Applications for Community Oncology

ASCO Data Review

July 17, 2025

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2025 ASCO Key Studies

Breast Cancer

- RAPID REVIEWS
  - *SERENA-6
  - DESTINY-Breast09
  - DESTINY-Breast06
  - AI for IHC HER2 Pathology
  - ASCENT-03
  - ASCENT-04
  - VERITAC-2
  - INAVO120
  - CompassHER2 pCR

GU/ GI Cancer

- *ATOMIC
- *MATTERHORN
- DESTINY-Gastric04
- ***RAPID REVIEWS***
  - BREAKWATER
  - PANOVA-3
  - AMPLITUDE

Other Notable Studies

- *NIVOPOSTOP
- KEYNOTE-689
- *VERIFY
- ***RAPID REVIEWS***
  - TROPION-Lung02
  - DELPHI-304
  - IMforte
  - TUXEDO-3
  - ROSELLA

* Plenary Session

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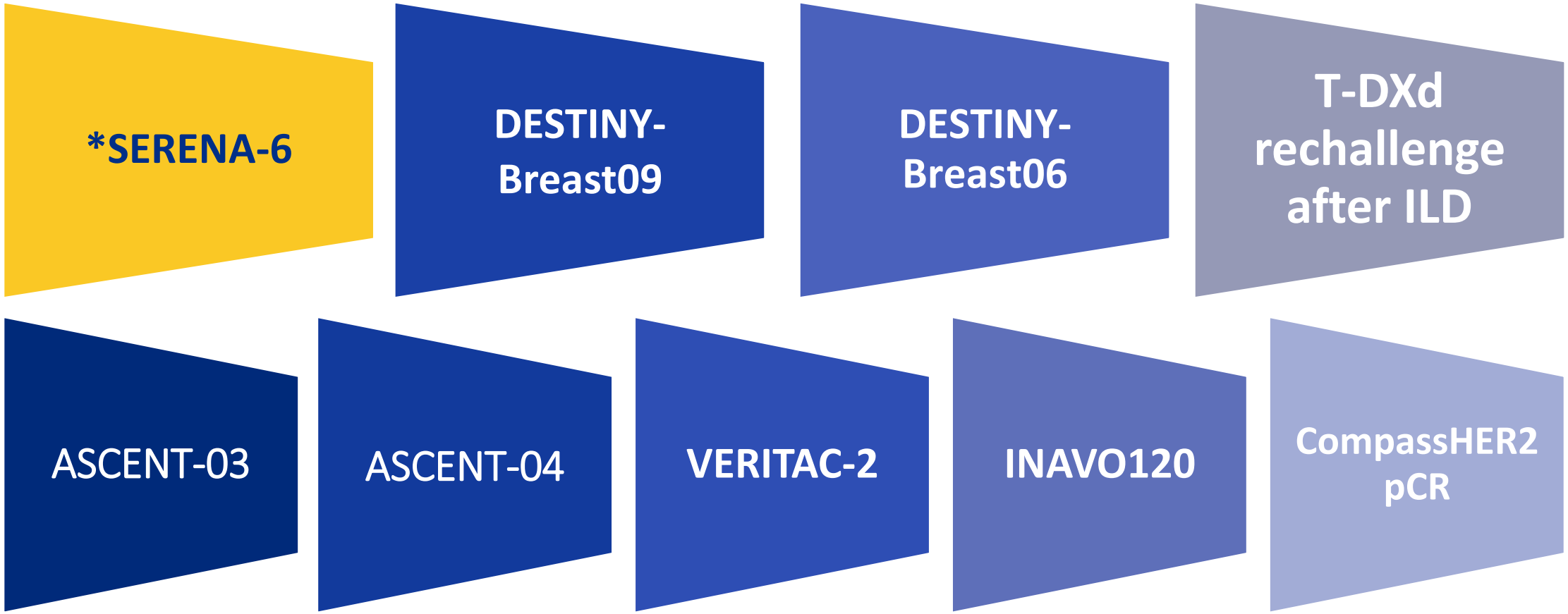
ASCO 2025: RAPID REVIEWS



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KEY DATA

SERENA-6: Camizestrant + CDK4/6i for emergent ESR1 mutations during 1L endocrine based therapy and before disease progression in HR+ HER2- mBC

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Study Design: Multicenter, randomized, double-blind phase III trial

Stratified by visceral disease (yes vs no); ESR1m detection (at first test vs later test); time since start of CDK4/6i + AI (<18 vs ≥18 mo); CDKi (palbociclib vs ribociclib vs abemaciclib)

- ER+/HER2- advanced breast cancer
- ≥6 mo of 1L AI + CDK4/6i (palbociclib, ribociclib, or abemaciclib)
- ctDNA-detected *ESR1*m
- **No evidence of disease progression**
- ECOG PS 0 -1

(N = 315*)

→ **Camizestrant** 75 mg QD + **Continued CDK4/6i** + AI placebo (n = 157)

→ **Continued AI** (anastrozole or letrozole) + **Continued CDK4/6i** + Camizestrant placebo (n = 158)

*Study population derived from 3256 patients screened for ESR1m during 1L AI + CDK4/6i.

Primary endpoint: PFS by investigator (RECIST v1.1)
Secondary endpoints: PFS2, OS, safety, PROs

Select Baseline Characteristics

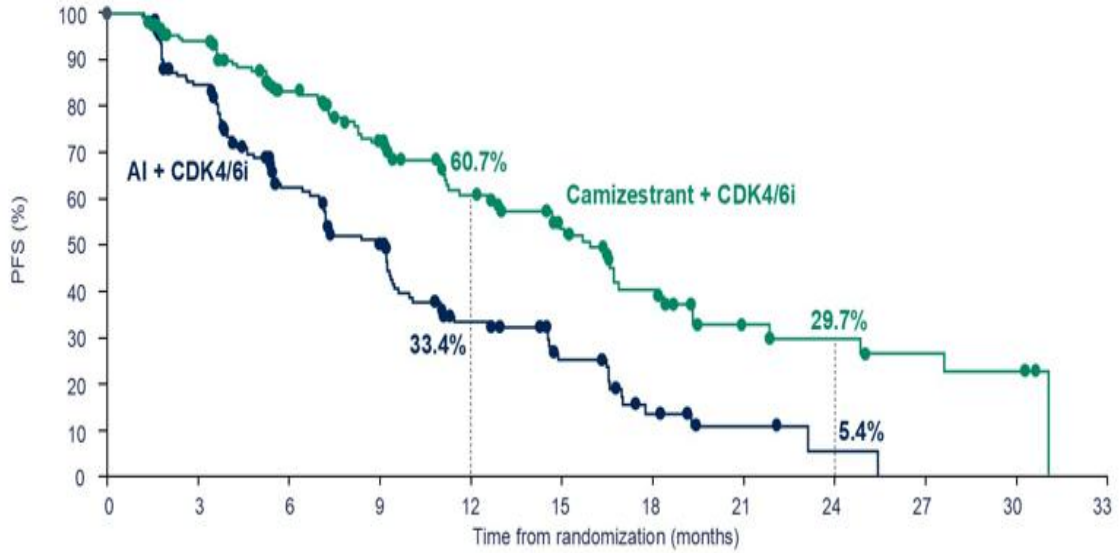
Characteristic	Cami + CDK4/6 (n = 157)	AI + CDK4/6i (n = 158)
Median age, yr (range)	61.0 (29-81)	60.5 (35-89)
Visceral metastasis, n (%)	66 (42)	71 (45)
Time since start of AI + CDK4/6i		
• ≥18 mo, n (%)	97 (62)	100 (63)
• <18 mo, n (%)	60 (48)	58 (37)
• Median, mo (range)	23 (7-96)	23 (6-96)
Time of ESR1m detection		
• At first test, n (%)	84 (54)	84 (53)
• At subsequent test,* n (%)	73 (47)	74 (47)
• Median, mo (range)	22 (4-95)	22 (6-96)
Most common ESR1m, n (%)		
• D538G	70 (45)	82 (52)
• Y537S	61 (39)	60 (38)
• Y537N	29 (19)	25 (16)
CDK4/6i continued at randomization, n (%)		
• Palbociclib	119 (76)	119 (75)
• Ribociclib	24 (15)	23 (15)
• Abemaciclib	14 (9)	16 (10)

*Subsequent tests performed every 2-3 mo after first test.

KEY DATA

SERENA-6: Camizestrant + CDK4/6i for emergent ESR1 mutations during 1L endocrine based therapy and before disease progression in HR+ HER2- mBC

Primary Endpoint: Progression-Free Survival

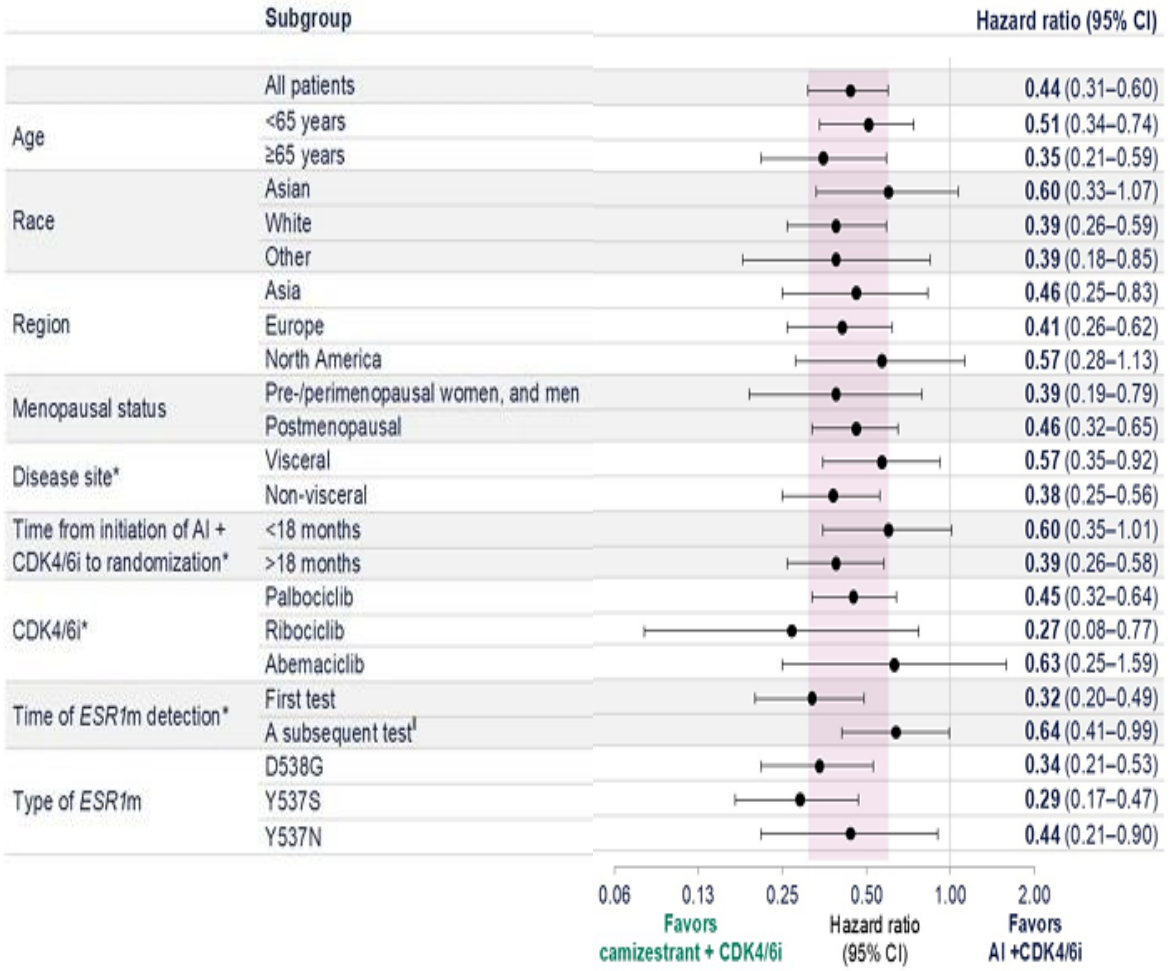


Number of patients at risk

Camizestrant + CDK4/6i	157	138	105	82	55	41	26	11	9	7	6	0
AI + CDK4/6i	158	124	73	55	29	17	7	3	1	0	0	0

Outcome	Cami + CDK4/6i (n = 157)	AI + CDK4/6i (n = 158)
PFS events	71	100
Median PFS, mo (95% CI)	**16.0** (12.7-18.2)	9.2 (7.2-9.5)
Adjusted hazard ratio (95% CI)	**0.44** (0.31-0.60); P <.00001	

Progression-Free Survival by Subgroup



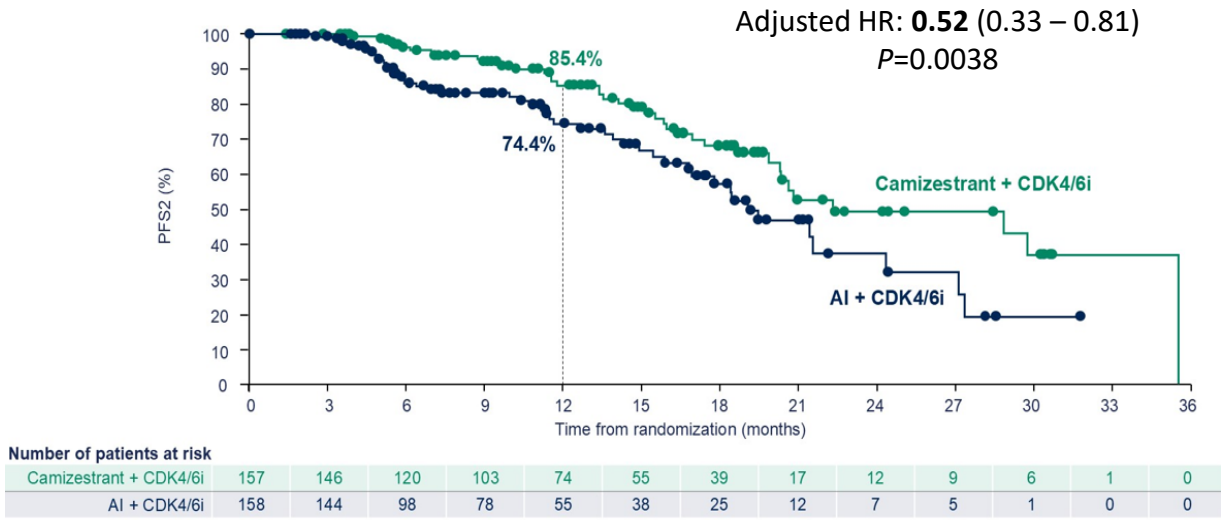
ASCO 2025 Abstr. LBA4; Bidard NEJM June 1, 2025 epub

KEY DATA

SERENA-6: Camizestrant + CDK4/6i for emergent ESR1 mutations during 1L endocrine based therapy and before disease progression in HR+ HER2- mBC

Secondary Endpoints

Second progression-free survival (PFS2)



Time to deterioration in global health status/quality of life (EORTC QLQ-C30)

	Cami + CDK4/6i (n = 157)	AI + CDK4/6i (n = 158)	Adjusted HR (95% CI)
Median TTD in global health status/QoL, mo (95% CI)	(n = 107) 23.0 (13.8-NE)	(n = 95) 6.4 (2.8-14.0)	**0.53** (0.33-0.82) P <.001

Safety

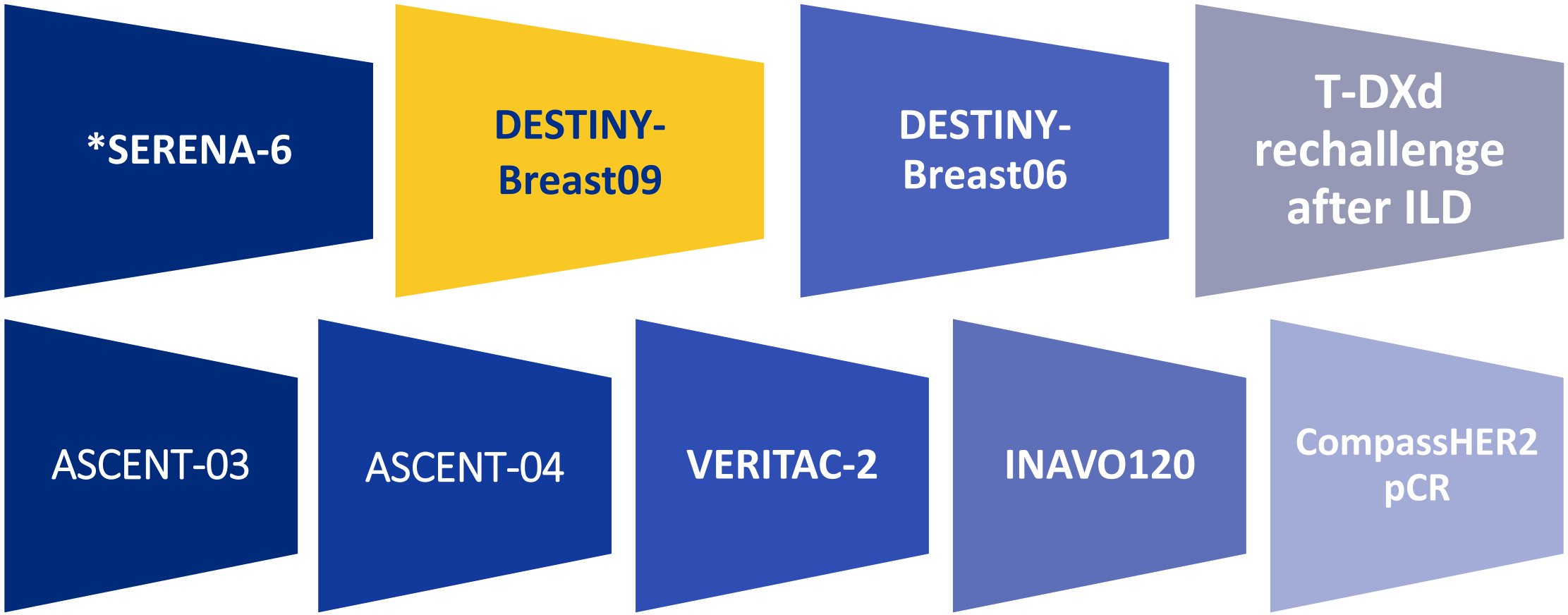
Outcome	Cami + CDK4/6i (n = 155)	AI + CDK4/6i (n = 155)
Any AE, n (%)	145 (94)	135 (87)
• Grade ≥3	93 (60)	71 (46)
Any Serious AE, n (%)	16 (10)	19 (12)
Any AE leading to discontinuation, n (%)		
• Camizestrant/AI	2 (1)	3 (2)
• CDK4/6i	2 (1)	2 (1)
• Both camizestrant/AI and CDK4/6i	1 (1)	2 (1)
Median treatment exposure, mo		
• Camizestrant/AI	10.1	6.3
• CDK4/6i	9.8	6.1
Mean relative dose intensity, %		
• Camizestrant/AI	99.6	99.7
• CDK4/6i	98.8	99.5

- Incidence rates of neutropenia were similar between treatment arms when adjusted for exposure time

Switching to camizestrant with continuation of CDK4/6i guided by ctDNA improves PFS and should be a new treatment strategy…not yet FDA approved

ASCO 2025 Abstr. LBA4; Bidard NEJM June 1, 2025 epub

ASCO 2025: RAPID REVIEWS



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KEY DATA

DESTINY-Breast09: Phase 3 T-DXd ± Pertuzumab vs Pertuzumab + Trastuzumab + Taxane in HER2+ mBC (Interim analysis)

Study Design: global, randomized phase 3 study

- HER2+* (IHC3+ or ISH+) advanced or mBC
- No previous chemo or HER2-targeted therapy for advanced or metastatic disease
- Previous chemo/HER2-targeted therapy allowed in neoadjuvant setting if >6 mo from metastatic disease diagnosis
- One prior line of ET for mBC permitted
- Asymptomatic/inactive brain mets allowed
- ECOG PS 0/1

(N = 1157)

Stratified by de novo vs recurrent mBC
HR+ or HR-; PIK3CAm detected vs non-detected

T-DXd 5.4 mg/kg q3w
(Blinded until final PFS analysis)
(n=387)

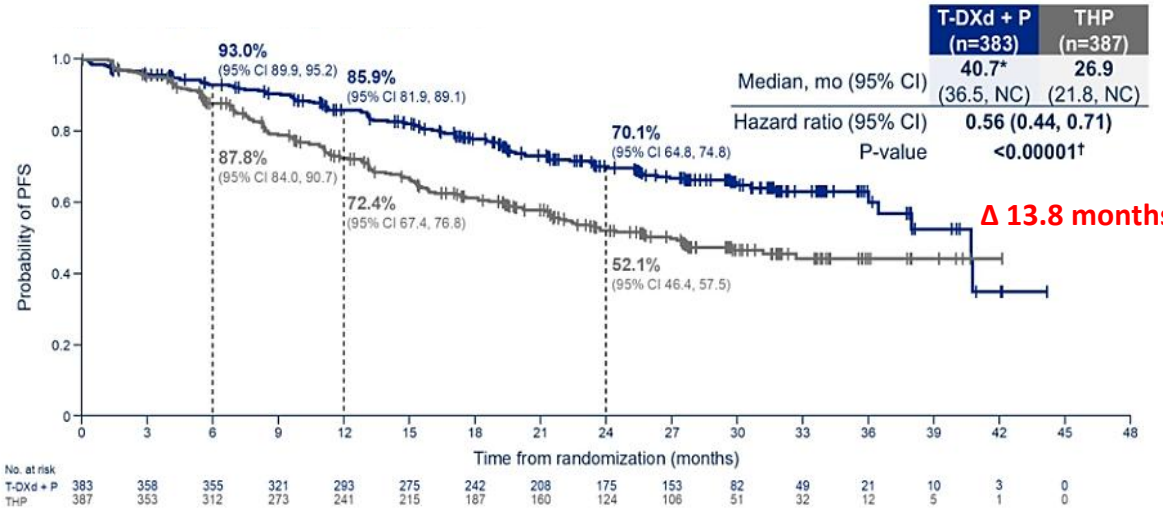
T-DXd 5.4 mg/kg q3w **+ Pertuzumab (n=383)**

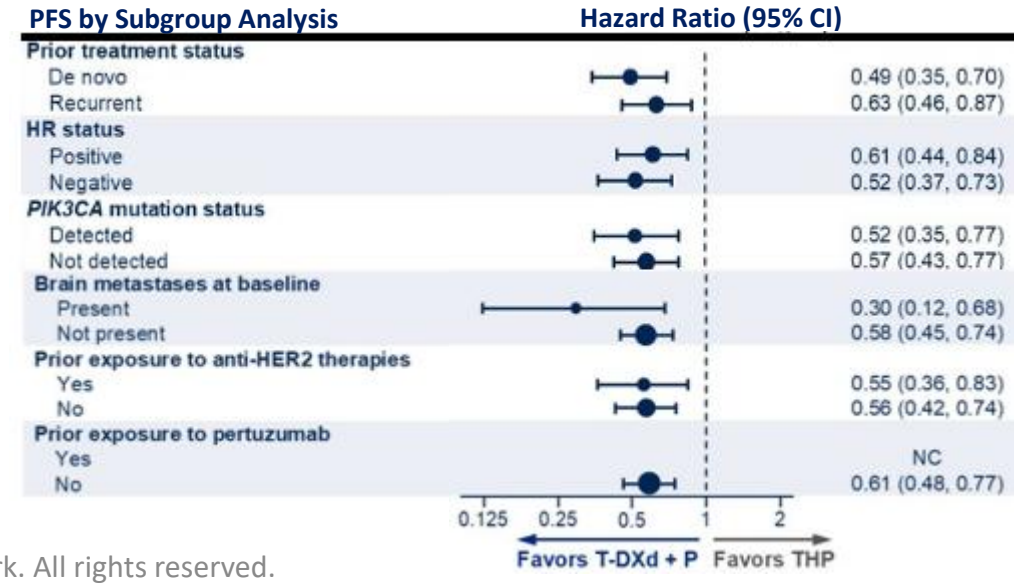
Taxane + Pertuzumab + Trastuzumab (TCP)†ǂ (n=387)

*Locally assessed and prospectively centrally confirmed.
†Investigator's choice: docetaxel or paclitaxel IV.
Concurrent use of ET (AI or tamoxifen) was allowed for those with HR positive disease after six cycles of T-DXd or discontinuation of taxane in the THP arm
Note: ~50% had *de novo* metastatic disease in each arm

Primary endpoint: PFS by BICR (per RECIST 1.1) up to 5 yr
Secondary endpoints: PFS by investigator, OS, ORR (BICR and investigator), DoR (BICR and investigator), PFS2, safety

Primary Endpoint: PFS by BICR





KEY DATA

DESTINY-Breast09: Phase 3 T-DXd ± Pertuzumab vs Pertuzumab + Trastuzumab + Taxane in HER2+ mBC (Interim analysis)

Secondary Endpoint: confirmed ORR

Median duration of response:
- T-DXd + P: **39.2** mo
- THP: 26.4 mo

Remaining in Response at 24-mo:
- T-DXd + P: **73.3%**
- THP: 54.9%

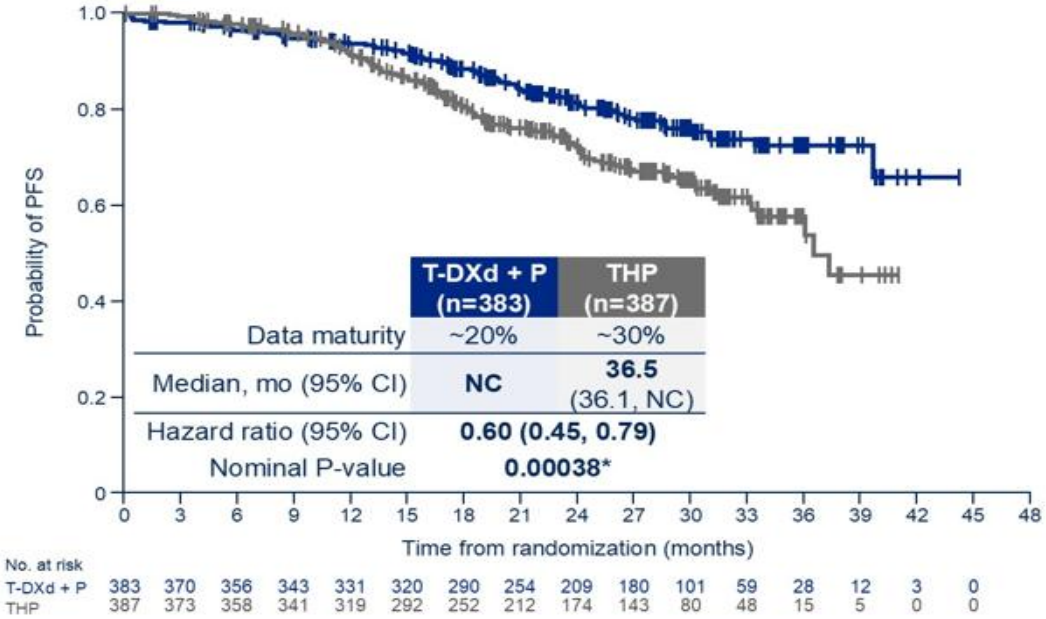
Stable disease:
- T-DXd + P: **9.9%**
- THP: 14.5%

Median total treatment duration:
- T-DXd + P: **21.7 mo** (range .3 to 44.5)
- THP: 16.9 mo (range 0.7 to 41.7)

Median treatment duration for taxanes:
- Docetaxel: 5.5 mo (range .7 to 37.4); median 8 cycles
- Paclitaxel: 4.4 mo (range 0.2 to 3.7); median 6 cycles

Note Secondary Endpoint: OS *- Immature, trend favoring T-DXD + P*

Secondary Endpoint: PFS2



PFS2 defined as the time from randomization to second progression (earliest progression event following first subsequent therapy) or death. Patients may have received more than one type of therapy; patients may have received trastuzumab and pertuzumab concurrently.

32.4% of patients in the T-DXd + P arm and 46.8% of patients in the THP arm proceeded to receive 2L therapy after treatment discontinuation
- Received HER2-directed therapies: 111 (29%) on T-DXd + P arm vs 166 (42.9%) on THP arm
- Received chemotherapy: 68 (17.8%) on T-DXd + P arm vs 57 (14.7%) on THP arm
- Received endocrine therapy: 19 (5%) on T-DXd + P arm vs 13 (3.4%) on THP arm

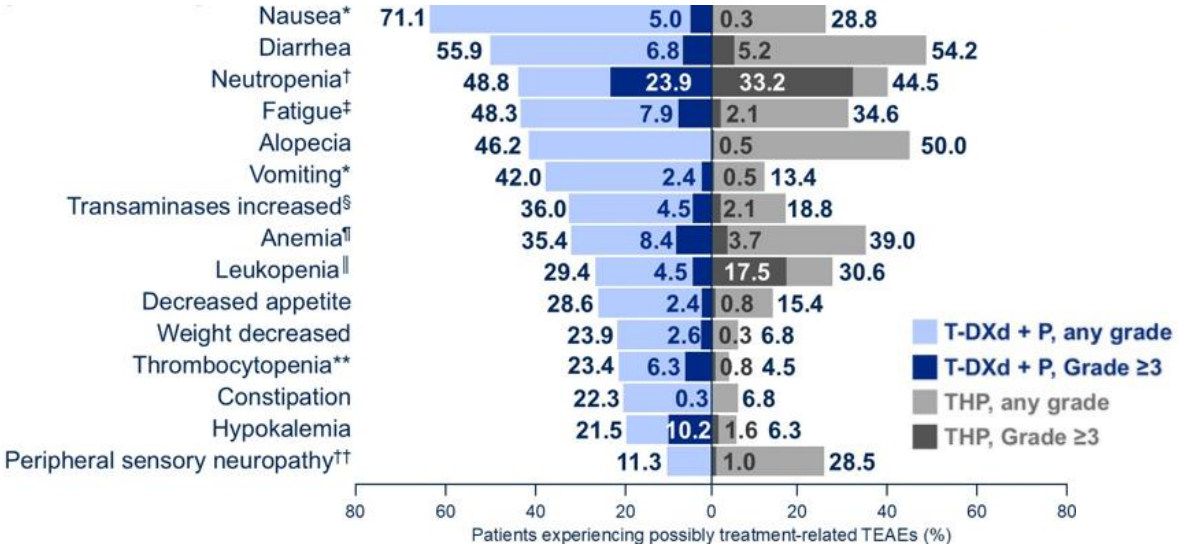
KEY DATA

DESTINY-Breast09: Phase 3 T-DXd ± Pertuzumab vs Pertuzumab + Trastuzumab + Taxane in HER2+ mBC (Interim analysis)

Safety

Safety Summary	T-DXd + P (n = 381)	THP (n = 382)
Total exposure, patient-yr	659.7	564.0
Any TEAE, n (%)	380 (99.7)	378 (99.0)
Possible TEAE (by INV), n (%) • Grade ≥3	373 (97.9) 209 (54.9)	369 (96.6) 200 (52.4)
Serious TEAE, n (%)	103 (27.0)	96 (25.1)
TEAE management/outcomes, n (%) • Treatment discontinuation • Dose interruptioduction • Death – Possible TRAE (by INV)*	 79 (20.7) 262 (68.8) 175 (45.9) 13 (3.4) 5 (1.3)	 108 (28.3) 187 (49.0) 76 (19.9) 3 (0.8) 1 (0.3)

The combination of T-DXD plus pertuzumab has the potential to be a new first-line standard of care for patients with HER2+ mBC… not yet FDA approved…



Event	T-DXd + P (n = 381)	THP (n = 382)
Adjudicated drug related ILD/pneumonitis, any	12.1%	1%
• Grade 1	4.5%	2%
• Grade 2	7.1%	0.5%
• Grade 3	---	---
• Grade 4	---	---
• Grade 5	0.5%	---
Left ventricular dysfunction, any	11%	7.1%
• Grade 1	1%	0.3%
• Grade 2	7.9%	5.0%
• Grade 3	1.8%	1.8%
• Grade 4	0.3%	---
• Grade 5	---	---

ASCO 2025 Abstr. 1008

CLEOPATRA THP		PATINA TH±P → Palbo + anti-HER2 + ET		DESTINY-Breast09 T-DXd + Pertuzumab	
Current Approved SoC		***Not yet FDA approved***			
• **No prior chemotherapy or biological treatment for metastatic disease**		• **6-8 cycles of treatment including trastuzumab with or without pertuzumab and taxane/vinorelbine** • **Completion of induction chemotherapy and no evidence of disease progression (CR, PR, or SD)**		• **No previous chemo or HER2-targeted therapy for advanced or metastatic disease** • **Previous chemo/HER2-targeted therapy allowed in neoadjuvant setting if >6 mo from metastatic disease diagnosis** • **One prior line of ET for mBC permitted**	
Pertuzumab + trastuzumab + docetaxel (n=402)	Placebo + trastuzumab + docetaxel (n=406)	**Palbociclib** + trastuzumab ± pertuzumab + endocrine therapy (n=261)	Placebo + trastuzumab ± pertuzumab + endocrine therapy (n=261)	**T-DXd** + pertuzumab (n=383)	Taxane + pertuzumab + trastuzumab (TCP)† (n=387)
Medium follow-up: 99.9 months	98.7 months	Medium follow-up: **52 months**		Medium follow-up: **29.2 months**	
mPFS: **18.7**	12.4 months	**mPFS: 44.3**	29.1 months	**mPFS: 40.7**	26.9 months
8-year landmark PFS rates: **16%** vs 10%		**HR: 0.74** (0.58 – 0.94); P = 0.0074		**HR: 0.56** (0.44 – 0.71); P = 0.00001	
mOS: **57.1**	40.8 months	*Not evaluable* (*OS immature*)	77 months	*Not calculable*	*Not calculable*
8-year landmark OS rate: **37%** vs 23%		**3-year OS rate: 87.0%** vs 84.7 %		HR 0.84 (*OS immature*)	

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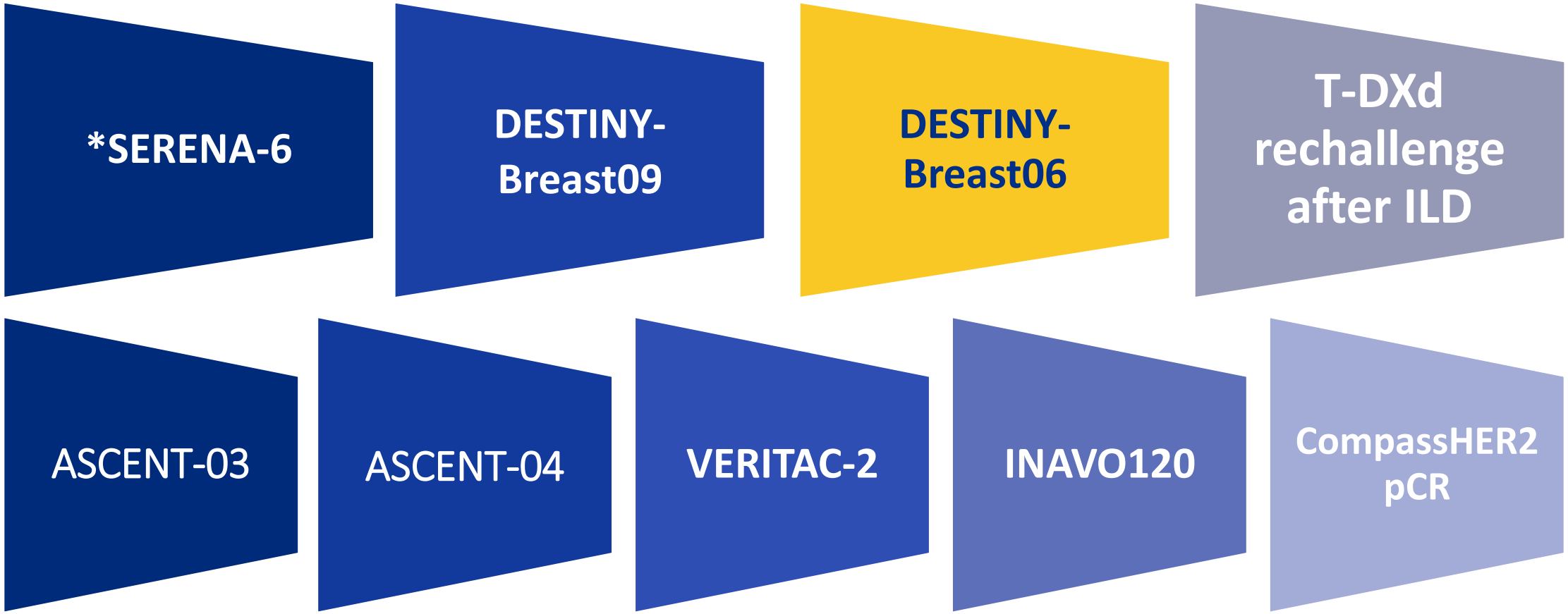

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KEY DATA

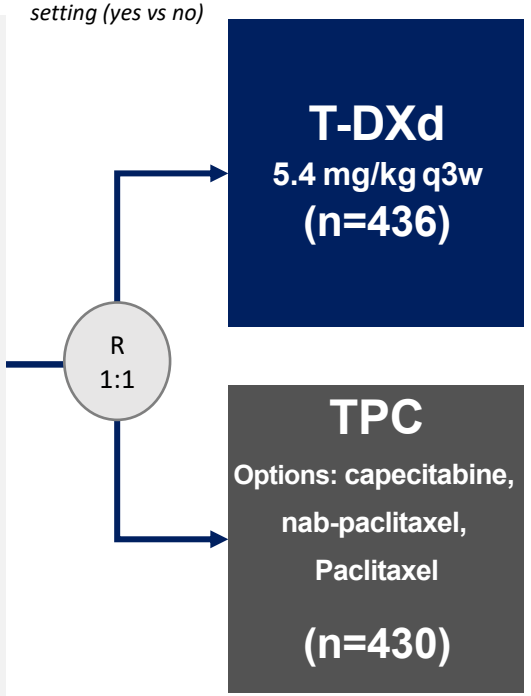
DESTINY-Breast06: Exploratory biomarker analysis of trastuzumab deruxtecan (T-DXd) vs TPC in HER2-low or ultralow HR+ mBC

Study Design: randomized, multicenter, open-label Phase 3 study

Stratified by Prior CDK4/6i use (yes vs no); HER2 expression (IHC 1+ vs IHC 2+/ISH− vs IHC 0 with membrane staining); Prior taxane in the non-metastatic setting (yes vs no)

- HR+ mBC
- HER2-low (IHC 1+ or IHC 2+/ISH−) or HER2-ultralow (IHC 0 with membrane staining)*
- **Chemotherapy naïve in the mBC setting**
- **Prior lines of therapy:**
  - ≥2 lines of ET ± targeted therapy for mBC **OR**
  - 1 line for mBC **AND** progression ≤6 months of starting first-line ET + CDK4/6i **OR**
  - Recurrence ≤24 months of starting adjuvant ET

(HER2-Low = 713; HER2-ultralow = 153)



Primary endpoints: PFS (BICR) in HER2-low
Key secondary endpoints: PFS (BICR) in ITT (HER2-low + ultralow); OS in HER2-low; OS in ITT (HER2-low + ultralow); PFS2 (investigator): second progression-free survival / time from randomization to second progression or death
Exploratory Endpoint: Biomarkers

- Blood samples at baseline, ctDNA via GuardantOMNI™
- Biomarker evaluable population:
  - *PIK3CA*, *AKT1*, *ESR1* and *BRCA1/2* mutations investigated
    - PI3K/AKT pathway mutation in 45% of patients
    - ESRI mutation in 51.5% of patients
    - BRCA1/2 in 7.7% of patients

Clinical outcomes in biomarker-evaluable and ITT populations

Overall	Biomarker-evaluable population (n=625)		ITT population (N=866)	
	T-DXd (n=318)	TPC (n=307)	T-DXd (n=436)	TPC (n=430)
mPFS, mos (95% CI)	13.9 (12.3 – 15.4)	8.2 (6.9 – 9.5)	13.2 (12.0 – 15.2)	8.1 (7.0 – 9.0)
HR (95% CI)	**0.63** (0.52 – 0.76)		**0.64** (0.54 – 0.76)	
Confirmed ORR, % (95% CI)	59.4 (53.8 – 64.9)	33.9 (28.6 – 39.5)	57.3 (52.5 – 62.0)	31.2 (26.8 – 35.8)

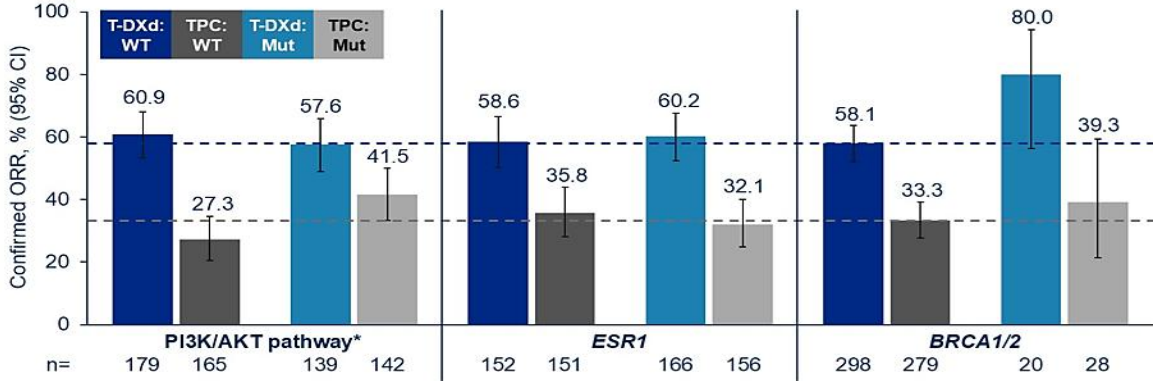
KEY DATA

DESTINY-Breast06: Exploratory biomarker analysis of trastuzumab deruxtecan (T-DXd) vs TPC in HER2-low or ultralow HR+ mBC

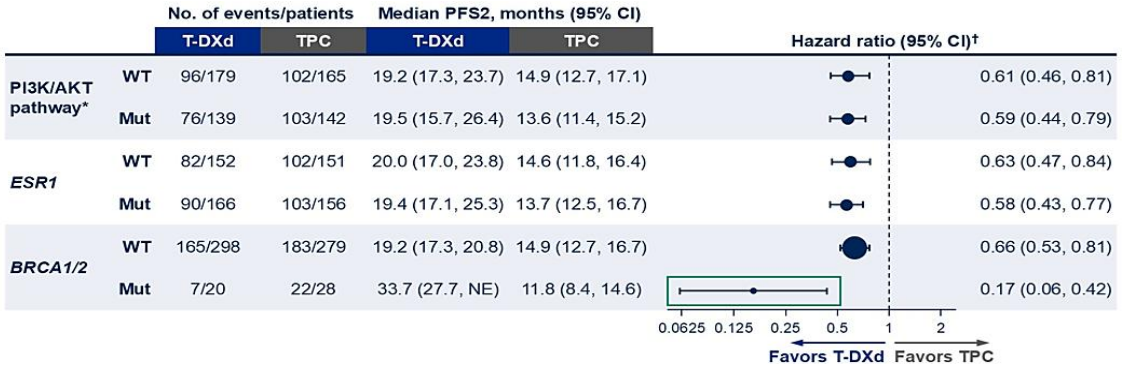
PFS (BICR) by baseline mutation status

		Wild type		Mutant	
		T-DXd	**TPC**	**T-DXd**	TPC
ESR1 mutation status	**mPFS, mos (95% CI)**	15.2 (12.3 – 17.3)	8.1 (6.9 – 9.6)	11.3 (9.8 – 13.5)	7.0 (5.6 – 9.3)
	HR (95% CI)	**0.59** (0.44 – 0.79)		**0.64** (0.49 – 0.83)	
BRCA1/2 mutation status	**mPFS, mos (95% CI)**	12.9 (10.9 – 14.5)	8.2 (6.9 – 9.6)	21.4 (15.2 – NE)	5.6 (4.1 – 6.9)
	HR (95% CI)	**0.69** (0.56 – 0.85)		**0.14** (0.05 – 0.33)	
PI3K/AKT Pathway mutation status	**mPFS, mos (95% CI)**	13.1 (11.1 – 15.4)	8.1 (6.8 – 9.6)	13.2 (9.9 – 15.5)	7.1 (6.0 – 9.5)
	HR (95% CI)	**0.61** (0.47 – 0.79)		**0.65** (0.48 – 0.87)	

Confirmed ORR (BICR) by baseline mutation status



PFS2 (investigator) by baseline mutation status



T-DXD is an effective treatment strategy regardless of mutational status for HR+, HER2-low or –ultralow mBC after prior endocrine-based therapy

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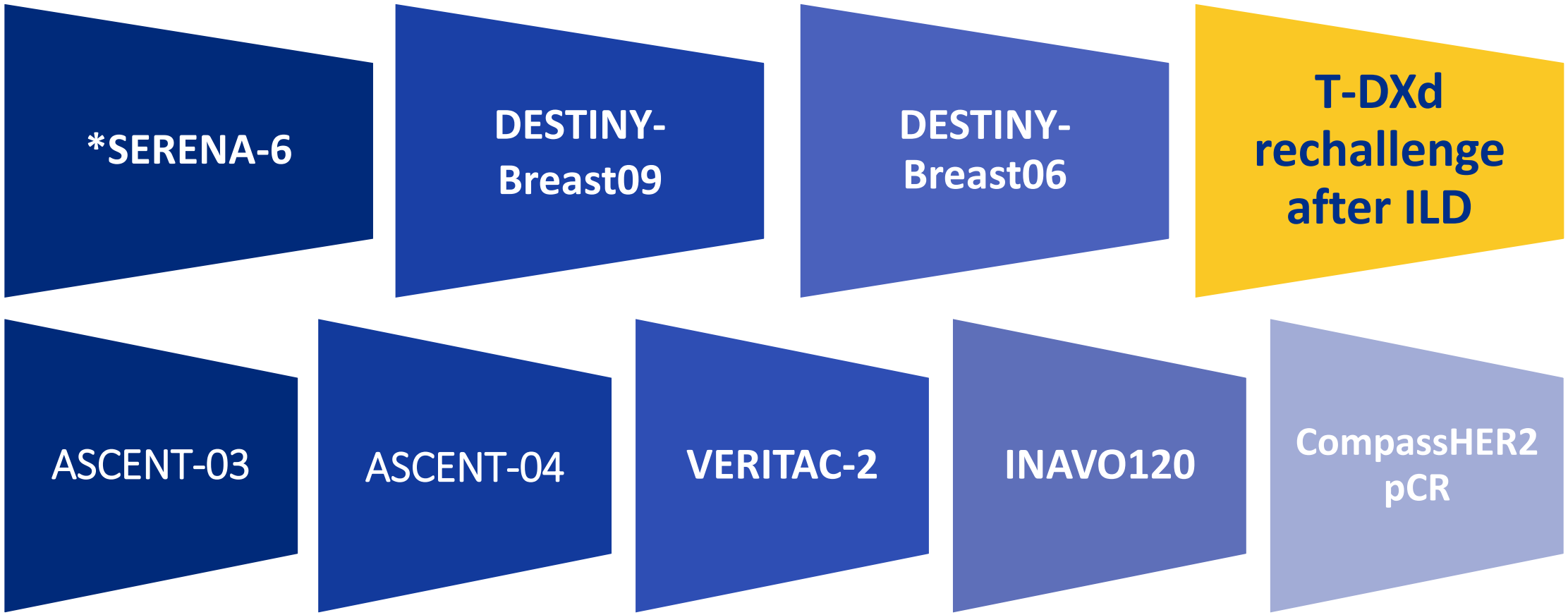

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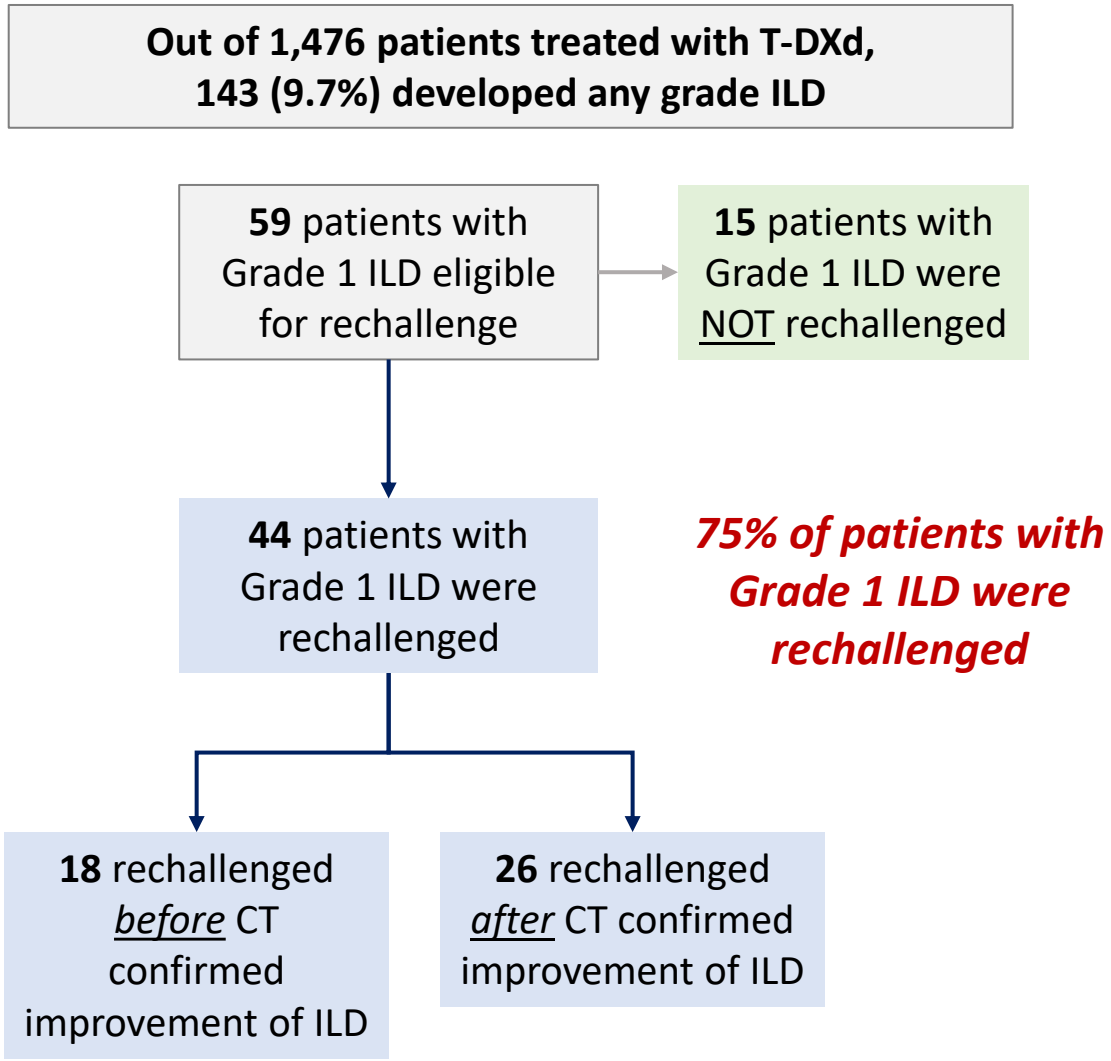
KEY DATA

Treatment rechallenge after trastuzumab-deruxtecan related ILD

Retrospective real-world study of patients treated with T-DXd for any cancer type at 5 US institutions from 2017 - 2024

- T-DXd carries a 12-15% risk of any grade interstitial lung disease/pneumonitis (ILD) and a 1-2% risk of fatal ILD (grade 5)
- Monitoring of symptoms and imaging is critical
- **Grade 1**: Imaging finding, asymptomatic
  - Hold treatment
  - Consider steroids
  - On resolution, option for rechallenge
- **Grade 2 or greater**: Symptomatic
  - Permanently discontinue treatment
  - Administer steroids



Powell CA et at., ESMO Open 2022; Rugo H et ESMO Open 2022
ASCO 2025 Abstr. 1015

KEY DATA

Treatment rechallenge after trastuzumab-deruxtecan related ILD

Retrospective real-world study of patients treated with T-DXd for any cancer type at 5 US institutions from 2017 - 2024

N, (%)	Rechallenged (n=44)	Not rechallenged (n=15)	Overall (n=59)
ILD onset from first T-DXd dose (days)	144 (77 – 216)	198 (123 – 334)	146 (81 – 246)
• Breast cancer • Other (GI, Gyn, Lung)	38 (86%) 6 (14%)	14 (93%) 1 (7%)	52 (88%) 7 (12%)
Age at 1st –DXd dose (years)	60 (52 – 68)	63 (48 – 72)	60 (52 – 69)
Prior # of Tx lines in ad/met setting	3 (1 – 4)	2 (2-5)	3 (1-4)
Renal impairment (CrCl <60 mL/min)	10 (23%)	3 (20%)	13 (22%)
Treated with steroids	**29 (66%)**	**6 (40%)**	**35 (59%)**
Duration of steroid treatment (days)	36 (21-76)	35 (25-49)	36 (21-75)
Radiographic ILD improvement (days)	**39 (22-84)**	**80 (64-99)**	**55 (24-84)***

*Radiographic ILD improvement was seen at a median of 29 days (IQR 20-70) for patients treated with steroids vs 82 days (IQR 50-108) without (p<0.001**)

Median time to rechallenge was **42** days from last dose before ILD

- 3 patients (7%), intervening therapy prior to rechallenge
- 27 patients (61%), rechallenged with the dose reduction
- 17 patients (38%), rechallenged while completing steroid taper

After rechallenge patients remained on T-DXd for a median of **215** days

12 (27%) patients developed recurrent ILD

- 9 with grade 1; 2 with grade 2; 1 with grade 3

Steroid use results in fast radiographic ILD improvement and rechallenge with T-DXd after grade 1 ILD is possible with limited, low-grade recurrence of ILD

ASCO 2025 Abstr. 1015

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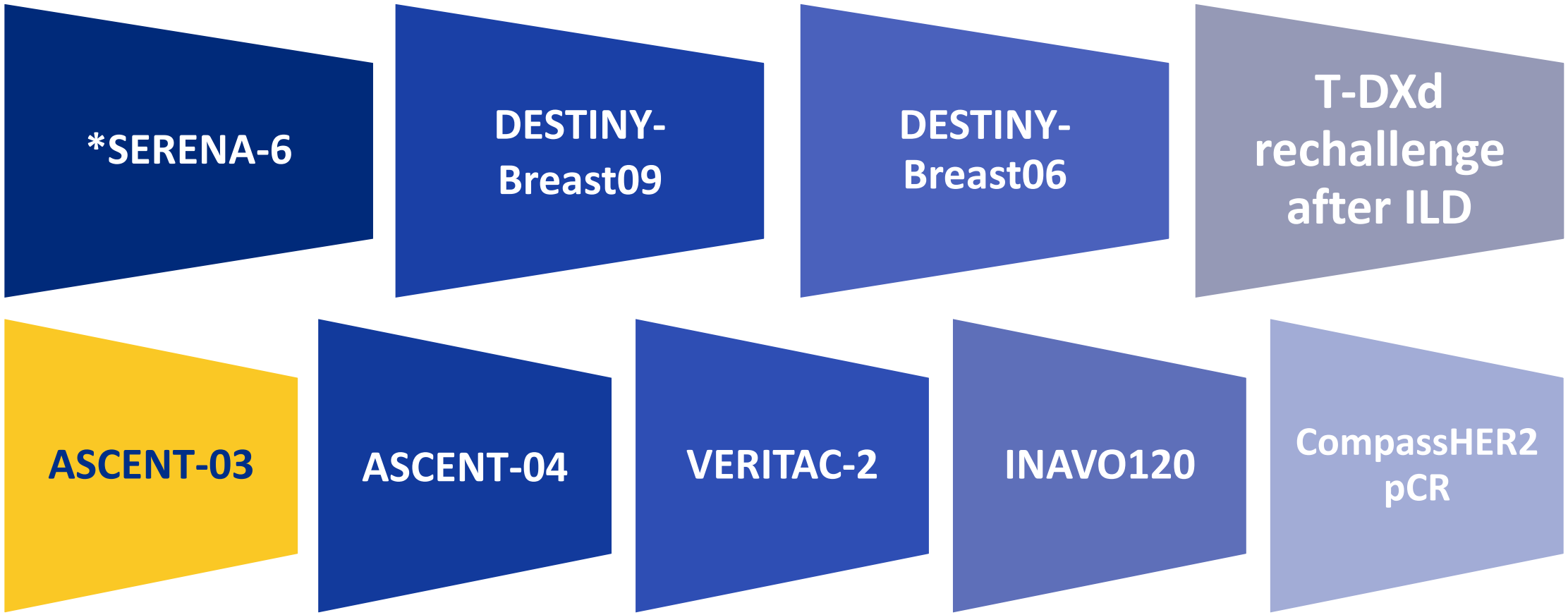

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REMINDER

ASCENT: *On April 7, 2021, the FDA granted regular approval to sacituzumab govitecan (Trodelvy, Immunomedics Inc.) for patients with unresectable locally advanced or metastatic TNBC who have received two or more prior systemic therapies, at least one of them for metastatic disease.*

Study Design: International, randomized, open-label phase III trial

Stratified by geography (N America vs rest of world), number of prior CT (2-3 vs >3), brain mets (yes vs no)

- Patients with mTNBC and ≥2 prior CT (no upper limit; could include PD within 12 mo of [neo]adjuvant tx
- Prior taxane
- RECIST v1.1 measurable disease
- Permitted brain mets if stable ≥4 wk before tx
- ECOG PS 0/1

(N = 529)

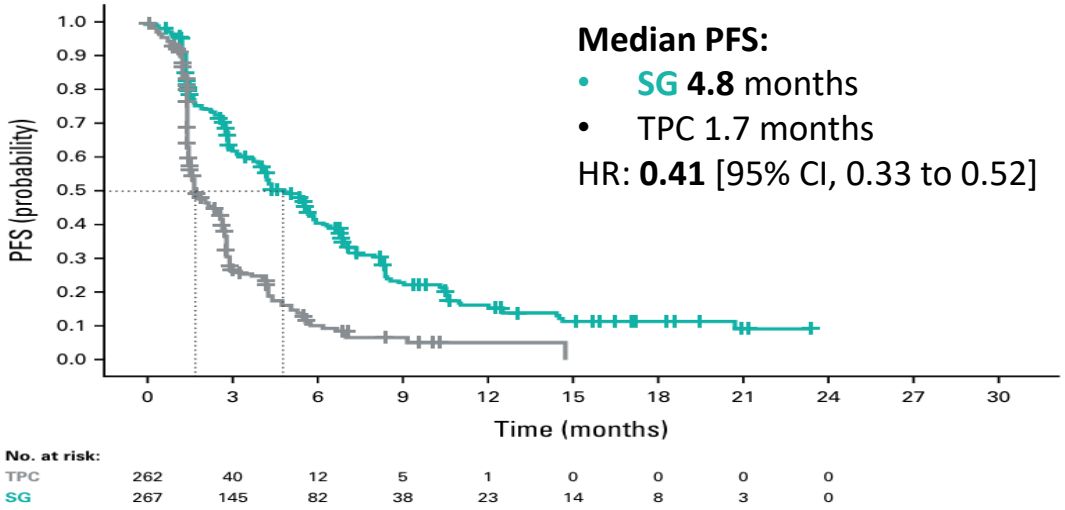
Sacituzumab govitecan
10 mg/kg IV on Days 1, 8 or 21-day cycle
(n = 267)

Physician's choice of single-agent CT*
(n = 262)

*Capecitabine, eribulin, gemcitabine, or vinorelbine.

Primary endpoint: PFS by BICR in patients without brain mets
Secondary endpoints: investigator-assessed PFS, OS, ORR, DoR, TTR, safety

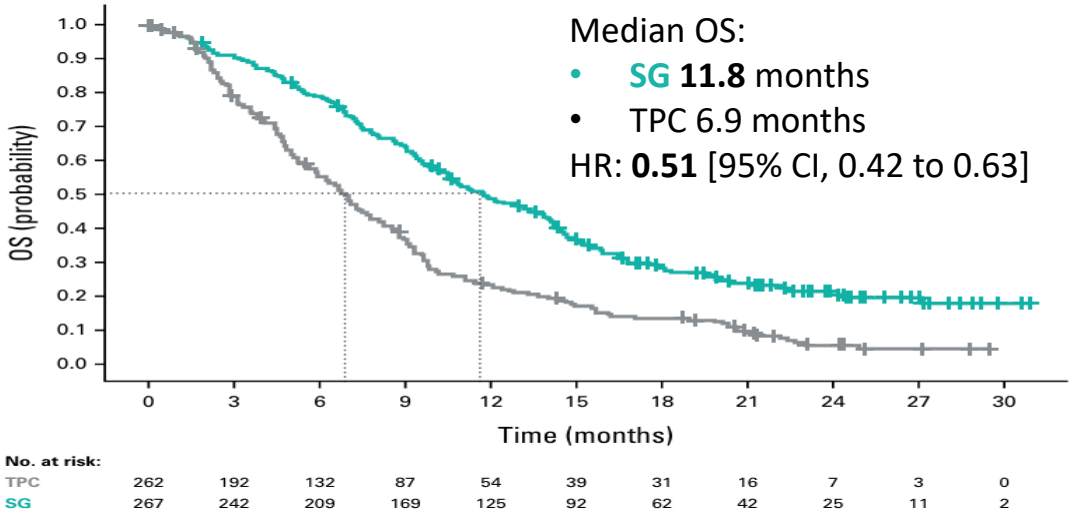
Primary Endpoint: PFS



Median PFS:
- SG **4.8** months
- TPC 1.7 months

HR: **0.41** [95% CI, 0.33 to 0.52]

Secondary Endpoint: OS



Median OS:
- SG **11.8** months
- TPC 6.9 months

HR: **0.51** [95% CI, 0.42 to 0.63]

J Clin Oncol 2024 42:1738-1744

KEY DATA

ASCENT-03: Sacituzumab govitecan in patients with previously untreated mTNBC with tumors lacking PD-L1 expression or patients previously treated with anti-PD-(L)1 in early-stage setting

Study Design

- Previously untreated locally advanced, unresectable, or metastatic TNBC
- PD-L1- by 22C3 CPS <10 or PD-L1+ by 22C3 CPS ≥10 in patients previously treated with an aPD-(L)1 agent in the curative setting
- ≥6 months since treatment in the curative setting
- Prior aPD-(L)1 use allowed in the curative setting
- PD-L1 and TNBC status centrally confirmed
- ECOG PS 0 or 1

N~540

Sacituzumab govitecan
10 mg/kg IV
Day 1 and 8 of a 21-day cycle

Gemcitabine 1000 mg/m2 + Carboplatin AUC 2 IV
Day 1 and day 8 of 21-day cycle

OR

Paclitaxel 90 mg/m2 IV
Day 1, 8, and 15 of 28-day cycle

OR

nab-Paclitaxel 100 mg/m2 IV
Day 1, 8, and 15 of 28-day cycle

Primary Endpoint: PFS
Secondary Endpoints: OS, ORR, DOR, TTR, Safety, PROs

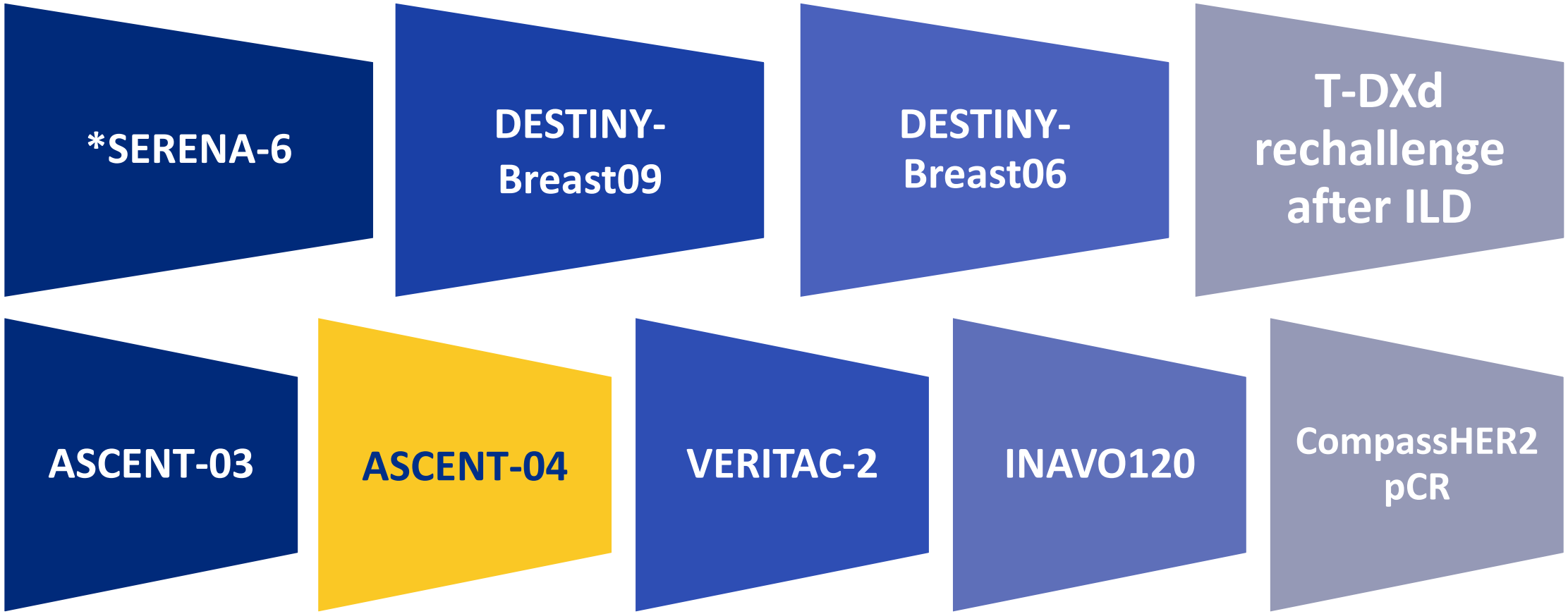
May 23rd 2025, press release:

Gilead Sciences, Inc. announced positive topline results from the Phase 3 ASCENT-03 study of Trodelvy® (sacituzumab govitecan-hziy). The study met its primary endpoint, demonstrating a highly statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to chemotherapy in patients with first-line metastatic triple-negative breast cancer (mTNBC) who are not candidates for PD-1/PD-L1 inhibitors, meaning they are PD-L1 negative or are ineligible to receive immunotherapy.

Detailed results from the ASCENT-03 study will be presented at a future medical meeting and discussed with regulatory authorities

ASCENT 03 Trodelvy Demonstrates Highly Statistically Significant Clinically Meaningful Improvement in Progression Free Survival in Patients With First line Metastatic Triple Negative Breast Cancer Who Are Not Candidates for Checkpoint Inhibitors

ASCO 2025: RAPID REVIEWS



* Plenary Session

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REMINDER

KEYNOTE-355: Pembrolizumab plus Chemotherapy in Advanced Triple-Negative Breast Cancer

On November 13, 2020, the FDA granted accelerated approval to pembrolizumab (KEYTRUDA, Merck & Co.) in combination with chemotherapy for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10) as determined by an FDA approved test.

Study Design:

Randomized, double-blind, multicenter phase III trial

Stratified by chemotherapy (taxane vs gem/carbo); PD-L1 tumor expression (CPS ≥1 vs <1); previous Tx with same class of chemotherapy for EBC (Y vs N)

- Adult patients with previously untreated locally recurrent inoperable or metastatic TNBC
- Completed curative intent treatment ≥6 mo before first recurrence
- ECOG PS 0/1

(N = 847)

Pembrolizumab + Chemotherapy* (n = 566)

*Investigator's choice of chemotherapy
- Nab-paclitaxel
- Paclitaxel
- Gem + carbo

Placebo + Chemotherapy* (n = 281)

Until progression, toxicity, or completion of 35 cycles of pembrolizumab /placebo

Primary endpoint: PFS and OS (PD-L1 CPS ≥10, PD-L1 CPS ≥1, and ITT)
Secondary endpoints: ORR, DoR, DCR, safety in full treated population

Coprimary Endpoints: PFS and OS

PFS	Pembrolizumab + CT	Placebo + CT	HR (95% CI)
PD-L1 CPS ≥10	(n = 220)	(n = 103)	0.66 (0.50-0.88)
• Median PFS, mo	**9.7**	5.6	
• 12-mo PFS, %	39.1	23.0	
PD-L1 CPS ≥1	(n = 425)	(n = 211)	0.75 (0.62-0.91)
• Median PFS, mo	7.6	5.6	
• 12-mo PFS, %	31.7	19.4	
ITT population	(n = 566)	(n = 281)	**0.82** (0.70-0.98)
• **Median PFS, mo**	**7.5**	**5.6**	
• 12-mo PFS, %	29.3	20.8	

OS	Pembrolizumab + CT	Placebo + CT	HR (95% CI)
PD-L1 CPS ≥10	(n = 220)	(n = 103)	0.73 (0.55-0.95) 1-sided *P* = .0093
• Median OS, mo	23.0	16.1	
• 18-mo OS, %	58.3	44.7	
• 24-mo OS, %	48.2	34.0	
PD-L1 CPS ≥1	(n = 425)	(n = 211)	0.86 (0.72-1.04) 1-sided *P* = .0563
• Median OS, mo	17.6	16.0	
• 18-mo OS, %	48.4	41.4	
• 24-mo OS, %	37.7	29.5	
ITT population	(n = 566)	(n = 281)	0.89 (0.76-1.05)
• Median OS, mo	17.2	15.5	
• 18-mo OS, %	47.8	41.8	
• 24-mo OS, %	35.5	30.4	

N Engl J Med. 2022 Jul 21;387(3):217-226.

KEY DATA

ASCENT-04: Sacituzumab Govitecan + Pembrolizumab in 1L setting for patient with PD-L1–Positive Advanced TNBC

Study Design: Global, multicenter, randomized, phase III trial

Stratified by curative treatment-free interval (de novo vs recurrence within 6-12 mo vs recurrence in >12 mo); region (US/Canada/W Europe vs RoW); prior anti–PD-1/PD-L1 (yes vs no)

- Previously untreated, locally advanced unresectable or metastatic TNBC
- PD-L1 positive (CPS ≥10 using 22C3 assay)
- ≥6 mo since curativetreatment (prior anti–PD-1/PD-L1 therapy allowed)

(N = 443)

Sacituzumab Govitecan + Pembrolizumab* (n = 221)

Chemotherapy + Pembrolizumab† (n = 222)

Treatment continued until BICR-verified disease progression or unacceptable toxicity

Crossover to 2L SG permitted upon progression

Note: (96 / 119 pts (81%) received SG monotherapy)

*SG 10 mg/kg IV D1, 8 + Pembro 200 mg D1 of 21-day cycle.

†Paclitaxel 90 mg/m^2 or nab-paclitaxel 100 mg/m^2 D1, 8, 15 of 28-day cycle or gemcitabine 1000 mg/m^2 + carboplatin AUC 2 D1, 8 of 21-day cycle; Pembro 200 mg D1 of 21-day cycle.

Primary endpoint: PFS by BICR

Secondary endpoints: OS and ORR by BICR (hierarchical testing), DoR by BICR, safety, QoL

Select Baseline Characteristics

Characteristic, n (%)	SG + Pembro (n = 221)	CT + Pembro (n = 222)
ECOG PS, n (%)		
• 0	156 (71)	154 (69)
• ≥1	65 (29)	67 (30)*
Curative tx-free interval		
• De novo	75 (34)	75 (34)
• Recurrence 6-12 mo	40 (18)	40 (18)
• Recurrence >12 mo	106 (48)	107 (48)
Metastatic sites		
• Lymph node	159 (72)	154 (69)
• Lung	111 (50)	95 (43)
• Bone	61 (28)	45 (20)
• Liver	55 (25)	57 (26)
• Brain	8 (4)	6 (3)
• Other	81 (37)	71 (32)
Prior anti–PD-1/PD-L1 therapy	9 (4)	11 (5)
CT selected†		
• Taxane	116 (52)	114 (51)
• Gem/carbo	105 (48)	108 (49)

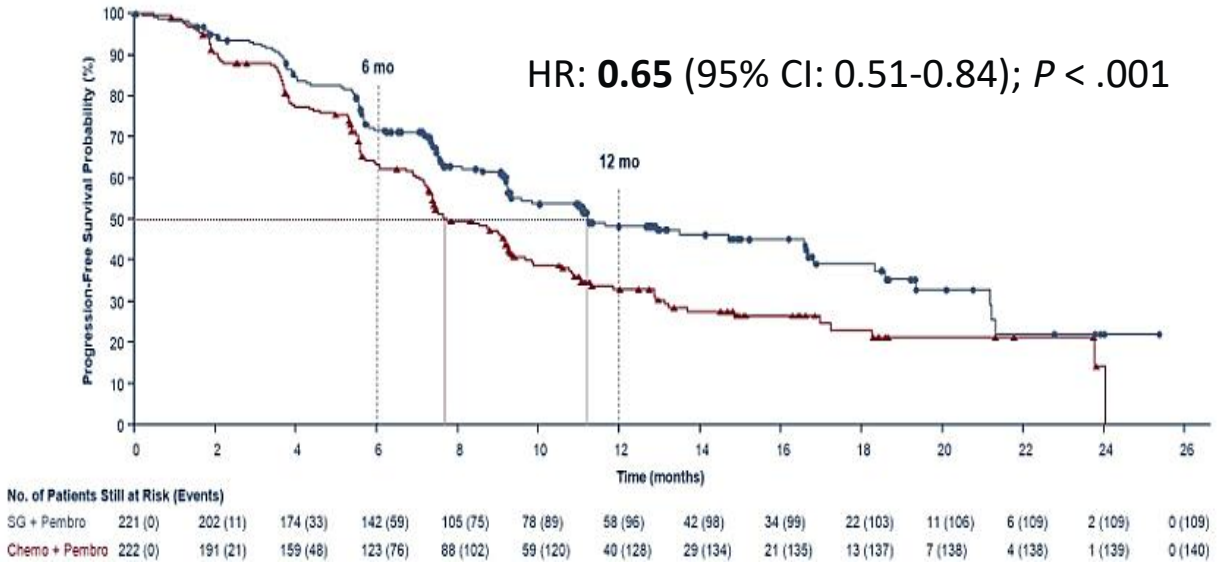
Note: Treatment arms were consistent for age, sex, race, geographical region

*1 patient had ECOG PS ≥2. †CT was selected prior to randomization; 2 randomized patients did not receive tx.

KEY DATA

ASCENT-04: Sacituzumab Govitecan + Pembrolizumab in 1L setting for patient with PD-L1–Positive Advanced TNBC

Primary Endpoint: PFS by BICR (ITT population)



	SG + Pembro (n = 221)	CT + Pembro (n = 222)
Events, n	109	140
Median PFS, mo (95% CI)	**11.2** (9.3-16.7)	**7.8** (7.3-9.3)
6-mo PFS, % (95% CI)	72% (65-77)	63% (56-69)
12-mo PFS, % (95% CI)	48% (41-56)	33% (26-40)

Median follow-up: 14.0 mo (range: 0.1-28.6)

PFS by subgroup analysis

	SG + Pembro		CT + Pembro		HR (95% CI)
	n	Median PFS, Mo (95% CI)	n	Median PFS, Mo (95% CI)	
Age					
• <65 yr	163	11.3 (9.3-16.8)	165	7.5 (7.0-9.2)	0.61 (0.45-0.82)
• ≥65 yr	58	11.1 (7.5-NR)	57	9.3 (7.3-13.2)	0.85 (0.52-1.39)
ECOG PS					
• 0	158	12.9 (9.3-16.8)	154	8.7 (7.3-9.9)	0.65 (0.48-0.88)
• ≥1	65	9.2 (7.5-18.3)	67	7.5 (5.6-9.3)	0.66 (0.43-1.03)
Geographic region					
• US/Canada/W Europe	85	11.7 (7.5-19.4)	85	7.4 (5.7-9.9)	0.65 (0.43-0.98)
• Rest of World	136	11.2 (9.3-16.7)	137	8.4 (7.4-9.3)	0.66 (0.48-0.91)
Curative tx-free interval					
• De novo	75	8.1 (7.3-18.6)	75	7.7 (6.1-11.9)	0.89 (0.59-1.34)
• Recurrence 6-12 mo	40	9.9 (5.7-16.8)	40	7.2 (4.4-9.1)	0.62 (0.36-1.08)
• Recurrence ≥12 mo	106	16.6 (11.0-NR)	107	8.7 (7.3-10.8)	0.52 (0.35-0.76)
Prior (neo)adjuvant anti–PD-1/PD-L1 therapy					
• Yes	9	7.5 (0.9-NR)	11	6.6 (2.1-NR)	1.08 (0.31-3.75)
• No	212	11.7 (9.3-16.8)	211	7.8 (7.4-9.3)	0.65 (0.50-0.84)
CT selected prior to randomization					
• Taxane	116	11.1 (8.6-16.7)	114	9.2 (7.2-12.9)	0.82 (0.58-1.17)
• Gem/carbo	105	11.3 (9.2-21.2)	108	7.4 (6.9-9.0)	0.52 (0.36-0.75)

KEY DATA

ASCENT-04: Sacituzumab Govitecan + Pembrolizumab in 1L setting for patient with PD-L1–Positive Advanced TNBC

Secondary Endpoints

Outcome	SG + Pembro (n = 221)	CT + Pembro (n = 222)
ORR, % (95% CI)	60 (52.9-66.3)	53 (46.4-59.9)
• Stratified OR (95% CI)	1.3 (0.9-1.9)	
Best overall response, n (%)		
• CR	28 (13)	18 (8)
• PR	104 (47)	100 (45)
• SD	70 (32)	70 (32)
– SD ≥6 mo	23 (10)	29 (13)
• PD	9 (4)	26 (12)
• NE	10 (5)	8 (4)
Median Time To Response, mo (range)	1.9 (1.0-9.3)	1.9 (1.1-11.4)
Median Duration of Response, mo (95% CI)	16.5 (12.7-19.5)	9.2 (7.6-11.3)
Median Overall Survival, mo (95% CI)	NR (25.6-NR)	NR (NR-NR)
• Events, n	53	61

Note: OS data immature at primary analysis (26% maturity rate)

Safety: AEs consistent with known profiles of SG and Pembro

Event, n (%)	SG + Pembro (n = 221)	CT + Pembro (n = 222)
TEAE	220 (>99)	219 (>99)
• Grade ≥3	158 (71)	154 (70)
Treatment-emergent SAE	84 (38)	68 (31)
• Treatment-related	61 (28)	42 (19)
TEAE leading to treatment d/c	26 (12)	68 (31)
TEAE leading to dose interruption	171 (77)	162 (74)
TEAE leading to dose reduction	78 (35)	96 (44)
TEAE leading to death	7 (3)	6 (3)
• Treatment-related	3 (1)	1 (<1)
Median Duration of treatment, mo	SG: 8.9 P: 8.5	CT: 6.2 P: 6.4

The combination of SG + P is a potential new treatment option for select patients previously untreated with PD-L1 positive locally advanced or metastatic TNBC

ASCO 2025: RAPID REVIEWS

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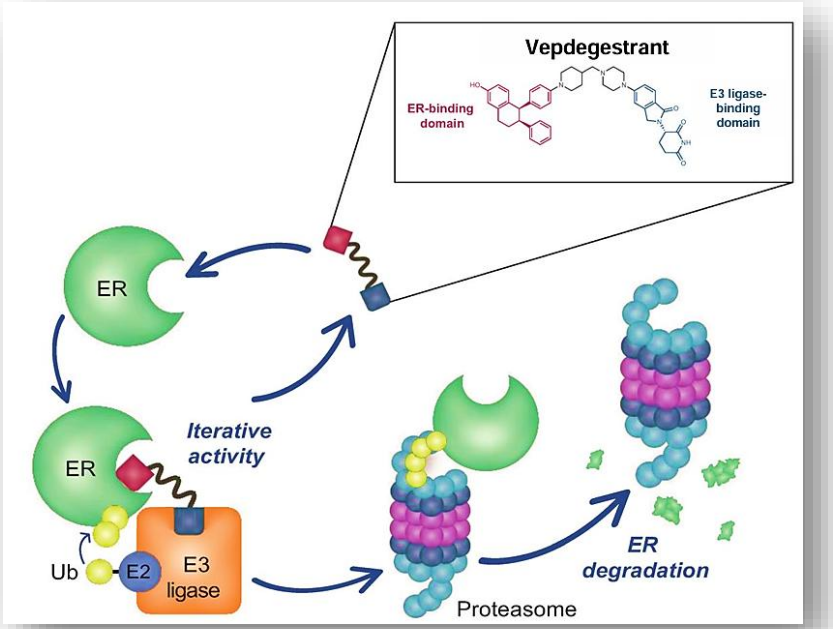
KEY DATA

VERITAC-2: Vepdegestrant, a potential oral therapy option for patients with previously treated ESR1-mutant ER+, HER2+ mBC

June 6, 2025: submission of a NDA to the FDA based on the results from VERITAC-2

Mechanism of Action

- Vepdegestrant is a selective oral PROTAC (PROteolysis TArgeting Chimera) estrogen receptor (ER) degrader that targets both wild-type and mutant estrogen receptors
- Vepdegestrant has a unique MOA that directly harnesses the ubiquitin-proteasome system to degrade estrogen receptors



Békés M, et al. Nat Rev Drug Discov 2022;21(3):181-200. Gough SM, et al. Clin Cancer Res. 2024;30(16):3549-3563.Hamilton EP, et al. Futur Oncol. 2024;20(32):2447–55

Study Design: International, open-label, randomized phase III study

Stratified by ESR1 *mutation (yes vs no) and visceral disease (yes vs no)*

- ER+/HER2- advanced or metastatic BC
- Prior therapy
  - 1 prior line of CDK4/6i + ET
  - ≤1 additional line of ET
  - Most recent ET given for ≥6 mo
  - **No prior chemotherapy** in advanced/metastatic setting
  - No prior SERD (e.g., fulvestrant, elacestrant)
- Radiological progression during or after last line of therapy

(N = 624)

28-day Treatment Cycles

Vepdegestrant
200 mg PO QD
(n = 313)

Fulvestrant
500 mg IM*
(n = 311)

*Day 1 and 15 of cycle 1; Day 1 thereafter.

Primary endpoint: PFS by BICR in all patients and *ESR1*m population
Secondary endpoints: OS, CBR and ORR by BICR, safety

Note: OS data is immature; ongoing follow-up

Data cutoff date: Jan 31, 2025

KEY DATA

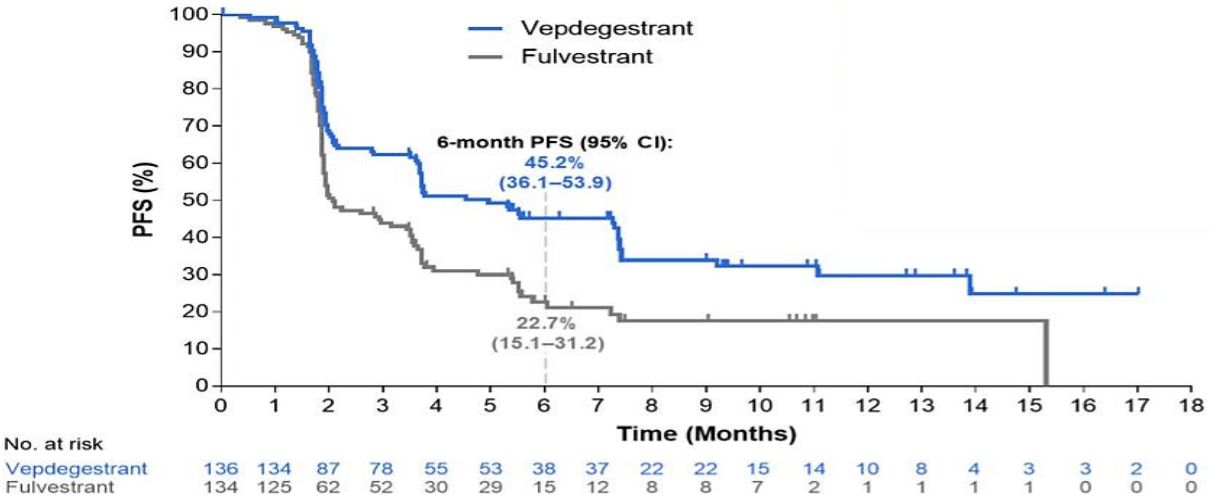
VERITAC-2: Vepdegestrant, a potential oral therapy option for patients with previously treated ESR1-mutant ER+, HER2+ mBC

Baseline characteristics

Characteristic, %	Patients With *ESR1*m		All Patients	
	Vep (n = 136)	Fulv (n = 134)	Vep (n = 313)	Fulv (n = 311)
Median age, yr (range)	60 (26-87)	60 (34-85)	60 (26-89)	60 (28-85)
Female, %	99	100	99	100
Postmenopausal, %	79	79	78	78
Race, %				
• White	43	51	47	46
• Black	3	4	2	2
• Asian	45	37	39	41
• Unknown/NR	9	7	12	9
ECOG PS 0/1, %	57/43	57/43	61/39	64/36
ESR1m, %	100	100	43	43
Sites of disease, %				
• Visceral	68	68	63	63
• Liver metastasis	46	44	40	36
• Bone only	18	18	18	20
Prior lines of therapy				
• 1 / 2	82 / 18	80 / 20	82 / 18	76 / 23

- 100% of patients had received prior endocrine therapy
- 100% of patients had received prior CDK4/6i

Primary Endpoint: Patients With *ESR1*m



Patients with ESR1m	Vepdegestrant (n = 136)	Fulvestrant (n = 134)
Median f/u, mo	7.4	6.0
Events, n (%)	79 (58)	95 (71)
Median PFS, mo (95% CI)	**5.0** (3.7-7.4)	**2.1** (1.9-3.5)
Stratified HR (95% CI)	**0.57** (0.42-0.77); 2-sided P <0.001	

PFS in all patients	Vepdegestrant (n = 313)	Fulvestrant (n = 311)
Median f/u, mo	7.4	7.2
Events, n (%)	186 (59)	198 (64)
Median PFS, mo (95% CI)	**3.7** (3.6-5.3)	**3.6** (2.2-3.8)
Stratified HR (95% CI)	**0.83** (0.68-1.02); 2-sided P = 0.07	

KEY DATA

VERITAC-2: Vepdegestrant, a potential oral therapy option for patients with previously treated ESR1-mutant ER+, HER2+ mBC

Secondary Endpoints

Outcome	Patients With ESR1m		All Patients	
	Vepdegestrant (n = 121)	Fulvestrant (n = 119)	Vepdegestrant (n = 274)	Fulvestrant (n = 272)
CBR by BICR	42.1	20.2	34.3	28.7
• OR (95% CI)	2.88 (1.57-5.39)		1.29 (0.89-1.91)	
• P Value	<0.001		0.16	
ORR by BICR	18.6 (n = 97)	4.0 (n = 100)	10.9 (n = 221)	3.6 (n = 222)
• OR (95% CI)	5.45 (1.69-22.73)		3.23 (1.38-8.71)	
• P Value	0.001		0.003	
Deaths,* n	43		80	

Safety

AEs, %	Vepdegestrant (n = 312)	Fulvestrant (n = 307)
TEAEs		
• Any	87	81
• Grade ≥3	**23**	**18**
• Serious	10	9
• Leading to tx discontinuation	3	1
• Leading to dose reduction	2	NA
TRAEs		
• Any	57	40
• Grade ≥3	**8**	3

- Elevated fatigue 27% any grade vep arm vs 16% any grade fulv arm
- **QT prolongation**:
  - 10% and 1% TEAEs in vepdegestrant and fulvestrant arms, respectively
- **QT interval substudy** (n = 88): no large QT-prolonging effect
  - Mild increase (11.1 ms) in mean QTcF from BL, with upper 90% CI (13.7 ms) <20 ms

In a head-to-head study with fulvestrant, vepdegestrant, a novel oral therapy, could be consider as a potential treatment option for patients with previously treated ESR1-mutant ER+, HER2- mBC

ASCO 2025 Abstr. LBA1000

COMPARISON

ESR1m, ER+/HER2- mBC

	VERITAC-2 International, open-label, randomized phase 3		DESTINY-Breast06 Randomized, multicenter, open-label Phase 3		EMERALD Randomized, open-label, phase 3	
			Biomarker evaluable population			
Patients with ESR1m	**Vepdegestrant (n = 136)**	**Fulvestrant (n = 134)**	**T-DXd (n=166)**	**TPC (n=156)**	**Elacestrant (n=115)**	**Fulvestrant or AI (n=113 total; 83 fulvestrant)**

Study Inclusion Criteria	• ER+/HER2- advanced or metastatic BC
	• **1 prior line of CDK4/6i + ET**
	• **≤1 additional line of ET**
	• Most recent ET given for ≥6 mo
	• **No prior chemotherapy** in advanced/metastatic setting
	• No prior SERD (e.g., fulvestrant, elacestrant)
			• HR+ , HER2-low or ultralow mBC
			• **Chemotherapy naïve** in the mBC setting
			• Prior lines of therapy:
			  • **≥2 lines of ET ± targeted therapy** for mBC OR
			  • 1 line for mBC AND progression ≤6 months of starting first-line ET + CDK4/6i OR
			  • Recurrence ≤24 months of starting adjuvant ET
					• ER+/HER2- advanced or metastatic BC
					• Progression on **1-2 lines of ET, at least one in combination with a CDK4/6i**
					• **≤1 line of chemotherapy** for advanced or metastatic disease	

Median PFS, mo (95% CI)	**5.0** (3.7-7.4)	2.1 (1.9-3.5)	**11.3** (9.8 – 13.5)	7.0 (5.6 – 9.3)	**3.8** (2.2 – 7.3)	1.9 (1.9 – 2.1)
Stratified HR (95% CI)	**0.57** (0.42-0.77) 2-sided P <0.001		**0.64** (0.49 – 0.83)		**0.55** (0.39 – 0.77) P=0.0005	

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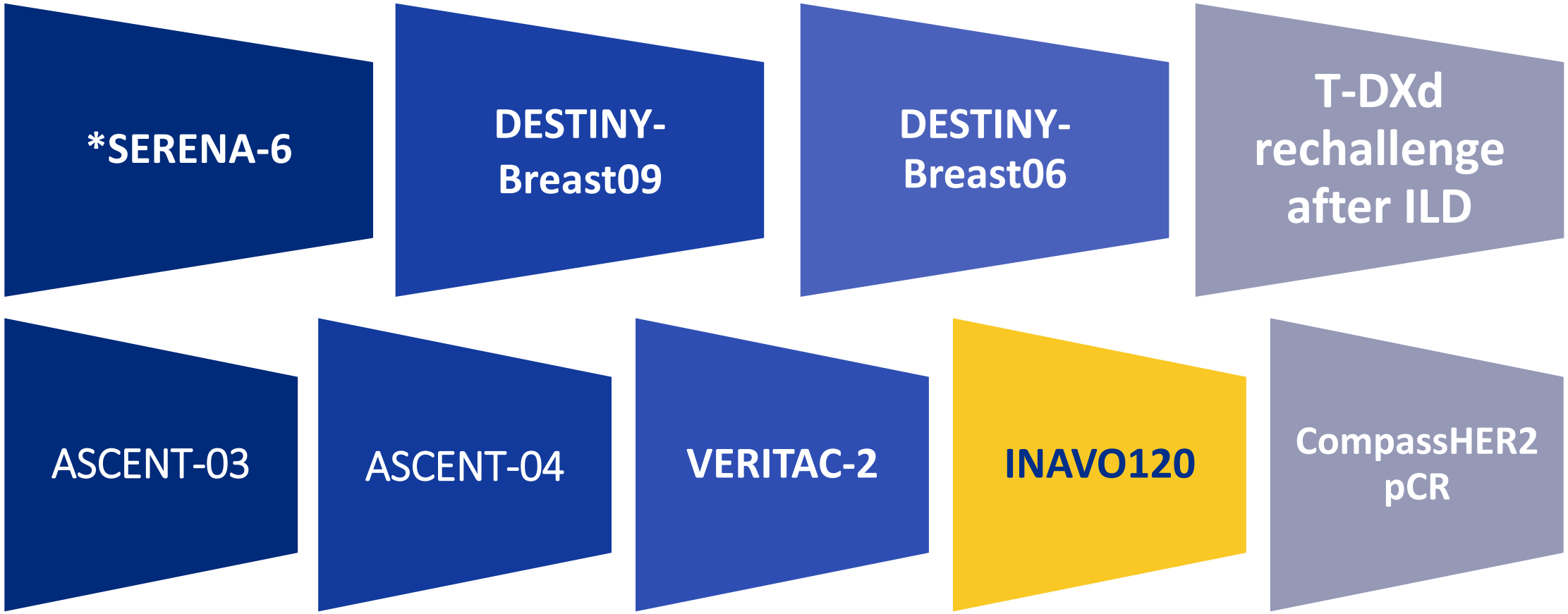

* Plenary Session

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KEY DATA

INAVO120: Final overall survival analysis of inavolisib + palbociclib + fulverstrant in 1L PIK3CA mutated HR+, HER2- endocrine resistant advanced BC

*On **October 10, 2024**, the FDA approved inavolisib (Itovebi, Genentech, Inc.) with palbociclib and fulvestrant for adults with endocrine-resistant, PIK3CA-mutated, HR+ve, HER2-ve, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy.*

Study Design: Randomized, double-blind, placebo-controlled, Phase 3 study

Stratified by Visceral Disease (Yes vs. No); Endocrine Resistance (Primary vs. Secondary)†; Region (North America/Western Europe; Asia; Other)

- PIK3CA-mutated, HR+, HER2- ABC by central ctDNA* or local tissue/ctDNA test
- Measurable disease
- Progression during/within 12 months of adjuvant ET completion
- No prior therapy for ABC
- Fasting glucose <126 mg/dL and HbA1C <6.0%

N =325

R 1:1

Inavolisib (9 mg QD PO) + **palbociclib** (125 mg PO QD D1–D21) + **fulvestrant** (500 mg C1D1/15 and Q4W)**

Until PD or toxicity

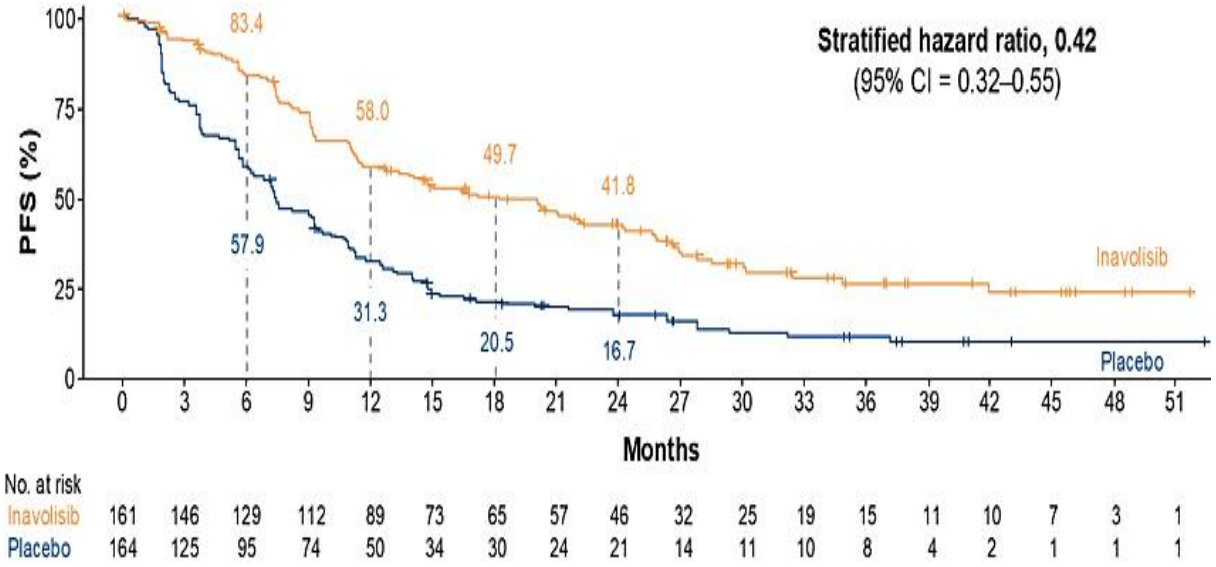
Placebo (PO QD) + **palbociclib** (125 mg PO QD D1–D21) + **fulvestrant** (500 mg C1D1/15 and Q4W)**

Enrollment period: December 2019 to September 2023

Primary endpoint: PFS by Investigator
Secondary endpoints: OS‡, ORR, BOR, CBR, DOR, PROs

Updated PFS

Median follow-up: 34.2 mo

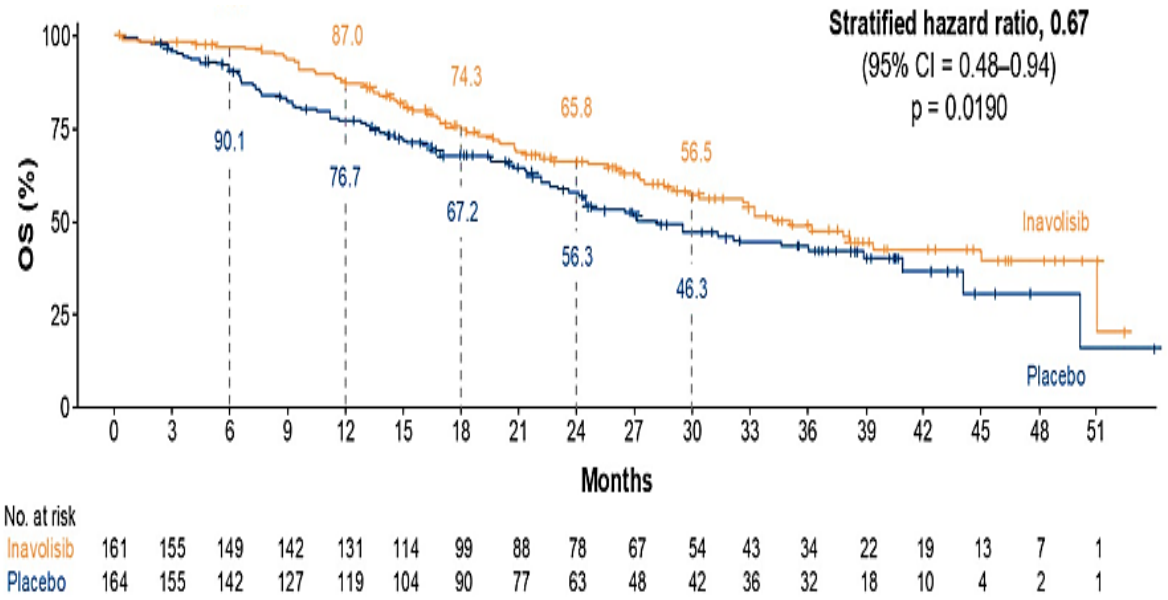


	Inavolisib (n = 161)	Placebo (n = 164)
Events, n (%)	103 (64.0)	141 (86.0)
Median PFS, mos (95% CI)	**17.2** (11.6-22.2)	7.3 (5.9-9.2)
	HR: **0.42** (95% CI: 0.32-0.55)	

KEY DATA

INAVO120: Final overall survival analysis of inavolisib + palbociclib + fulverstrant in 1L PIK3CA mutated HR+, HER2- endocrine resistant advanced BC

Final Overall Survival



	Inavolisib (n = 161)	Placebo (n = 164)
Deaths, n (%)	72 (44.7%)	82 (50.0%)
Median OS, mos (95% CI)	**34.0** (28.4 – 44.8)	27.0 (22.8 – 38.7)
	HR: **0.67** (95% CI: 0.48-0.94); *p*=0.0190	

OS by Subgroup analysis

Subgroup	Patients, n		Median OS, months		Hazard ratio (95% CI)
	Inavolisib	Placebo	Inavolisib	Placebo	
All patients	161	164	34.0	27.0	0.76 (0.55–1.04)
Age					
<65 years	136	130	36.0	26.8	0.65 (0.46–0.92)
≥65 years	25	34	14.4	NR	1.65 (0.77–3.51)
Geographic region					
Asia	58	62	32.7	27.0	0.78 (0.45–1.34)
North America or Western Europe	63	64	30.2	29.3	0.95 (0.56–1.59)
Other	40	38	36.0	16.6	0.53 (0.28–0.98)
ECOG performance status score at baseline					
0	100	106	39.2	36.0	0.69 (0.45–1.05)
1	60	58	27.1	26.8	0.85 (0.52–1.38)
Menopausal status at randomization					
Pre-menopausal	52	52	32.7	23.9	0.67 (0.38–1.19)
Post-menopausal	104	111	34.0	28.0	0.81 (0.55–1.19)
Visceral disease					
No	29	36	38.0	40.7	1.06 (0.46–2.46)
Yes	132	128	33.0	24.1	0.70 (0.50–0.99)
Liver metastasis at enrollment					
No	84	73	38.0	36.0	0.87 (0.53–1.44)
Yes	77	91	28.8	21.9	0.72 (0.48–1.10)
No. of organs with metastases at enrollment					
1	21	32	NR	31.9	0.77 (0.28–2.10)
2	58	46	44.8	24.1	0.51 (0.28–0.90)
≥3	82	86	28.8	24.2	0.86 (0.57–1.30)
Resistance to endocrine therapy					
Primary	54	58	25.9	22.8	0.69 (0.42–1.14)
Secondary	107	105	37.7	34.3	0.77 (0.51–1.16)
Hormone receptor status					
ER-positive, PR-negative	45	45	25.9	38.7	1.16 (0.65–2.08)
ER-positive, PR-positive	113	113	39.2	24.5	0.60 (0.41–0.88)
Previous endocrine therapy					
Aromatase inhibitor and tamoxifen	18	19	NR	NR	1.15 (0.38–3.44)
Aromatase inhibitor only	60	71	26.3	24.2	0.89 (0.56–1.41)
Tamoxifen only	82	73	44.8	36.0	0.68 (0.42–1.11)

KEY DATA

INAVO120: Final overall survival analysis of inavolisib + palbociclib + fulverstrant in 1L PIK3CA mutated HR+, HER2- endocrine resistant advanced BC

ORR and DoR

Outcome	Inavolisib (n = 161)	Placebo (n = 164)
ORR, %	**62.7%**	28.0%
• Difference (95% CI)	34.7 (24.5-44.8); P <.0001	

	Inavolisib (n = 101)	Placebo (n = 46)
Median DoR, mo (95% CI)	**19.2** (14.7-28.3)	11.1 (8.5-20.2)
• Events, n (%)	58 (57.4)	33 (71.7)

	Inavolisib (n = 161)	Placebo (n = 164)
Median time to first subsequent CT, mo (95% CI)	**35.6** (25.4-NR)	12.6 (10.4-16.1)
• Events, n (%)	64 (39.8%)	94 (57.3%)
• Hazard ratio (95% CI)	**0.43** (0.30-0.60)	

OS by Subgroup analysis

AEs, n (%)	Inavolisib (n = 161)	Placebo (n = 163)
Any grade	161 (100)	163 (100)
• Grade 3/4	146 (90.7)	138 (84.7)
• Grade 5*	6 (3.7)	2 (1.2)
• Serious	44 (27.3)	22 (13.5)
AE leading to treatment discontinuation		
• Inavolisib/placebo	11 (6.8)	1 (0.6)
• Palbociclib	10 (6.2)	0
• Fulvestrant	6 (3.7)	0
AE leading to dose reduction		
• Inavolisib/placebo	24 (14.9)	6 (3.7)
• Palbociclib	65 (40.4)	56 (34.4)

- Inavolisib associated with higher frequency of some AEs i.e., hyperglycemia (63.4% vs 13.5%), stomatitis or mucosal inflammation (55.3% vs 28.8%), ocular toxicities (29.2% vs 16.0%), rash (26.7% vs 19.6%), diarrhea (52.2% vs 16.0%), nausea (29.2% vs 19.6%)

Adding inavolisib to palbociclib and fulvestrant may be considered a new standard of care that can benefit select patients with PIK3CA-mutated, HR +ve, HER2 -ve advanced breast cancer…the hyperglycemia with this regimen is a huge clinical problem - particularly knowing that they excluded patients with diabetes.

COMPARISON

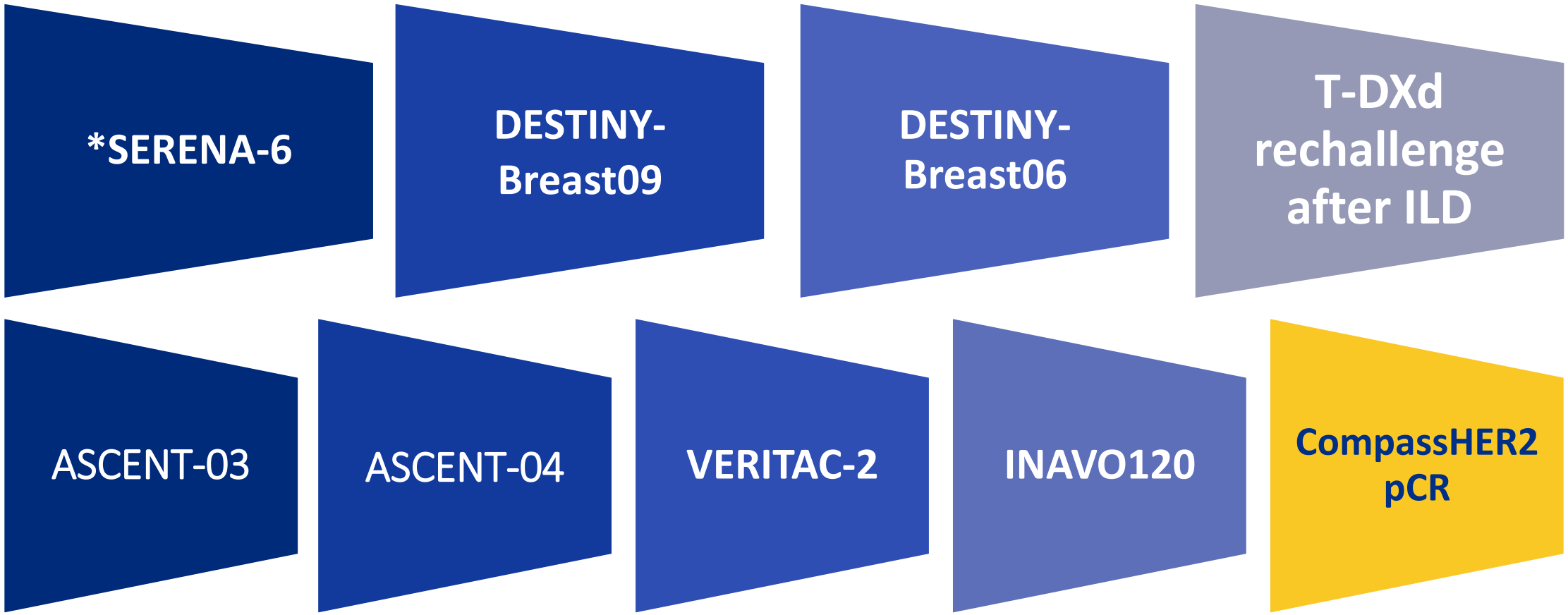
PI3K/AKT Pathway

	INAVO120 Randomized, double-blind, placebo-controlled, Phase 3		DESTINY-Breast06 Randomized, multicenter, open-label Phase 3	
Patients with PI3K/AKT Pathway mutation status	**Inavolisib + palbociclib + fulvestrant (n=161)**	**Placebo + palbociclib + fulvestrant (n=164)**	*Biomarker evaluable population* **T-DXd (n=166)**	**TPC (n=156)**

Study Inclusion Criteria	• PIK3CA-mutated, HR+, HER2- ABC by central ctDNA* or local tissue/ctDNA test
	• Measurable disease
	• Progression during/within 12 months of adjuvant ET completion
	• **No prior therapy for advanced BC**
	• Fasting glucose <126 mg/dL and HbA1C <6.0%
			• HR+ , HER2-low or ultralow mBC
			• **Chemotherapy naïve** in the mBC setting
			• Prior lines of therapy:
			  • **≥2 lines of ET ± targeted therapy for mBC** OR
			  • 1 line for mBC AND progression ≤6 months of starting first-line ET + CDK4/6i OR
			  • Recurrence ≤24 months of starting adjuvant ET	

Median PFS, mo (95% CI)	**17.2** (11.6-22.2)	7.3 (5.9-9.2)	**13.2** (9.9 – 15.5)	7.1 (6.0 – 9.5)
Stratified HR (95% CI)	HR: **0.42** (0.32 - 0.55)		**0.65** (0.48 – 0.87)	
ORR	**62.7%**	28.0%	**57.6%**	41.5%

ASCO 2025: RAPID REVIEWS



* Plenary Session

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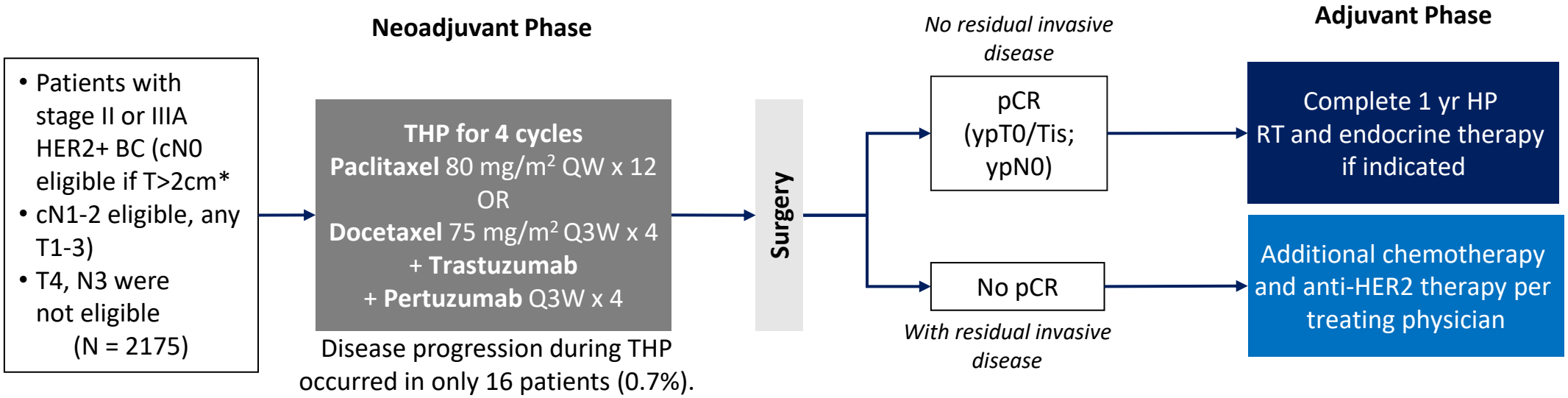
KEY DATA

CompassHER2 pCR: Can we predict using clinicopathologic factors and molecular tools who will achieve pCR and benefit from less intensive chemotherapy in operable HER2+ BC?

Study Design: Single-arm phase II trial



Disease progression during THP occurred in only 16 patients (0.7%).

Is 4 cycles of THP enough?

*ER+ cT2-3cm, cN0 capped at 20% of total participants; ER+ defined as ≥1% ER+

Primary endpoint: 3-yr RFS > 92% in patients with pCR overall and in ER+/HER2+ and ER-/HER2+ cohorts
Secondary endpoints: 3-yr iDFS, DDFS, DRFS, RFI, OS, breast cancer-specific survival in patients with pCR; 3-yr EFS in all patients; safety and tolerability; biomarkers2

Current analysis: includes clinical factors, HER2Dx pCR likelihood score, generated from the HER2Dx test that incorporates 27 genes associated with immune activation (14 genes), luminal differentiation (5 genes), tumor cell proliferation (4 genes), and HER2 amplicon (4 genes, including ERBB2)

KEY DATA

CompassHER2 pCR: Can we predict using clinicopathologic factors and molecular tools who will achieve pCR and benefit from less intensive chemotherapy in operable HER2+ BC?

pCR Rates by Clinicopathologic Factors Univariable Analysis

pCR (ypT0/Tis ypN0)	All Patients (n = 2141*)	ER-/HER2+ (n = 774*)	ER+/HER2+ (n = 1337*)
All patients, % (95% CI)	**43.8** (41.6-45.9)	**63.7** (60.2- 67.1)	**32.5** (30-35)
Age, %			
• <50 yr	43.6	63.5	34.0
• 50-70 yr	47	67.9	34.2
• >70 yr	31.9	48.7	21.1
ECOG PS, %			
• 0	44.7	65.4	32.9
• 1	37.4	51.6	29.7
Grade, %			
• 1	26.9	60	21.1
• 2	37.2	63	27.9
• 3	49.5	64	37.9
ER+ cells			
• 0	63.7	63.7	--
• 1-10	62.5	--	62.5
• 11-70	51.6	--	51.6
• >70	22.5	--	22.5
HER2 IHC			
• 3+	50.3	67.6	39.3
• 2+	11.9	26.0	8.0
Taxane			
• Paclitaxel	46.5	68.5	34.2
• Docetaxel	39.3	55.9	29.7

Association Between HER2Dx pCR Score and Observed pCR Rate

ER- (n = 230)

Parameter	High HER2Dx (n = 147)	Medium HER2Dx (n = 70)	Low HER2Dx (n = 13)	P Value for HER2Dx High vs Low
Patients %	64	30	6	
pCR rate, %	70	74	31	<0 .01

ER+ (n = 339)

	High HER2Dx (n = 36)	Medium HER2Dx (n = 89)	Low HER2Dx (n = 263)	P Value for HER2Dx High vs Low
Patients %	11	26	63	
pCR rate, %	58	61	18	<0 .01

ER-negative status, lower ER expression (≤70%) in ER+ tumors, HER2 IHC of 3+ (vs IHC 2+/ISH+), weekly paclitaxel and higher HER2DX pCR score are all associated with improved pCR in patients with Stage II and III HER2+ BC

Note in trials with 6-8 pre-operative cycles of THP the pCR rate ~20% higher

ASCO 2025:

Breast Cancer

Key Takeaways

Q&A
@EdithAPerezMD

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SERENA-6: *Switching to camizestrant with continuation of CDK4/6i guided by ctDNA improves PFS and should be a new treatment strategy…not yet FDA approved…*

DESTINY-Breast09: *The combination of T-DXD plus pertuzumab has the potential to be a new first-line standard of care for patients with HER2+ mBC…not yet approved…more to come…*

DESTINY-Breast06: *T-DXD is an effective treatment strategy regardless of mutational status for HR+, HER2-low or –ultralow mBC after prior endocrine-based therapy…FDA approved since January 2025*

Treatment rechallenge after trastuzumab-deruxtecan related ILD: *Steroid use results in fast radiographic ILD improvement and rechallenge with T-DXd after grade 1 ILD is possible with limited, low-grade recurrence of ILD*

ASCENT-03: *Positive topline results from the Phase 3 ASCENT-03 study of sacituzumab govitecan-hziy suggest benefit for 1L metastatic TNBC patients…not yet approved in earlier line setting, more to come…*

ASCENT-04: *The combination of sacituzumab govitecan-hziy plus pembrolizumab is a potential new treatment option for select patients previously untreated with PD-L1 positive locally advanced or metastatic TNBC…not yet approved…more to come…*

VERITAC-2: *Vepdegestrant, benefitted patients with previously treated ESR1-mutant ER+, HER2- mBC: mPFS 5.0 mos. EMERALD, elacestrant vs fulvestrant in ESR1m, ER+/HER2- mBC ≤1 prior chemo: mPFS 3.8 mos HR 0.55*

INAVO120: *Adding inavolisib to palbociclib and fulvestrant is a new standard of care that can benefit select patients with PIK3CA-mutated, HR+ve, HER2-ve advanced breast cancer…the hyperglycemia with this regimen is a huge clinical problem - particularly knowing that they excluded patients with diabetes*

CompassHER2 pCR: *Clinicopathologic factors and HER2DX scores can be utilized to identify patients who have no residual disease after THP and surgery, and can forgo further chemotherapy*

2025 ASCO Key Studies

Breast Cancer

- RAPID REVIEWS
  - *SERENA-6
  - DESTINY-Breast09
  - DESTINY-Breast06
  - AI for IHC HER2 Pathology
  - ASCENT-03
  - ASCENT-04
  - VERITAC-2
  - INAVO120
  - CompassHER2 pCR

GU/ GI Cancer

- *ATOMIC
- *MATTERHORN
- DESTINY-Gastric04
- ***RAPID REVIEWS***
  - BREAKWATER
  - PANOVA-3
  - AMPLITUDE

Other Notable Studies

- *NIVOPOSTOP
- KEYNOTE-689
- *VERIFY
- ***RAPID REVIEWS***
  - TROPION-Lung02
  - DELPHI-304
  - IMforte
  - TUXEDO-3
  - ROSELLA

* Plenary Session

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CLINICAL QUESTION

ATOMIC

* Plenary Session

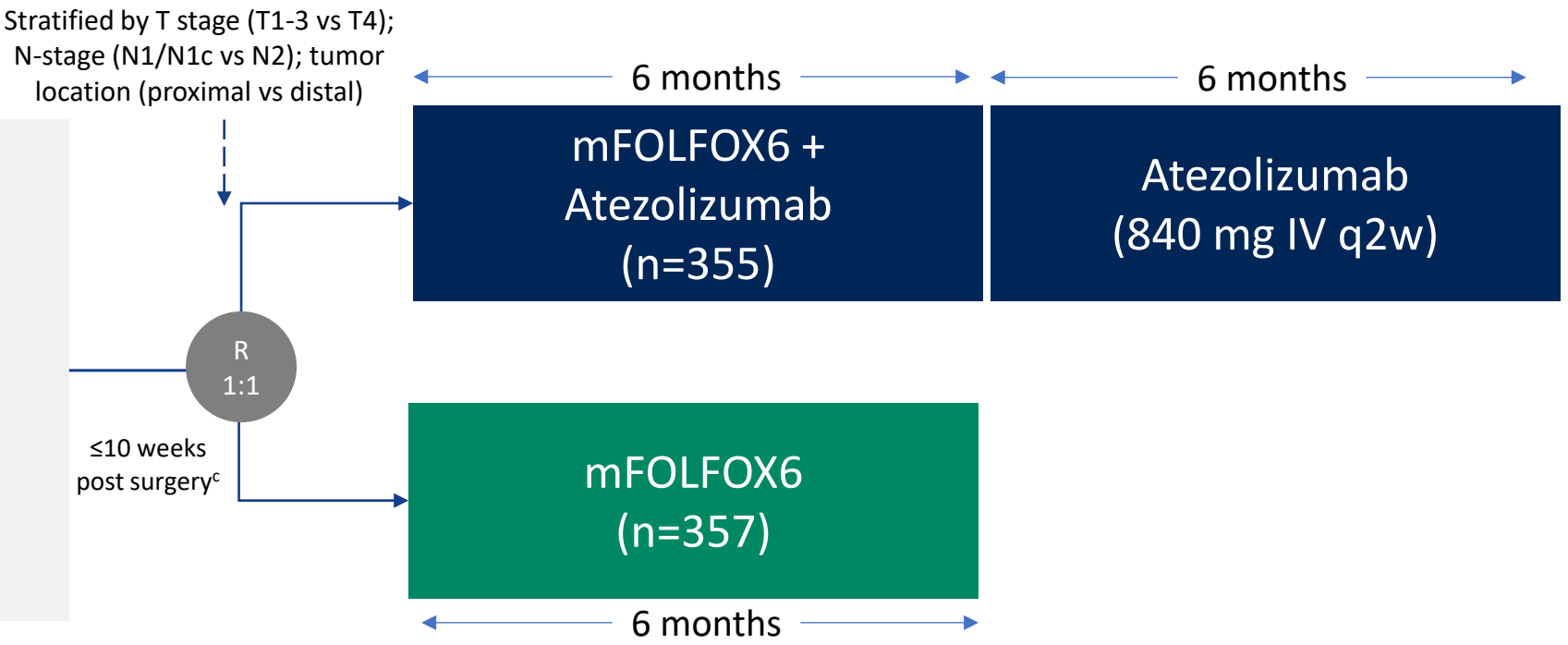
Does the addition of atezolizumab to standard of care chemotherapy benefit patients with stage III deficient mismatch repair dMMR colon cancer?

KEY DATA

ATOMIC: Phase 3 of mFOLFOX6 +/- atezolizumab for 1 year

Study Design: Randomized, multicenter, open label phase 3 study

- Age ≥12 years old
- Histologically confirmed, R_0 resected stage III colon adenocarcinoma
- dMMR by Immunohistochemistry[a,b]
- ECOG PS ≤2
- No prior chemotherapy or radiation



Primary endpoints: Disease-free survival (DFS)
Secondary endpoints: Overall survival (OS), adverse event (AE) profile

Data cutoff (Feb 4, 2025)
median follow-up was 37.1 months
(Q1, Q3: 24.2, 55.7)

[a]dMMR by immunohistochemistry (IHC) locally or at site-selected reference laboratory. Retrospective central confirmation of dMMR also performed. [b]Lynch syndrome included. [c]One cycle of mFOLFOX6 prior to randomization permitted.

KEY DATA

ATOMIC: Phase 3 of mFOLFOX6 +/- atezolizumab for 1 year

Baseline characteristics

	mFOLFOX6 + Atezo (n = 355)	mFOLFOX6 (n = 357)
Median age, years (Q1 - Q3, range)	65 (51.0 - 73.0)	63 (48.0 - 73.0)
Sex, n		
• Female	186 (52.4%)	206 (57.7%)
• Male	169 (47.6%)	151 (42.3%)
Race, n		
• White	302 (85.1%)	305 (85.4%)
• Black	28 (7.9%)	22 (6.2%)
• Other	25 (6.0%)	30 (8.4%)
Primary tumor site, n		
• Proximal	301 (84.8%)	296 (82.9%)
• Distal	53 (14.9%)	57 (16.0%)
• Multiple	1 (0.3%)	4 (1.1%)

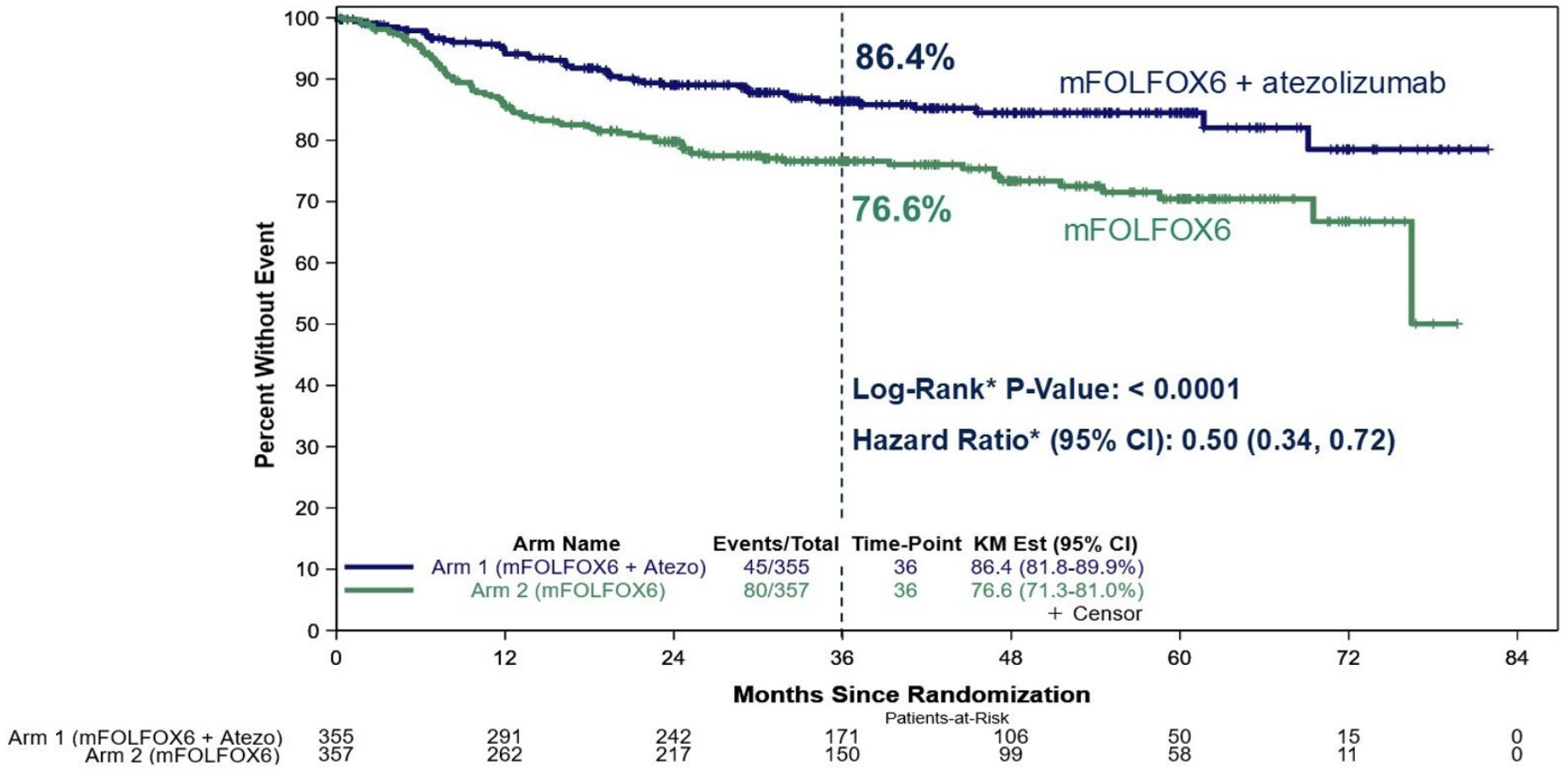
Q1, first quartile
Q3, third quartile

	mFOLFOX6 + Atezo (n = 355)	mFOLFOX6 (n = 357)
T stage, n		
• Tx	0	1 (0.3%)
• T1	11 (3.1%)	4 (1.1%)
• T2	30 (8.5%)	22 (6.2%)
• T3	202 (56.9%)	216 (60.5%)
• T4	112 (31.5%)	114 (31.9%)
N stage, n		
• N1/N1c	226 (63.7%)	225 (63.0%)
• N2	129 (36.3%)	132 (37.0%)
Risk group,* n		
• Low	164 (46.2%)	164 (45.9%)
• High	191 (53.8%)	193 (54.1%)
ECOG PS, n		
• 0	238 (67.0%)	225 (63.0%)
• 1	111 (31.3%)	127 (35.6%)
• 2	6 (1.7%)	5 (1.4%)

KEY DATA

ATOMIC: Phase 3 of mFOLFOX6 +/- atezolizumab for 1 year

Primary Endpoint: Disease-free survival (DFS)



Confirmed dMMR by central reference laboratory: Log-Rank P-Value: 0.0007, HR (95% CI): 0.53 (0.36,0.79)

*Stratified by randomization factors

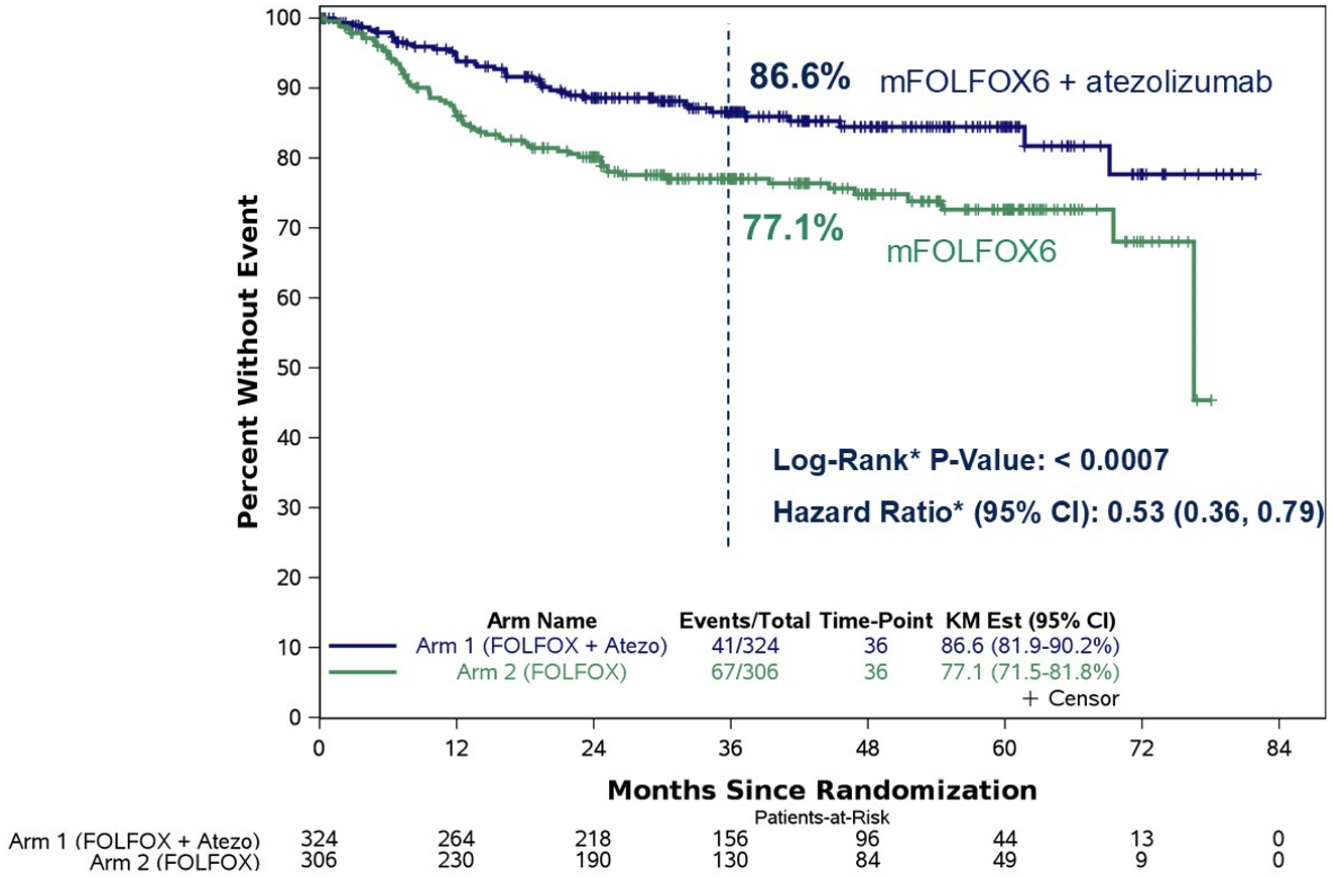
Median follow-up = 37.2 mos

KEY DATA

ATOMIC: Phase 3 of mFOLFOX6 +/- atezolizumab for 1 year

Secondary Endpoints

DFS: dMMR by central reference lab



*Stratified by randomization factors
Median follow-up = 37.2 mos

Overall survival

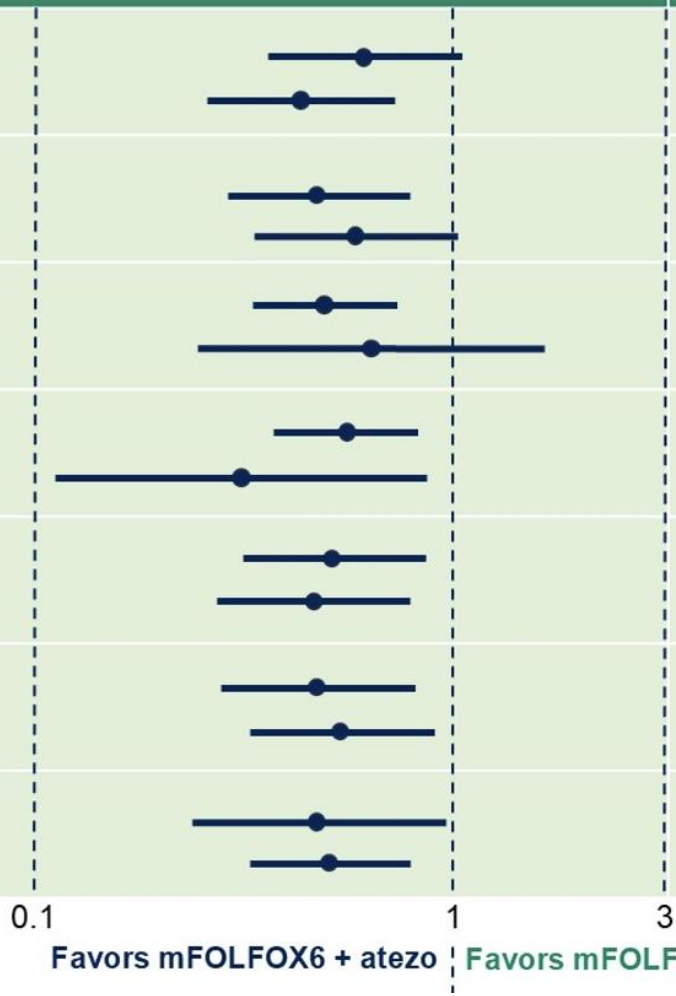
- OS data are not mature
- Median (Q1, Q3) OS follow-up:
  - 42.5 (27.9, 60.5) months
- The OS comparison may be confounded by subsequent immunotherapy

KEY DATA

ATOMIC: Phase 3 of mFOLFOX6 +/- atezolizumab for 1 year

DFS by Subgroup

		mFOLFOX6 + Atezo	mFOLFOX6	HR (95% CI)
Age	< 65 year	22/173	36/187	0.61 (0.36, 1.04)
	≥ 65 year	23/182	44/170	0.43 (0.26, 0.72)
Sex	Female	24/186	50/206	0.48 (0.29, 0.77)
	Male	21/169	30/151	0.58 (0.33, 1.01)
Race	White	38/302	69/305	0.50 (0.33, 0.74)
	Other	7/53	11/52	0.63 (0.25, 1.63)
Tumor Location	Proximal	40/301	65/296	0.56 (0.38, 0.83)
	Distal	5/53	14/57	0.31 (0.11, 0.87)
T-Stage	Tx/T1-T3	23/243	44/243	0.51 (0.31, 0.85)
	T4	22/112	36/114	0.46 (0.27, 0.79)
N-Stage	$N1/N1_c$	21/226	41/225	0.48 (0.28, 0.81)
	N2	24/129	39/132	0.54 (0.33, 0.90)
Risk Group	Low*	12/164	25/164	0.47 (0.24, 0.94)
	High*	33/191	55/193	0.51 (0.33, 0.78)
		Events/Patients	Events/Patients	



*Low (Tx-T3 and N1/N1c); High (T4 or N2)

KEY DATA

ATOMIC: Phase 3 of mFOLFOX6 +/- atezolizumab for 1 year

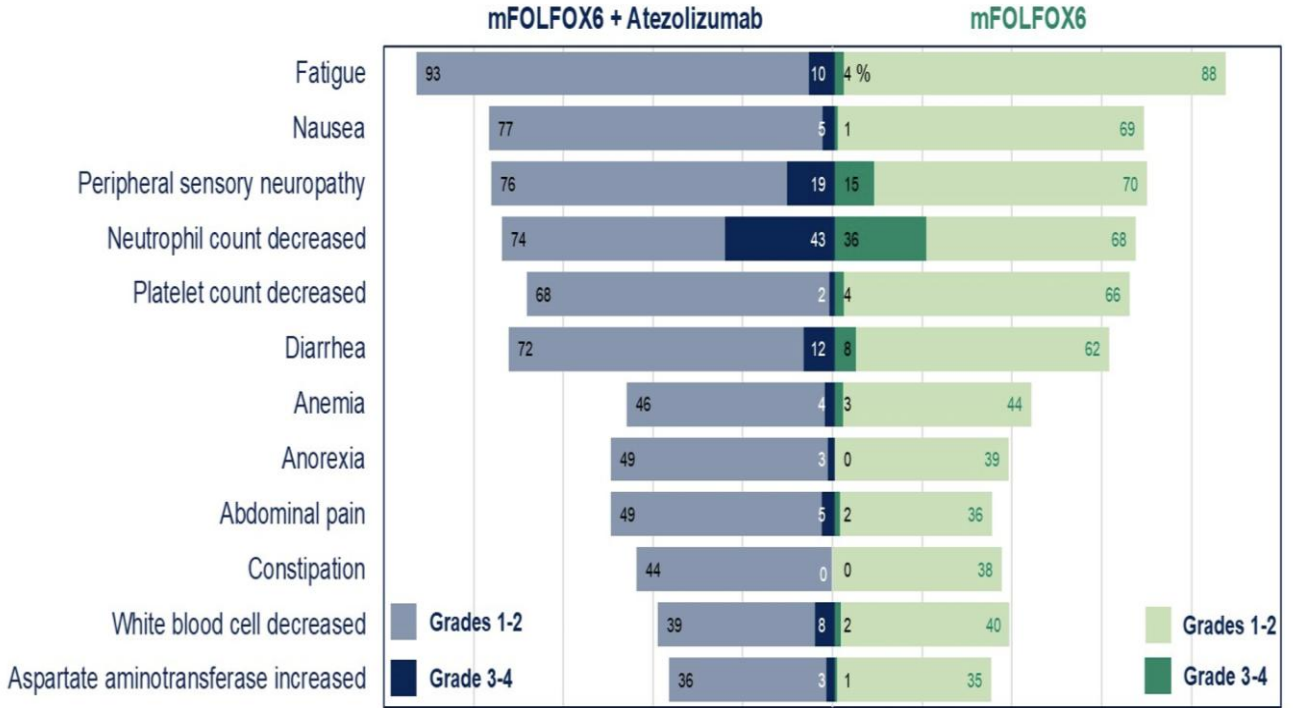
Safety Summary

	mFOLFOX6 + Atezo (n = 346)#	mFOLFOX6 (n = 334)#
Any Grade AE, (n)	100% (346)	95.1 % (329)
• Treatment-related	99.7% (345)	94.2% (326)
Grade 3-4 AE, (n)	83.8% (290)	69.1% (239)
• Treatment-related	72.3% (250)	59.2% (205)
Grade 5 AE, (n)	1.7% (6)	0.6% (2)
• Treatment-related	0.6% (2)*	0.0% (0)

Immune-Related AEs

	mFOLFOX6+ Atezo (n = 346)#		mFOLFOX6 (n = 334)#	
	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4
Adrenal insufficiency	0.3%	0.9%	0%	0%
Hyperglycemia	17.9%	2.6%	9.0%	1.2%
Hypothyroidism	20.5%	0%	3.6%	0%
Colitis	5.5%	1.2%	0.6%	0%
Diarrhea	60.1%	12.1%	53.3%	8.4%
Generalized muscle weakness	7.8%	0.9%	3.3%	0%
Maculopapular rash	13.3%	0.9%	6.0%	0%

AEs Occurring in >35% of Evaluable* Patients



Neutrophil count decrease

Grade 3, n	**100 (28.9%)**	**97 (29.0%)**
Grade 4, n	**49 (14.2%)**	**23 (6.9%)**

#Recived at least one dose of treatment

*1 sudden death NOS (possibly related); 1 sepsis (possibly related)

*Evaluable patients: received at least 1 treatment dose

ASCO 2025. Abstr. LBA1

Efficacy of Neoadjuvant IO in dMMR Colon Cancer

Study	Treatment Regimen	Treatment duration	No. of patients	pCR or cCR rate	Grade 3-4 AEs
NICHE-2 *N Engl J Med*. 2024;390(21):1949-1958.	NIVO + IPI	4 weeks	115	68%	5%
Xu et al., ASCO 2024	Sintilimab ± IBI310	6 weeks	101	78% vs 47%	10% (mono) 6% (dual)
NICHE-3 *Nat Med.* 2024;30(11):3284-3290.	NIVO + relatlimab	8 weeks	59	68%	10%
PICC *Lancet Gastroenterol Hepatol.* 2022;7(1):38-48.	Toripalimab + celecoxib	12 weeks	34	88%	3%
PICC *Lancet Gastroenterol Hepatol.* 2022;7(1):38-48.	Toripalimab *(w/o celecoxib)*	12 weeks	34	65%	3%
NEOPRISM	Pembro	6 weeks	32	58%	6%
IMHOTEP *Ann Oncol.* 2024;35(suppl 2):S429.	Pembro	4-8 weeks	77	47% (1 cycle) 68% (2 cycles)	13%
N Engl J Med 2025;392:2297-2308	Dostarlimab	6 months	22	82%	6%

SUMMARY

ATOMIC

- The addition of PD-L1 inhibitor (atezolizumab) to mFOLFOX6 is practice-changing and, if approved, could be considered a new standard of care adjuvant treatment for patients with dMMR stage III colon cancer
  - Not yet FDA approved or included in the NCCN Guidelines
- The safety of mFOLFOX6 + atezolizumab was in line with the known safety profiles of each individual therapy
  - Increase in non-febrile neutropenia was manageable

IMPACT

The addition of PD-L1 inhibitor (atezolizumab) to mFOLFOX6 is practice changing and, if approved, could be considered a new standard of care adjuvant treatment for patients with dMMR stage III colon cancer

Emergence of neoadjuvant IO (without chemo) is gaining momentum but the combination of IO and chemo in the adjuvant setting with ATOMIC has set a high bar

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2025 ASCO Key Studies

Breast Cancer

- RAPID REVIEWS
  - *SERENA-6
  - DESTINY-Breast09
  - DESTINY-Breast06
  - AI for IHC HER2 Pathology
  - ASCENT-03
  - ASCENT-04
  - VERITAC-2
  - INAVO120
  - CompassHER2 pCR

GU/ GI Cancer

- *ATOMIC
- *MATTERHORN
- DESTINY-Gastric04
- ***RAPID REVIEWS***
  - BREAKWATER
  - PANOVA-3
  - AMPLITUDE

Other Notable Studies

- *NIVOPOSTOP
- KEYNOTE-689
- *VERIFY
- ***RAPID REVIEWS***
  - TROPION-Lung02
  - DELPHI-304
  - IMforte
  - TUXEDO-3
  - ROSELLA

* Plenary Session

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CLINICAL QUESTION

MATTERHORN

* Plenary Session

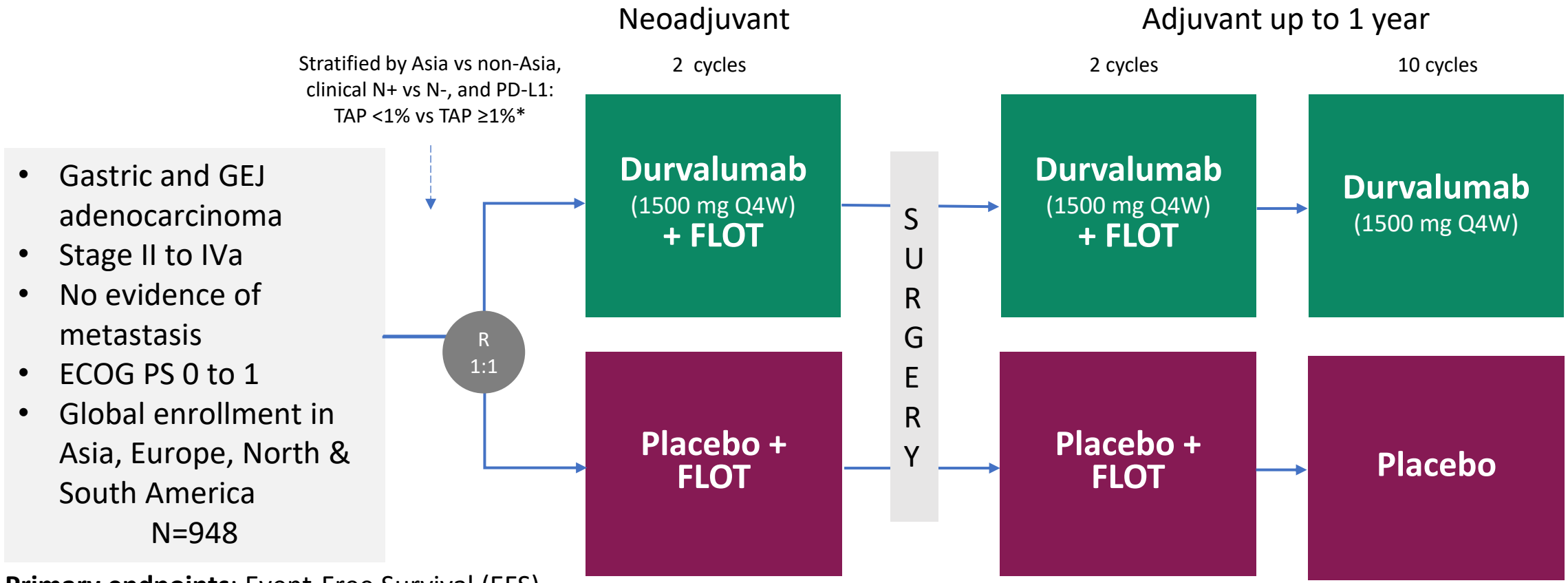
Does the addition of the PD-L1 inhibitor durvalumab to standard of care neoadjuvant/adjuvant FLOT chemotherapy benefit patients with resectable Gastric/Gastroesophageal Junction Cancer (GC/GEJC)?

ASCO 2025. Abstr. LBA5

KEY DATA

MATTERHORN: neoadjuvant/adjuvant FLOT +/- durvalumab

Study Design: Global, phase 3, randomized, double-blind, placebo-controlled study



- Gastric and GEJ adenocarcinoma
- Stage II to IVa
- No evidence of metastasis
- ECOG PS 0 to 1
- Global enrollment in Asia, Europe, North & South America

N=948

Primary endpoints: Event-Free Survival (EFS)

Secondary endpoints: Overall Survival (OS), Path Complete Response (pCR), Disease-Free Survival (DFS)

FLOT: 5-Fluorouracil 2600 mg/m^2, leucovorin 200 mg/m^2, oxaliplatin 85 mg/m^2, docetaxel 50 mg/m^2, on Days 1 and 15 Q4W, 4 doses (two cycles) pre-and post-operative: durvalumab: 150 mg on day 1 Q4W, 2 doses (two cycles) of durvalumab or placebo pre- and post-operative, followed by 10 dose of post-operative durvalumab or placebo monotherapy. Participants underwent surgery 4-8 weeks after last dose of neoadjuvant therapy. Adjuvant began 4-12 weeks post-surgery. Durvalumab / placebo monotherapy may be continued if FLOT is discontinued due to toxicity.

*Measured by IHC using VENTANA PD-L1 (SP263) CDx Assay (Roche Diagnosis; IUO)

KEY DATA

MATTERHORN: neoadjuvant/adjuvant FLOT +/- durvalumab

Baseline characteristics

	Durvalumab + FLOT (n = 474)*	Placebo + FLOT (n = 474)*
Median age, yr (range)	62 (26-84)	63 (28-83)
Male	69%	75%
Geographic region		
• Non-Asia	81%	81%
• **Asia**	**19%**	**19%**
ECOG PS		
• 0	71%	77%
• 1	29%	23%
Site of tumor		
• Gastric	68%	67%
• **GEJ**	**32%**	**33%**
Primary tumor stage		
• **T4**	**25%**	**25%**
• Non-T4	75%	75%

	Durvalumab + FLOT (n = 474)*	Placebo + FLOT (n = 474)*
Clinical lymph node status[a]		
• **N+**	**69%**	**70%**
PD-L1 expression by TAP		
• <1%	10%	10%
• ≥1%	90%	90%
Histology type[b]		
• Intestinal	52%	50%
• Diffuse	27%	25%
• Unspecified/mixed/other	21%	25%
MSI status[c]		
• **MSI-high**	**5%**	**5%**
• Not MSI-high	64%	65%
• Not evaluable/missing	31%	30%

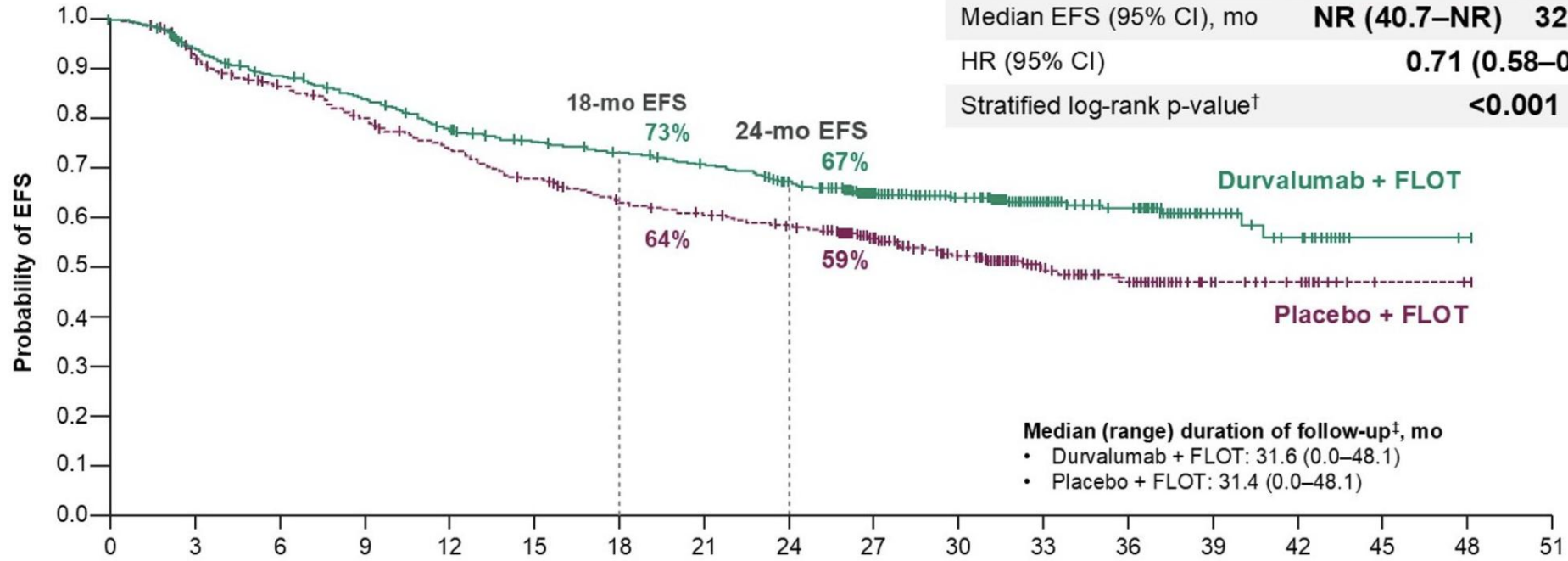
*Full analysis set (all randomized participants regardless of treatment received). [†]As recorded at randomization on the Interactive Response Technology System or Randomization and Trial Supply Management. [b]Measured by IHC using VENTANA PD-L1 (SP263) CDx Assay (Roche Diagnostic: IUO. [c]MSI was measured by a clinical trial assay based on FoundationOne CDx in a research use only capacity.

KEY DATA

MATTERHORN: neoadjuvant/adjuvant FLOT +/- durvalumab

Primary Endpoint: Event-Free Survival (EFS)

	Durvalumab + FLOT (n=474)*	Placebo + FLOT (n=474)*
Median EFS (95% CI), mo	NR (40.7–NR)	32.8 (27.9–NR)
HR (95% CI)	0.71 (0.58–0.86)	
Stratified log-rank p-value†	<0.001	



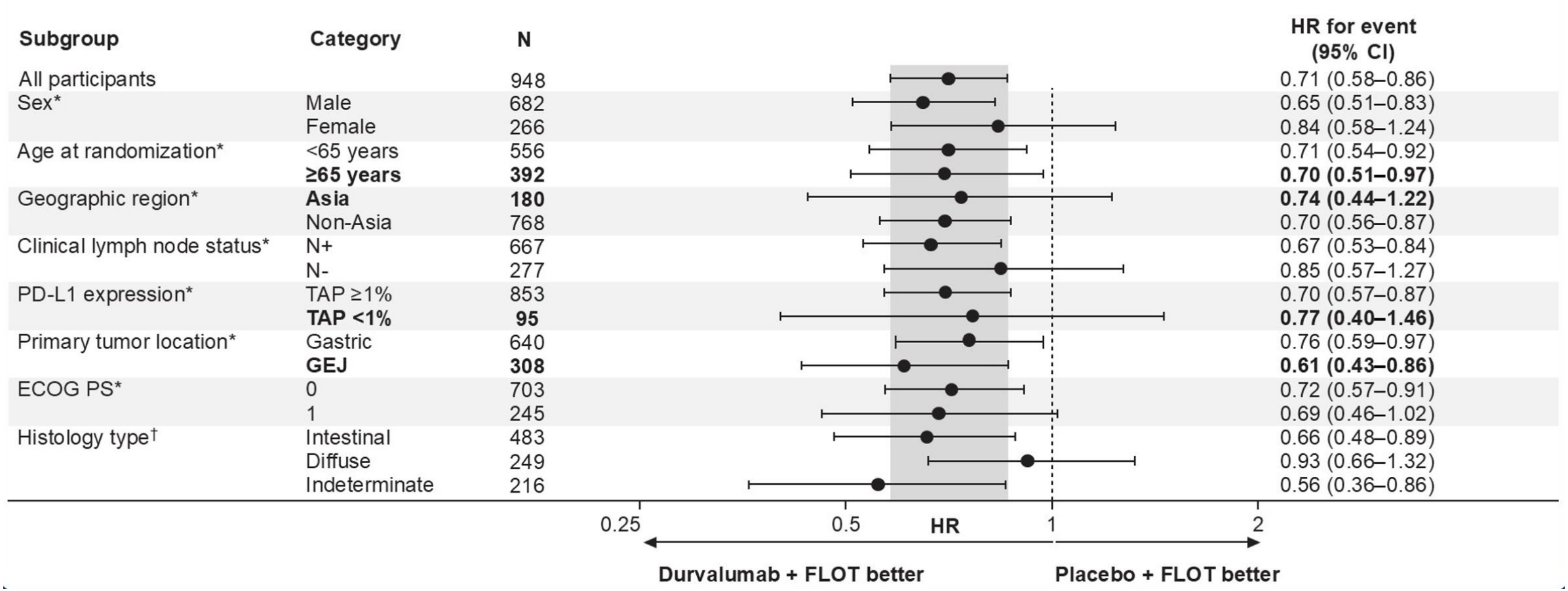
No. of participants at risk																		Total events
Durvalumab + FLOT	474	436	404	381	351	334	320	307	288	234	187	107	88	33	20	2	1	0	167
Placebo + FLOT	474	429	392	360	329	302	278	264	249	202	160	89	65	26	21	2	1	0	218

KEY DATA

MATTERHORN: neoadjuvant/adjuvant FLOT +/- durvalumab

Event Free Survival in Key Subgroups

Subgroup	Category	N	HR for event (95% CI)
All participants		948	0.71 (0.58–0.86)
Sex*	Male	682	0.65 (0.51–0.83)
	Female	266	0.84 (0.58–1.24)
Age at randomization*	<65 years	556	0.71 (0.54–0.92)
	≥65 years	**392**	**0.70 (0.51–0.97)**
Geographic region*	**Asia**	**180**	**0.74 (0.44–1.22)**
	Non-Asia	768	0.70 (0.56–0.87)
Clinical lymph node status*	N+	667	0.67 (0.53–0.84)
	N-	277	0.85 (0.57–1.27)
PD-L1 expression*	TAP ≥1%	853	0.70 (0.57–0.87)
	TAP <1%	**95**	**0.77 (0.40–1.46)**
Primary tumor location*	Gastric	640	0.76 (0.59–0.97)
	GEJ	**308**	**0.61 (0.43–0.86)**
ECOG PS*	0	703	0.72 (0.57–0.91)
	1	245	0.69 (0.46–1.02)
Histology type†	Intestinal	483	0.66 (0.48–0.89)
	Diffuse	249	0.93 (0.66–1.32)
	Indeterminate	216	0.56 (0.36–0.86)



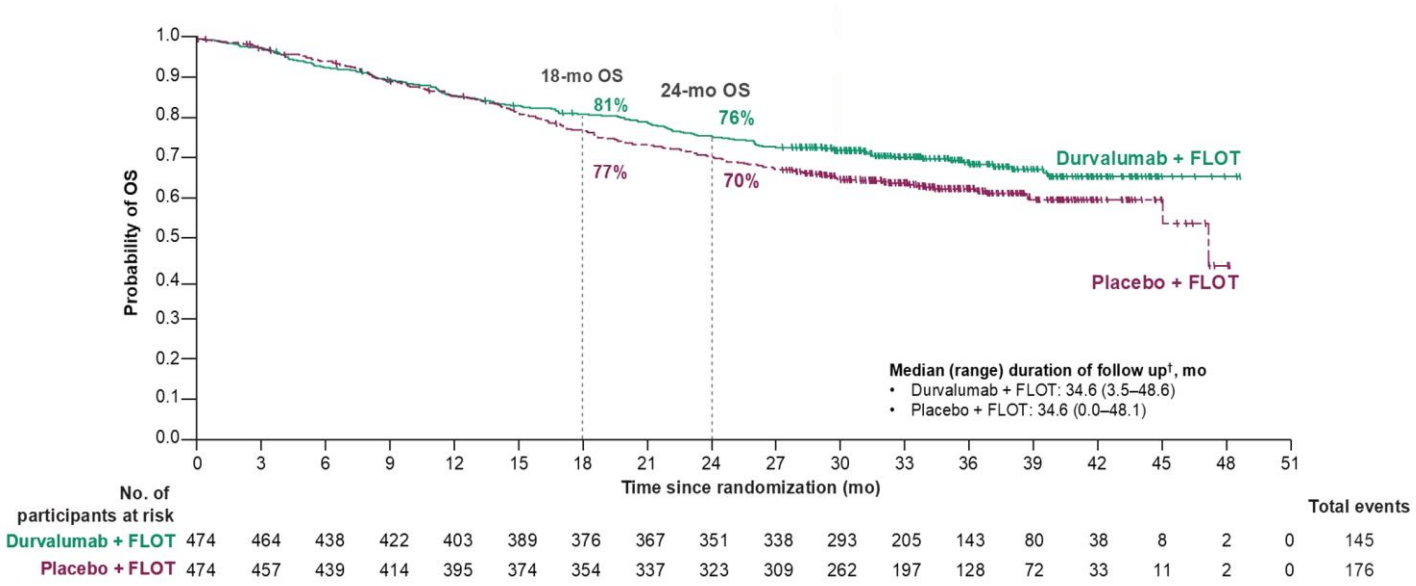
*Pre-specified per protocol. †Assessed post hoc per local laboratory

KEY DATA

MATTERHORN: neoadjuvant/adjuvant FLOT +/- durvalumab

Key Secondary Endpoints

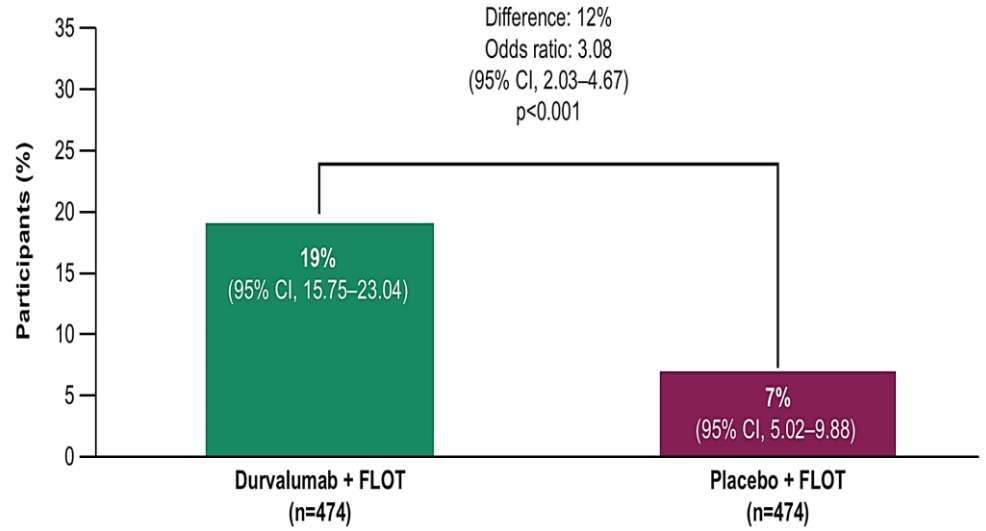
Overall Survival



	Durvalumab + FLOT (n = 474)	Placebo + FLOT (n = 474)
Median OS (95% CI), mo	NR (NR-NR)	47.2 (45.1-NR)
▪ HR (95% CI)	0.78 (0.62-0.97)	
▪ Stratified log-rank P	.025*	

*significance threshold *P* <.0001

pCR

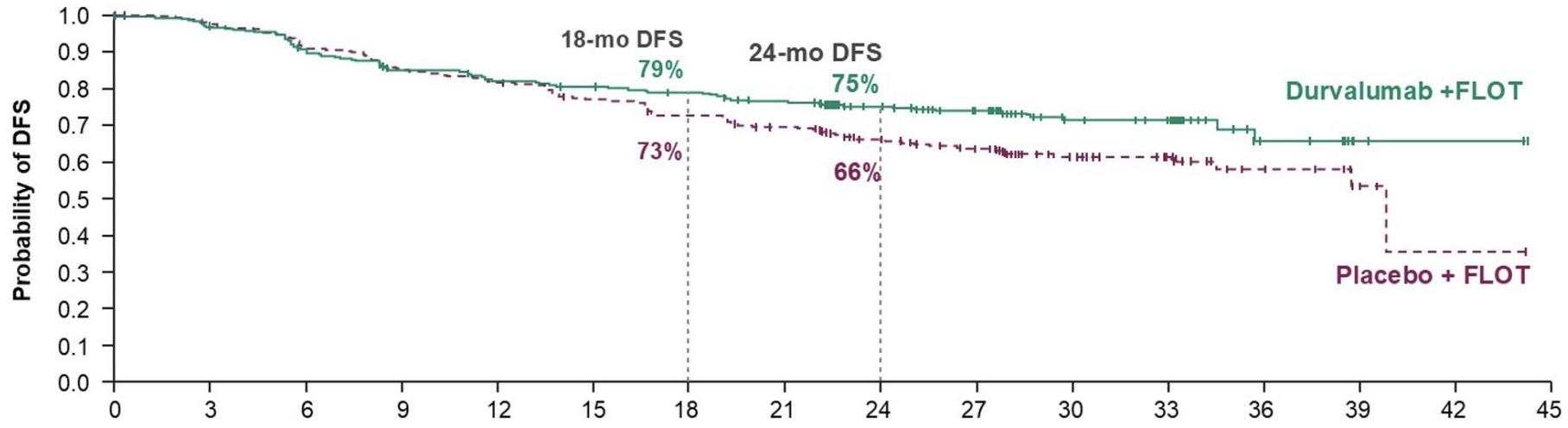


KEY DATA

MATTERHORN: neoadjuvant/adjuvant FLOT +/- durvalumab

Secondary Endpoint: Disease-Free Survival (DFS)

	Durvalumab + FLOT (n=339)	Placebo + FLOT (n=323)
Median DFS (95% CI), mo	**NR (NR–NR)**	**39.8 (38.7–NR)**
HR (95% CI)	**0.70 (0.53–0.93)**	



No. of participants at risk																	Total events
Durvalumab + FLOT	339	327	305	283	272	265	258	244	184	168	81	74	19	3	2	0	90
Placebo + FLOT	323	315	293	275	262	245	230	217	157	142	72	56	23	4	2	0	119

KEY DATA

MATTERHORN: neoadjuvant/adjuvant FLOT +/- durvalumab

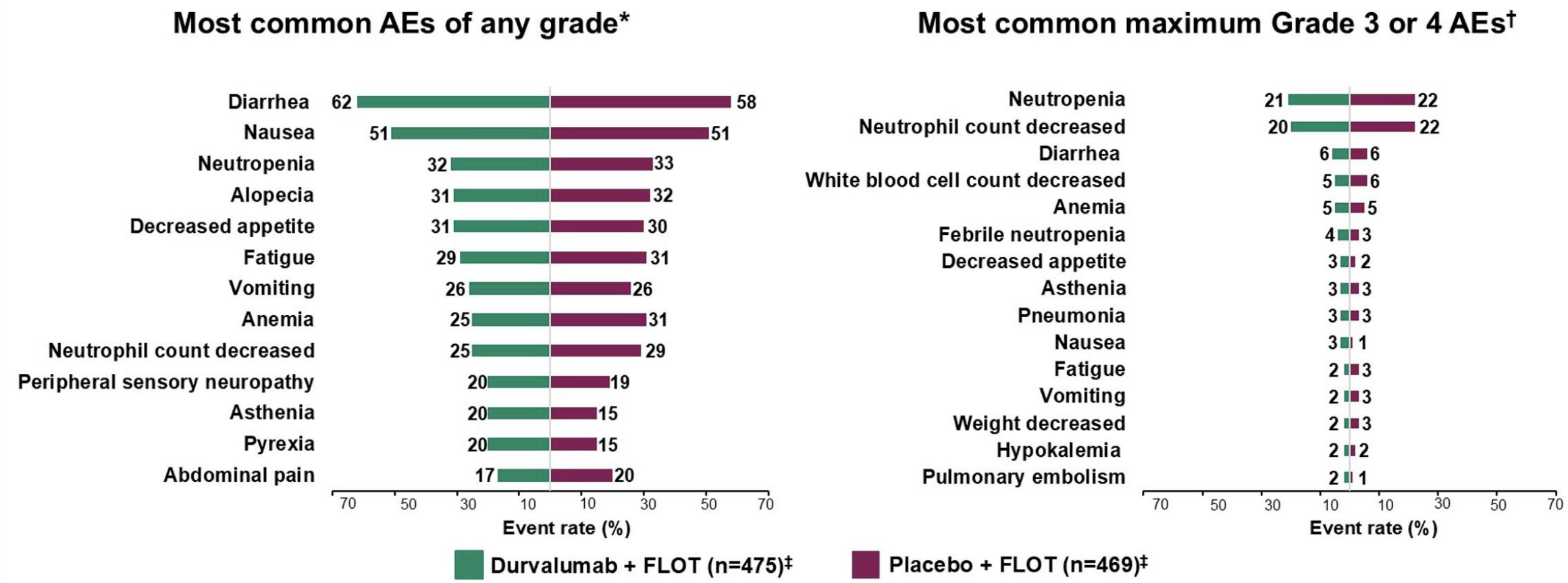
Safety

	Durvalumab + FLOT (n = 475)	Placebo + FLOT (n = 469)
Any grade AEs	**99%**	**99%**
• Possibly related to any study treatment	95%	95%
Grade 3 or 4 AEs	**72%**	**71%**
• Possibly related to any study treatment	60%	59%
Serious AE	**48%**	**44%**
AE Leading to discontinuation of any study treatment	**30%**	**23%**
Durvalumab or placebo	10%	6%
Any FLOT	25%	20%
AE with outcome of death	**5%**	**4%**
• Possibly related to durvalumab or placebo	1%	<1%
• Possibly related to FLOT	1%	<1%
ImAE (any grade)*	**23%**	**7%**
Grade 3 or 4 immune-mediated AE	7%	4%
Any AE leading to surgery not being performed	**1%**	**<1%**
Any AE leading to a delay in surgery†	**2%**	**3%**

*Excludes AEs of special interest group of infusion or hypersensitivity reactions. †A surgical delay is defined as surgery occurring >8 weeks (56 days) after the last dose of neoadjuvant treatment.

MATTERHORN: neoadjuvant/adjuvant FLOT +/- durvalumab

Common AEs



*AEs of any grade occurred in ≥20% of participants in any treatment group. †Grade 3 or 4 AEs occurred in ≥2% of any treatment group. ± Safety analysis set (participants who received at least one dose of study treatment); one participant in the placebo + FLOT group received a single dose of durvalumab and is, therefore, included in the durvalumab + FLOT group for the safety analysis.

SUMMARY

MATTERHORN

IMPACT

- The addition of durvalumab to neoadjuvant/adjuvant FLOT could be a new treatment option for patients with localized gastric and GEJ cancers
  - Significant improvement in EFS (HR: 0.71; 95% CI: 0.58-0.86, P <.001), consistent across subgroups
  - Increased pCR: 19% vs 7% (OR: 3.08; 95% CI: 2.03-4.67; P <.001)
- EFS benefit was consistent across subgroups and geographic regions
- Rates of AEs were expected, no new safety concerns were identified
- Early OS data trending positive (HR 0.78)
  - Final OS analysis pending; 33.9% maturity at interim analysis

Neoadjuvant/adjuvant durvalumab with chemotherapy (FLOT) benefits patients with localized gastric and GEJ adenocarcinoma and could be a new treatment option

Not yet FDA approved

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2025 ASCO Key Studies

Breast Cancer

- RAPID REVIEWS
  - *SERENA-6
  - DESTINY-Breast09
  - DESTINY-Breast06
  - AI for IHC HER2 Pathology
  - ASCENT-03
  - ASCENT-04
  - VERITAC-2
  - INAVO120
  - CompassHER2 pCR

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- DESTINY-Gastric04
- ***RAPID REVIEWS***
  - BREAKWATER
  - PANOVA-3
  - AMPLITUDE

Other Notable Studies

- *NIVOPOSTOP
- KEYNOTE-689
- *VERIFY
- ***RAPID REVIEWS***
  - TROPION-Lung02
  - DELPHI-304
  - IMforte
  - TUXEDO-3
  - ROSELLA

* Plenary Session

cornerstone specialty network™

CLINICAL QUESTION

DESTINY-Gastric04

Does trastuzumab deruxtecan (T-DXd) improve outcomes compared to ramucirumab plus paclitaxel in patients with HER2+ metastatic gastric or gastroesophageal junction adenocarcinoma (GC/GEJA) in the second-line setting?

On January 15, 2021, the FDA approved fam-trastuzumab deruxtecan-nxki (Enhertu, Daiichi Sankyo) for adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen based on the phase 2 DESTINY-Gastric01 trial.

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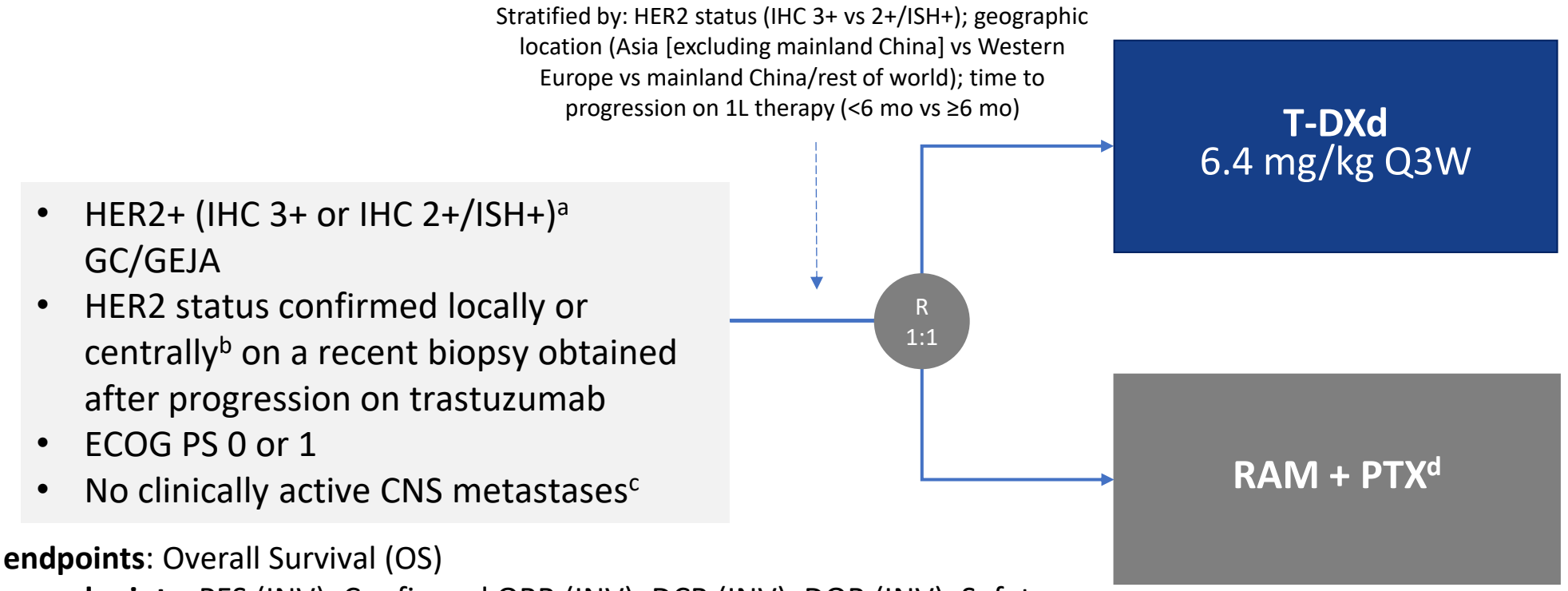
ASCO 2025. Abstr. LBA4002

KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

Study Design: Global, multicenter, randomized, phase 3 trial



Primary endpoints: Overall Survival (OS)
Secondary endpoints: PFS (INV), Confirmed ORR (INV), DCR (INV), DOR (INV), Safety
Exploratory endpoints: PROs

[a]As classified by the 2017 ASCO-CAP guidelines for HER2 testing in gastroesophageal adenocarcinoma. [b]Study protocol originally mandated HER2 status be determined centrally but was later amended to allow local determination. [c]Clinically active CNS metastases were defined as being untreated and symptomatic or requiring therapy with corticosteroids or anticonvulsants. Patients with clinically inactive CNS metastases could be enrolled. [d]RAM administered as 8 mg/kg on days 1 and 15of reach 28-day cycle and PTX administered as 80 mg/m^2 on days 1, 8, and 15 of 28-day cycle.

KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

Baseline characteristics

	T-DXd (n = 246)	RAM + PTX (n = 248)
Age, median (range), years	63.2 (21.1-84.1)	64.3 (31.9-87.0)
Male, n	187 (76.0%)	205 (82.7%)
Geography,[a] n		
• Asia (ex-China)	57 (23.2%)	60 (24.2%)
• Western Europe	140 (56.9%)	139 (56.0%)
• Other*	49 (19.9%)	49 (19.8%)
Race, n		
• White	116 (47.2%)	130 (52.4%)
• Black	0	2 (0.8%)
• Asian	101 (41.1%)	97 (39.1%)
• Other	28 (11.4%)	19 (7.7%)
ECOG PS		
• 0/1	39.4%/60.2%	35.5%/63.7%
• 2/missing	0.4%/0%	0.4%/0.4%
Primary tumor location, n		
• Gastric	153 (62.2%)	149 (60.1%)
• GEJ	93 (37.8%)	99 (39.9%)

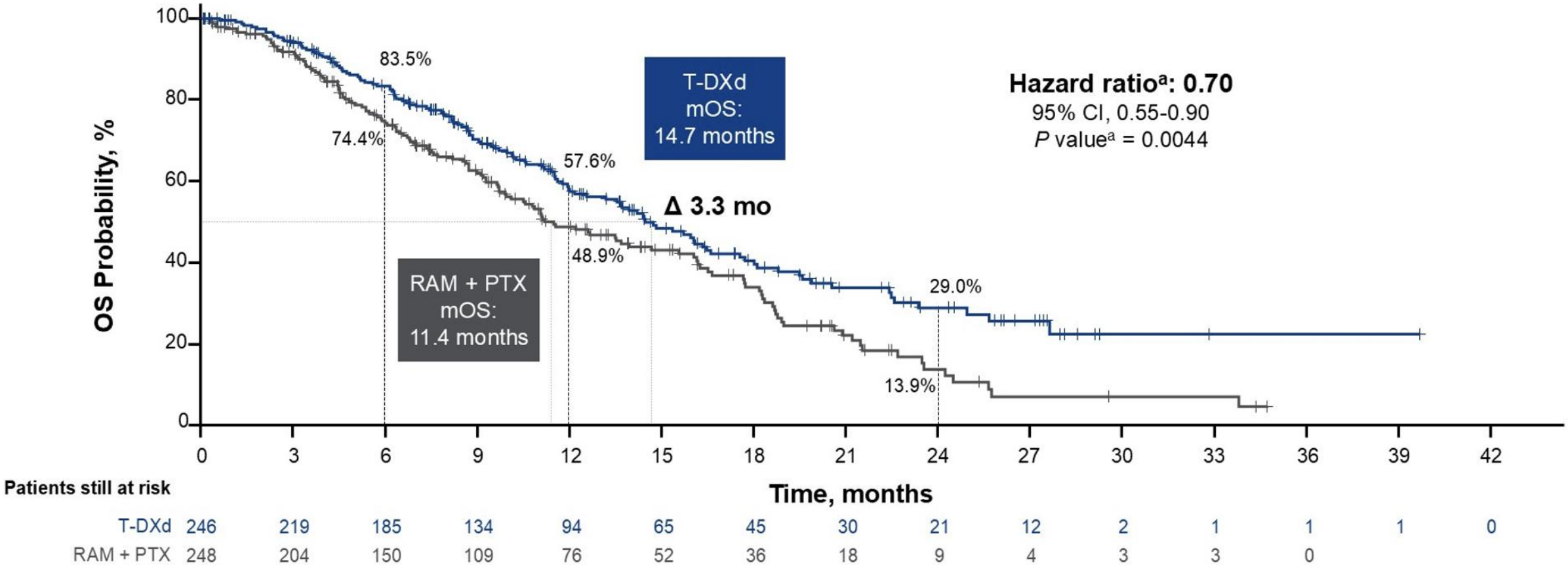
	T-DXd (n = 246)	RAM + PTX (n = 248)
HER2 status,[a,b] n		
• IHC 2+/ISH+	39 (15.9%)	40 (16.1%)
• IHC 3+	207 (84.1%)	208 (83.9%)
TTP on 1L therapy,[a] n		
• <6 mo	61 (24.8%)	61 (24.6%)
• ≥6 mo	185 (75.2%)	187 (75.4%)
Prior treatment with ICI, n	39 (15.9%)	38 (15.3%)
Metastatic sites, n		
• <2	73 (29.7%)	75 (30.2%)
• ≥2	173 (70.3%)	173 (69.8%)
Liver metastases, n	147 (59.8%)	158 (63.7%)
Brain metastases, n	16 (6.5%)	18 (7.3%)

[a]Stratification factor by interactive response therapy. [b]Local or central HER2 status.

KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

Primary Endpoint: Overall Survival (OS)

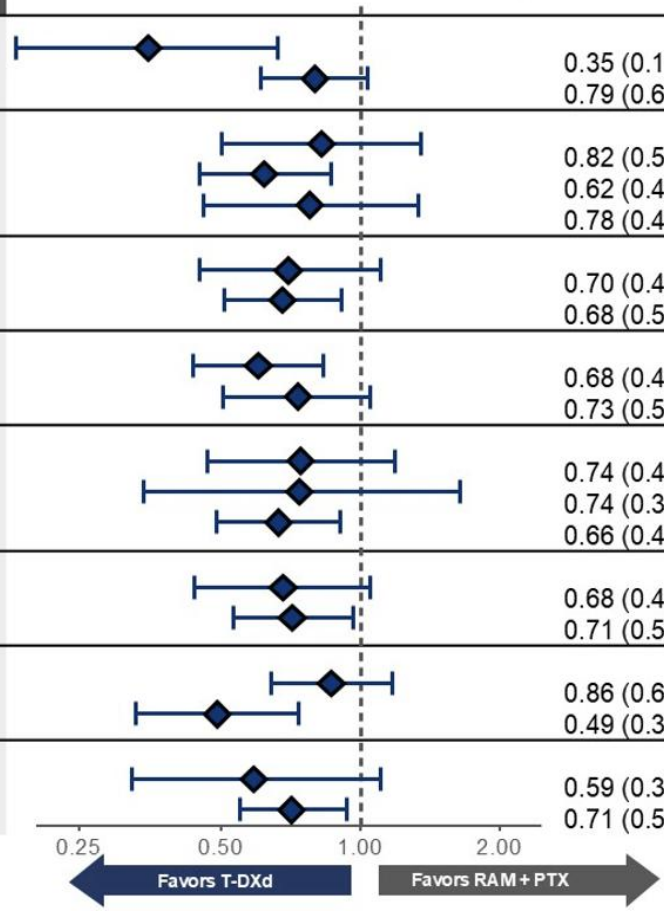


KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

Overall Survival by Subgroups

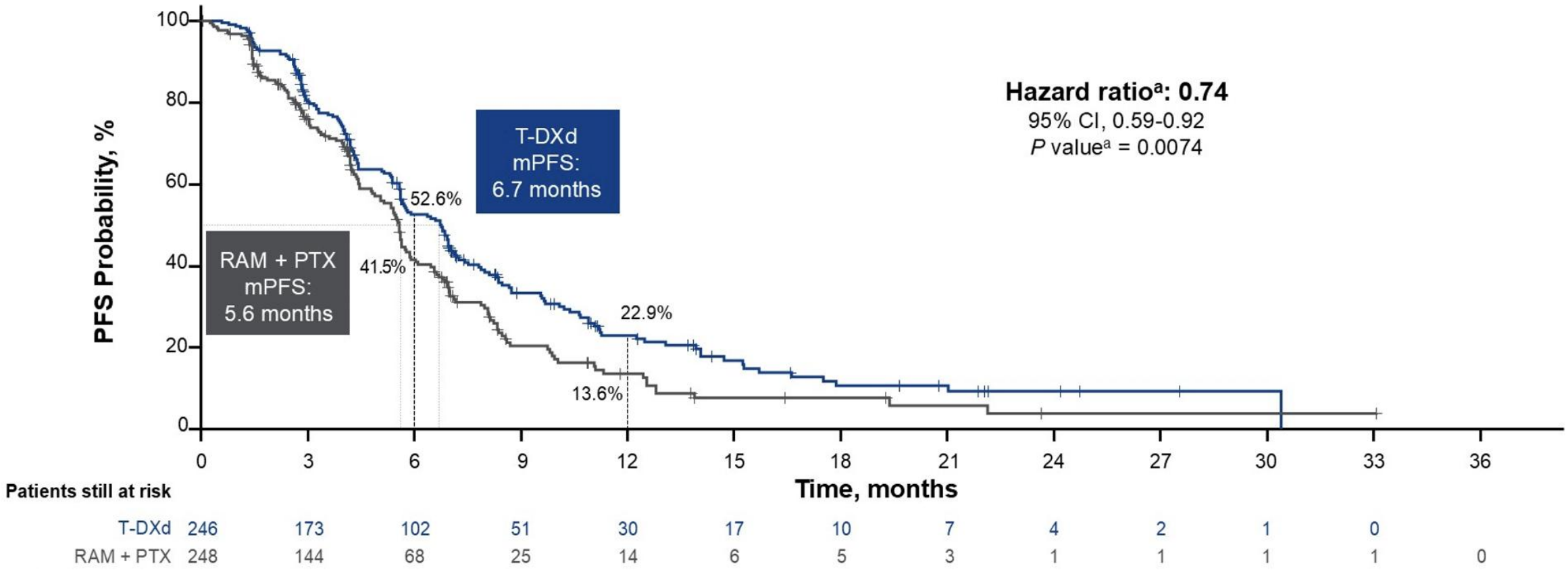
	No. of Events/No. of Patients		OS, median (95% CI), months		Hazard Ratio (95% CI)
	T-DXd	RAM + PTX	T-DXd	RAM + PTX	
HER2 IHC status					
IHC 2+/ISH+	17/39	25/40	17.7 (9.1-NE)	7.4 (4.5-10.7)	0.35 (0.18-0.66)
IHC 3+	107/207	117/208	14.4 (11.9-16.4)	13.4 (10.8-16.5)	0.79 (0.61-1.03)
Geography					
Asia (excluding China)	31/57	34/60	14.4 (10.5-19.4)	16.1 (10.8-18.9)	0.82 (0.50-1.34)
Western Europe	67/140	79/139	15.7 (11.9-18.8)	11.1 (8.7-15.5)	0.62 (0.45-0.86)
Mainland China/ROW	26/49	29/49	14.8 (8.7-NE)	9.7 (7.4-16.0)	0.78 (0.46-1.33)
Time to progression on 1L					
<6 months	38/61	38/61	10.2 (8.1-14.4)	7.3 (5.0-10.1)	0.70 (0.45-1.10)
≥6 months	86/185	104/187	16.3 (13.7-19.4)	13.5 (11.0-17.6)	0.68 (0.51-0.91)
Age					
<65 years	69/140	75/130	15.7 (12.1-18.1)	11.1 (9.6-16.1)	0.68 (0.49-0.94)
≥65 years	55/106	67/118	13.7 (10.5-17.5)	11.5 (8.9-16.6)	0.73 (0.51-1.05)
Histologic subtype					
Intestinal	35/69	38/66	16.6 (11.5-20.5)	12.6 (9.9-18.3)	0.74 (0.47-1.18)
Diffuse	15/25	11/19	9.4 (7.9-16.0)	8.7 (4.6-16.1)	0.74 (0.34-1.64)
Others	74/152	93/163	14.7 (11.9-19.4)	11.1 (9.2-16.1)	0.66 (0.49-0.90)
ECOG PS					
0	38/97	45/88	18.1 (13.1-27.6)	17.6 (12.6-20.6)	0.68 (0.44-1.05)
1 or 2	86/149	96/159	13.9 (10.2-16.0)	9.9 (7.7-11.4)	0.71 (0.53-0.96)
Primary tumor location					
Gastric	83/153	83/149	11.9 (10.1-14.8)	11.4 (9.6-16.1)	0.86 (0.64-1.17)
GEJA	41/93	59/99	18.0 (14.7-22.5)	11.5 (9.2-16.2)	0.49 (0.33-0.74)
Prior treatment with ICI					
Yes	18/39	24/38	16.3 (10.2-NE)	10.1 (7.4-18.6)	0.59 (0.32-1.10)
No	106/207	118/210	14.4 (11.9-17.5)	12.6 (9.9-16.1)	0.71 (0.55-0.93)



KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

Key Secondary Endpoints: PFS

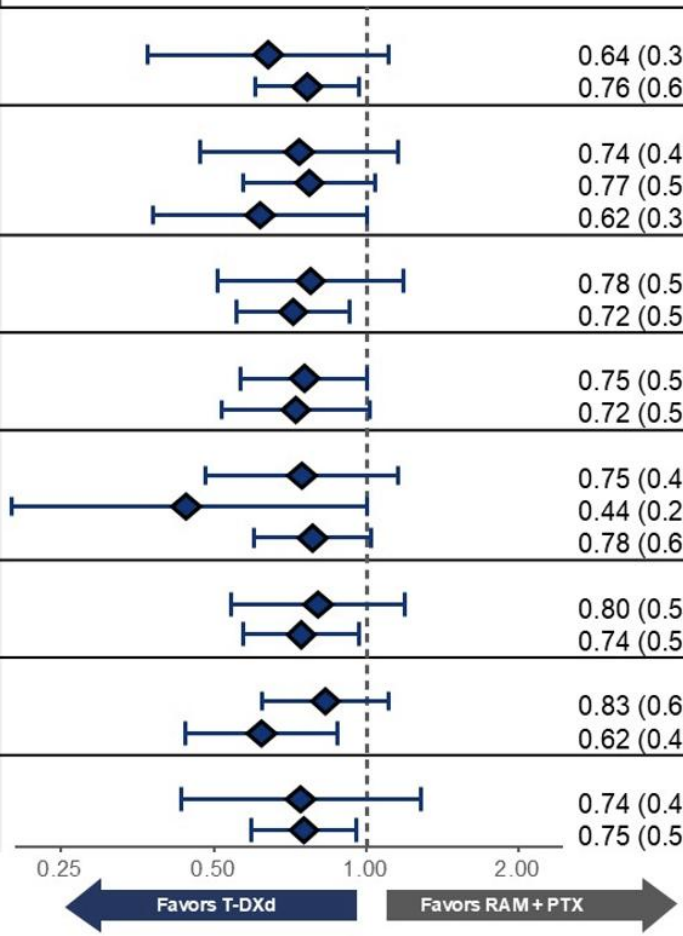


KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

PFS by Subgroups

	No. of Events/No. of Patients		PFS, median (95% CI), months		Hazard Ratio (95% CI)
	T-DXd	RAM + PTX	T-DXd	RAM + PTX	
HER2 IHC status					
IHC 2+/ISH+	27/39	27/40	4.4 (3.0-9.7)	3.6 (2.4-5.4)	0.64 (0.37-1.11)
IHC 3+	139/207	129/208	6.7 (5.6-7.1)	5.6 (5.1-6.4)	0.76 (0.60-0.97)
Geography					
Asia (excluding China)	39/57	37/60	6.9 (4.4-10.9)	5.4 (4.0-8.1)	0.74 (0.47-1.16)
Western Europe	94/140	83/139	5.9 (5.6-6.9)	5.6 (4.8-5.9)	0.77 (0.57-1.04)
Mainland China/ROW	33/49	36/49	7.2 (4.2-9.6)	5.6 (4.4-7.0)	0.62 (0.38-1.00)
Time to progression on 1L					
<6 months	49/61	41/61	5.4 (4.0-5.7)	4.2 (2.8-5.0)	0.78 (0.51-1.18)
≥6 months	117/185	115/187	6.9 (5.9-8.1)	5.6 (5.4-6.6)	0.72 (0.55-0.93)
Age					
<65 years	96/140	86/130	6.8 (5.7-7.5)	5.6 (4.2-6.4)	0.75 (0.56-1.00)
≥65 years	70/106	70/118	5.7 (5.3-7.8)	5.6 (4.8-6.5)	0.72 (0.52-1.01)
Histologic subtype					
Intestinal	47/69	36/66	6.3 (5.1-8.7)	4.9 (4.2-5.6)	0.75 (0.48-1.67)
Diffuse	13/25	13/19	6.9 (5.6-14.0)	4.2 (2.6-8.0)	0.44 (0.20-1.00)
Others	106/152	107/163	6.7 (5.6-7.2)	5.6 (5.3-6.5)	0.78 (0.60-1.02)
ECOG PS					
0	63/97	43/88	6.9 (5.6-8.3)	6.0 (4.4-7.9)	0.80 (0.54-1.19)
1 or 2	103/149	113/159	6.3 (5.1-7.0)	5.5 (4.4-5.7)	0.74 (0.57-0.97)
Primary tumor location					
Gastric	102/153	86/149	5.9 (5.1-7.4)	5.6 (4.4-6.8)	0.83 (0.62-1.10)
GEJA	64/93	70/99	6.9 (5.7-8.0)	5.5 (4.4-5.8)	0.62 (0.44-0.88)
Prior treatment with ICI					
Yes	28/39	27/38	7.2 (4.4-9.6)	5.4 (4.2-8.1)	0.74 (0.43-1.27)
No	138/207	129/210	6.4 (5.6-7.0)	5.6 (4.8-5.8)	0.75 (0.59-0.95)



KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

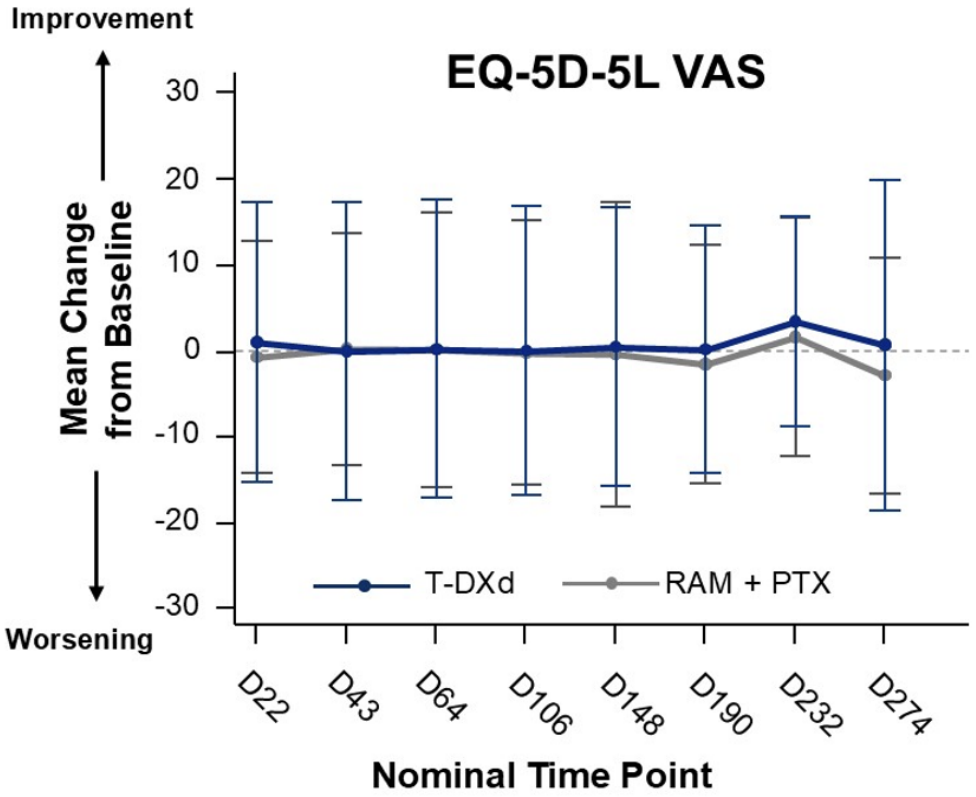
Key Secondary Endpoints: Confirmed ORR and DOR

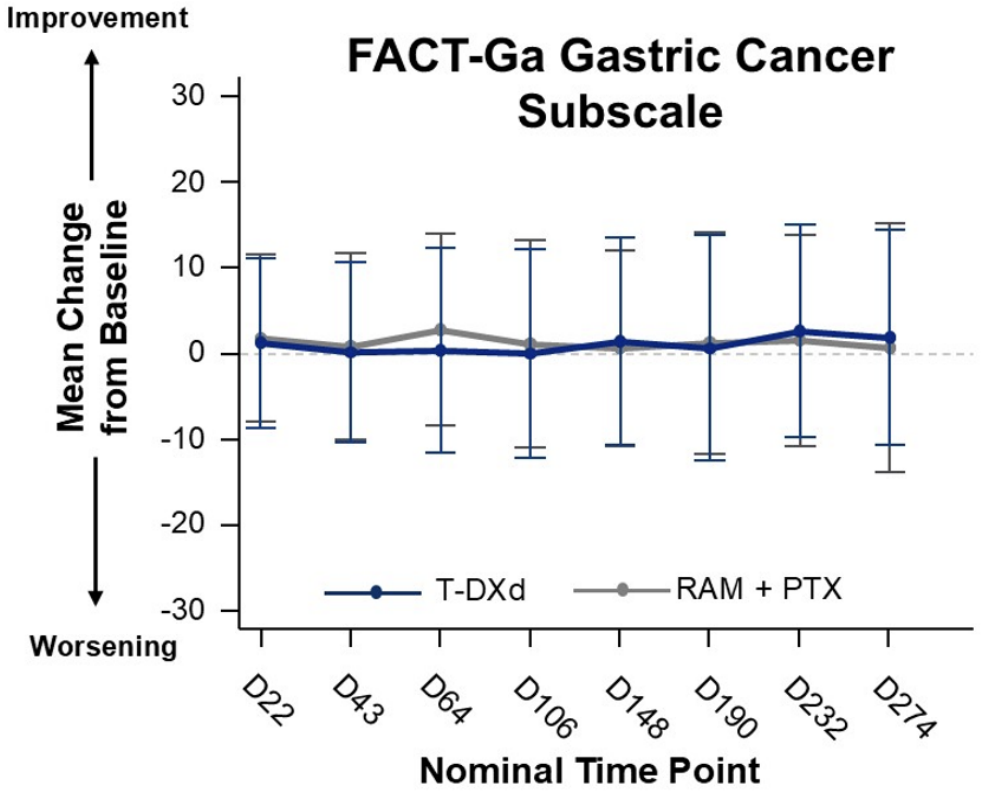
	T-DXd (n = 246)	RAM + PTX (n = 248)
Confirmed ORR (95% CI)	**44.3% (37.8-50.9)**	**29.1% (23.4-35.3)**
• P value • Difference (95% CI)	0.0006 15.1% (6.1-24.2)	
DOR, median (95% CI), mo	**7.4 (5.7-10.1)**	**5.3 (4.1-5.7)**
DCR (95% CI)	**91.9% (87.7-95.1)**	**75.9% (70.0-81.2)**
Confirmed BOR, n		
• CR	7 (3.0%)	3 (1.3%)
• PR	97 (41.3%)	66 (27.8%)
• SD	112 (47.7%)	111 (46.8%)
• PD	13 (5.5%)	22 (9.3%)
• NE	6 (2.6%)	35 (14.8%)

KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

Exploratory endpoint: Patient-Reported Outcomes





D, day; EQ-5D-5L, EuroQol 5-Dimension, 5-Level; FACT-Ga, Functional Assessment of Cancer Therapy-gastric; HRQOL, health-related quality of life; PTX, paclitaxel; RAM, ramucirumab; T-DXd, trastuzumab deruxtecan; VAS, visual analog scale.
[a]Median treatment duration was 5.4 months with T-DXd and 4.6 months with RAM + PTX. [b]Baseline completion rates for the EQ-5D-5L VAS and FACT-GA subscale were 98.2% and 99.1%, respectively, in the T-DXd arm, and 99.5% and 97.5% in the RAM + PTX arm. [c]Results for an arm were no longer considered informative once the number of patients who had the specified visit dropped below 10%, which occurred after D274. [d]Defined as a ≥10 point change from baseline.

KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

Safety Summary

	T-DXd (n = 244)	RAM + PTX (n = 233)
Any TEAE, n	244 (100%)	228 (97.9%)
• Drug related	227 (93.0%)	213 (91.4%)
Grade ≥3 TEAEs, n	166 (68.0%)	172 (73.8%)
• Drug related	122 (50.0%)	126 (54.1%)
Serious TEAEs, n	100 (41.0%)	101 (43.3%)
• Drug related	45 (18.4%)	41 (17.6%)
TEAEs associated with dose discontinuation, n	35 (14.3%)	40 (17.2%)
• Drug related	28 (11.5%)	31 (13.3%)
TEAEs associated with dose interruption, n	137 (56.1%)	141 (60.5%)
• Drug related	94 (38.5%)	119 (51.1%)
TEAEs associated with dose reduction, n	77 (31.6%)	87 (37.3%)
• Drug related	76 (31.1%)	84 (36.1%)
TEAEs associated with death, n	22 (9.0%)	35 (15.0%)
• Drug related[a]	4 (1.6%)	2 (0.9%)

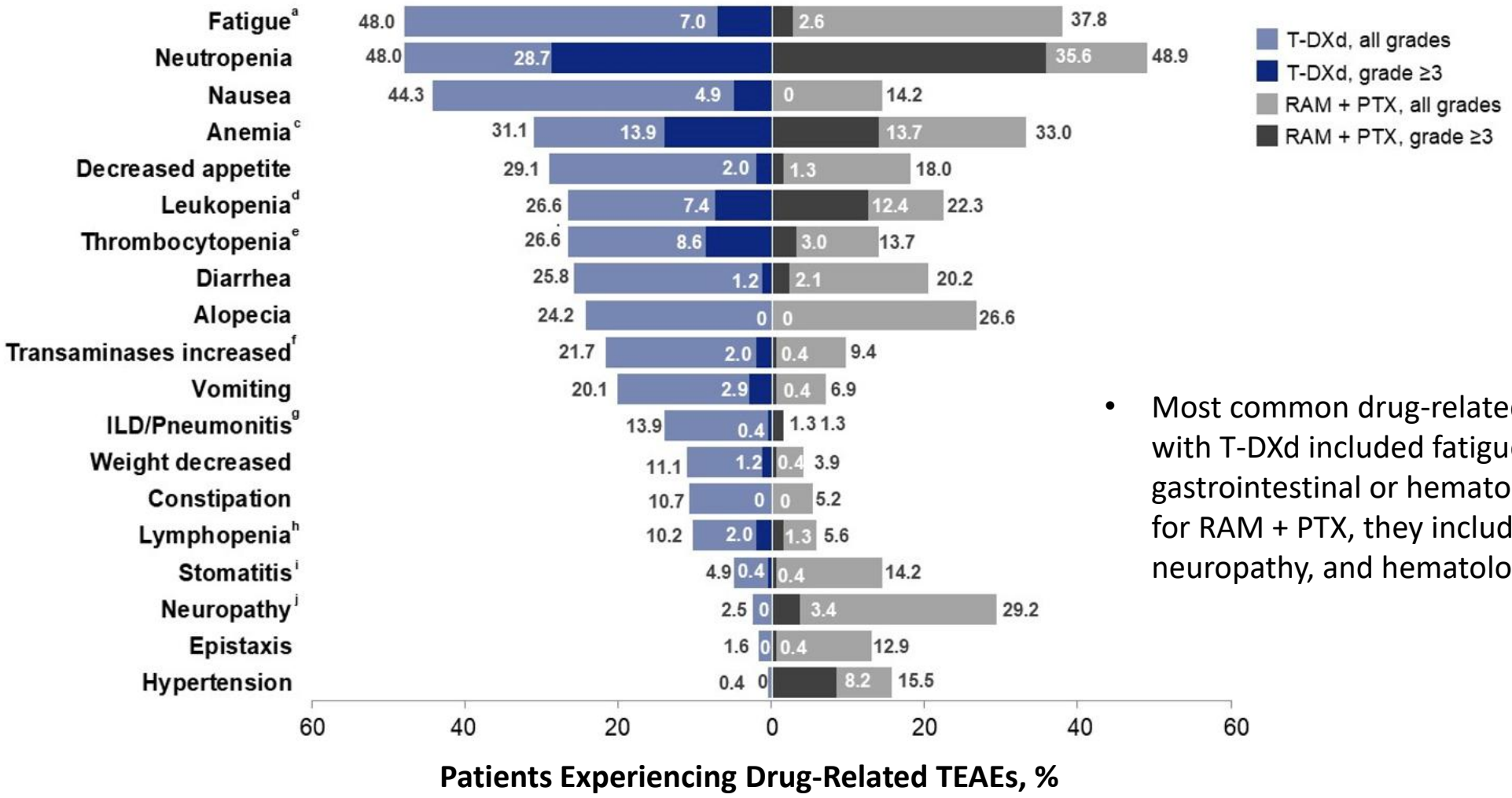
- Median treatment duration:
  - **T-DXd:** 5.4 mo (range, 0.7-30.3 mo)
  - **RAM + PTX:** 4.6 mo (range, 0.9-34.9 mo)
- Similar incidence of the drug-related grade ≥3 TEAEs, serious TEAEs, treatment discontinuations, and deaths were observed in the 2 arms

[a]Drug-related adverse events that were associated with death occurred in 4 patients (1.6%) who received T-DXd (upper gastrointestinal hemorrhage, intestinal obstruction, sudden death, and death not otherwise specified in 1 patient each) and in 2 patients (0.9% who received RAM + PTX (gastric perforation and ILD in 1 patient each).

KEY DATA

DESTINY-Gastric04: Phase 3 of T-DXd vs Ramucirumab + Paclitaxel in 2L

Drug-Related TEAEs in ≥10% of Patients



- Most common drug-related TEAEs with T-DXd included fatigue or AEs of gastrointestinal or hematologic nature; for RAM + PTX, they included fatigue, neuropathy, and hematologic AEs

SUMMARY

DESTINY-Gastric04

IMPACT

- DESTINY-Gastric04 is the first phase 3 trial of ENHERTU in HER2-positive advanced gastric cancer
- T-DXd demonstrated a statistically significant and clinically meaningful improvement in OS compared with RAM + PTX in patients with HER2+ metastatic GC/GEJA in the 2L setting
  - Median OS: 14.7 vs 11.4 mo (HR: 0.70; *P* = 0.0044)
  - Improvement also noted in PFS, confirmed ORR, DCR, and DoR with T-DXd vs RAM +PTX
- No new safety signals were reported and patient-reported QoL was maintained

Trastuzumab deruxtecan should be considered as a standard second-line therapy for patients with metastatic HER2-positive gastric cancer with prior progression on a trastuzumab-containing regimen

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ASCO 2025: RAPID REVIEWS

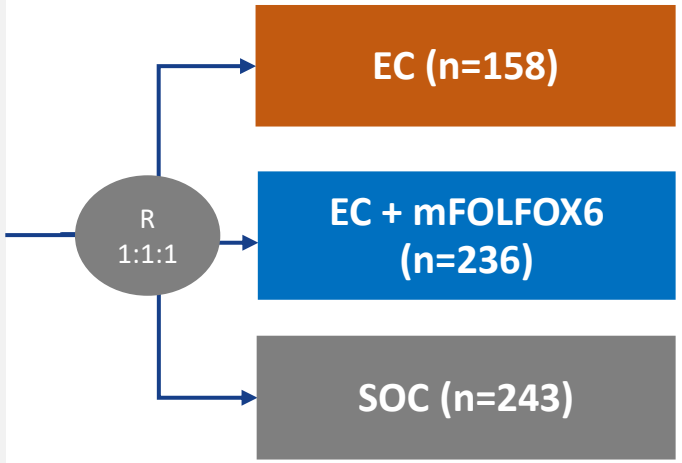
KEY DATA

BREAKWATER: 1L encorafenib + cetuximab + mFOLFOX6 PSF and updated OS analyses in BRAF V600E-mutant metastatic colorectal cancer

Study Design: Open-label, multicenter, phase 3 study

Stratified by US/Canada vs Europe vs Rest of World and ECOG PS (0 vs 1)

- Age ≥16 years (or ≥18 based on country)
- No prior systemic treatment for metastatic disease
- Measurable disease (RECIST 1.1)
- BRAF V600E-mutant mCRC by local or central laboratory testing
- ECOG PS 0 or 1
- Adequate bone marrow, hepatic, and renal function



Data cutoff: January 6, 2025

Primary endpoint: PFS by BICR, ORR by BICR

Secondary endpoints: OS

Select Baseline Characteristics

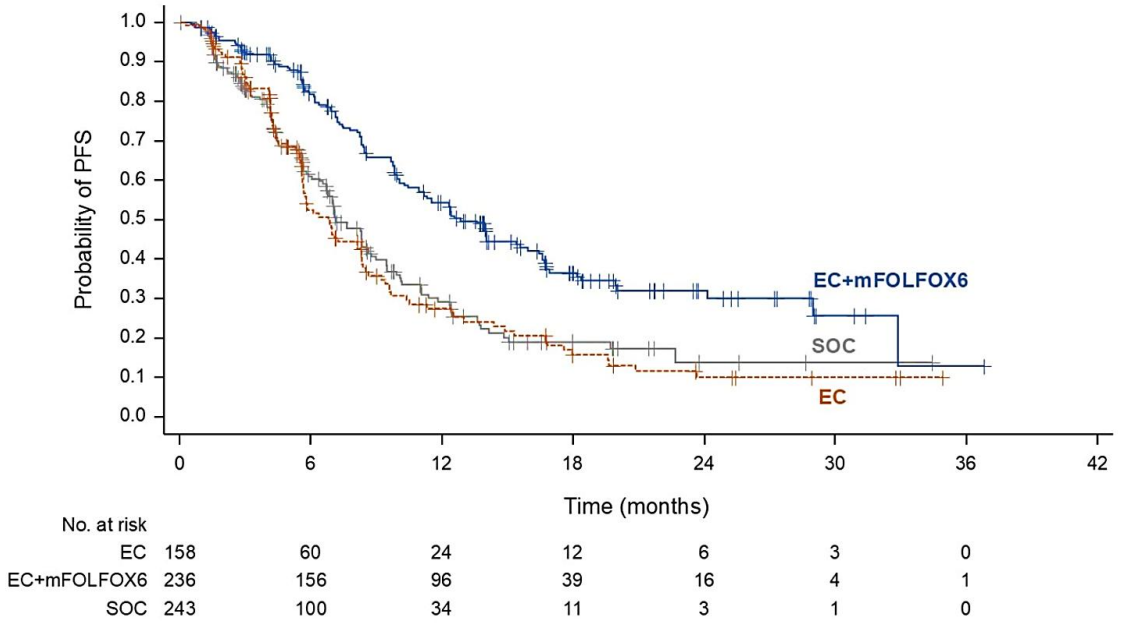
Characteristic	EC (n = 158)	EC + mFOLFOX-6 (n = 236)	SOC (n = 243)
Median age, yr (range)	59 (26-84)	60 (24-81)	62 (28-84)
ECOG PS, n			
▪ 0	79 (50.0%)	128 (54.2%)	131 (53.9%)
▪ 1	74 (46.8%)	104 (44.1%)	98 (40.3%)
No. of organs involved*			
▪ ≤2	86 (54.4%)	119 (50.4%)	127 (52.3%)
▪ ≥3	72 (45.6%)	117 (49.6%)	116 (47.7%)
Liver metastases*	94 (59.5%)	147 (62.3%)	160 (65.8%)
CEA at baseline			
▪ ≤5 µg/L	50 (31.6%)	64 (27.1%)	63 (25.9%)
▪ >5 µg/L	102 (64.6%)	167 (70.8%)	163 (67.1%)
CRP at baseline			
▪ ≤10 mg/L	91 (57.6%)	125 (53.0%)	118 (48.6%)
▪ ≥10 mg/L	61 (38.6%)	105 (44.5%)	108 (44.4%)

*Based on blind independent central review

KEY DATA

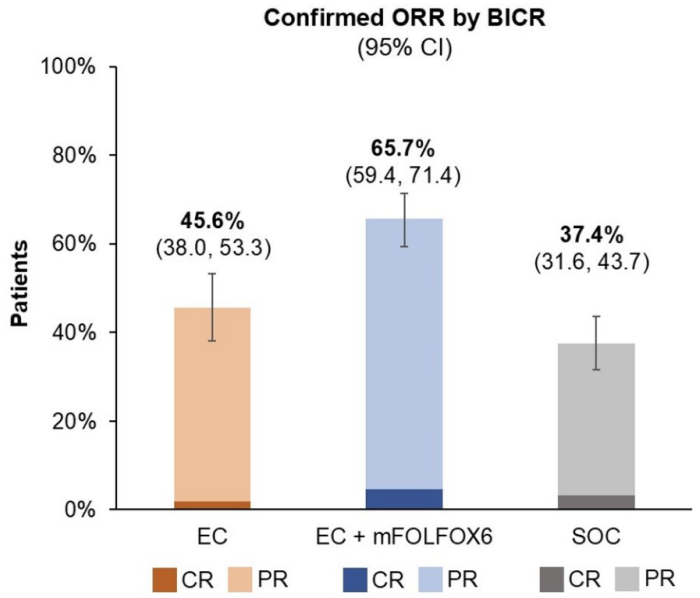
BREAKWATER: 1L encorafenib + cetuximab + mFOLFOX6, PFS and updated OS analyses in BRAF V600E-mutant metastatic colorectal cancer

Primary Endpoint: PFS by BICR



	EC N=158	EC + mFOLFOX6 n=236	SOC n=243
No. of events, n	102 (64.6%)	122 (51.7%)	132 (54.3%)
Median PFS, months (95% CI)	6.8 (5.7, 8.3)	12.8 (11.2, 15.9)	7.1 (6.8, 8.5)

Primary Endpoint: ORR by BICR



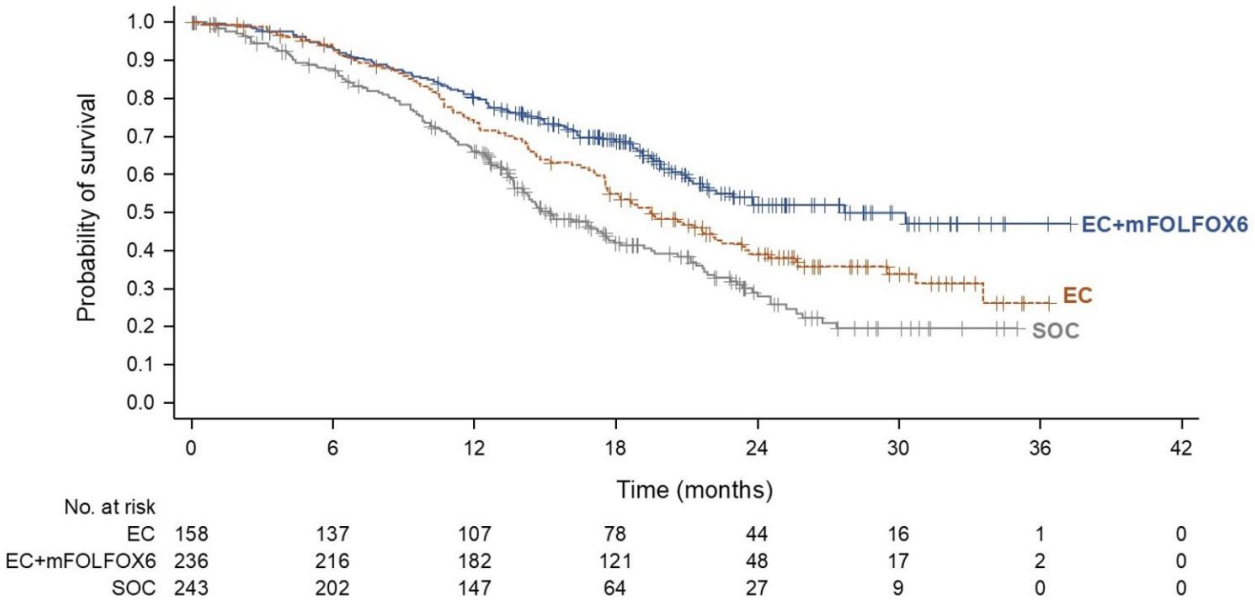
cORR, n	EC N=158	EC+mFOLFOX6 N=236	SOC N=243
CR	3 (1.9%)	11 (4.7%)	8 (3.3%)
PR	69 (43.7%)	144 (61.0%)	83 (34.2%)
SD	57 (36.1%)	50 (21.2%)	85 (35.0%)
PD	12 (7.6%)	8 (3.4%)	21 (8.6%)

	EC N=72	EC+mFOLFOX6 N=155	SOC N=91
TTR, median (range), weeks	6.6 (4.3 to 86.4)	7.0 (5.1 to 103.6)	7.3 (5.4 to 48.0)
DOR, median (95% CI), months	7.0 (4.2, 11.6)	13.9 (10.9, 18.5)	10.8 (7.6, 13.4)
Patients with a DOR of ≥6 months, n	29 (40.3%)	110 (71.0%)	38 (41.8%)
Patients with a DOR of ≥12 months, n	15 (20.8%)	54 (34.8%)	16 (17.6%)

KEY DATA

BREAKWATER: 1L encorafenib + cetuximab + mFOLFOX6 PSF and updated OS analyses in BRAF V600E-mutant metastatic colorectal cancer

Secondary Endpoints: Overall Survival



	EC N=158	EC + mFOLFOX6 n=236	SOC n=243
No. of events, n	92 (58.2%)	94 (39.8%)	148 (60.9%)
Median OS, months (95% CI)	19.5 (17.6, 22.5)	30.3 (21.7, NE)	15.1 (13.7, 17.7)

*Sepsis (preferred term).

Safety Summary	EC (n = 153)	EC + mFOLFOX-6 (n = 232)	SOC (n = 229)
Duration of treatment, median (range), weeks	27.0 (2.0-153.6)	49.8 (1.3-161.9)	25.9 (2.0-150.0)
All causality			
• TEAE	149 (97.4%)	232 (100%)	227 (99.1%)
• Grade 3 or 4 TEAE	65 (42.5%)	189 (81.5%)	153 (66.8%)
• Grade 5 TEAE	4 (2.6%)	10 (4.3%)	10 (4.4%)
• Serious TEAE	46 (30.1%)	107 (46.1%)	89 (38.9%)
• TEAE leading to permanent d/c	20 (13.1%)	62 (26.7%)	40 (17.5%)
• TEAE leading to dose reduction	16 (10.5%)	152 (65.5%)	124 (54.1%)
• TEAE leading to dose interruption	63 (41.2%)	212 (91.4%)	168 (73.4%)
Treatment-related			
• AE related to any drug	136 (88.9)	232 (100%)	272 (94.%8)
• Grade 3 or 4 TREA	24 (15.7%)	177 (76.3%)	134 (58.5%)
• Grade 5	0	0	1 (0.4)*
• Serious AE related to any drug	10 (6.5%)	45 (19.4%)	50 (21.8%)

EC + mFOLFOX6 is practice-changing 1L therapy as a new SOC for BRAF V600E-mutant mCRC

On December 20, 2024, the FDA granted accelerated approval to encorafenib (Braftovi, Array BioPharma Inc., a subsidiary of Pfizer Inc.) with cetuximab and mFOLFOX6 for patients with metastatic colorectal cancer (mCRC) with a BRAF V600E mutation, as detected by an FDA-approved test.

ASCO 2025: RAPID REVIEWS

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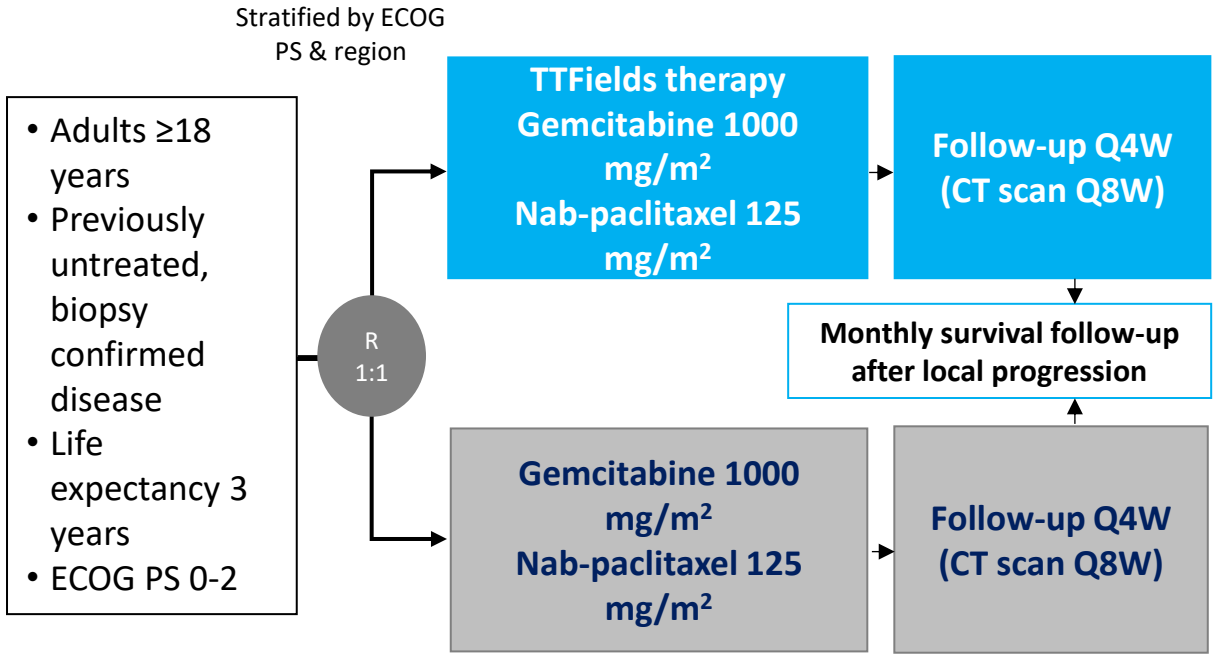
KEY DATA

PANOVA-3: Phase 3 study of Tumor Treating Fields (TTFields) with gemcitabine and nab-paclitaxel (GnP) for locally advanced pancreatic adenocarcinoma (LA-PAC)

Study Design: Phase 3 study



Primary endpoint: OS

Secondary endpoints: PFS, local PFS, pain-free survival, 1-yr survival rate, ORR, safety

Enrollment: March 2018 – March 2023
Data cutoff: October 16, 2024

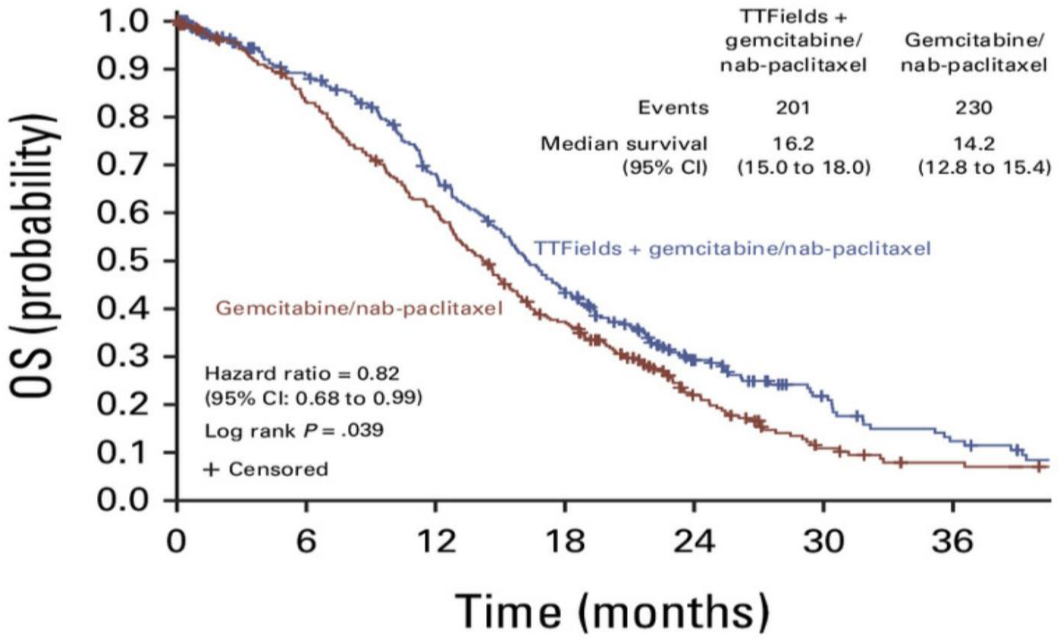
Select Baseline Characteristics

	TTFields + GnP (n=285)	GnP (n = 286)	Overall (n=571)
Median age (range), years	67 (31, 90)	67.5 (40, 88)	67 (31, 90)
Gender, n			
• Male	147 (51.6%)	125 (43.7%)	272 (47.6%)
• Female	138 (48.4%)	161 (56.3%)	299 (52.4%)
ECOG PS, n			
• 0	109 (38.2%)	111 (38.8%)	220 (38.5%)
• 1	166 (58.2%)	163 (57.0%)	329 (57.6%)
• 2	10 (3.5%)	12 (4.2%)	22 (3.9%)
CA 19-9, n			
• Normal (≤37 U/mL)	48 (16.8%)	44 (15.4%)	92 (16.1%)
• Elevated (38-1,000 U/mL)	140 (49.1%)	152 (53.1%)	292 (51.1%)
• High (>1,000 U/mL)	88 (30.9%)	79 (27.6%)	167 (29.2%)
• Untested	9 (3.2%)	11 (3.8%)	20 (3.5%)

KEY DATA

PANOVA-3: Phase 3 study of Tumor Treating Fields (TTFields) with gemcitabine and nab-paclitaxel (GnP) for locally advanced pancreatic adenocarcinoma (LA-PAC)

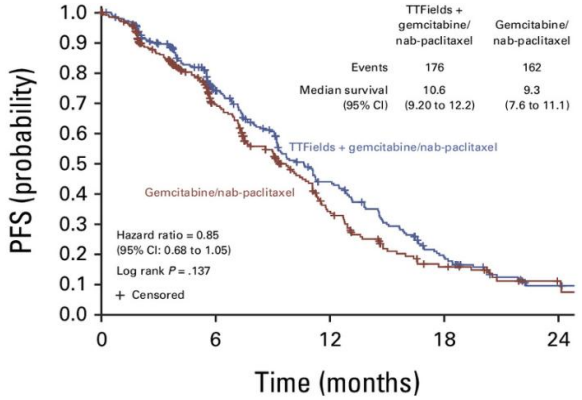
Primary Endpoint: OS



Number at risk:

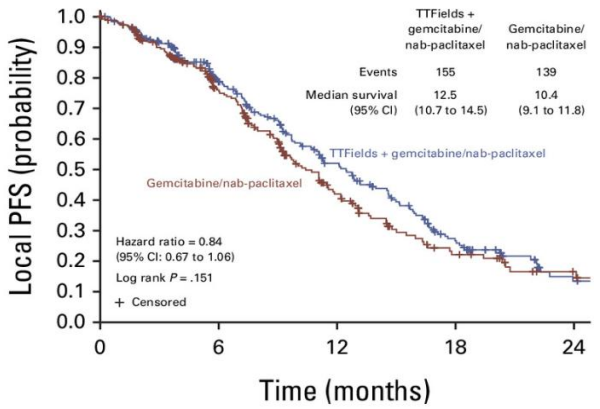
TTFields + gemcitabine/ nab-paclitaxel	285	224	166	104	50	26	14
Gemcitabine/ nab-paclitaxel	286	228	164	98	41	16	9

Secondary Endpoint: PFS and local PFS



Number at risk:

TTFields + gemcitabine/ nab-paclitaxel	285	153	79	30	9
Gemcitabine/ nab-paclitaxel	286	133	50	17	6



Number at risk:

TTFields + gemcitabine/ nab-paclitaxel	285	162	90	36	9
Gemcitabine/ nab-paclitaxel	286	139	56	20	8

Safety Summary

AE, n (%)	TTFields + GnP (n = 274)		GnP (n = 273)	
	All grades	Grade ≥3	All grades	Grade ≥3
Serious AE	147 (53.6%)	143 (52.2%)	131 (48.0%)	130 (47.6%)
AE leading to device discontinuation	23 (8.4%)		NA	
AE leading to chemotherapy discontinuation	47 (17.2%)		43 (15.8%)	
AE leading to death	17 (6.2%)		16 (5.9%)	

TTFields with GnP is a potential new standard paradigm for unresectable LA-PAC

ASCO 2025 Abstr. LBA4005; J Clin Oncol. 2025 May 31:JCO2500746.

ASCO 2025: RAPID REVIEWS

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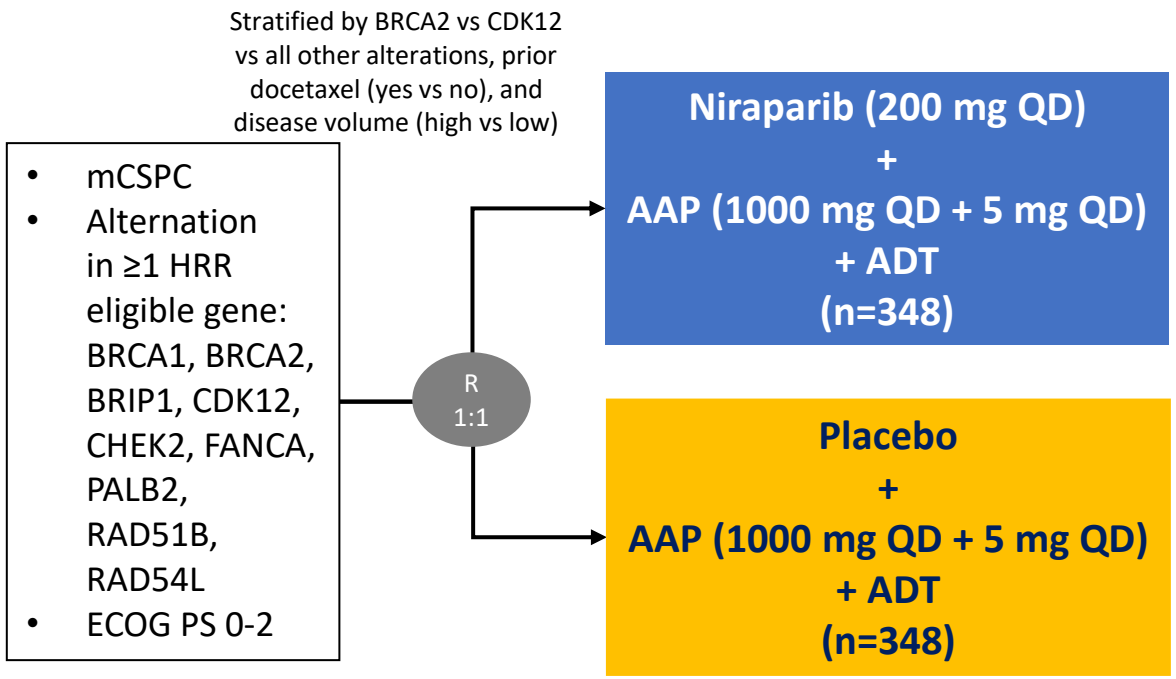
KEY DATA

AMPLITUDE: Niraparib and abiraterone acetate plus prednisone for metastatic castration-sensitive prostate cancer patients with alterations in homologous recombination repair genes

Study Design: Randomized, double-blind, placebo-controlled trial



Prior allowed treatments in mCSPC: ADT ≤6 months, Docetaxel ≤6 cycles, APP ≤45 days, Palliative RT

Data cutoff: January 7, 2024

Primary endpoint: rPFS by investigator review
Secondary endpoints: Time to symptomatic progression, OS, safety

Select Baseline Characteristics

	Niraparib + AAP (n=348)	Placebo + AAP (n = 348)
Median age (range), years	68 (40-88)	67 (40-92)
Median PSA at initial diagnosis (range, ng, mL	112 (0.1-17475)	102 (0.1-15900)
ECOG PS score, n		
• 0	242 (70%)	218 (63%)
• ≥1	106 (30%)	130 (37%)
Gleason score at initial diagnosis, 8, n	**276 (79%)**	**262 (75%)**
Metastatic stage at diagnosis, M1 (Synchronous), n	**301 (86%)**	**302 (87%)**
Disease volume, High, n	**269 (77%)**	**271 (78%)**
Prior docetaxel use in mCSPC, n	**54 (16%)**	**56 (16%)**
Site of metastases, n		
• Bone only	146 (42%)	154 (44%)
• Visceral	57 (16%)	54 (16%)
• Lymph nodes	173 (50%)	161 (46%)
BRCA alternation, n	191 (55%)	196 (56%)

KEY DATA

AMPLITUDE: Niraparib and abiraterone acetate plus prednisone for metastatic castration-sensitive prostate cancer patients with alterations in homologous recombination repair genes

Endpoints

	Niraparib + AAP (n=348)	Placebo + AAP (n = 348)
Primary Endpoint		
• **Median rPFS, months**		
• **BRCAm**	NE	26.0
• **HRRm (ITT)**	NE	29.5
Secondary Endpoints		
Median time to symptomatic progression, months		
• **BRCAm**	NE	NE
• **HRRm**	NE	NE
Median OS, months		
• **BRCAm**	NE	NE
• **HRRm**	NE	NE

Safety Summary

	Niraparib + AAP (n = 347)*	Placebo + AAP (n = 348)
TEAEs	346 (>99%)	341 (98%)
Treatment-related TEAEs	309 (89%)	257 (74%)
Grade 3 or 4 TEAEs	261 (75%)	205 (59%)
Treatment-related grade 3 or 4 TEAEs	193 (56%)	105 (30%)
SAEs	136 (39%)	96 (28%)
Treatment-related SAEs	44 (13%)	11 (3%)
TEAs leading to treatment discontinuation	**51 (15%)**	**36 (10%)**
TEAEs leading to dose reduction	76 (22%)	24 (7%)
TEAEs leading to death	14 (4%)	7 (2%)

*One randomized patient never received the study treatment

Niraparib and abiraterone acetate plus prednisone could become a new treatment for patients with mCSPC and HRR gene alteration

ASCO 2025:

GI/GU *Cancer*

Key Takeaways

Q&A

@SujithKalmadiMD

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ATOMIC: *Atezolizumab plus mFOLFOX6 could be considered a new standard adjuvant treatment for patients with stage III deficient DNA mismatch repair colon cancer... not yet FDA approved*

MATTERHORN: *Perioperative durvalumab with chemotherapy (FLOT) could be a new standard treatment for patients with localized gastric and GEJ adenocarcinoma... not yet FDA approved*

DESTINY-Gastric04: *Trastuzumab deruxtecan should be considered as a standard second-line therapy for patients with metastatic HER2-positive gastric cancer... FDA approved since January 2021*

BREAKWATER: *Encorafenib plus cetuximab with mFOLFOX6 is could be a new standard first-line therapy for patients with BRAF V600E-mutant metastatic colorectal cancer... FDA approval since December 2024*

PANOVA-3: *Tumor Treating Fields (radiation) with gemcitabine and nab-paclitaxel is a potential new standard paradigm for unresectable locally advanced pancreatic adenocarcinoma... not yet FDA approved*

AMPLITUDE: *Niraparib and abiraterone acetate plus prednisone could become a new standard treatment for patients with metastatic castration-sensitive prostate cancer with alterations in homologous recombination repair genes... not yet FDA approved*

2025 ASCO Key Studies

Breast Cancer

- RAPID REVIEWS
  - *SERENA-6
  - DESTINY-Breast09
  - DESTINY-Breast06
  - AI for IHC HER2 Pathology
  - ASCENT-03
  - ASCENT-04
  - VERITAC-2
  - INAVO120
  - CompassHER2 pCR

GU/ GI Cancer

- *ATOMIC
- *MATTERHORN
- DESTINY-Gastric04
- ***RAPID REVIEWS***
  - BREAKWATER
  - PANOVA-3
  - AMPLITUDE

Other Notable Studies

- *NIVOPOSTOP
- KEYNOTE-689
- *VERIFY
- ***RAPID REVIEWS***
  - TROPION-Lung02
  - DELPHI-304
  - IMforte
  - TUXEDO-3
  - ROSELLA

* Plenary Session

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NIVOPOSTOP

* Plenary Session

Does nivolumab added to radio-chemotherapy benefit patients with resected head and neck squamous cell carcinoma at high risk of relapse?

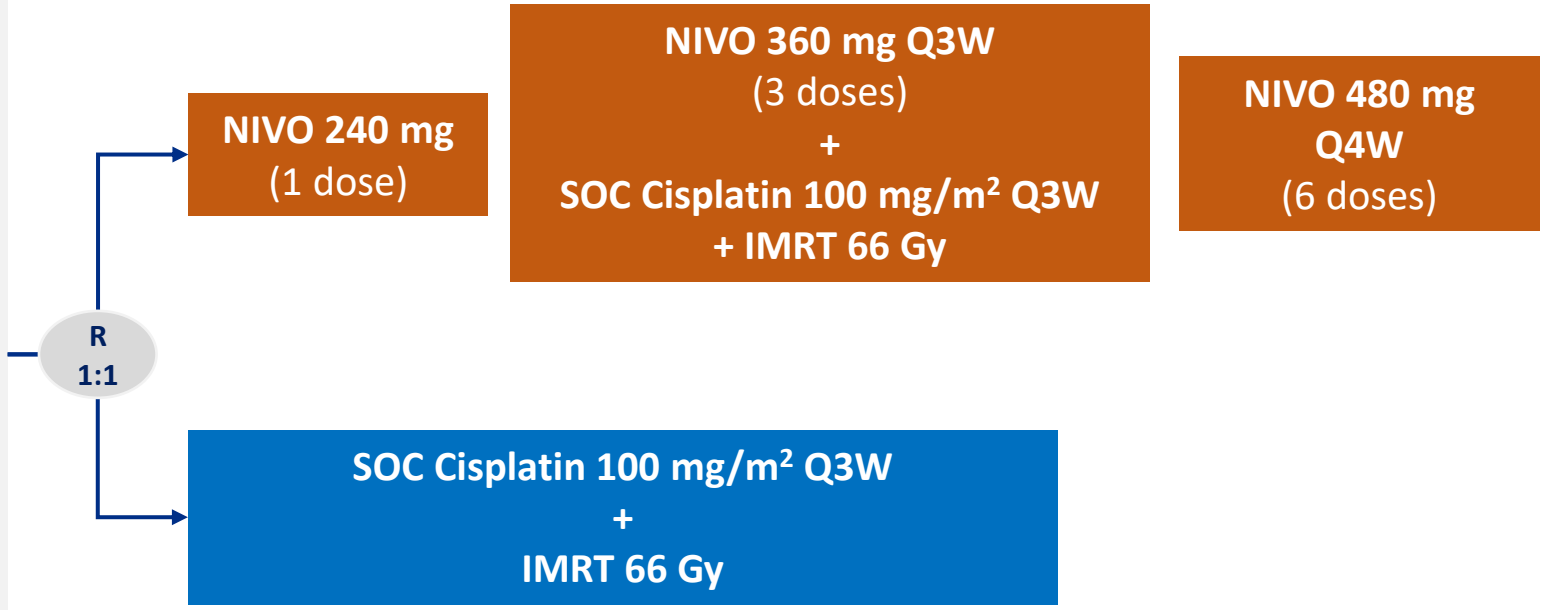
KEY DATA

NIVOPOSTOP: Nivolumab plus SOC for treatment of high-risk LA-HNSCC

Study Design: Multicenter, open-label, randomized, phase 3 investigator sponsored study

- Adult patients < 75 y/o
- ECOG PS 0-1
- SCC of the oral cavity, oropharynx, larynx, or hypopharynx with
  - Complete macroscopic surgical resection
  - Stage III or IV
  - High-risk pathological features of relapse (high-risk features are extracapsular extension or + margins, multiple peri-neural invasions and numerous involved nodes)

N=680



Primary endpoint: Disease-free survival (DFS) per investigator assessments

Secondary endpoints: Overall survival (OS), Safety

ASCO 2025. Abstr. LBA2

KEY DATA

NIVOPOSTOP: Nivolumab plus SOC for treatment of high-risk LA-HNSCC

Baseline characteristics

	NIVO + CRT (n=332[a])	CRT (n=334[a])
Median age (IQR), y	59 (53-65)	59 (53-64)
Sex		
• Male	250 (75%)	257 (77%)
• Female	82 (25%)	77 (23%)
ECOG PS		
• 0	169 (51%)	168 (50%)
• 1	163 (49%)	166 (50%)
Smoking status		
• Current	179 (54%)	161 (48%)
• Former	108 (33%)	109 (33%)
• Never	45 (14%)	64 (19%)
Median no. packs-years (IQR)	40 (25-50)	40 (25-45)

	NIVO + CRT (n=332[a])	CRT (n=334[a])
Tumor site and p16 status		
• Oral cavity	192 (58%)	193 (58%)
• Hypopharynx	43 (13%)	40 (12%)
• Larynx	40 (12%)	41 (12%)
• OPC p16-	41 (12%)	43 (13%)
• OPC p16+	16 (5%)	17 (5%)

[a]Analysis was based on 666 patients randomized before the data cut off when the required number of DFS events was reached.

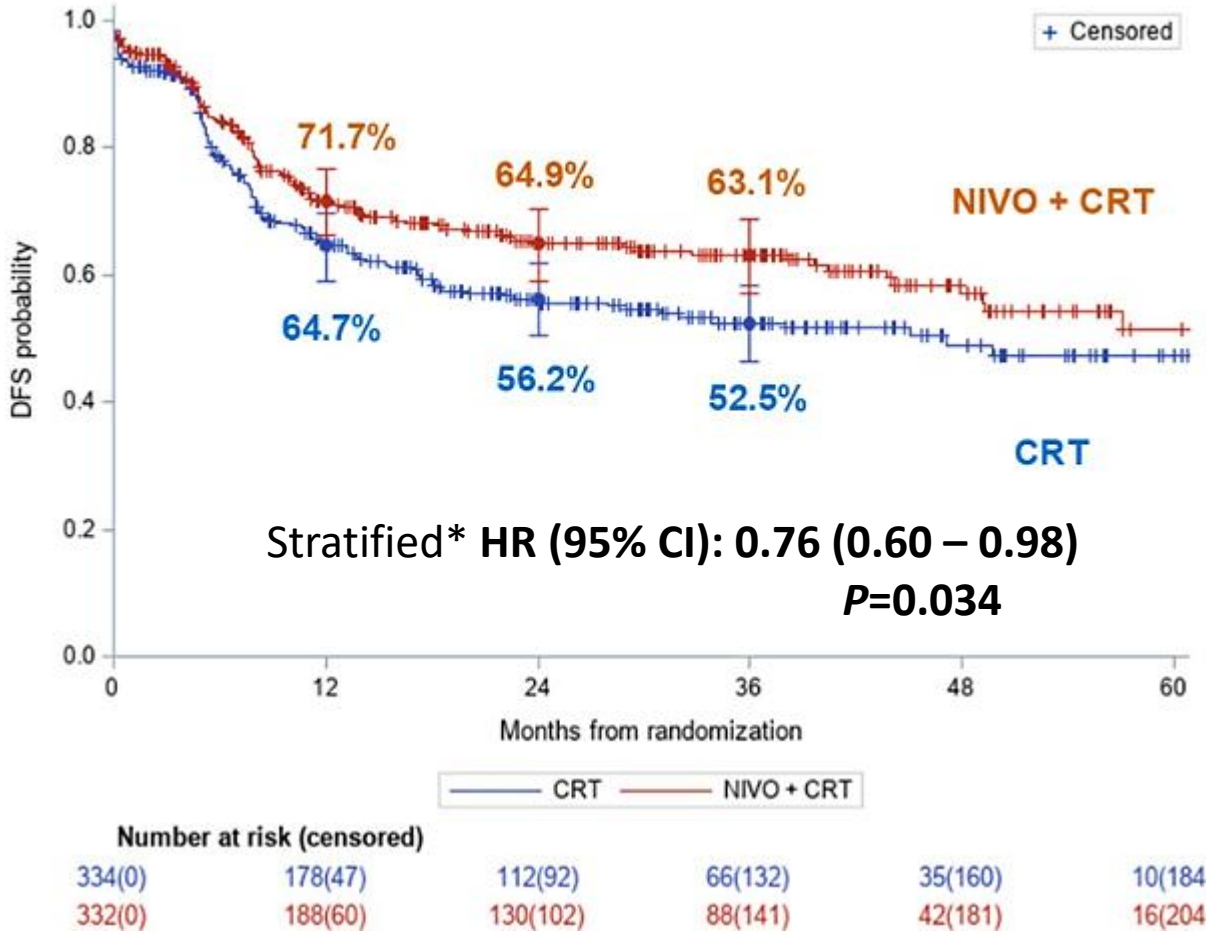
OPS: Oropharyngeal cancer; IQR: Interquartile Range; CRT: cisplatin + radiation

Data cut-off date: April 30, 2024

KEY DATA

NIVOPOSTOP: Nivolumab plus SOC for treatment of high-risk LA-HNSCC

Primary Endpoint: Disease-free survival (DFS) per investigator assessments



Stratified* **HR (95% CI): 0.76 (0.60 – 0.98)**

***P*=0.034**

*HR stratified for p16 status (OPC p16 positive vs OPC p16 negative and non –OPC) in Cox model

Specific DFS events

	NIVO + CRT	CRT
DFS events, n	112	140
• Loco-regional	39	61
• Loco-regional + distant	16	22
• Distant	37	40
• Death	20	17

Analysis based on 252 DFS events at the data cutoff pf April 30th, 2024

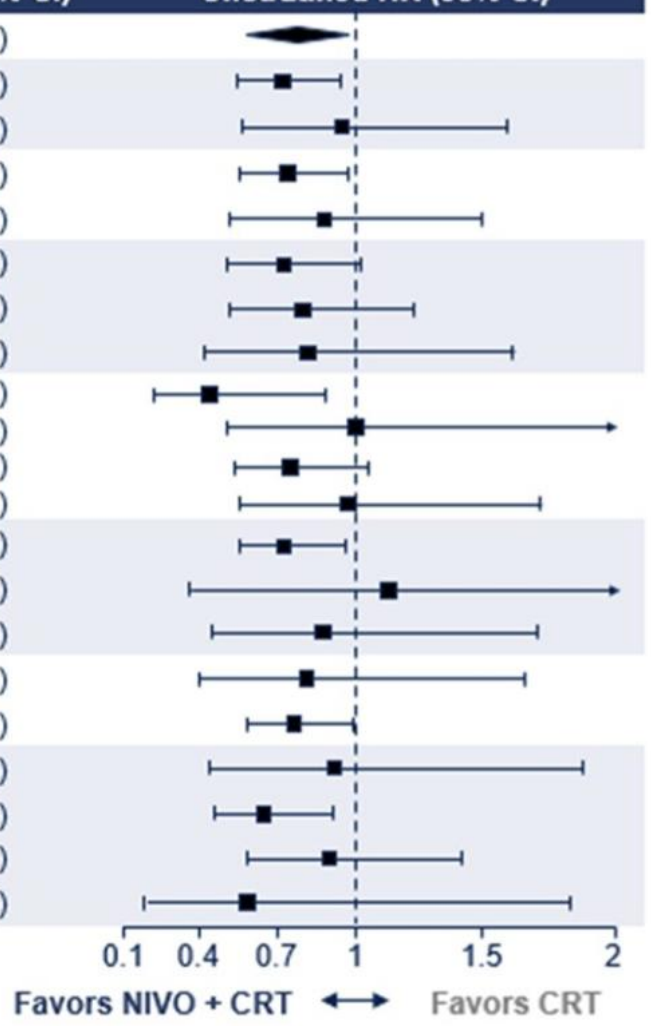
Median follow up: 30.3 months

KEY DATA

NIVOPOSTOP: Nivolumab plus SOC for treatment of high-risk LA-HNSCC

Disease Free Survival in Subgroups

Subgroup		No. events/N	Unstratified HR (95% CI)
All patients		252/666	0.77 (0.60–0.98)
Age	< 65 years	195/515	0.71 (0.54–0.95)
	≥ 65 years	57/151	0.95 (0.56–1.59)
Sex	Male	196/507	0.74 (0.56–0.98)
	Female	56/159	0.88 (0.52–1.49)
Smoking status	Current smoker	131/340	0.72 (0.51–1.02)
	Former smoker	85/217	0.80 (0.52–1.22)
	Never smoker	36/109	0.82 (0.41–1.61)
Tumor site	Hypopharynx	37/83	0.44 (0.22–0.88)
	Larynx	32/81	1.00 (0.50–2.00)
	Oral cavity	135/385	0.75 (0.54–1.06)
	Oropharynx	48/117	0.97 (0.55–1.71)
p16 status	Non-OPC	204/549	0.73 (0.55–0.96)
	p16-positive OPC	12/33	1.13 (0.36–3.51)
	p16-negative OPC	36/84	0.87 (0.45–1.70)
pStage	I-III	31/113	0.81 (0.40–1.64)
	IV	221/553	0.76 (0.58–0.99)
PD-L1 CPS	< 1	30/78	0.92 (0.45–1.88)
	1-19	126/298	0.65 (0.46–0.92)
	≥ 20	80/246	0.91 (0.58–1.41)
	Unknown	16/44	0.59 (0.19–1.83)



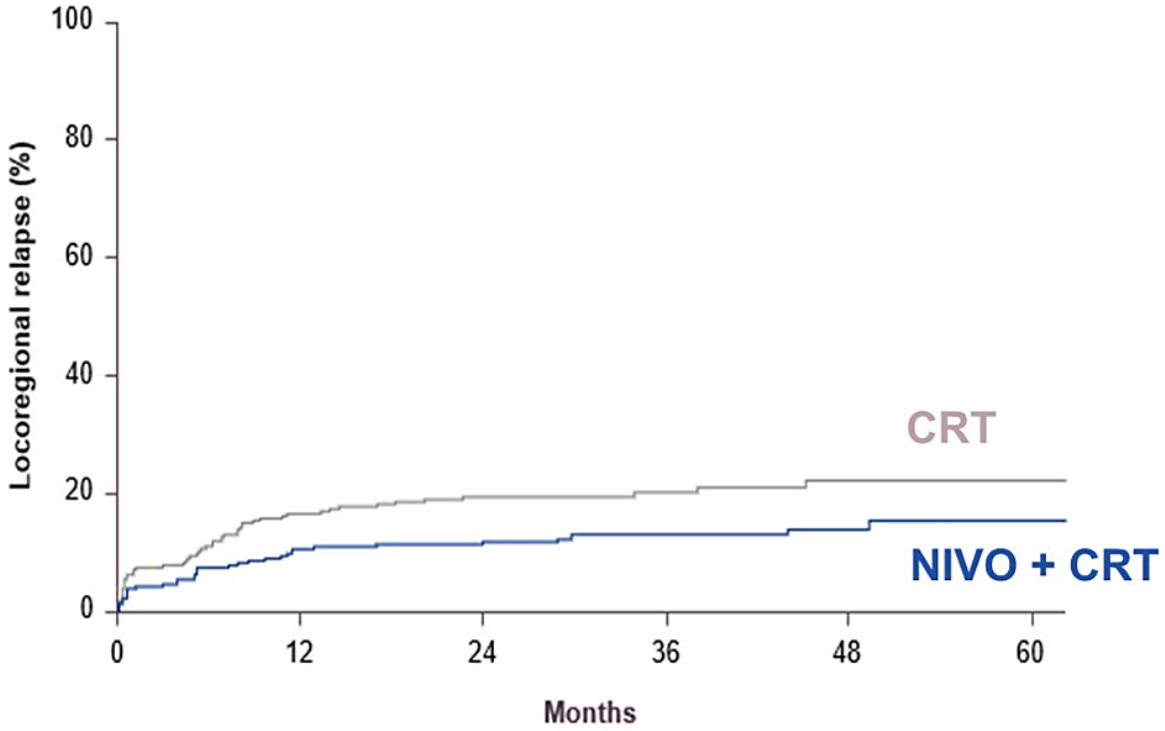
OPC: Oropharyngeal cancer

ASCO 2025. Abstr. LBA2

KEY DATA

NIVOPOSTOP: nivolumab plus SOC for treatment of high-risk LA-HNSCC

Cumulative incidence of local regional relapses alone



	NIVO + CRT (N=332)	CRT (N=334)
Events, n	39	61
Cumulative Incidence, %		
1-year	11	16
2-year	12	19
3-year	13	20
Stratified sub-HR (95% CI)	0.63 (0.42-0.94)	

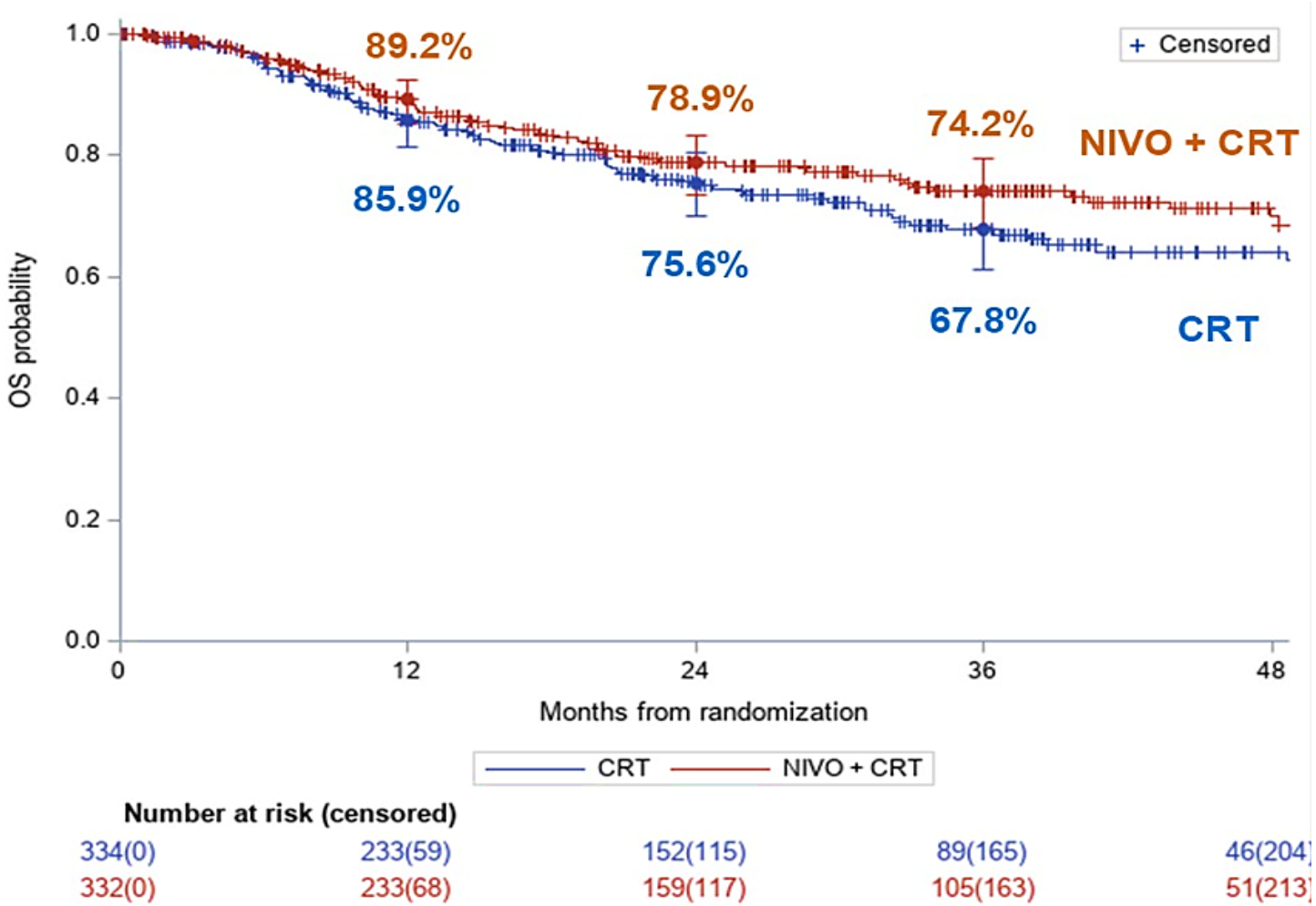
Sub-distribution HR stratified for p16 status (OPC p16 positive vs OPC p16 negative and non-OPC) in Fine-Gray model

CRT: cisplatin + radiation

KEY DATA

NIVOPOSTOP: nivolumab plus SOC for treatment of high-risk LA-HNSCC

Secondary Endpoint: Overall Survival (descriptive*)



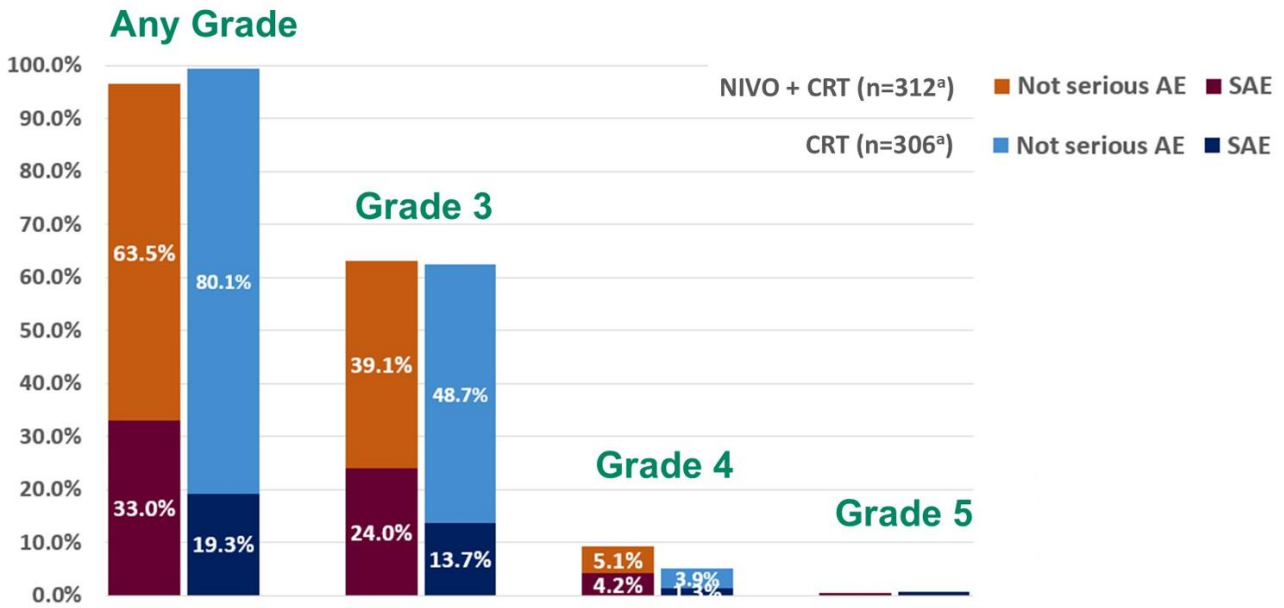
*Note: OS could not be formally tested since the pre-specified number of deaths was not reached.

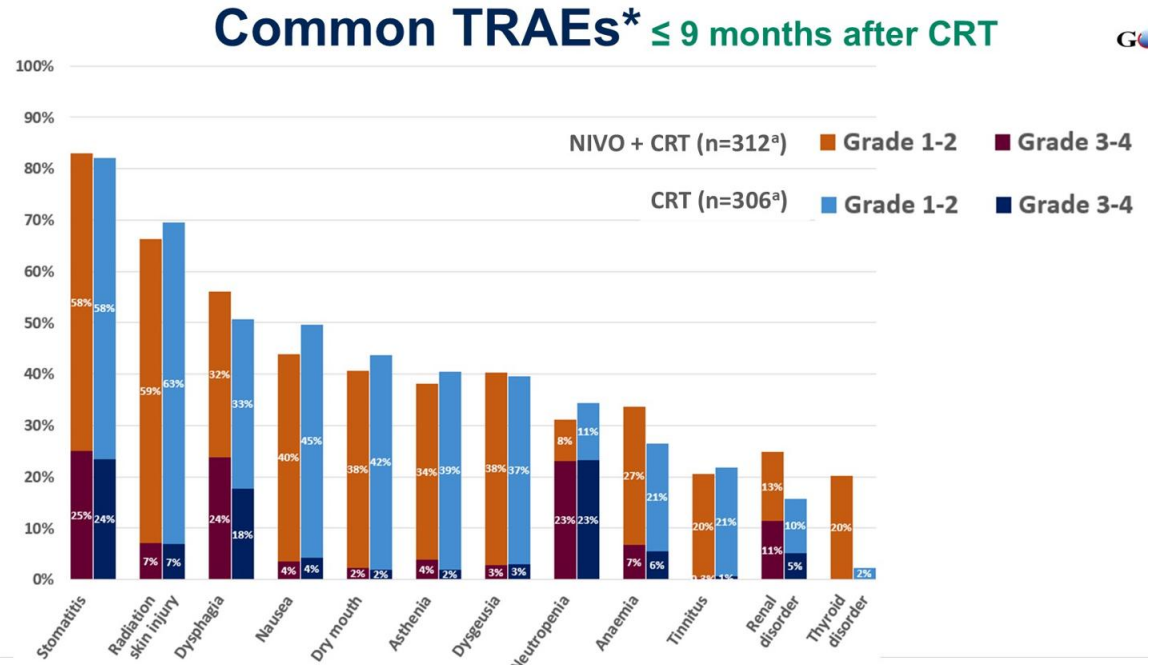
At data cutoff, 158 patients died.

KEY DATA

NIVOPOSTOP: nivolumab plus SOC for treatment of high-risk LA-HNSCC

Safety: Treatment Related Adverse Events (TRAE)*





Late TRAEs > 9 months after CRT	NIVO + CRT (n = 234)				CRT (n = 235)			
	Any grade	Grade 3	Grade 4	Grade 5	Any grade	Grade 3	Grade 4	Grade 5
Late treatment-related AEs								
Any, n	78 (33.3%)	10 (4.3%)	0	0	72 (30.6%)	8 (3.4%)	0	0
Serious, n	3 (1.3%)	3 (1.3%)	0	0	1 (0.4%)	1 (0.4%)	0	0
Late nivolumab-related AEs								
Any, n	10 (4.3%)	2 (0.9%)	0	0	N/A	N/A	N/A	N/A
Serious, n	2 (0.9%)	2 (0.9%)	0	0	N/A	N/A	N/A	N/A

*Maximal grade of any TRAE per patient

[a]Safety evaluated in 618 patients who received at least one dose of any study treatment

SUMMARY

NIVOPOSTOP

- The benefit-risk ratio of adding nivolumab to post operative SOC cisplatin-RT appears to be favorable
  - The primary endpoint was met: DFS significantly improved (HR: 0.76)
  - Moderate increased toxicity, without increase in treatment-related deaths

IMPACT

Post-operative nivolumab added to SOC cisplatin-RT benefited patients with resected high-risk LA-SCCHN and could be a potential new standard of care treatment option

2025 ASCO Key Studies

Breast Cancer

- RAPID REVIEWS
  - *SERENA-6
  - DESTINY-Breast09
  - DESTINY-Breast06
  - AI for IHC HER2 Pathology
  - ASCENT-03
  - ASCENT-04
  - VERITAC-2
  - INAVO120
  - CompassHER2 pCR

GU/ GI Cancer

- *ATOMIC
- *MATTERHORN
- DESTINY-Gastric04
- ***RAPID REVIEWS***
  - BREAKWATER
  - PANOVA-3
  - AMPLITUDE

Other Notable Studies

- *NIVOPOSTOP
- KEYNOTE-689
- *VERIFY
- ***RAPID REVIEWS***
  - TROPION-Lung02
  - DELPHI-304
  - IMforte
  - TUXEDO-3
  - ROSELLA

* Plenary Session

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CLINICAL QUESTION

KEYNOTE-689

Does adding neoadjuvant/adjuvant pembrolizumab to standard of care (chemo + RT) benefit patients with advanced head and neck squamous cell carcinoma (HNSCC)?

ASCO 2025. Abstr. 6012

FDA APPROVAL

*On **June 12, 2025**, the FDA approved **pembrolizumab** (Keytruda, Merck) for adults with resectable locally advanced head and neck squamous cell carcinoma (HNSCC) whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, as a single agent as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without cisplatin after surgery, and then as a single agent.*

This is the first approval for HNSCC in 6 years and the first overall perioperative approval for locally advanced HNSCC

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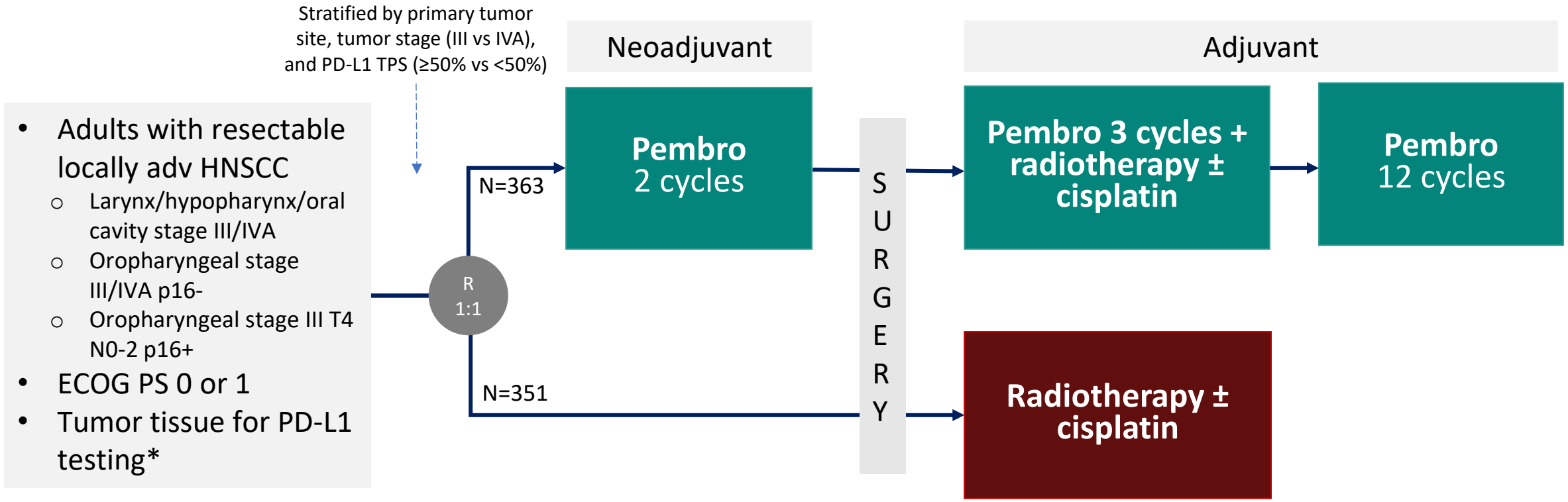
KEY DATA

KEYNOTE-689: neo/adj pembro for HNSCC

Study Design: Open-label, randomized, phase 3 study



Primary endpoint: EFS per RECIST 1.1 by BICR

Secondary endpoints: Major pathological response by BIPR (mPR; ≤10% residual invasive SCC in resected primary tumor + all sampled regional lymph nodes), OS, Safety

Exploratory endpoints: Locoregional failure rate, DMFS, second cancers

Median follow up (time from randomization to data cutoff date): 38.3 months (9.0 – 66.5)

*Assessed by PD-L1 IHC 22C3 pharmDx; TPS=% tumor cells with membranous PD-L1 staining; CPS=number of PD-L1-straining cells + total # viable tumor cells x 100.

ASCO 2025. Abstr #6012; N Engl J Med 2025;393:37-50

KEYNOTE-689: neo/adj pembro for HNSCC

Baseline Characteristics

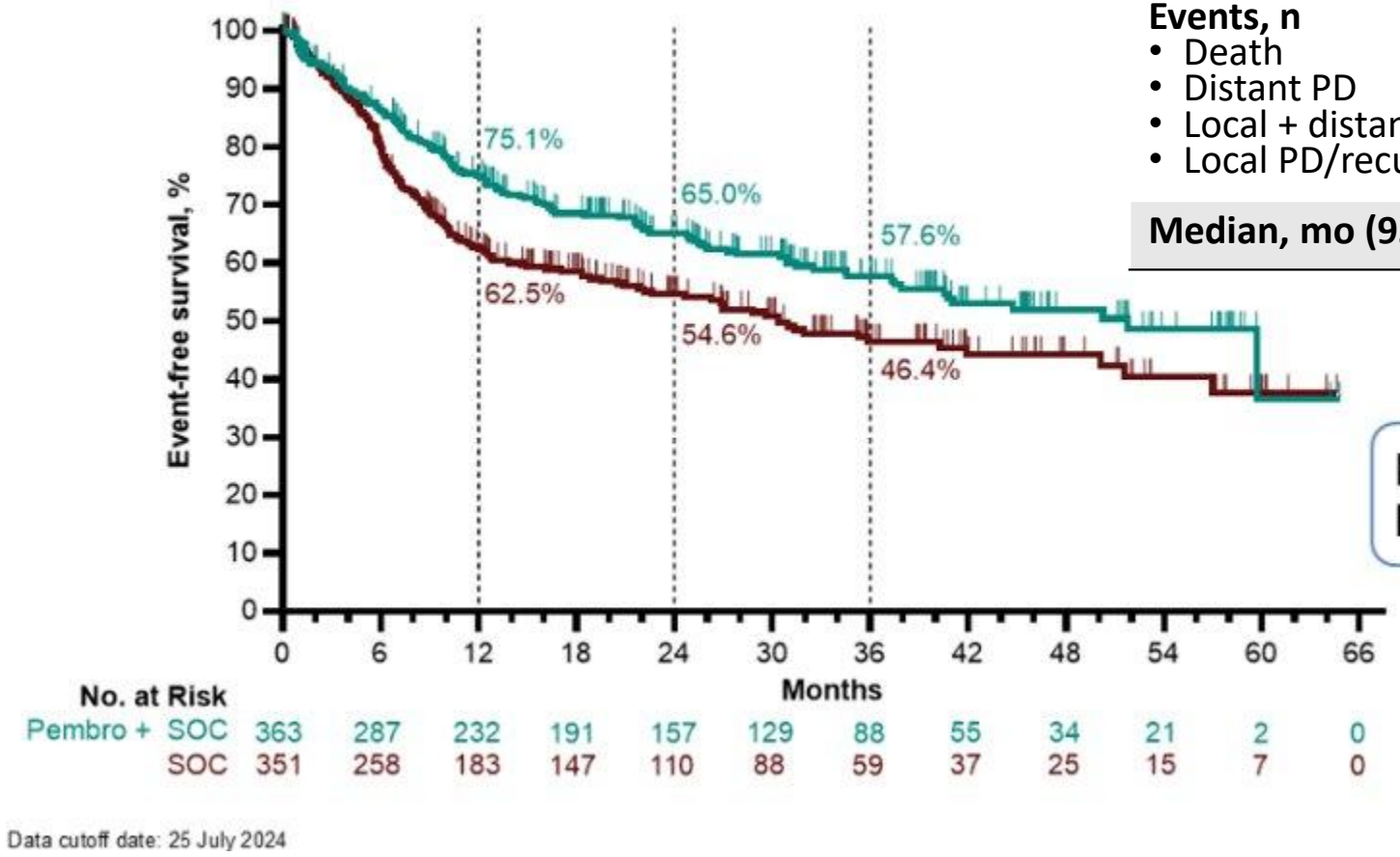
	Pembro + SoC	SoC
Median age (range), years	60.0 (29-82)	61.0 (22-87)
Male, n (%)	286 (78.8%)	277 (78.9%)
Current/ former smoker, n (%)	293 (80.7%)	267 (76.1%)
Alcohol use—yes, n (%)	150 (68.9%)	238 (67.8%)
Primary tumor site, n (%)		
• Oral cavity	219 (60.3%)	213 (60.7%)
• Larynx	81 (22.3%)	73 (20.8%)
• Hypopharynx	28 (7.7%)	26 (7.4%)
• Oropharynx	35 (9.6%)	38 (10.8%)
• Missing	0	1 (0.3%)
Positive HPV status, n (%)	12 (3.3%)	15 (4.3%)
PD-L1 CPS ≥10, n (%)	234 (64.5%)	231 (65.8%)
PD-L1≥1, n (%)	347 (95.6%)	335 (95.4%)

KEY DATA

KEYNOTE-689: neo/adj pembro for HNSCC

Primary Endpoint: EFS by BICR

All participants



Data cutoff date: 25 July 2024

	Pembro + SoC (N=363)	SOC (N=351)
Events, n	136 (37.5%)	159 (45.3%)
• Death	67 (18.5%)	64 (18.2%)
• Distant PD	26 (7.2%)	51 (14.5%)
• Local + distant PD	4 (1.1%)	7 (2.0%)
• Local PD/recurrence	39 (10.7%)	37 (10.5%)
Median, mo (95% CI)	**51.8** (37.5-NR)	**30.4** (21.8-50.1)

HR 0.73, 95% CI 0.58–0.92, P=.0041*

NR, not reached.
*Significance boundary was met at IA1.

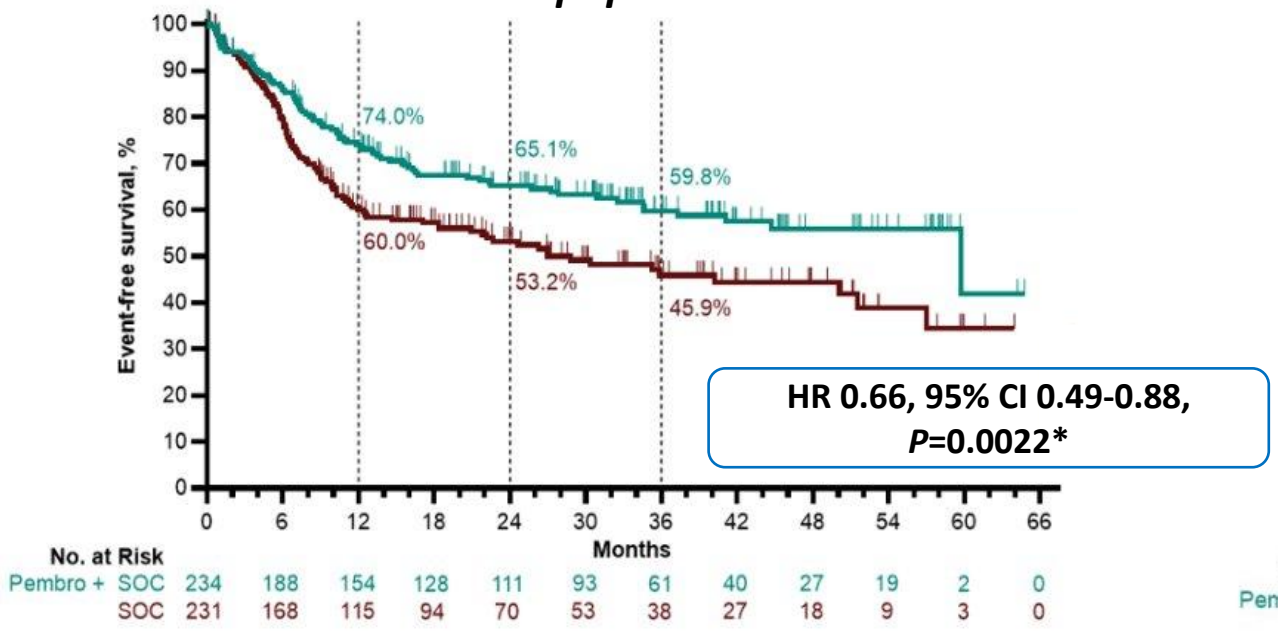
KEY DATA

KEYNOTE-689: neo/adj pembro for HNSCC

BICR's EFS by PD-L1 status

BICR: Blind independent central review

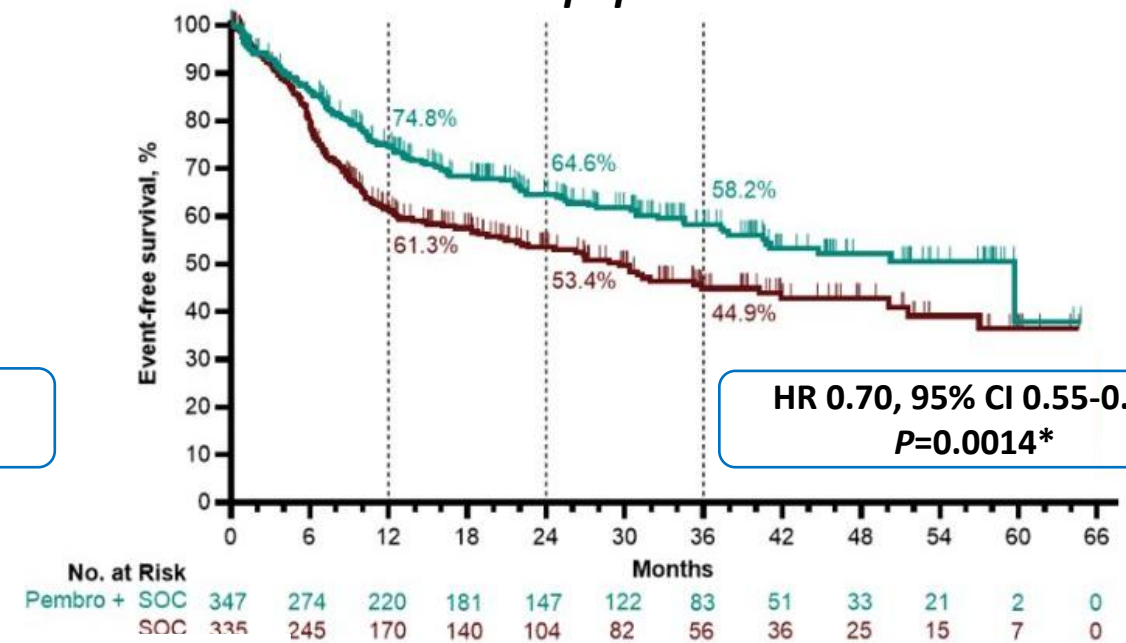
CPS ≥10 population



HR 0.66, 95% CI 0.49-0.88, *P*=0.0022*

	Pembro + SoC (n=234)	SOC (n=231)
Events, n	85 (36.3%)	107 (46.3%)
Median, mo (95% CI)	59.7 (41.1-NR)	26.9 (18.9-51.5)

CPS ≥1 population



HR 0.70, 95% CI 0.55-0.89, *P*=0.0014*

	Pembro + SOC (n=347)	SOC (n=335)
Events, n	128 (36.9%)	156 (46.6%)
Median, mo (95% CI)	59.7 (37.9-NR)	29.6 (19.5-41.9)

NR, not reached. *Significant boundary was met at Interim Analysis 1.

Data cutoff date: 25 July 2024
Median follow-up: 38.3 months (9.0-66.5).

KEYNOTE-689:neo/adj pembro for HNSCC

Secondary endpoints

Pathological Response by CPS, for all Participants

	CPS ≥10 Population		CPS ≥1 Population		All Participants	
	Pembro + SOC (n=234)	SOC (n=231)	Pembro + SOC (n=347)	SOC (n=335)	Prembro + SOC (n=363)	SOC (n=351)
mPR, n (%)	32 (13.7%)	0	34 (9.8%)	0	34 (9.4%)	0
Estimated difference (95% CI)	13.7 (9.7-18.7)		9.8 (7.0-13.3)		9.3 (6.7-12.8)	
P value*	<0.00001		<0.00001		<0.00001	
pCR, n (%)	10 (4.3)	0	11 (3.2)	0	11 (3.0)	0
Estimated difference (95% CI)	4.2 (2.1 – 7.6)		3.1 (1.6 – 5.6)		3.0 (1.5 – 5.3)	

MPR (≤10% residual invasive SCC) and pCR evaluated by blinded independent pathology review.

*Significance boundary was met at Interim Analysis 1

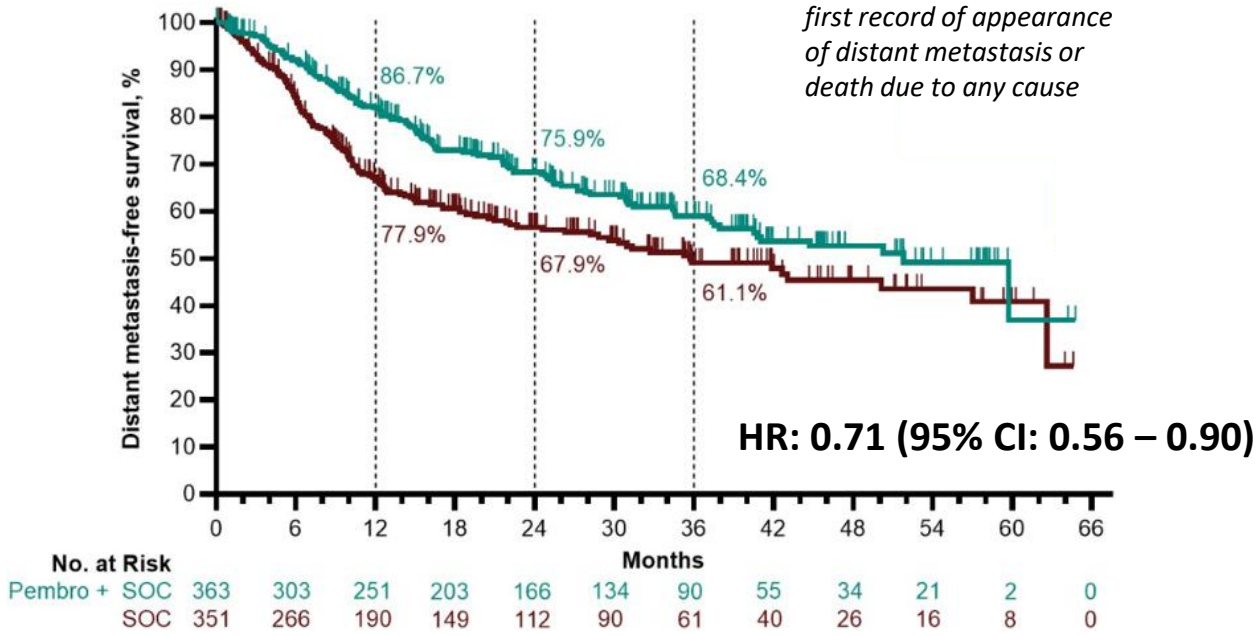
CPS: Combined positive score

KEYNOTE-689: neo/adj pembro for HNSCC

Exploratory Endpoints

Distant metastasis-free survival, All Participants

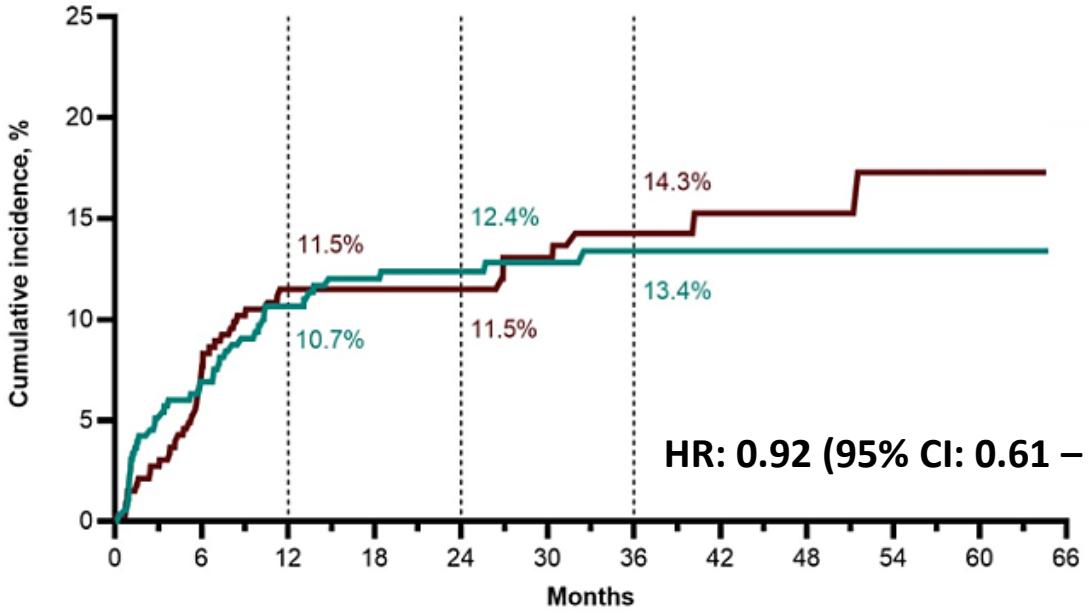
DMFS: time from randomization to date of first record of appearance of distant metastasis or death due to any cause



HR: 0.71 (95% CI: 0.56 – 0.90)

	Pembro + SOC (n=363)	SOC (n=351)
Events, n	127 (35.0%)	148 (42.2%)
Median, mo (95% CI)	51.8 (37.9-NR)	35.7 (26.3-57.0)

Time to Locoregional Failure, All Participants



HR: 0.92 (95% CI: 0.61 – 1.41)

	Pembro + SOC (n=363)	SOC (n=351)
Events, n	136 (37.5%)	159 (45.3%)

KEYNOTE-689: neo/adj pembro for HNSCC

Summary of Safety, As-Treated Population

	Pembro + SoC (n=361)	SOC (n=315)
Median (range) duration of therapy, mo	9.1 (0.03-22.3)	2.9 (0.03-7.2)
Treatment-related adverse events, n		
• Any grade	294 (81.4%)	258 (81.9%)
• Grade ≥3	161 (44.6%)	135 (42.9%)
• Serious	69 (19.1%)	33 (10.5%)
• Led to discontinuation	64 (17.7%)	39 (12.4%)
• Led to death	4 (1.1%)a	1 (0.3%)b
Immune-mediated adverse events, n		
• Any grade	156 (43.2%)	32 (10.2%)
• Grade ≥3	36 (10.0%)	2 (0.6%)

[a]Renal failure, COVID-19 pneumonia, death, and pneumonitis (n=1 each). [b]Acute kidney injury.
As-treated population included all pts with ≥1 dose study treatment (including surgery only).

Data cutoff date: 25 July 2024

KEYNOTE-689: Pembro + SOC		NIVOPOSTOP: Nivo + CRT		KEYNOTE-412: Pembro + CRT		JAVELIN Head and Neck 100: Avelumab + CRT	
FDA approved June 12, 2025		***Not yet FDA approved***		***Did not meet primary endpoint***		***Did not meet primary endpoint***	
• **Larynx/hypopharynx/oral cavity stage III/IVA** • **Oropharyngeal stage III/IVA p16-** • **Oropharyngeal stage III T4 N0-2 p16+** • **ECOG PS 0 to 1**		• **SCC of the oral cavity, oropharynx, larynx, or hypopharynx with complete macroscopic surgical resection** • **Stage III or IV, and high-risk pathological features of relapse**		• **Locally advanced HNSCC** • **Oropharyngeal p16 positive (T4, N3), oropharyngeal p16 negative (any T3-T4, any N2a-3)** • **Larynx, hypopharynx/ oral cavity (any T3-4, any N2a-3)**		• **Historically confirmed oropharynx, hypopharynx, larynx, or oral cavity** • **Previously untreated**	
Neoadj Pembro→ Adj Pembro + radiotherapy ± cisplatin (n = 363)	Adj Radiotherapy ± cisplatin (n = 351)	**Adj Nivolumab** + cisplatin + IMRT (n=332)	Cisplatin + IMRT (n=334)	**Pembrolizumab** + cisplatin-radiotherapy (n=402)	Placebo+ cisplatin-radiotherapy (n=402)	**Avelumab**+ cisplatin-radiotherapy (n=350)	Placebo+ cisplatin-radiotherapy (n=347)
Median follow-up: **38.3 months**		Median follow-up: **30.3 months**		Median follow-up: **47.7 months**		Median follow-up: **14.6**	14.8 months
mEFS: 51.8	30.4 months	**3-year DFS: 63.1%** vs 52.5%		**mEFS: NR**	46.6 months	**mPFS: NR**	NR
HR: 0.73 (0.58-0.92); *P* = 0.0041		**HR: 0.76** (0.60-0.98); *P* = 0.034		***Significance threshold: p≤0.024** **HR: 0.83** (0.68-1.03); *P* = 0.043*		**HR: 1.21** (0.93–1.57) *P* = 0.92	
mDMFS: 51.8	35.7 months	*OS immature*		**mOS: NR**	NR	**mOS: NR**	NR
HR: 0.71 (0.56-0.90)		**3-year OS rate: 74.2%** vs 67.8%		**Estimated 3-year OS rate: 72%** vs 70%		**HR: 1.31** (0.93-1.85) *P* = 0.94	
ASCO 2025. Abstr. #6012		ASCO 2025. Abstr. LBA2		Lancet Oncol. 2024 May;25(5):572-587		Lancet Oncol. 2021 April;22(4):450-462	

KEYNOTE-689

SUMMARY

- The addition of neoadjuvant and adjuvant pembrolizumab to SOC improved EFS in resectable LA HNSCC irrespective of PD-L1 status
- OS benefit did not reach statistical significance at first interim analysis; additional follow-up is ongoing
- Neoadjuvant pembrolizumab did not alter surgical completion rate
- No new safety signals observed in the neoadjuvant, concurrent with (chemo)radiotherapy, and adjuvant pembrolizumab settings

IMPACT

Neoadjuvant pembrolizumab followed by surgery and adjuvant pembrolizumab concurrent with and after postoperative (chemo)radiotherapy benefits patients and should be a new standard of care in the treatment of patients with resectable locally advanced head and neck cancer

Now FDA approved!

cornerstone specialty network™

2025 ASCO Key Studies

Breast Cancer

- RAPID REVIEWS
  - *SERENA-6
  - DESTINY-Breast09
  - DESTINY-Breast06
  - AI for IHC HER2 Pathology
  - ASCENT-03
  - ASCENT-04
  - VERITAC-2
  - INAVO120
  - CompassHER2 pCR

GU/ GI Cancer

- *ATOMIC
- *MATTERHORN
- DESTINY-Gastric04
- ***RAPID REVIEWS***
  - BREAKWATER
  - PANOVA-3
  - AMPLITUDE

Other Notable Studies

- *NIVOPOSTOP
- KEYNOTE-689
- *VERIFY
- ***RAPID REVIEWS***
  - TROPION-Lung02
  - DELPHI-304
  - IMforte
  - TUXEDO-3
  - ROSELLA

* Plenary Session

cornerstone specialty network™

* Plenary Session

Does the hepcidin mimetic rusfertide added to standard of care benefit patients with polycythemia vera (PV)?

Rusfertide is a first-in-class subcutaneous peptide mimetic of the endogenous hormone hepcidin, the principal regulator of iron homeostasis

ASCO 2025. Abstr. LBA3

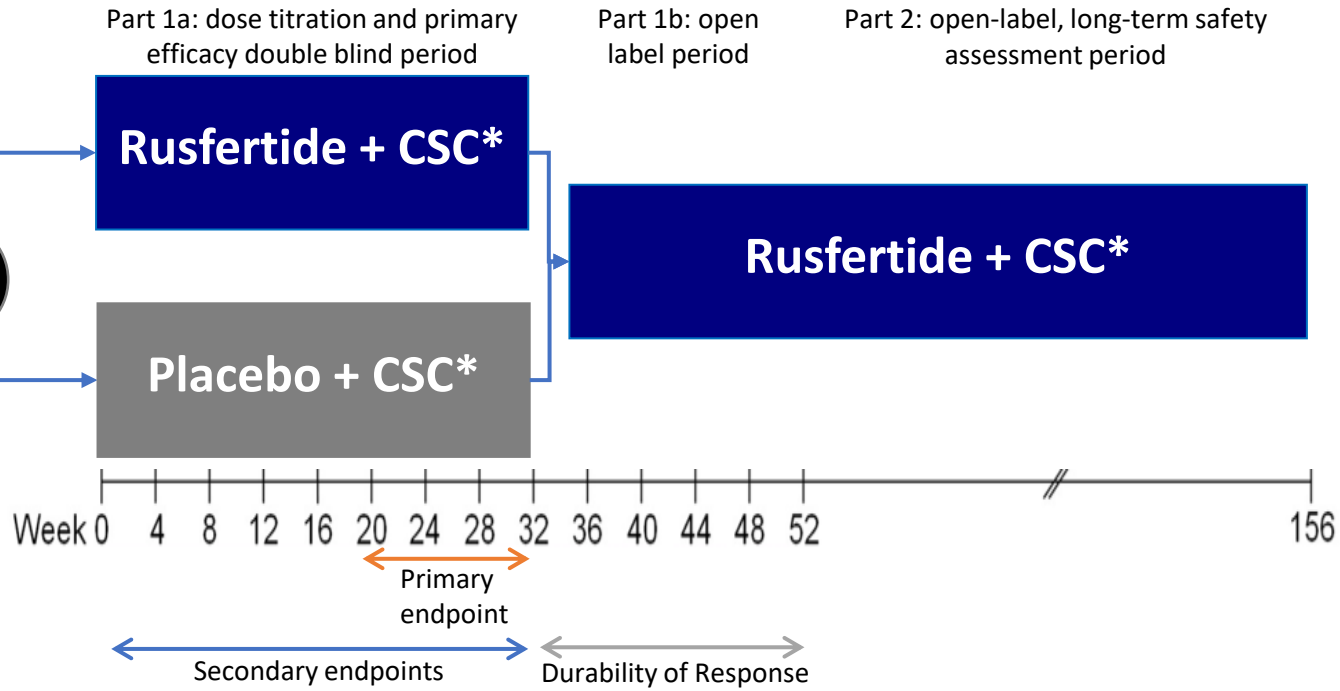
KEY DATA

VERIFY: Rusfertide + SOC as treatment for PV

Study Design: Phase 3, double-blind, placebo-controlled study

- ≥3 PHL (28 weeks prior) OR
- ≥5 PHL (1 year prior)

N=293



*PHL≠CRT
CRT: cytoreductive therapy;
CSC: current standard of care
PHL: phlebotomy

Starting dose (rusfertide/placebo): 20 mg SC QW
Allowed dosing levels: 10 - 90 mg

Primary endpoint: **Weeks 20-32**, Clinical response (absence of phlebotomy eligibility, i.e., confirmed hematocrit (Hct) ≥45% and ≥3% higher than baseline or Hct ≥ 48%)
Secondary endpoints: **Weeks 0-32**, Mean number of phlebotomies, proportion of patients with Hct <45%, mean change from baseline in PROMIS Fatigue SF-8a Score, and mean change from baseline in MFSAF TSS7

Data cutoff: January 7, 2025

KEY DATA

VERIFY: Rusfertide + SOC as treatment for PV

Baseline Characteristics

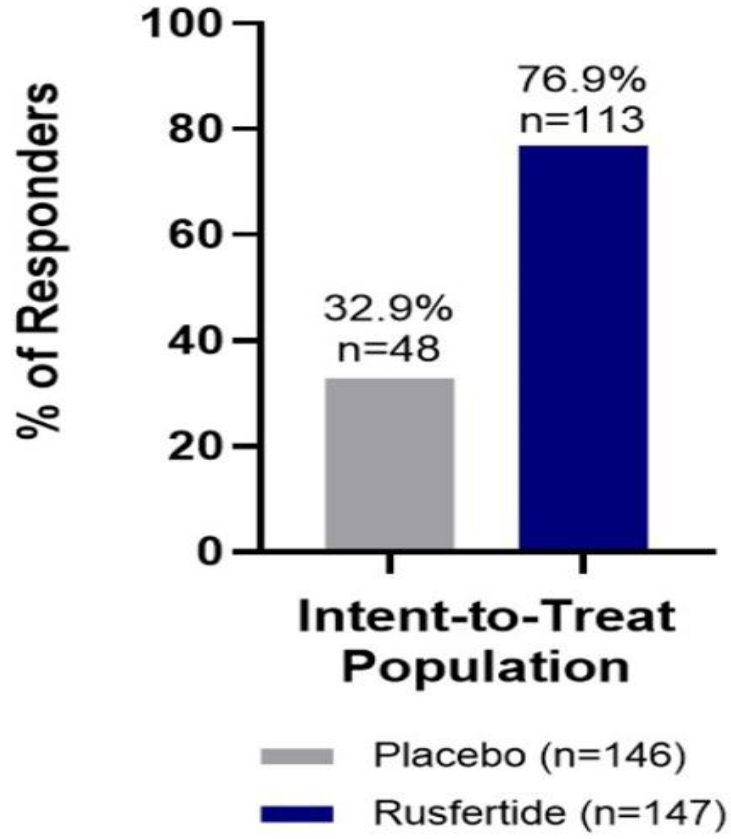
	Placebo + CSC (n=146)	Rusfertide + CSC (n=147)	Total (N=293)
Median age (range), years	57 (27-82)	58 (28-86)	57 (27-86)
Gender, n			
• Male	108 (74.0%)	106 (72.1%)	214 (73.0%)
• Female	38 (26.0%)	41 (27.9%)	79 (27.0%)
Risk Category, n			
High Risk (age ≥60 years old and/or prior TE)	70 (47.9%)	66 (44.9%)	136 (46.4%)
Disease Characteristics			
• Age at PV diagnosis (years), median (range)	51 (22-81)	53 (17-84)	52 (17-84)
• PV duration (years), median (range)	3 (0.2-29.2)	2.8 (0.2-26.4)	2.9 (0.2-29.2)
Phlebotomy History – 28 Weeks Prior to Study Treatment			
• Number of TPs, mean ± SD	4.1 ± 1.4	4.2 ± 1.6	4.2 ± 1.5
• Patient requiring ≥7 TPs, n	7 (4.8%)	16 (10.9%)	23 (7.8%)

TE, thromboembolic event
TP, therapeutic phlebotomy

KEY DATA

VERIFY: Rusfertide + SOC as treatment for PV

Primary Endpoint: Clinical response (Week 20-32)



	Placebo + CSC (n=146)	Rusfertide + CSC (n=147)
Responders[a], n	48 (32.9%)	113 (76.9%)
p-value*	<0.0001	
Non-responders, n	98 (67.1%)	34 (23.1%)

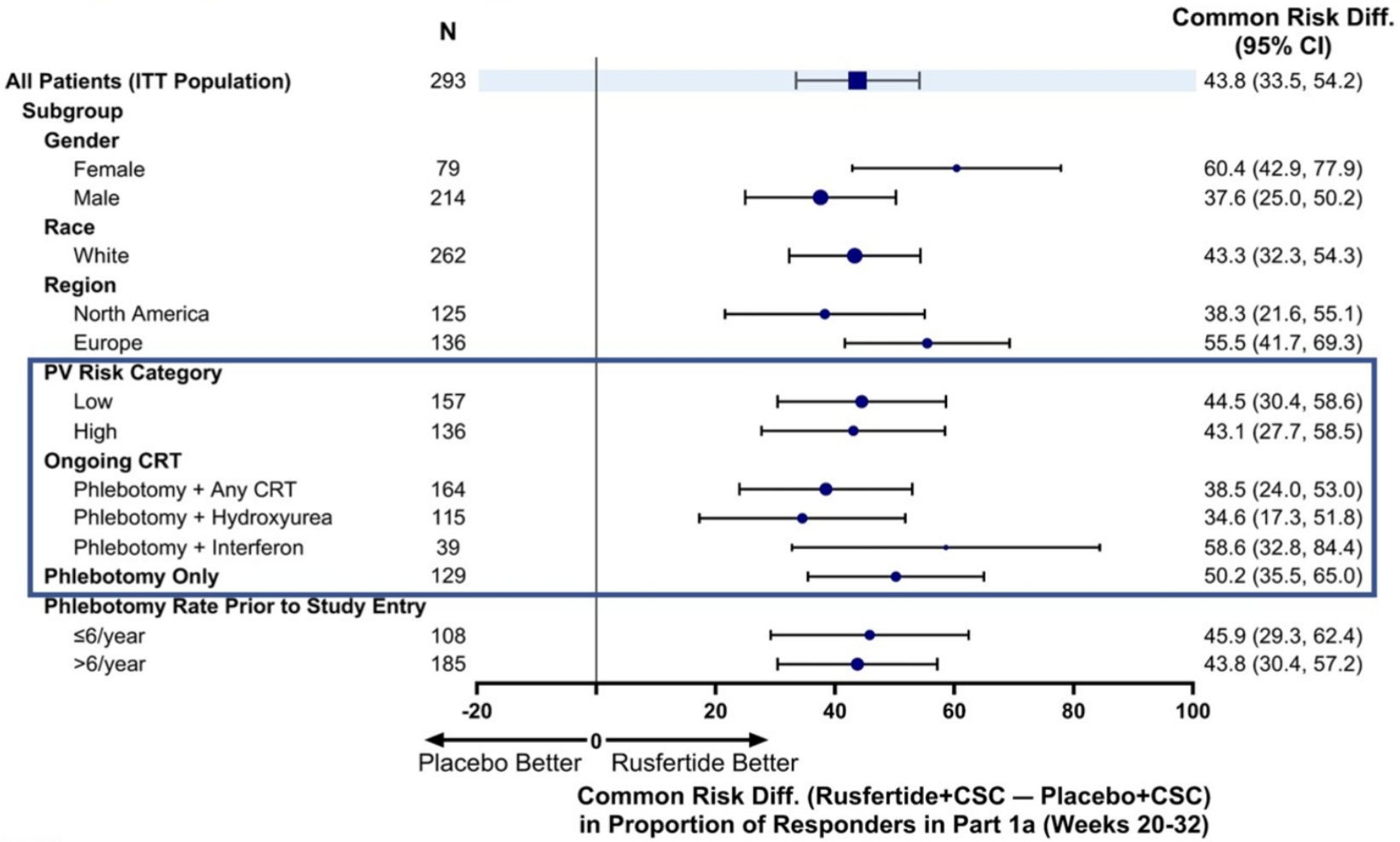
[a]Responder = absence of phlebotomy eligibility (confirmed Hct ≥45% and ≥3% higher than baseline Hct OR Hct ≥48%), no phlebotomies, and completion of Part 1a.

CSC: current standard of care

*p-value based on Cochran-Mantel-Haenszel test

VERIFY: Rusfertide + SOC as treatment for PV

Clinical response across subgroups

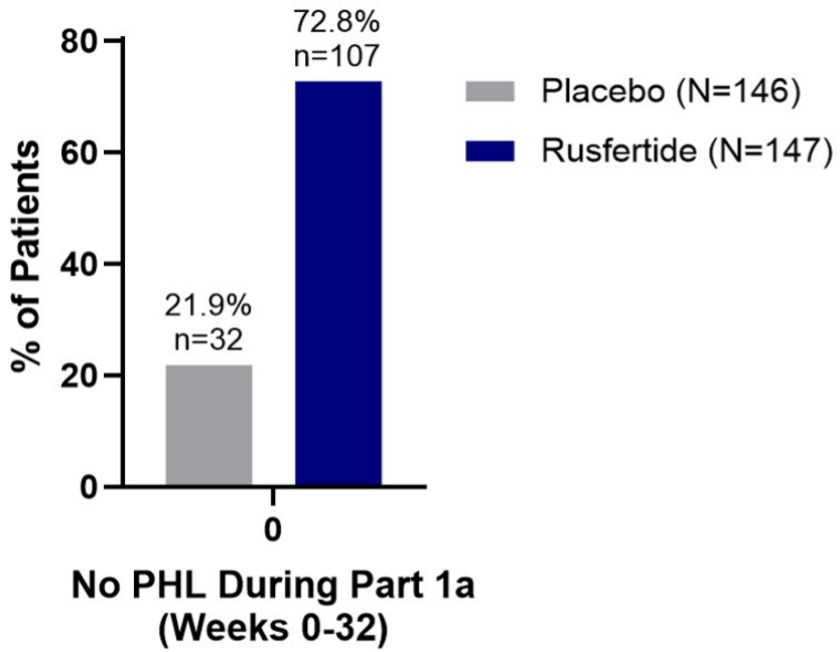


CRT: cytoreductive therapy

VERIFY: Rusfertide + SOC as treatment for PV

Secondary Endpoints

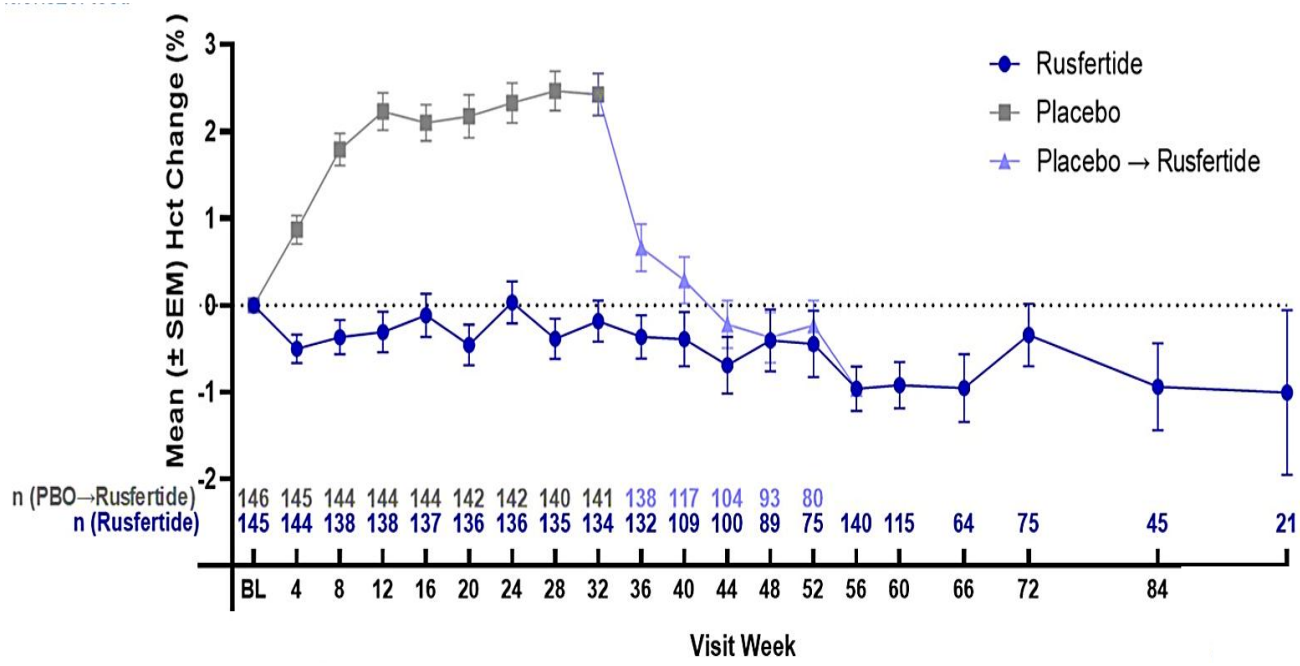
Number of Phlebotomies at week 32



No PHL During Part 1a (Weeks 0-32)

	Placebo + CSC (n=146)	Rusfertide + CSC (n=147)
Mean (Std Dev)	1.8 (1.5)	0.5 (1.2)
p-value	<0.0001	

Hct <45% at week 32



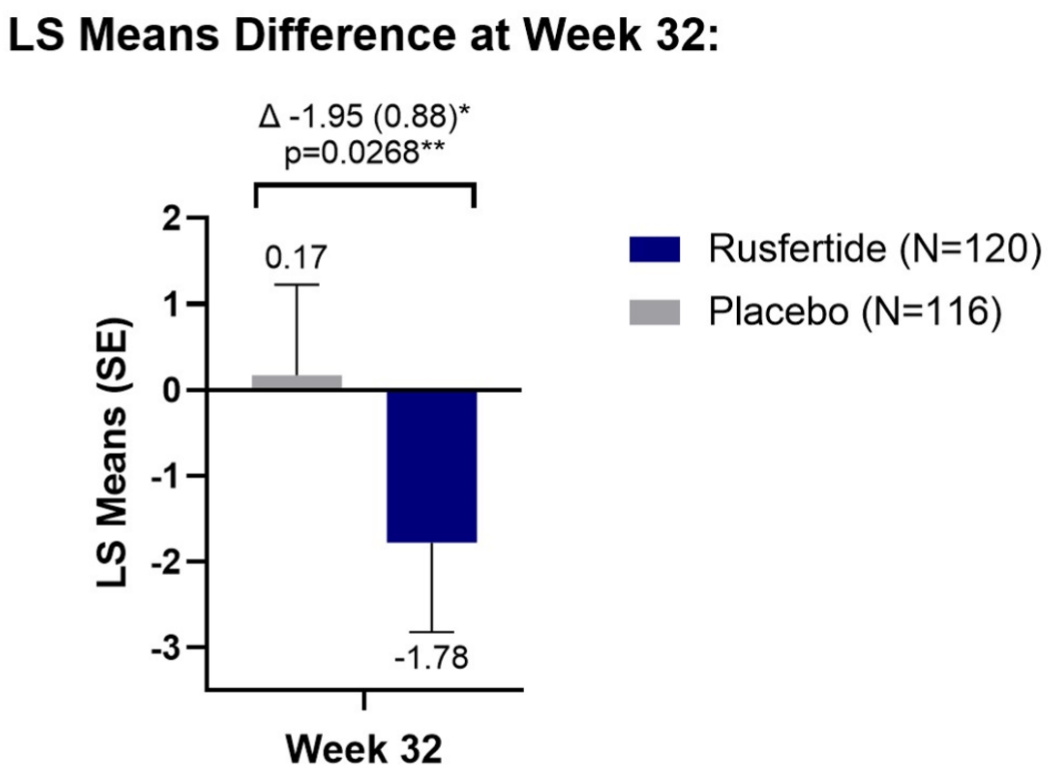
	Placebo + CSC (n=146)	Rusfertide + CSC (n=147)
Hct <45% (baseline through week 32), n (%)	21 (14.4%)	92 (62.6%)
p-value	<0.0001	

CSC: current standard of care

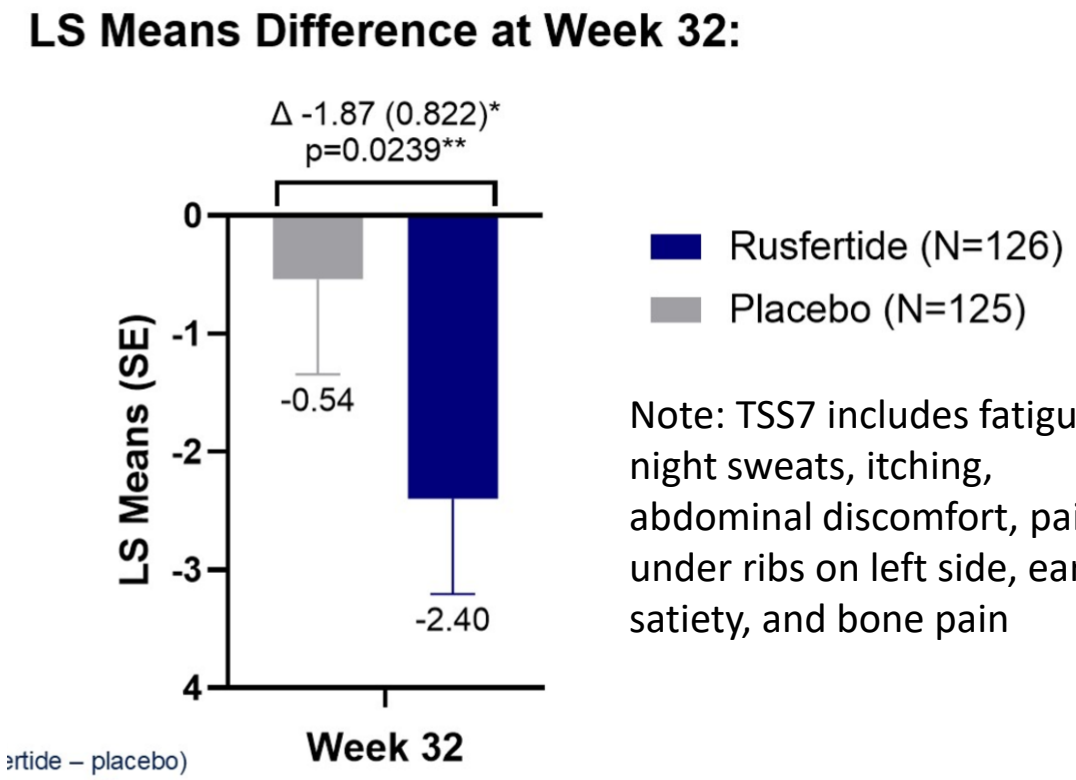
VERIFY: Rusfertide + SOC as treatment for PV

Secondary Endpoints

PROMIS Fatigue SF-8a Total T-score at week 32



MFSAF TSS7 at week 32



Note: TSS7 includes fatigue, night sweats, itching, abdominal discomfort, pain under ribs on left side, early satiety, and bone pain

PROMIS: patient-reported outcomes measurement information system

MFSAF: Myelofibrosis Symptom Assessment Form

TSS7: Total Symptom Score (TSS) derived from a 7-item subset of a larger symptom assessment tool

TSS7 myelofibrosis symptom assessment form version 4.0 total symptom score dash 7 item

KEY DATA

VERIFY: Rusfertide + SOC as treatment for PV

Safety

Most Frequent TEAEs	Placebo + CSC (n=146)	Rusfertide + CSC (n=145)
Patients with at least 1 TEAE	126 (86.3%)	129 (89%)
Injection site reaction	48 (32.9%)	81 (55.9%)
Anemia	6 (4.1%)	23 (15.9%)
Fatigue	23 (15.8%)	22 (15.2%)
Headache	17 (11.6%)	15 (10.3%)
COVID-19	16 (11.0%)	14 (9.7%)
Pruritus	14 (9.6%)	14 (9.7%)
Diarrhea	8 (5.5%)	12 (8.3%)
Dizziness	9 (6.2%)	12 (8.3%)
Arthralgia	12 (8.2%)	11 (7.6%)
Constipation	11 (7.5%)	11 (7.6%)
Abdominal distension	8 (5.5%)	10 (6.9%)
Thrombocytosis	0	10 (6.9%)

Cancer Events	Placebo + CSC (n=146)	Rusfertide + CSC (n=145)
Patients with ≥1 Cancer Event, n	7 (4.8%)	1 (0.7%)
Basal cell carcinoma	3 (2.1%)	0
Squamous cell carcinoma	1 (0.7%)	1 (0.7%)
1 (0.7%)	1 (0.7%)	0
Colorectal cancer	1 (0.7%)	0
Prostate cancer	1 (0.7%)	0

Median treatment exposure was 32 weeks in both groups

- Medium (min – max) dose was 30 (10 – 90) mg in the rusfertide group
- Serious AEs occurred in 3.4% in the rusfertide group and 4.8% in the placebo group (none related to rusfertide)
- Discontinuations rates due to TEAEs were 2.7% in the placebo group and 5.5% in the rusfertide group

RESPONSE-2: Ruxolitinib		VERIFY: Rusfertide + CSC	
FDA approval ***Dec 4, 2014***: for the treatment of polycythemia vera in adults who have had an inadequate response to or are intolerant of hydroxyurea		***Not yet approved***	
• **PV requiring phlebotomy** • **Spleen volume greater than 450 cm^3** • **Resistant/ intolerant to hydroxyurea** • **No prior systemic therapy**		• **Three or more phlebotomy 28 weeks prior or five or more phlebotomy 1 year prior**	
Open-label, randomized, phase 3b study Median follow-up: 5 years (260 weeks)		Ongoing, global, randomized, placebo-controlled trial	
Ruxolitinib, 10 mg twice daily (n=74)	Best available therapy* (n=75)	**Rusfertide** + CSC (n=147)	Placebo + CSC (n=146)
Cross over allowed at week 28+: 58 (77%) of BAT crossed over to Rux; 97 pts received Rux until week 260 (59 Rux + 38 BAT cross over arm)		**Primary endpoint**: Clinical responders (absence of phlebotomy eligibility)	
		77%	Weeks 20-32: p <0.0001 33%
Hematocrit control		Hematocrit control	
22% (95% CI 13–33)	*Not reported due to small n of responders*	**62.6%**	p <0.0001 14.4%
60/74 required phlebotomies	106 /75 required phlebotomies	40/147 required phlebotomies	114/146 required phlebotomies
5-year OS: 96%	91%	**---**	---

The Lancet Hematology Volume 9, Issue 7e480-e492July 2022

ASCO 2025. Abstr. LBA3

**BAT included: hydroxyurea (n=38), interferon or pegylated interferon (n=9), pipobroman (n=5), lenalidomide (n=1), or no treatment (n=22)*

SUMMARY

VERIFY

- Rusfertide added to current standard of treatment (phlebotomy ± cytoreductive therapy) could be a new treatment option for patients with polycythemia vera
  - Not yet FDA approved
- Rusfertide resulted in a statistically significant reduction in the mean number of PHLs and improved Hct control
- Demonstrate a statistically significant improvement in the PROMIS Fatigue SF-8a and MFSAF PROs in pts with PV
- Manageable safety profile consistent with prior studies

IMPACT

Rusfertide plus phlebotomy ± cytoreductive therapy improved patient outcomes and could be a potential new treatment option for patients with PV

Rusfertide has received Orphan Drug designation and Fast Track designation from the U.S. FDA

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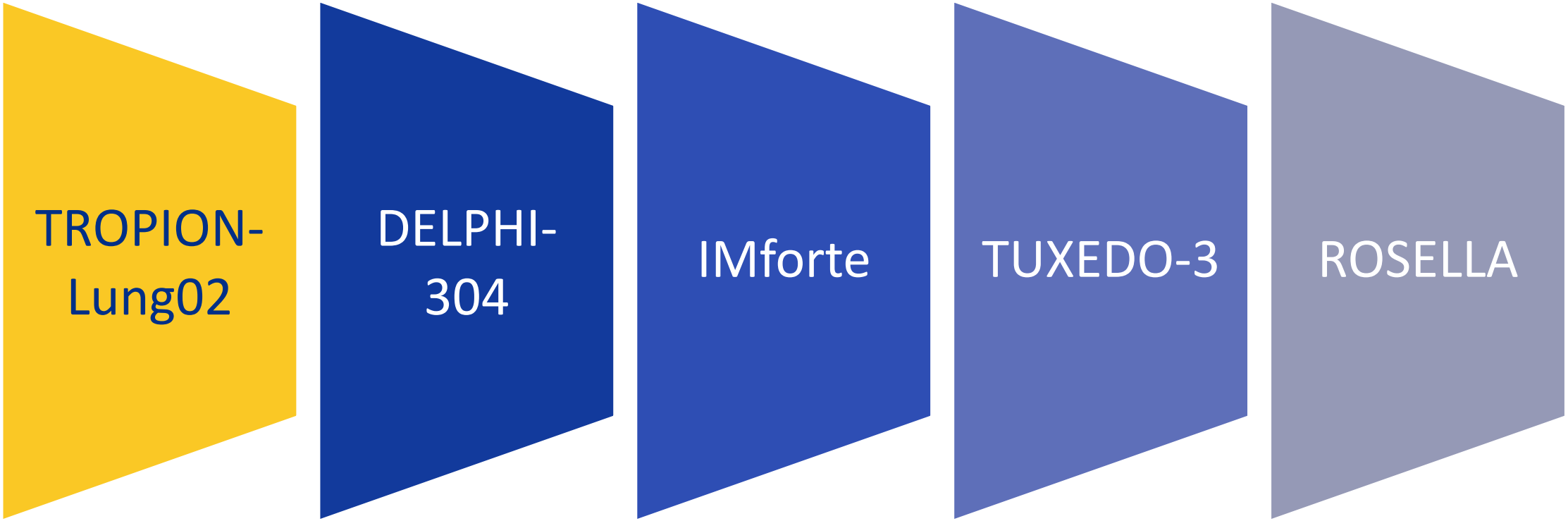
ASCO 2025: RAPID REVIEWS



KEY DATA

TROPION-Lung02: Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab with or without chemotherapy in 1L mNSCLC

Final report

Study Design: Multicenter, open-label, *phase 1b: safety* and efficacy in advanced or metastatic NSCLC without actionable genomic alterations

- Advanced or metastatic NSCLC ***without*** actionable genomic alterations*
- ≤1 line of Platinum-based CT (cohorts 1 and 2) or treatment-naive (cohort 2 [enrolled after June 30, 2022] and 3-6)

**EGFR, ALK, ROS1, NTRK, BRAF, RET,* or *MET.*

Primary objectives: safety and tolerability

Secondary objectives: efficacy

Exploratory retrospective testing of outcomes based on TROP2 biomarker analyses

Data cut-off: April 29, 2024

First-line Patients Only

Cohort 1 (n = 2)	**Dato-DXd** 4 mg/kg IV Q3W + **Pembrolizumab** 200 mg IV Q3W
Cohort 2 (n = 40)	**Dato-DXd** 6 mg/kg IV Q3W + **Pembrolizumab** 200 mg IV Q3W
Cohort 3 (n = 14)	**Dato-DXd** 4 mg/kg IV Q3W + **Pembrolizumab** 200 mg IV Q3W + **Carboplatin** AUC 5
Cohort 4 (n = 26)	**Dato-DXd** 6 mg/kg IV Q3W + **Pembrolizumab** 200 mg IV Q3W + **Carboplatin** AUC 5
Cohort 5 (n = 8)	**Dato-DXd** 4 mg/kg IV Q3W + **Pembrolizumab** 200 mg IV Q3W + **Cisplatin** 75 mg/m^2
Cohort 6 (n = 6)	**Dato-DXd 6** mg/kg IV Q3W + **Pembrolizumab** 200 mg IV Q3W + **Cisplatin** 75 mg/m^2

Baseline Characteristic	Doublet (n = 42)	Triplet (n = 54)
Median age, yr (range)	65 (48-83)	64 (33-78)
Male, n	32 (76.2%)	34 (63.0%)
Asian race, n	31 (73.8%)	23 (42.6%)
Histology, n		
• Nonsquamous	32 (76.2%)	40 (74.1%)
• Squamous	10 (23.8%)	14 (25.9%)
History of brain metastases, n	4 (9.5%)	10 (18.5%)
ECOG PS 1, n	24 (57.1)	33 (61.1%)
Dato-DXd dosing, n		
• 4 mg/kg	2 (4.8%)	22 (40.7%)
• 6 mg/kg	40 (95.2%)	32 (59.3%)
PD-L1 expression, n		
• <50%	30 (71.4%)	40 (74.1%)
• ≥50%	5 (11.9%)	10 (18.5%)
• NE	7 (16.7%)	4 (7.4%)

KEY DATA

TROPION-Lung02: Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab with or without chemotherapy in 1L mNSCLC

Primary Endpoint: Safety (summary)

Event, n (%)	Doublet (n = 42)	Triplet (n = 54)
TRAE, n	39 (92.9%)	54 (100%)
• Grade ≥3	17 (40.5%)	30 (55.6%)
TEAEs associated with dose modifications		
• Dose reduction of any drug	8 (19.0%)	14 (25.9%)
• Dose reduction of Dato-DXd	8 (19.0%)	7 (13.0%)
• Discontinuation of any drug	14 (33.3%)	20 (37.0%)
• Discontinuation of Dato-DXd	13 (31.0%)	16 (29.6%)
Serious TRAEs, n	5 (11.9%)	12 (22.2%)
• Grade ≥3	4 (9.5%)	9 (16.7%)
AEs of special interest		
• Oral mucositis/stomatitis	26 (61.9%)	22 (40.7%)
– Grade 3	2 (4.8%)	1 (1.9%)
• Adjudicated drug-related ILD/pneumonitis	11 (26.2%)	14 (25.9%)
– Grade 3	2 (4.8%)	1 (1.9%)
• Ocular surface events	9 (21.4%)	18 (33.3%)
– Grade 3	1 (2.4%)	2 (3.7%)

Secondary Endpoint: Efficacy

Parameter	Doublet (n = 42)	Triplet (n = 54)
Confirmed ORR, n (%) [95% CI]	23 (**54.8%**) [38.7-70.2]	30 (55.6%) [41.4-69.1]
Median DoR, mo (95% CI)	**20.1** (9.7-NE)	13.7 (5.7-NE)
DCR, n (%) [95% CI]	37 (**88.1%**) [74.4-96.0]	48 (88.9%) [77.4-95.8]
Median TTR, mo (Range)	1.4 (1.2-7.0)	1.4 (1.2-9.6)
Median PFS, mo (95% CI)	**11.2** (8.2-21.3)	6.8 (5.5-11.1)
Median OS, mo (95% CI)	NE (19.2-NE)	17.4 (9.1-NE)

Efficacy benefit regardless of PD-L1 expression
Safety profile was consistent with the known toxicities of each agent, and no new safety signals

More to come…TROPION-Lung07 (1L mNSCLC, PD-L1 <50%) and TROPION-Lung08 (1L mNSCLC, PD-L1 ≥50%)

ASCO 2025 Abstr. #8501

Recent FDA Approval: *Dato-DXd Monotherapy*

*On **June 23, 2025**, the FDA granted accelerated approval to **datopotamab deruxtecan-dlnk** (Datroway, Daiichi Sankyo, Inc.) for adults with **locally advanced or metastatic EGFR-mutated NSCLC** who have received **prior EGFR-directed therapy and platinum-based chemotherapy***

- Pooled subgroup of 114 patients (**TROPION-Lung05 and TROPION-Lung01**)
- Locally advanced or metastatic EGFR-mutated NSCLC
- Prior treatment with an EGFR-directed therapy and platinum-based chemotherapy
- Received datopotamab deruxtecan-dlnk at the recommended dose of 6 mg/kg (up to a maximum of 540 mg for patients ≥ 90 kg), as an intravenous infusion once every 3 weeks, until disease progression or unacceptable toxicity.

The major efficacy outcome measures were confirmed overall response rate (ORR) and duration of response (DOR) determined by blinded independent central review per RECIST v1.1.

- ORR: 45% (95% CI: 35, 54)
- Median DOR: 6.5 months (95% CI: 4.2, 8.4)

TROPION-Lung05 (NCT04484142): multicenter, single-arm trial
TROPION-Lung01 (NCT04656652): multicenter, open-label, randomized controlled trial

FDA grants accelerated approval to datopotamab deruxtecan-dlnk for EGFR-mutated non-small cell lung cancer | FDA

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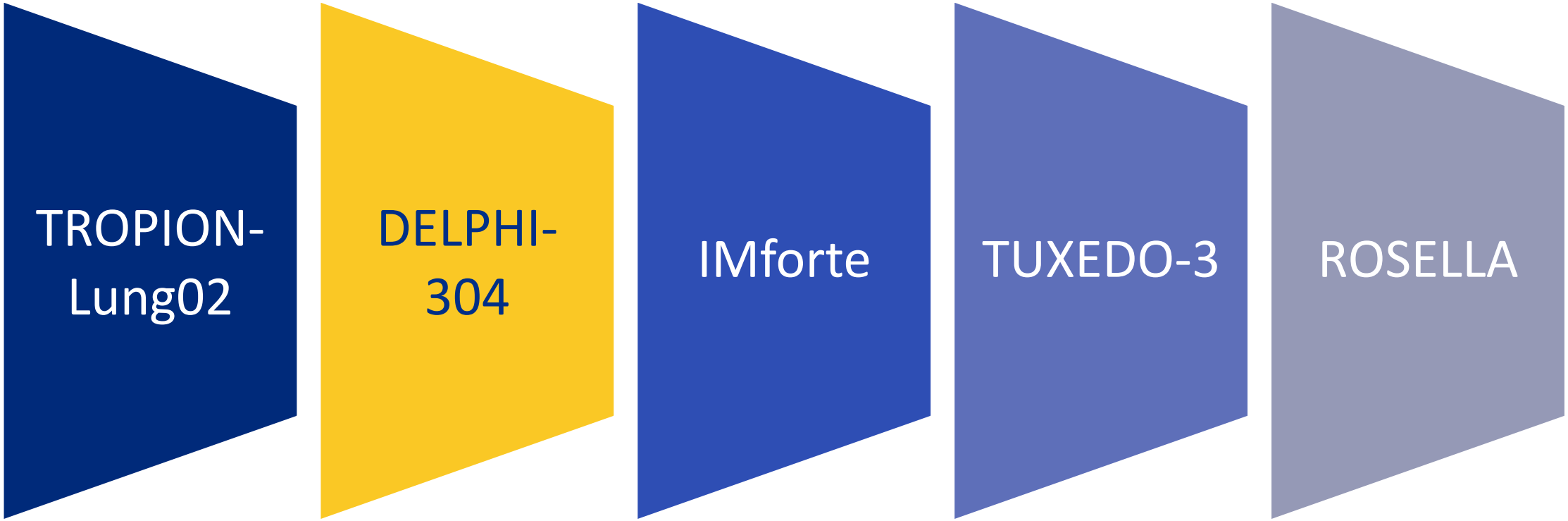
ASCO 2025: RAPID REVIEWS



KEY DATA

DELLphi-304: Tarlatamab as a 2L treatment for SCLC

Study Design: randomized controlled phase 3 study

Stratified by: prior anti PD L1 exposure (yes or no), chemotherapy free interval (<90 days vs ≥ 90 days to <180 days vs ≥ 280 days); Presence of (previous/current) brain metastases (yes or no); Intended chemotherapy (topotecan/amrubicin vs lurbinectedin)

- Histologically or cytologically confirmed SCLC
- Progression after 1L platinum-based chemo ± anti PD-(L)1
- ECOG PS 0 or 1
- Asymptomatic, treated or untreated brain metastases

R 1:1

- Tarlatamab (n=254)
- Chemotherapy* (n=255)

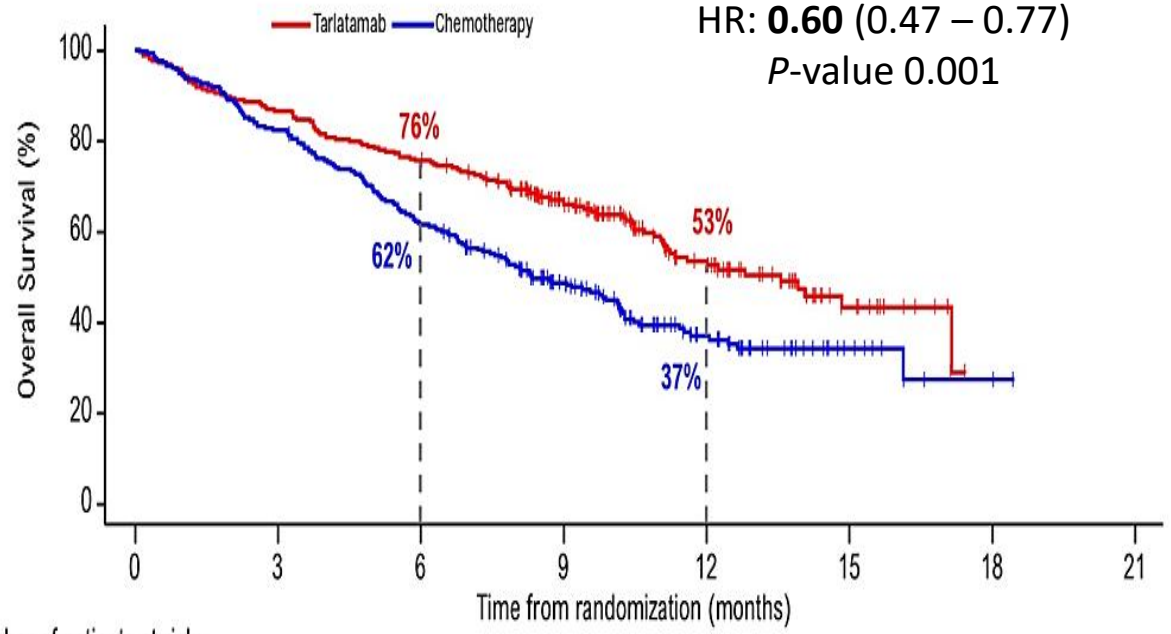
*Topotecan (n=185); amrubicin (n=23);lurbinectedin (n=47)

Primary Endpoint: OS

Secondary Endpoint: PFS, PROs, OR, DCR, DOR, Safety

Primary Endpoint: Overall Survival

mOS: Tarlatamab **13.6** mos
Chemotherapy **8.3** mos
HR: **0.60** (0.47 – 0.77)
P-value 0.001



Number of patients at risk:

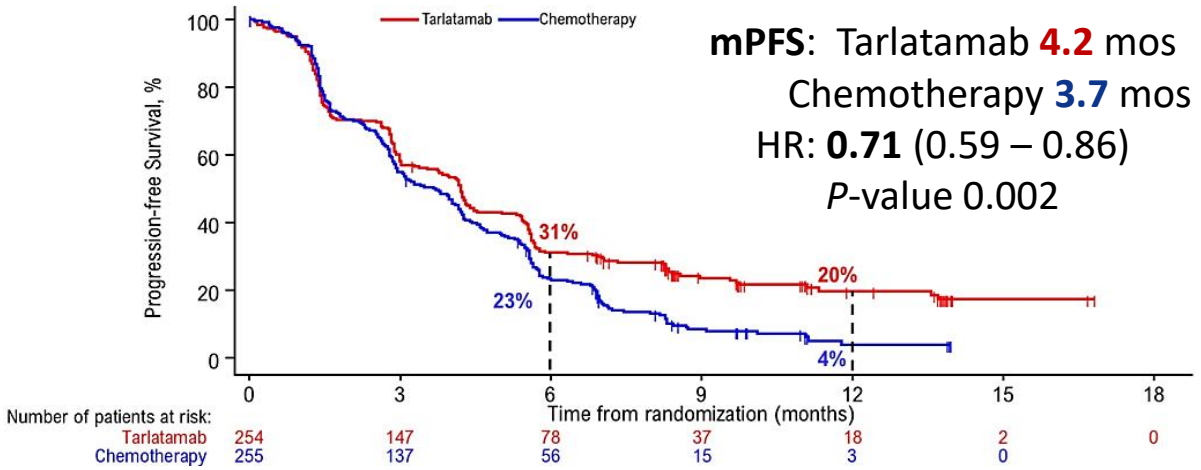
Tarlatamab	254	220	192	131	60	17	0
Chemotherapy	255	210	156	97	42	9	2	0

KEY DATA

DELLphi-304: Tarlatamab as a 2L treatment for SCLC

Primary analysis

Key Secondary Endpoint: Progression-Free Survival



mPFS: Tarlatamab **4.2** mos
Chemotherapy **3.7** mos
HR: **0.71** (0.59 – 0.86)
P-value 0.002

Safety Summary (Safety analysis set, at least one dose of Tx)	**Tarlatamab (n=252)**	**Chemotherapy (n=244)**
Median duration of treatment, mos	4.2 (<1 – 17)	2.5 (<1 – 15)
• All grade TEAEs, n (%)	249 (99%)	243 (100%)
• All grade TRAEs, n (%)	235 (93%)	223 (91%)
• Grade 3 TREAs, n (%)	67 (27%)	152 (62%)
• Serious TRAEs, n (%)	70 (28%)	75 (31%)
• TRAEs, dose interruption/reduction, n (%)	48 (19%)	134 (55%)
• TRAEs, discontinuation, n (%)	7 (3%)	15 (6%)
• Tx-related grade 5 events, n (%)	1 (0.4%)	4 (2)

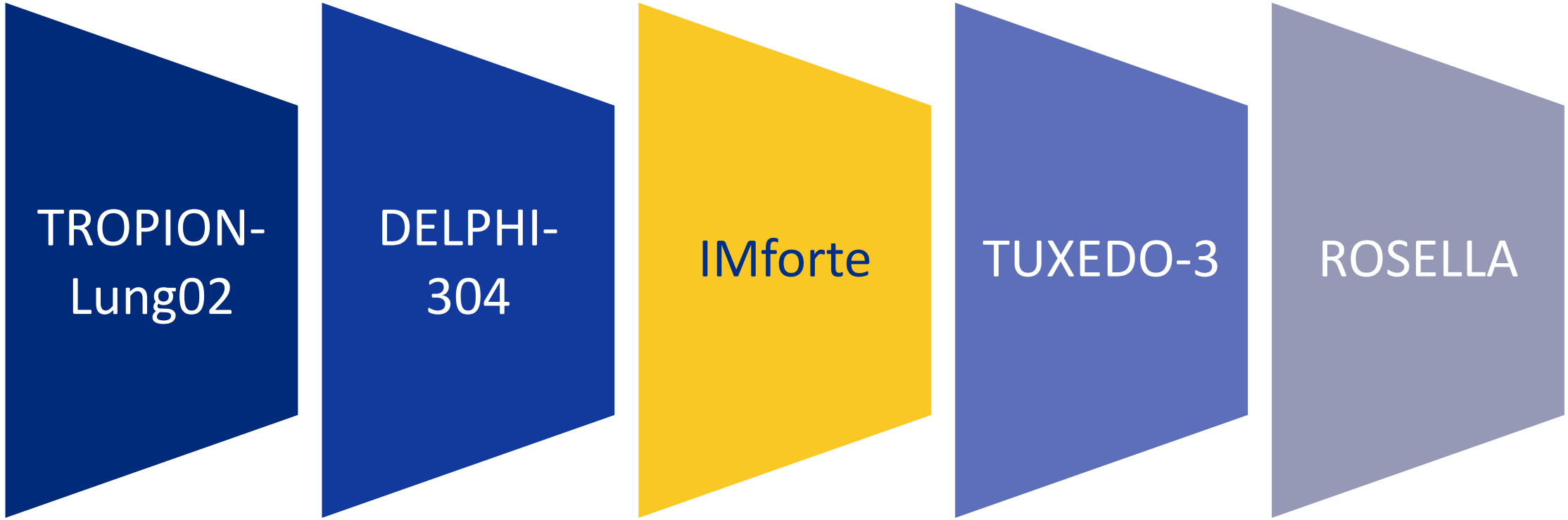
Response Data and Summary

	Tarlatamab (n=254)	**Chemotherapy (n=255)**
Best overall Response, n (%)		
• CR	3 (1%)	0 (0%)
• PR	84 (34%)	52 (20%)
• SD	84 (33%)	112 (44%)
• PD	56 (22%)	50 (20%)
• Not evaluable	25 (10%)	41 (16%)
ORR, %	**35%** (29-41)	**20%** (16-26)
Median duration of Response, mos	6.9	5.5
Median time to objective response, mos	1.5	1.4
Ongoing response at data cutoff, n (%)	42 (47%)	8 (15%)

Tarlatamab previously granted accelerated approval (May 2024) based on the phase 2 DELLphi-301 study

Phase 3 DELLphi-304 trial confirms survival benefit of tarlatamab in SCLC compared to SoC chemotherapy

ASCO 2025: RAPID REVIEWS



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Press Release

IMforte Lurbinectedin and atezolizumab combination granted US FDA priority review for first line maintenance treatment of ES-SCLC

Study Design

- Ongoing phase III, randomized, multicenter maintenance trial
- Evaluating the efficacy, safety, and pharmacokinetics of lurbinectedin plus atezolizumab compared with standard-of-care, first-line maintenance with atezolizumab alone in adults (aged ≥18 years) with ES-SCLC, following induction therapy with carboplatin, etoposide, and atezolizumab.
- The primary endpoints for this study are OS and independent review facility-assessed PFS

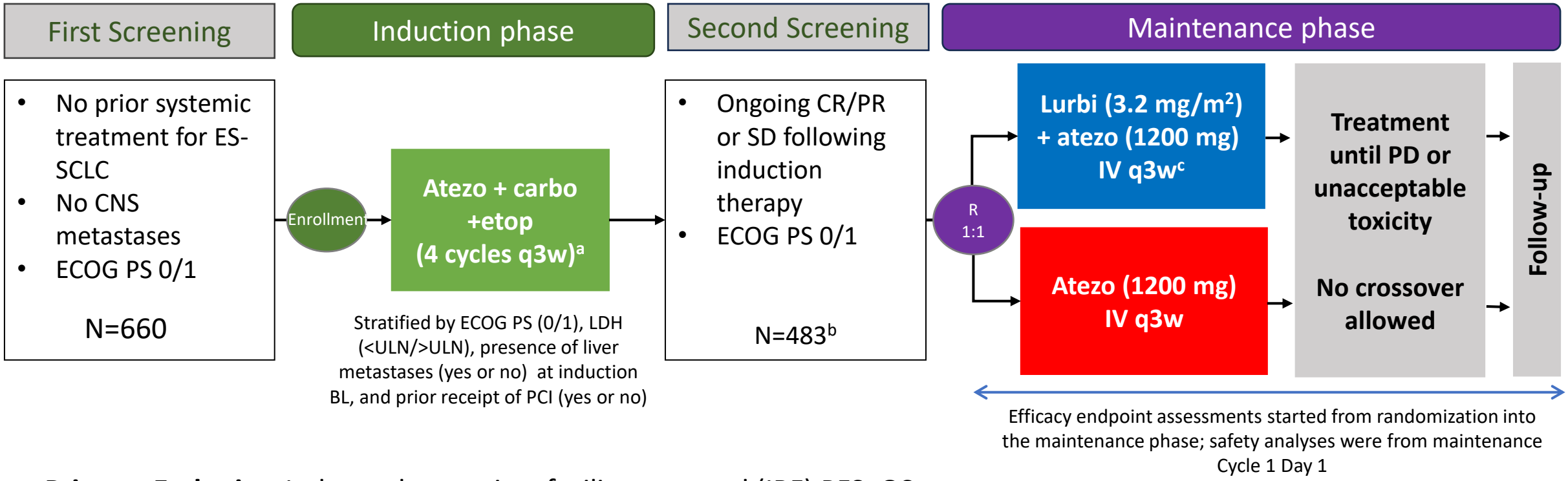
- ***Press release**: DUBLIN, **June 10, 2025** /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced the U.S. Food and Drug Administration (FDA) has accepted the supplemental New Drug Application (sNDA) for Zepzelca® (lurbinectedin) in combination with atezolizumab (Tecentriq®) as a first-line maintenance treatment for people with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab, carboplatin, and etoposide for Priority Review.*
- *A Prescription Drug User Fee Act (PDUFA) action date of October 7, 2025.*

https://investor.jazzpharma.com/news-releases/news-release-details/zepzelcar-lurbinectedin-and-atezolizumab-tecentriqr-combination

KEY DATA

IMforte: Lurbinectedin to 1L chemo + Atezolizumab treatment for ES-SCLC in patients without progression after chemo

Study Design: Global, open-label, randomized phase 3 trial



Primary Endpoint: Independent review facility-assessed (IRF) PFS, OS

Secondary Endpoint: INV-PFS, ORR, DOR, Safety

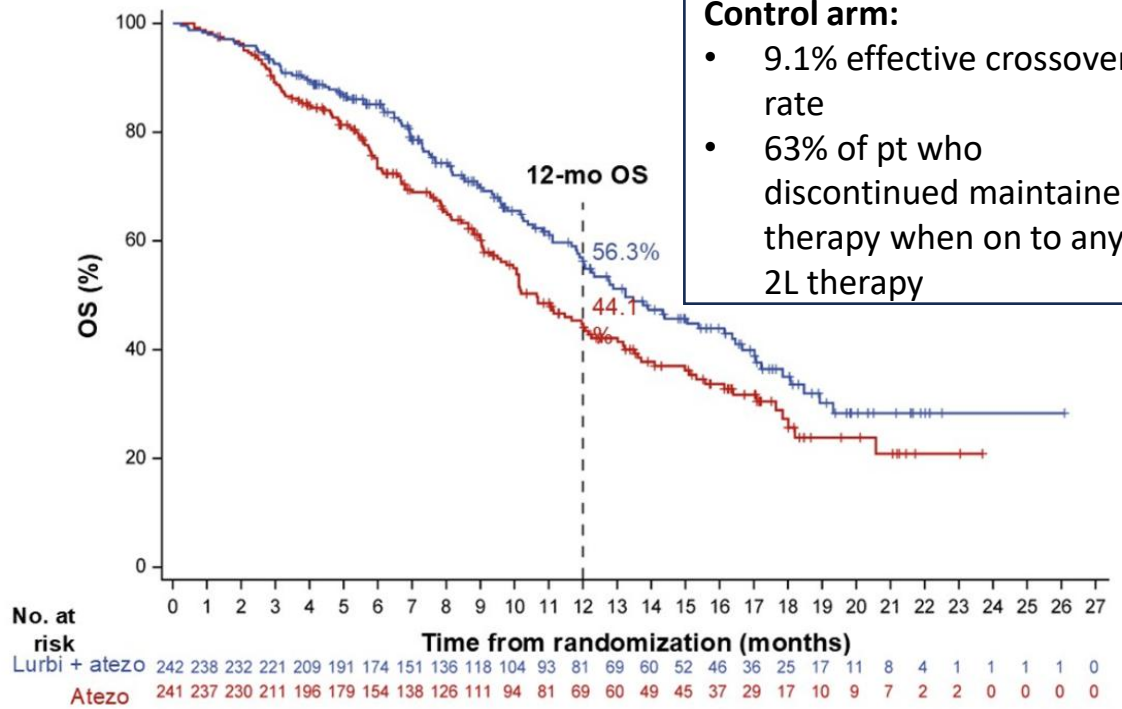
Clinical cutoff: July 29, 2024

[a]Administered per standard dose. [b]73% of patients continued from induction to maintenance. [c]With prophylactic granulocyte colony-stimulating factor and anti-emetics.

KEY DATA

IMforte: Lurbinectedin to 1L chemo + Atezolizumab treatment for ES-SCLC in patients without progression after chemo

OS benefits in 1L ES-SCLC



Control arm:

- 9.1% effective crossover rate
- 63% of pt who discontinued maintained therapy when on to any 2L therapy

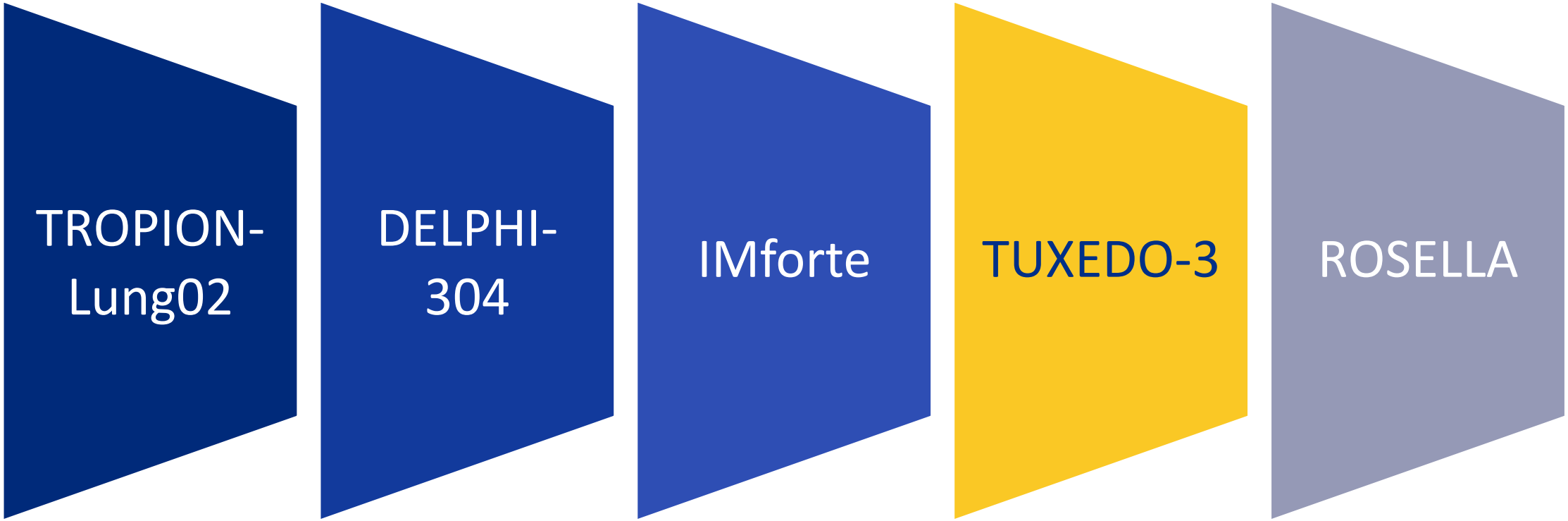
OS*	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n	113 (46.7%)	136 (56.4%)
OS, median (95% CI), mo	13.2 (11.9, 16.4)	10.6 (9.5, 12.2)
Stratified HR (95% CI)	0.73 (0.57, 0.95)	
Stratified *P* value (2-sided)	0.0174	
a boundary (2-sided)	0.0313	

Efficacy vs Toxicity

Patients with ≥1 AE, n	Lurbi + atezo (n=242)	Atezo (n=240)
All-cause AEs	235 (97.1%)	194 (80.8%)
Grade ¾ AEs	92 (38.0%)	53 (22.1%)
Treatment-related Grade ¾ AEs	62 (25.6%)	14 (5.8%)
Grade 5 AEs	12 (5.0%)	6 (2.5%)
Treatment-related Grade 5 AEs	2 (0.8%)	1 (0.4%)
Serious AEs	75 (31.0%)	41 (17.1%)
AEs leading to discontinuation of any study drug	15 (6.2%)	8 (3.3%)
AEs leading to dose interruption/modification of any study drug	92 (38.0%)	33 (13.8%)

Lurbinectedin + 1L chemo + ICI improved survival in ES-SCLC in patient without progression after chemo

ASCO 2025: RAPID REVIEWS



KEY DATA

TUXEDO-3: patritumab deruxtecan (HER3-DXd) in active brain mets (breast cancer, NSCLC) and in solid tumors with leptomeningeal disease

Study Design: open-label single-arm, three cohort, non-comparative phase 2 trial

- ≥18 yrs old
- **mBC with active brain mets (N=20; cohort 1)**
  - ≥1 measurable (≥10 mm) brain lesions
- **AdvNSCLC with active brain mets (N=20; cohort 2)**
  - ≥1 measurable (≥10 mm) brain lesions
- **Any adv solid tumor with type I/II LMD (N=20; cohort 3)**
- ≥1 line of systemic therapy in the adv setting
- KPS ≥70%
- ECOG PS ≤2
- LVEF ≥50%

HER3-DXd

5.6 mg/kg IV every 21 days until PD, discontinuation or death

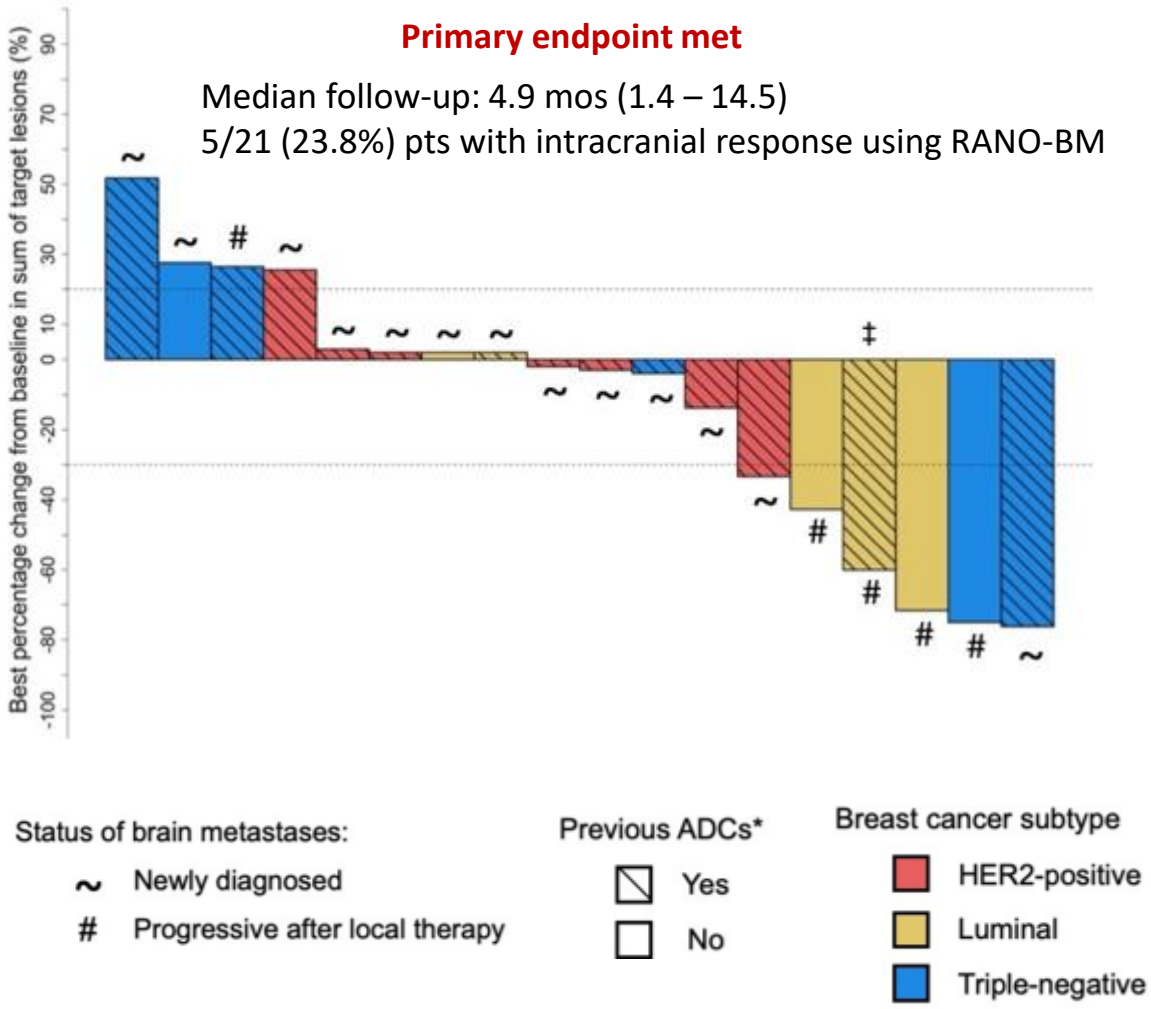
Primary Endpoints:

- **Cohort 1**: intracranial ORR (met if ≥15% pts with response)
- **Cohort 2**: intracranial ORR (met if ≥15% pts with response)
- **Cohort 3**: 3-month OS rate (met if ≥15% pts alive after 3-mos)

Primary Endpoint: Metastatic BC with active brain mets

Primary endpoint met

Median follow-up: 4.9 mos (1.4 – 14.5)
5/21 (23.8%) pts with intracranial response using RANO-BM



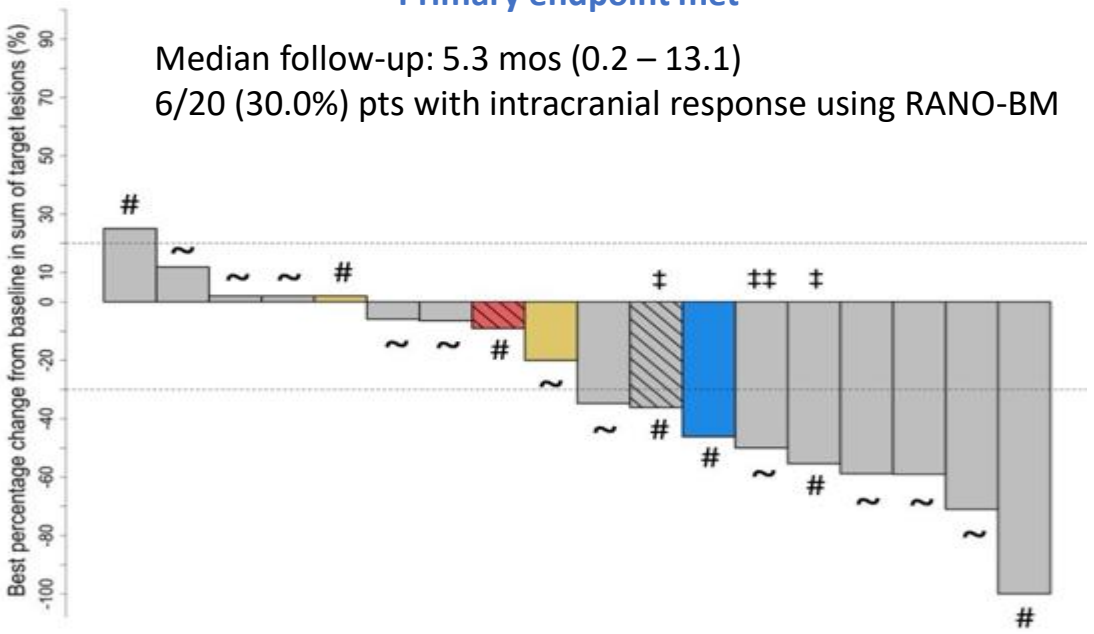
KEY DATA

TUXEDO-3: patritumab deruxtecan (HER3-DXd) in active brain mets (breast cancer, NSCLC) and in solid tumors with leptomeningeal disease

Primary Endpoint: Metastatic NSCLC with active brain mets

Primary endpoint met

Median follow-up: 5.3 mos (0.2 – 13.1)
6/20 (30.0%) pts with intracranial response using RANO-BM



Status of brain metastases:
~ Newly diagnosed
# Progressive after local therapy

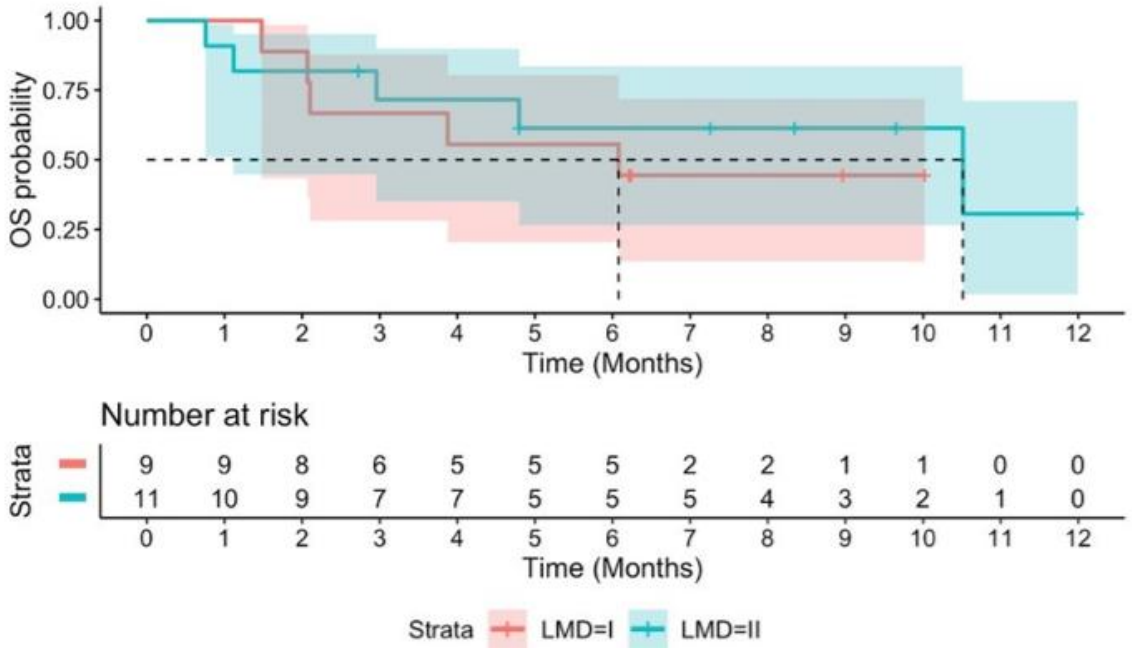
Histologic type
Squamous
Non-squamous

Activating driver mutations
Non-mutated
EGFR (common)
EGFR (uncommon)
KRAS G12C

Primary Endpoint: Metastatic Solid Tumors with LMD

Primary endpoint met

Median follow-up: 5.4 mos (0.8 – 12.0)
13/20 (65.0%) pts alive after 3-mos



HER2-DXd has potential to benefit patients with active brain mets or leptomeningeal disease

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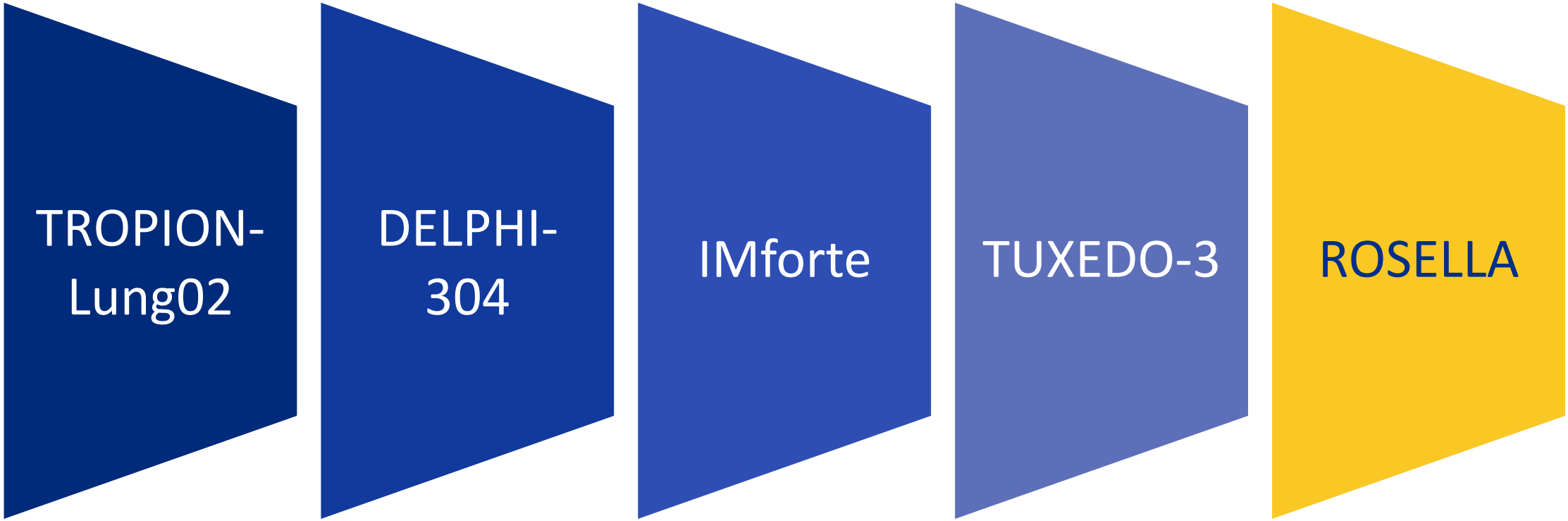


KEY DATA

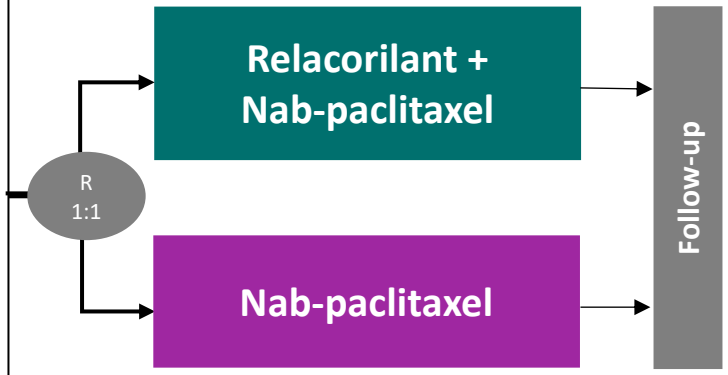
ROSELLA: Relacorilant in Combination with Nab-Paclitaxel vs Nab-Paclitaxel monotherapy in patients with Platinum-Resistant Ovarian Cancer

Relacorilant, is a selective glucocorticoid receptor modulator; on July 14, 2025, a NDA was submitted to the FDA based on ROSELLA with a PDUFA date of December 30, 2025

Study Design: Phase 3, randomized, open-label, global multicenter study

- Epithelial ovarian, primary peritoneal or fallopian tube cancer
- ECOG PS 0 or 1
- Progression <6 mo after the last dose of platinum therapy (excluding no response to, or progression in <1 mo of primary platinum)
- 1-3 prior lines of therapy
- Prior bevacizumab required

Stratified by prior lines of therapy (1 vs >1) and region (N America vs Europe vs Korea, Australia, and Latin America)



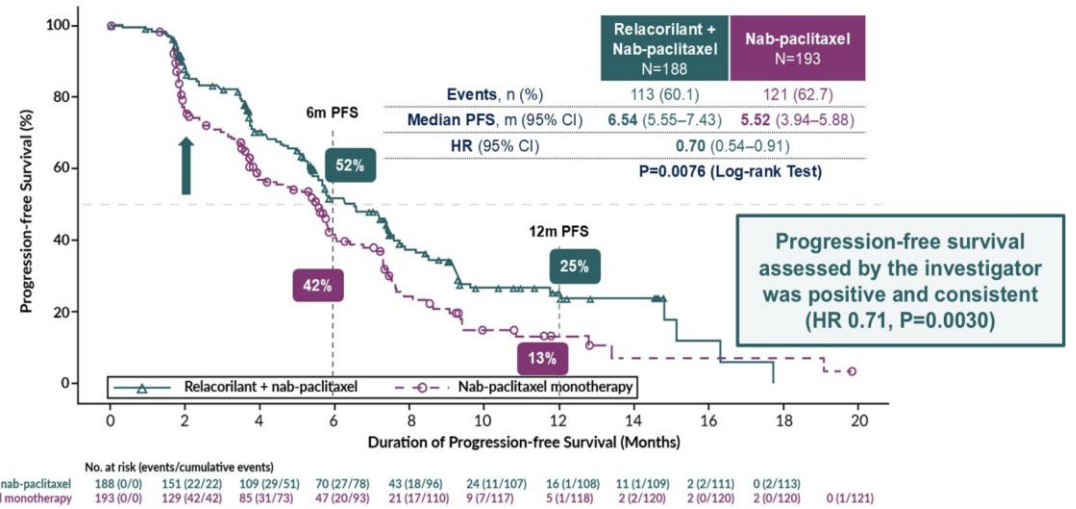
Data cutoff: 24 February 2025

***381 women were in the phase 3 trial**

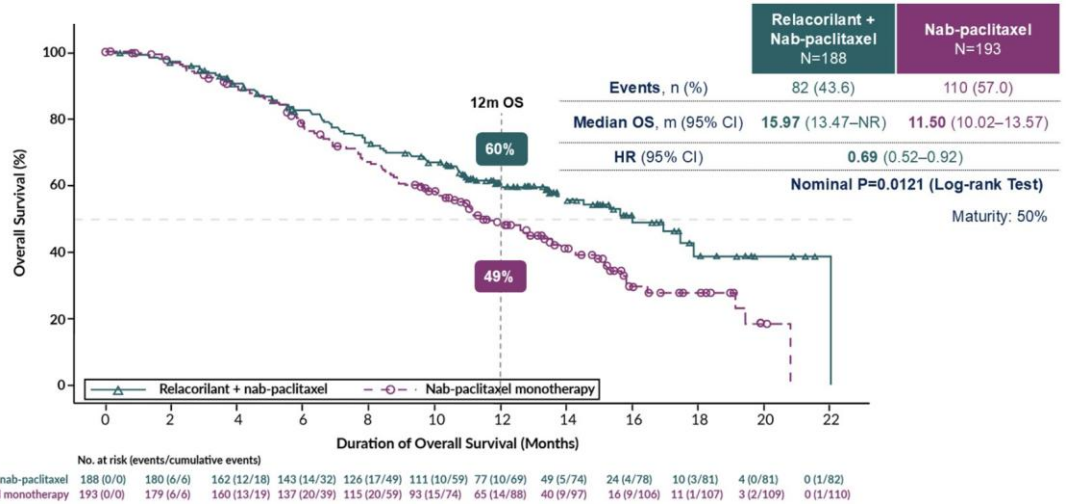
Primary Endpoint: PFS by RECIST v1.1 per blinded independent central review, OS

Secondary Endpoint: PFS by RECIST v1.1 Investigator, ORR, DoR, CBR (RECISTS v1.1), response by CA-125 GCIG criteria, combine response (RECIST v1.1 and CA-125 GCIG criteria), Safety

PFS assessed by blinded review



Overall Survival



KEY DATA

ROSELLA: Relacorilant in Combination with Nab-Paclitaxel vs Nab-Paclitaxel monotherapy in patients with Platinum-Resistant Ovarian Cancer

Secondary Endpoints:

	Relacorilant + Nab-paclitaxel (N=188)	Nab-paclitaxel (N=190)
Objective Response Rate, n	69 (36.9%)	58 (30.1%)
	6.8% improvement P=0.17 (Stratified Cochran-Mantel-Haenszel Test)	
• **Complete Response, n**	6 (3.2%)	4 (2.1%)
• **Partial Response, n**	63 (33.7%)	54 (28.0%)
• **Stable Disease, n**	77 (41.2%)	68 (35.2%)
• **Progressive Disease, n**	32 (17.1%)	52 (26.9%)
• **Not Evaluable, n**	9 (4.8%)	15 (7.8%)
Clinical Benefit Rate, n (Response or stable disease maintained for 24 weeks)	96 (51.1%)	75 (38.9%)
	12.2% improvement P=0.016 (Stratified Cochran-Mantel-Haenszel Test)	

Safety Summary	Relacorilant + Nab-paclitaxel (N=188)	Nab-paclitaxel (N=190)
Weeks of Nab-paclitaxel Therapy, mean (range)	23.2 (0.1-90.3)	18.6 (0.1-68.1)
Any TEAEs, n	188 (100%)	189 (99.5%)
Grade ≥3 TEAEs	140 (74.5%)	113 (59.5%)
Serious AEs, n	66 (35.1%)	45 (23.7%)
All Death on treatment or within 30 days of the last dose, n	10 (5.3%)	8 (4.2%)
Dose reductions of Relacorilant Due to TEAEs, n	13 (6.9%)	--
Dose reductions of Nab-paclitaxel Due to TEAEs, n	91 (48.4%)	60 (31.6%)
Interruptions of Nap-paclitaxel (+ Relacorilant) Due to TEAEs, n	137 (72.9%)	104 (54.7%)
Discontinuation of Nab-pacilaxel (+ Relacorilant) Due to TEAEs, n	17 (9.0%)	15 (7.9%)

Adding relacorilant to nab-paclitaxel improved survival for patients with platinum-resistant ovarian cancer

ASCO 2025 Abstr. #5507

ASCO 2025:

Other Cancers

Key Takeaways

Q&A

@EricSchaeferMD

NIVOPOSTOP: *Post-operative nivolumab added to SOC cisplatin-RT benefited patients for resected high-risk LA-SCCHN and could be proposed as a new standard treatment… not yet FDA approved*

KEYNOTE-689: *Neoadjuvant pembrolizumab followed by surgery and adjuvant pembrolizumab concurrent with and after postoperative (chemo)radiotherapy could be a new standard of care in the treatment of patients with resectable locally advanced head and neck cancer… FDA approved since June 2025*

VERIFY: *Rusfertide plus phlebotomy ± cytoreductive therapy improved patient outcomes and should be considered as a new treatment option for patients with PV... not yet FDA approved*

TROPION-Lung02: *Dato-DXd + pembrolizumab ± platinum chemotherapy showed encouraging activity in patients with NSCLC in 1L and 2L setting. More to come…TROPION-Lung07 (1L mNSCLC, PD-L1 <50%) and TROPION-Lung08 (1L mNSCLC, PD-L1 ≥50%)*

DELLPHI-304: *Phase 3 study confirmed that 2L tarlatamab improved medical survival compared to chemo SOC... accelerated FDA approval granted in May 2024*

IMforte: *Lurbinectedin + 1L chemo+ICI improved survival in ES-SCLC in patient without progression after chemo... not yet FDA approved*

TUXEDO-3: *HER3-DXd showed activity to benefit patients with active brain mets or leptomeningeal disease… not yet FDA approved*

ROSELLA: *Adding Relacorilant to nab-paclitaxel improved mOS in patients with platinum-resistant ovarian cancer... not yet FDA-approved…PDUFA date Dec 30, 2025*

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