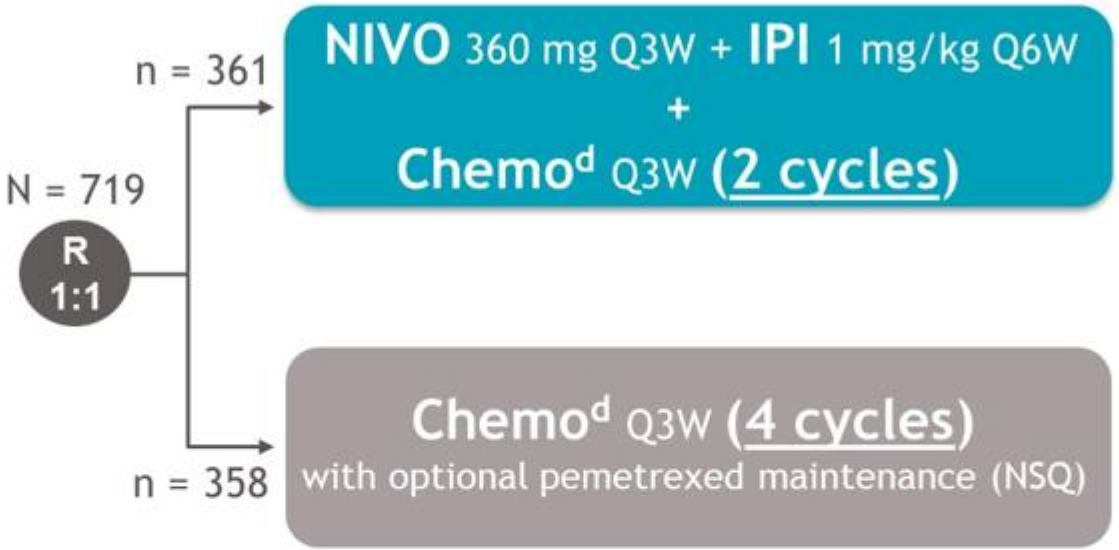
CheckMate -9LA Clinical Trial

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)



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

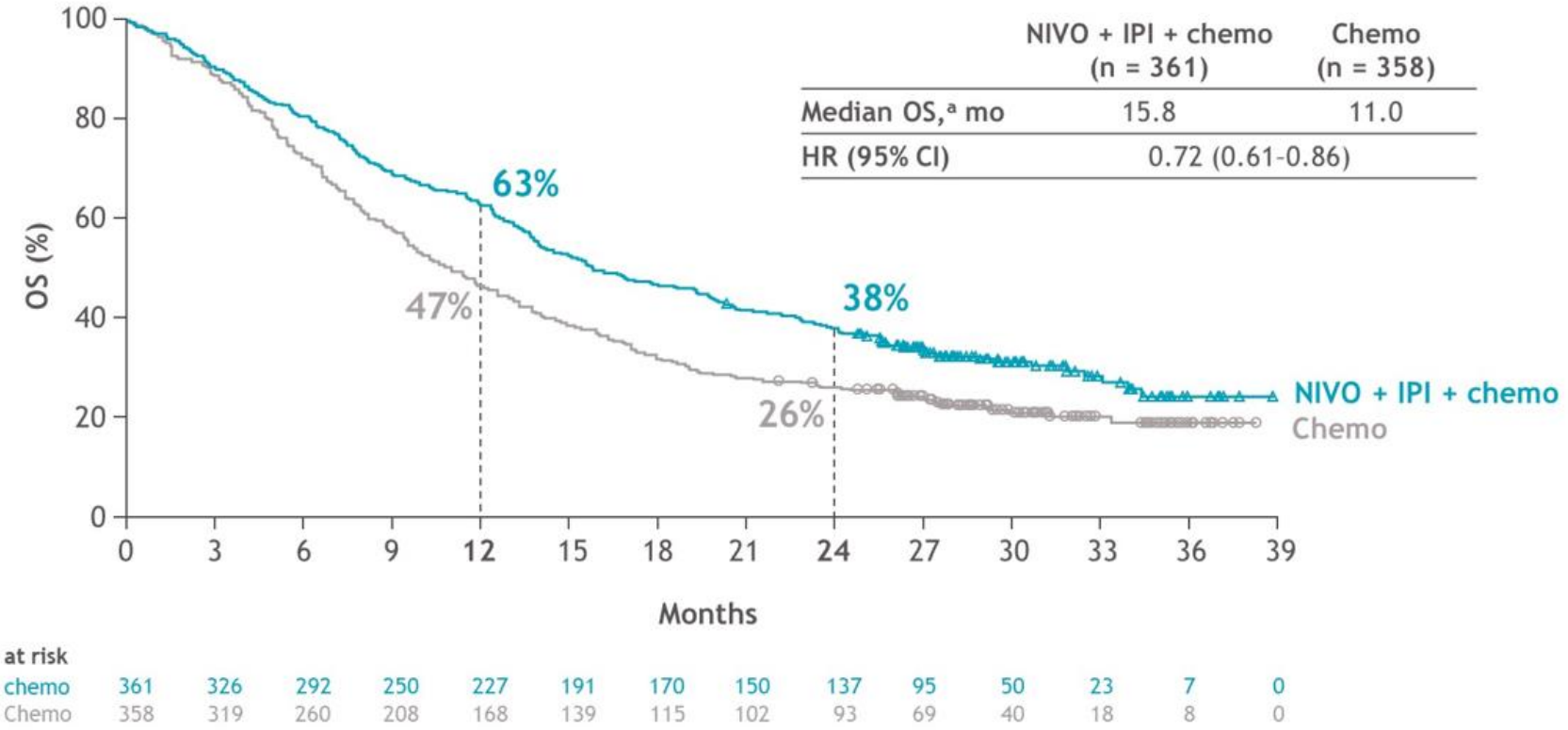
DBL: February 18, 2021; minimum / median follow-up for OS: 24.4 months / 30.7 months.

[a]NCT03215706; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [d]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [e]Hierarchically statistically tested.

KEY DATA

CheckMate -9LA Clinical Trial

2-year update NIVO + IPI + Chemo vs Chemo in 1L NSCLC: OS in all randomized patients



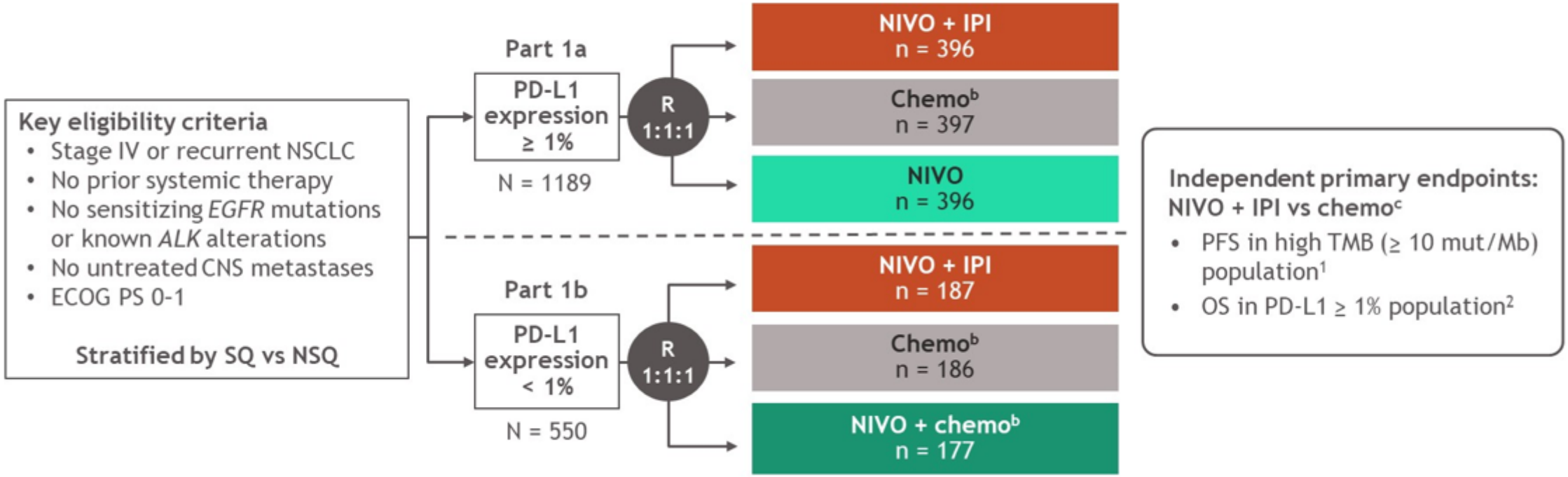
Minimum follow-up: 24.4 months

[a]95% CI: 13.9 – 19.7 (NIVO + IPI + Chemo) and 9.5 – 12.7 (Chemo)

KEY DATA

CheckMate -227 Clinical Trial

Study Design: NIVO + IPI versus chemotherapy as a 1L treatment for advanced NSCLC
Updated 4-year efficacy and safety results

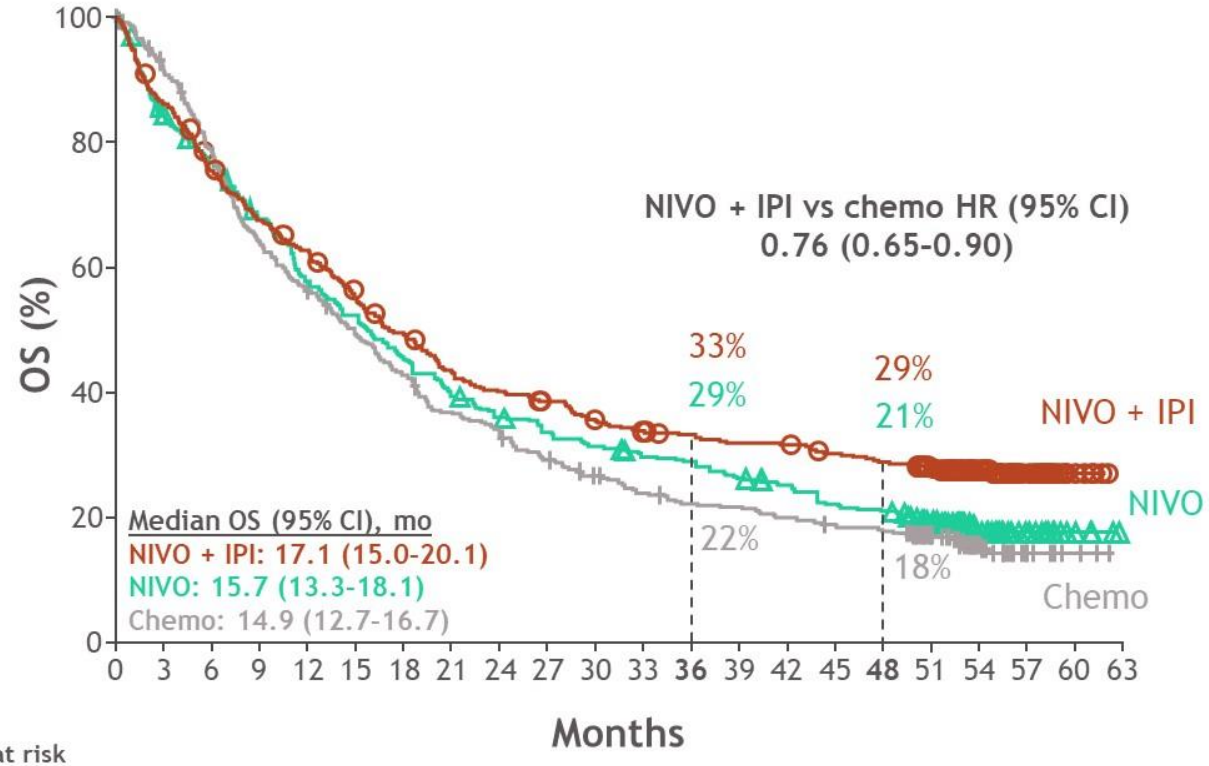


Database lock: February 18, 2021; minimum / median follow-up for OS: 49.4 months / 54.8 months.

Treatment was continued until disease progression, unacceptable toxicity, or for 2 years for immunotherapy. [a]NCT02477826; [b]NSQ: pemetrexed + cisplatin or carboplatin, Q3W for ≤ 4 cycles, with optional pemetrexed maintenance following chemo or NIVO + pemetrexed maintenance following NIVO + chemo; SQ: gemcitabine + cisplatin, or gemcitabine + carboplatin, Q3W for ≤ 4 cycles; [c]Both endpoints were met; results were previously reported. 1. Hellmann MD, et al. *N Engl J Med* 2018;378:2093-2104; 2. Hellmann MD, et al. *N Engl J Med* 2019;381:2020-2031.

4-year OS in patients with PD-L1 ≥ 1%

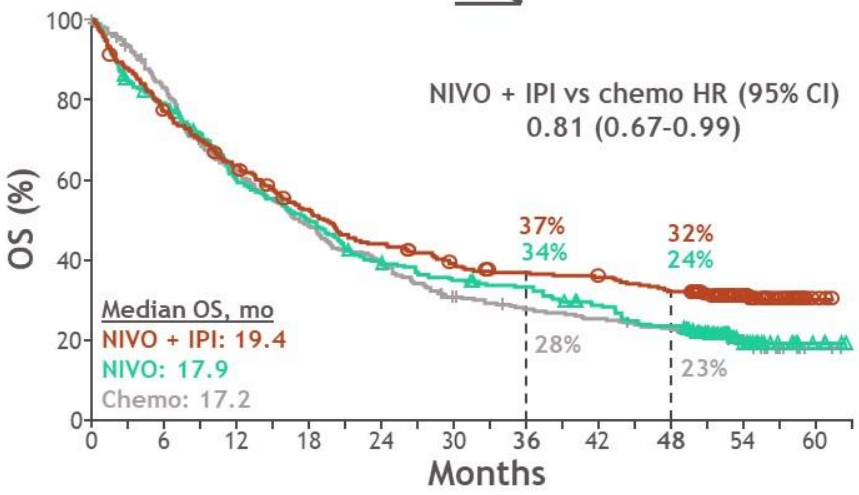
All patients (NSQ + SQ)



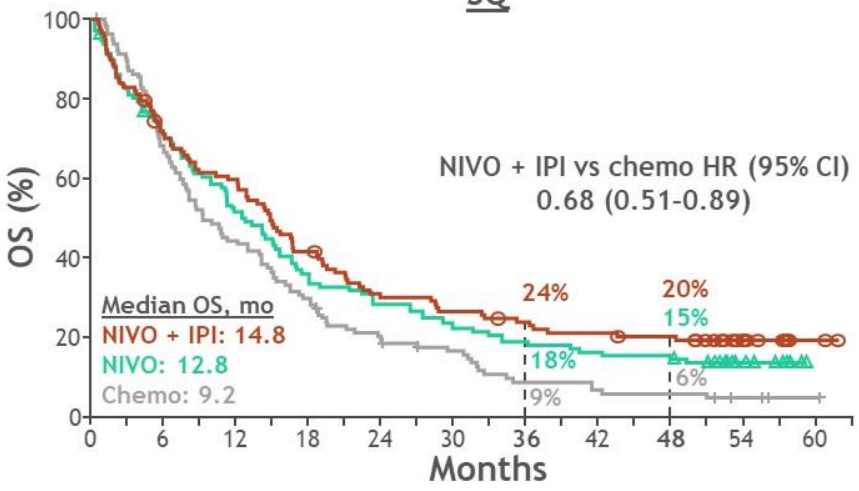
No. at risk

NIVO + IPI	396	341	295	264	244	212	190	165	153	145	132	124	121	116	114	108	103	84	58	23	5	0
NIVO	396	330	299	265	220	201	176	153	139	129	119	112	108	98	91	80	76	61	31	15	4	0
Chemo	397	358	306	250	218	190	166	141	126	112	98	87	80	78	72	66	63	46	24	7	3	0

NSQ



SQ

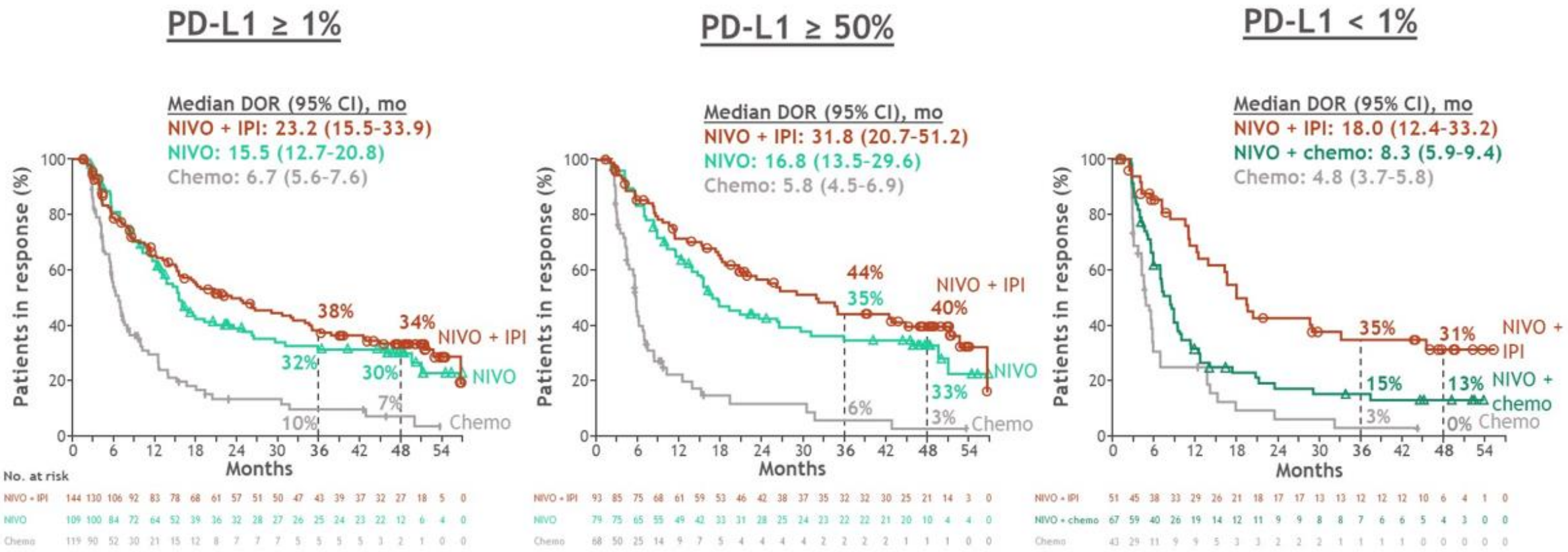


In all patients with PD-L1 ≥ 1% (NSQ + SQ) with a PFS event (per BICR), subsequent systemic therapy was received by 34% in the NIVO + IPI arm, 46% in the NIVO arm, and 49% in the chemo arm; subsequent immunotherapies by 7%, 9%, and 40%; and subsequent chemo by 32%, 45%, and 25%, respectively.

KEY DATA

CheckMate -227 Clinical Trial

4 Year Update: DOR



ASCO 2021 Abstract #: 9016

KEY DATA

CheckMate -9LA and CheckMate -227 Clinical Trials

	CheckMate -9LA 2 year update		CheckMate -227 4 year update	
Treatment Arms	NIVO +IPI + Chemo	Chemo	NIVO + IPI	Chemo
Median OS, months (%) PD-L1 < 1%	17.7 months (37%)	9.8 months (22%)	**17.2 months (24%)**	**12.2 months (10%)**
HR (95% CI)	0.67 (0.51 – 0.88)		0.64 (0.51 – 0.81)	
Median OS, months (%) PD-L1 ≥1%	15.8 months (41%)	10.9 months (28%)	17.1 months (29%)	14.9 months (18%)
HR (95% CI)	0.70 (0.56 – 0.89)		0.76 (0.65 – 0.90)	
Median OS, months (%) PD-L1 ≥50%	18.9 months (45%)	12.9 months (32%)	21.2 months (37%)	14.0 months (20%)
HR (95% CI)	0.67 (0.46 – 0.97)		0.66 (0.52 – 0.84)	

ASCO 2021 Abstract #: 9000 and 9016

SUMMARY

CheckMate -9LA and CheckMate -227 Clinical Trials

CheckMate -9LA: At 2 years: OS, PFS and DOR benefits were maintained across key subgroups. Updated results continue to support NIVO + IPI + 2 cycles of chemotherapy as an efficacious 1L treatment option for patients with advanced NSCLC.

CheckMate -227: At 4 years: OS, PFS and DOR benefits were maintained. Updated results continue to support NIVO + IPI as an efficacious 1L treatment option regardless of PD-L1 expression for patients with advanced NSCLC.

The longest follow-up of any Phase 3 trial for an immunotherapy combination in non-small cell lung cancer

IMPACT

CheckMate -9LA and CheckMate -227 Clinical Trials

Nivolumab (Opdivo®) plus ipilimumab (Yervoy®)-based combinations continue to demonstrate long-term survival benefits in the 1L setting for patients with NSCLC

When and why?

- Compare across studies - squamous cell!
- CNS activity
- Prior Chemo/adjuvant

2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
• OlympiA* • MONALEESA-3 • PALOMA-3 • ASCENT • DESTINY-Breast01 • OUTBACK*	• IMpower010 • CodeBreaK100 • CheckMate -9LA • CheckMate -227	• VISION* • KEYNOTE-564*	• DESTINY-Gastric01 • CheckMate -648

* 2021 ASCO Annual Meeting Plenary Session

cornerstone specialty network™

CLINICAL QUESTION

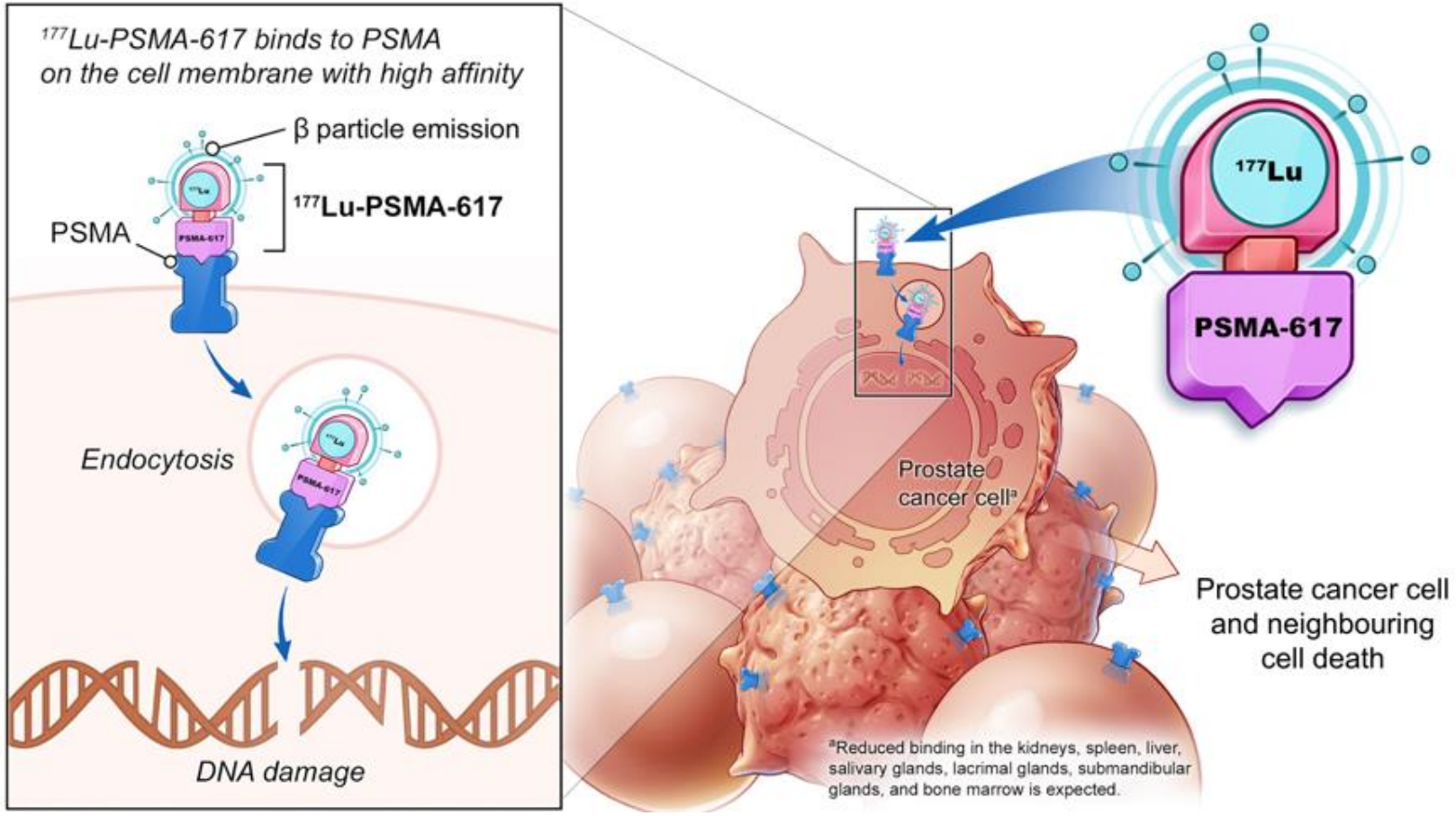
VISION Clinical Trial

Does targeted radioligand therapy benefit patients with PSMA-positive mCRPC who have received previous androgen (≥1) and taxane (1-2) regimes?

KEY DATA

VISION Clinical Trial

^{177}Lu-PSMA-617 targeted radioligand therapy



J Clin Oncol 39, 2021 (suppl 15); ASCO 2021 abstr LBA4

KEY DATA

VISION Clinical Trial

Study Design: a phase III study assessing lutetium-177-PSMA-617 in patients with metastatic castration-resistant prostate cancer

Eligible patients

- Previous treatment with both
  - ≥ 1 androgen receptor pathway inhibitor
  - 1 or 2 taxane regimens
- Protocol-permitted standard of care (SOC) planned before randomization
  - Excluding chemotherapy immunotherapy, radium-223, investigational drugs
- ECOG performance status 0–2
- Life expectancy > 6 months
- PSMA-positive mCRPC on PET/CT with ^{68}Ga-PSMA-11

- Randomization stratified by
  - ECOG status (0–1 or 2)
  - LDH (high or low)
  - Liver metastases (yes or no)
  - Androgen receptor pathway inhibitors in SOC (yes or no)
- CT/MRI/bone scans
  - Every 8 weeks (treatment)
  - Every 12 weeks (follow-up)
  - Blinded independent central review

Centrally read PSMA PET imaging criteria

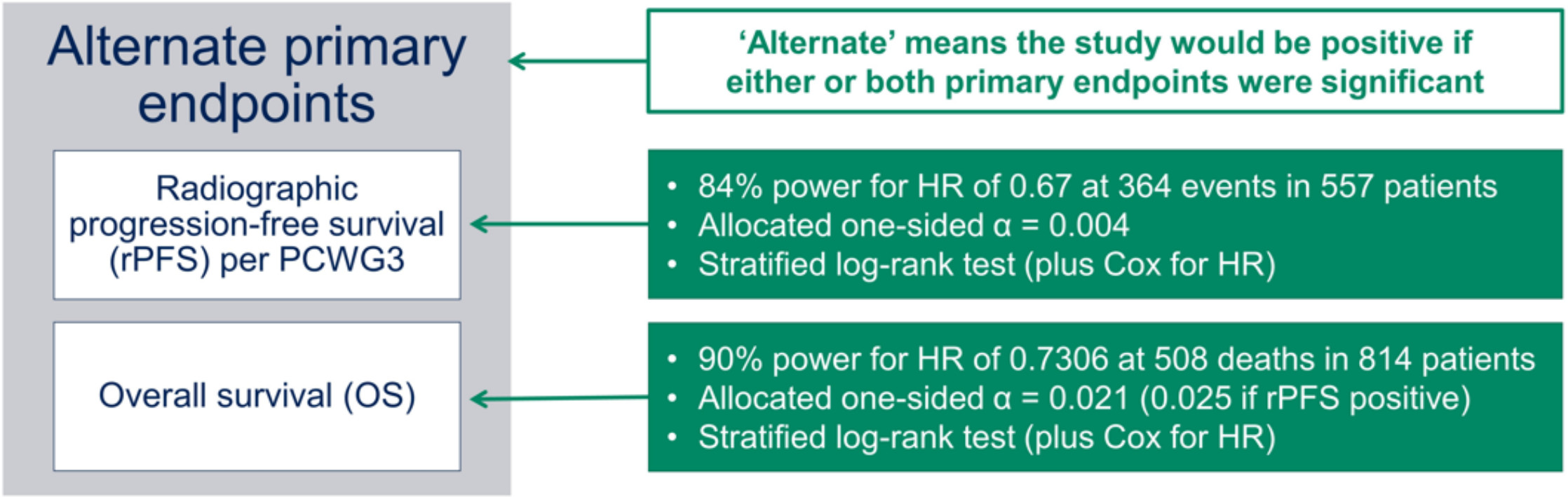
- ≥ 1 PSMA-positive metastatic lesion
  - Positive = ^{68}Ga uptake > liver
- No PSMA-negative metastatic lesions
  - Bone with soft tissue component ≥ 1.0 cm
  - Lymph node ≥ 2.5 cm
  - Solid organ ≥ 1.0 cm

Note: demographic characteristics, baseline features, and prior treatments were well balanced between the two treatment groups.

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

KEY DATA

VISION Clinical Trial



Key secondary endpoints: time to first symptomatic skeletal event (SSE), RECIST v1.1 overall response rate, RECIST v1.1 disease control rate

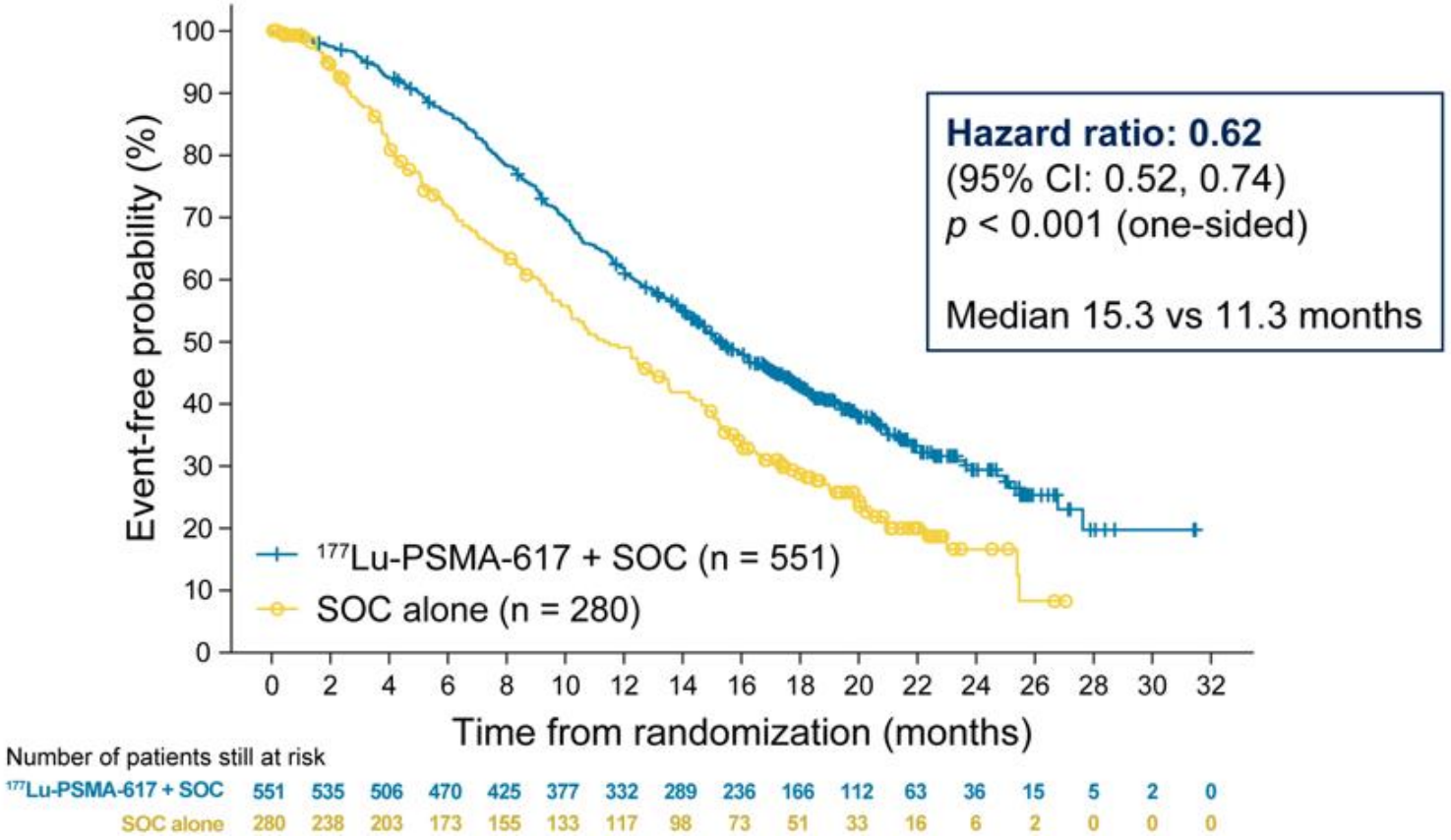
Other secondary endpoints: Safety and tolerability, biomarkers including PSA, health-related quality of life and pain

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

KEY DATA

VISION Clinical Trial

Primary Endpoint: ^{177}Lu-PSMA-617 + SOC prolonged OS compared to SOC alone, in the overall cohort of all randomized patients (n=831) by a median of 4 months



- Overall survival in the **rPFS analysis subset** (n=581), revealed that treatment with ^{177}Lu-PSMA-617 + SOC significantly improved overall survival by a median of **4.2** months (median OS, 14.6 vs 10.4 months; HR, 0.63 [95% CI: 0.51, 0.7]), compared to SOC alone.

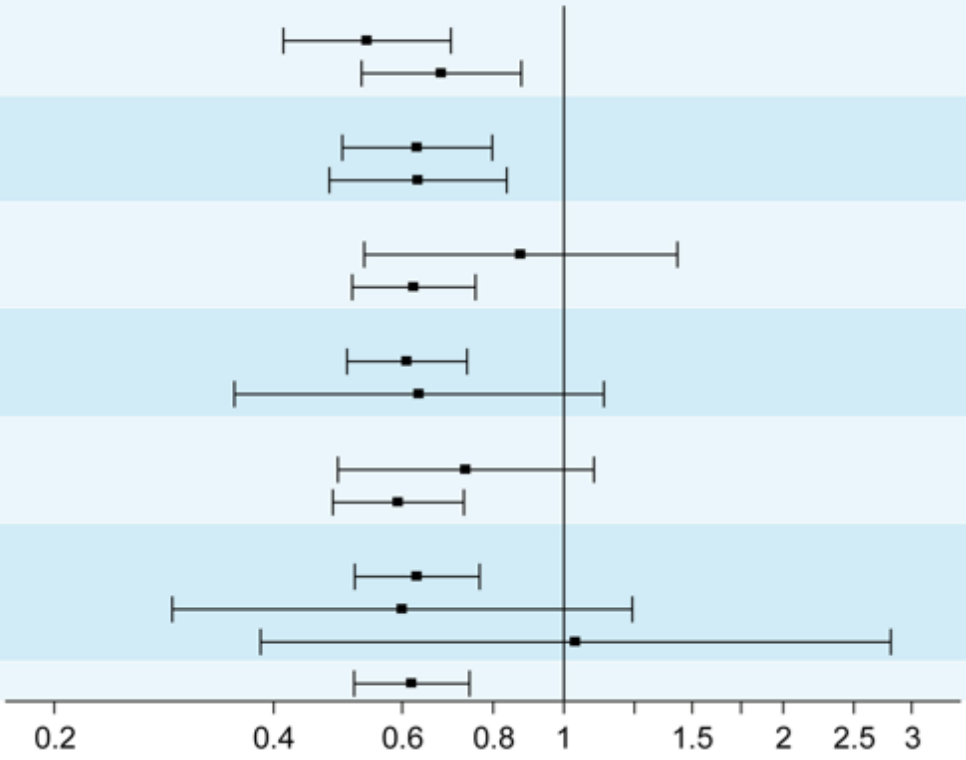
J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

KEY DATA

VISION Clinical Trial

Overall survival across subgroups

Subgroup	^{177}Lu-PSMA-617 + SOC (n = 551)	SOC alone (n = 280)	Hazard ratio (95% CI)
Androgen receptor pathway inhibitors as part of planned SOC			
Yes	243	146	0.54 (0.41, 0.70)
No	308	134	0.68 (0.53, 0.87)
LDH			
≤ 260 IU/L	368	182	0.63 (0.50, 0.80)
> 260 IU/L	182	97	0.63 (0.48, 0.84)
Liver metastases			
Yes	48	34	0.87 (0.53, 1.43)
No	503	246	0.62 (0.51, 0.76)
ECOG score			
0 or 1	510	258	0.61 (0.50, 0.74)
2	41	22	0.63 (0.35, 1.13)
Age			
< 65 years	145	60	0.73 (0.49, 1.10)
≥ 65 years	406	220	0.59 (0.48, 0.73)
Race			
White	486	235	0.63 (0.52, 0.77)
African American or Black	34	21	0.60 (0.29, 1.24)
Asian	9	11	1.04 (0.38, 2.81)
All patients	551	280	0.62 (0.52, 0.74)

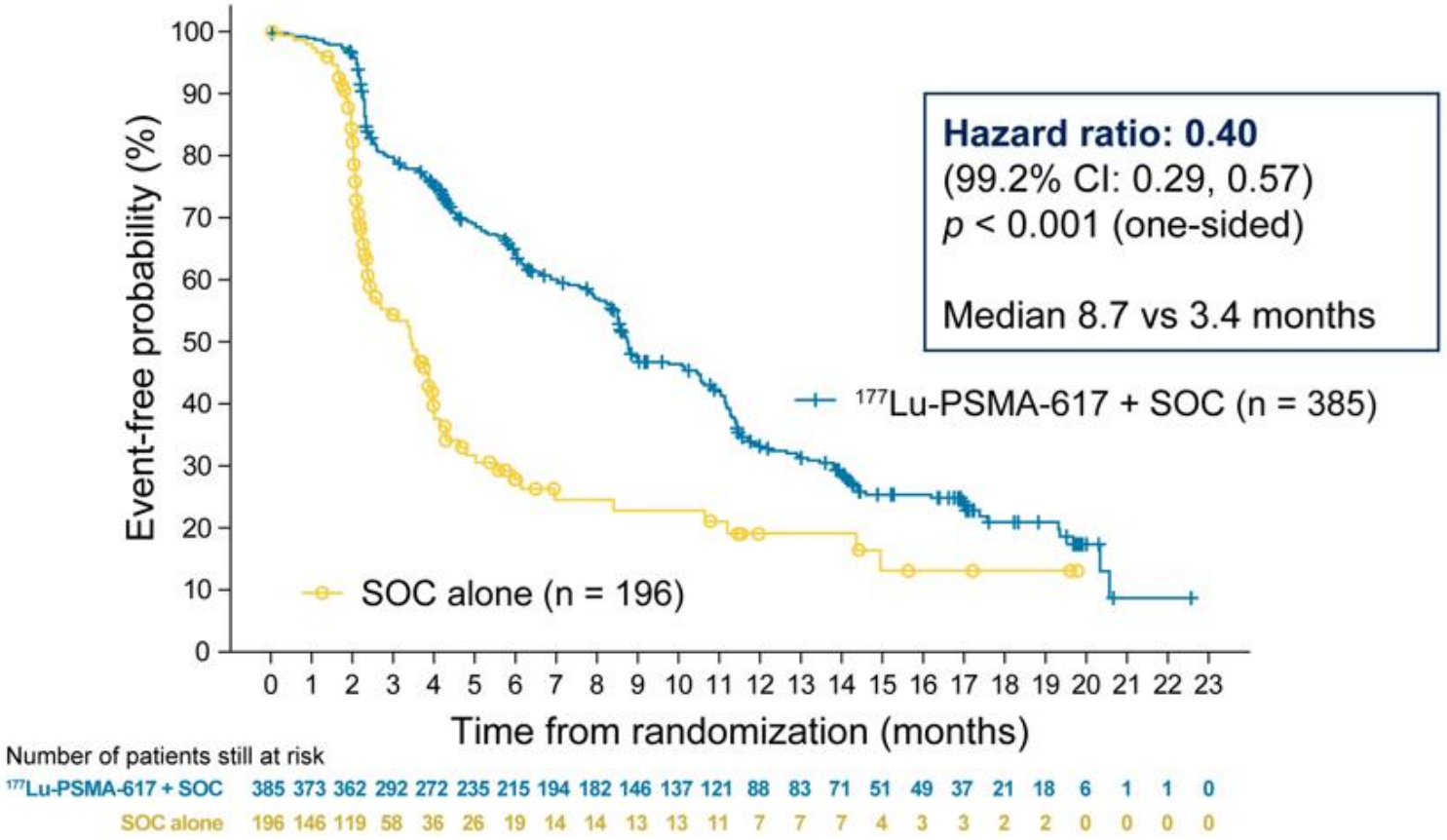


J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

KEY DATA

VISION Clinical Trial

Primary Endpoint: ^{177}Lu-PSMA-617 + SOC improved rPFS compared to SOC alone by a median of 5.3 months



- ^{177}Lu-PSMA-617 + SOC in the **whole randomized cohort** (n=831) revealed that rPFS was significantly improved by a median of **5.2** months (median rPFS, 8.8 vs 3.6 months; HR, 0.42 [99.2% CI: 0.32, 0.58]).

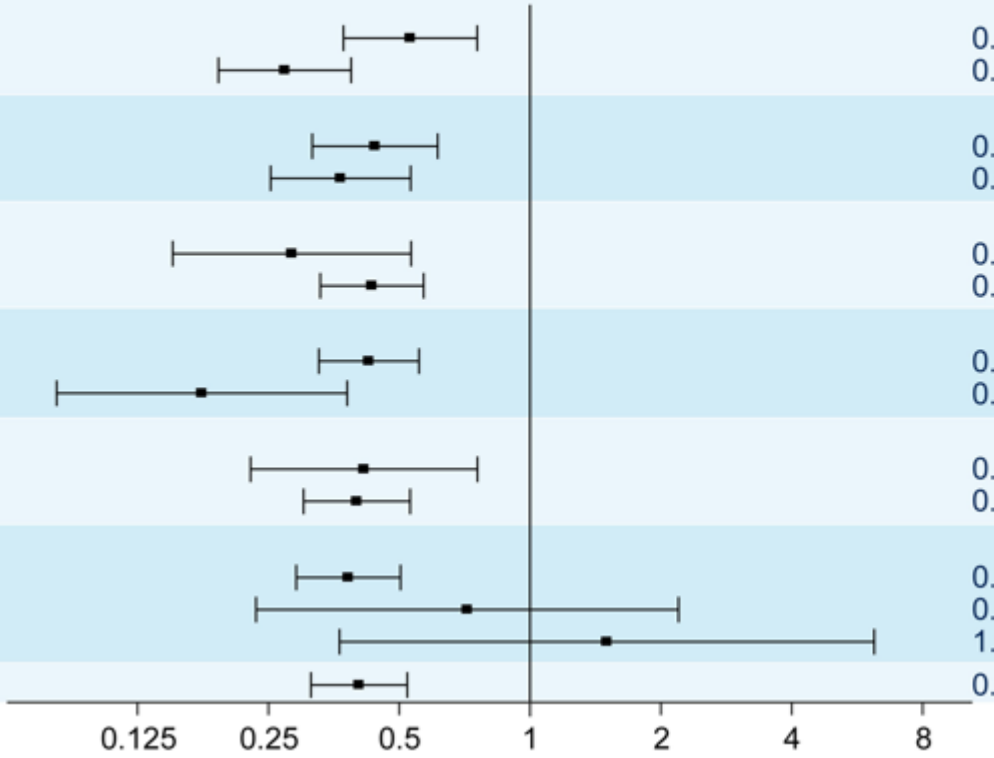
J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

KEY DATA

VISION Clinical Trial

rPFS across subgroups

Subgroup	^{177}Lu-PSMA-617 + SOC (n = 385)	SOC alone (n = 196)	Hazard ratio (95% CI)
Androgen receptor pathway inhibitors as part of planned SOC			
Yes	170	107	0.53 (0.37, 0.76)
No	215	89	0.27 (0.19, 0.39)
LDH			
≤ 260 IU/L	244	120	0.44 (0.32, 0.61)
> 260 IU/L	140	75	0.37 (0.25, 0.53)
Liver metastases			
Yes	37	22	0.28 (0.15, 0.53)
No	348	174	0.43 (0.33, 0.57)
ECOG score			
0 or 1	352	179	0.43 (0.33, 0.56)
2	33	17	0.18 (0.08, 0.38)
Age			
< 65 years	96	39	0.42 (0.23, 0.76)
≥ 65 years	289	157	0.40 (0.30, 0.53)
Race			
White	336	166	0.38 (0.29, 0.50)
African American or Black	29	14	0.72 (0.23, 2.20)
Asian	6	9	1.50 (0.36, 6.19)
All patients	385	196	0.40 (0.31, 0.52)

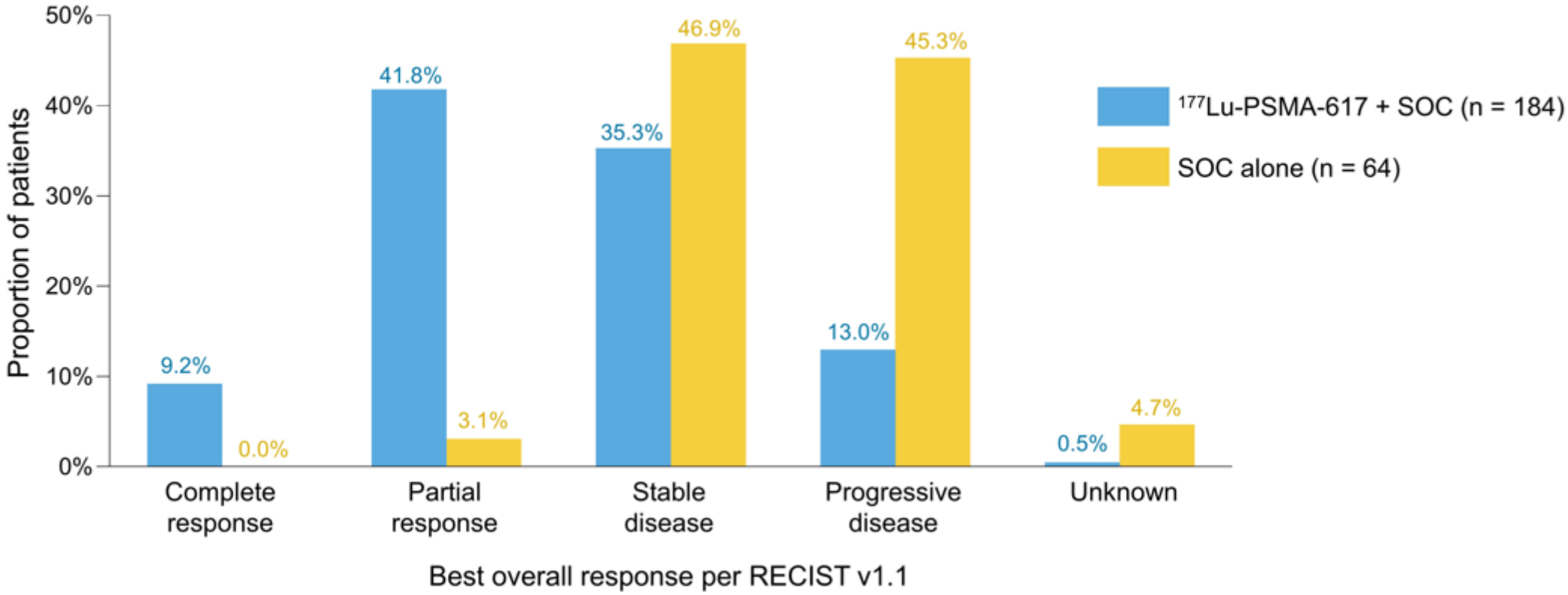


J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

KEY DATA

VISION Clinical Trial

Secondary Endpoint: ^{177}Lu-PSMA-617 improved RECISTv1.1 responses



J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

KEY DATA

VISION Clinical Trial

There was a higher rate of high-grade (Grade 3-5) treatment-emergent adverse events observed with ^{177}Lu-PSMA-617 versus SOC alone (28.4% vs 3.9%)

Patients, n (%)	All grades		Grade 3–5	
	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)
Any TEAE	451 (85.3)	59 (28.8)	150 (28.4)	8 (3.9)
Serious	49 (9.3)	5 (2.4)	43 (8.1)	5 (2.4)
Grade 5	–	–	5 (0.9)	0 (0.0)

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

KEY DATA

VISION Clinical Trial

Treatment with ^{177}Lu-PSMA-617 + SOC was associated with increased rates of bone marrow suppression, xerostomia, and nausea and vomiting

Patients, n (%)	All grades		Grade 3–5	
	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)
Fatigue	260 (49.1)	60 (29.3)	37 (7.0)	5 (2.4)
Bone marrow suppression	251 (47.4)	36 (17.6)	124 (23.4)	14 (6.8)
Leukopenia	66 (12.5)	4 (2.0)	13 (2.5)	1 (0.5)
Lymphopenia	75 (14.2)	8 (3.9)	41 (7.8)	1 (0.5)
Anemia	168 (31.8)	27 (13.2)	68 (12.9)	10 (4.9)
Thrombocytopenia	91 (17.2)	9 (4.4)	42 (7.9)	2 (1.0)
Dry mouth	208 (39.3)	2 (1.0)	0 (0.0)	0 (0.0)
Nausea and vomiting	208 (39.3)	35 (17.1)	8 (1.5)	1 (0.5)
Renal effects	46 (8.7)	12 (5.9)	18 (3.4)	6 (2.9)
Second primary malignancies	11 (2.1)	2 (1.0)	4 (0.8)	1 (0.5)
Intracranial hemorrhage	7 (1.3)	3 (1.5)	5 (0.9)	2 (1.0)

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

SUMMARY

VISION Clinical Trial

- ^{177}Lu-PSAM-617 extended overall survival and delayed radiographic disease progression in patients with prior androgen and taxane regimens
  - 40% reduction of risk of death and a 4-month improvement in median OS (HR, 0.62; 95% CI, 0.52-0.74; *P* <.001)
  - 60% reduction in risk of progression (HR, 0.40; 99.2% CI, 0.29-0.57; P <.001) with a 5.3-month improvement in median rPFS
- There were no unexpected or concerning safety related AEs associated with ^{177}Lu-PSAM-617 and in general was well tolerated

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

VISION Clinical Trial

^{177}Lu-PSMA-617 improves rPFS and prolongs OS compared with SOC alone in men with advanced-stage PSMA-positive mCRPC and should be adopted as SOC treatment

FDA APPROVAL

VISION Clinical Trial

June 16, 2021: The FDA granted breakthrough therapy designation to ^{177}Lu-PSMA-617 for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC).

The designation is supported by data from the phase 3 VISION trial (NCT03511664)

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2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
• OlympiA* • MONALEESA-3 • PALOMA-3 • ASCENT • DESTINY-Breast01 • OUTBACK*	• IMpower010 • CodeBreaK100 • CheckMate -9LA • CheckMate -227	• VISION* • KEYNOTE-564*	• DESTINY-Gastric01 • CheckMate -648

* 2021 ASCO Annual Meeting Plenary Session

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CLINICAL QUESTION

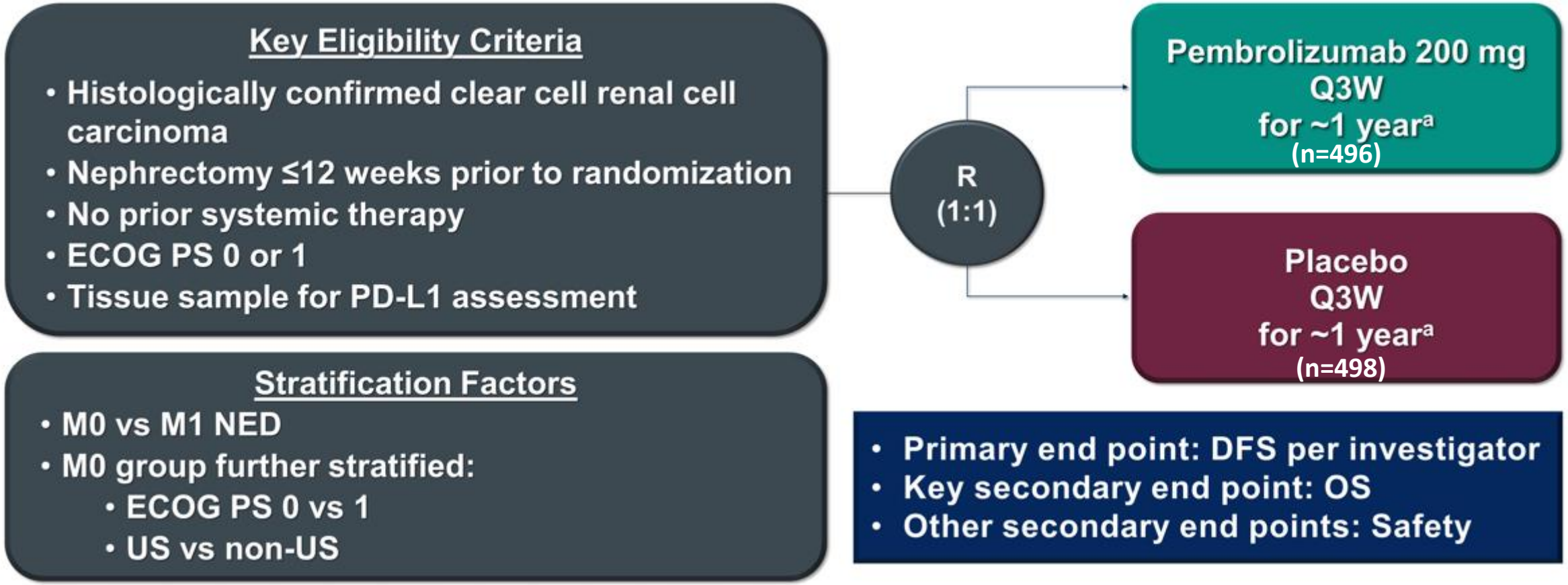
KEYNOTE-564 Clinical Trial

Does adjuvant immunotherapy pembrolizumab (Keytruda®) benefit patients with renal cell carcinoma post nephrectomy ?

KEY DATA

KEYNOTE-564 Clinical Trial

A Phase 3, double bind, multicenter trial of pembrolizumab vs placebo following nephrectomy in patients with clear cell renal cell carcinoma (n=994)

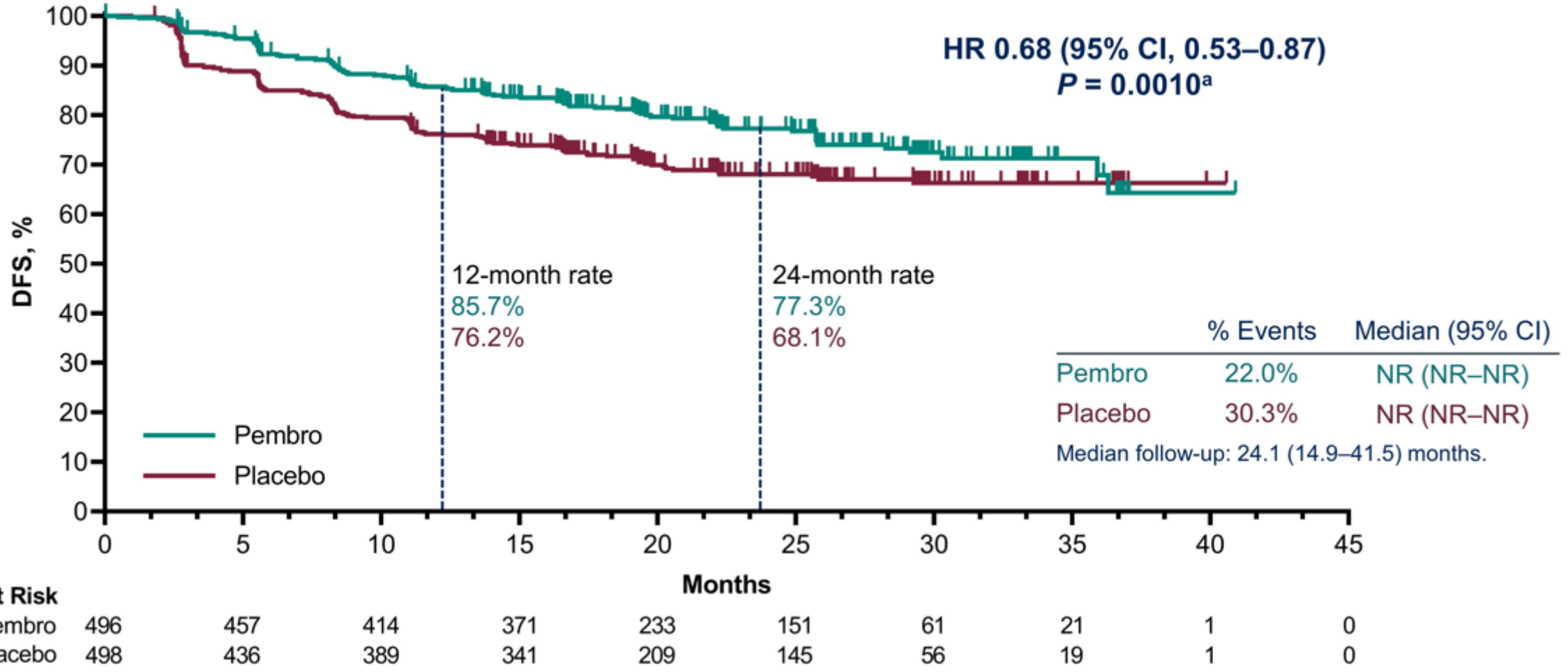


ASCO 2021 abstr 546

KEY DATA

KEYNOTE-564 Clinical Trial

DFS by Investigator, ITT population

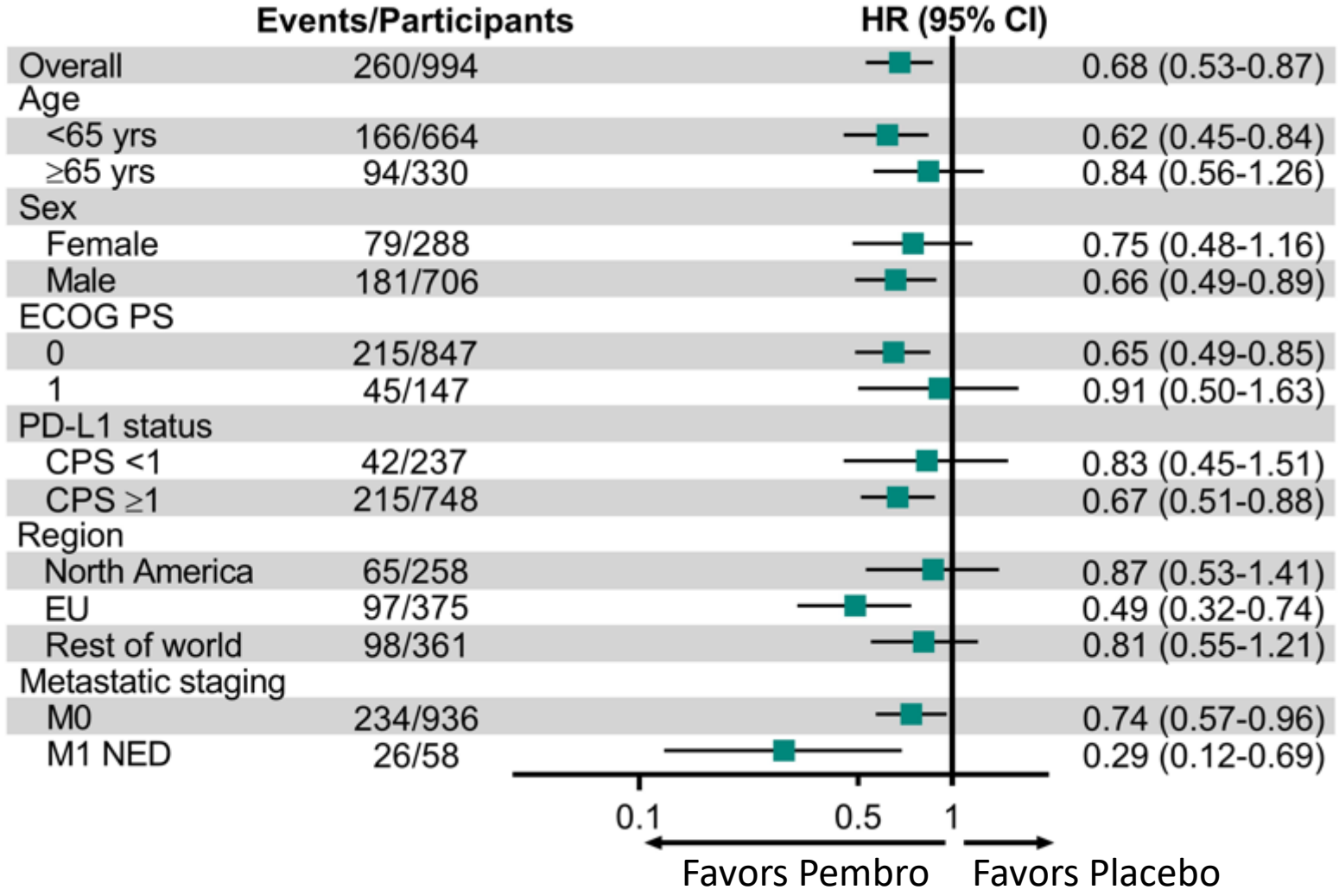


ASCO 2021 abstr 546

KEY DATA

KEYNOTE-564 Clinical Trial

DFS by Investigator by subgroups, ITT population



ASCO 2021 abstr 546

KEY DATA

KEYNOTE-564 Clinical Trial

Interim OS results, ITT population

ASCO 2021 abstr 546

KEY DATA

KEYNOTE-564 Clinical Trial

Safety Results

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

- Treatment with pembrolizumab was associated with increased rates of hypothyroidism and hyperthyroidism
  - Low incidence of high-dose corticosteroid treatment for immune-mediated AEs

ASCO 2021 abstr 546

SUMMARY

KEYNOTE-564 Clinical Trial

- Adjuvant pembrolizumab post nephrectomy demonstrated a statistically significant and clinically meaningful improvement in DFS versus placebo
- Benefit was consistent across subgroups, including the M1 NED populations and could be considered as a treatment option for these patients
- Safety results were within expectations and no new safety signals were observed

ASCO 2021 abstr 546

KEYNOTE-564 Clinical Trial

Keynote-564 is the first positive phase 3 study of an adjuvant immunotherapy (pembrolizumab, Keytruda®) for renal cell carcinoma and is a potential new standard of care in the adjuvant setting for RCC

2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
• OlympiA* • MONLEESA-3 • PALOMA-3 • ASCENT • DESTINY-Breast01 • OUTBACK*	• IMpower010 • CodeBreaK100 • CheckMate -9LA • CheckMate -227	• VISION* • KEYNOTE-564*	• DESTINY-Gastric01 • CheckMate -648

* 2021 ASCO Annual Meeting Plenary Session

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INDICATION

DESTINY-Gastric01 Clinical Trial

ENHERTU® (Fam-trastuzumab deruxtecan-nxki) is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen.

FDA approval: January 15, 2021

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DESTINY-Gastric01 Clinical Trial

Does fam-trastuzumab deruxtecan-nxki (T-DXd, ENHERTU®) provide benefit for patients with human epidermal growth factor receptor 2-positive advanced gastric cancer or gastroesophageal junction adenocarcinoma?

Final overall survival results

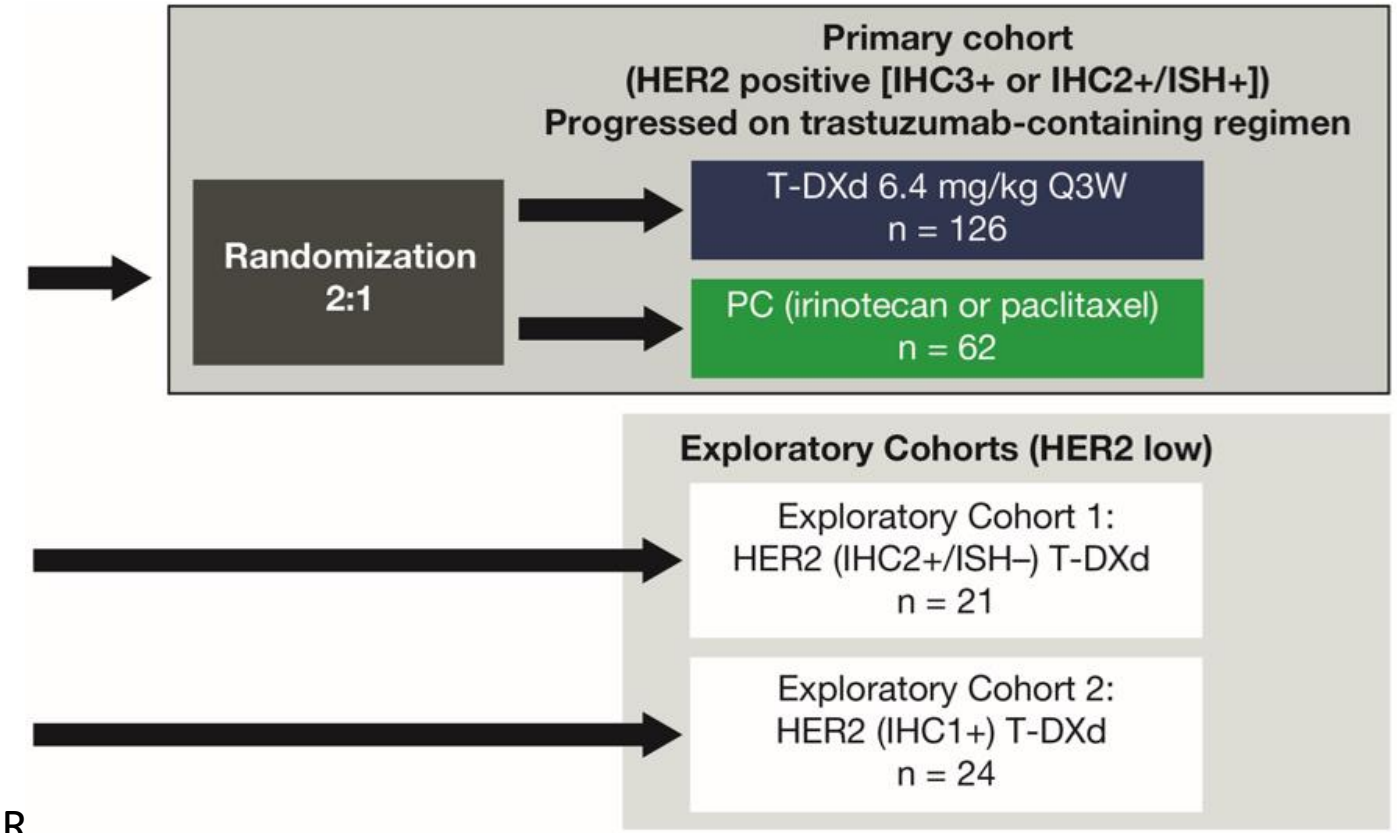
KEY DATA

DESTINY-Gastric01 Clinical Trial

Study Design: Phase 2, open-label, multicenter, randomized trial

Study population:

- HER2-expressing advanced gastric or GEJ adenocarcinoma
- ≥2 prior regimens; must include fluoropyrimidine and a platinum agent



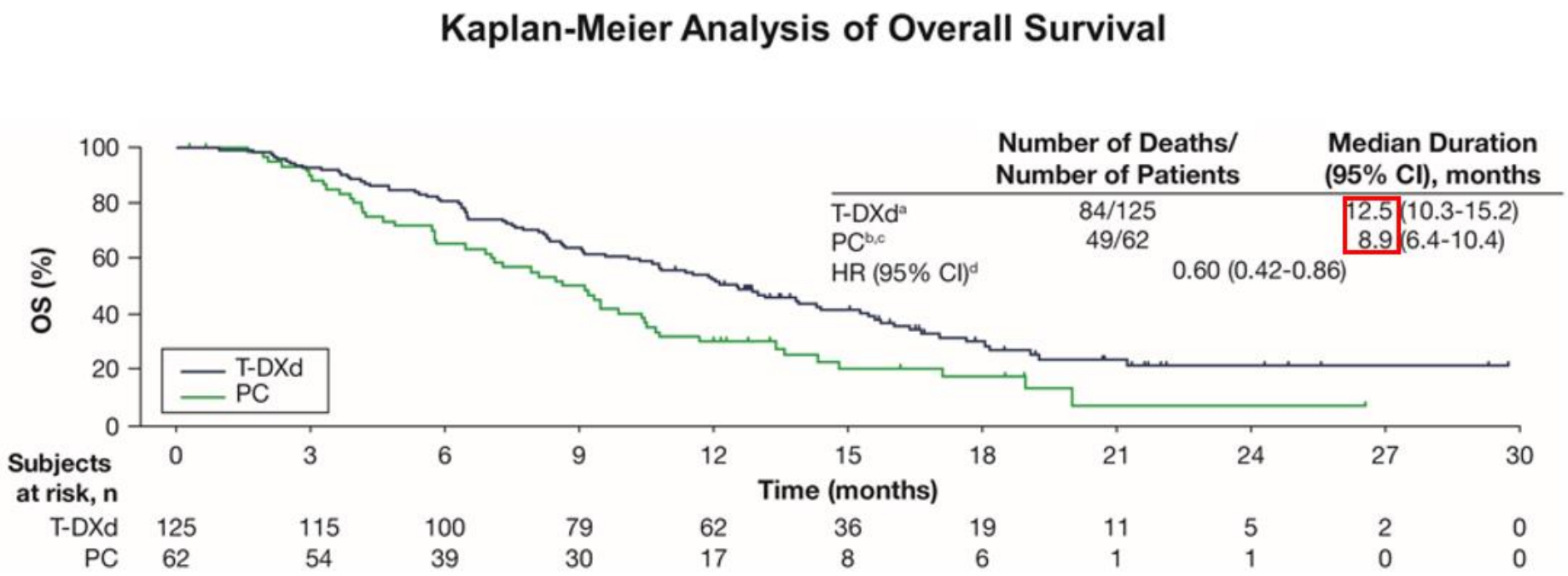
Primary endpoint: ORR by ICR

Secondary Endpoints: OS, DOR, PFS, confirmed ORR, and safety

J Clin Oncol 39, 2021 (suppl 15; abstr 4048)

KEY DATA

DESTINY-Gastric01 Clinical Trial



At primary analysis: 101 OS events, 54% maturity
Updated analysis: 133 OS events, 71% maturity

J Clin Oncol 39, 2021 (suppl 15; abstr 4048)

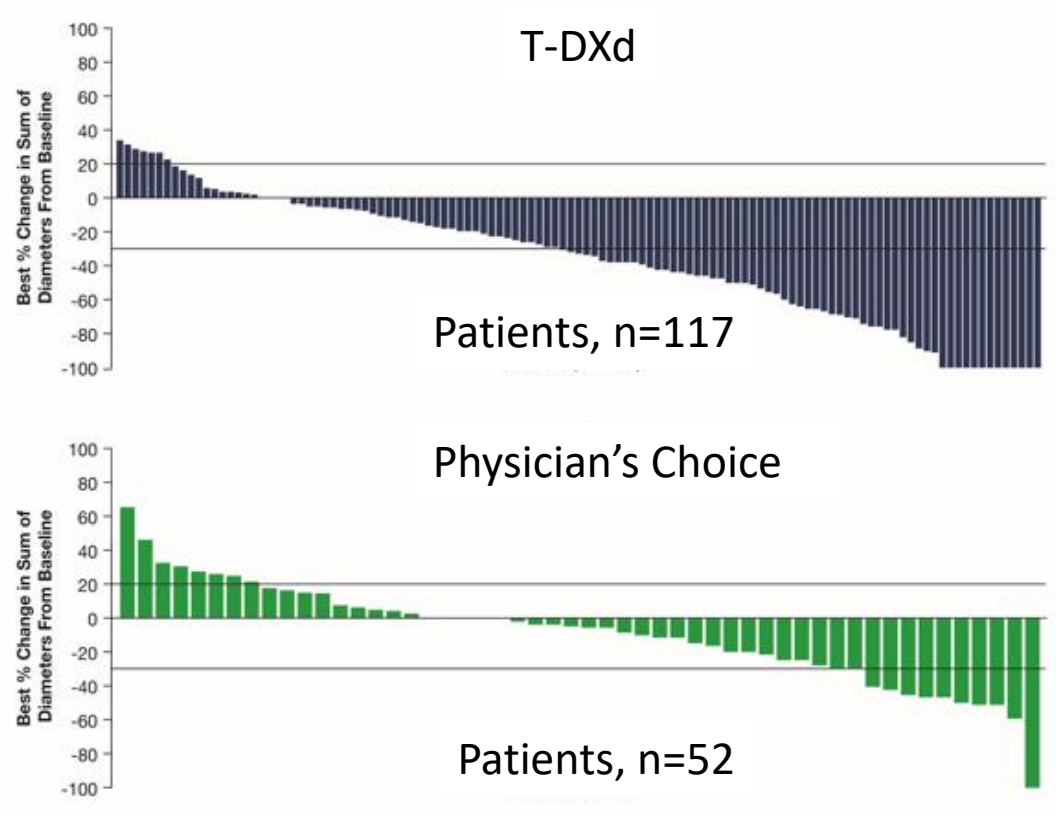
KEY DATA

DESTINY-Gastric01 Clinical Trial

ORR and other efficacy endpoints

	T-DXd n = 119	PC Overall n = 56
ORR (CR + PR) by ICR, n (%)[a]	61 (51.3) 95% CI, 41.9-60.5	8 (14.3) 95% CI, 6.4-26.2
	P < 0.0001[b]	
CR	11 (9.2)	0
PR	50 (42.0)	8 (14.3)
SD	42 (35.3)	27 (48.2)
PD	14 (11.8)	17 (30.4)
Not evaluable	2 (1.7)	4 (7.1)
Confirmed ORR (CR + PR) by ICR, n (%)[a]	50 (42.0) 95% CI, 33.0-51.4	7 (12.5) 95% CI, 5.2-24.1
CR	10 (8.4)	0
PR	40 (33.6)	7 (12.5)
SD	52 (43.7)	28 (50.0)
PD	14 (11.8)	17 (30.4)
Not evaluable	3 (2.5)	4 (7.1)
Confirmed DCR (CR + PR + SD), n (%)[a]	102 (85.7) 95% CI, 78.1-91.5	35 (62.5) 95% CI, 48.5-75.1
Confirmed DOR, median, months	12.5 95% CI, 5.6-NE	3.9 95% CI, 3.0-4.9
PFS, median, months	5.6 95% CI, 4.3-6.9	3.5 95% CI, 2.0-4.3
	P = 0.0003[c]	
TTR, median, months	1.5 95% CI, 1.4-1.7	1.6 95% CI, 1.3-1.7

Best percentage change from baseline in tumor size for individual pts



J Clin Oncol 39, 2021 (suppl 15; abstr 4048)

KEY DATA

DESTINY-Gastric01 Clinical Trial

Safety Results

	T-DXd n = 125			PC Overall n = 62		
		Grade			Grade	
Preferred Term, %	Any	3	4	Any	3	4
Neutrophil count decreased[b]	64.8	38.4	12.8	35.5	16.1	8.1
Nausea	63.2	5.6	0	46.8	1.6	0
Decreased appetite	60.8	16.8	0	45.2	12.9	0
Anemia[c]	57.6	38.4	0	30.6	21.0	1.6
Platelet count decreased[d]	40.0	9.6	1.6	6.5	1.6	1.6
White blood cell count decreased[e]	38.4	20.8	0	35.5	8.1	3.2
Malaise	34.4	0.8	0	16.1	0	0
Diarrhea	32.8	2.4	0	32.3	1.6	0
Vomiting	26.4	0	0	8.1	0	0
Pyrexia	24.8	0	0	16.1	0	0
Constipation	24.8	0	0	24.2	0	0
Lymphocyte count decreased[f]	23.2	7.2	4.8	3.2	0	1.6
Alopecia	22.4	0	0	14.5	0	0
Fatigue	21.6	7.2	0	24.2	3.2	0

- Grade ≥3 AEs occurred in 85.6% of T-DXd patients vs 56.5% with PC
  - The most common were decreased neutrophil count (51.2%, 24.2%), anemia (38.4%, 22.6%), and decreased white blood cell count (20.8%, 11.3%)
- 16 patients (12.8%) had T-DXd–related ILD, as determined by an independent adjudication committee
  - There were 13 grade 1 or 2, two grade 3, one grade 4, and no grade 5 events
  - There were four ILD events since the primary analysis; one grade 1 and three grade 2
  - Among the 16 total ILD events, the median time to first onset was 102.5 days (range, 36-638 days)
  - There were no ILD events in the PC arm
- There was one T-DXd-related death from pneumonia (non-ILD), as reported in the primary analysis
- There were no AE-related deaths in the PC arm

J Clin Oncol 39, 2021 (suppl 15; abstr 4048)

SUMMARY

DESTINY-Gastric01 Clinical Trial

- T-DXd demonstrated clinically meaningful OS benefit (~40% reduced risk of death) and clinically relevant improvement in ORR compared with PC standard chemotherapy in HER2+ advanced gastric or GEJ cancer

- Overall safety was manageable and consistent with the primary analysis
  - The most common AEs were gastrointestinal or hematologic in nature
  - 16 patients (12.8%) had T-DXd related ILD; most were grade 1 or 2

Post-hoc exploratory biomarker analysis and efficacy in HER2+ and HER2-low advanced gastric cancer was presented at the ESMO World Congress on Gastrointestinal Cancer
30 June – 3 July 2021; Abstract# O-14

J Clin Oncol 39, 2021 (suppl 15; abstr 4048)

DESTINY-Gastric01 Clinical Trial

Updated OS results support continued use of fam-trastuzumab deruxtecan-nxki (T-DXd, ENHERTU®) as an effective treatment option for patients with HER2+ advanced gastric or GEJ adenocarcinoma who have received a prior trastuzumab-based regimen

2021 ASCO Key Studies

Breast and Gynecologic Cancer	Lung Cancer	Genitourinary Cancer	Gastrointestinal Cancer
• OlympiA* • MONLEESA-3 • PALOMA-3 • ASCENT • DESTINY-Breast01 • OUTBACK*	• IMpower010 • CodeBreaK100 • CheckMate -9LA • CheckMate -227	• VISION* • KEYNOTE-564*	• DESTINY-Gastric01 • CheckMate -648

* 2021 ASCO Annual Meeting Plenary Session

CLINICAL QUESTION

CheckMate -648 Clinical Trial

Does the addition of nivolumab (Opdivo®) in the 1L setting provide benefit to patients with advanced esophageal squamous cell carcinoma (ESCC)?

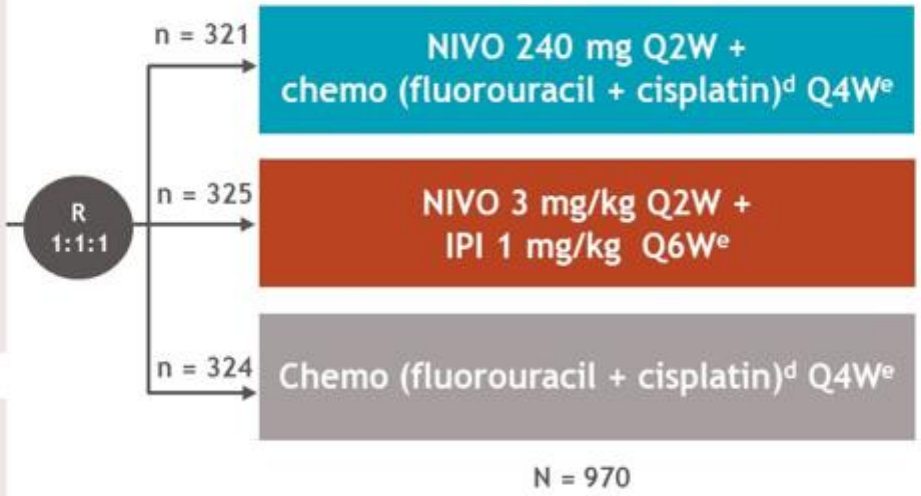
KEY DATA

CheckMate -648 Clinical Trial

A phase III study of first-line nivolumab (Opdivo®) plus ipilimumab (Yervoy®) versus nivolumab plus chemotherapy for patients with advanced esophageal squamous cell carcinoma (ESCC)

Key eligibility criteria
- Unresectable advanced, recurrent or metastatic ESCC
- ECOG PS 0-1
- No prior systemic treatment for advanced disease
- Measurable disease

Stratification factors
- Tumor cell PD-L1 expression (≥ 1% vs < 1%[b])
- Region (East Asia[c] vs rest of Asia vs ROW)
- ECOG PS (0 vs 1)
- Number of organs with metastases (≤ 1 vs ≥ 2)



Primary endpoints:
- OS and PFS[f] (tumor cell PD-L1 ≥ 1%)

Secondary endpoints:
- OS and PFS[f] (all randomized)
- ORR[f] (tumor cell PD-L1 ≥ 1% and all randomized)

At data cutoff (January 18, 2021) the minimum follow-up was 12.9 months

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4001)

KEY DATA

CheckMate -648 Clinical Trial

Duration and Discontinuation

All treated	NIVO + chemo (n = 310)	NIVO + IPI (n = 322)	Chemo (n = 304)
Median duration of treatment, months (range)	5.7 (0.1-30.6)	2.8 (0.0-24.0)	3.4 (0.0-19.5)
Discontinued treatment, n (%)	285 (92)	301 (93)	300 (99)
Reasons for treatment discontinuation, n (%)			
Disease progression	184 (59)	174 (54)	193 (63)
AE related to treatment	33 (11)	59 (18)	40 (13)
AE not related to treatment	28 (9)	19 (6)	12 (4)
Patient request	15 (5)	13 (4)	20 (7)
Other[a]	25 (8)	36 (11)	35 (12)

55% of all randomized patients received subsequent treatment

- The predominant subsequent treatment across all 3 treatment arms was chemo
- Subsequent immunotherapy was received by ~5% of patients in the NIVO-containing arm and 16% in the chemo arm

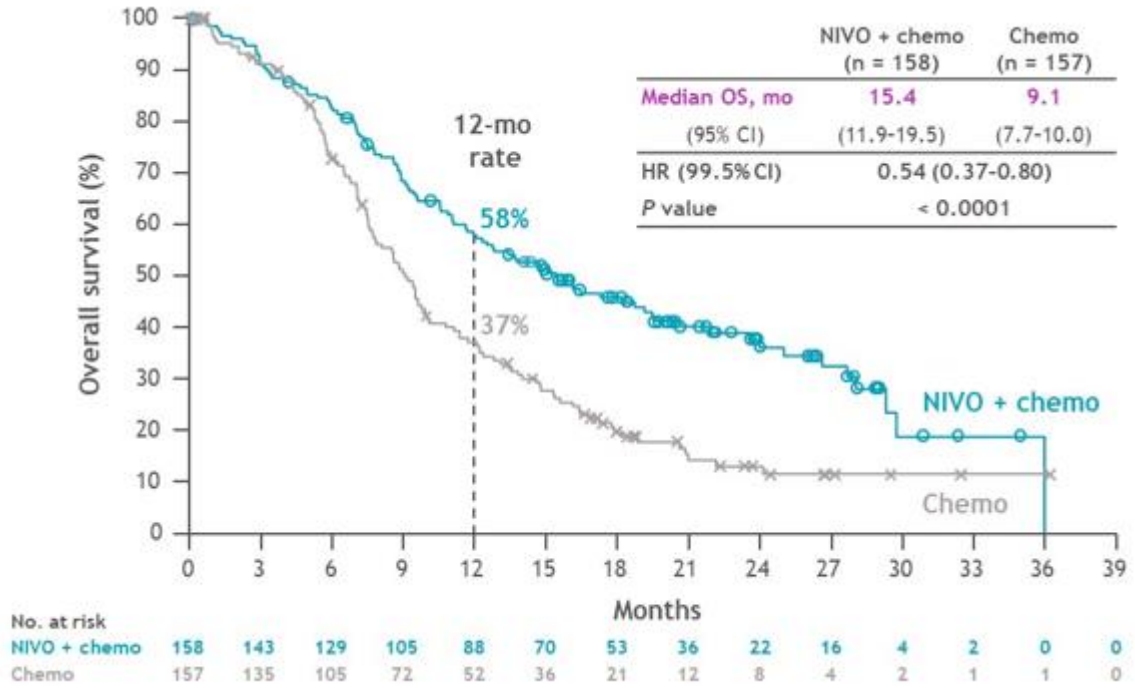
J Clin Oncol 39, 2021 (suppl 15; abstr LBA4001)

KEY DATA

CheckMate -648 Clinical Trial

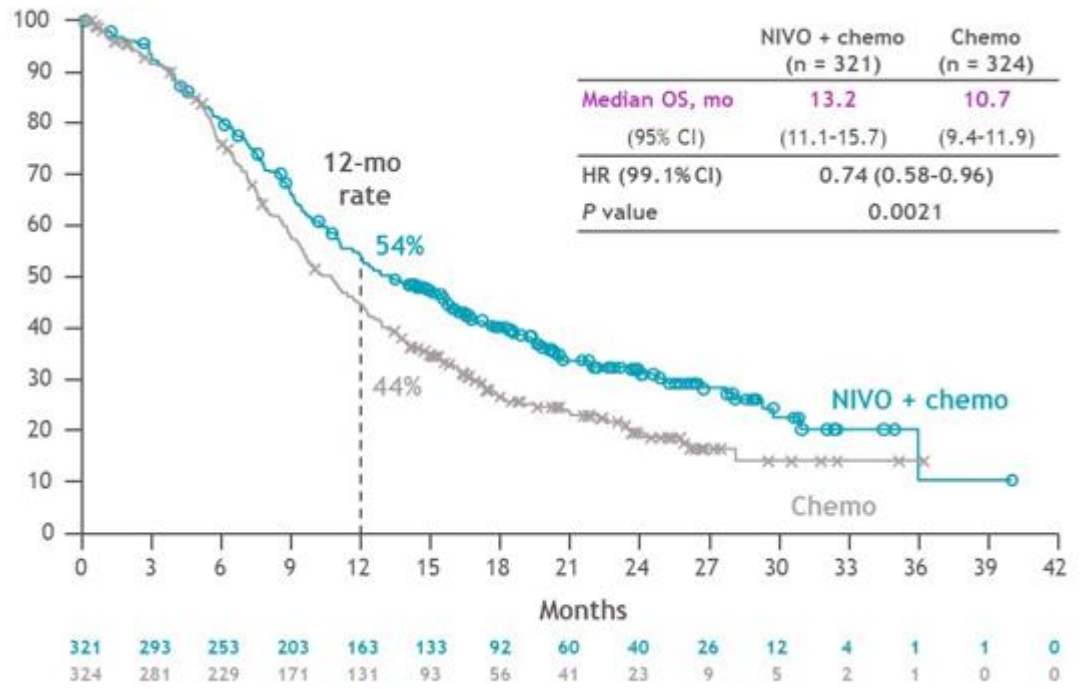
Overall survival: NIVO + chemo vs chemo alone

Primary endpoint (tumor cell PD-L1 ≥ 1%)



	NIVO + chemo (n = 158)	Chemo (n = 157)
Median OS, mo	15.4	9.1
(95% CI)	(11.9-19.5)	(7.7-10.0)
HR (99.5% CI)	0.54 (0.37-0.80)	
P value	< 0.0001	

All randomized



	NIVO + chemo (n = 321)	Chemo (n = 324)
Median OS, mo	13.2	10.7
(95% CI)	(11.1-15.7)	(9.4-11.9)
HR (99.1% CI)	0.74 (0.58-0.96)	
P value	0.0021	

Superior OS with NIVO + chemo vs chemo in tumor cell PD-L1≥ 1% and all randomized populations

- Tumor cell PD-L1 ≥ 1%: 46% reduction in the risk of death and a 6.3-month improvement in median OS
- All randomized: 26% reduction in the risk of death and a 2.5-month improvement in median OS

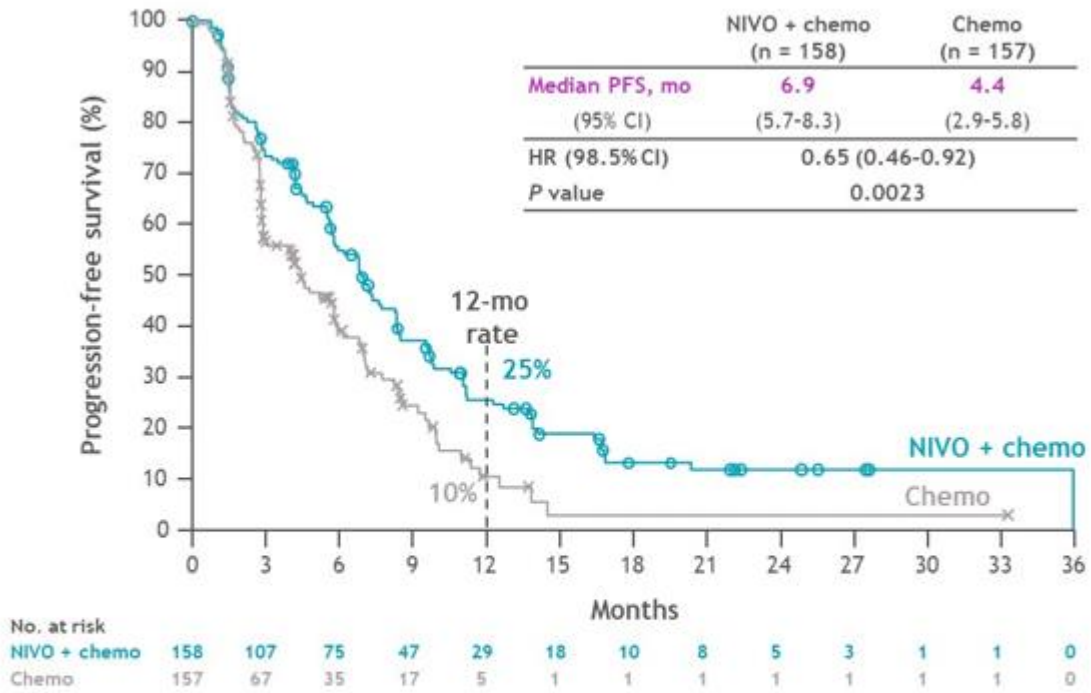
J Clin Oncol 39, 2021 (suppl 15; abstr LBA4001)

KEY DATA

CheckMate -648 Clinical Trial

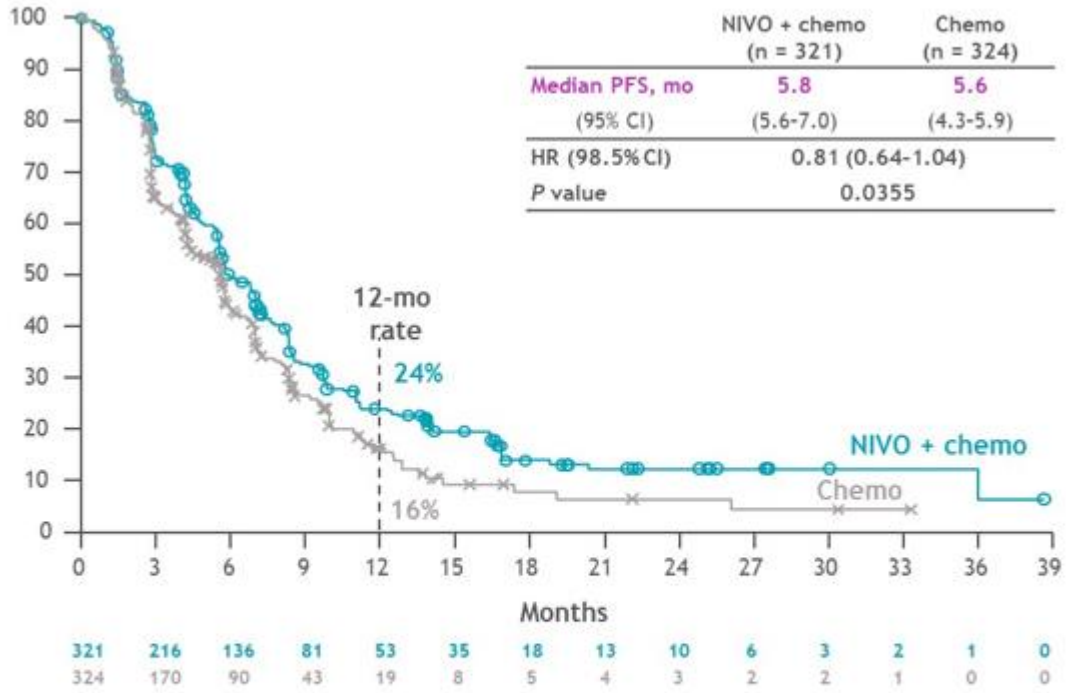
PFS: NIVO + chemo vs chemo alone

Primary endpoint (tumor cell PD-L1 ≥ 1%; per BICR)



	NIVO + chemo (n = 158)	Chemo (n = 157)
Median PFS, mo	6.9	4.4
(95% CI)	(5.7-8.3)	(2.9-5.8)
HR (98.5% CI)	0.65 (0.46-0.92)	
P value	0.0023	

All randomized (per BICR)



	NIVO + chemo (n = 321)	Chemo (n = 324)
Median PFS, mo	5.8	5.6
(95% CI)	(5.6-7.0)	(4.3-5.9)
HR (98.5% CI)	0.81 (0.64-1.04)	
P value	0.0355	

- Primary endpoint of PFS per BICR met in patients with tumor cell PD-L1 ≥ 1%
- Prespecified significance boundary for PFS per BICR not met in all randomized patients
- Improved PFS per INV[b] with HR of 0.53 (95% CI, 0.41-0.69) in tumor cell PD-L1 ≥ 1% and 0.69 (95% CI, 0.58-0.83) in all randomized populations

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4001)

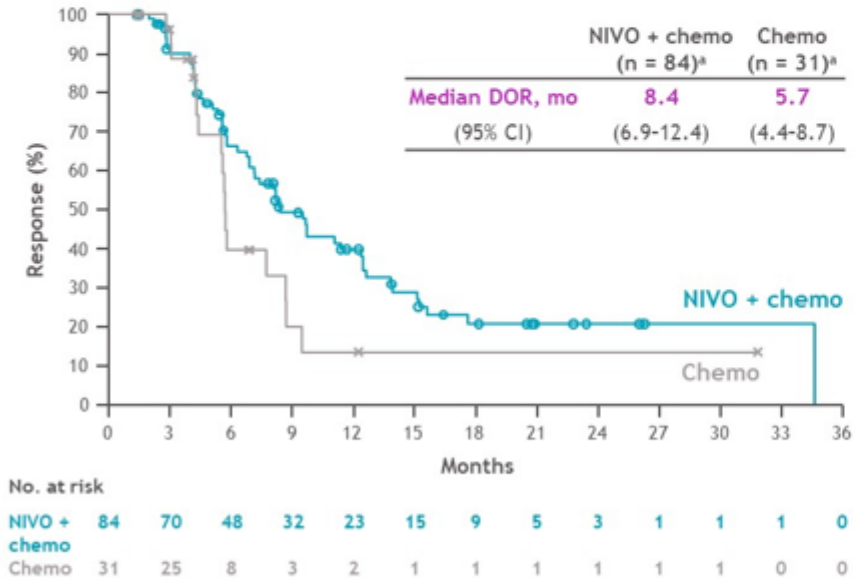
KEY DATA

CheckMate -648 Clinical Trial

Response and duration of response: NIVO + chemo vs chemo alone

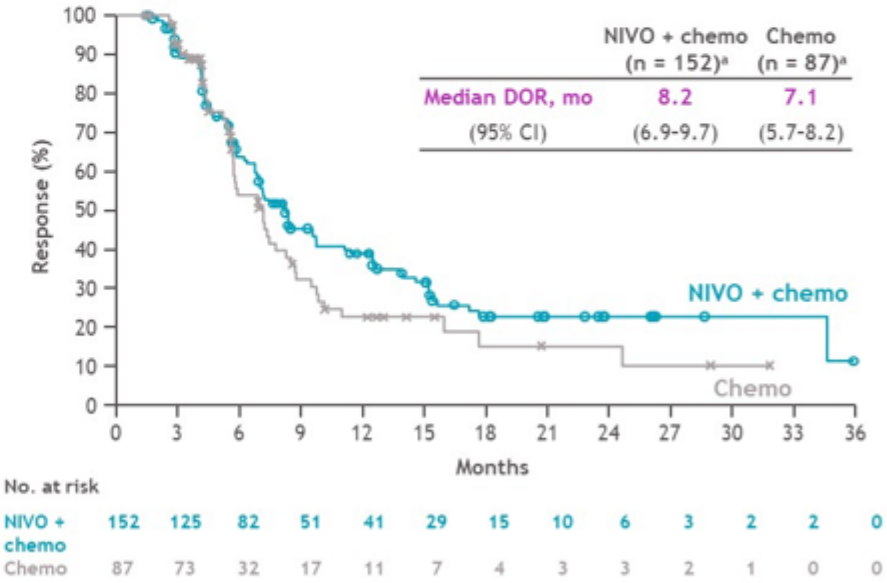
Tumor cell PD-L1 ≥ 1%

Response per BICR	NIVO + chemo (n = 158)	Chemo (n = 157)
ORR, % (95% CI)	53 (45-61)	20 (14-27)
CR	16	5
PR	37	15
SD	25	46
PD	14	15



All randomized

Response per BICR	NIVO + chemo (n = 321)	Chemo (n = 324)
ORR, % (95% CI)	47 (42-53)	27 (22-32)
CR	13	6
PR	34	21
SD	32	46
PD	13	12



[a]Number of responders.

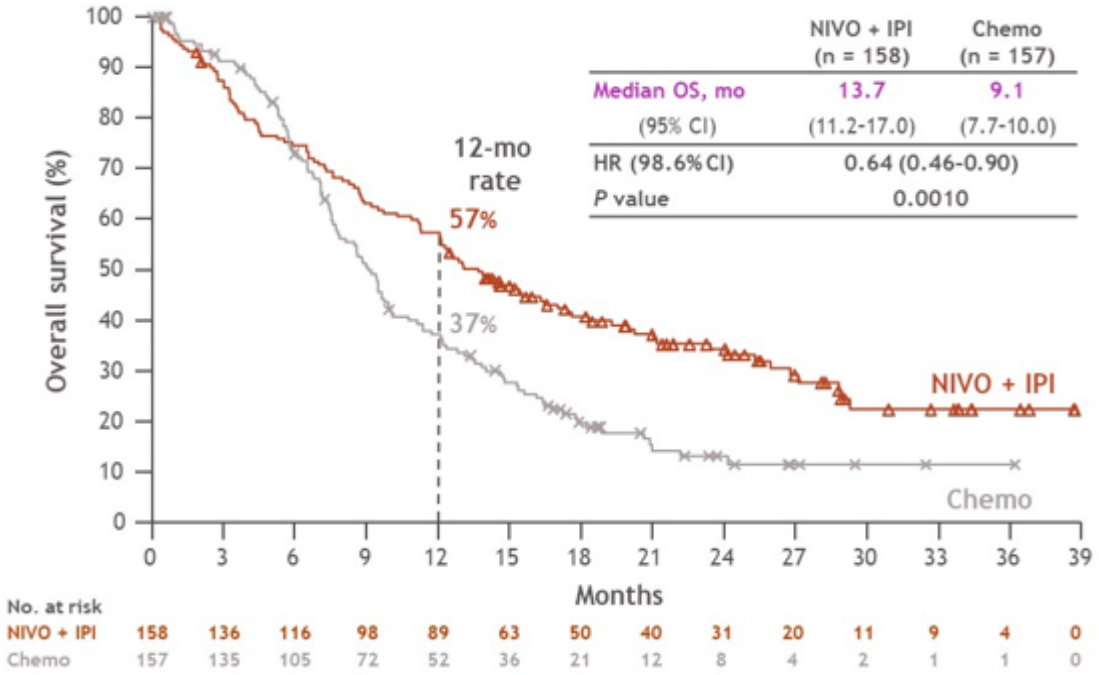
J Clin Oncol 39, 2021 (suppl 15; abstr LBA4001)

KEY DATA

CheckMate -648 Clinical Trial

Overall survival: NIVO + IPI vs chemo alone

Primary endpoint (tumor cell PD-L1 ≥ 1%)

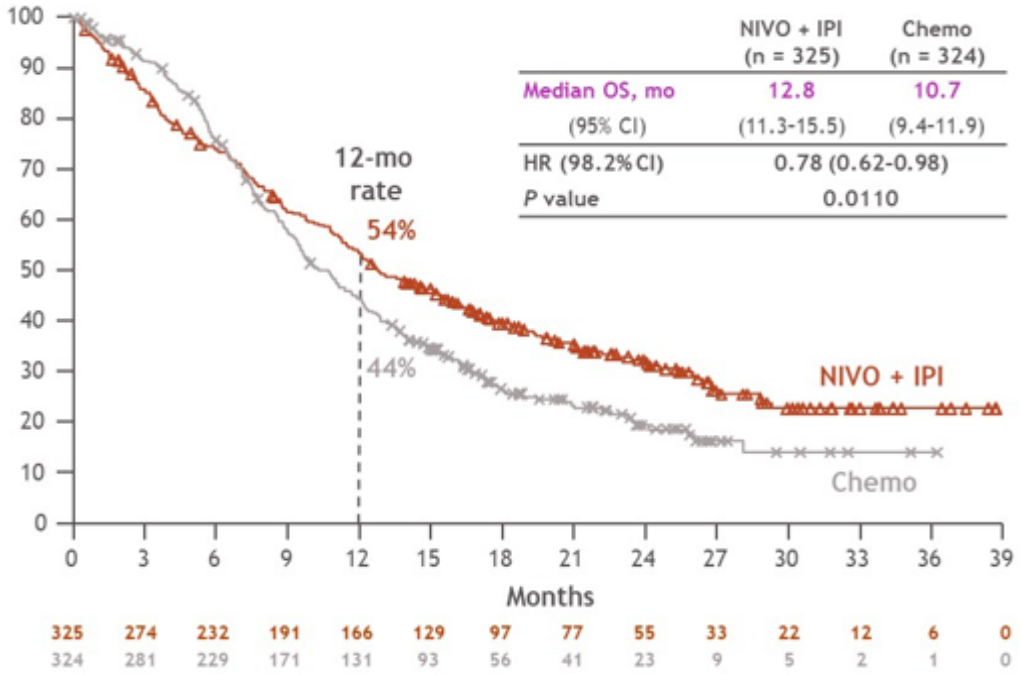


	NIVO + IPI (n = 158)	Chemo (n = 157)
Median OS, mo	13.7	9.1
(95% CI)	(11.2-17.0)	(7.7-10.0)
HR (98.6% CI)	0.64 (0.46-0.90)	
P value	0.0010	

No. at risk

NIVO + IPI	158	136	116	98	89	63	50	40	31	20	11	9	4	0
Chemo	157	135	105	72	52	36	21	12	8	4	2	1	1	0

All randomized



	NIVO + IPI (n = 325)	Chemo (n = 324)
Median OS, mo	12.8	10.7
(95% CI)	(11.3-15.5)	(9.4-11.9)
HR (98.2% CI)	0.78 (0.62-0.98)	
P value	0.0110	

NIVO + IPI	325	274	232	191	166	129	97	77	55	33	22	12	6	0
Chemo	324	281	229	171	131	93	56	41	23	9	5	2	1	0

- Superior OS with NIVO + IPI vs chemo in tumor cell PD-L1 ≥ 1% and all randomized populations
  - Tumor cell PD-L1 ≥ 1%: 36% reduction in the risk of death and a 4.6-month improvement in median OS
  - All randomized: 22% reduction in the risk of death and a 2.1-month improvement in median OS

[a]Minimum follow-up 12.9 months.

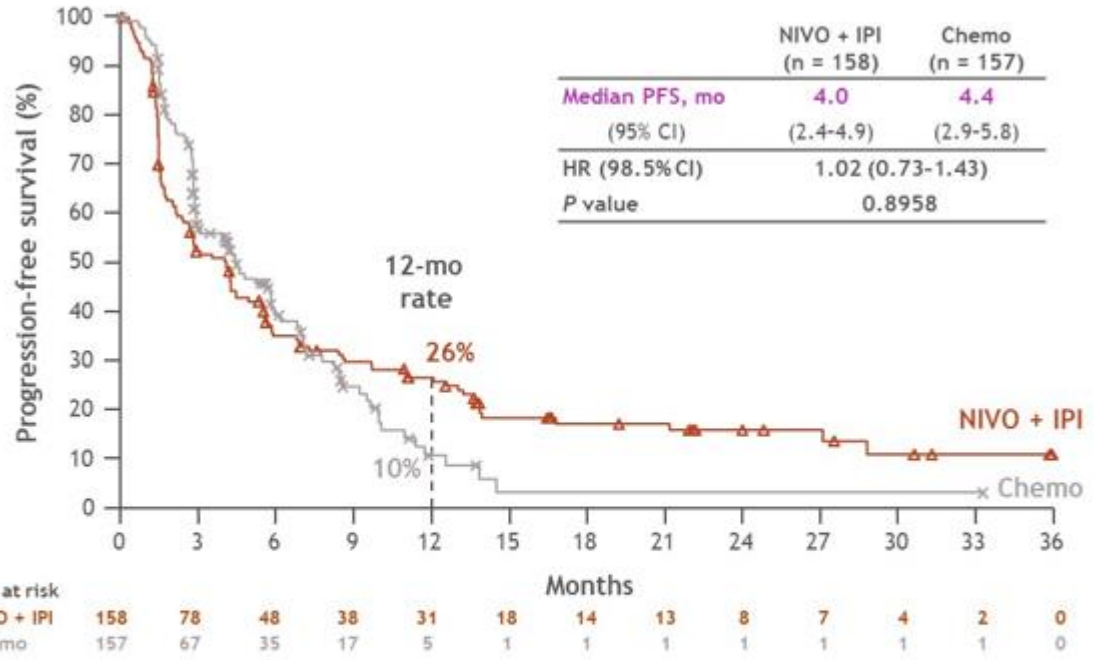
J Clin Oncol 39, 2021 (suppl 15; abstr LBA4001)

KEY DATA

CheckMate -648 Clinical Trial

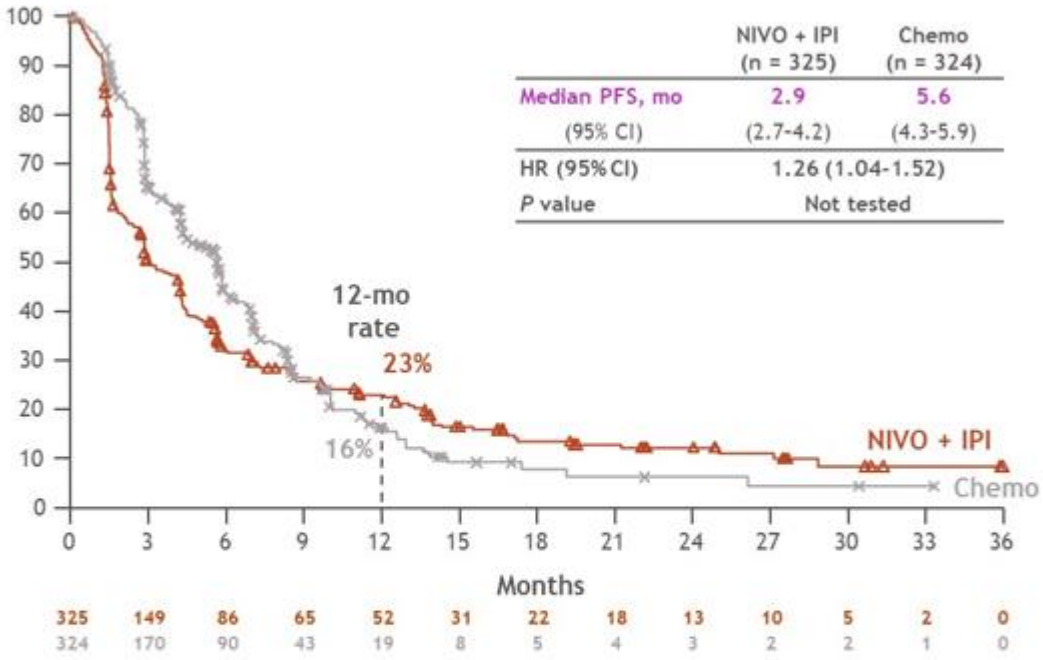
PFS: NIVO + IPI vs chemo alone

Primary endpoint (tumor cell PD-L1 ≥ 1%; per BICR)



	NIVO + IPI (n = 158)	Chemo (n = 157)
Median PFS, mo	4.0	4.4
(95% CI)	(2.4-4.9)	(2.9-5.8)
HR (98.5% CI)	1.02 (0.73-1.43)	
P value	0.8958	

All randomized (per BICR)



	NIVO + IPI (n = 325)	Chemo (n = 324)
Median PFS, mo	2.9	5.6
(95% CI)	(2.7-4.2)	(4.3-5.9)
HR (95% CI)	1.26 (1.04-1.52)	
P value	Not tested	

- Primary endpoint of PFS per BICR not met in patients with tumor cell PD-L1 ≥ 1%
- PFS per BICR not hierarchically tested in all randomized patients
- Directionally improved PFS per INV[b] with HR of 0.83 (95% CI, 0.64-1.07) in tumor cell PD-L1 ≥ 1% and 1.01 (95% CI, 0.85-1.21) in all randomized populations

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4001)

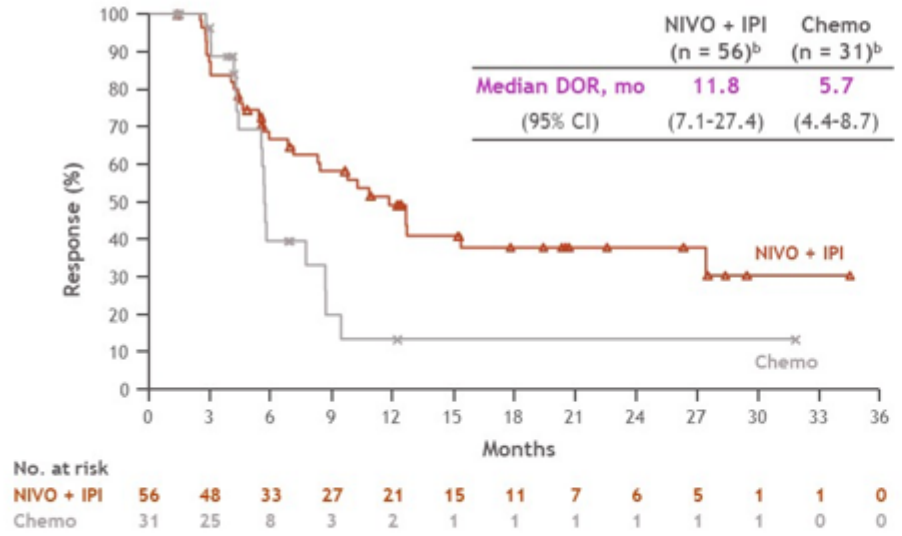
KEY DATA

CheckMate -648 Clinical Trial

Response and duration of response: NIVO + IPI vs chemo alone

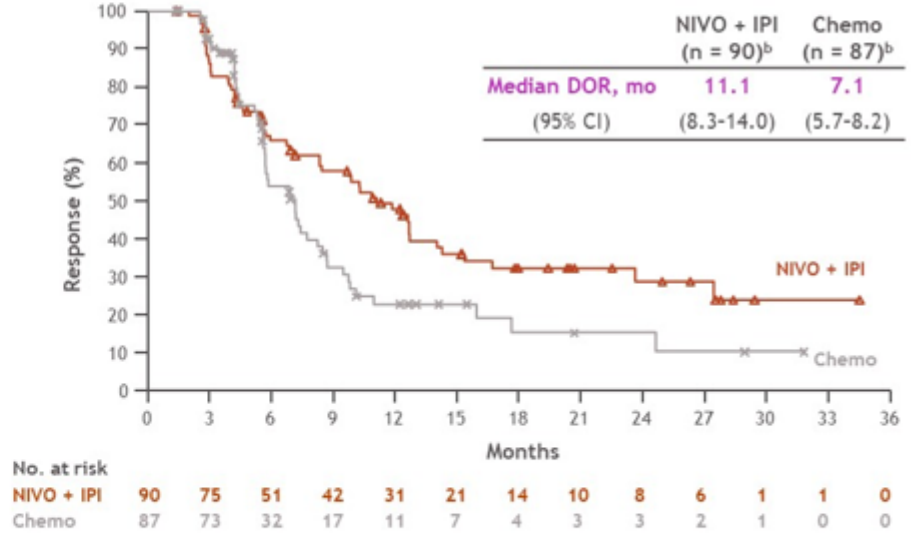
Tumor cell PD-L1 ≥ 1%

Response per BICR	NIVO + IPI (n = 158)	Chemo (n = 157)
ORR, % (95% CI)	35 (28-43)	20 (14-27)
CR[a]	18	5
PR[a]	18	15
SD	27	46
PD	30	15



All randomized

Response per BICR	NIVO + IPI (n = 325)	Chemo (n = 324)
ORR, % (95% CI)	28 (23-33)	27 (22-32)
CR	11	6
PR	17	21
SD	32	46
PD	32	12



[a]Percentages may not add up to ORR due to rounding; [b]Number of responders.

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KEY DATA

CheckMate -648 Clinical Trial

Treatment-Related Adverse Events

All treated,[a] n (%)	NIVO + chemo (n = 310)		NIVO + IPI (n = 322)		Chemo (n = 304)	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
Any TRAEs[b]	297 (96)	147 (47)	256 (80)	102 (32)	275 (90)	108 (36)
Serious TRAEs[b]	74 (24)	57 (18)	103 (32)	73 (23)	49 (16)	38 (13)
TRAEs leading to discontinuation[b,c]	106 (34)	29 (9)	57 (18)	41 (13)	59 (19)	14 (5)
Treatment-related deaths[d]	5 (2)[e]		5 (2)[f]		4 (1)[g]	

- Most common any-grade TRAEs (≥ 10%) included:
  - NIVO + chemo and chemo arms: nausea, decreased appetite, and stomatitis
  - NIVO+ IPI arm: rash, pruritus, and hypothyroidism
- The incidence of TRAEs in patients with tumor cell PD-L1 ≥ 1% was consistent with all treated patients across all arms

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4001)

SUMMARY

CheckMate -648 Clinical Trial

- NIVO is the first PD-1 inhibitor to demonstrate superior OS and durable responses in combination with either chemo or IPI versus chemo alone, in previously untreated patients with advanced ESCC
  - Statistically significant and clinically meaningful OS benefit was observed with NIVO + chemo and NIVO + IPI for patients with tumor cell PD-L1 ≥ 1% and all randomized patients
  - Clinically meaningful PFS benefit and higher ORR with NIVO + chemo
  - Longer duration of response with NIVO-containing regimens

- No new safety signals were identified with NIVO + chemo or NIVO + IPI

J Clin Oncol 39, 2021 (suppl 15; abstr LBA4001)

CheckMate -648 Clinical Trial

NIVO (Opdivo®) is the first PD-1 inhibitor when combined with either chemo or IPI (Yevroy®) to show superior OS benefit in previously untreated patients with advanced ESCC and either combination offers a potential new 1L treatment option