

ASCO Update 2026

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Disclosure

- No Conflicts

Objectives

At the end of this presentation participants will be able to:

1. Identify recently presented efficacy data that may impact the standard of care
2. Describe patient populations that should be considered for these new treatments
3. Recognize the potential toxicity associated with these new treatments

Pre Q1. Which of the following is true about treatment of Pancreatic Cancer Patients?

- a. Immunotherapy is replacing cytotoxic chemotherapy
- b. A novel TKI is replacing cytotoxic chemotherapy
- c. Sequencing therapy makes this a chronic disease
- d. Cytotoxic chemotherapy is highly effective

Pre Q2. Which of the following is true about adjuvant NSCLC treatment?

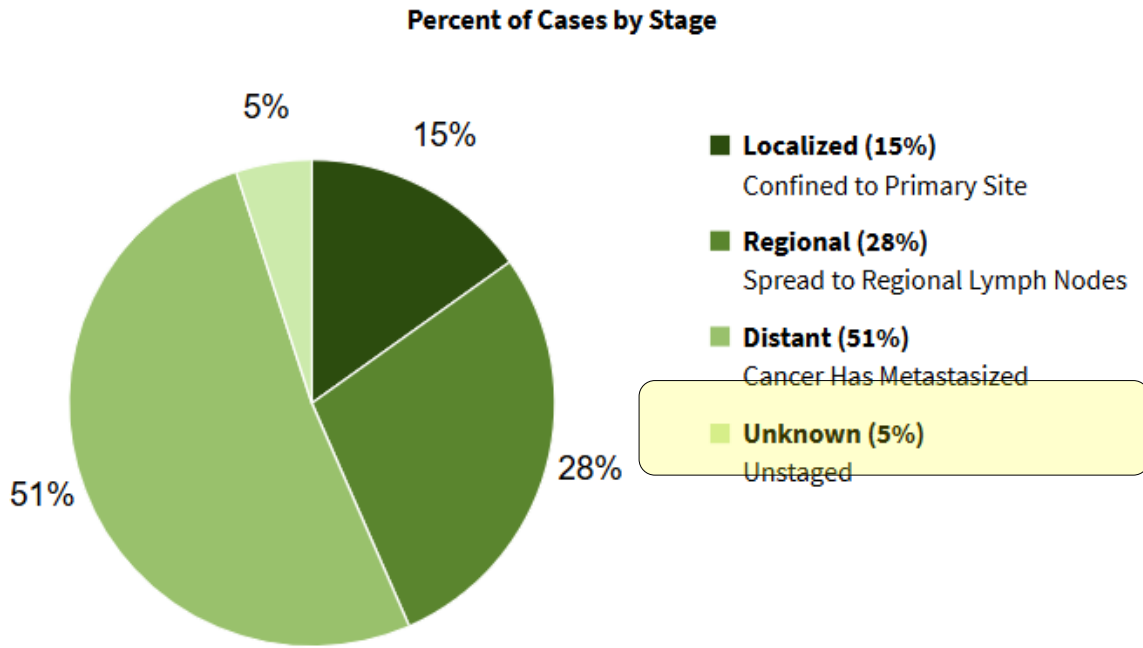
- a. Adjuvant therapy of any type provides minimal to no OS benefit
- b. Antibody directed cytotoxic therapy has expanded into adjuvant NSCLC therapy
- c. An adjuvant RET inhibitor appears to be a significant improvement
- d. Adjuvant TKI therapy beyond EGFR and ALK inhibitors has failed to show promise

Another step in Personalized Treatment

Outline and trials discussed

- Pancreatic Cancer: Daraxonrasib (RASolute 302 trial)
- Lung Cancer: Adjuvant Selpercatinib for RET+ NSCLC (Libretto-432), Ivonescimab plus chemotherapy (HARMONi-6)
- Breast Cancer: Adjuvant Girecestrant (LidERA)
- Colorectal Cancer: Encorafenib + cetuximab + FOLFIRI (Breakwater)
- Treatment De-escalation: Chemotherapy avoidance for N+ high risk breast cancer patients (OPTIMA), 3 months of adjuvant CRC therapy instead of 6 months based on ctDNA (GALAXY ctDNA Insight)

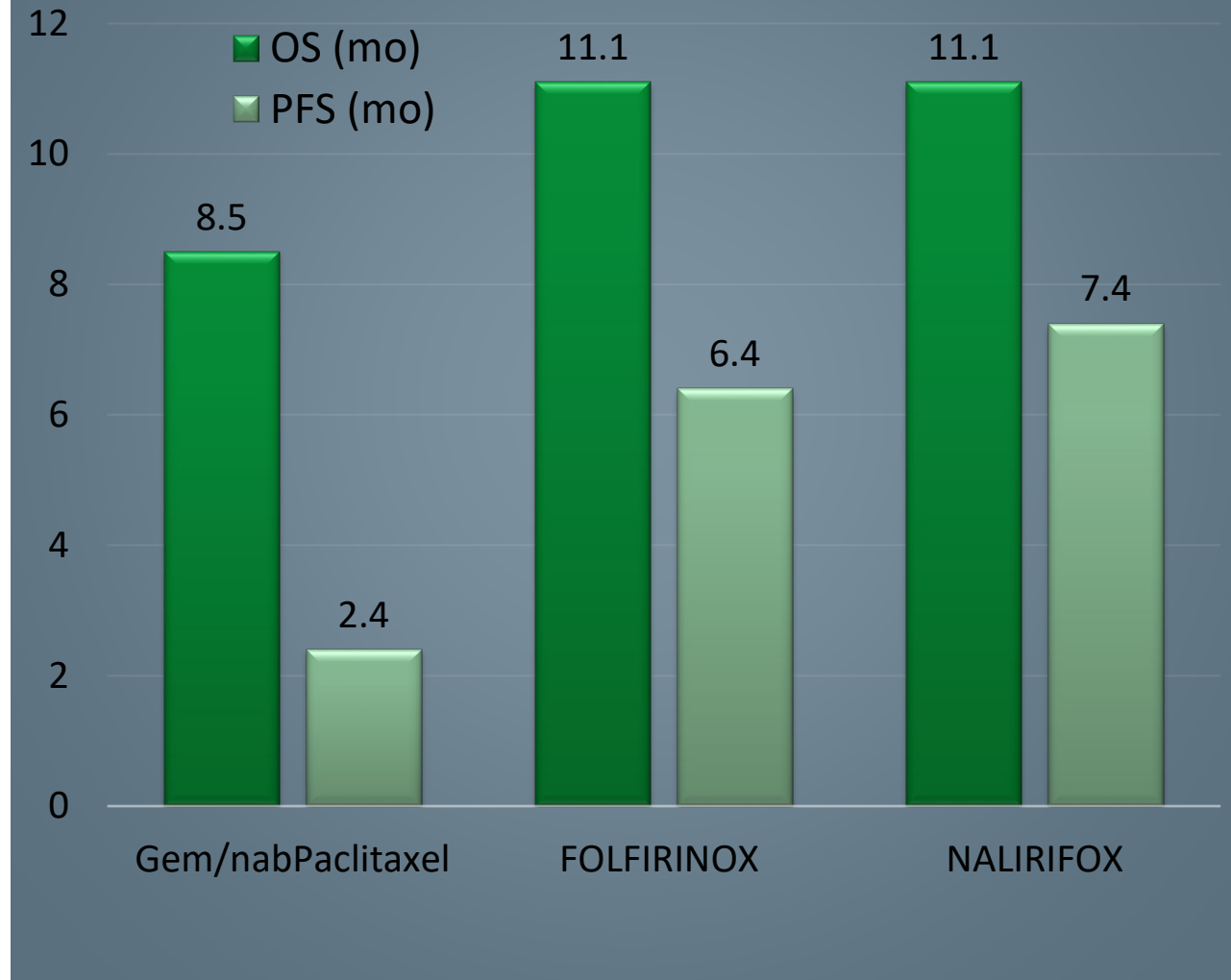
Pancreatic Cancer



Median OS from 2nd line treatment is ~ 4 months

Preferred 2nd line therapy is clinical trial

First Line Tx for ADV/Metastatic Disease



Pancreatic Cancer – RASolute 302

2nd Line pancreatic ductal carcinoma

Previously treated mPDAC

Stratified by:

- Performance status (0 or 1)
- Presence of Mets at original Dx
- Liver metastases
- Ras mutational status (G12, G13, or Q61, or none identified)

Primary objective: RAS G12-mut - PFS and OS

Secondary objectives: PFS, OS, ORR



Daraxonrasib 300 mg po daily

N=248

Investigator's Choice of:

Gem/nab-Paclitaxel Or
5FU based regimen

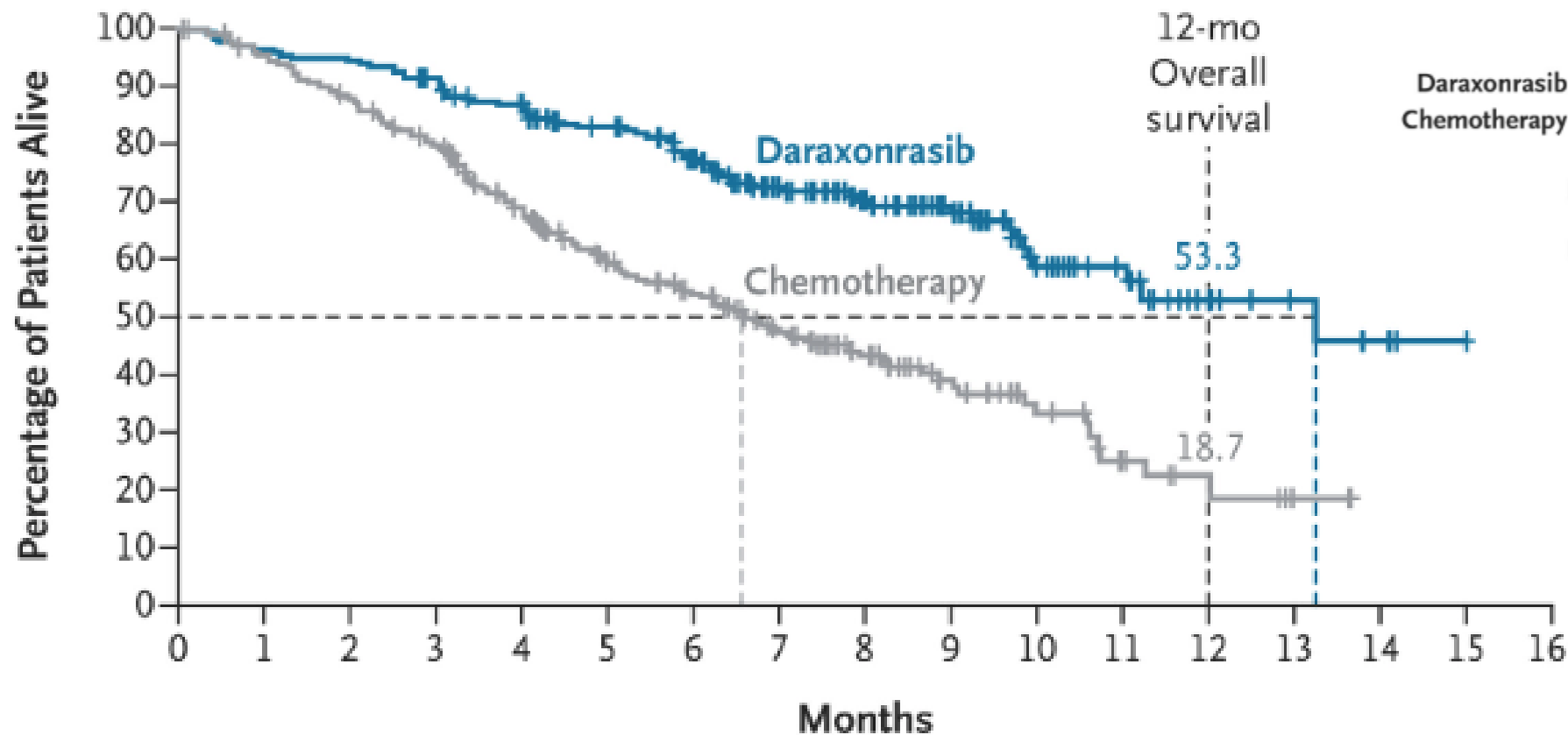
N=252

Demographics – RASolute 302

Characteristic		Daraxonrasib (n = 248)	Chemotherapy (n = 252)
Mean age, yr		66 (30-88)	65 (36-86)
Women		47%	43%
Race:	White	69%	66%
	Asian	12%	11%
	Black	3%	6%
ECOG PS	0	52%	47%
	1	48%	53%
Prior Regimen: FOLFIRINOX		40%	42%
Gem/nabPaclitaxel		38%	37%
NALIRIFOX		2%	1%
Prior Whipple Procedure		23%	22%
Liver Metastases		70%	70%
RAS Mutation:	G12D or G12V	79%	78%
	other G12 mut	13%	14%
	G13 or Q61 or None	8%	8%

Overall Survival – RASolute 302 (primary endpoint)

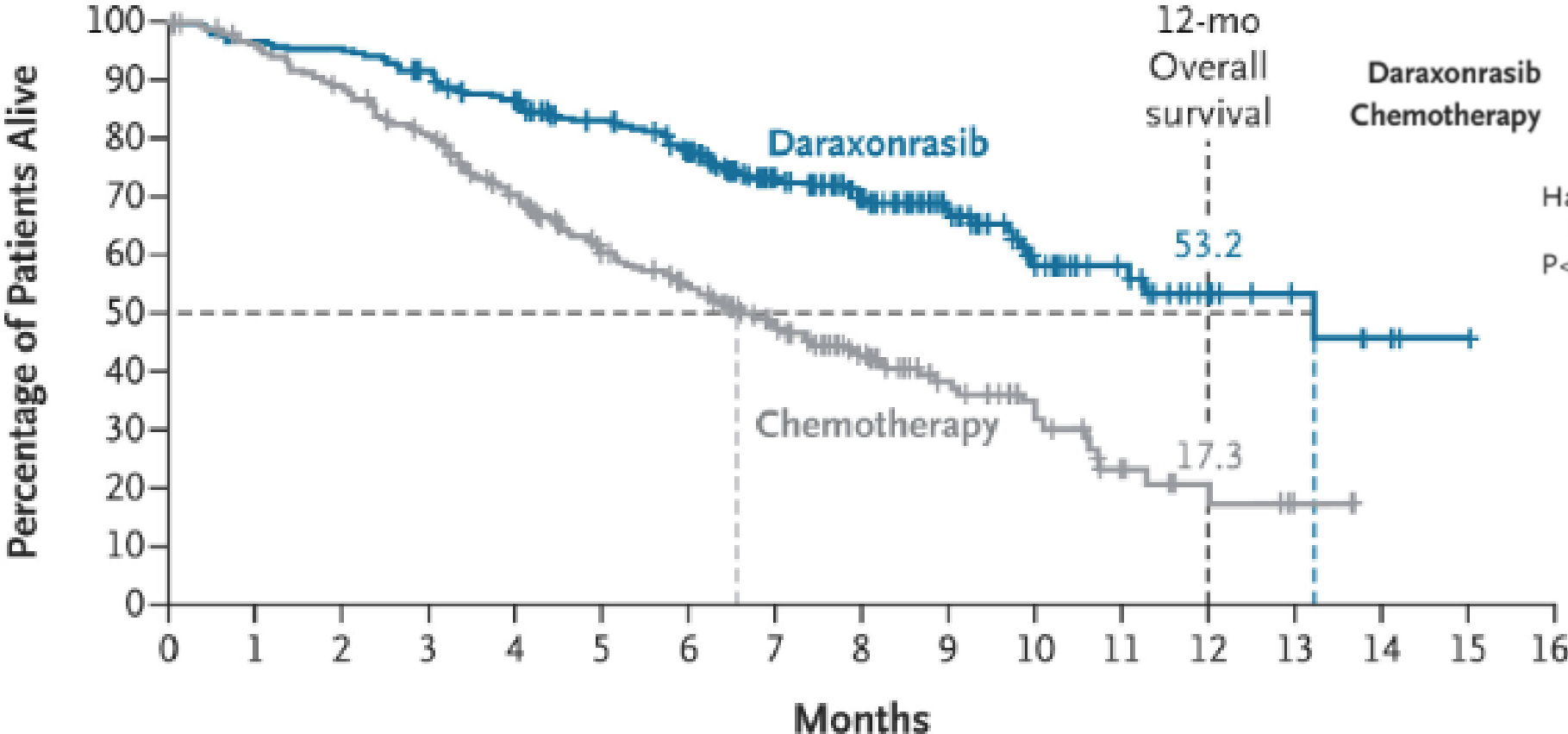
Overall Survival in the RAS G12 Population



NOTE: 13.2 months is longer than any first line trial

Overall Survival – RASolute 302 (ALL pts)

Overall Survival in the Overall Population



	No. of Patients	No. of Events (%)	Median Overall Survival (95% CI) mo
Daraxonrasib	248	79 (32)	13.2 (10.0–NR)
Chemotherapy	252	141 (56)	6.7 (5.8–8.0)

Hazard ratio for death, 0.40 (95% CI, 0.30–0.53)
P<0.001

NOTE: 13.2 months is longer than any first line trial

Toxicity (select common) – RASolute 302

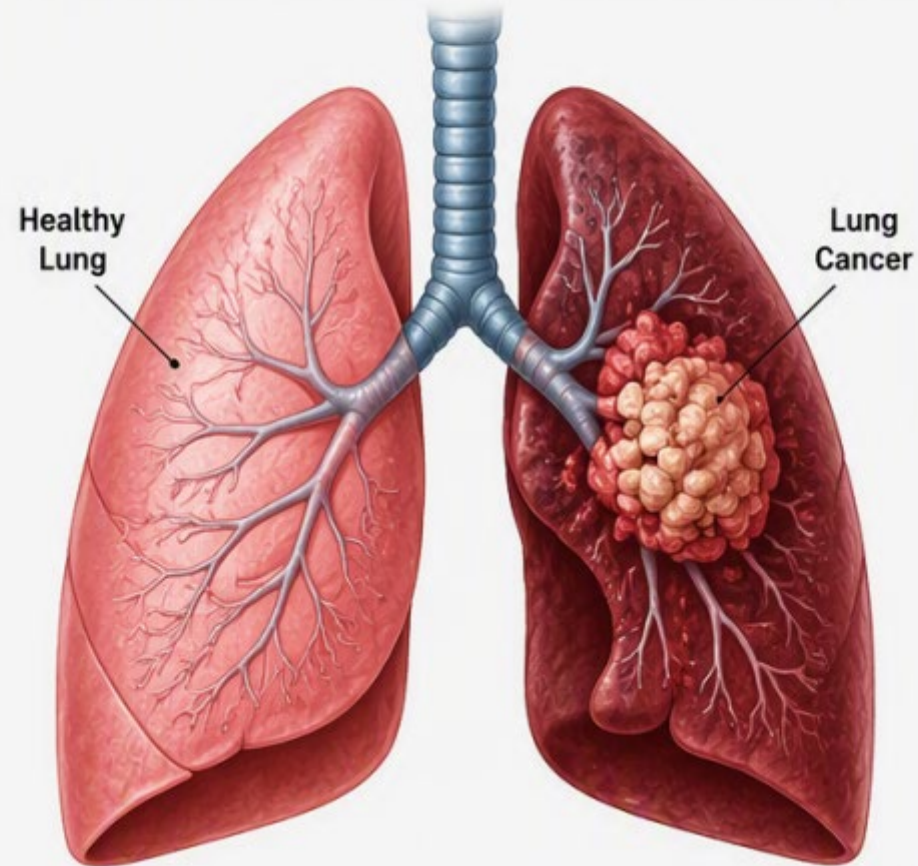
Event	Daraxonrasib (n = 241)	Chemotherapy (n = 214)
Any (grade 3/4/5)	10% (62%)	98% (70%)
AE leading to discontinuation	1%	11%
Rash all grades (grade 3+)	86% (14%)	6% (0%)
Diarrhea all grades (grade 3+)	58% (5%)	40% (7%)
Stomatitis all grades (grade 3+)	53% (12%)	17% (3%)
Nausea all grades (grade 3+)	47% (2%)	40% (2%)
Fatigue all grades (grade 3+)	23% (4%)	44% (6%)
Anemia all grades (grade 3+)	18% (4%)	40% (16%)
Neutropenia all grades (grade 3+)	8% (2%)	38% (28%)
ALT all grades (grade 3+)	10% (2%)	10% (1%)

Daraxonrasib is being reviewed by the FDA

**Stay Tuned for Limitations:
line of therapy or genetically restricted?**

LUNG CANCER

KNOW IT. DETECT IT. TAKE ACTION.



RET mutated NSCLC – LIBRETTO-432 Trial

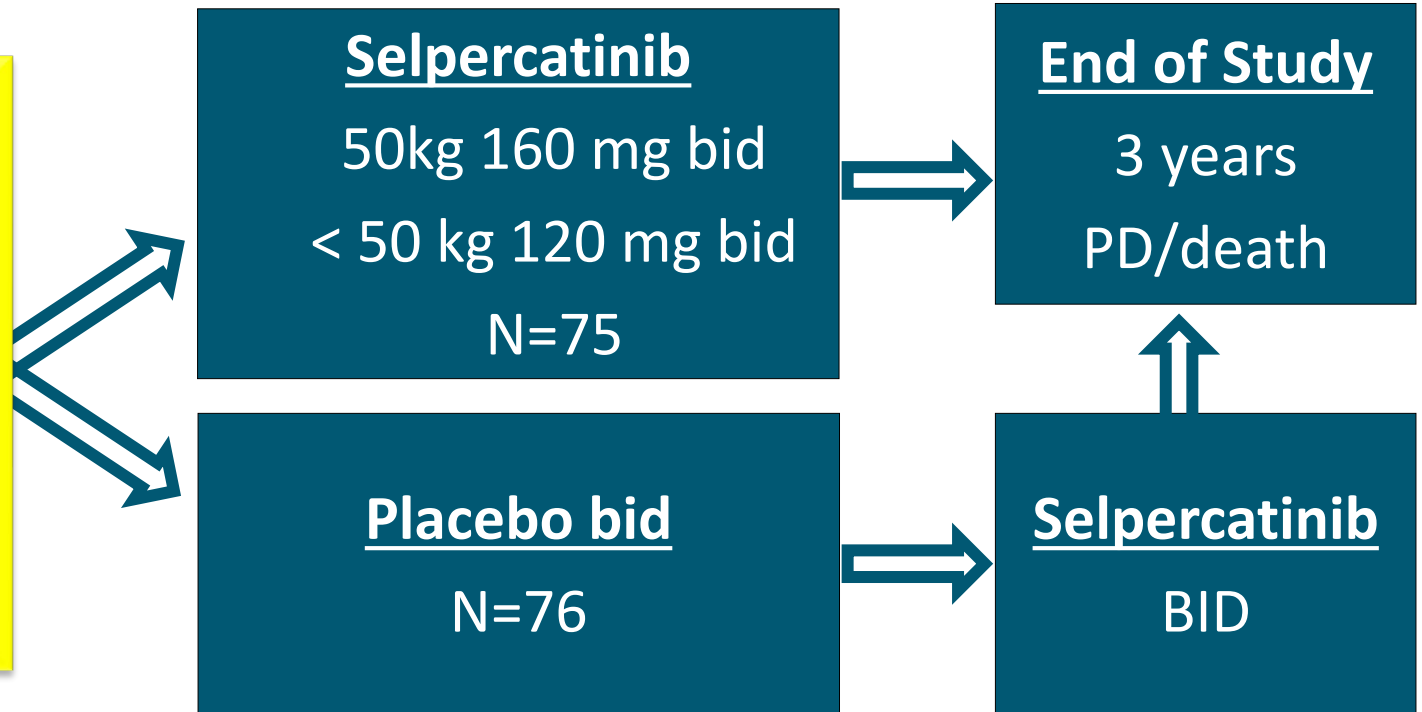
Adjuvant Therapy for NSCLC

Stage IB-IIIa

Ret fusion positive

Prior Tx with definitive surgery of radiotherapy

No evidence of disease recurrence or Progression following definitive therapy

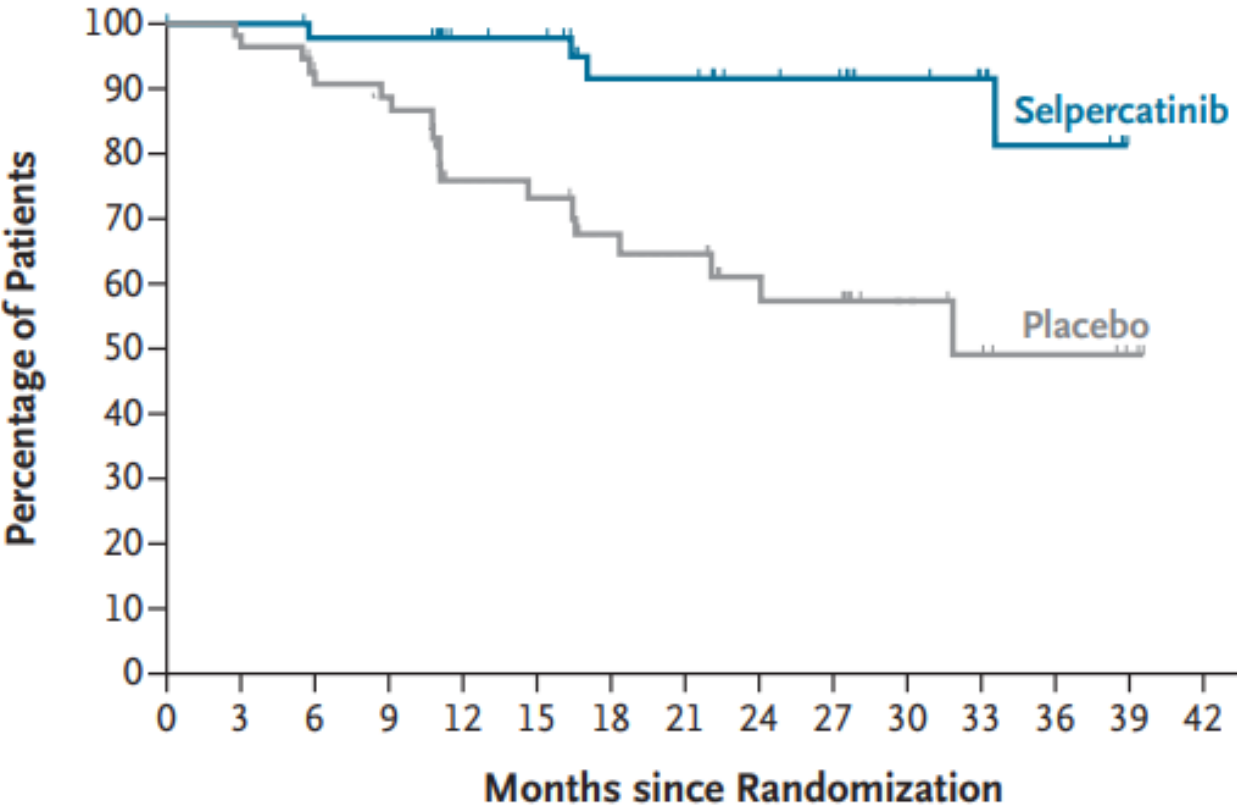


Primary objective: EFS in stage II-IIIa RET fusion + patients

Secondary objectives: EFS in all patients, Safety and Tolerability

RET mutated NSCLC – LIBRETTO-432 Trial

Event-free Survival in the Primary Analysis Population



Investigator-assessed EFS (stage II–IIIA)

	Selpercatinib (n=54)	Placebo (n=55)
Events, n	4	19
24-month EFS, rate (95%CI)	92% (75.4, 97.2)	61% (44.2, 74.3)
HR (95%CI); p-value	0.17 (0.058, 0.509); 0.0003	

Investigator-assessed EFS (stage IB–IIIA)

	Selpercatinib (n=75)	Placebo (n=76)
Events, n	4	20
24-month EFS, rate (95%CI)	94% (81.5, 98.0)	70% (55.5, 80.1)
HR (95%CI); p-value	0.16 (0.056, 0.485); 0.0002	

RET mutated NSCLC – LIBRETTO-432 Trial

- Key results (cont.)

TEAEs, n (%)	Selpercatinib (n=75)	Placebo (n=76)
Any	75 (100)	74 (97.4)
Grade ≥3	50 (66.7)	18 (23.7)
Led to study treatment discontinuation ^a	13 (17.3)	1 (1.3)
Led to dose modifications	66 (88.0)	35 (46.1)
Dose interruptions	58 (77.3)	20 (26.3)
Dose reductions	41 (54.7)	6 (7.9)
Serious in ≥1	17 (22.7)	10 (13.2)
Serious led to discontinuation	2 (2.7)	1 (1.3)

	Selpercatinib (n=75)		Placebo (n=76)	
TEAEs, n (%)	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Patients with ≥1 (≥20%)	75 (100)	50 (66.7)	74 (97.4)	18 (23.7)
ALT increased	47 (62.7)	13 (17.3)	14 (18.4)	1 (1.3)
AST increased	45 (60.0)	14 (18.7)	12 (15.8)	2 (2.6)
Diarrhea	29 (38.7)	3 (4.0)	13 (17.1)	0
Dry mouth	30 (40.0)	0	12 (15.8)	0
Cough	20 (26.7)	0	18 (23.7)	0
Bilirubin increased	20 (26.7)	1 (1.3)	11 (14.5)	0
Hypertension	23 (30.7)	8 (10.7)	8 (10.5)	2 (2.6)
Constipation	17 (22.7)	0	10 (13.2)	0
Hyperuricemia	15 (20.0)	0	8 (10.5)	0

- Conclusions

- In patients with stage IB–IIIA RET fusion-positive NSCLC, adjuvant selpercatinib significantly prolonged EFS versus placebo with a safety profile consistent with prior findings

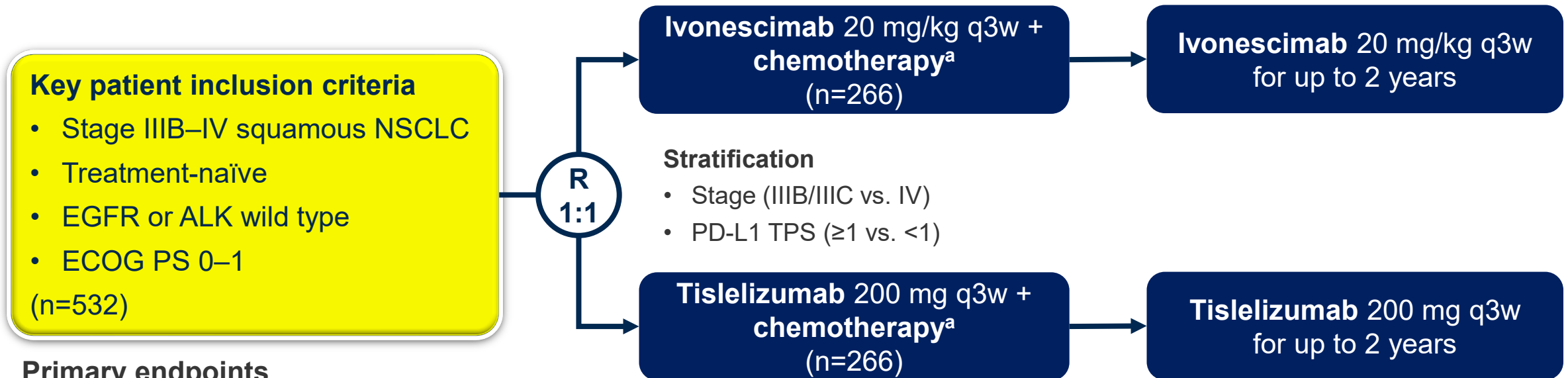
^aMost common reason for selpercatinib discontinuation: ALT increased (n=4); AST increased (n=2); interstitial lung disease (n=2).

**Adjuvant Selpercatinib
is arguably a new SOC
for early stage resected
RET+ NSCLC**

Adv/Met Squam NSCLC - HARMONi-6 trial

- **Study objective**

- To evaluate OS at a pre-specified interim analysis with 1L ivonescimab + chemotherapy vs tislelizumab + chemotherapy in patients with advanced squamous NSCLC



Primary endpoints

- PFS (IRRC, RECIST v1.1)

Secondary endpoints

- OS, PFS (investigator-assessed), ORR, DCR, DoR, TTR, safety

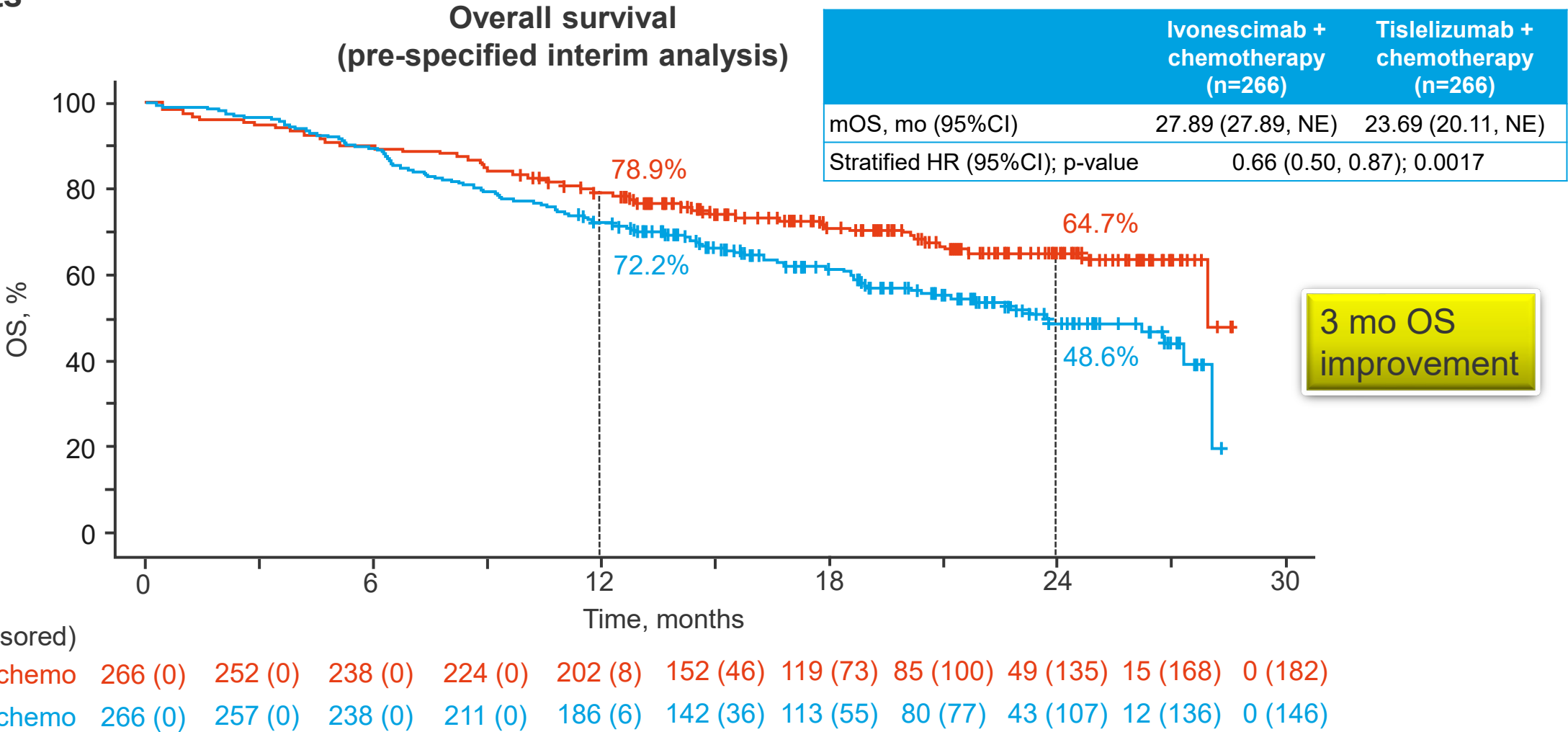
Ivonescimab: A bispecific mab that binds VEGF and PD1

Tislelizumab: An anti-PD1 mab

^aCarboplatin AUC5 q3w + paclitaxel 175 mg/m² q3w (up to 4 cycles).

Adv/Met Squam NSCLC - HARMONi-6 trial

- Key results



Adv/Met Squam NSCLC - HARMONi-6 trial

- Key results (cont.)

AEs, n (%)	Ivonescimab + chemotherapy (n=266)	Tislelizumab + chemotherapy (n=265)
TRAE	264 (99.2)	263 (99.2)
Grade ≥3	184 (69.2)	156 (58.9)
Serious	110 (41.4)	91 (34.3)
Led to treatment discontinuation	14 (5.3)	12 (4.5)
Led to death	10 (3.8)	11 (4.2)
Grade ≥3 irAE	34 (14)	36 (14)

- Conclusions

This bispecific antibody appears safe and effective in Squamous histology NSCLC, albeit with increased toxicity

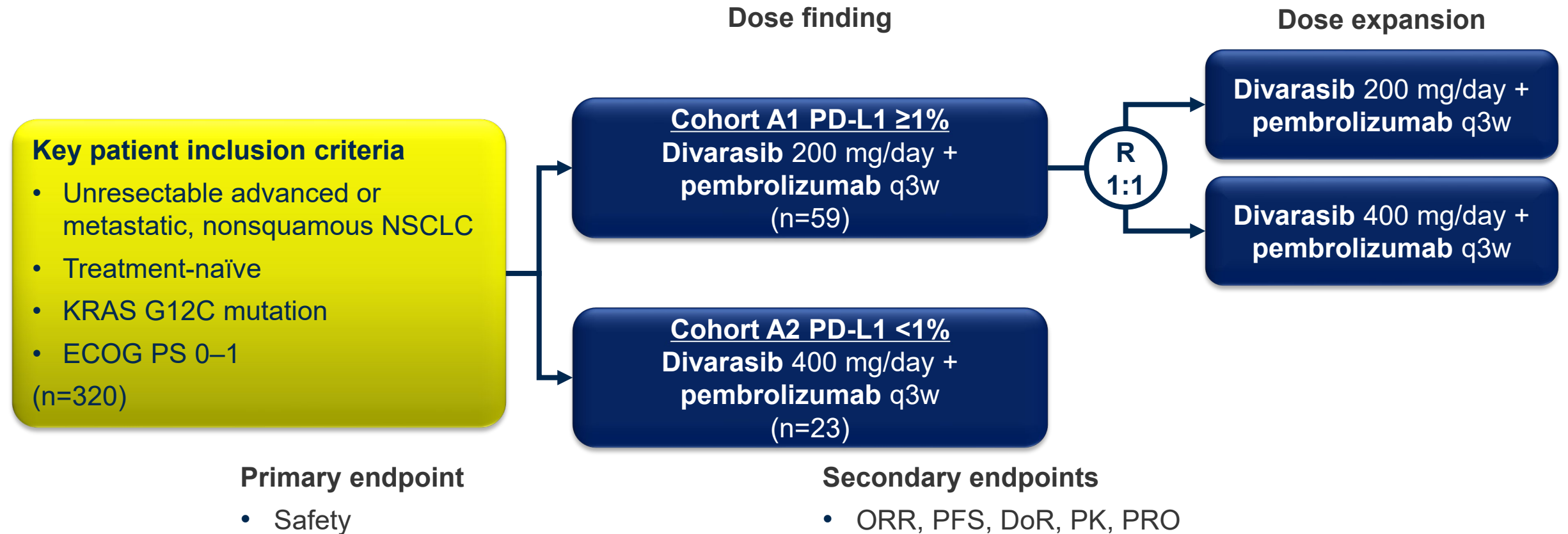
TRAEs occurring in ≥15% of patient, %	Ivonescimab + chemo		Tislelizumab + chemo	
	All grade	Grade ≥3	All grade	Grade ≥3
Alopecia	66.2	-	61.5	-
Anemia	57.1	7.1	60.8	4.9
Neutrophil count decreased	47.0	32.3	44.5	26.0
White blood cell count decreased	38.0	10.9	37.0	9.4
Proteinuria	34.2	4.5	18.7	-
Platelet count decreased	32.3	3.0	28.3	3.0
Hypoesthesia	28.2	-	26.0	-
Appetite decreased	25.6	2.3	25.7	0.8
ALT increased	22.6	0.8	23.0	0.4
AST increased	21.1	1.1	19.6	1.9
Pain in extremity	19.9	1.1	14.0	0.4
Hypertriglyceridemia	19.5	1.9	14.7	2.3
Hypoalbuminemia	19.5	-	11.7	-
Hypothyroidism	18.8	0.4	14.3	-
Hyperuricemia	16.9	0.4	18.7	-
Nausea	16.2	0.8	20.0	-

**Bispecific PD1/VEGF
combined with
chemotherapy for
Squam NSCLC is Coming**

RAS G12C mut NSCLC - Krascendo-170 Trial

- **Related Background**

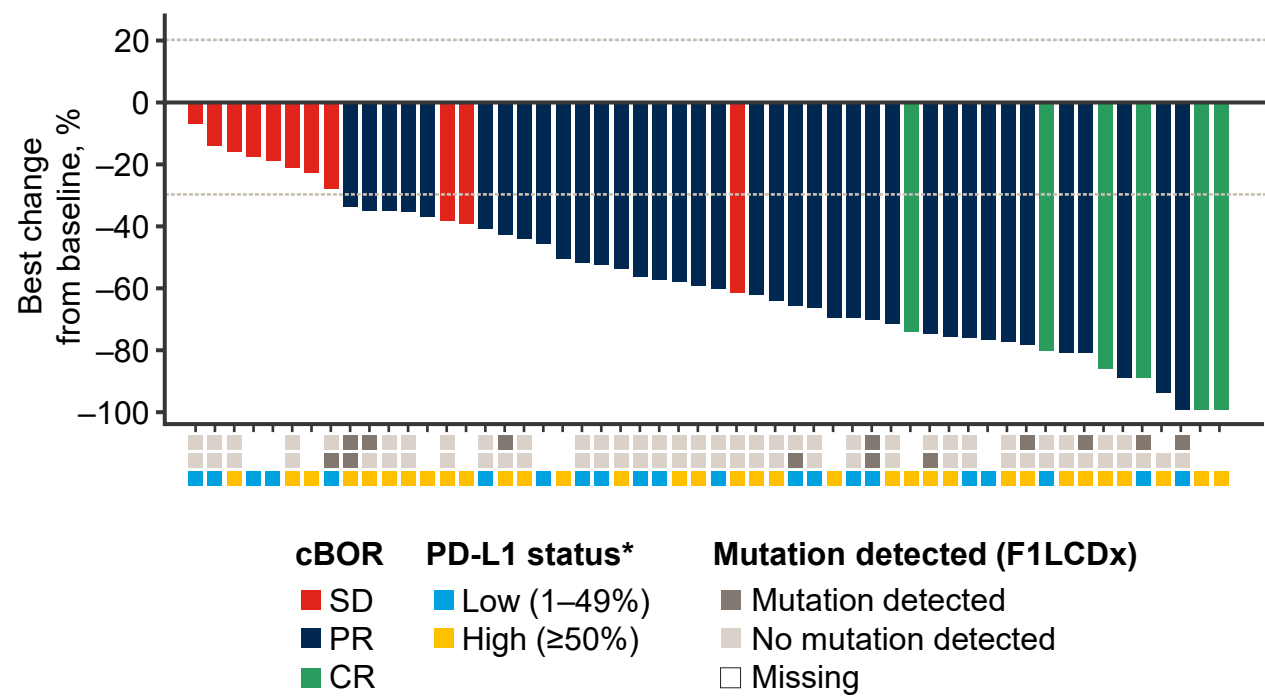
- 1st line Sotorasib + chemo – ORR 65% PFS 11mo.



RAS G12C mut NSCLC - Krascendo-170 Trial

- Key results

Confirmed ORR in PD-L1 positive cohort



PD-L1 positive cohort	Divarasib + pembrolizumab (n=59)
Confirmed ORR , n (%) [95%CI]	43 (72.9) [59.7, 83.6]
BOR, n (%)	
CR	6 (10.2)
PR	37 (62.7)
SD	11 (18.6)
NE	5 (8.5)
Median time to first response, days (range)	43 (36–164)
Median DoR, mo (95%CI)	NE (14.5, NE)
mPFS, mo (95%CI)	19.3 (12.4, NE)
6-mo PFS rate, % (95%CI)	83.5 (73.6, 93.3)

RAS G12C mut NSCLC - Krascendo-170 Trial

- Key results (cont.)

PD-L1 negative cohort	Divarasib + pembrolizumab (n=23)	Safety in Cohorts A1 and A2, n (%)	Divarasib + pembrolizumab (n=78) ^a	TRAEs occurring in ≥20% in Cohorts A1 and A2, n (%)	Divarasib + pembrolizumab (n=78)	
					Any grade	Grade 3–4
Unconfirmed ORR , n (%) [95%CI]	16 (69.6) [47.1, 86.8]	Any grade AE	78 (100)	Diarrhea	58 (74.4)	14 (17.9)
BOR, n (%)		Grade ≥3	60 (76.9) ^a	Nausea	50 (64.1)	1 (1.3)
PR	16 (69.6)	Serious	39 (50.0)	Vomiting	36 (46.2)	1 (1.3)
SD	4 (17.4)	Any grade TRAE	77 (98.7)	ALT increased	41 (52.6)	18 (23.1)
PD	1 (4.3)	Grade 3–4	51 (65.4)	AST increased	38 (48.7)	14 (17.9)
NE	2 (8.7)	Serious	22 (28.2)	Lipase increased	23 (29.5)	7 (9.0)
Median time to first response, days (range)	40.5 (36–120)	Led to divarasib dose reduction	41 (52.6)	Appetite decreased	24 (30.8)	0
		Led to dose interruption	54 (69.2)	Amylase increased	16 (20.5)	3 (3.8)
		Led to study treatment discontinuation	10 (12.8)			

- Conclusions

- In patients with advanced KRAS G12C-mutant NSCLC, 1L divarasib + pembrolizumab demonstrated encouraging antitumor activity across PD-L1 subgroups with a manageable safety profile

^aFour patients had grade 5 AEs.

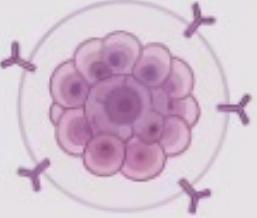
**Second Generation
KRAS G12C inhibitors
combined with ICI for
NSCLC is Coming**



BREAST CANCER SUBGROUPS

Breast cancers are not all the same.
Molecular subtyping helps guide prognosis and treatment.



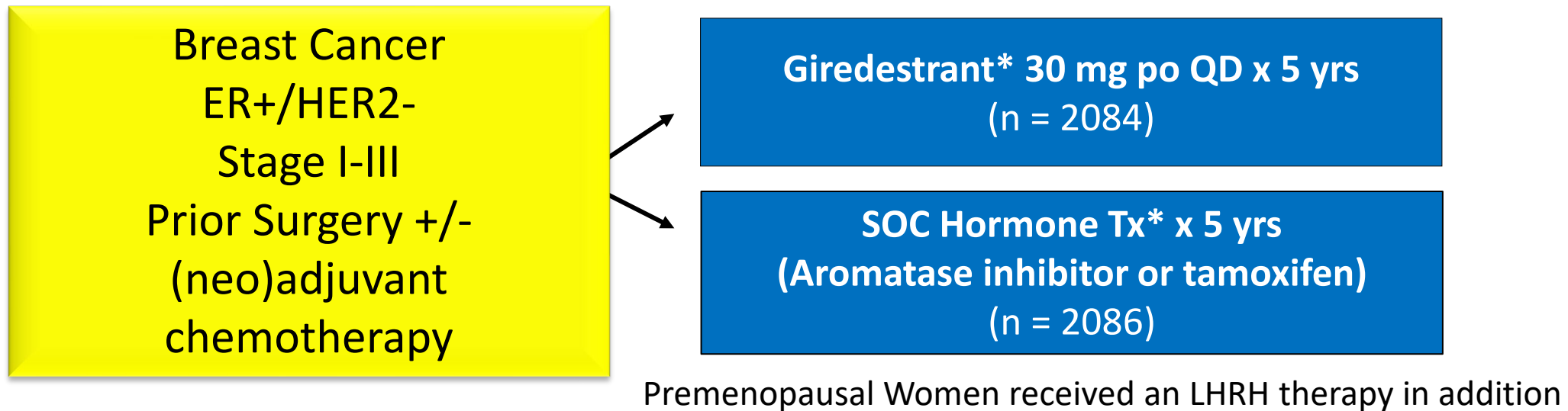
HR+/HER2- (Luminal A / Luminal B)	HER2+/HR-	HR+/HER2+ (Luminal HER2)	TRIPLE NEGATIVE (HR-/HER2-)
			
HR (Estrogen Receptor) ✓ HER2 (Human Epidermal Growth Factor Receptor 2) ✗	HR (Estrogen Receptor) ✗ HER2 (Human Epidermal Growth Factor Receptor 2) ✓	HR (Estrogen Receptor) ✓ HER2 (Human Epidermal Growth Factor Receptor 2) ✓	HR (Estrogen Receptor) ✗ HER2 (Human Epidermal Growth Factor Receptor 2) ✗
• Most common subtype • Generally slower growing • Best prognosis	• May be more aggressive • Higher risk of recurrence without targeted therapy • Prognosis improved with HER2-targeted treatment	• Intermediate prognosis • Benefits from both hormone therapy and HER2-targeted therapy	• Often more aggressive • Higher risk of early recurrence • Fewer targeted treatment options
 TREATMENT IMPLICATIONS Endocrine (hormone) therapy is the mainstay; chemotherapy may be considered based on individual risk.	 TREATMENT IMPLICATIONS HER2-targeted therapy (e.g., trastuzumab, pertuzumab, T-DM1) + chemotherapy.	 TREATMENT IMPLICATIONS Combination of endocrine therapy + HER2-targeted therapy +/- chemotherapy.	 TREATMENT IMPLICATIONS Chemotherapy is the mainstay; immunotherapy may be an option in select patients (e.g., PD-L1 positive).



Improvement on Aromatase Inhibitors or Tamoxifen?

Adjuvant Hormone Therapy – LidERA

- Multicenter, open-label, randomized global phase III study



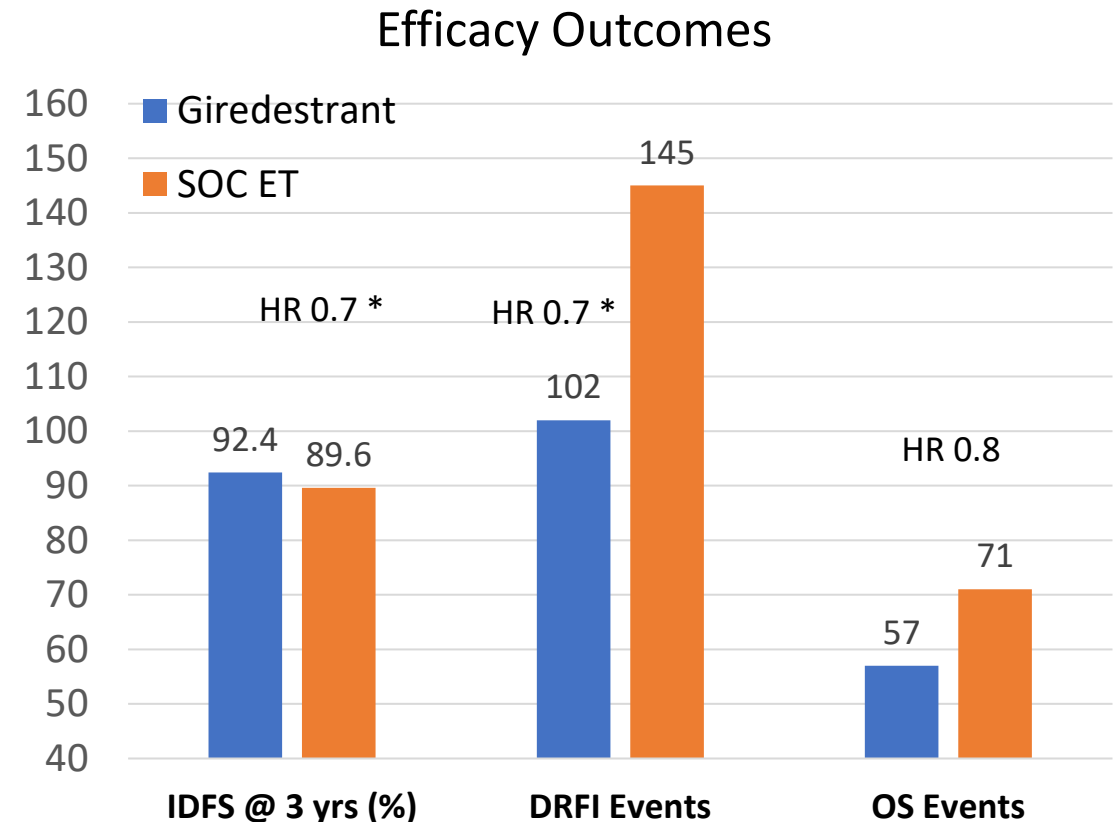
- **Primary endpoint:** Invasive Disease-Free Survival (IDFS)
- **Key secondary endpoints:** Distant Recurrence-Free Interval (DRFI), safety and tolerability

Adjuvant Hormone Therapy – LidERA Interim Analysis

After a median F/U of 32.3 months.

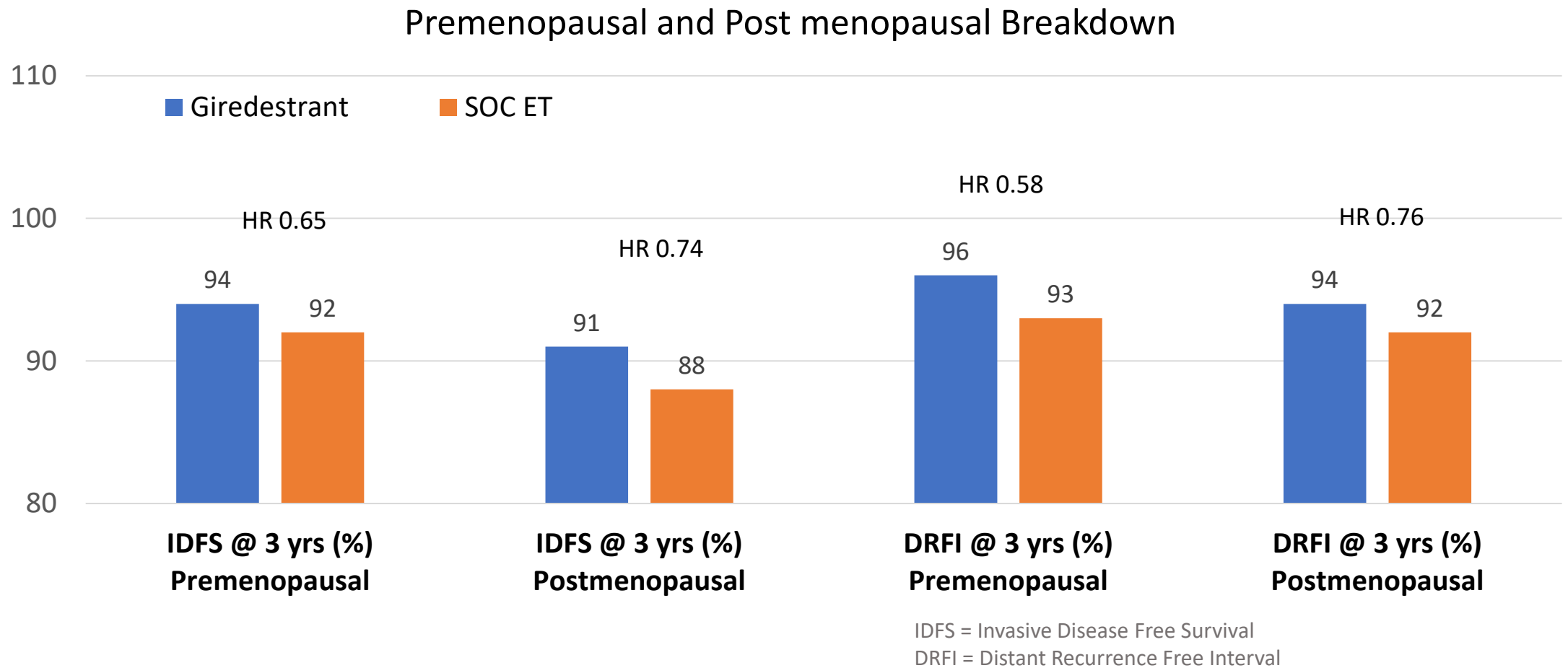
- Median Age 54 yrs; 59% postmenopausal
- Stage: I = 13%, II = 47%, III = 40%
- Most common AEs

Event	Giredestrant	SOC ET
Arthralgia	48%	47%
Headache	15%	13%
Hot flush	27%	29%
Hypertension (g3/4)	3%	2%
Discontinue due to AE	5%	8%

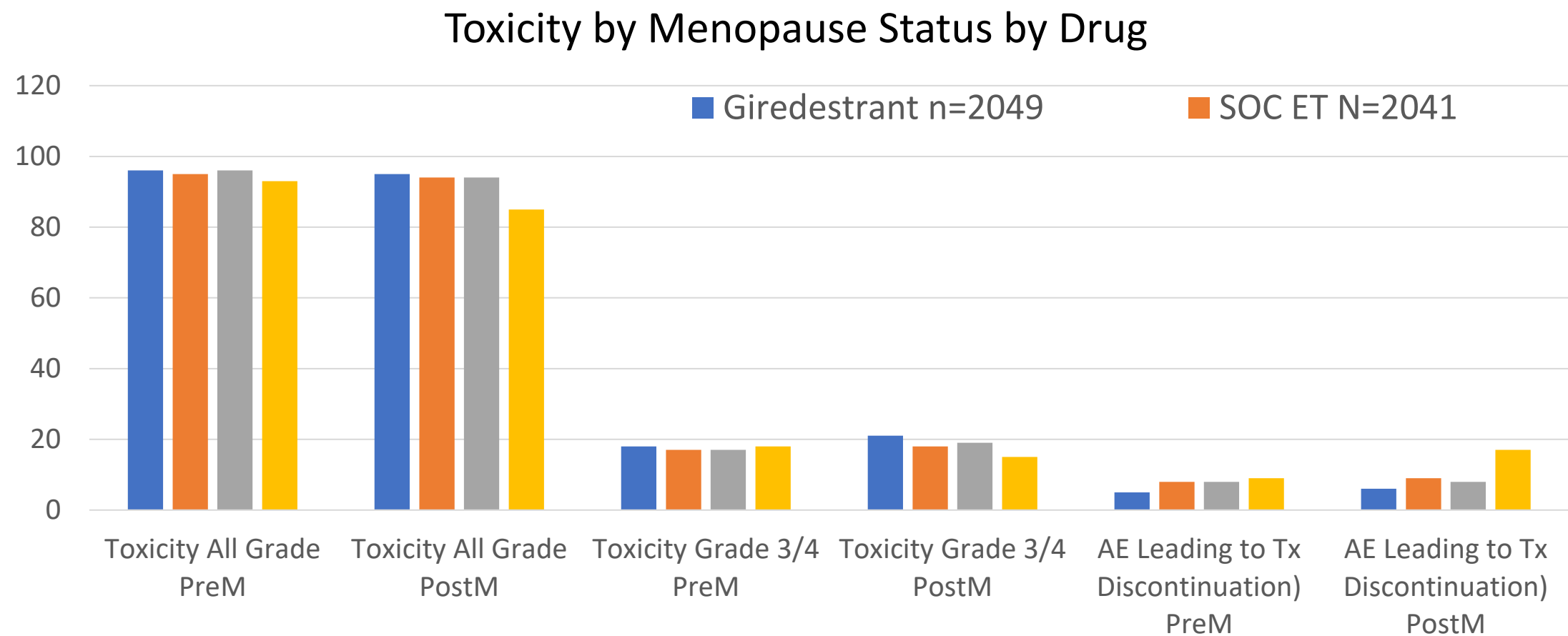


IDFS = Invasive Disease Free Survival
DRFI = Distant Recurrence Free Interval
OS = Overall Survival
* Statistically significant

Adjuvant Hormone Therapy – LidERA Interim Analysis

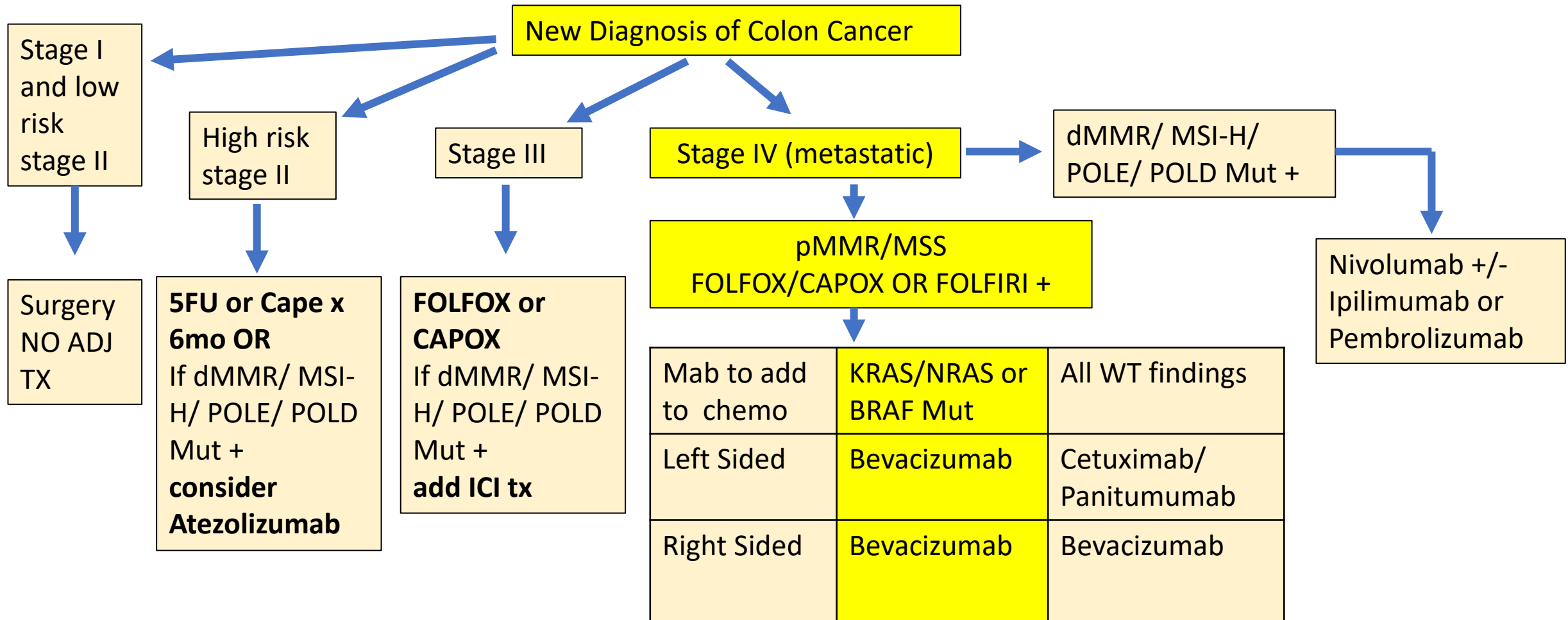


Adjuvant Hormone Therapy – LidERA Interim Analysis



**GIREDESTRANT LOOKS
LIKE IT COULD BECOME
THE NEW HORMONE
THERAPY FOR eBC**

Colorectal Cancer Subgroups (First Line Tx)



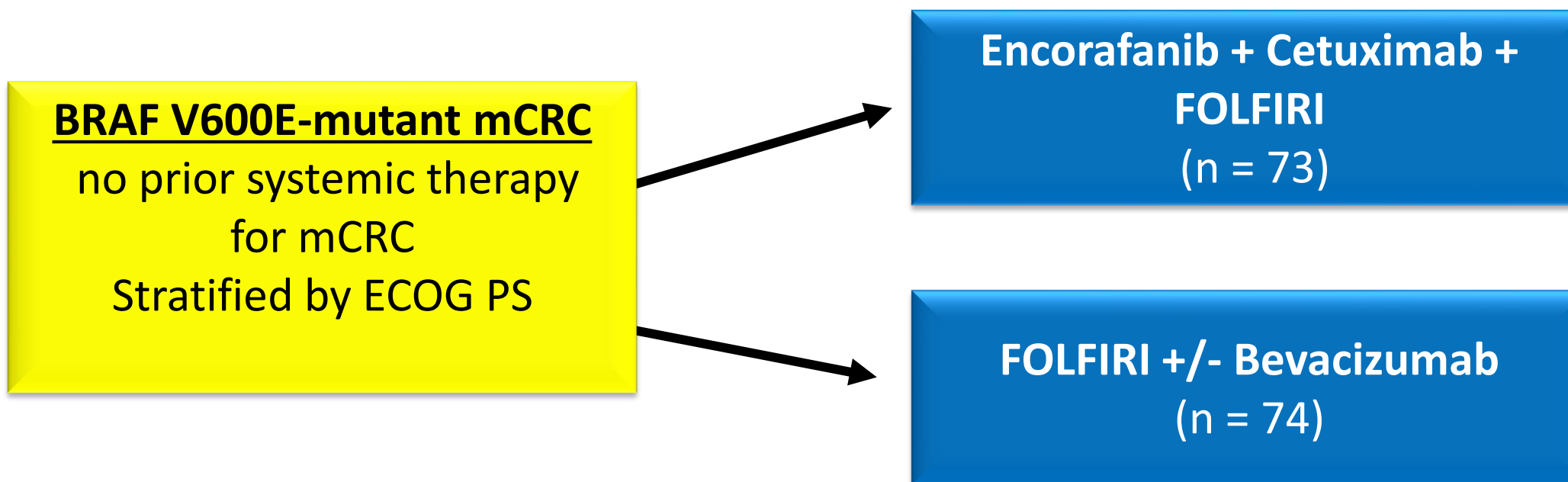
BRAF, NRAS, KRAS mutations

Group – Variable	FOLFOX-Panitumumab	FOLFOX
No RAS or BRAF mut – OS	28.3 mo (n=228)	20.9 mo (n=218)
BRAF only mut – OS	10.5 mo (n=24)	9.2 mo (n=29)
KRAS mut in exon 2 – OS	15.5 mo (n=221)	19.2 mo (n=219)
BRAF or RAS mut – OS Includes NRAS mut	15.3 mo (n=296)	18.0 mo (n=305)

PFS results reflect same trend of no benefit/deliterious when mutations present and panitumumab used

Breakwater Cohort 3: Study Schema

- Multicenter, randomized, open-label phase III trial



This is a comparison between Arms D and E of a larger study (Arm A: Encorafenib + cetuximab discontinued and arm D and E added with amendment 5)

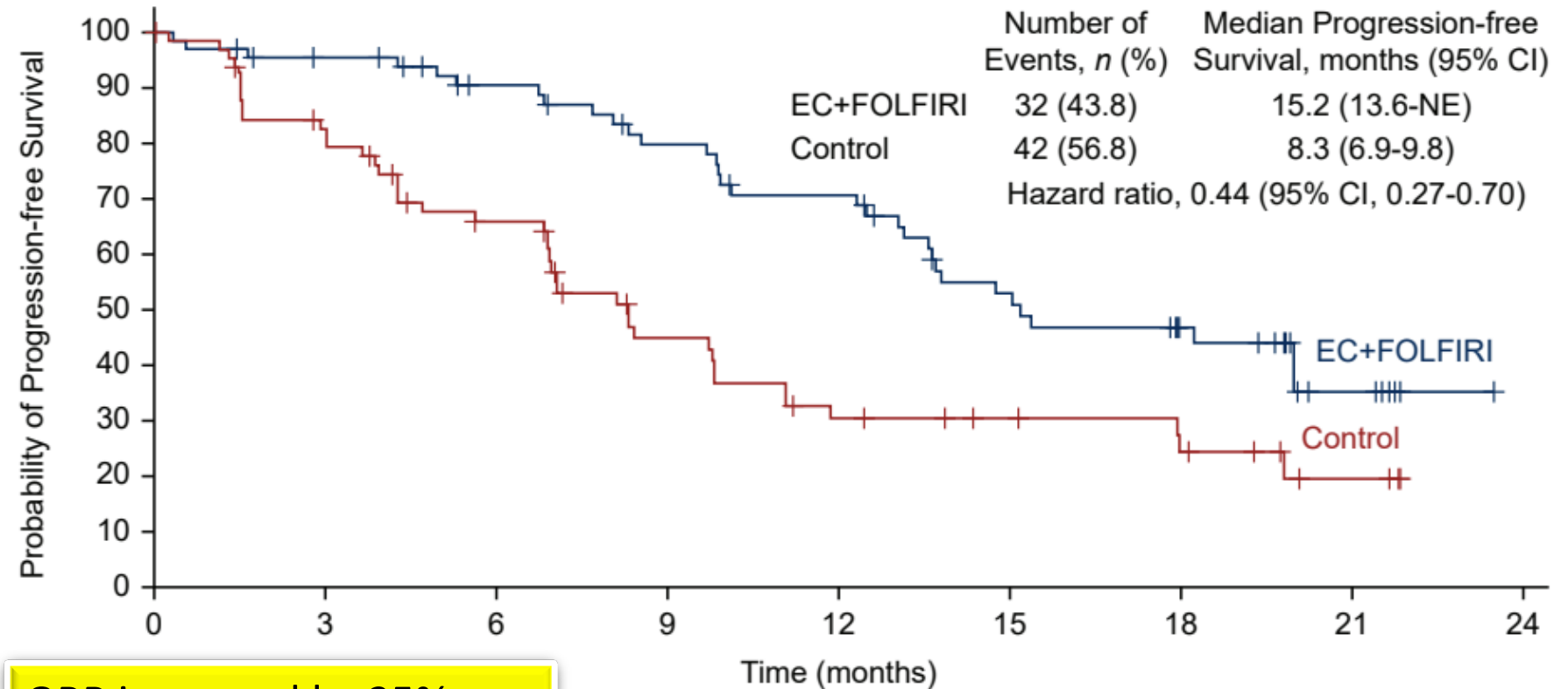
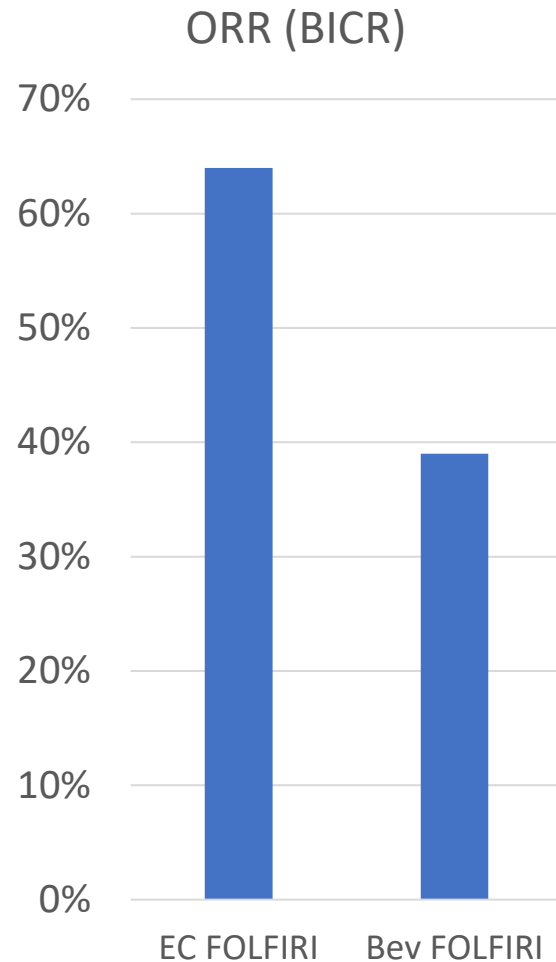
- **Primary endpoint:** ORR ITT (BICR)
- **Key secondary endpoints:** PFS (BICR), OS, and safety

Breakwater Cohort 3- Demographics

Characteristic	EC FOLFIRI (n = 73)	FOLFIRI Bev (n = 74)
Median age, yr (range)	62 (28-81)	61 (29-84)
Female, n (%)	40 (55)	39 (53)
Race, n (%) - White - Asian	41 (56) 29 (40)	49 (66) 20 (27)
ECOG PS, n (%) 0 1	47 (64) 24 (33)	41 (55) 27 (37)
Side of Tumor, n (%) - Left - Right	31 (43) 41 (56)	36 (49) 38 (51)

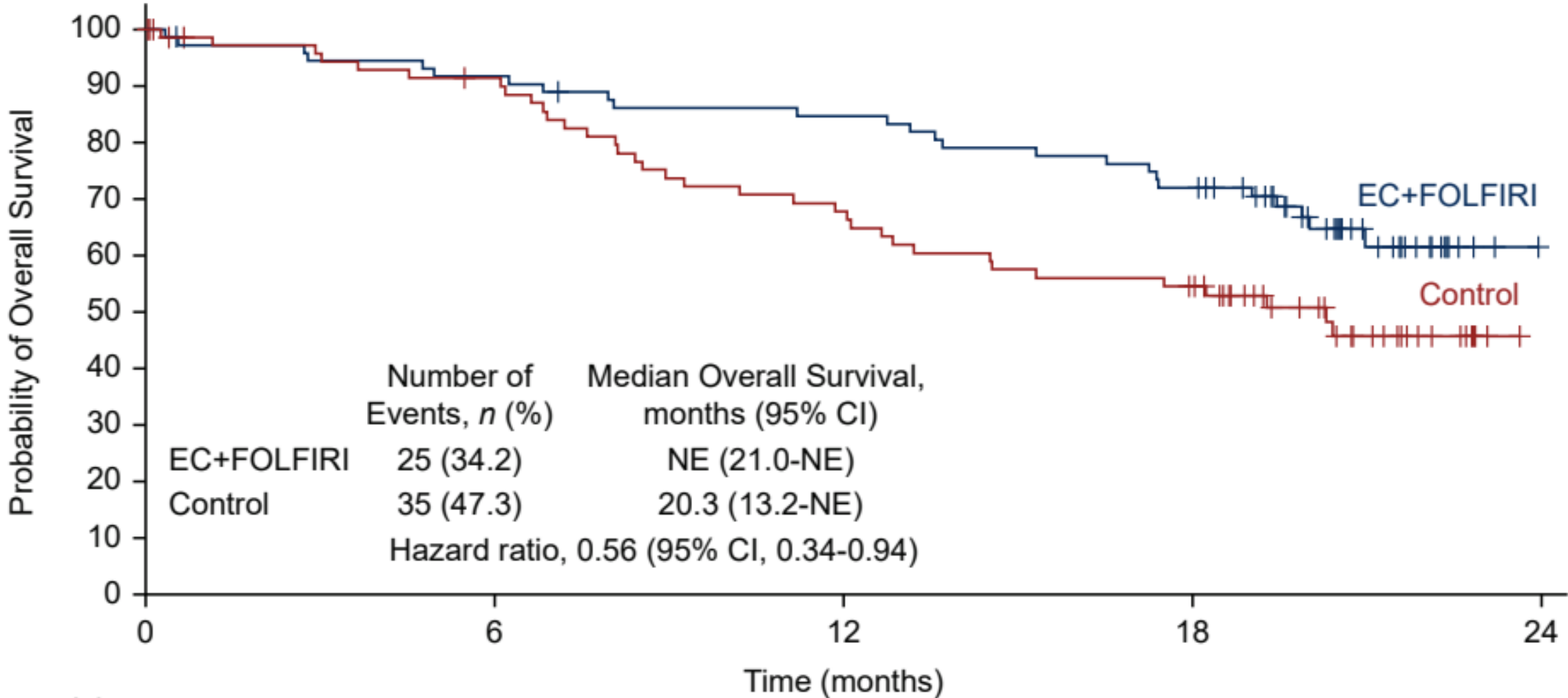
Characteristic, n (%)	EC FOLFIRI (n = 73)	FOLFIRI Bev (n = 74)
Stage IV at initial diagnosis, n (%)	54 (74)	47 (64)
No. of organs involved < 3 3+	38 (52) 35 (48)	34 (46) 40 (54)
Liver Metastasis Yes	43 (59)	46 (62)
<i>MSI-H/dMMR-</i> positive	0 (0)	0 (0)

Breakwater Cohort 3- Efficacy



ORR increased by 25%
PFS increased by 7 months

Breakwater Cohort 3- Efficacy



Toxicity (Select) – Breakwater Cohort-3

Event	EC FOLFIRI (n = 71)	FOLFIRI Bev (n = 68)
Treatment-emergent AE (G3-5)	100% (70%)	99% (81%)
AE leading to discontinuation (any Rx)	16%	10%
Treatment Related AE leading to DEATH	1 (1%)	1 (1%)
Adverse Event	All grades (G3+)	All grades (G3+)
Nausea	65% (3%)	59% (2%)
Vomiting	51% (3%)	32% (0%)
Inc Lipase	20% (11%)	6% (6%)
Diarrhea	59% (13%)	50% (9%)
Neutropenia	35% (18%)	29% (21%)
Fatigue	35% (3%)	40% (3%)
Anemia	45% (14%)	27% (2%)
Constipation	32% (1%)	29% (2%)

Met BRAF V600E + CRC
1st line therapy may
include Encorafenib +
Cetuximab + FOLFIRI

SAME OUTCOMES. LESS TOXICITY.

De-escalate treatment without compromising effectiveness

MORE TREATMENT



HIGHER TOXICITY RISK



Fatigue



Neuropathy



Diarrhea



Rash



Hospitalization

- More treatment
- Higher treatment burden
- More toxicity



SAME TUMOR CONTROL



PROGRESSION-FREE
SURVIVAL



OVERALL SURVIVAL



RESPONSE RATE



LESS TREATMENT



LOWER TOXICITY RISK



More Energy



Better Quality
of Life



Fewer Side
Effects

- Less treatment
- Lower toxicity
- Better quality of life

Adjuvant Chemotherapy or Not - OPTIMA

- Multicenter, open-label, randomized global phase III study, non-inferiority design

Breast Cancer

- ER+/HER2-
- 40+ years old
- 0-9 nodes
- Recommended to receive chemotherapy (N0 & T>30mm, or N+)

Chemo + Hormone Tx x 5 yrs
(n = 2214)

PAM50
(n = 2215)

68% Endocrine Therapy Alone
32% Chemo + Endocrine Therapy

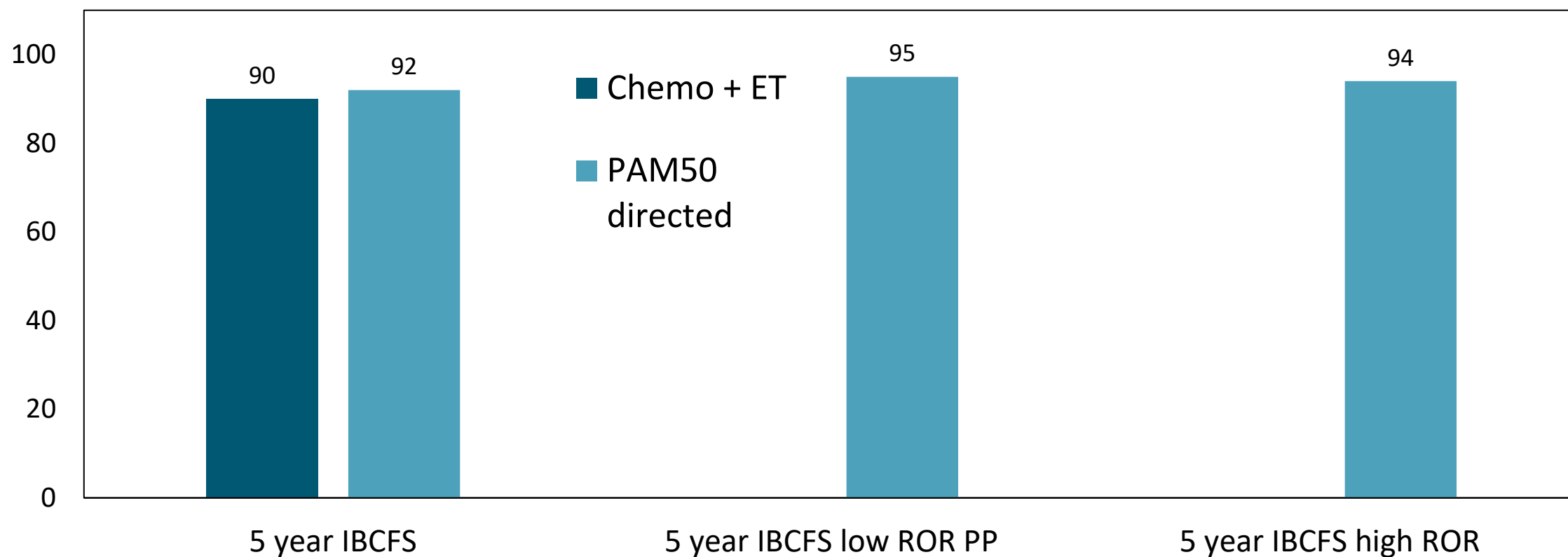
Well Balance groups:

- Postmenopausal 62%
- pN1 73%
- pN0/pN1mi 8%
- pN2 19%

Pam50 – Prosigna 50 gene test. ROR score 60+ get chemo, those with an ROR score < 60 receive endocrine therapy alone (adjuvant abemaciclib permitted, ovarian suppression given to pre-menopausal women)

- **Primary endpoint:** 5-year Invasive Breast Cancer Free Survival (IBCFS)
- **Key secondary endpoints:** Distant Recurrence-Free Interval (DRFI), safety and tolerability

Chemo + Endocrine Tx vs PAM50 directed - OPTIMA

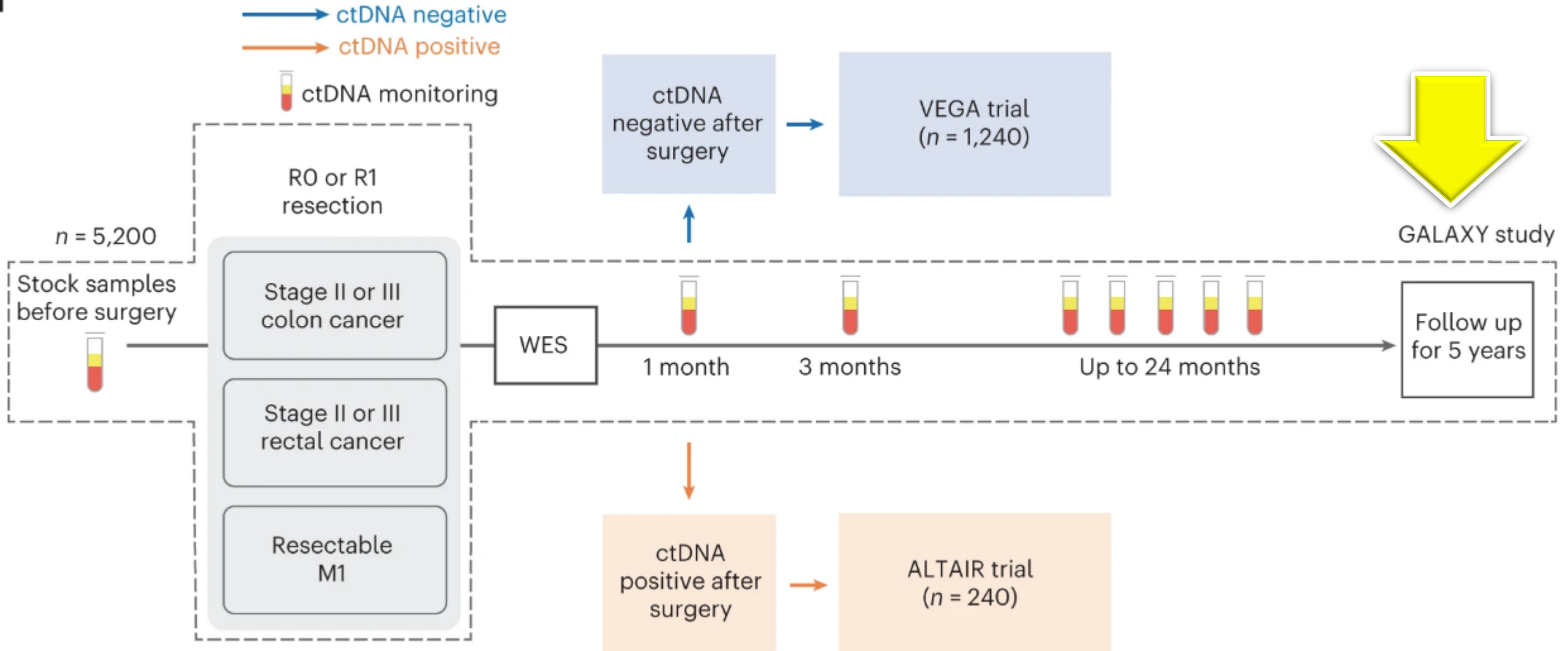


Median of 3.9 years of follow-up

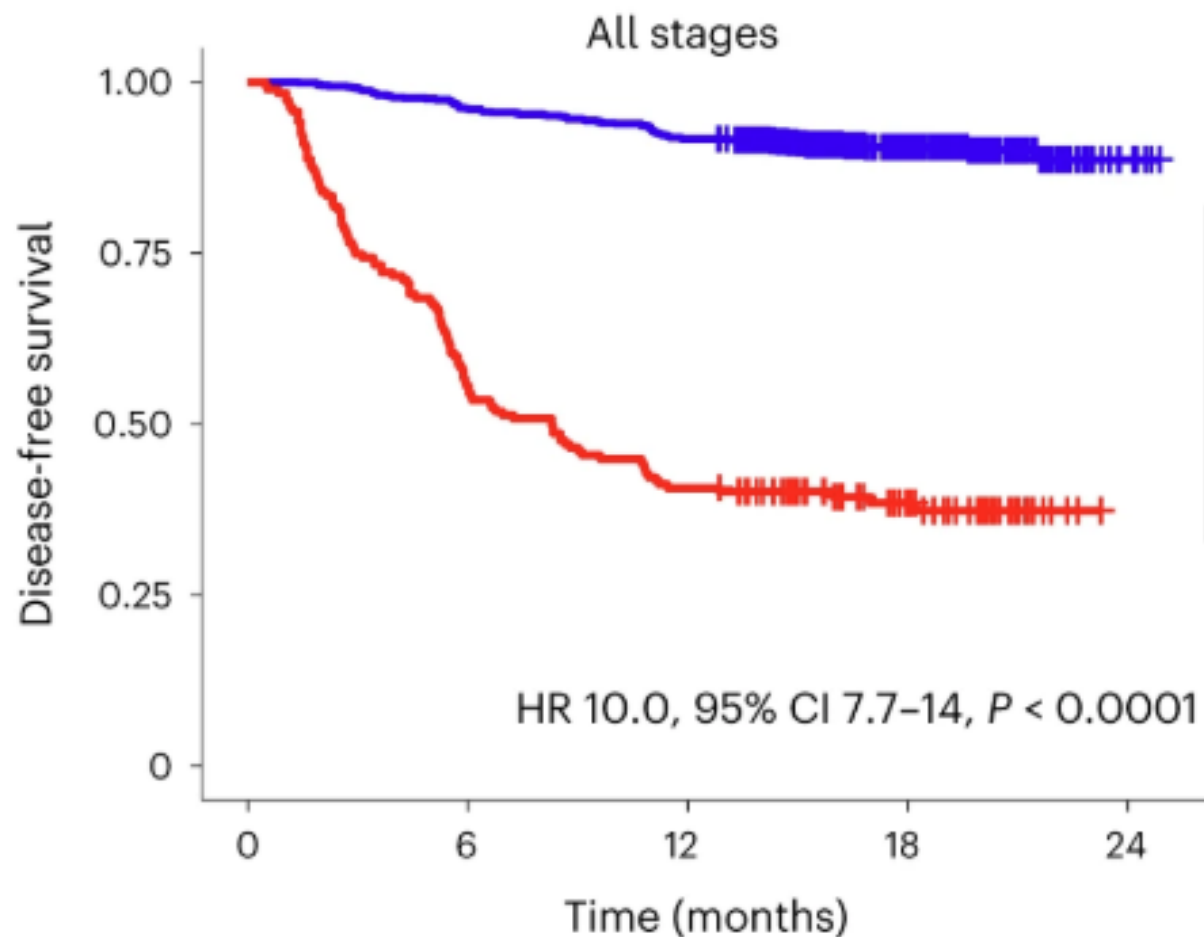
Non-Inferiority met HR=0.99 [90% CI 0.81- 1.20], NI p = 0.013

Adjuvant Chemotherapy or Not - GALAXY

a



Benefit of Adjuvant Chemo in Resected stage I-IV CRC



ctDNA at 4 weeks post-op

ctDNA	Number of events	6M-DFS (95% CI)	12M-DFS (95% CI)	18M-DFS (95% CI)
ctDNA negative	81 out of 852	96.1% (94.6-97.2)	91.7% (89.6-93.3)	90.5% (88.3-92.3)
ctDNA positive	115 out of 187	55.6% (48.2-62.64)	40.6% (33.6-47.6)	38.4% (31.4-45.5)

ctDNA negative at 4 weeks, patients have minimal benefit from Adjuvant Chemotherapy – BUT some still have recurrence.

KEY QUESTION: Does the 12-week ctDNA test capture patients who would benefit from Adj Chemotherapy

Adjuvant Chemotherapy or Not - Galaxy

Colorectal Cancer

- Surgical Resection
- ctDNA negative at 4 weeks post-op (n = 1034)

ctDNA at 12 Weeks Negative
(n=998)

ctDNA at 12 Weeks Positive
Observation or
Adjuvant Chemotherapy
(n=36)

2-year DFS

Obs = 84.1%
ACT = 87.1%
HR 0.8 p=0.1744

2-year DFS

Obs = 2.5%
ACT = 45.5%
HR 0.3 p=0.0165

Demographics: 48% Female, Colon CA 74%

Stage Distribution:

11% Stage I / Low Risk Stage II,
72% High Risk Stage II/Stage III,
17% stage IV

Median age 69 (25-93)

Median time to ACT 6.7 weeks (3-12)

Conclusion:

Clear role for obtaining a 12 ctDNA

Patients who convert from ctDNA neg to positive at 12 weeks benefit from Adjuvant Chemotherapy

ASCO 2026 Summary

- Pancreatic Cancer
 - 2nd line therapy with **Daraxonrasib** is BETTER than chemotherapy (coming soon)
- Lung Cancer
 - RET+ early-stage Lung cancer adjuvant therapy should consist of **Selpercatinib**
 - Squamous Histology metastatic NSCLC has improved outcomes when **Ivonescimab** (bispecific PD1/VEGF mab) is added to chemotherapy
 - KRAS G12C+ metastatic NSCLC 1st line treatment **Divarasisb** + Pembrolizumab
- Breast Cancer
 - HR+/HER2- early-stage Breast Cancer found **Giredestrant** (a new SERD) is better than AI or Tam in both pre and post menopausal women.
- CRC
 - BRAF V600E mut CRC – 1st line **Encorafenib + Cetuximab** + FOLFIRI is better
- De-escalation
 - Genetic testing can identify high risk Breast Cancer Patients who can **avoid chemo**
 - ctDNA at 4 and 12-weeks can identify adjuvant CRC patients who can **avoid or should receive adjuvant chemo**



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