2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

CLINICAL QUESTION

DESTINY-Breast03 Clinical Trial

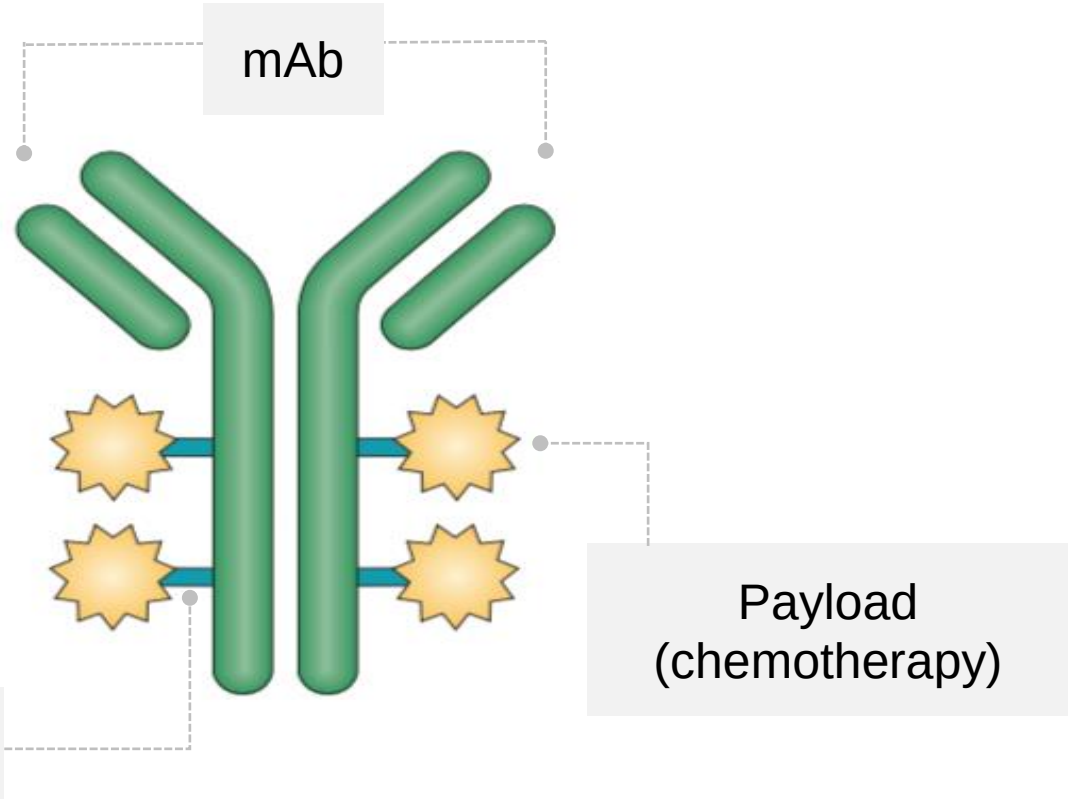
Does the use of fam-trastuzumab deruxtecan-nxki (T-DXd, ENHERTU®) in the 2L setting benefit pts with HER2+ MBC, when compared with T-DM1?

cornerstone specialty network™

Antibody Drug Conjugates (ADCs)

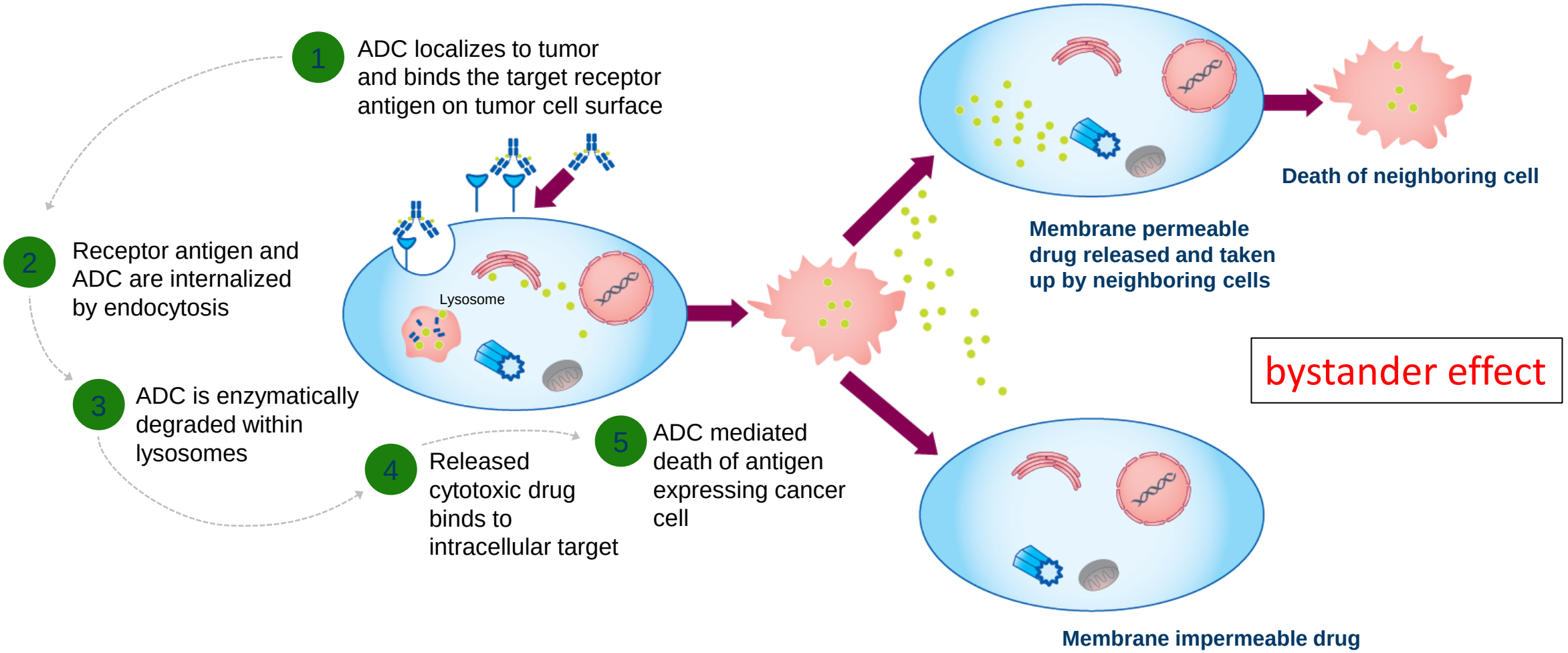
- ADCs are a class of cancer therapies that combine antigen specificity and potent cytotoxicity in a single molecule
- Offer increased therapeutic index of anticancer agents

Structure of ADC



Drago JZ, Modi S, Chandarlapaty S. Nature Reviews Clinical Oncology 18 (6), 327-344, 2021

ADCs Provide Efficient Targeted Delivery of Cytotoxic Drugs



Trail PA, et al. *Pharmacol Ther.* 2018;181:126-142.

HER2 ADCs/ISACs for Breast Cancer and in Clinical Development for Solid Tumors with HER2 Expression (Data prior to ESMO Sept 2021)

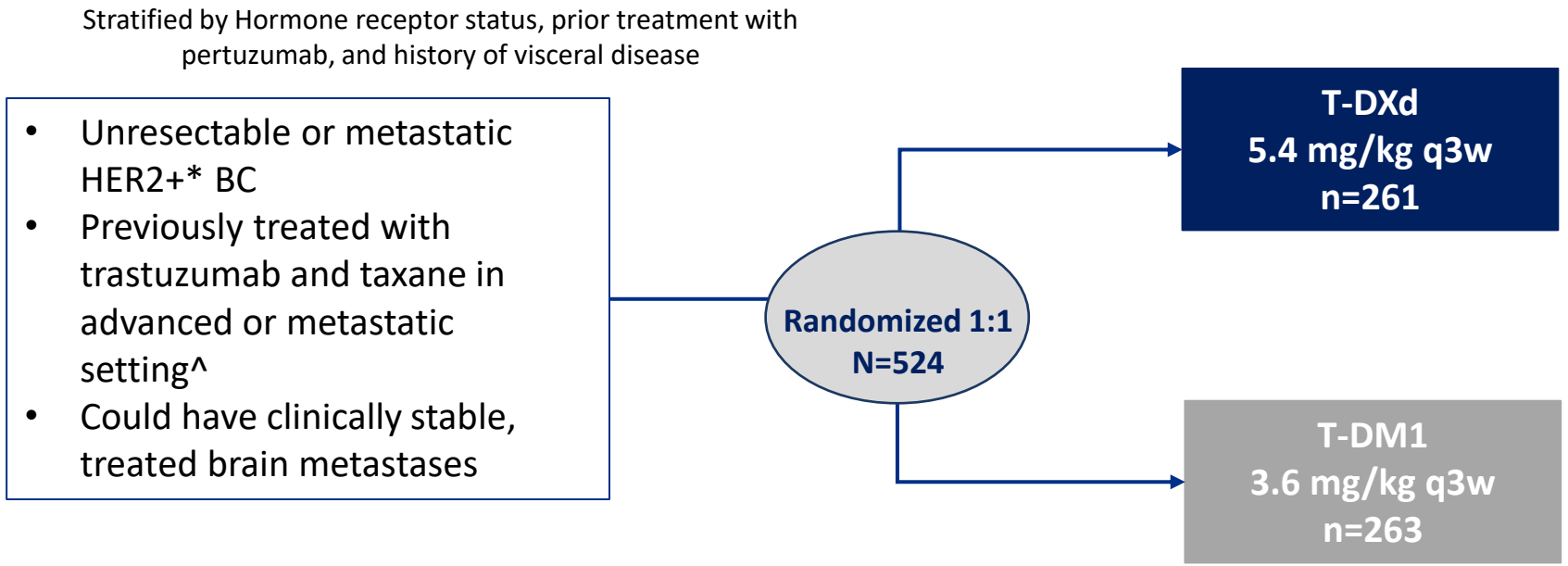
Agent	Anti-HER2 Ab/Payload	Drug:Ab ratio	Linker drug	ORR (%)	Phase	Clinical Trial
TDM1	Trastuzumab/ DM1 (anti-tubulin)	3.5	Non-cleavable	43.6	FDA Approved III	
Trastuzumab deruxtecan (DS-8201a)	Trastuzumab /deruxtecan (topo I inhibitor)	8	Cleavable	62	FDA Approved III	NCT03248492 NCT03529110 NCT03523585
SYD985	Anti-HER2 mAb/ duocarmycin derivative (alkylator)	2.8	Cleavable	33	III	NCT03262935
XMT-1522	XMT-1519/ monomethyl auristatin(anti-tubulin)	12	Cleavable	pending	I	NCT02952729
ARX788	Anti-HER2 mAb/ auristatin analog AS5269 (anti-tubulin)	1.9	Non-cleavable	pending	II/III	NCT03255070
PF-06804103	Trastuzumab-derived Ab/Aur-06380101	4	Cleavable	Pending	I	NCT03284723
ZW49	ZW 25/auristatin		Cleavable	pending	I	NCT03821233
MRG002	Anti-HER2 IgG1/MMAE (anti-tubulin)	NA	NA	NA	I	NCT04492488 NCT04742153
RC48-ADC	Hertuzumab/MMAE (anti-tubulin)	4	Cleavable	pending	I/II	NCT04280341
BDC-1001	Trastuzumab/TLR7/8 agonist	NA	Non-cleavable	pending	I/II	NCT04278144
A166	Trastuzumab/Duostatin-5 (microtubule inhibitor)	NA	Cleavable	33	I	NCT03602079

Ferraro E, Drago JZ, Modi S. Br Can Res 2021

KEY DATA

DESTINY-Breast03 Clinical Trial

Study Design: Phase 3 open-label, multicenter study



*HER2 IHC3+ or IHC2+/ISH+ based on central confirmation
^Progression during or <6 months after completing adjuvant therapy involving trastuzumab and taxane

- **Primary End Point:** PFS (Blinded ICR)
- **Secondary Endpoints:** OS, ORR (BIDR and investigator), DOR (BICR), PFS (investigator), safety

KEY DATA

DESTINY-Breast03 Clinical Trial

Baseline Characteristics

	Randomized to T-DXd (n=261)	Randomized to T-DM1 (n=263)
Age, Median (range), years	54.3 (27.9 – 83.1)	54.2 (20.2 – 83.0)
Female, %	99.6	99.6
Region, %		
• Europe	20.7	19.0
• Asia	57.1	60.8
• North America	6.5	6.5
• Rest of World	15.7	13.7
HER2 Status (IHC, %)		
• 3+	89.7	88.2
• 2+ (ISH amplified)	9.6	11.4
• 1+ / not evaluable /not examined	0.4 / 0.4 / 0	0 / 0.4 / 0
ECOG PS, %: 0 / 1 / missing	59.0 / 40.6 / 0.4	66.5 / 33.1 / 0.4
Hormone Receptor, %: +ve / -ve	50.2 / 49.8	51.0 / 49.0
Brain Mets, %	23.8	19.8
Visceral Disease, %	70.5	70.3

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA1).

KEY DATA

DESTINY-Breast03 Clinical Trial

Prior Therapies

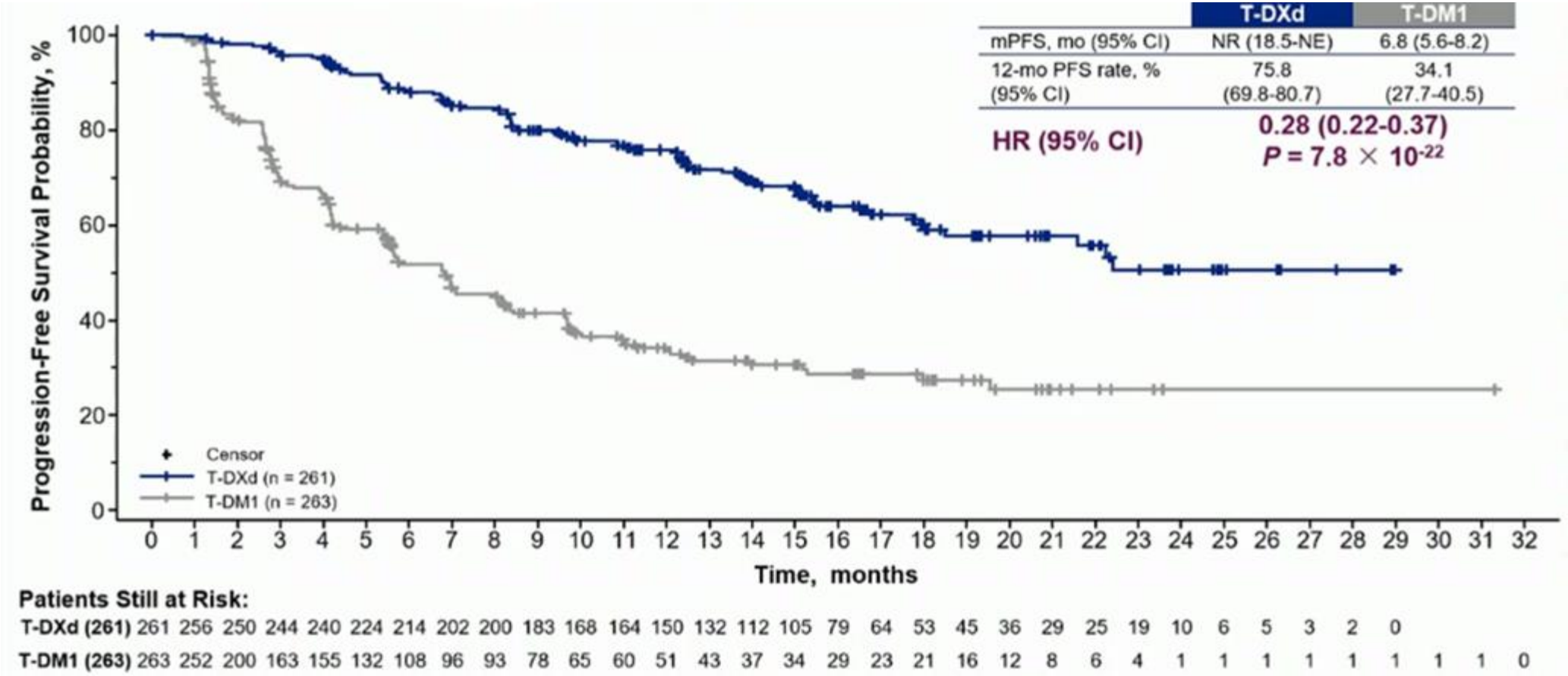
	Randomized to T-DXd (n=261)	Randomized to T-DM1 (n=263)
Prior Treatment for mBC, n (%): Yes / No	240 (92%) / 21 (8%)	234 (89%) / 29 (11%)
Prior lines of therapy in the metastatic setting (includes "rapid progressors" as one line of treatment)		
• 0	2 (0.8)	3 (1.1)
• 1	130 (49.8)	123 (46.8)
• 2	56 (21.5)	65 (24.7)
• 3	35 (13.4)	35 (13.3)
• 4	15 (5.7)	19 (7.2)
• ≥5	23 (8.8)	18 (6.8)
Prior Cancer Therapy, %		
• Trastuzumab	99.6	99.6
• Pertuzumab	62.1	60.1
• Other anti-HER2		
• Anti-HER2 TKI	16.1	13.7
• Other anti-HER2 antibody or ADC	0.8	1.1

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA1).

KEY DATA

DESTINY-Breast03 Clinical Trial

Primary Endpoint: PFS by BICR



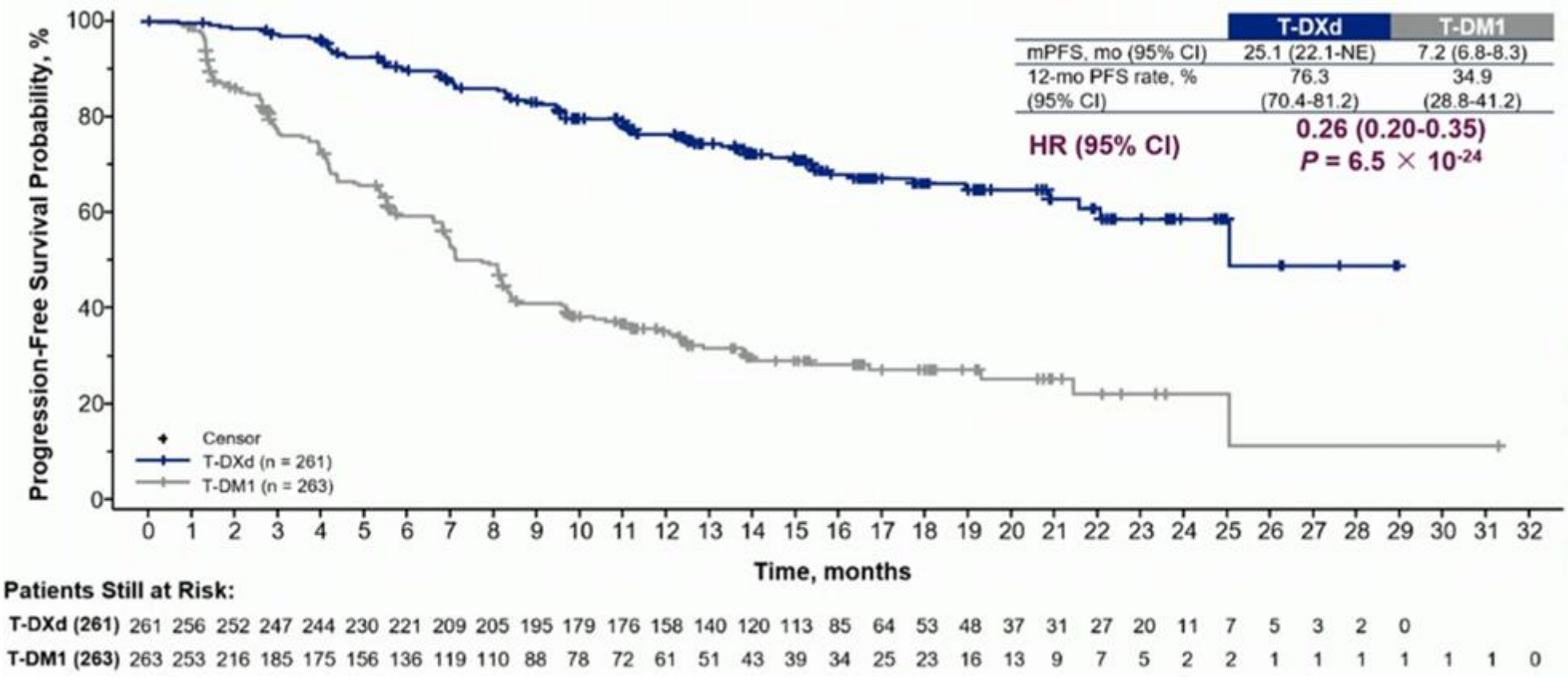
Median PFS follow up for T-DXd was 15.5 months (range 15.1 – 16.6) and for T-DM1 was 13.9 months (range 11.8 – 15.1)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA1).

KEY DATA

DESTINY-Breast03 Clinical Trial

Secondary Endpoint: PFS by Investigator Assessment



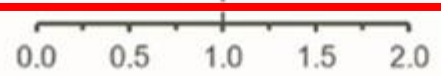
European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA1).

KEY DATA

DESTINY-Breast03 Clinical Trial

PFS in Key Subgroups

		Number of Events		Median PFS (mo, 95% CI)		HR (95% CI)
		T-DXd	T-DM1	T-DXd	T-DM1	
All patients		87/261	158/263	NE (18.5-NE)	6.8 (5.6-8.2)	0.2840 (0.2165-0.3727)
Hormone Receptor Status	Positive (n = 272)	46/133	84/139	22.4 (17.7-NE)	6.9 (4.2-9.8)	0.3191 (0.2217-0.4594)
	Negative (n = 248)	41/126	73/122	NE (18.0-NE)	6.8 (5.4-8.3)	0.2965 (0.2008-0.4378)
Prior Pertuzumab Treatment	Yes (n = 320)	57/162	98/158	NE (18.5-NE)	6.8 (5.4-8.3)	0.3050 (0.2185-0.4257)
	No (n = 204)	30/99	60/105	NE (16.5-NE)	7.0 (4.2-9.7)	0.2999 (0.1924-0.4675)
Visceral Disease	Yes (n = 384)	72/195	123/189	22.2 (16.5-NE)	5.7 (4.2-7.0)	0.2806 (0.2083-0.3779)
	No (n = 140)	15/66	35/74	NE (NE-NE)	11.3 (6.8-NE)	0.3157 (0.1718-0.5804)
Prior Lines of Therapy[a]	0-1 (n = 258)	46/132	75/126	22.4 (17.9-NE)	8.0 (5.7-9.7)	0.3302 (0.2275-0.4794)
	≥2 (n = 266)	41/129	83/137	NE (16.8-NE)	5.6 (4.2-7.1)	0.2828 (0.1933-0.4136)
Brain Metastases	Yes (n = 114)	31/62	31/52	15.0 (12.6-22.2)	5.7 (2.9-7.1)	0.3796 (0.2267-0.6357)
	No (n = 410)	56/199	127/211	NE (22.4-NE)	7.0 (5.5-9.7)	0.2665 (0.1939-0.3665)



HR (T-DXd vs T-DM1)

[a]Rapid progressors on (neo)adjuvant therapy were included
Line of therapy does not include endocrine therapy

DESTINY-Breast03 Clinical Trial

Adverse Events of Special Interest

Adjudicated as drug-related ILD/pneumonitis, n (%)						
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
T-DXd (n=257)	7 (2.7)	18 (7.0)	2 (0.8)	0	0	27 (10.5)
T-DM1 (n=261)	4 (1.5)	1 (0.4)	0	0	0	5 (1.9)

- There were no grade 4 or 5 adjudicated drug-related ILD/pneumonitis events observed with T-DXD

LVEF decrease, n (%)						
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
T-DXd (n=257)	1 (0.4)	6 (2.3)	0	0	0	7 (2.7)
T-DM1 (n=261)	0	1 (0.4)	0	0	0	1 (0.4)

- In the T-DXd arm, all reported adverse events of LVEF decrease were asymptomatic and no cases of cardiac failure occurred

SUMMARY

DESTINY-Breast03 Clinical Trial

- Clinically meaningful and statistically significant improvement in PFS compared to T-DM1
  - PFS HR of 0.28 (P = 7.8 x 10^{-22})
- Consistent benefit across key subgroup and efficacy endpoints
  - Confirmed ORR for T-DXD of 79.9% vs 34.3% for T-DM1 (CR, 16.1% vs 8.7%, respectively)
  - Including patients with stable brain mets
  - CR/PR/stable disease: 96.6% for T-DXD vs 76.8% for T-DM1
- Encouraging OS trend at the time of the first interim analysis
  - 12-month OS rate for T-DXd was 94.1% vs 85.9% for T-DM1
- Continue to be aware of and monitor for ILD/pneumonitis

October 4, 2021: The U.S. Food and Drug Administration (FDA) has granted ENHERTU® (fam-trastuzumab deruxtecan-nxki) Breakthrough Therapy Designation (BTD) in the U.S. for the treatment of adult patients with unresectable or metastatic HER2+ breast cancer who have received one or more prior anti-HER2-based regimens.

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA1).

DESTINY-Breast03 Clinical Trial

Use of fam-trastuzumab deruxtecan-nxki (T-DXd, ENHERTU®) in the 2L setting should become standard of care for patients with HER2+ metastatic breast cancer

2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

CLINICAL QUESTION

TULIP Clinical Trial

Does use of SYD985 provide benefit for pts with HER2+ MBC with progression during or after at least two HER2-targeting treatment regimens for locally advanced or metastatic disease or progression during or after ado-trastuzumab emtansine (T-DM1) treatment?

cornerstone specialty network™

KEY DATA

TULIP Clinical Trial

Study Design: Phase 3 multicenter study

Stratified by region, # of prior treatment lines for LABC or MBC, prior treatment with Pertuzumab

- HER2+ LABC or MBC with ≥ 2 therapies for metastatic disease or T-DM1 for metastatic disease
- Treated brain mets allowed

Randomized 2:1
N=437

SYD985
1.2 mg/kg IV q3w
(n=291)

Physician's choice combination
(n=146)
(Lapatinib + Capecitabine
Trastuzumab + Capecitabine
Trastuzumab + Vinorelbine
Trastuzumab + Erilbulin)

Continue treatment until progression or unacceptable toxicity

- **Primary End Point:** PFS (centrally assessed)
- **Secondary Endpoints:** PFS (investigator assessed), OS, ORR, HRQOL

Trial was powered to detect a HR of 0.65 at $P<0.05$ assuming:

- Median time to progression of 4.1 months in the PC group
- 20% dropout in PC group and 30% dropout in SYD985 group. Following DMC recommendations (Sept 2019) dropout was updated to 30% and 40% respectively (Drop out refers to pt not having event of interest (centrally assessed PFS) during the period of observation for any reason)

KEY DATA

TULIP Clinical Trial

Demographics and Baseline Characteristics

	SYD985 (n=261)	Physician's choice (n=263)
Age, Median (range), years	56.0 (24 – 84)	58.0 (34 – 86)
Race, n (%)		
• White	202 (69.4)	95 (65.1)
• Not disclosed	54 (18.6)	30 (20.5)
• Asian	29 (10.0)	17 (11.6)
• Other	6 (2.0)	2 (2.8)
Time from MBC diagnosis to study entry (years), median (range)	3.6 (0.0 – 18.6)	2.9 (0.0 – 19.5)
Median # of prior treatments	4.0 (1 – 16)	5.0 (1 – 14)
Previous systemic anti-HER2 cancer therapy in MBC setting, n (%)		
• Trastuzumab	260 (89.3)	126 (86.3)
• Ado-Trastuzumab Emtansine	255 (87.6)	128 (87.7)
• Pertuzumab	177 (60.8)	84 (57.5)
• Lapatinib	101 (34.7)	43 (29.5)
• Neratinib	16 (5.5)	2 (1.4)
• Tucatinib/Placebo*	9 (3.1)	10 (6.8)
• Margetuximab	6 (2.1)	0
• Fam-Trastuzumab deruxtecan	6 (2.1)	2 (1.4)

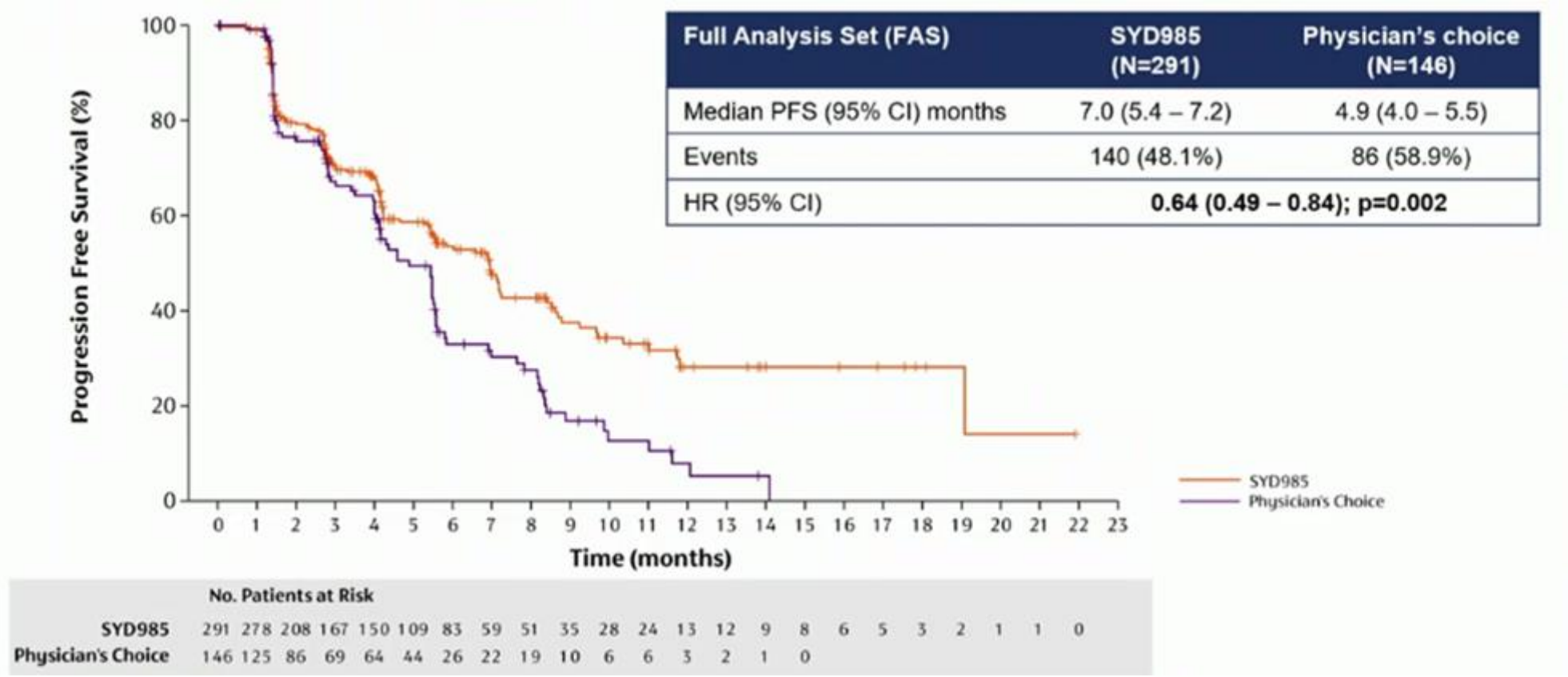
*4 patients received Tucatinib (2 SYD, 2 PC) and 15 patients received Tucatinib/Placebo (7 SYD, 8 PC)

KEY DATA

TULIP Clinical Trial

Centrally Reviewed PFS

Full Analysis Set (FAS)	SYD985 (N=291)	Physician's choice (N=146)
Median PFS (95% CI) months	7.0 (5.4 – 7.2)	4.9 (4.0 – 5.5)
Events	140 (48.1%)	86 (58.9%)
HR (95% CI)	**0.64 (0.49 – 0.84); p=0.002**	



European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA15).

KEY DATA

TULIP Clinical Trial

Safety – AEs of Special Interest

- Eye toxicity: 78.1% of SYD985 vs 29.2% of physician's choice treatment
  - Grade ≥3 for 21.2% of SYD985 treated patients
  - Discontinuation in 20.8% of SYD985 patients
  - Dose modification in 22.9% of SYD985 patients
    - Risk mitigation strategy: Patients with prior keratitis excluded, prophylactic lubricating eye drops, regular eye exams, Grade 3 or higher keratitis stop treatment, Grade 3 conjunctivitis delay treatment until reduced to Grade 2

- ILD/pneumonitis: 7.6% (n=22) of SYD985 patients (not reported for physician's choice)
  - Grade ≥3 for 2.4 % of SYD985 treated patients
  - Discontinuation in 5.2% (n=15) SYD985 patients
  - Dose modification in 2.1% (n=6) SYD985 patients
    - Risk mitigation strategy: Patients with prior pneumonitis excluded, CT scans for lung changes, diagnostic work up for new or worsening respiratory symptoms, Grade 2 or higher pneumonitis stop treatment, Grade 1 delay treatment until resolution

- Fatal Cases: 2.1% (n=6) of SYD985 patients (not reported for physician's choice)
  - Related: Respiratory failure (0.3%, n=1); Pneumonia (0.3%, n=1); pneumonitis (0.7%, n=2)
  - Not related: Acute respiratory failure (0.3%, n=1); COVID-19 pneumonia (0.3%, n=1)

SUMMARY

TULIP Clinical Trial

- PFS was significantly improved with SYD985 (7 months) compared to standard Physician's choice combination treatment (4.9 months), HR 0.64, *P = 0.0002*
- Ocular toxicity is the most prevalent safety event (78%)
- ILD/pneumonitis reported in 7.6% 2.4% of patients, including 2.4% ≥grade 3
  Continue to be aware of and monitor for ILD/pneumonitis

TULIP Clinical Trial

Use of SYD985 may be a future option for patients with 2+ prior regimens for pts with metastatic HER2+ breast cancer.

Eye toxicity a challenge

2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

FDA APPROVAL

KEYNOTE-522 Clinical Trial

On July 26, 2021, the Food and Drug Administration approved pembrolizumab (Keytruda, Merck) for high-risk, early-stage, triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.

Approved based on results from the KEYNOTE-522 Phase 3 trial (NCT03036488)

cornerstone specialty network™

CLINICAL QUESTION

KEYNOTE-522 Clinical Trial

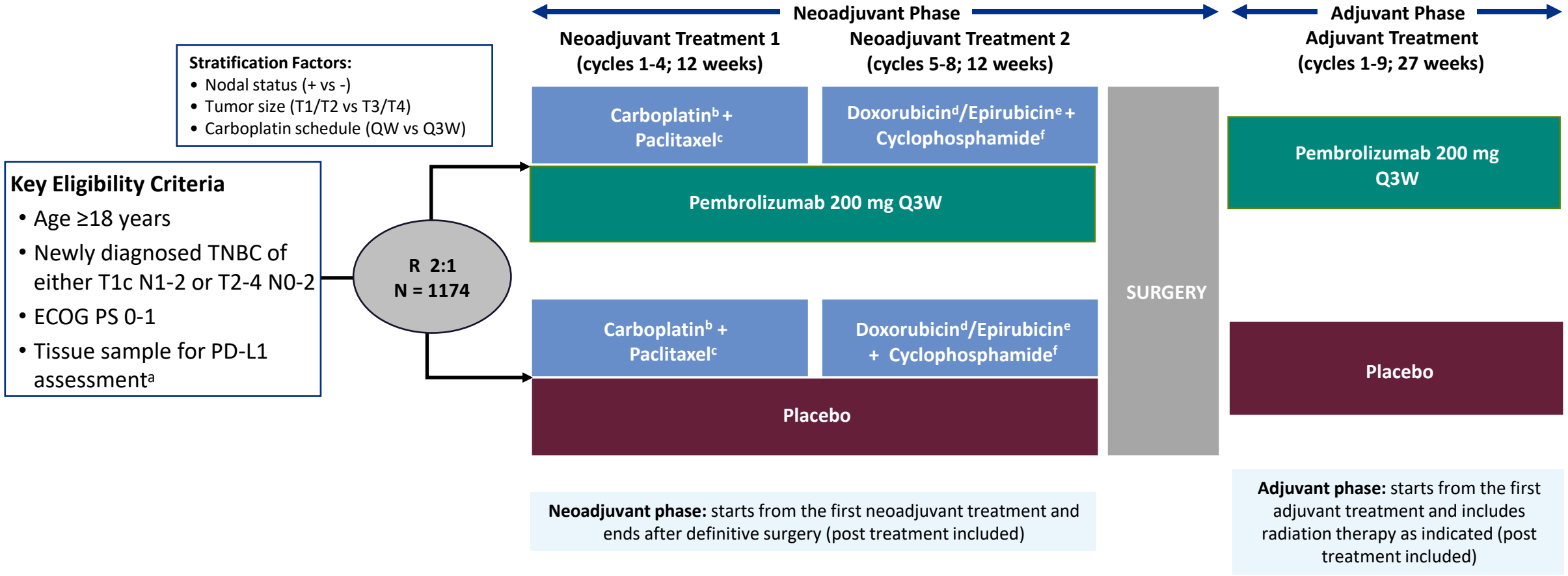
Does use of pembrolizumab in combination with chemotherapy in the neoadjuvant setting followed by pembrolizumab as a single agent in the adjuvant setting improve outcome for patients with early TNBC?

cornerstone specialty network™

KEY DATA

KEYNOTE-522 Clinical Trial

Study Design: Phase 3 multicenter study



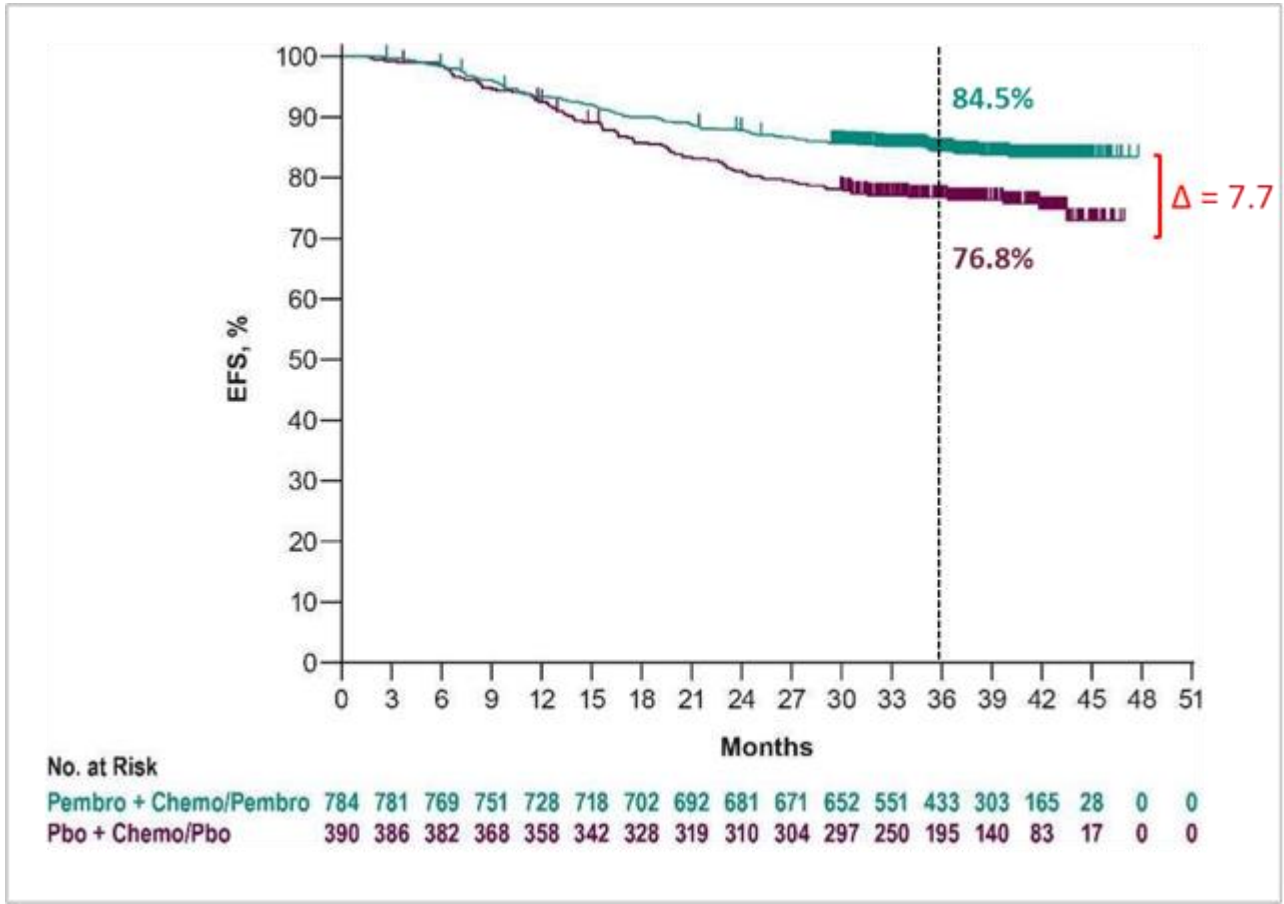
[a]Must consist of at least 2 separate tumor cores from the primary tumor. [b]Carboplatin dose AUC 5 q3w or AUC 1.5 qw. [c]Paclitaxel dose was 80 mg/m^2 qw. [d]Doxorubicin dose 60 mg/m^2 q3w. [e]Epirubicin dose 90 mg/m^2 q3w. [f]Cyclophosphamide dose 600 mg/m^2 q3w.

Ref. Schmit et al. ESMO Virtual Plenary July 2021

KEY DATA

KEYNOTE-522 Clinical Trial

Statistically Significant and Clinically Meaningful EFS



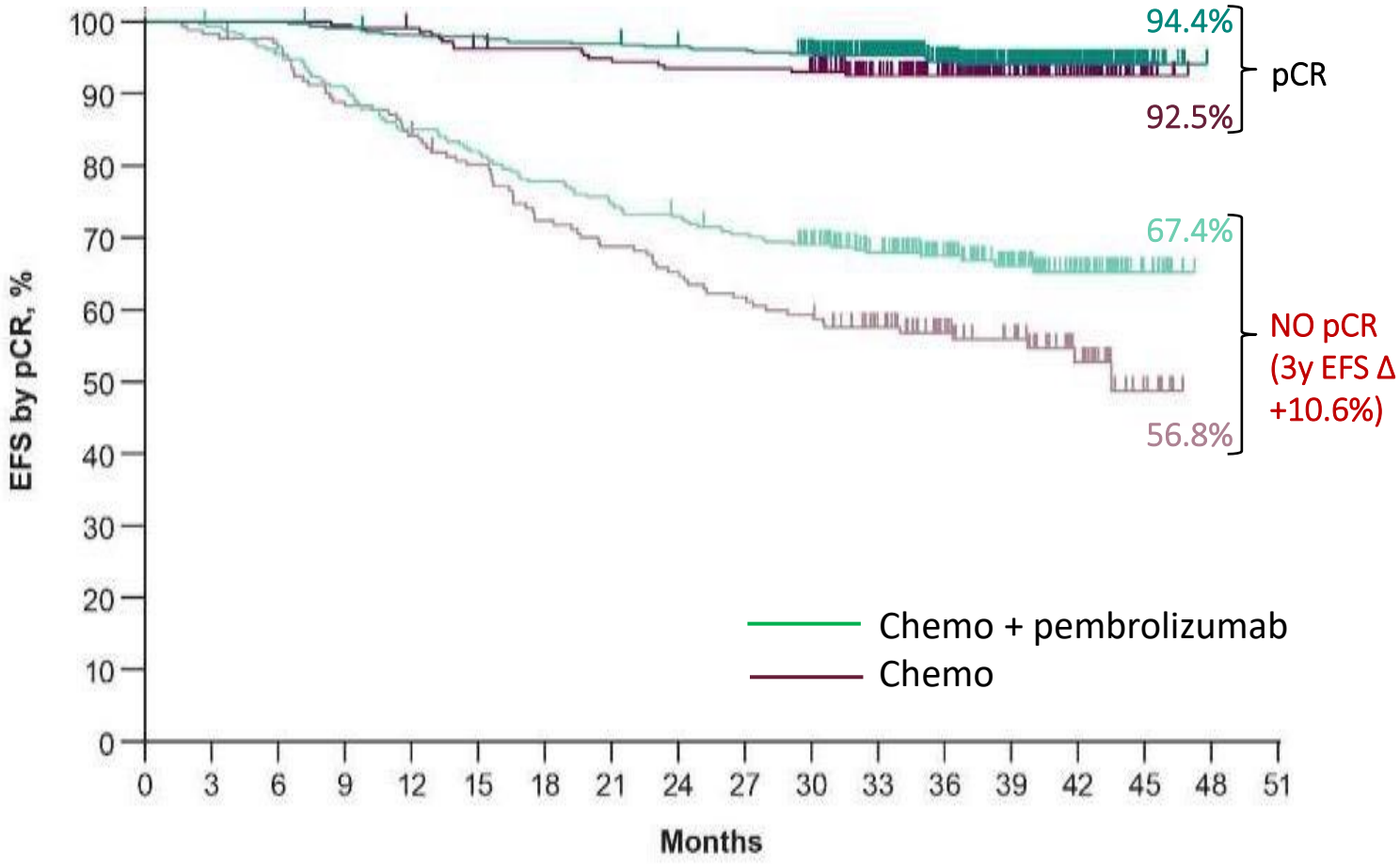
	Events	HR (95%CI)	P-value
Pembro + Chemo/ Pembro	15.7%	0.63[a] (0.48-0.82)	0.00031[b]
Pbo + Chemo/Pbo	23.8%		

[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors.
[b]Prespecified P-value boundary of 0.00517 reached at this analysis.
Data cutoff date: March 23, 2021.

KEY DATA

KEYNOTE-522 Clinical Trial

Outcome Based on pCR vs no pCR (Residual Disease)



Most benefit with pembrolizumab addition observed in patients with a worse prognosis; namely those not achieving pCR

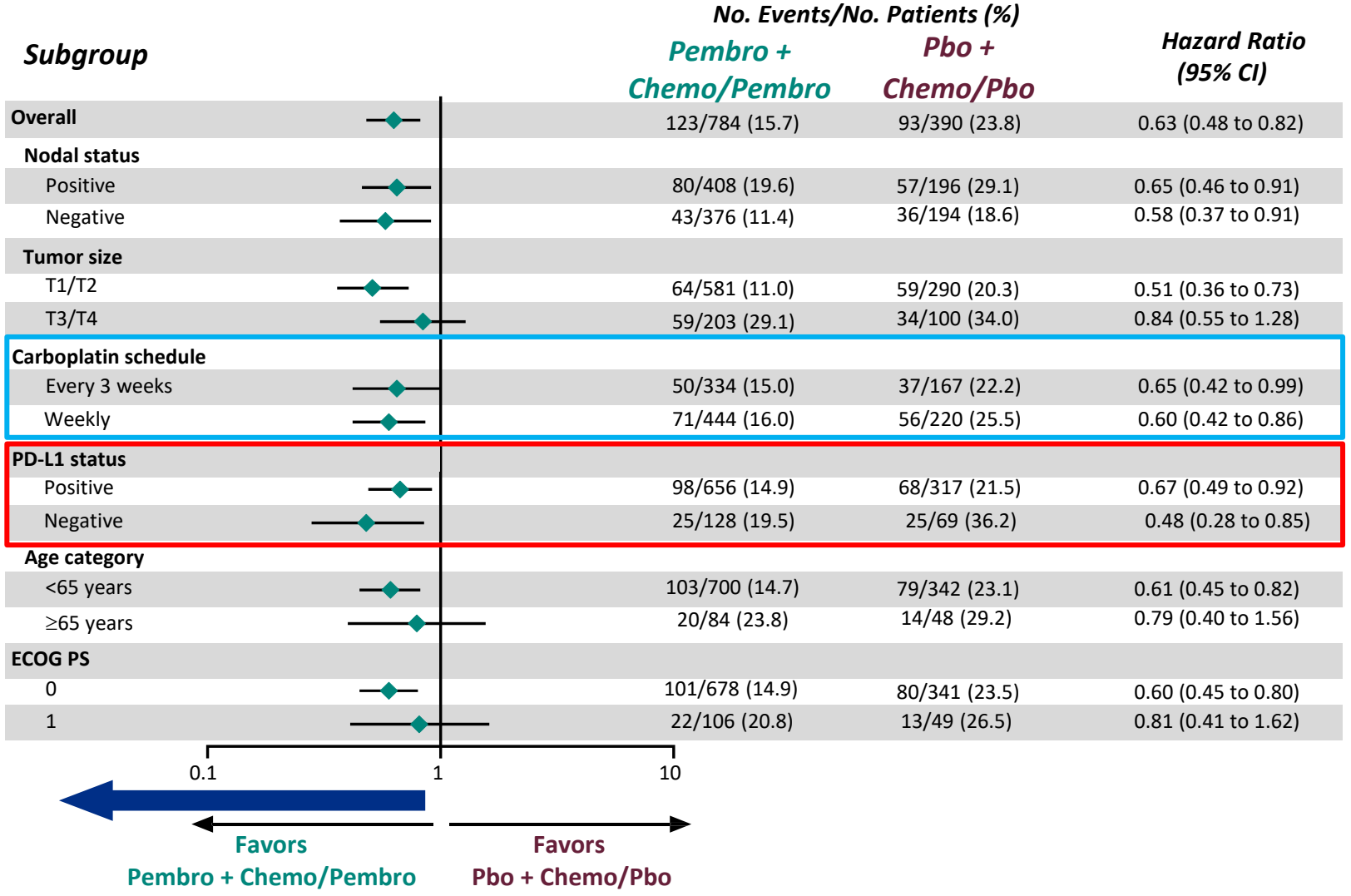
Research question:
How to identify this population up front?

ESMO 2021: European Society for Medical Oncology (ESMO) Congress 2021 (VP7_2021).

KEY DATA

KEYNOTE-522 Clinical Trial

Subgroup Analysis



EFS benefit with pembrolizumab consistent in all subgroups

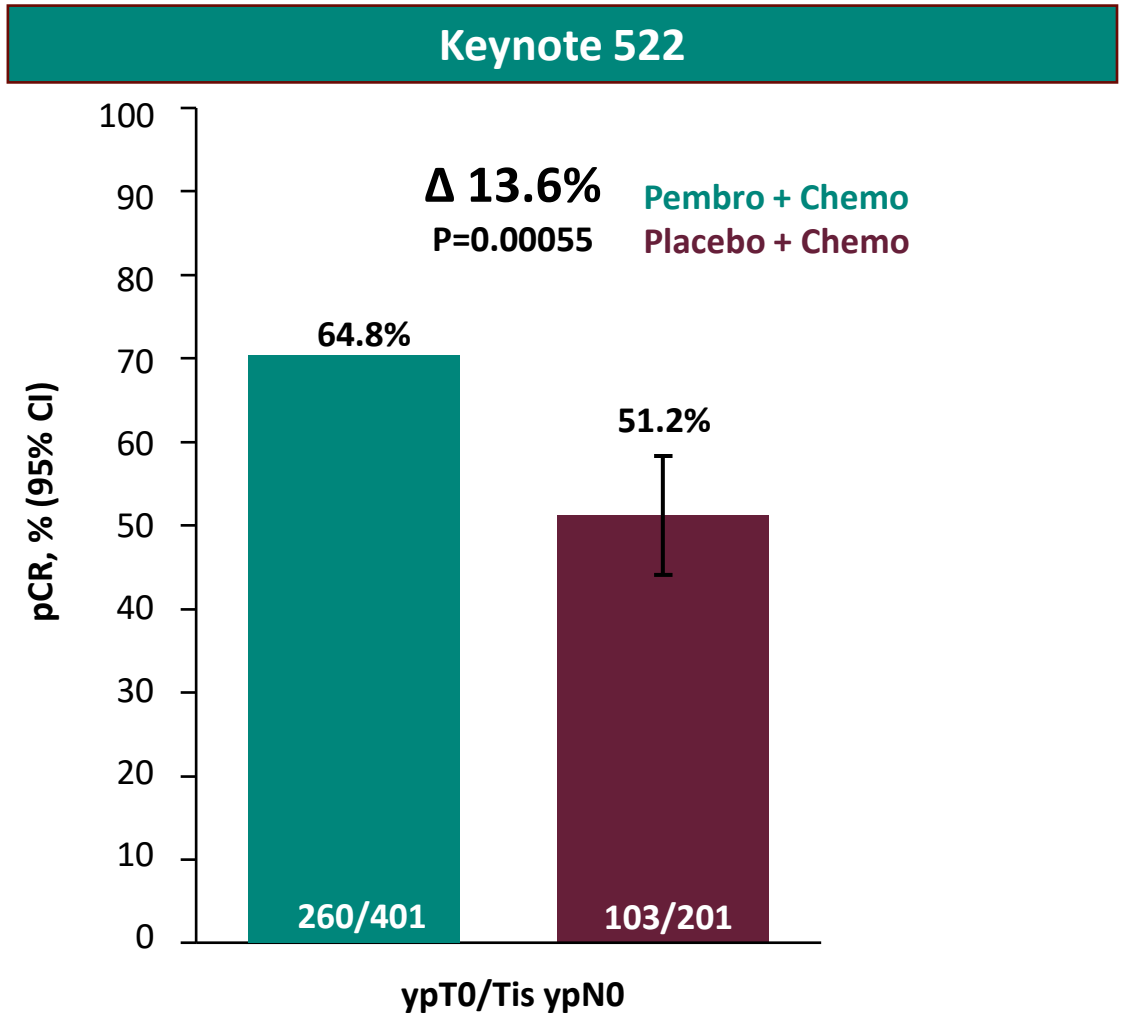
PD-L1 not predictive

ESMO 2021: European Society for Medical Oncology (ESMO) Congress 2021 (VP7_2021).

KEY DATA

KEYNOTE-522 pCR Data

pCR Data of Neoadjuvant Chemo +/- Pembrolizumab

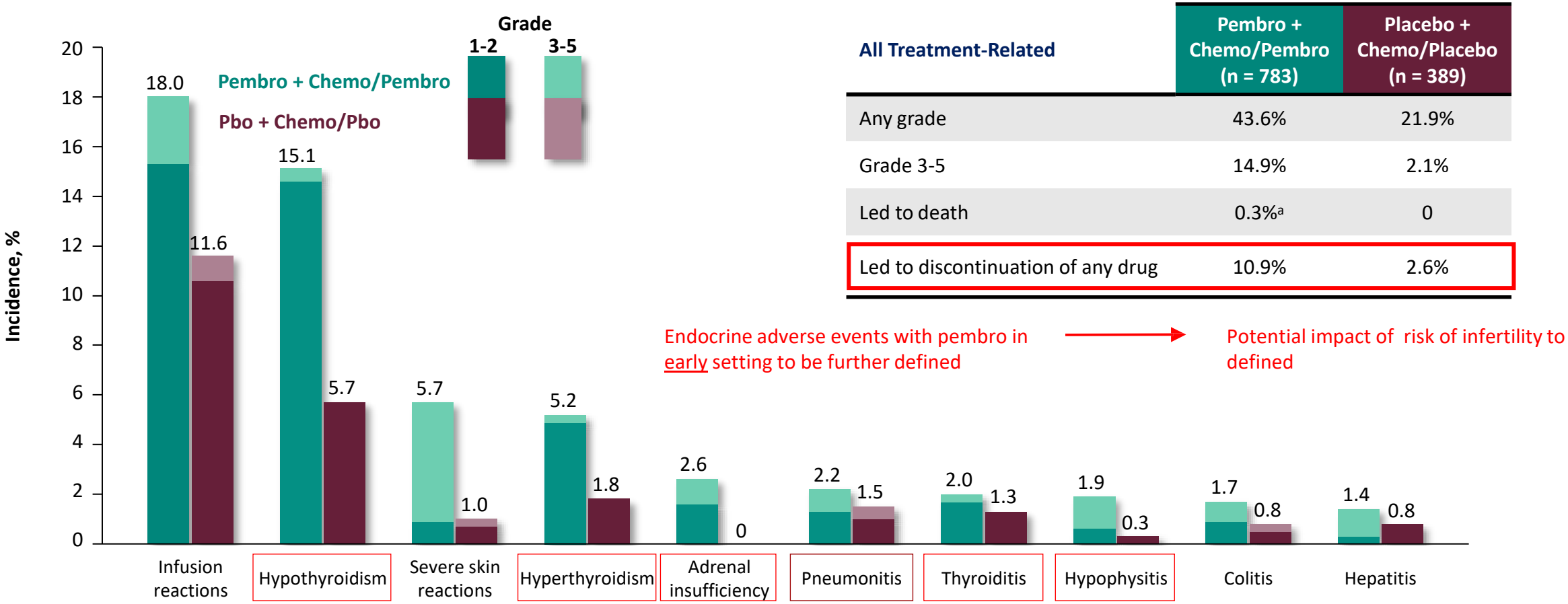


Schmid P, et al. ESMO virtual July 2021

KEY DATA

KEYNOTE-522 Clinical Trial

Immune-Related AEs in Combined Phases



All Treatment-Related	Pembro + Chemo/Pembro (n = 783)	Placebo + Chemo/Placebo (n = 389)
Any grade	43.6%	21.9%
Grade 3-5	14.9%	2.1%
Led to death	0.3%[a]	0
Led to discontinuation of any drug	10.9%	2.6%

Endocrine adverse events with pembro in early setting to be further defined → Potential impact of risk of infertility to be defined

Immune-Mediated AEs and Infusion Reactions with Incidence ≥ 10 Patients

[a]1 patient from pneumonitis and 1 patient from autoimmune encephalitis. Considered regardless of attribution to treatment or immune relatedness by the investigator. Related terms included in addition to preferred terms listed.
Data cutoff date: March 23, 2021.

Integrating CPI with Other Options for Patient Management

- **During the conduct of KEYNOTE-522, other treatments have emerged for <u>TNBC not achieving pCR:</u>**
  - **CREATE-X →** post-neoadjuvant capecitabine improves DFS & OS
  - **OlympiA →** post-neoadjuvant olaparib improves DFS in pts with BRCA tumors (could be TNBC or high-risk HR+)

- **Pembrolizumab alone?**

Pragmatism will be required to maximize the benefit achieved with our new treatments

CPI = checkpoint inhibitor

SUMMARY

KEYNOTE-522 Clinical Trial

- Neoadjuvant Pembro added to chemotherapy
  - Improved pCR (ypT0/Tis ypN0; 65% vs 51%, *P* =0.00055)
- Neoadjuvant Pembro added to chemotherapy followed by adjuvant Pembro
  - Improvement in EFS at 3 years (84% vs 77%, *P* =0.00031)
- Benefit of Pembro demonstrated for patients who did not achieve pCR to either chemo or chemo + Pembro
- Most immune-mediated AEs occurred in the neoadjuvant stage, were low grade and manageable with treatment interruption, steroid administration, and or hormone replacement – still an issue to consider

ESMO 2021: European Society for Medical Oncology (ESMO) Congress 2021 (VP7_2021).

KEYNOTE-522 Clinical Trial

Use of pembrolizumab with chemotherapy in the neoadjuvant setting followed by single agent pembrolizumab in the adjuvant setting provides benefit for patients with early stage triple negative breast cancer irrespective of PD-L1 status

2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

FDA APPROVAL

Recent PD-1 antibody approvals for the treatment of PD-L1+ TNBC

2019

- Accelerated approval of **atezolizumab**, in combo with nab-paclitaxel (based on IMpassion 130 trial)
  - Endpoints- PFS (in ITT and PD-L1+); OS (in ITT and PD-L1+)

2020

- **Accelerated approval for pembrolizumab, in combination with chemotherapy for advanced/metastatic PD-L1+TNBC (based on KEYNOTE-355 trial)**
  - Endpoint- PFS

2021

- IMpassion 131: adding atezolizumab to paclitaxel *did not* improve PFS or OS in either the PD-L1+ or the ITT subjects
  - ODAC meeting April 27-29, 2021 voted to maintain the atezolizumab + nab-paclitaxel accelerated approval
  - *August 27, 2021: Genentech press release withdrawing accelerated approval*

- ***Full approval of pembrolizumab in combination with chemotherapy***
  - Endpoints- PFS (in CPS≥ 10)

Summary of Companion Assays for PD-L1 Tissue Testing

Two companion diagnostics are approved by the FDA for PD-L1 testing in metastatic TNBC

- SP142 assay with IC scoring for atezolizumab
- 22C3 assay with tumor and IC scoring by combined positive score for pembrolizumab

Antibody clone	Assay	Platform	PD-L1 scoring for breast cancer	Companion diagnostic status	Companion diagnostic approval for TNBC
SP142	VENTANA PD-L1 (SP142)	VENTANA	IC score=the percentage of the tumor area containing ICs labeling with PD-L1 at any intensity above background	Yes	IC score ≥1% indicates eligibility for atezolizumab (+nab-paclitaxel)
22C3	PD-L1 IHC 22C3 pharmDx	Dako	CPS=number of PD-L1 staining cells (including TCs, lymphocytes, and macrophages) divided by the total number of viable TCs multiplied by 100	Yes	CPS≥10 indicates eligibility for pembrolizumab (+chemotherapy)
28–8	PD-L1 IHC 28–8 pharmDx	Dako	Not applicable	No	None
SP263	VENTANA PD-L1 (SP263)	VENTANA	Not applicable	Not for breast cancer	None

CLINICAL QUESTION

KEYNOTE-355 Clinical Trial

Does the use of pembrolizumab in combination with chemotherapy in the 1L setting benefit patients with metastatic TNBC based on PD-L1 expression?

cornerstone specialty network™

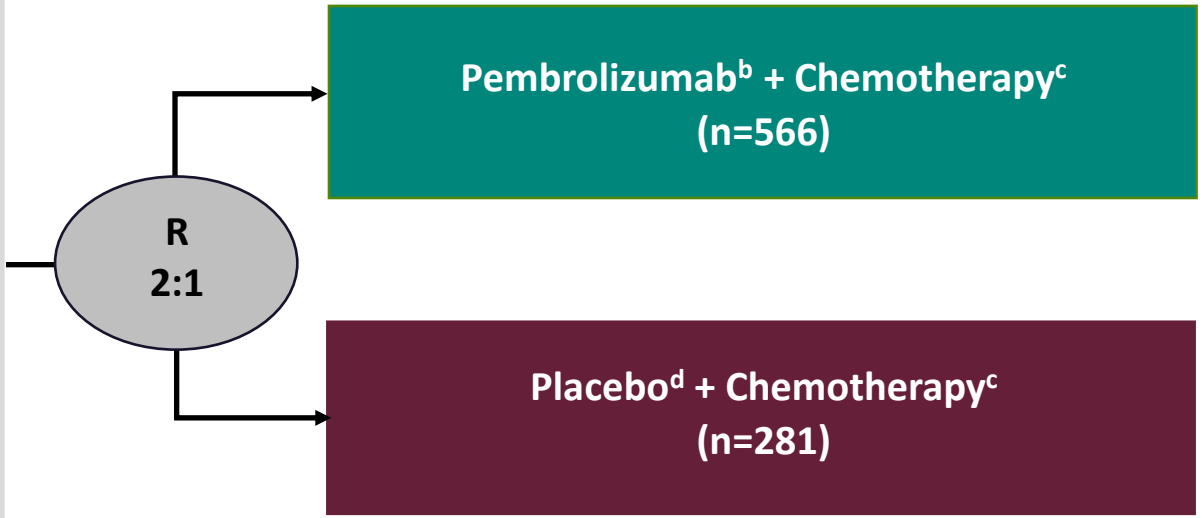
KEY DATA

KEYNOTE-355 Clinical Trial

Study Design: Phase 3 study

Stratification Factors:
- Chemotherapy on study (taxane or gemcitabine-carboplatin)
- PD-L1 tumor expression (CPS ≥ 1 or CPS < 1)
- Prior treatment with same class chemotherapy in the neo/adjuvant setting

Key Eligibility Criteria
- Age ≥18 years
- Central determination of TNBC and PD-L1 expression[a]
- Previously untreated locally recurrent inoperable or metastatic TNBC
- De novo metastasis or completion of treatment with curative intent ≥ 6 months prior to first disease recurrence
- ECOP status 0 or 1
- Life expectancy of 12 weeks from randomization
- Adequate organ function
- No systemic steroids
- No active CNS mets
- No active autoimmune disease
- N=847



[a]Based on a newly obtained tumor sample from a locally recurrent inoperable or metastatic site (an archival tumor sample was used with permission from the study sponsor if a new tumor biopsy was not obtainable). [b]Pembrolizumab 200 mg IV q3w. [C]PChemotherapy dosing regimens are as follows: Nab-paclitaxel 100 mg/m^2 IV on days 1, 8 and 15 every 28 days; Paclitaxel 90 mg/m^2 IV on days 1, 8, and 15 every 28 days; Gemcitabine 1000 mg/m^2/carboplatin AUC 2 on days 1 and 8 every 21 days. [d]Normal saline.
Ref. Schmit et al. ESMO Virtual Plenary July 2021

KEY DATA

KEYNOTE-355 Clinical Trial

Overall Survival

Population	Treatment (n/N)	Median OS, mo	Events	HR (95% CI)	P-value
PD-L1 CPS ≥ 10	**Pembro + CT** (155/220)	**23.0**	70.5%	**0.73** (0.55-0.95)	0.0093
	Placebo + CT (84/103)	**16.1**	81.6%		
PD-L1 CPS ≥ 1	**Pembro + CT** (336/425)	17.6	79.1%	0.86 (0.72-1.04)	0.0563
	Placebo + CT (177/211)	16.0	83.9%		
ITT	**Pembro + CT** (460/566)	17.2	81.3%	0.89 (0.76-1.05)	-
	Placebo + CT (238/281)	15.5	84.7%		

Data cutoff: June 15, 2021

ESMO 2021: European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA16).

KEY DATA

KEYNOTE-355 Clinical Trial

Progression-Free Survival

Population	Treatment (n/N)	Median OS, mo	Events	HR (95% CI)
PD-L1 CPS ≥ 10	**Pembro + CT** (144/220)	**9.7**	65.5%	**0.66** (0.50-0.88)
	Placebo + CT (81/103)	**5.6**	78.6%	
PD-L1 CPS ≥ 1	**Pembro + CT** (299/425)	7.6	70.4%	0.75 (0.62-0.91)
	Placebo + CT (166/211)	5.6	78.8%	
ITT	**Pembro + CT** (406/566)	7.5	71.7%	0.82 (0.70-0.98)
	Placebo + CT (217/281)	5.6	77.2%	

Data cutoff: June 15, 2021

ESMO 2021: European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA16).

SUMMARY

KEYNOTE-355 Clinical Trial

- Pembrolizumab added to chemotherapy
  - Reduced the risk of death by 27% (HR=0.73 [95% CI, 0.55-0.95]; p=0.0093) in patients with mTNBC whose tumors expressed PD-L1 (CPS ≥10
    - Increased median OS by 6.9 months (23.0 months [95% CI, 19.0-26.3] vs. 16.1 months [95% CI, 12.6-18.8])

  - Associated AEs led to discontinuation in 18.3% of pts compared to 11.0% of patients in the chemotherapy arm

ESMO 2021: European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA16).

KEYNOTE-355 Clinical Trial

Adding pembrolizumab to chemotherapy in the 1L setting improves PFS and OS for patients with metastatic TNBC whose tumors express PD-L1 (CPS ≥10)

2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

CLINICAL QUESTION

BEVERLY Clinical Trial

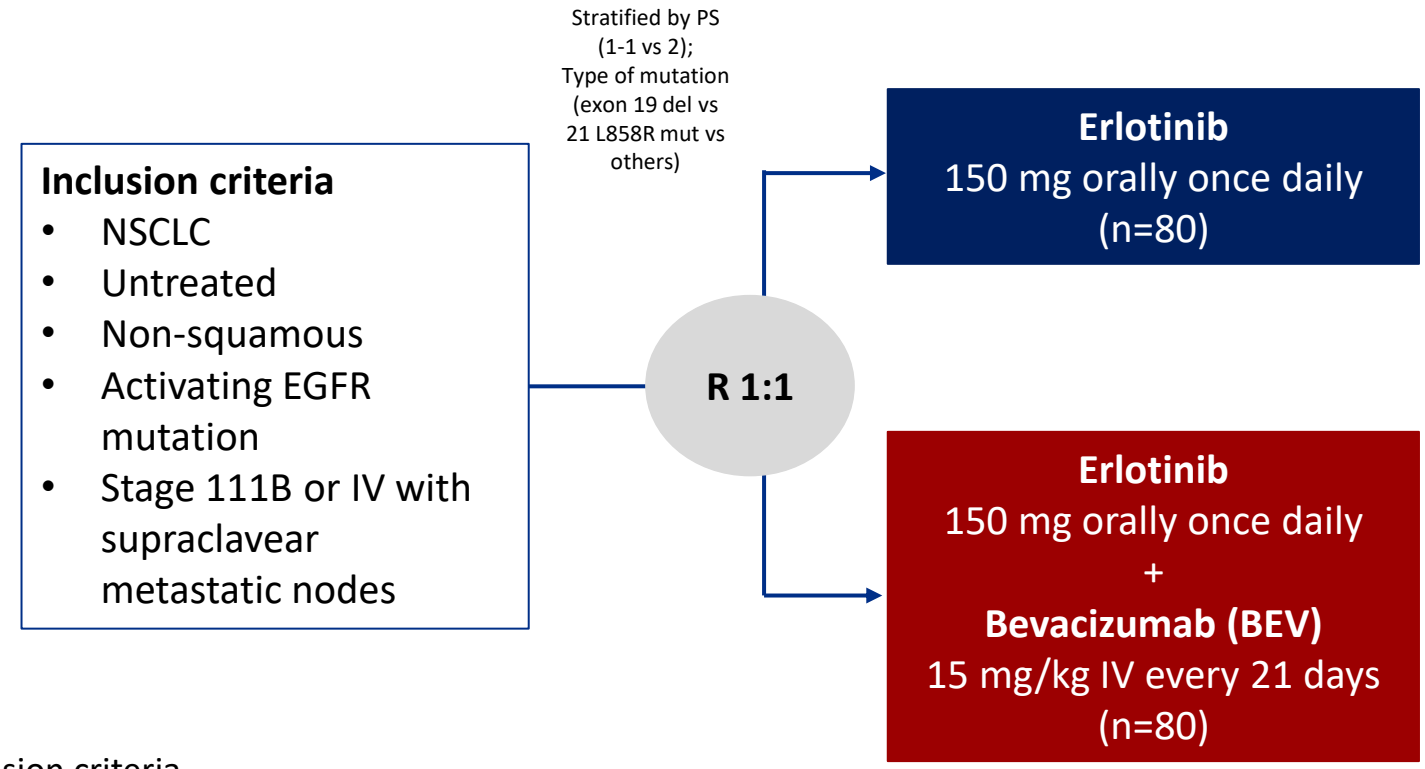
Does the addition of bevacizumab to erlotinib in the 1L setting benefit patients with EGFR mutated advanced or metastatic non-squamous NSCLC ?

cornerstone specialty network™

KEY DATA

BEVERLY Clinical Trial

Study Design: Phase 3 randomized trial



Primary End Point: PFS

Main exclusion criteria

- EGFR T790M mutation and exon 20 insertions or a squamous component
- Brain metastasis
- Concomitant pathologies/ lab alterations/ concomitant medications that contraindicate the use of erlotinib or bevacizumab

KEY DATA

BEVERLY Clinical Trial

Patient Demographics and Baseline Characteristics

Characteristic, n (%)	Erlotinib n=80	Erlotinib + BEV n=80
Median age, years (range)	67.7 (60.7 – 73.6)	65.9 (57.9 – 71.8)
Male / Female, n (%)	30 (37.5) / 50 (62.5)	28 (35.0) / 52 (65.0)
Smoking history, n (%)		
Never	37 (46.3)	46 (57.5)
Former/current	43 (53.8)	34 (42.5)
Stage, n (%)		
IIIB	5 (6.3)	3 (3.8)
IV	75 (93.8)	77 (96.3)
Performance Status, n (%)		
0	47 (58.8)	52 (65.0)
1	29 (36.3)	26 (32.5)
2	4 (5.0)	2 (2.5)
EGFR mutation type, n (%)		
Exon 19 deletion	44 (55.0)	44 (55.0)
Exon 21 L858R mutation	32 (40.0)	34 (42.5)
Other	4 (5.0)	2 (2.5)

cornerstone specialty network

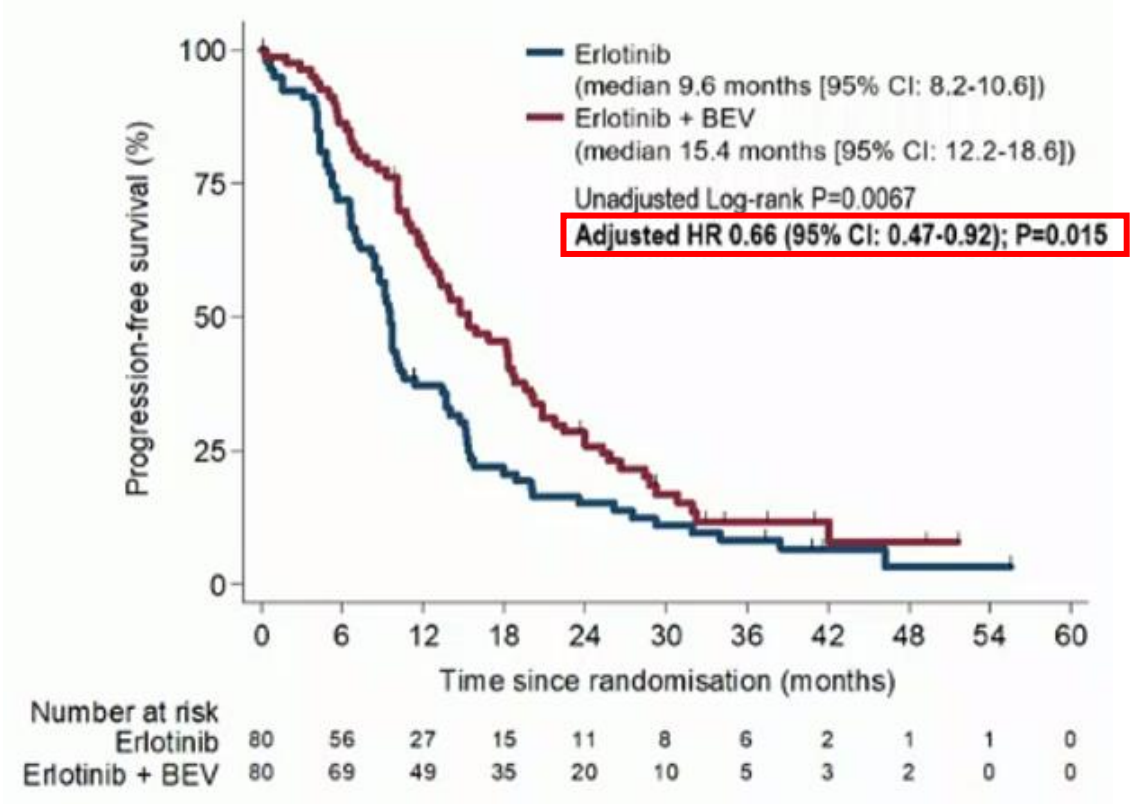
European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

KEY DATA

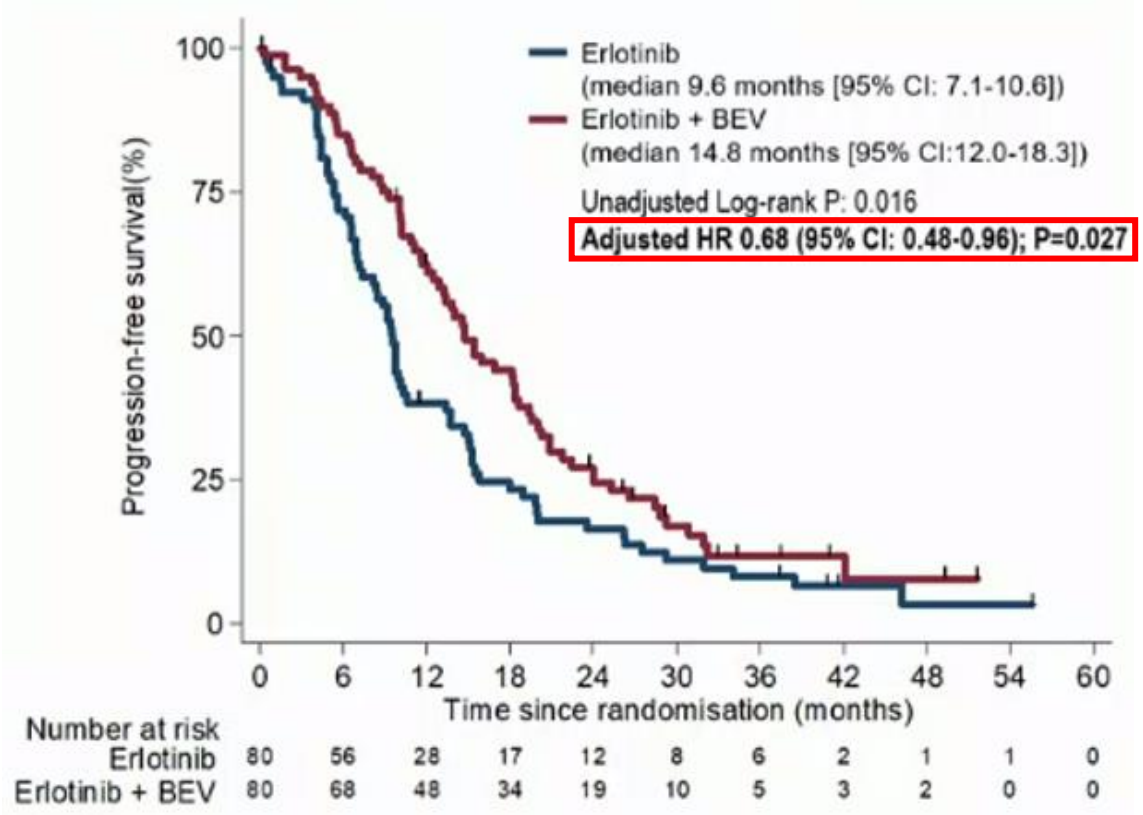
BEVERLY Clinical Trial

Progression-Free Survival

Investigator-assessed



BICR



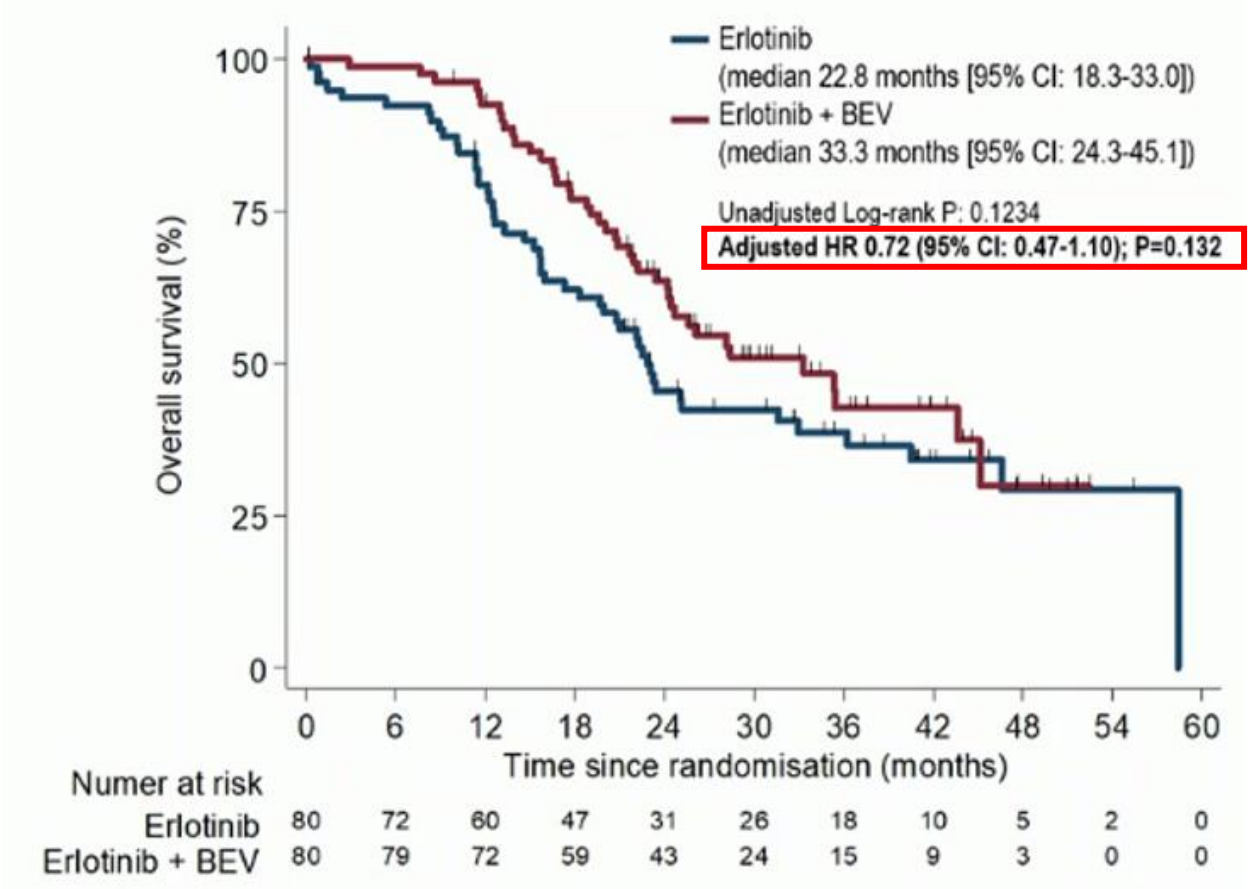
cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

KEY DATA

BEVERLY Clinical Trial

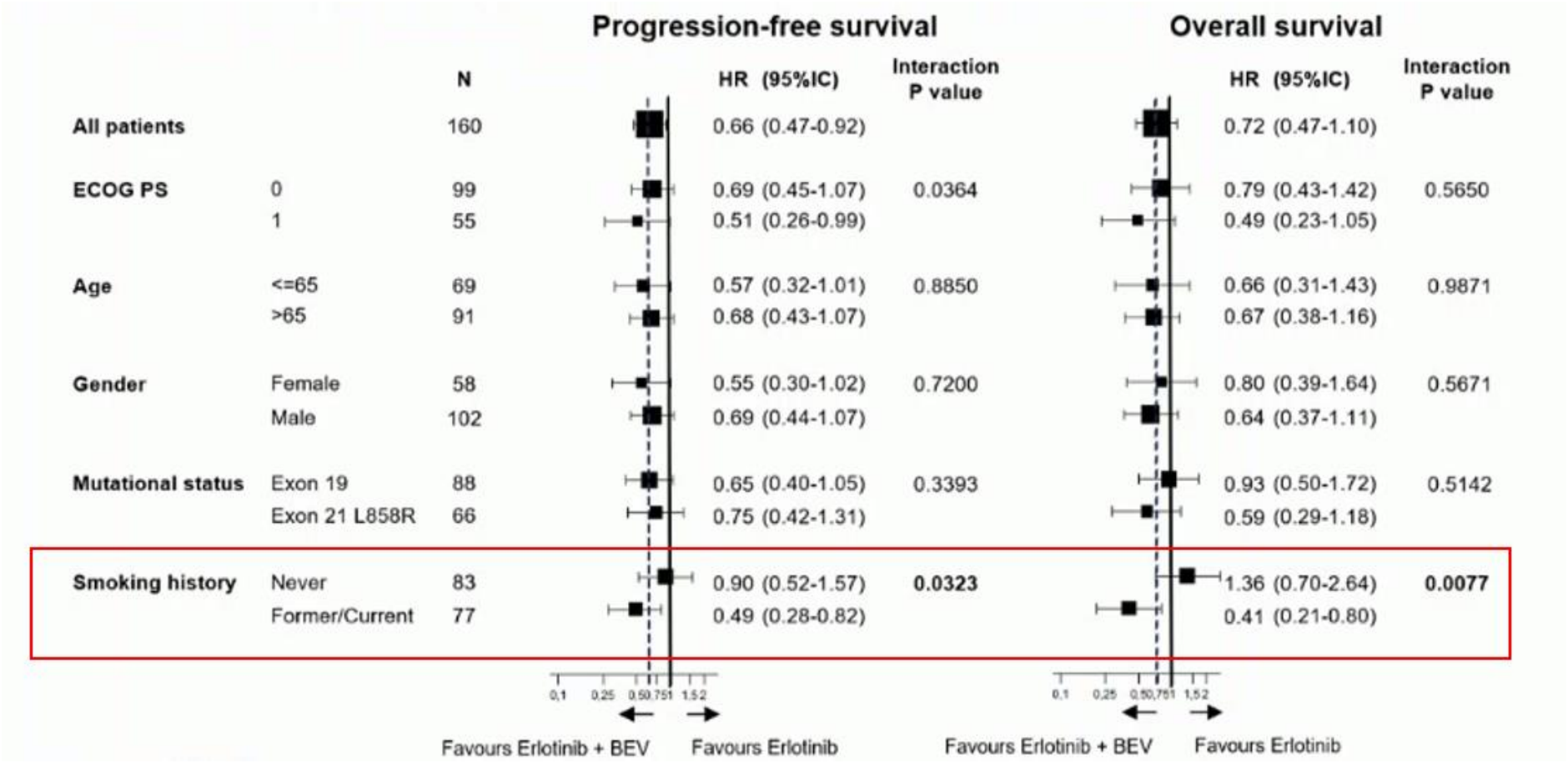
Overall Survival



European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

BEVERLY Clinical Trial

Exploratory Subgroup Analyses of PFS and OS



KEY DATA

BEVERLY Clinical Trial

Objective Response Rate

	Investigator-assessed		Blinded Independent Centrally Reviewed	
	Erlotinib (n=80)	**Erlotinib + BEV (n=80)**	**Erlotinib (n=80)**	**Erlotinib + BEV (n=80)**
Responders (CR + PR)	40 (50.0%) 95% CI: 39.0%-60.9%	**56** (70.0%) 95% CI: 60.0% - 80.0%	43 (53.8%) 95% CI: 39.0%-60.9%	**57** (71.3%) 95% CI: 60.0% - 80.0%
	P 0.01		*P 0.02*	
CR	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)
PR	39 (48.8%)	**55 (68.8%)**	42 (52.5%)	**56 (70.0%)**
SD	29 (36.3%)	18 (22.5%)	26 (32.5%)	17 (21.3%)
PD	11 (13.8%)	6 (7.5%)	11 (13.8%)	6 (7.5%)

cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

KEY DATA

BEVERLY Clinical Trial

Safety

More frequent (>5%) or significantly difference severe side effects

	Erlotinib		Erlotinib + BEV	
	Grade 0-2 (%)	Grade ≥3 (%)	Grade 0-2 (%)	Grade ≥3 (%)
Diarrhea	76 (96.2%)	3 (3.8%)	76 (95.0%)	4 (5.0%)
Fatigue	79 (100%)	0 (0%)	0 (0%)	5 (6.3%)
AST increased	75 (94.9%)	4 (5.1%)	79 (98.8%)	1 (1.3%)
Proteinuria	78 (98.7%)	1 (1.3%)	75 (93.8%)	5 (6.3%)
Hypertension	**75 (94.9%)**	**5 (5.1%)**	**61 (76.3%)**	**19 (23.8%)***
Thromboembolic event	78 (98.7%)	1 (1.3%)	76 (95.0%)	4 (5.0%)
Rash	**66 (83.5%)**	**13 (16.5%)**	**53 (66.3%)**	**27 (33.8%)****

Note: one toxic death was reported with erlotinib + BEV due to intracranial hemorrhage

- **P = 0.001; ** P = 0.01*
- Proteinuria was significantly more frequent with BEV (*P=0.004*) when considering all grades

cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

KEY DATA

BEVERLY Clinical Trial

Post-study anti-cancer therapies

	Erlotinib	Erlotinib + BEV
Discontinued study treatment , n (%)	78 (99%)	71 (89%)
No post-treatment anti-cancer therapy, n (%)	11 (14%)	8 (11%)
Missing information	11 (14%)	14 (20%)
First post-treatment anticancer therapy, n (%)	56 (72%)	49 (69%)
Osimertinib	**32 (57%)**	**24 (49%)**
Erlotinib (out of the study)	7 (13%)	8 (16%)
Gefitinib	---	3 (6%)
Platinum-based chemotherapy	16 (29%)	13 (27%)
Single agent chemotherapy	1 (2%)	1 (2%)

cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

SUMMARY

BEVERLY Clinical Trial

- The addition of Bevacizumab to 1L Erlotinib significantly increased PFS
  - mPFS 15.4 vs 9.6 months; HR 0.66, 95% CI: 0.47 -0.92; *P=0.015*
- Overall response rate was significantly increased (70% vs 50%)
- Overall survival trend improved with the addition of bevacizumab although not significant
  - mOS 33.3 vs 22.8 months; HR 0.72; 95% CI: 0.47-1.10; *P =0.132*
- No unexpected safety issues

cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

BEVERLY Clinical Trial

Bevacizumab in combination with erlotinib provides benefit as a 1L option for patients with EGFR mutation-positive NSCLC who cannot receive osimertinib

2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

FDA APPROVAL

On May 21, 2021, the Food and Drug Administration granted accelerated approval to amivantamab-vmjw (Rybrevant, Janssen Biotech, Inc.), a bispecific antibody directed against epidermal growth factor (EGF) and MET receptors, for adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.

The FDA also approved the Guardant360® CDx (Guardant Health, Inc.) as a companion diagnostic for amivantamab-vmjw to identify patients who harbor the EGFR exon 20 insertion mutation.

cornerstone specialty network™

CLINICAL QUESTION

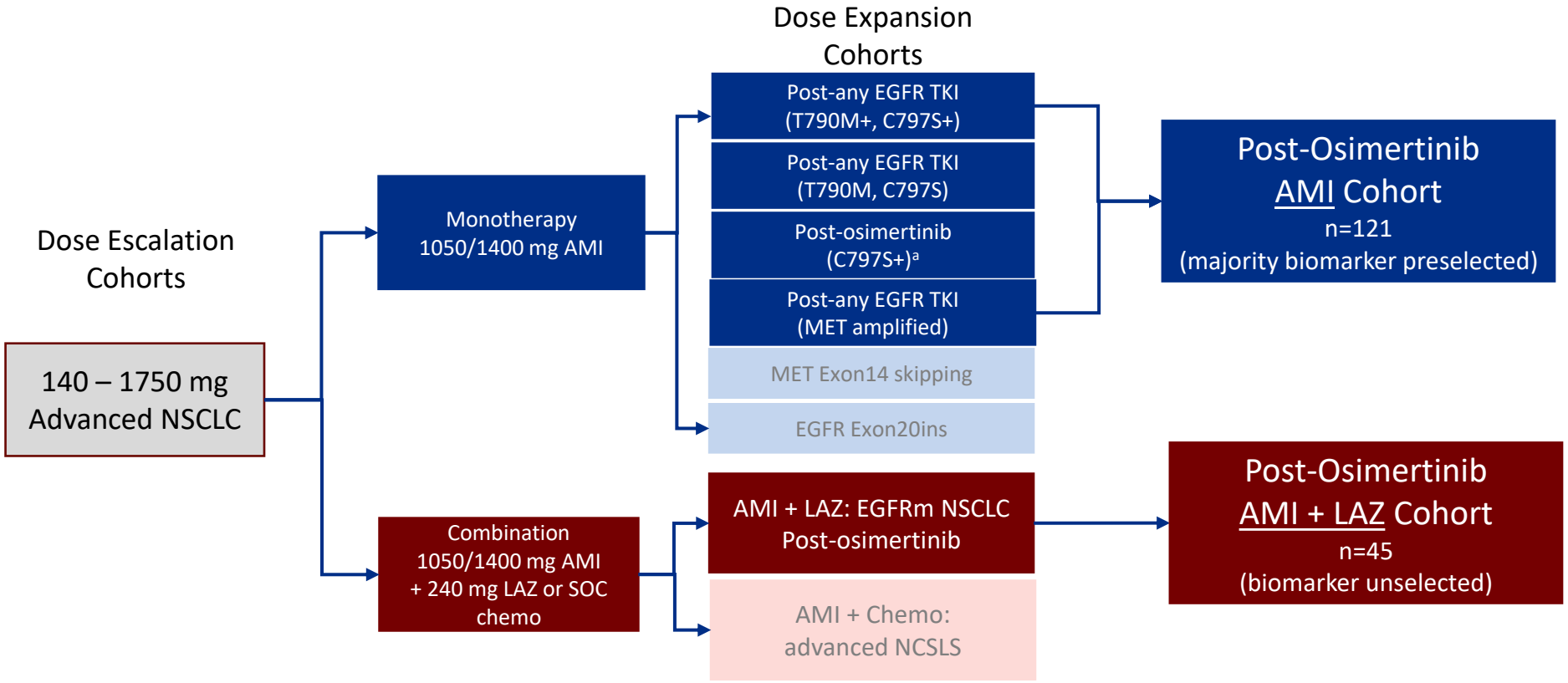
CHRYSALIS Clinical Trial

Does amivantamab in combination with lazertinib benefit patients with EGFR-mutant NSCLC post osimertinib?

KEY DATA

CHRYSALIS Clinical Trial

Study Design: Phase 1



Data cutoff: April 19, 2021

[a]The first 33 patients were unselected before the cohort was amended to select only for C797S.

KEY DATA

CHRYSALIS Clinical Trial

Patient Demographics and Baseline Characteristics

Characteristic, n (%)	AMI n=121	AMI + LAZ n=45
Median age, years (range)	63 (37-83)	65 (39-85)
Male / Female	41 (34) / 80 (66)	20 (44) / 25 (56)
Race		
Asian	69 (57)	19 (42)
White	35 (29)	20 (44)
Black	6 (5)	2 (4)
Other	11 (9)	4 (9)
History of brain mets	31 (26)	13 (29)
Smoking History, Yes	48 (40)	20 (44)
Median prior lines, n (range)	**3** (1-4)	**2** (1-4)
3rd generation EGFR TKI	121 (100)	45 (100)
Platinum-based chemotherapy	53 (44)	7 (16)[a]
EGFR/MET-based resistance[b]	103 (**85**)	17 (**38**)
C797S	69 (57)	7 (16)
MET amp (≥3 copies)	40 (33)	5 (11)

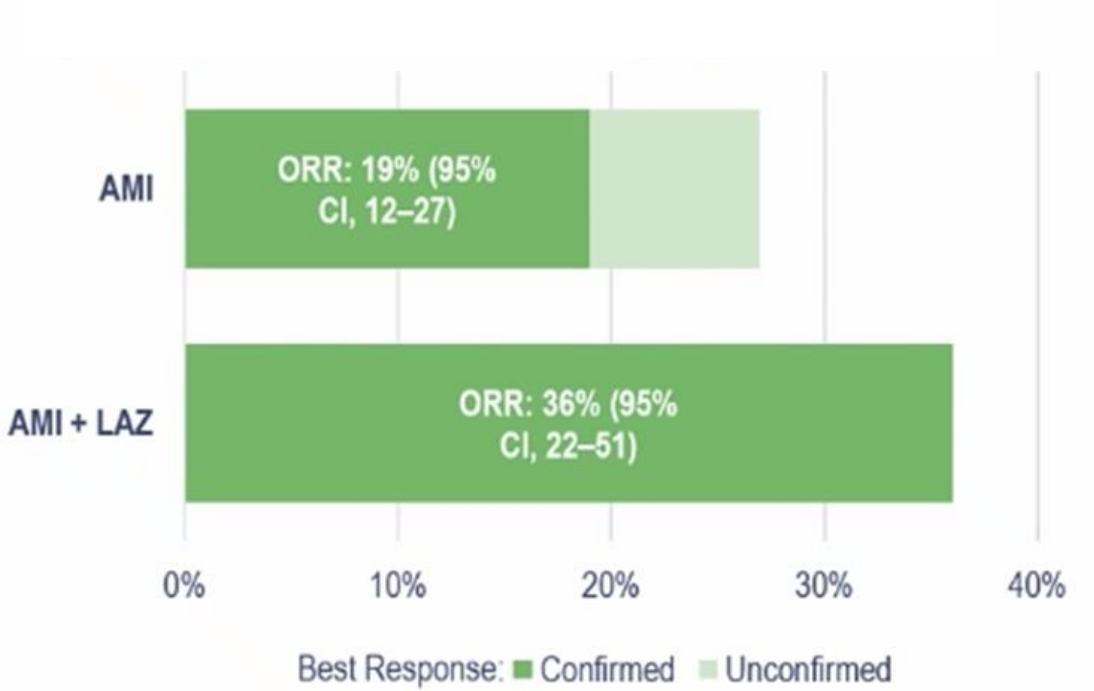
[a]Seven patients had limited platinum exposure (<2 cycles) given before first EGFR TKI

[b]Guardant360 or Thermofischer/Foundation Medicine local or central testing EGFR-based Osimertinib resistance and MET-based osimertinib resistance. Some patients had more than 1 identified resistance mechanism.

KEY DATA

CHRYSALIS Clinical Trial

Efficacy of AMI monotherapy and AMI + LAZ combination



	AMI (n=121)	AMI + LAZ (n=45)
Best Response	27%	36%
Confirmed ORR (95% CI)	**19%** (12-27)	**36%** (22-51)
CR	0	1 (2%)
PR	23 (19%)	15 (33%)
SD	53 (44%)	14 (31%)
PD	39 (32%)	11 (24%)
NE	6 (5%)	4 (9%)
mDOR (95% CI)	**5.9 mo** (4.2-12.6)	**9.6 mo** (5.3 – NR)
CBR (95% CI)	**48%** (39-57)	**64%** (49-78)
mPFS (95% CI)	4.2 mo (3.2-5.3)	4.9 mo (3.7-9.5)
mF/U (range)	6.9 mo (0.7-38.6)	11.1 mo (1.0-15.0)

*ORR among patients with identified EGFR/MET-based Osimertinib resistance was 18% for AMI and 47% for AMI + LAZ

Additional of lazertinib to amivantamab was associated with numerically higher objective response rate and longer duration of response after progression on osimertinib

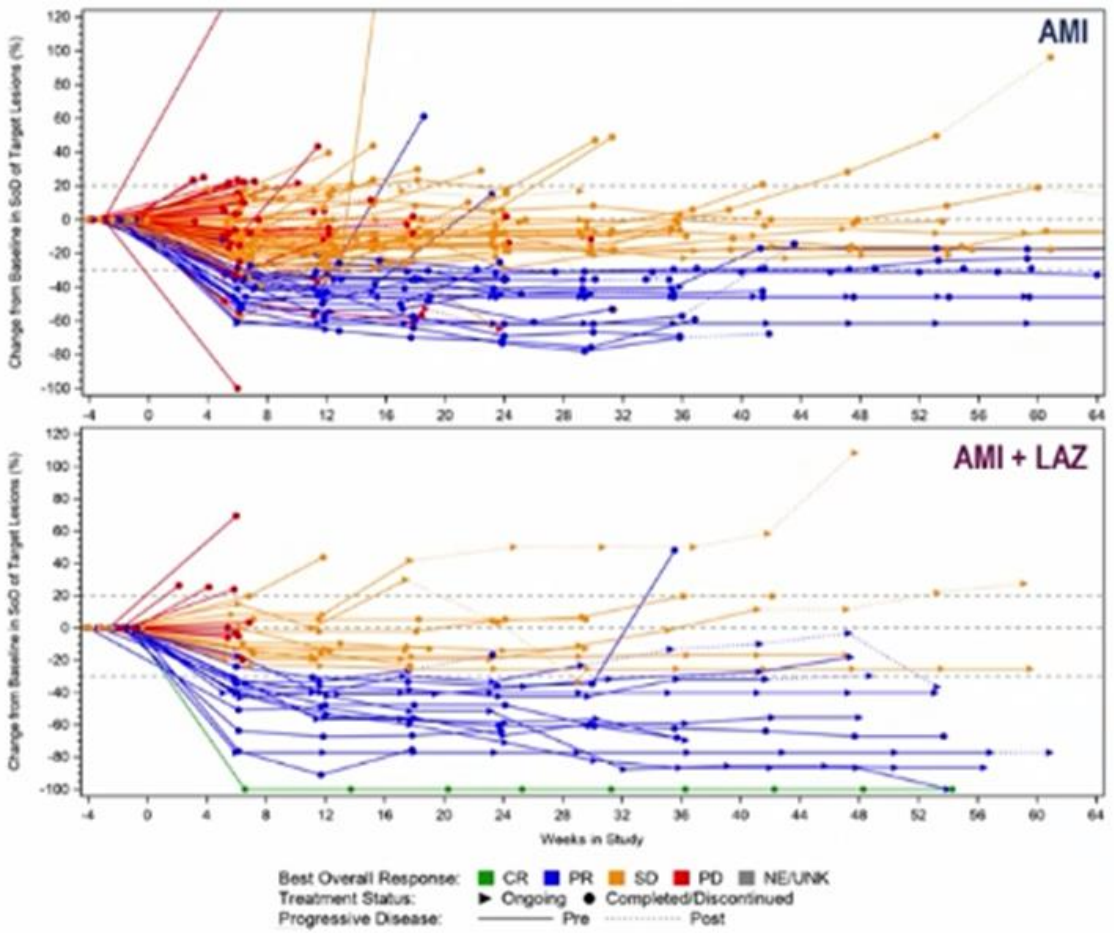
cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

KEY DATA

CHRYSALIS Clinical Trial

Efficacy of AMI monotherapy and AMI + LAZ combination



AMI (n=121)

- Median time on treatment **3.7** month (range, 0.03 – 32.2)
  - Among responders **8.3** months (range, 2.8 – 32.2)
- **39%** had responses ≥ 6 months
- CNS progression was documented among 17% of patients with 13% being new CNS lesions

AMI + LAZ (n=45)

- Median time on treatment **5.6** month (range, 0.5 – 14.8)
  - Among responders **12.0** months (range, 4.1 – 14.6)
- **69%** had responses ≥ 6 months
- CNS progression was documented among 7% of patients with 4% being new CNS lesions

cornerstone specialty network™

KEY DATA

CHRYSALIS Clinical Trial

Safety Profile

TEAE (≥20%, with AMI monotherapy), n (%)	AMI, n=121	AMI + LAZ, n=45
Infusion-related reaction	83 (69)	35 (78)
Paronychia	45 (37)	22 (49)
Acneiform dermatitis	34 (28)	23 (51)
Hypoalbuminemia	31 (26)	17 (38)
Rash	32 (26)	12 (27)
Constipation	31 (26)	12 (27)
Nausea	29 (24)	20 (44)
Dyspnea	28 (23)	1 (24)
Pruritis	27 (22)	14 (31)

- Safety profile is consistent with that reported from earlier data cutoffs; no new safety signals identified
- Diarrhea reported in 7% of AMI and 22% of AMI + LAZ patients
- Pneumonitis/ILD reported in 2% of AMI and 4% of AMI + LAZ patients

- Additional AEs of ≥20% in AMI + LAZ cohort: peripheral edema (38%), dry skin (29%), stomatitis (27%), fatigue (27%), increased AST (22%), dizziness (22%), hypocalcemia (20%), vomiting (20%), headache (20%)

cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

SUMMARY

CHRYSALIS Clinical Trial

- Amivantamab plus Lazertinib after Osimertinib improved ORR and DOR over amivantamab monotherapy alone
  - AMI + LAZ: ORR **36%** (95% CI, 22-51) ; mDOR **9.6** months (95% CI 5.3 - NR)
  - AMI monotherapy: ORR 19% (95% CI, 12-27) ; mDOR 5.9 months (95% CI 4.2 – 12.6)
  - CNS progression was low with AMI + LAZ (17%) and with AMI monotherapy (7%)

- The safety profile for both arms was consistent with previously reported experience; no new safety signals identified

cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

CHRYSALIS Clinical Trial

Use of amivantamab in combination with lazertinib after osimertinib provides greater benefit than amivantamab monotherapy for some patients with EGFR-mutated advanced or metastatic NSCLC

More to come…

2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

CLINICAL QUESTION

CHRYSALIS-2 Clinical Trial

Does amivantamab in combination with lazertinib benefit patients with EGFR-mutant NSCLC post osimertinib and post chemotherapy?

cornerstone specialty network™

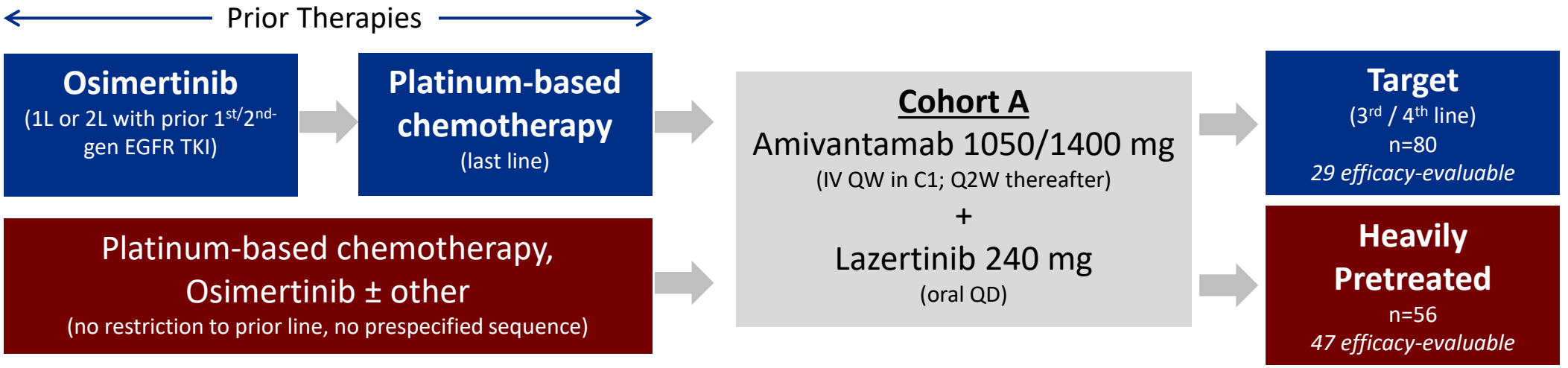
KEY DATA

CHRYSALIS-2 Clinical Trial

Study Design: Phase 1

Key Eligibility Criteria:

- Metastatic advanced NSCLC
- EGFR Exon19del or L858R



End Points:

ORR, PFS, OS, DOR, clinical benefit rate (CBR), adverse events

KEY DATA

CHRYSALIS-2 Clinical Trial

Demographics and Baseline Characteristics

Characteristic, n (%)	Target (n=80)	Heavily Pretreated (n=56)
Median age, years (range)	62 (31-82)	63 (39-83)
Male / Female	31 (39%) / 49 (61%)	19 (34%) / 37 (66%)
Race		
Asian	49 (61%)	34 (61%)
White	20 (25%)	14 (25%)
Black	0	1 (2%)
Other	11 (14%)	7 (13%)
History of brain mets	34 (43%)	22 (39%)
Smoking History, Yes	23 (29%)	18 (32%)
Median prior lines, n (range)		
2-3 lines	76 (95%)	17 (30%)
≥4 lines	4 (5%)	39 (70%)
ECOG PS		
0	24 (30%)	19 (34%)
1	56 (70%)	37 (66%)

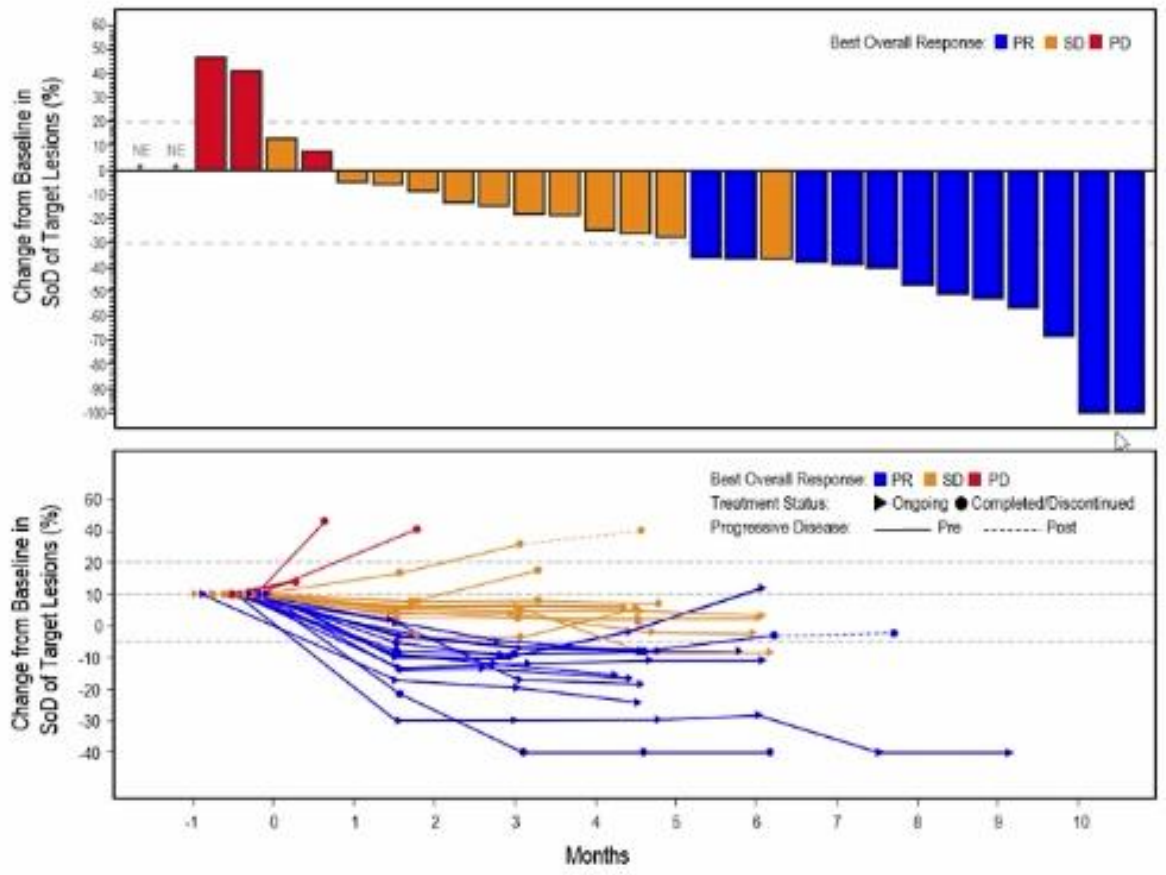
cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

KEY DATA

CHRYSALIS-2 Clinical Trial

Target Population: Antitumor activity of amivantamab + lazertinib



Among 29 efficacy-evaluable patients at a median follow-up of 4.6 months (range, 0.4 -9.6):

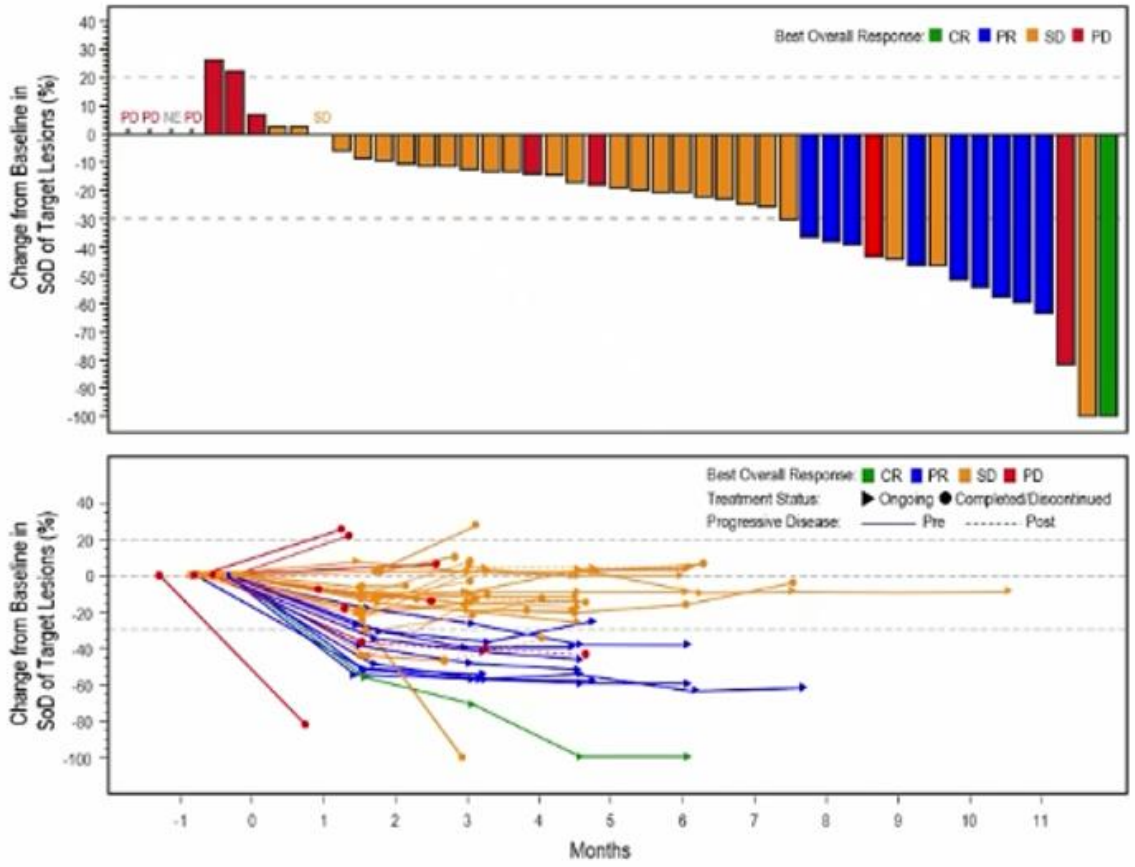
- ORR = 41% (95% CI: 24 – 61)
- CBR = 69% (95% CI: 49-85)
- Median time on treatment 4.2 months (range, 0.03 – 8.4)
- Responses observed early
  - mTTR = 1.4 months (range, 1.4 – 4.4)
- 8 out of 12 patients who responded are progression-free and remain on treatment
- 5 out of 12 patients with stable disease remain on treatment (longest at 6.9+ months)

cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

CHRYSALIS-2 Clinical Trial

Heavily Pretreated: Antitumor activity of amivantamab + lazertinib



Among 47 efficacy-evaluable patients at a median follow-up of 4.5 months (range, 0.3 – 9.7):

- ORR = 21% (95% CI: 11 – 36)
- CBR = 51% (95% CI: 36 – 66)
- Median time on treatment 3.7 months (range, 0.03 – 9.7)
- Responses observed early
  - mTTR = 1.5 months (range, 1.3 – 4.2)
- 10 out of 10 patients who responded are progression-free and remain on treatment
- 10 out of 26 patients with stable disease remain on treatment (longest at 9.6+ months)

cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

KEY DATA

CHRYSALIS-2 Clinical Trial

Safety Profile

TEAE (≥10%), n (%)	All Grade	Grade ≥3
Infusion-related reaction	91 (67%)	12 (9%)
Stomatitis	50 (37%)	2 (2%)
Acneiform dermatitis	47 (35%)	6 (4%)
Paronychia	47 (35%)	4 (3%)
Rash	46 (34%)	3 (2%)
Hypoalbuminemia	40 (29%)	6 (4%)
Vomiting	28 (21%)	0
Increased alanine aminotransferase	27 (20%)	4 (3%)
Decreased appetite	27 (20%)	1 (1%)
Asthenia	26 (19%)	2 (2%)
Diarrhea	26 (19%)	0
Dry Skin	26 (19%)	0

TEAE (≥10%), n (%)	All Grade	Grade ≥3
Nausea	25 (18%)	2 (2%)
Peripheral edema	24 (18%)	1 (1%)
Headache	23 (17%)	0
Increased aspartate aminotransferase	22 (16%)	3 (2%)
Constipation	22 (16%)	0
Fatigue	22 (16%)	3 (2%)
Thrombocytopenia	20 (15%)	1 (1%)
Dyspnea	18 (13%)	8 (6%)
Pruritis	18 (13%)	1 (1%)
Myalgia	14 (10%)	0
Skin fissures	14 (10%)	0

- Safety profile is consistent with previously-reported experience with the combination regimen
- 50 patients (37%) had treatment-related grade ≥3 AEs
- 4 patients (3%) had pneumonitis/ILD
- AEs leading to dose discontinuation reported in 11%, dose reduction in 18%, and dose interruption in 46%
- No new safety signals were identified

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

SUMMARY

CHRYSALIS-2 Clinical Trial

- Amivantamab plus lazertinib demonstrated antitumor activity for patients that progressed on both osimertinib and platinum-based chemotherapy (with no approved targeted therapy options)
  - In the target population, ORR was 41% and CBR was 69%
  - In the heavily treated population, ORR was 21% and CBR was 51%
- Activity is comparable to previously reported post-osimertinib, chemotherapy-naïve population suggesting that intervening chemotherapy does not impact amivantamab plus lazertinib activity
- Safety profile was consistent with previously reported; no new safety signals identified

cornerstone specialty network™

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #1192MO).

CHRYSALIS-2 Clinical Trial

Use of amivantamab in combination with lazertinib provided benefit to patients with EGFR-mutant NSCLC after both osimertinib and platinum chemotherapy

More to come…

2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

CLINICAL QUESTION

KRYSTAL-1 Clinical Trial

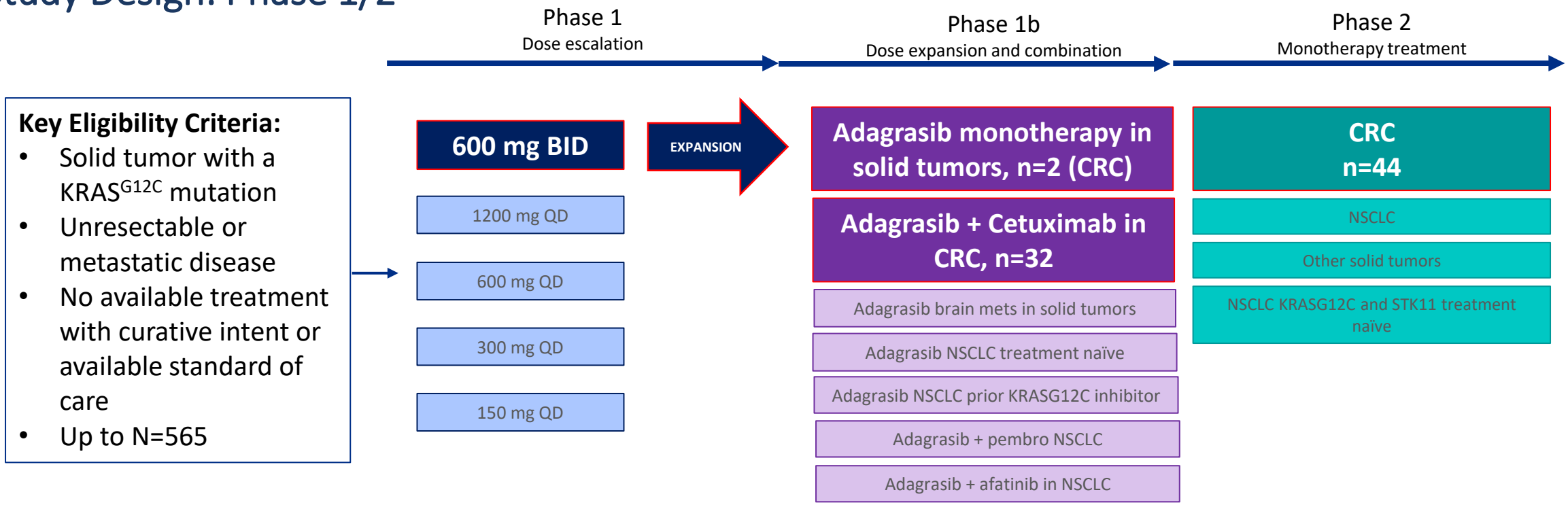
Does adagrasib (MRTX849) with or without cetuzimab benefit patients with colorectal cancer harboring a $KRAS^{G12C}$ mutation?

cornerstone specialty network™

KEY DATA

KRSYTAL-1 Clinical Trial

Study Design: Phase 1/2



Phase 1 Endpoints

- **Primary End Point: S**afety, MTD, PK, RP2D
- **Secondary Endpoints:** OR, DOR, PFS, OS

Phase 2 Endpoints

- **Primary End Point:** ORR (RECIST1.1)
- **Secondary Endpoints:** Safety

- Previously reported data demonstrated the clinical activity of adagrasib in patients with pretreated CRC with a $KRAS^{G12C}$ mutation
- Preliminary data for adagrasib 600 mg BID as monotherapy (n=2 in Phase 1/1b and n=44 in Phase 2; median follow-up 8.9 months) and in combination with cetuximab (n=32; median follow-up 7 months) in patients with pretreated CRC with a $KRAS^{G12C}$ mutation
- Data as of 25 May 2021 (adagrasib monotherapy), 9 July (adagrasib + cetuximab)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA6).

KEY DATA

KRSYTAL-1 Clinical Trial

Demographics and Baseline Characteristics

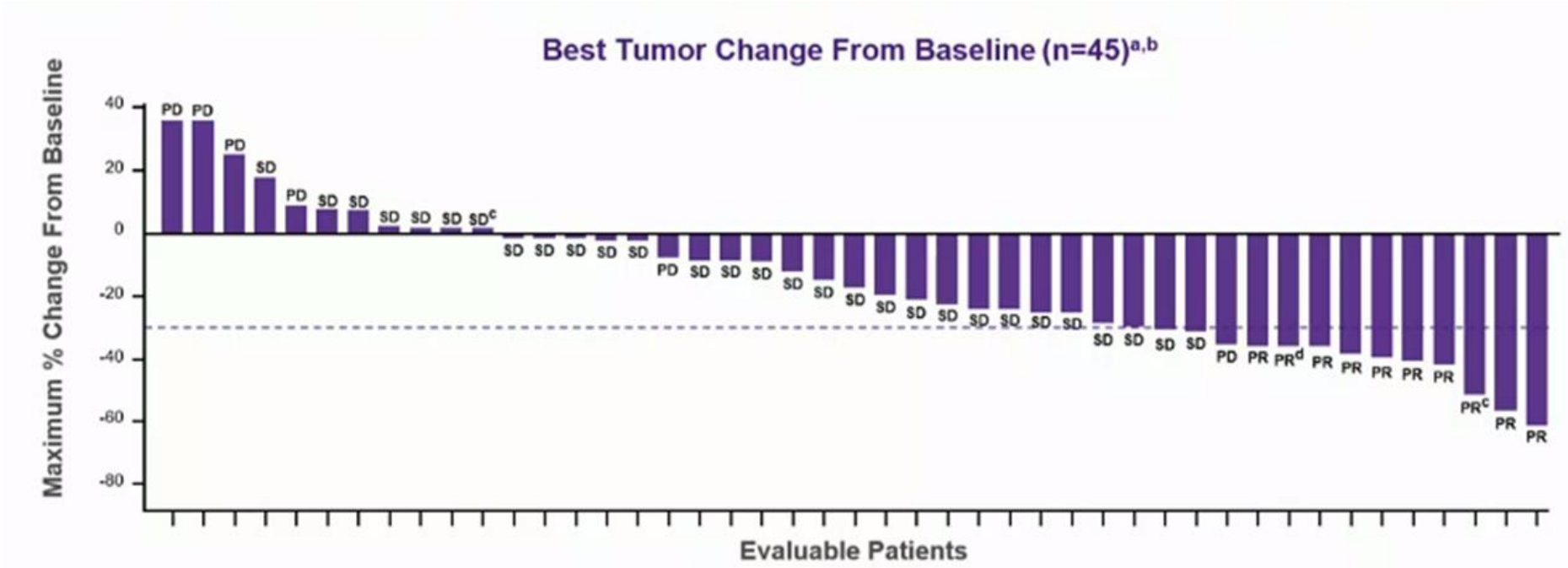
	Adagrasib monotherapy (n=46)	Adagrasib + Cetuximab (n=32)
Median age, y (range)	58 (29-79)	61 (41-74)
Female, n (%)	23 (50%)	17 (53%)
Race, n (%)		
White	35 (76%)	26 (81%)
Black	6 (13%)	4 (13%)
Asian	3 (7%)	2 (6%)
Other	2 (4%)	0 (0%)
ECOG PS, n (%) 0 / 1	23 (50%) / 23 (50%)	14 (44%) / 18 (56%)
Prior lines of systemic anticancer therapy, median (range)	3 (1-10)	3 (1-8)
Prior lines of systemic anticancer therapy, %: 1 / 2 / 3 / ≥4	20% / 26% / 20% / 35%	9% / 25% / 34% / 31%
Prior systemic anticancer therapy, (%)		
Fluoropyrimidine/oxaliplatin/irinotecan	100% / 98% / 80%	100% / 100% / 88%
Anti-VEGF	83%	84%
Anti-EGFR biological therapy	2%	0%
Regorafenib and /or trifluridine/tipiracil	22%	19%
Molecular status, n (%)		
BRAF V600E	0/44 (0%)	0/30 (0%)
MSI-H or dMMR	1/35 (3%)	0/19 (0%)
EGFR amplification	1/35 (3%)	1/28 (4%)
TP53	23/24 (68%)	18/26 (69%)
PIK3CA	5/36 (14%)	3/26 (12%)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA6).

KEY DATA

KRSYTAL-1 Clinical Trial

Adagrasib in patients with advanced CRC: Best overall response



- Response rate was 22% (10/45), including 1 unconfirmed PR
- SD was observed in 64% (29/45) of patients
- Clinical benefit (DCR) was observed in 87% (39/45) of patients
- No apparent association between response rate and molecular status was shown in an exploratory analysis

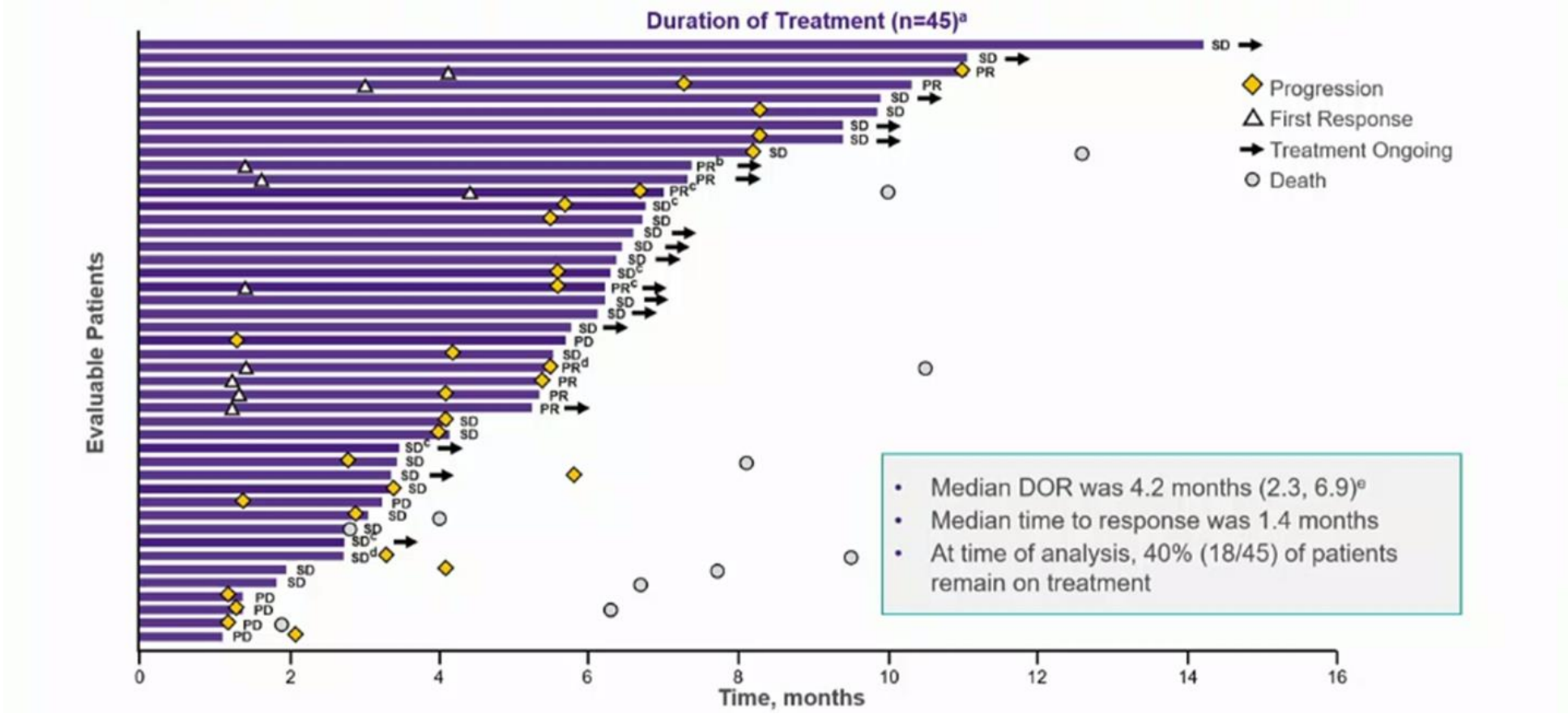
Data as of 25 May 2021 for monotherapy (median follow-up of 8.9 months)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA6).

KEY DATA

KRSYTAL-1 Clinical Trial

Adagrasib in patients with advanced CRC: Duration of Treatment

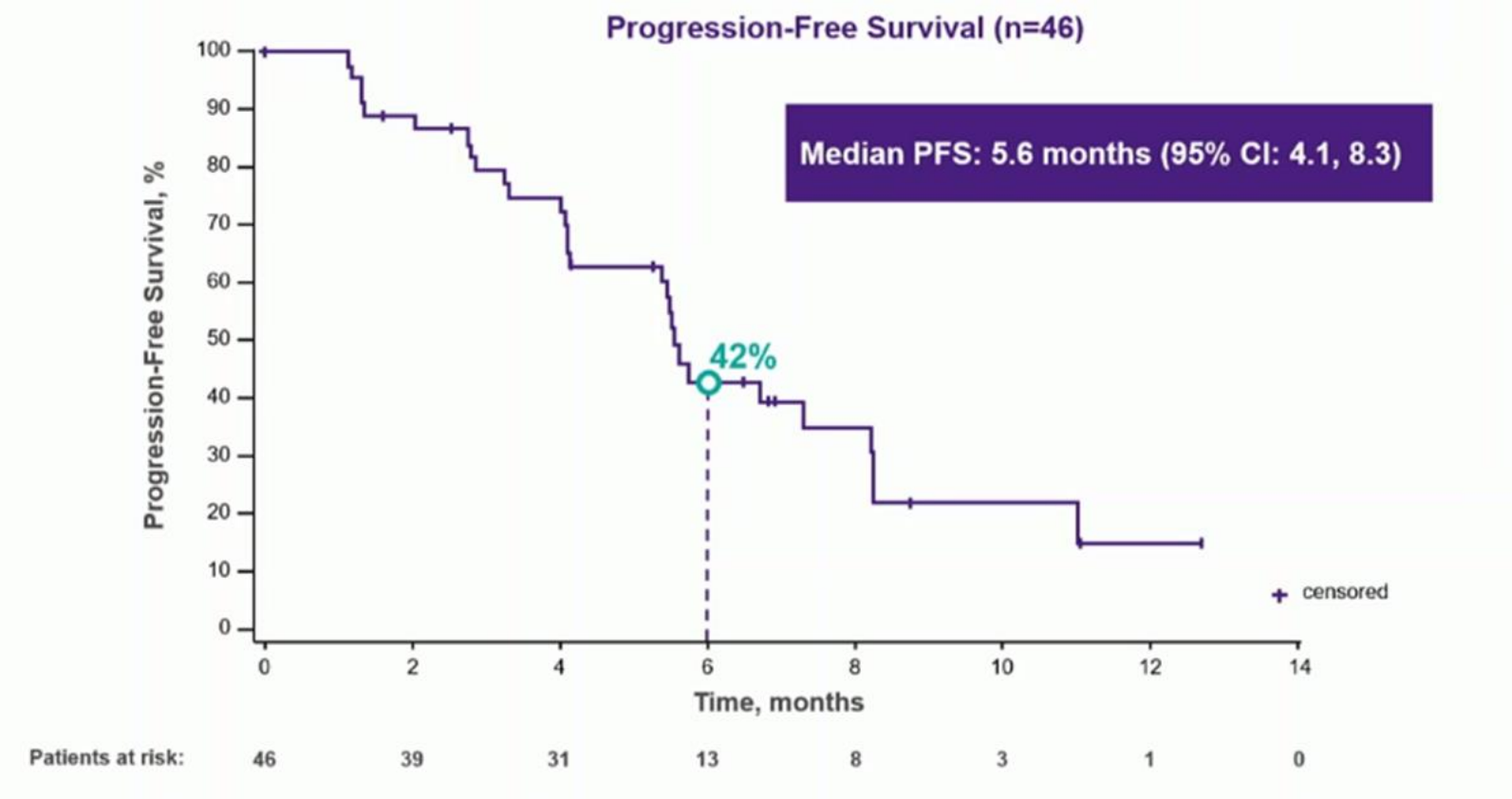


Data as of 25 May 2021 for monotherapy (median follow-up of 8.9 months)

KEY DATA

KRSYTAL-1 Clinical Trial

Adagrasib in patients with advanced CRC: Progression-Free Survival



Data as of 25 May 2021 for monotherapy (median follow-up of 8.9 months)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA6).

KEY DATA

KRSYTAL-1 Clinical Trial

Adagrasib in patients with advanced CRC: Treatment-Related Adverse Events

Most Frequent TRAEs	Adagrasib Monotherapy[a] (n=46)	
TRAEs,[b,c] %	**Any Grade**	**Grades 3-4**
Any TRAEs	91%	30%
Most frequent TRAEs, %		
Diarrhea	63%	7%
Nausea	57%	0%
Fatigue	46%	4%
Vomiting	46%	0%
Decreased appetite	15%	0%
Peripheral edema	15%	0%
AST increase	13%	4%
QT prolongation	13%	2%
ALT increase	11%	4%
Anemia	11%	2%

- No Grade 5 TRAEs
- No TRAEs that led to discontinuation

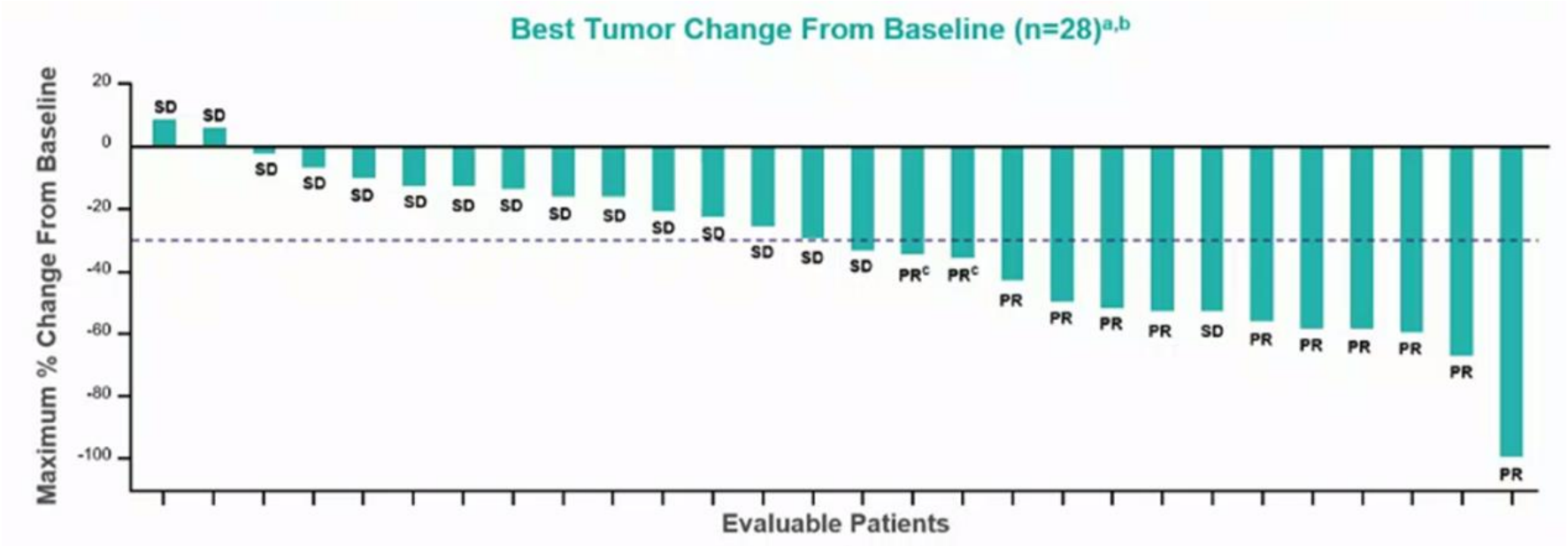
Data as of 25 May 2021 for monotherapy (median follow-up of 8.9 months)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA6).

KEY DATA

KRSYTAL-1 Clinical Trial

Adagrasib + Cetuximab in patients with advanced CRC: Best Overall Response



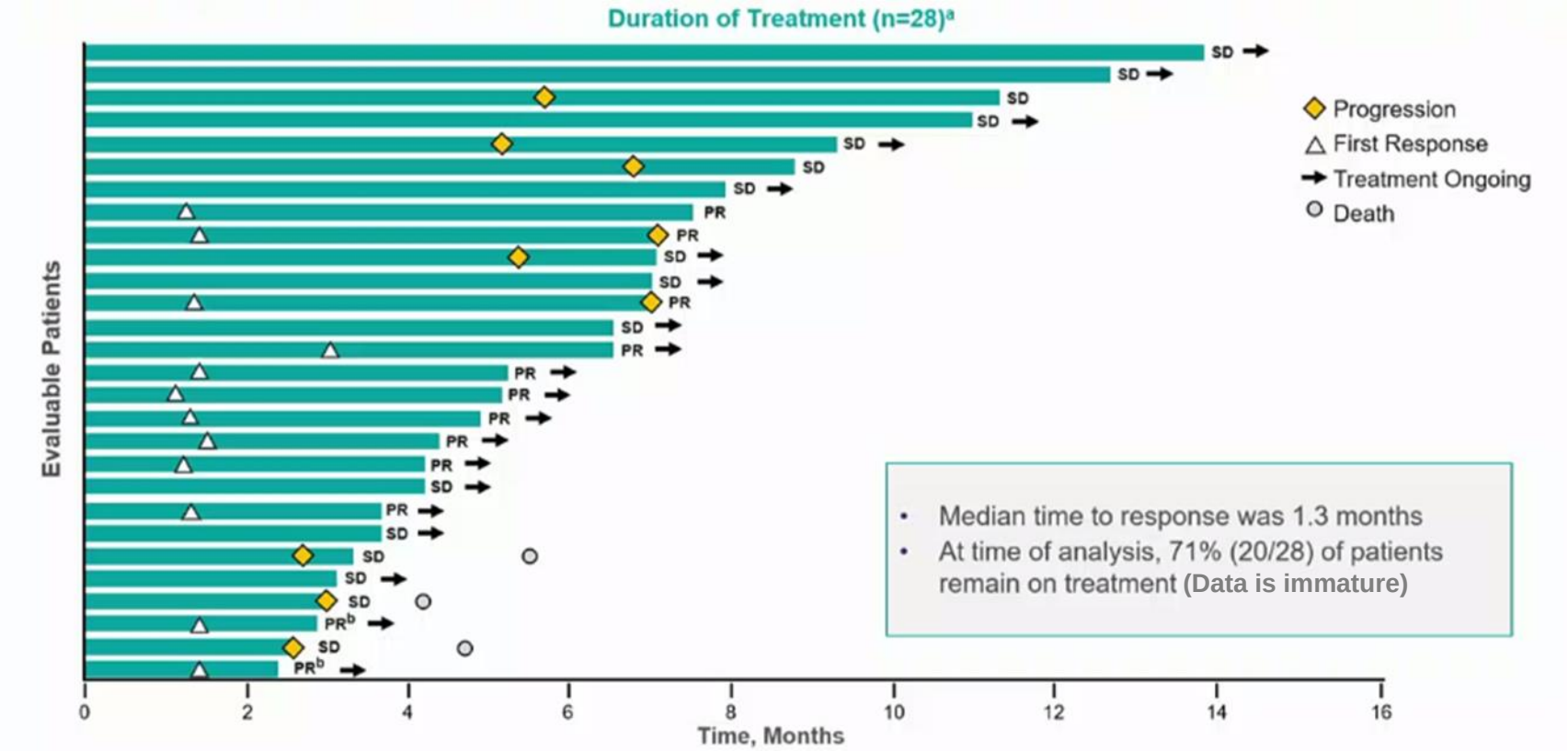
- Response rate was 43% (12/28), including 2 unconfirmed PR
- SD was observed in 57% (16/28) of patients
- Clinical benefit (DCR) was observed in 100% (28/28) of patients
- No apparent association between response rate and molecular status was shown in an exploratory analysis

Data as of 9 July 2021 (median follow-up of 7 months)

KEY DATA

KRSYTAL-1 Clinical Trial

Adagrasib + Cetuximab in patients with advanced CRC: Duration of Treatment



Data as of 9 July 2021 (median follow-up of 7 months)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA6).

KEY DATA

KRSYTAL-1 Clinical Trial

Adagrasib + Cetuximab in patients with advanced CRC: Treatment-Related Adverse Events

Most Frequent TRAEs	Adagrasib + Cetuximab (n=32)	
TRAEs,[a,b] %	Any Grade	Grades 3-4
Any TRAEs	100%	16%
Most frequent TRAEs, %		
Nausea	63%	0%
Diarrhea	56%	3%
Vomiting	50%	0%
Fatigue	47%	0%
Dermatitis acneiform	44%	3%
Dry skin	38%	0%
Headache	28%	0%
Rash maculopapular	22%	0%
Dyspepsia	19%	0%
Infusion-related reaction	19%	3%
Peripheral edema	19%	0%
Rash	19%	0%
Stomatitis	19%	3%
Decreased appetite	16%	0%
Dizziness	16%	0%
QT prolongation	16%	3%
ALT increase	13%	0%
Dyspnea	13%	0%
Hypomagnesemia	13%	0%

- No Grade 5 TRAEs
- 6% (n=2) of TRAEs led to discontinuation

Data as of 9 July 2021 (median follow-up of 7 months)

SUMMARY

KRSYTAL-1 Clinical Trial

- Adagrasib monotherapy demonstrated promising clinical activity (response rate of 22%) and broad disease control (DCR of 87%) in heavily pretreated patients with CRC harboring a $KRAS^{G12C}$ mutation
- Adagrasib plus cetuzimab demonstrated encouraging clinical activity (response rate of 43%) and broad disease control (DCR of 100%) in heavily pretreated patients with CRC harboring a $KRAS^{G12C}$ mutation
- Adagrasib is tolerable and has a manageable safety profile, both as a monotherapy and when combined with cetuximab
- Adagrasib with cetuximab is being evaluated in the 2L setting in the KRYSTAL-10 Phase 3 open-label clinical trial in patients with $KRAS^{G12C}$ mutant CRC
    - Adagrasib [600mg BID] + cetuximab (n=210) in a 1:1 ratio against FOLFIRI or mFOLFOX6 (n=210) after progression on 1L fluoropyrimidine-based regimen containing oxaliplatin or irinotecan

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA6).

KRSYTAL-1 Clinical Trial

Use of adagrasib in combination with cetuximab should be considered as a potential treatment option for patients with CRC harboring a $KRAS^{G12C}$ mutation

More to come…

2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

CLINICAL QUESTION

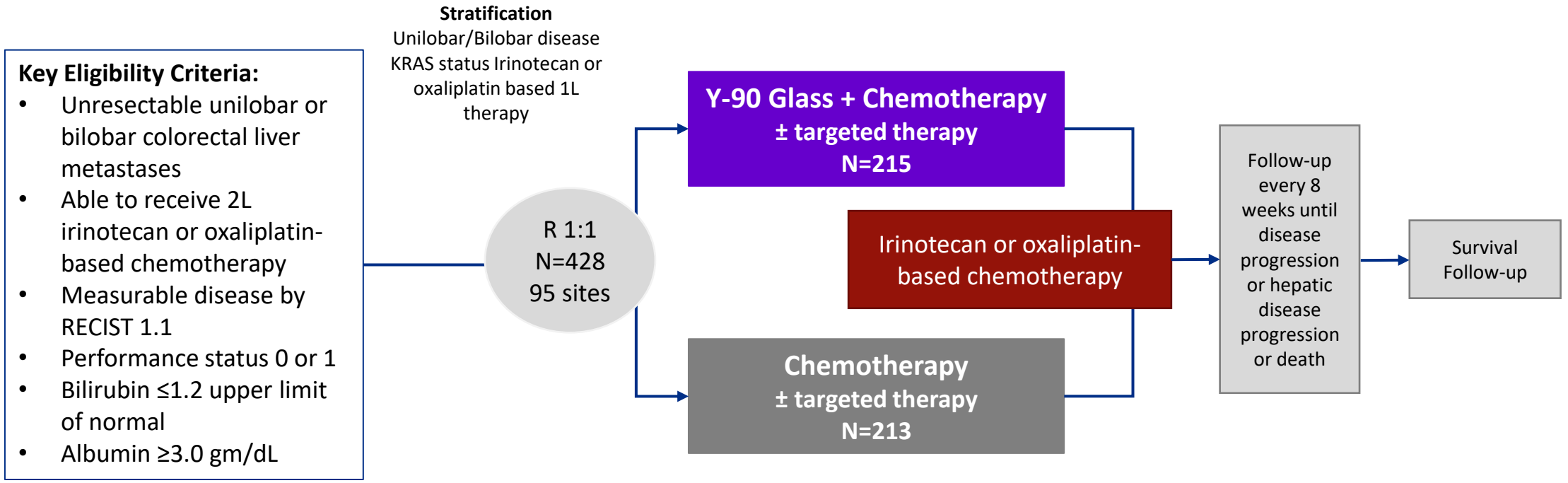
EPOCH Clinical Trial

Does the addition of radioembolization (Y-90) to standard of care chemotherapy provide benefit for patients with colorectal cancer liver metastases after progression on 1L treatment?

KEY DATA

EPOCH Clinical Trial

Study Design: Phase 3, randomized, open-label, international , multicenter trial



Primary Endpoints: PFS and hepatic PFS (hPFS) by BICR (one-sided p≤ 0.00248)
Secondary Endpoints: OS, TTSP, ORR by BICR, DCR by BICR, TTDQoL

TARE with Y-90 glass microspheres (TheraSphere, Boston Scientific Corporation)
Cycle 1 = chemotherapy, T-90 TARE replace Cycle 2, Cycle 3 resume chemotherapy ± targeted therapy (VEGF or EGFR inhibitors)

KEY DATA

EPOCH Clinical Trial

Demographics and Baseline Characteristics

	Y-90 + Chemo (N=215)	Chemo (N=213)
Median Age	63.0 years	60.0 years
Male	135 (62.8%)	138 (64.8%)
Region		
North America	63 (29.3%)	56 (26.3%)
Europe	131 (60.9%)	145 (68.1%)
Asia	21 (9.8%)	12 (5.6%)
ECOG 0	119 (55.3%)	133 (62.4%)
Albumin ≥ LLN	182 (84.7%)	177 (83.1%)
CEA ≥ 35 ng/mL	116 (54.0%)	105 (49.3%)
KRAS Status		
Mutant	100 (46.5%)	101 (47.4%)
Wild type	115 (53.5%)	112 (52.6%)

	Y-90 + Chemo (N=215)	Chemo (N=213)
Bilobar disease	176 (81.9%)	173 (81.2%)
Liver Tumor Burden[a]		
< 10%	124 (57.7%)	121 (56.8%)
≥ 10% to < 25%	54 (25.1%)	47 (22.1%)
≥ 25%	29 (13.5%)	28 (13.1%)
Maximum Liver Lesion Size ≥ 40 mm[a]	162 (75.3%)	142 (66.7%)
Primary tumor in situ	83 (38.6%)	69 (32.4%)
Left side primary tumor	150 (69.8%)	136 (63.8%)
Extrahepatic Lesions at Baseline	113 (52.6%)	95 (44.6%)
Number of Lesions		
< 3	25 (11.6%)	21 (9.9%)
3-5	40 (18.6%)	38 (17.8%)
6-10	54 (25.1%)	60 (28.2%)
> 10	88 (40.9%)	77 (36.2%)
Missing	8 (3.7%)	17 (8.0%)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA21).

KEY DATA

EPOCH Clinical Trial

Treatment Characteristics

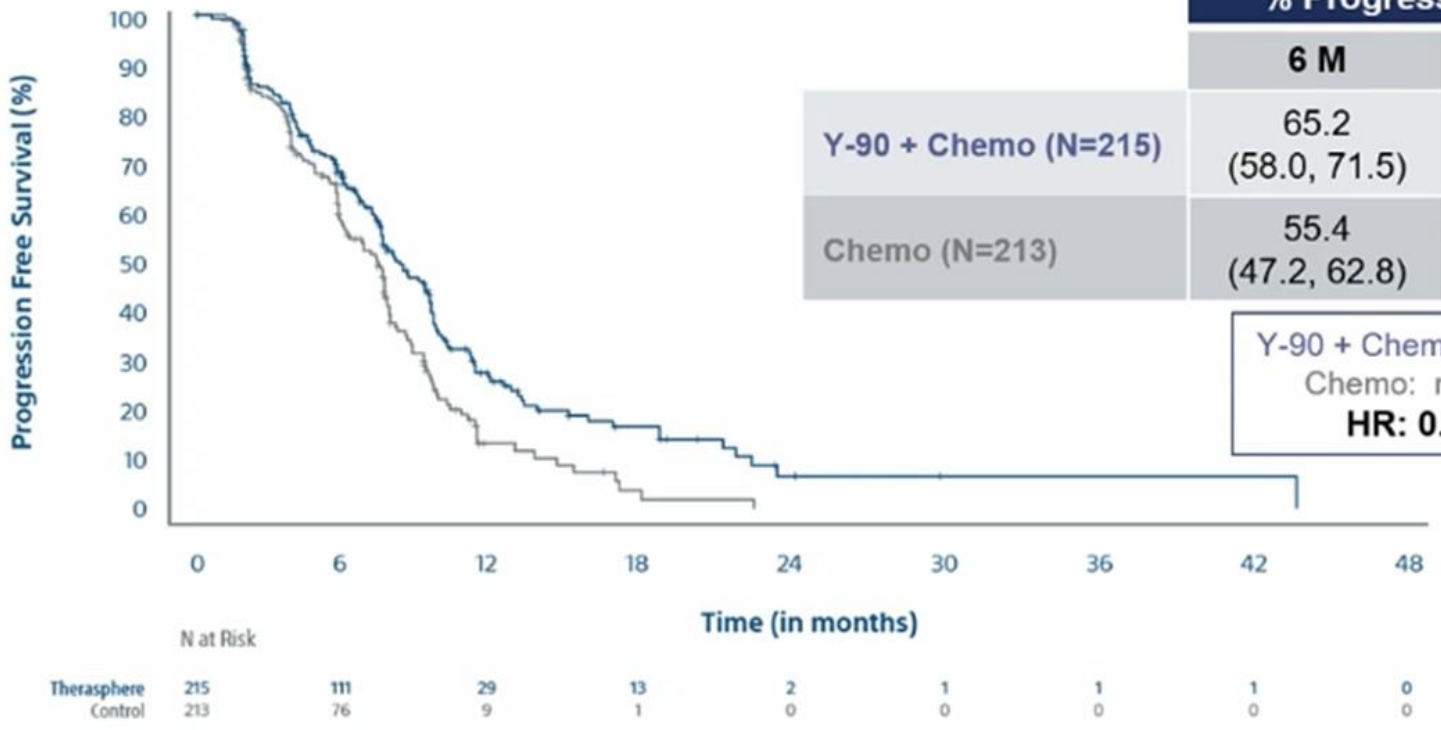
	Y-90 + Chemo (N=215)	Chemo (N=213)
Received Assigned Therapy	187 (87.0%)	191 (89.7%)
2nd Line Chemo Administered	203 (94.4%)	191 (89.7%)
Irinotecan-based	130 (60.5%)	123 (57.7%)
Mean Number of Cycles / Median of Average Dose per Cycle	9.0 / 180 mg/m^2	9.5 / 180 mg/m^2
Oxaliplatin-based	73 (34.0%)	68 (31.9%)
Mean Number of Cycles / Median of Average Dose per Cycle	8.5 / 85 mg/m^2	8.8 / 85 mg/m^2
Biological Agent	88 (40.9%)	93 (43.7%)
Aflibercept / Ramucirumab	9 (4.2%) / 0	11 (5.2%) / 1 (0.5%)
Bevacizumab	74 (34.4%)	65 (30.5%)
Cetuximab	5 (2.3%)	10 (4.7%)
Panitumumab	2 (0.9%)	6 (2.8%)
Y-90 Treatment		
Median absorbed dose to perfused volume prior to progression by investigator determination, Gy (range)	117 (61.7, 156)	NA
Median time to Y-90, days (range)	25 (12-90)	NA

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA21).

KEY DATA

EPOCH Clinical Trial

Progression-Free Survival



	% Progression-Free Survival (95% CI)		
	6 M	12 M	18 M
Y-90 + Chemo (N=215)	65.2 (58.0, 71.5)	25.8 (18.9, 33.1)	16.7 (10.6, 23.9)
Chemo (N=213)	55.4 (47.2, 62.8)	13.2 (7.5, 20.5)	1.8 (0.2, 8.1)

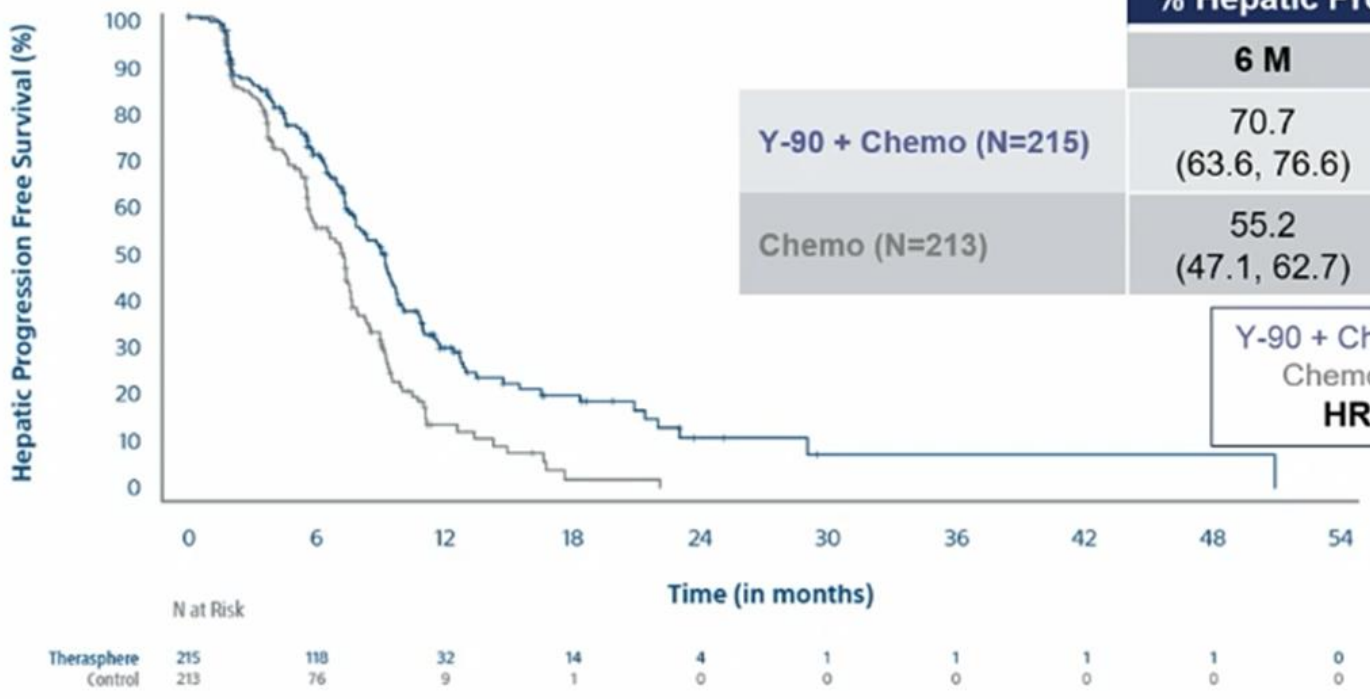
Y-90 + Chemo: median 8.0 M (95% CI: 7.2, 9.2)
Chemo: median 7.2 M (95% CI: 5.7, 7.6)
HR: 0.69 (0.54, 0.88); p=0.0013

Kaplan-Meier for PFS according to RECIST 1.1 by BICR
Log rank, one-sided p. Success criteria for the study were met (both PFS and hPFS p-values ≤0.00248)
Patient who received subsequent mCRC therapy prior to their last tumor assessment or PD or death were censored at their last tumor assessment prior to subsequent mCRC therapy.
Patients who had PD or death immediately after ≥2 missed visits were censored at the last tumor assessment prior to the 2 missed visits.

KEY DATA

EPOCH Clinical Trial

Hepatic Progression-Free Survival



	% Hepatic Progression-Free Survival (95% CI)		
	6 M	12 M	18 M
Y-90 + Chemo (N=215)	70.7 (63.6, 76.6)	29.8 (22.4, 37.6)	19.8 (13.0, 27.6)
Chemo (N=213)	55.2 (47.1, 62.7)	13.5 (7.7, 20.9)	1.9 (0.2, 8.3)

Y-90 + Chemo: median 9.1 M (95% CI: 7.8, 9.7)
Chemo: median 7.2 M (95% CI: 5.7, 7.6)
HR: 0.59 (0.46, 0.77); p<0.0001

Kaplan-Meier for PFS according to RECIST 1.1 by BICR
Log rank, one-sided p. Success criteria for the study were met (both PFS and hPFS p-values ≤0.00248)
Patient who received subsequent mCRC therapy prior to their last tumor assessment or PD or death were censored at their last tumor assessment prior to subsequent mCRC therapy.
Patients who had PD or death immediately after ≥2 missed visits were censored at the last tumor assessment prior to the 2 missed visits.

KEY DATA

EPOCH Clinical Trial

Treatment Effect on PFS and hPFS in Patient Subgroups

Key characteristics of interest associated with a PFS benefit with Y-90 + chemotherapy:

- Tumors with KRAS mutation
- Hepatic tumor burden ≥10% to <25%
- < 3 lesions
- Left-sided primary tumor
- Addition of a biologic agent

Key characteristics of interest associated with a hPFS benefit with Y-90 + chemotherapy:

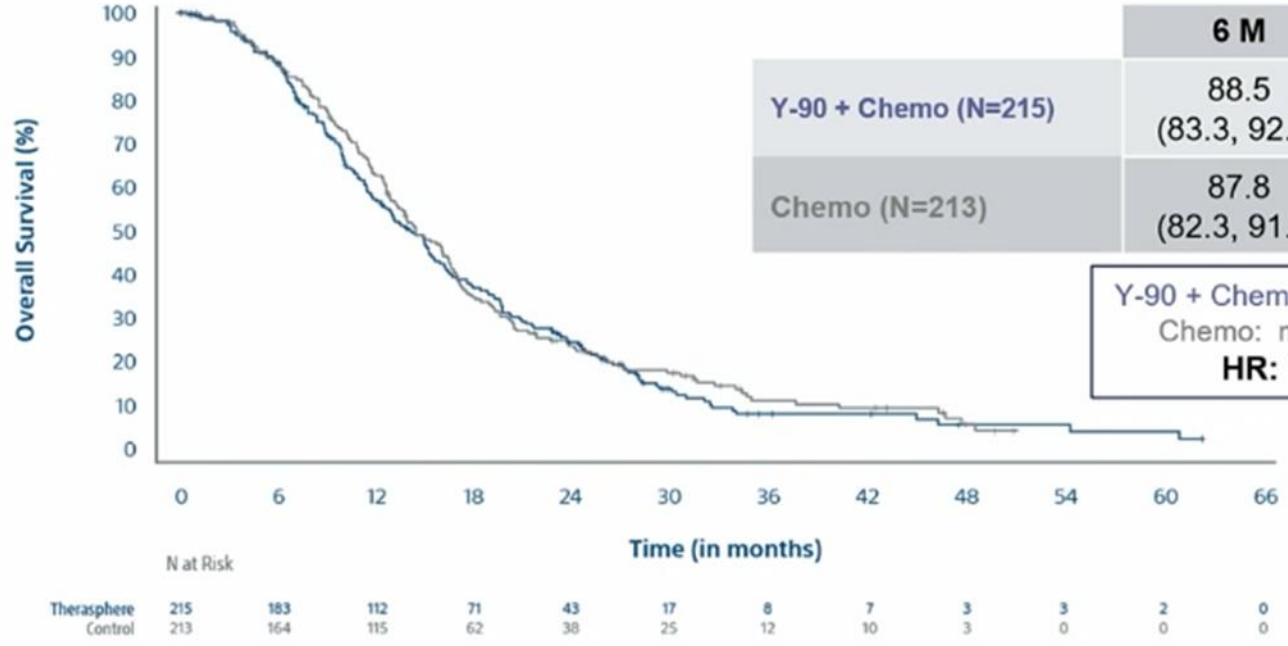
- Tumors with KRAS mutation
- Hepatic tumor burden <25%
- < 3 lesions
- Left- or right-sided primary tumor
- Addition of a biologic agent

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA21).

KEY DATA

EPOCH Clinical Trial

Overall Survival



	% Overall Survival (95% CI)		
	6 M	12 M	18 M
Y-90 + Chemo (N=215)	88.5 (83.3, 92.1)	56.3 (49.2, 62.8)	36.4 (29.7, 43.1)
Chemo (N=213)	87.8 (82.3, 91.7)	62.4 (55.0, 68.9)	34.3 (27.5, 41.2)

Y-90 + Chemo: median 14.0 M (95% CI: 11.8, 15.5)
Chemo: median 14.4 M (95% CI: 12.8, 16.4)
HR: 1.07 (0.86, 1.32); p=0.7229

Kaplan-Meier for overall survival. For each patient not known to have died, overall survival is censored at the time of last date known to be alive.
Log-rank, one sided p.

KEY DATA

EPOCH Clinical Trial

Response Rate

Response*	Y-90 + Chemo (N=215)	Chemo (N=213)
Overall response Rate		
(CR + PR), n (%) 95% CI	73 (34.0%) (28.0%, 40.5%)	45 (21.1%) (16.2%, 27.1%)
Best Response (n, %)		
Complete response	2 (0.9%)	3 (1.4%)
Partial Response	71 (33.0%)	42 (19.7%)
Stable Disease	98 (45.6%)	110 (51.6%)
Progressive Disease	27 (12.6%)	27 (12.7%)

*By RECIST 1.1

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA21).

KEY DATA

EPOCH Clinical Trial

Treatment-Emergent Adverse Events

	Y-90 + Chemo (N=187)	Chemo (N=207)
Any TEAEs (n, %)	181 (96.8%)	194 (93.7%)
Chemotherapy-Related TEAEs	172 (92.0%)	189 (91.3%)
Adverse Device Events (ADEs)	103 (55.1%)	0
Angiographic Procedure-Related TEAEs	55 (29.4%)	2 (1.0%)
TEAEs with CTCAE ≥ Grade 3	128 (68.4%)	102 (49.3%)
Serious TEAEs	70 (37.4%)	43 (20.8%)
Serious Treatment Emergent ADEs	20 (10.7%)	0
TEAEs Leading to Fatal Outcome	8 (4.3%)	4 (1.9%)
TEAEs Requiring Discontinuation of Chemotherapy	24 (12.8%)	25 (12.1%)

TEAEs collected until disease progression by investigator assessment or 30 days after discontinuation of study therapy, whichever came first.
Safety population based on treatment received.
TEAEs are adverse events which were not present at the initiation of chemotherapy or angiogram or worsened in severity following the first dose of chemotherapy or date of angiogram.

SUMMARY

EPOCH Clinical Trial

- Addition of Y-90 TARE to chemotherapy increased PFS from 7.2 moths to 8.0 months and hPFS from 7.2 to 9.1 months
  - PFS: HR 0.69, 1-sided p=0.0013; hPFS: HR 0.59, 1-sided p<0.0001
- No significant differences were noted in OS
- Overall response rate was nominally better in the Y-90 arm compared to the chemotherapy alone arm
- There were no new, unexpected safety signals
  - Chemotherapy-related adverse events were comparable between groups
- Y-90 did not compromise ability to receive additional chemotherapy

EPOCH Clinical Trial

The addition of Y-90 TARE to chemotherapy improved PFS and hPFS outcomes in the 2L setting for patients with colorectal liver metastases

2021 ESMO Key Studies

Breast Cancer

- DESTINY-Breast03*
- TULIP
- KEYNOTE-522^
- KEYNOTE-355

Lung Cancer

- BEVERLY
- CHRYSALIS
- CHRYSALIS-2

GU/GI Cancer

- KRYSTAL-1**
- EPOCH
- PEACE-1**

*2021 ESMO Presidential Symposium 1 and **2021 ESMO Presidential Symposium 2
^2021 ESMO Virtual Plenary Debate Session

cornerstone specialty network™

CLINICAL QUESTION

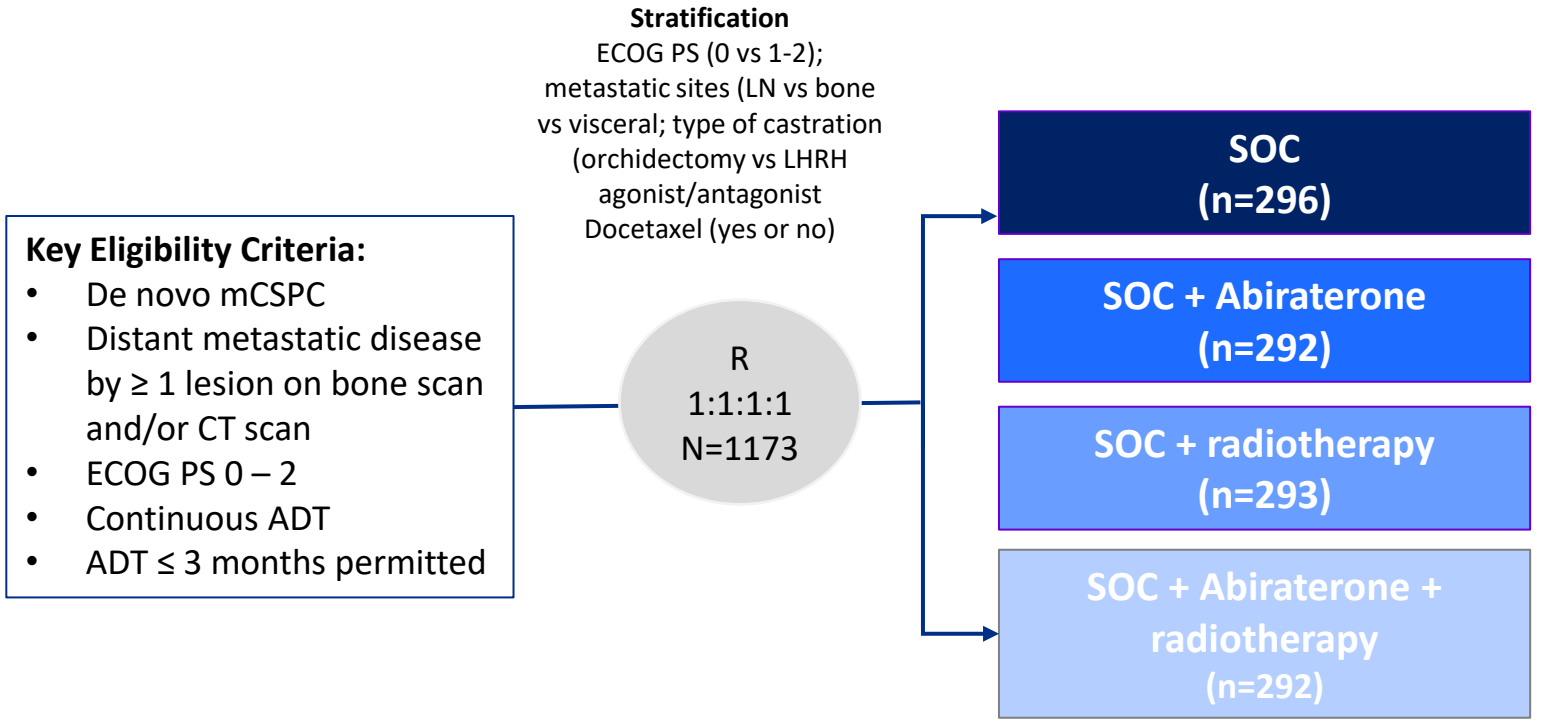
PEACE-1 Clinical Trial

Does the addition of abiraterone acetate plus prednisone improve survival in patients with *de novo* metastatic castration-sensitive prostate cancer?

KEY DATA

PEACE-1 Clinical Trial

Study Design: Phase 3



Standard Treatments:

- ADT continuously (LHRH agonist/antagonist or bilateral orchiectomy)
- +/- Docetaxel 75 mg/m^2/3w x 6 (G-CSF recommended)

Experimental Treatments:

- Abiraterone 1000 mg/d + prednisone 5 mg x 2/d until disease progression or intolerance (concomitant to docetaxel)
- Radiotherapy (RXT) of the prostate 74 Gy in 37 fractions (after docetaxel is completed)

Primary Endpoints: PFS and hepatic PFS (hPFS) by BICR
Secondary Endpoints: OS, TTSP, ORR by BICR, DCR by BICR, TTDQoL

TARE with Y90 glass microspheres (TheraSphere, Boston Scientific Corporation)
Cycle 1 = chemotherapy, T-90 TARE replace Cycle 2, Cycle 3 resume chemotherapy ± targeted therapy (VEGF or EGFR inhibitors)

KEY DATA

PEACE-1 Clinical Trial

Patient Characteristics (ADT + docetaxel population)

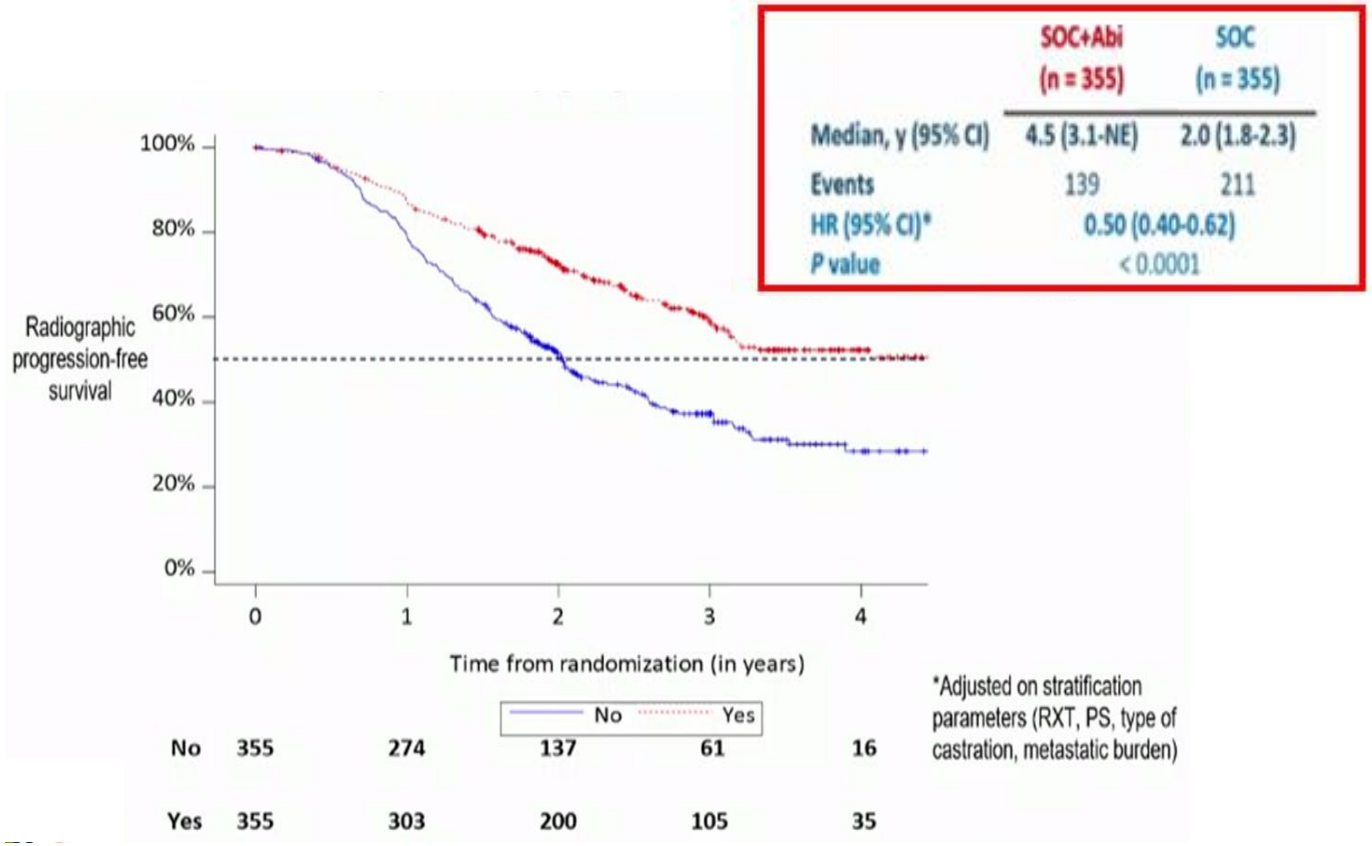
	SOC (+/- RXT) + Abiraterone (n=355)	SOC (+/- RXT) (n=355)
Median age, y (IQR)	66 (60-70)	66 (59-70)
ECOG PS score, n (%)		
0	250 (70)	246 (69)
1-2	105 (30)	109 (31)
Gleason score at initial diagnosis, n (%)		
≤7	79 (23)	71 (21)
≥8	270 (77)	276 (79)
Median time from diagnosis, m (IQR)	2.2 (1.6 – 3.0)	2.2 (1.4 – 2.9)
Metastatic sites, n (%)		
Lymph nodes only	27 (8)	29 (8)
Bone without visceral	287 (81)	279 (79)
Visceral	41 (12)	47 (13)
Disease burden, n (%)		
Low	131 (37)	123 (35)
High	224 (63)	232 (65)
Median baseline PSA, ng/mL (IQR)	13.7 (2.4 – 58.9)	12.0 (3.0 – 59.9)
Docetaxel, n (%)	355 (100)	355 (100)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA5).

KEY DATA

PEACE-1 Clinical Trial

rPFS with Abiraterone in the ADT + docetaxel (+/- RXT) population



	High volume metastatic burden		Low volume metastatic burden	
	SOC + Abi (n=255)	SOC (n=231)	SOC + Abi (n=129)	SOC (n=122)
Median, y (95%CI)	**4.1** (2.7 – NE)	**1.6** (1.4 – 2.0)	NE (3.1 – NE)	2.7 (2.5 – NE)
Events	97	156	41	55
HR (95% CI)*	**0.47** (0.36 – 0.60)		**0.58** (0.39 – 0.87)	
P value	< 0.0001		0.006	

*Adjusted on stratification parameters (RXT, PS, type of castration, metastatic burden

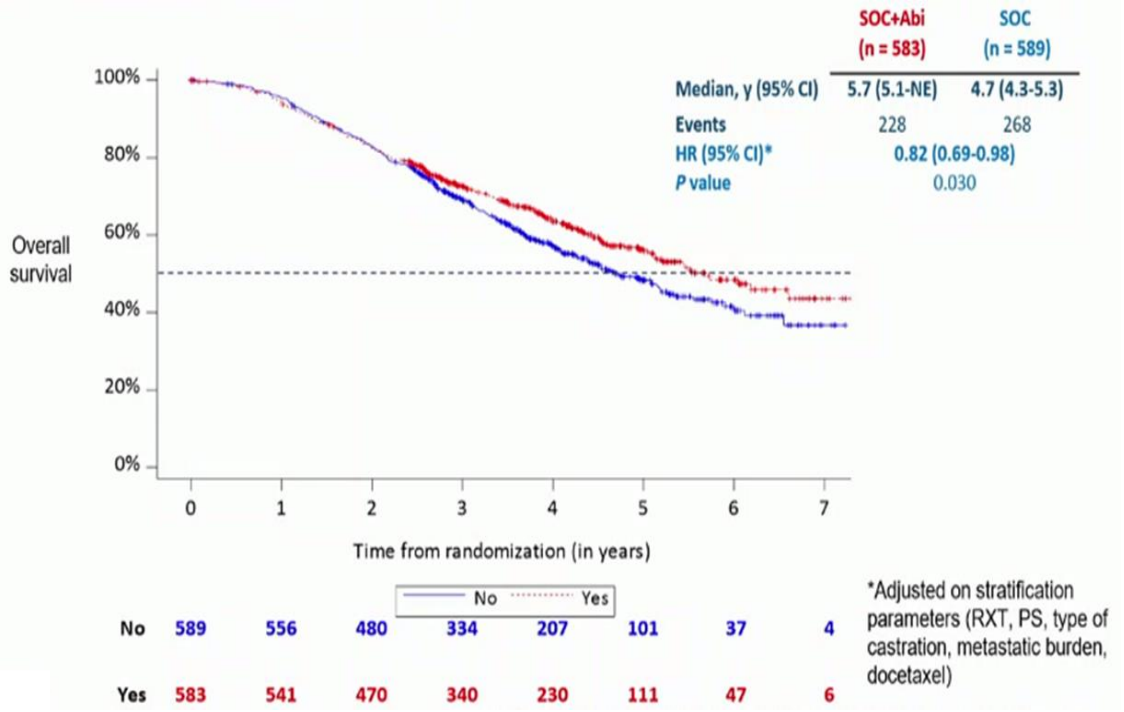
European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA5).

KEY DATA

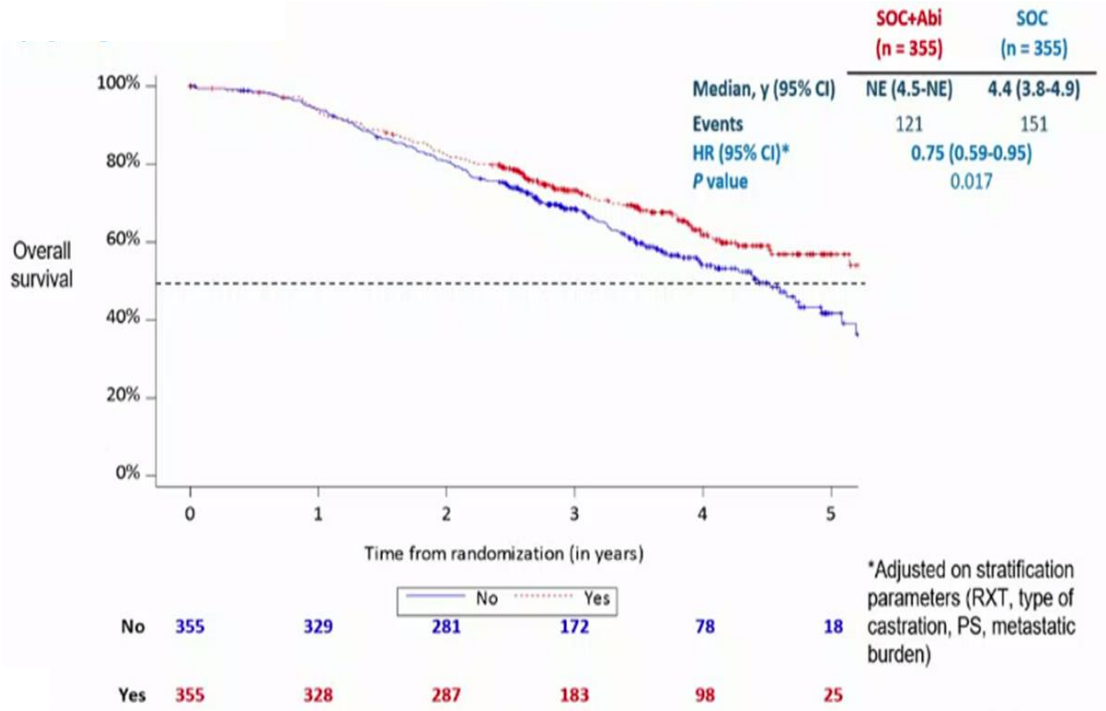
PEACE-1 Clinical Trial

Overall Survival

OS: Overall population



OS: With Abiraterone in the ADT + docetaxel (+/-RXT) population



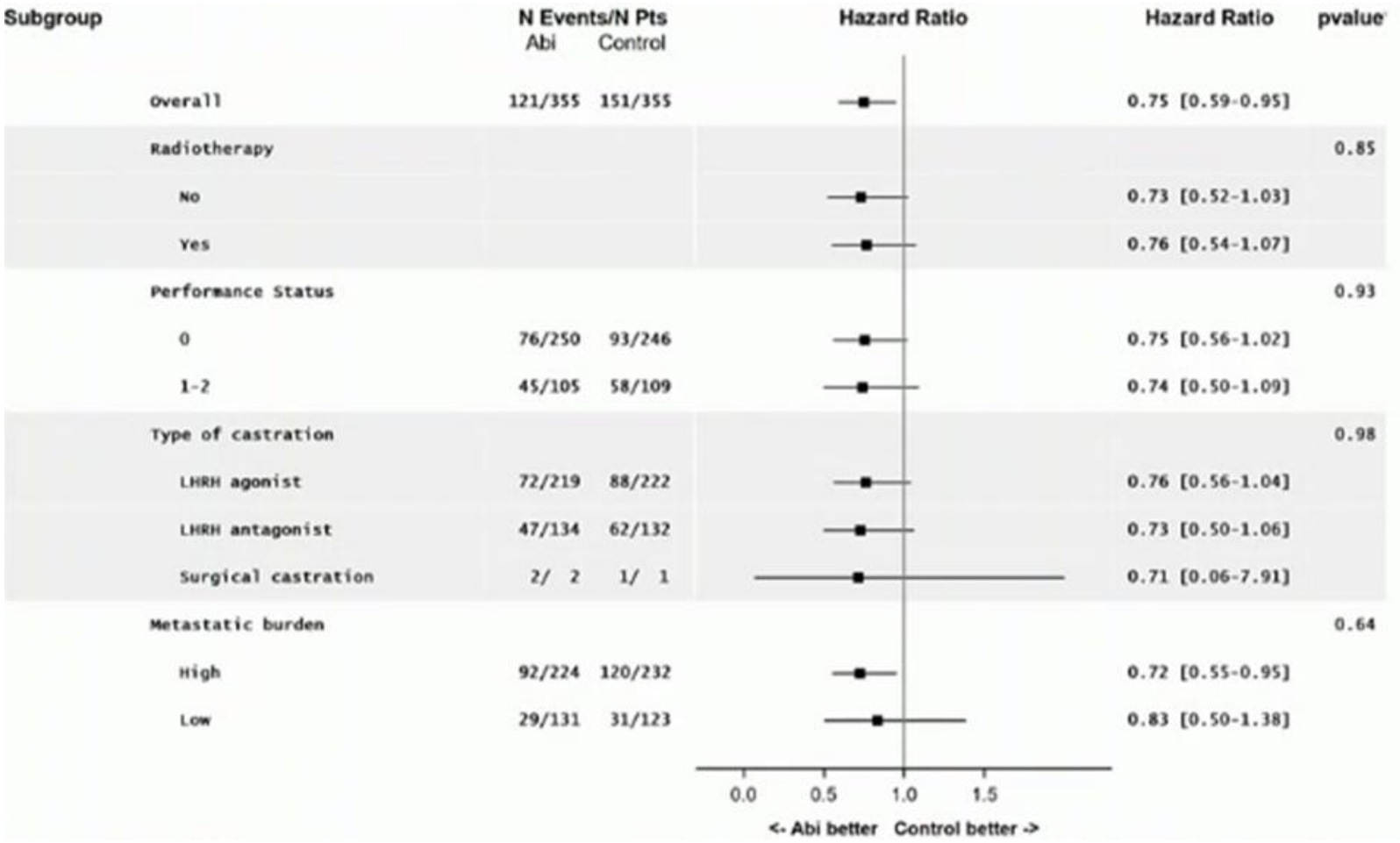
25% reduction in the risk of death

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA5).

KEY DATA

PEACE-1 Clinical Trial

Subgroup Analysis of Overall Survival



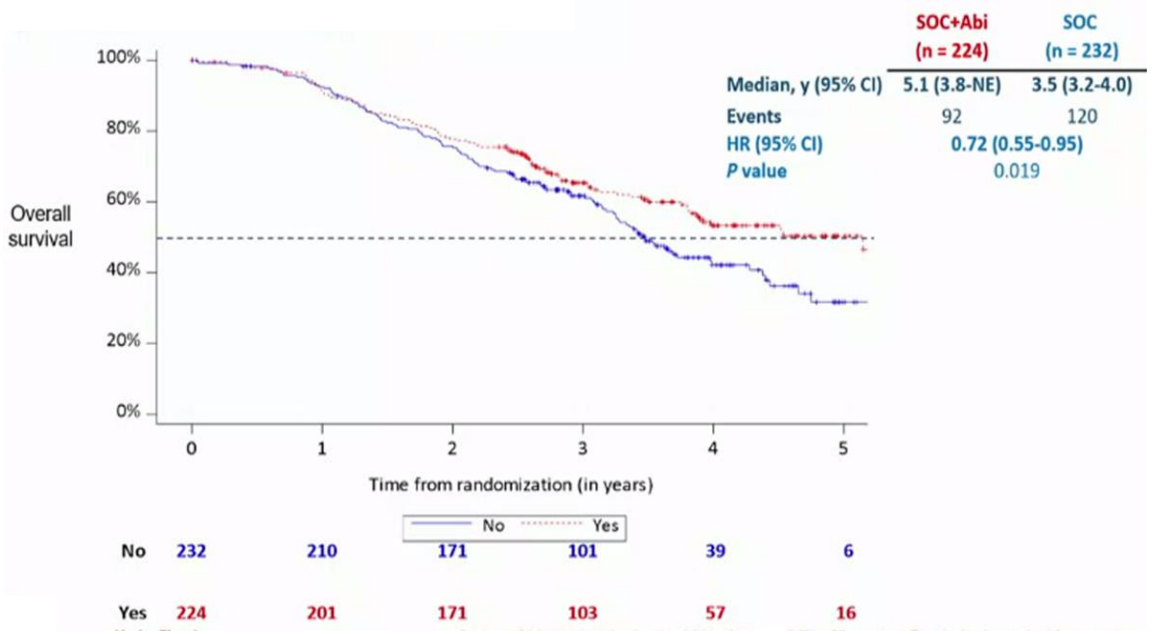
European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA5).

KEY DATA

PEACE-1 Clinical Trial

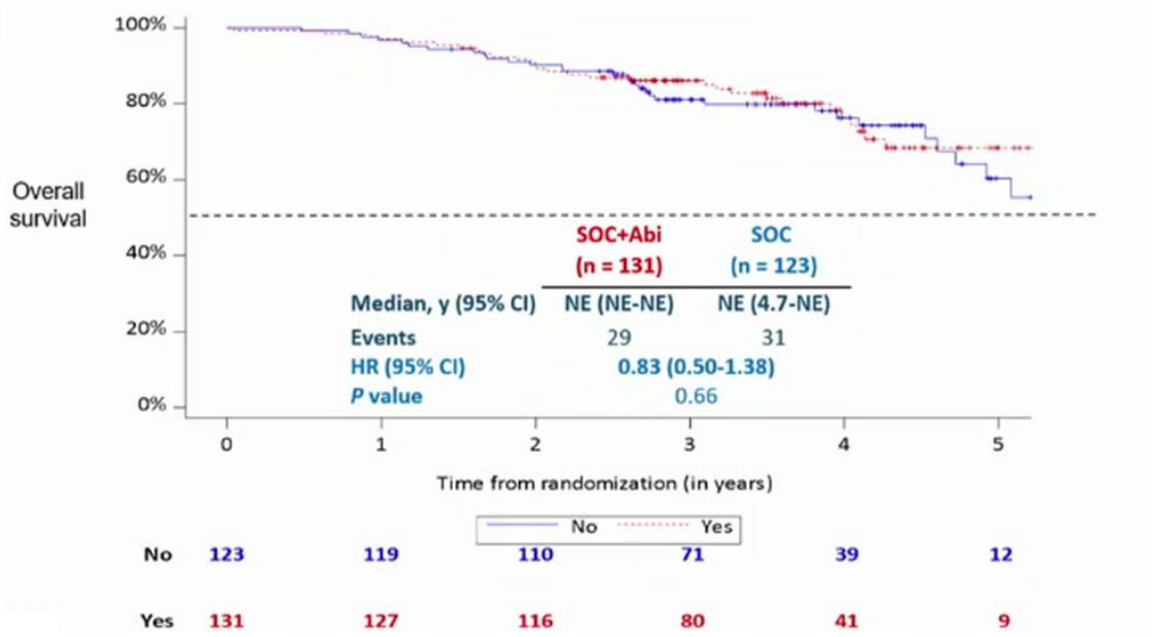
Overall Survival

OS with Abiraterone in the ADT + docetaxel (+/-RXT): High-volume patients



Benefit of more than 1.5 years

OS with Abiraterone in the ADT + docetaxel (+/-RXT) population: Low-volume patients



European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA5).

KEY DATA

PEACE-1 Clinical Trial

Treatments beyond progression: ADT + docetaxel population

At least one treatment, n (%)	SOC (+/- RXT) + Abiraterone n_{CRPC} = 141	SOC (+/- RXT) n_{CRPC} = 263
Life-prolonging treatment	104 (74)	221 (**84**)
Next generation HT	65 (46)	213 (**81**)
Abiraterone	22 (16)	153 (58)
Enzalutamide	57 (40)	119 (45)
Docetaxel	29 (21)	25 (10)
Cabazitaxel	84 (60	114 (43)
Radium 223	3 (2)	11 (4)
Lu-PSMA	2 (1)	3 (1)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA5).

KEY DATA

PEACE-1 Clinical Trial

Grade 3 – 5 Toxicity

Toxicity, n (%)	SOC (+/- RXT) + Abiraterone n_{CRPC}=141	SOC (+/- RXT) n_{CRPC}=263
Neutropenia	34 (10)	32 (9)
Febrile neutropenia	18 (5)	19 (5)
Liver	20 (6)	2 (1)
Hypertension	76 (22)	45 (13)
Hypokalemia	11 (3)	1 (0)
Cardiac	6 (2)	5 (1)
Fatigue	10 (3)	15 (4)
Gastro-intestinal	14 (4)	18 (5)
Grade 5	7 (2)	3 (1)

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA5).

SUMMARY

PEACE-1 Clinical Trial

- Addition of abiraterone to ADT + docetaxel significantly improved rPFS by 2.5 years in men with *de novo* metastatic prostate cancer
- Overall survival was improved with a 25% reduction in the risk of death
  - 84% of mCRPC patient in the control group received at least one life prolonging treatment
- Median lifetime gain of more than 1.5 years for men with high-volume metastases
  - OS data for low-volume metastases immature
- Toxicity was as expected with no apparent synergistic side effects from this combination

European Society for Medical Oncology (ESMO) Congress 2021 (Abstract #LBA5).

PEACE-1 Clinical Trial

The combination of ADT + docetaxel + abiraterone provides rPFS and OS benefit for men with de novo high-volume mCSPC and should be considered practice changing