ESMO 2019 Update

29 September 2019

NASDAQ: GTHX

Agenda

6:45 – 6:50 p.m.	**Welcome & G1 Overview** **Mark Velleca, M.D., Ph.D.,** *Chief Executive Officer*
6:50 – 7:05 p.m.	**Breast Cancer State of the State c. 2019** **Lisa Carey, M.D., FASCO,** *Chief of Hematology/Oncology and Physician-in-Chief, N.C. Cancer Hospital* *Associate Director of Clinical Sciences, Lineberger Comprehensive Cancer Center*
7:05 – 7:15 p.m.	**ESMO Data Review: Trilaciclib and G1T48** **Raj Malik, M.D.,** *Chief Medical Officer and Senior Vice President, R&D*
7:15 – 7:30 p.m.	**Q&A with Dr. Carey, Dr. Malik and Dr. Velleca**
7:30 – 7:40 p.m.	**Pipeline Development Strategy and Regulatory Milestones** **Raj Malik, M.D.,** *Chief Medical Officer and Senior Vice President, R&D*
7:40 – 7:50 p.m.	**Commercial Opportunity and Strategy** **John Demaree,** *Chief Commercial Officer*
7:50 – 8:05 p.m.	**Q&A with Dr. Malik, Mr. Demaree and Dr. Velleca**
8:05 – 8:10 p.m.	**Upcoming Catalysts and Closing Remarks** **Mark Velleca, M.D., Ph.D.,** *Chief Executive Officer*

Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "expect," "plan," "anticipate," "estimate," "intend" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Forward-looking statements in this presentation include, but are not limited to, the therapeutic potential of trilaciclib, lerociclib and G1T48, the expected timing of data availability from ongoing clinical trials, the expected timing of initiation of future clinical trials, and the timing for the commencement and completion of marketing applications in the U.S. and Europe for trilaciclib in SCLC, and are based on the Company's expectations and assumptions as of the date of this presentation. Each of these forward-looking statements involves risks and uncertainties. Factors that may cause the Company's actual results to differ from those expressed or implied in the forward-looking statements in this presentation are discussed in the Company's filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" sections contained therein and include, but are not limited to, the Company's ability to complete clinical trials for, obtain approvals for and commercialize any of its product candidates; the Company's initial success in ongoing clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials; the inherent uncertainties associated with developing new products or technologies and operating as a development-stage company; the Company's development of a CDK4/6 inhibitor to reduce chemotherapy-induced myelosuppression is novel, unproven and rapidly evolving and may never lead to a marketable product; and market conditions. Except as required by law, the Company assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

Welcome & G1 Overview

Mark Velleca, M.D., Ph.D.
Chief Executive Officer

Small molecule therapeutics for big oncology indications

Trilaciclib

- ✓ Breakthrough Therapy Designation; begin rolling NDA submission for SCLC in 4Q19, expect to complete in 2Q20
- ✓ Preliminary OS benefit in mTNBC; initiating Phase 3 trial in 2H20
- ✓ Initiating Phase 3 mCRC trial in 2H20

G1T48

- ✓ Best-in-class potential
- ✓ Differentiated chemistry, favorable tolerability
- ✓ Initiating Phase 3 1L combo trial with CDK4/6i in 2H20

Lerociclib

- ✓ Less neutropenia and favorable tolerability – advantages in breast cancer (BC) adjuvant setting
- ✓ Data + dose identification in 4Q19 to support pivotal trials
- ✓ Initiating Phase 3 1L BC trial in 2H20

All three therapies have potential to **improve outcomes for women with breast cancer** in advanced/ metastatic and adjuvant settings

Trilaciclib regulatory update

Small cell lung cancer

- Breakthrough Therapy Designation (BTD)
- Pre-NDA meeting with Hematology Division completed
- **Will begin rolling NDA submission in 4Q19; expect to complete submission in 2Q20**
- Anticipate MAA submission in 2H20

Triple-negative breast cancer

- Productive interactions with Oncology Division
- Received feedback on Phase 2 data and comments on preliminary Phase 3 trial design
- **Expect to initiate Phase 3 trial in 2H20**

Catalysts across all programs in 2019/2020

	INDICATION/COMBO	4Q19	1H20	2H20
trilaciclib IV - CDK4/6i	1st-line SCLC (+ etop/carbo)	Begin rolling NDA submission for SCLC	Complete NDA submission for SCLC	MAA filing for SCLC
	1st-line SCLC (+ etop/carbo/Tecentriq)			
	2nd/3rd-line SCLC (+ topotecan)			
	Metastatic TNBC (+ gem/carbo)			Initiate Phase 3 TNBC trial
	Metastatic CRC (5-FU regimens)			Initiate Phase 3 mCRC trial
lerociclib Oral - CDK4/6i	ER+, HER2- BC (+ Faslodex)	Present additional Phase 1b/2a data		Initiate Phase 3 BC trial
	EGFRm NSCLC (+ Tagrisso)			
G1T48 Oral - SERD	ER+, HER2- BC			Initiate Phase 3 CDK4/6i combination trial + Present additional data

Well funded with $325M cash at end of 2Q19; anticipate 2019 YE cash of $260-270M

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UNC CANCER CARE

Breast Cancer State of the State c. 2019

Lisa A. Carey M.D., FASCO
University of North Carolina
Lineberger Comprehensive Cancer Center

Disclosures

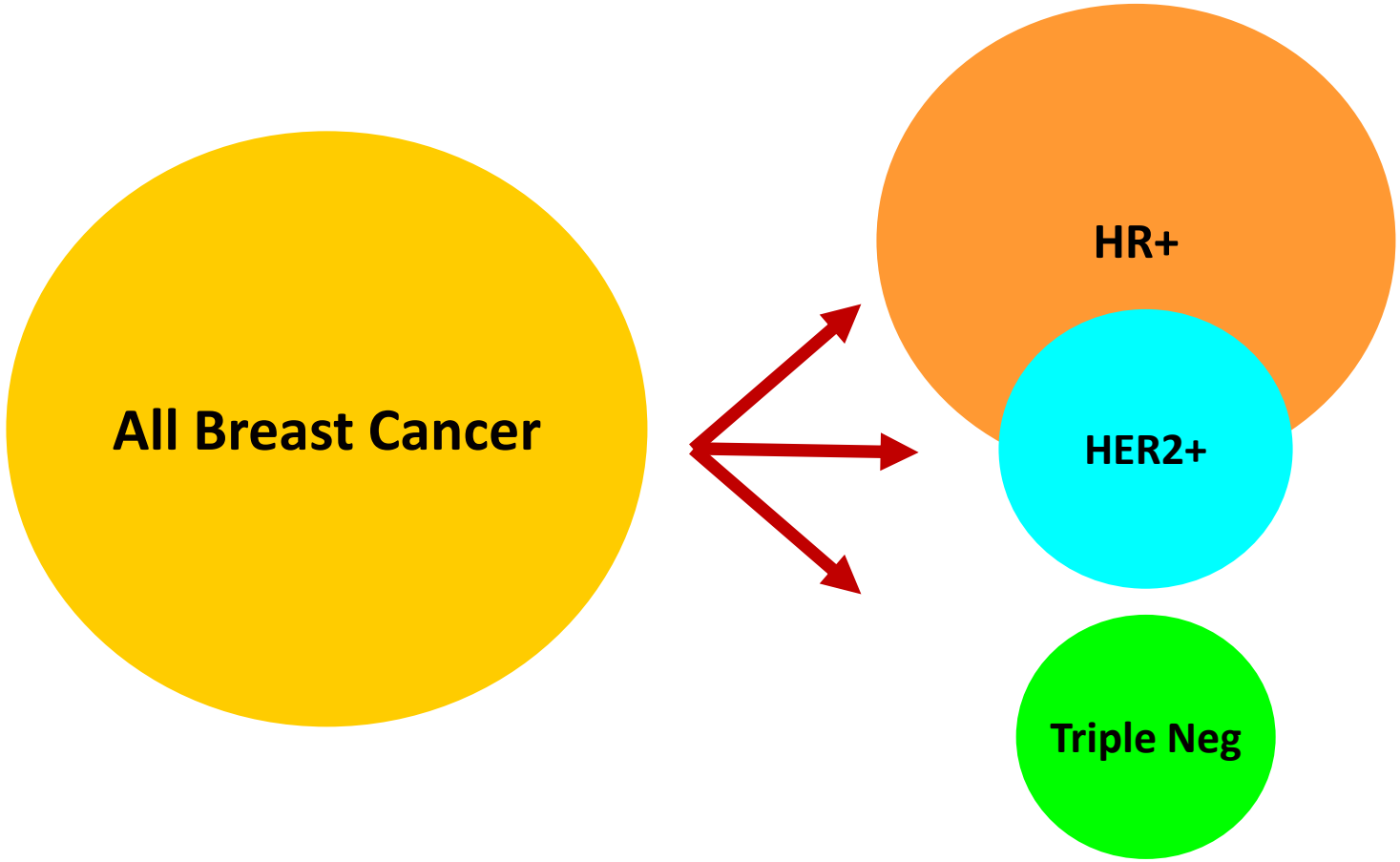
- **Research funding (to my institution): Innocrin, Nanostring, Novartis, Roche, Seattle Genetics**

- **Advisory or consultant role (no personal compensation): G1 Therapeutics, Innocrin, Lilly, Novartis, Seattle Genetics**

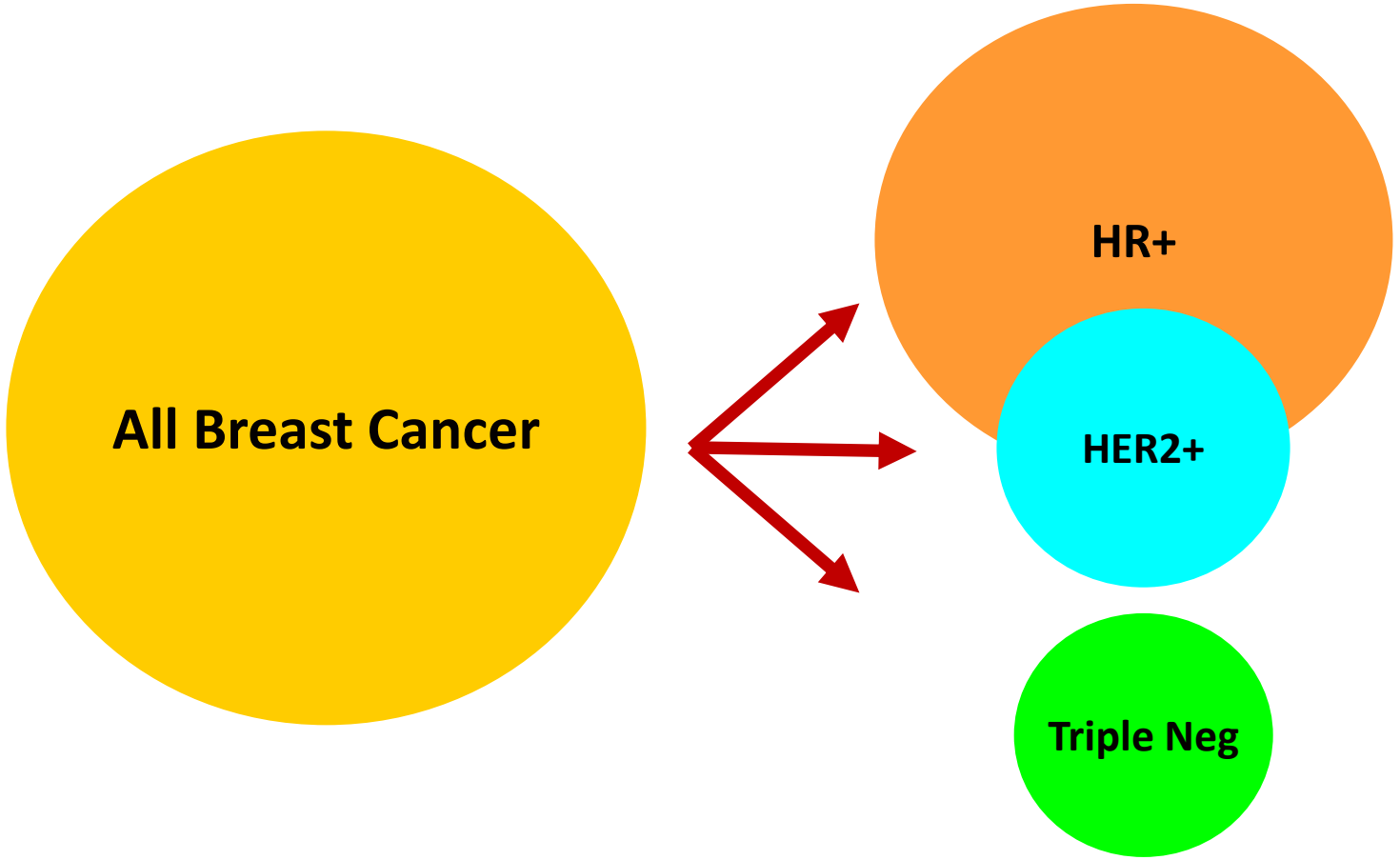
Epidemiology of Breast Cancer

- ~ 270,000 new cases per year in the U.S. (+2,500 men) in 2018
- 85% curable
- 3.5 million breast cancer survivors (currently in treatment and completed treatment) in the U.S.

Clinical Receptor Phenotype



Clinical Receptor Phenotype: Systemic Therapy



Primary Rx:

Endocrine-based

Anti-HER2-based

Chemo-based

Goals of Therapy

Stages I-III / Nonmetastatic

- Cure
- No long-term toxicity

Stage IV / Metastatic

- Control
- Tolerability (acute and chronic)

Goals of Therapy

Stages I-III / Nonmetastatic

- Cure
- No long-term toxicity

Metastatic

- Control
- Tolerability (acute and chronic)

Goals of therapy markedly differ

Willing to tolerate more acute toxicity in order to complete Rx

Balance toxicity and outcome

Decision-making Regarding Need for Medical Therapy

If distant metastases present, mainstay of lifelong therapy is medical.

If nonmetastatic, type and aggressiveness of treatment vary by:

- Tumor size and appearance (grade)
- Local lymph node involvement
- Targetable receptors (ER, PR, HER2)
- Patient factors (comorbidities, age, etc.)
- Genomic assays (in ER+ HER2-)
  - E.g. Oncotype Dx Recurrence Score, Prosigna, Mammaprint

Medical therapy given to reduce risk of recurrence in nonmetastatic disease = "neoadjuvant" or "adjuvant" therapy

Modern (Neo) Adjuvant Therapy

Hormone receptor (ER, PR) + (regardless of HER2):

- Antiestrogen pills (5-10 years)
- Chemotherapy (several months) if high risk

HER2+ (regardless of hormone receptors):

- Chemotherapy (several months)
- Anti-HER2 therapy (1-3 drugs for 1-2 years)

“Triple negative” (all receptors negative):

- Chemotherapy for up to 1 year

Modern (Neo) Adjuvant Therapy

Hormone receptor (ER, PR) + (regardless of HER2):

- Antiestrogen pills (5-10 years)
- Chemotherapy (several months) if high risk

HER2+ (regardless of hormone receptors):

- Chemotherapy (several months)
- Anti-HER2 therapy (1-3 drugs for 1-2 years)
  - Trastuzumab + pertuzumab + neratinib
  - Trastuzumab emtansine in residual disease after neoadjuvant chemotherapy + trastuzumab

"Triple negative" (all receptors negative):

- Chemotherapy for up to 1 year
  - Capecitabine x 6m in residual disease after neoadjuvant chemotherapy

Future directions:

Tailoring (less vs more) in all

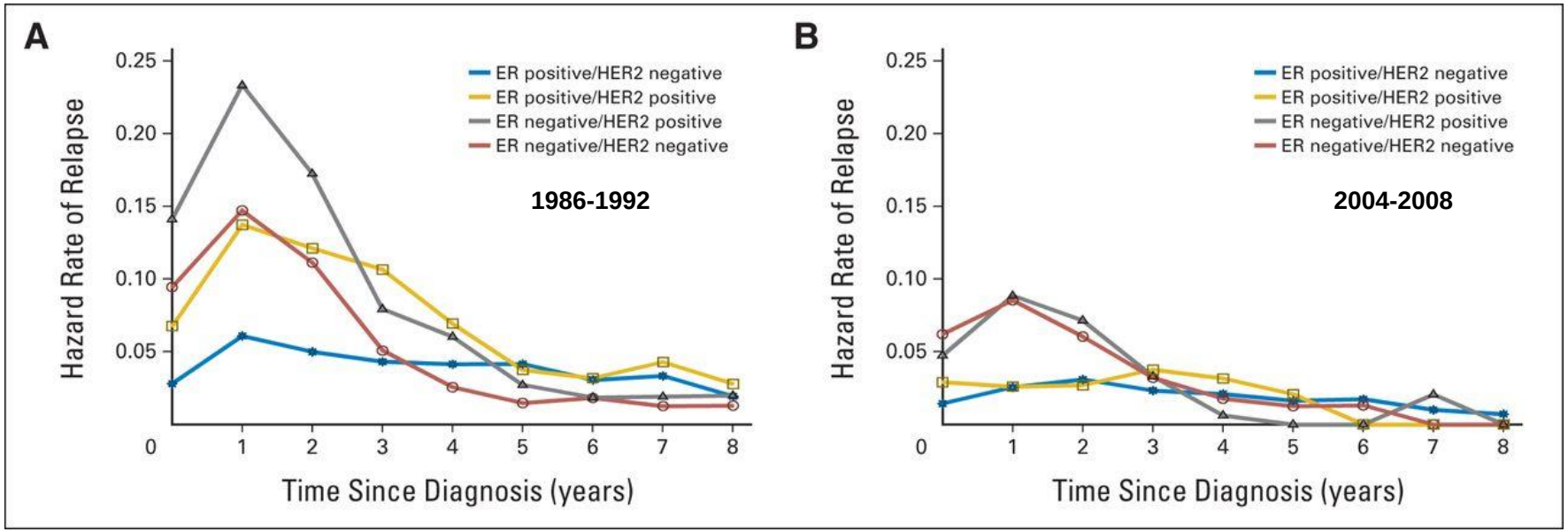
CDK4/6 inhibitors (soon!)
PI3K / mTOR inhibitors
Better endocrine Rx (oral SERDs!)
Genomics to determine duration of Rx

Better anti-HER2 drugs
CDK4/6 inhibitors
Immunotherapy
Molecular assays to determine Rx

Immunotherapy
Optimized management of toxicities

Breast Cancer Outcomes Have Improved

- **Better chemotherapy drugs and approaches**
- **Better endocrine therapy**
- **Development of anti-HER2 therapy**

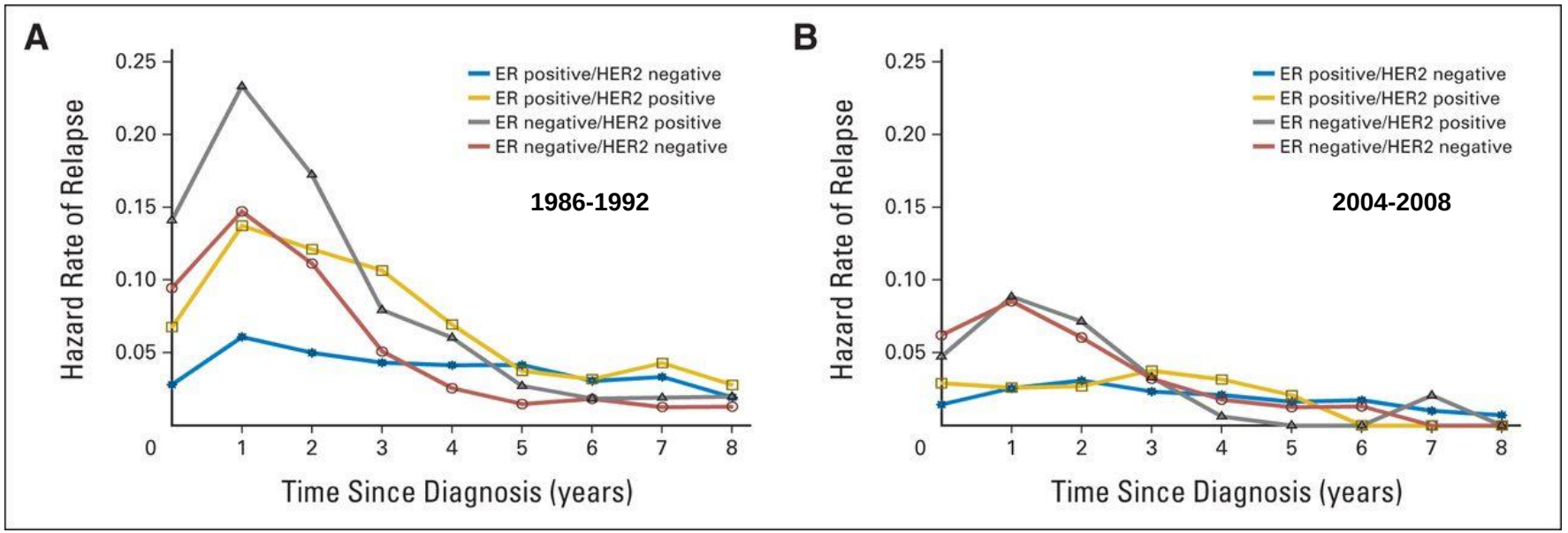


Cossetti R J et al. JCO 2015

Nonmetastatic Breast Cancer Outcomes Have Improved

- **Better chemotherapy drugs and approaches**
- **Better endocrine therapy**
- **Development of anti-HER2 therapy**

Cost has also increased! Reason for focus on rational Rx

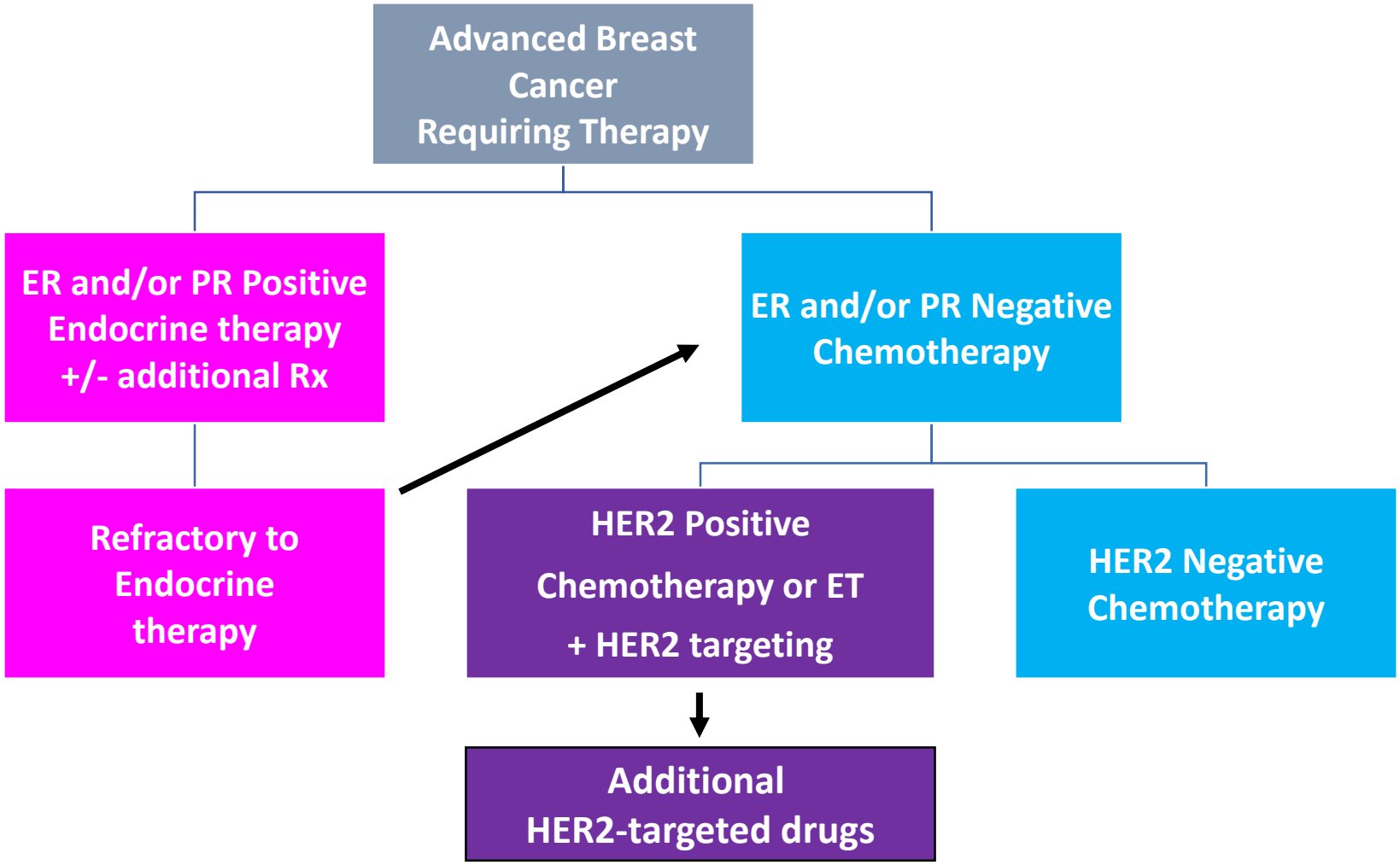


Cossetti R J et al. JCO 2015

Epidemiology of Metastatic Breast Cancer

- **Approximately 40,000 deaths per year in the U.S., but declining because of advances in therapy, especially in HER2+ disease**
- **Median survival ~3 years, but highly variable**
- **Prevalent population in U.S. ≈200,000 women**

Treatment Based on Tumor Phenotype



ASCO Guidelines: General Principles

ER+ HER2-

- Endocrine (usually) preferable to chemotherapy in 1st line
- Targeted agents added to ET (CDK4/6, mTOR, PI3K inhibitors)

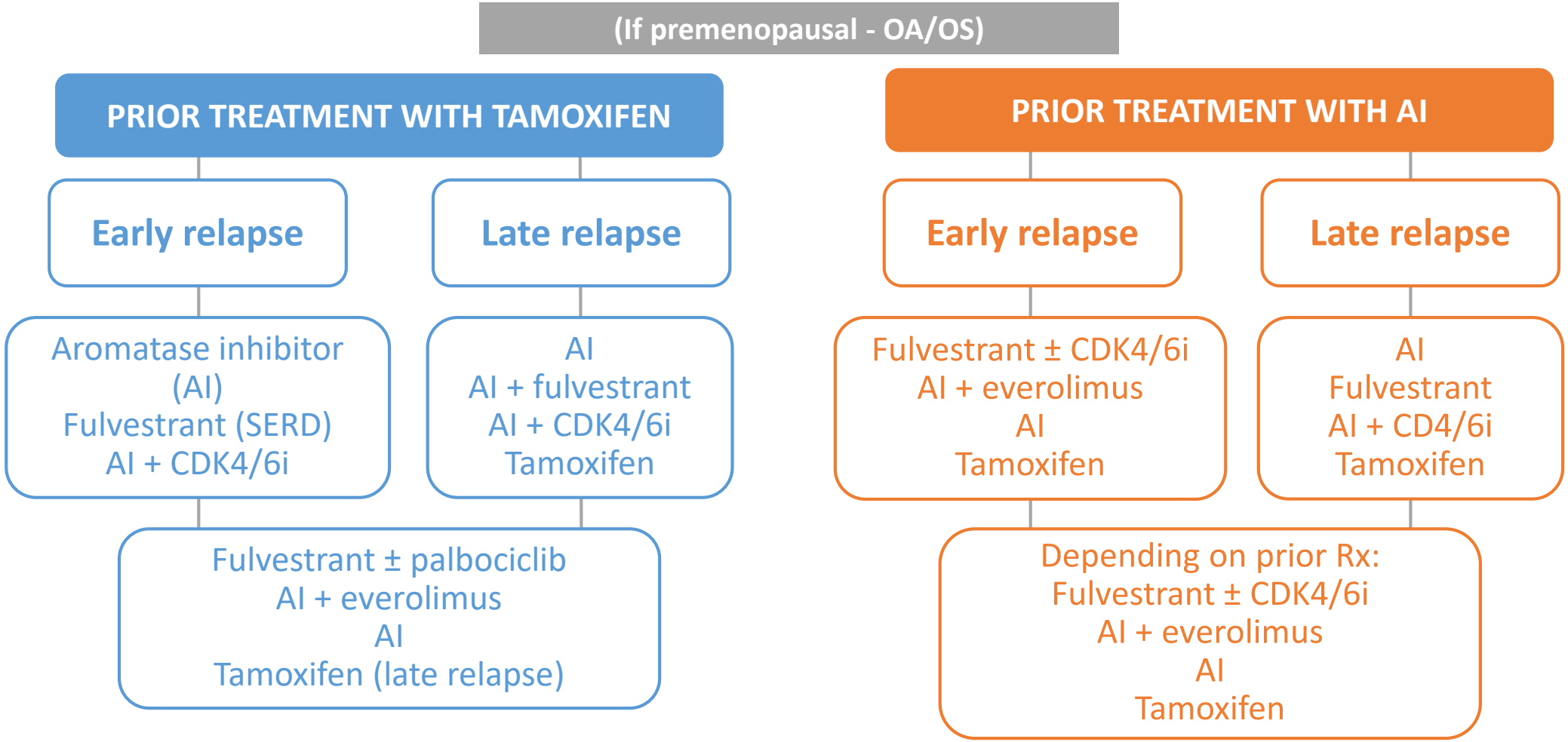
Any HER2- receiving chemotherapy

- Single agent chemotherapy preferable to combination
  - Exception: symptomatic, immediately life-threatening
- Longer duration ↑ outcome but must be balanced against ↑ toxicity
- No single optimal 1st or later chemotherapy
  - Factors: prior Rx, toxicity, performance status, comorbidity, patient preference

HER2+

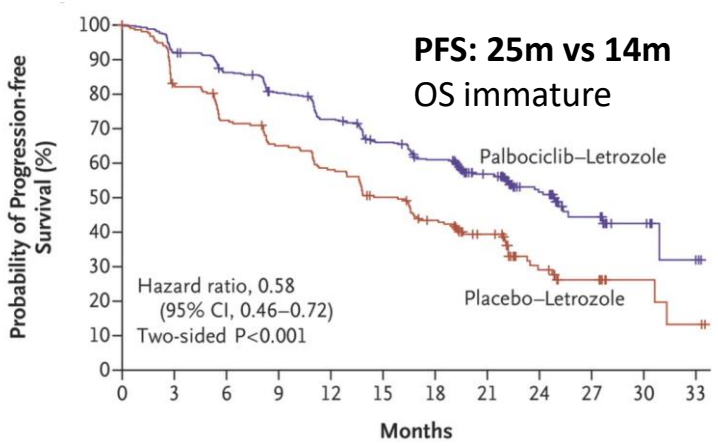
- HER2-directed Rx is mainstay
- 1st-line: taxane + trastuzumab + pertuzumab; 2nd-line: T-DM1
- HR+ HER2+ may consider ET + HER2-Rx or ET alone in selected cases

Endocrine Rx Algorithm in ER+/HER2-



CDK4/6 Inhibitor Effect in HR+ HER2-

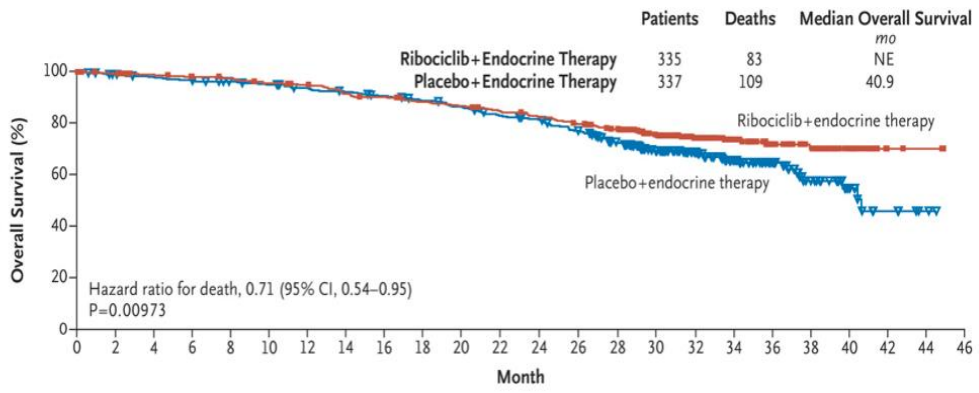
PALOMA2: Ph 3 letrozole ± palbo 1st L



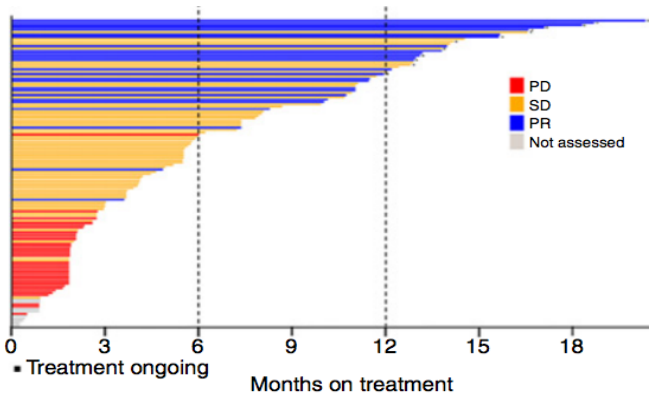
PFS: 25m vs 14m
OS immature

- **Similar PFS impact CDK 4/6i across lines of Rx (~ HR 0.50)**
- **OS ↑ in pretreated pts with abemaciclib, ribociclib, (palbo trial immature). HR ~ 0.70-75.**
- **No apparent interaction with PIK3CAmt, ESR1mt etc.**
- **Abemaciclib single agent activity, different toxicity profile**
- **Widely used. More toxic than ET alone.**
- **Being studied in (neo)adjuvant, HER2+**

MONALEESA7: Ph 3 ET ± ribo 1st L pre/perimen

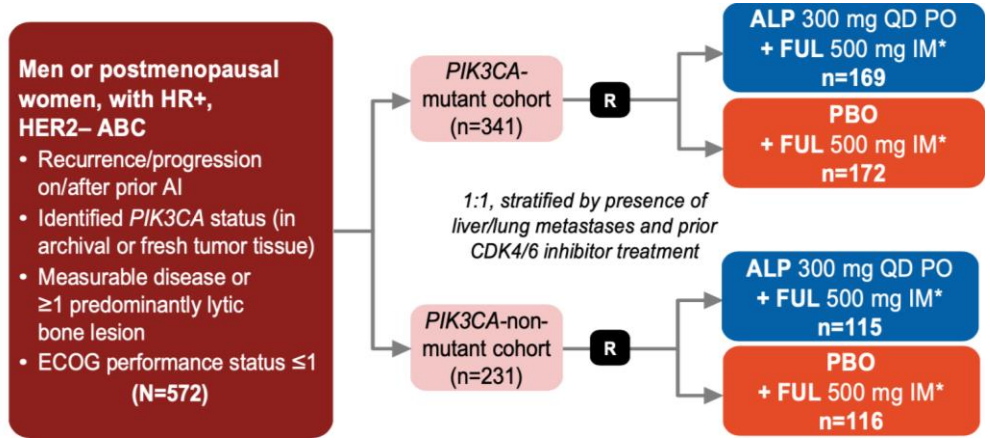


MONARCH1: Abema single agent



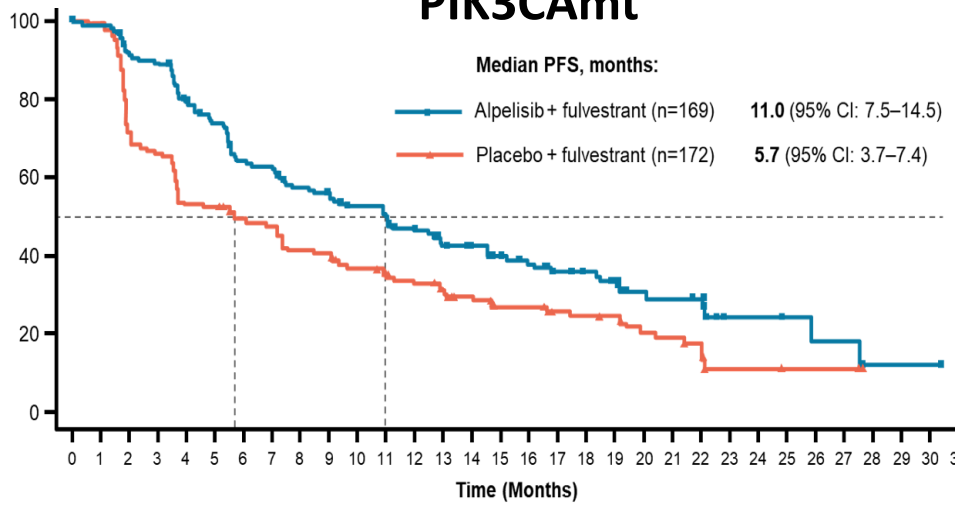
Alpelisib Added to Fulvestrant in PreRx PIKC3CA mt HR+ HER2-

SOLAR1

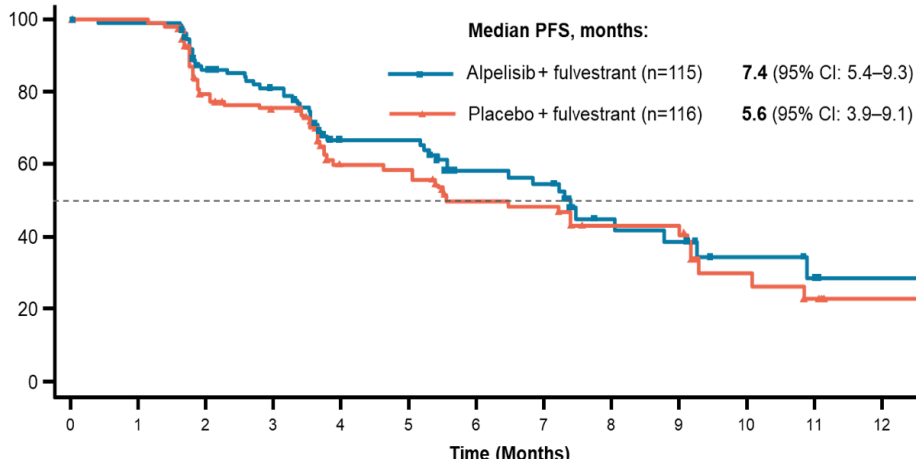


PFS HR 0.65 in mutant group. No OS yet.
Toxicity – hyperglycemia (40%), rash (10%)

PIK3CAmt



PIK3CAwt



Andre F, NEJM 2019

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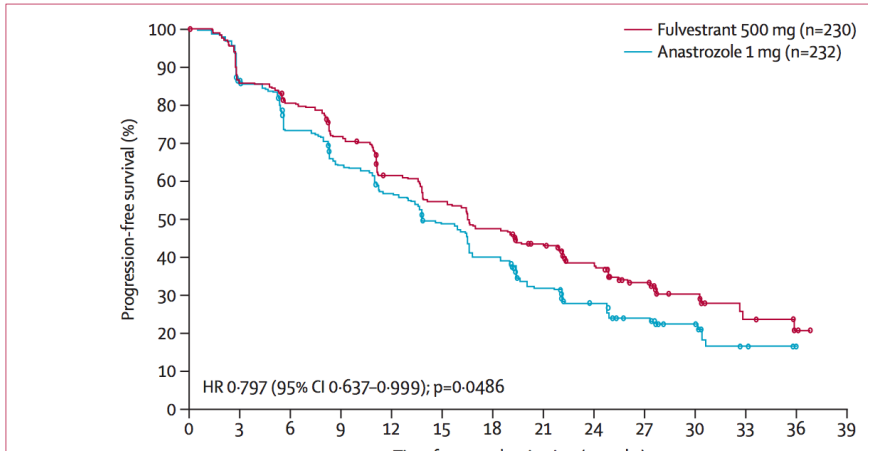
Fulvestrant vs AI: 1st-Line

FALCON study: Phase III trial

	Fulvestrant	Anastrozole	P-value
CR+ PR	46%	45%	NS
CBR	78%	74%	NS
PFS*	17m	14m	0.049

ET-naïve!

OS 5.5m improvement in Phase II FIRST trial



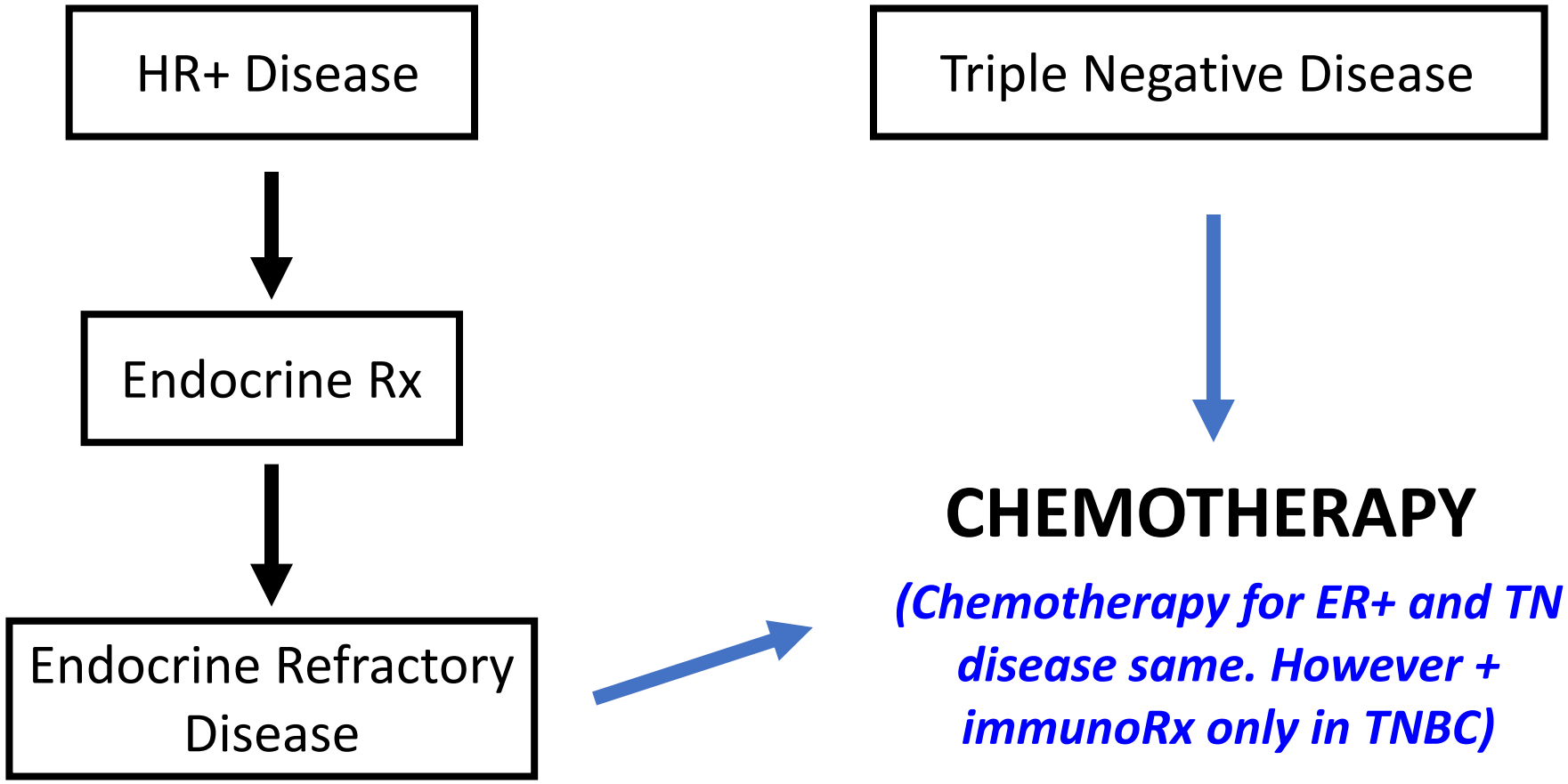
Robertson JFR et al, Lancet 2016

Fulvestrant as single agent =/> AI in 1st line endocrine Rx

Considerations:

1. **Prior adjuvant AI (if anything) should augment difference**
2. **CDK 4/6i trials usually AI 1st-line, fulvestrant later**
3. **IM administration is an obstacle – little enthusiasm for adjuvant setting**

Chemotherapy in HER2-Negative Breast Cancer



Chemotherapy Options

Anthracyclines
- **Doxorubicin**
- **Epirubicin**
- **Liposomal doxorubicin**

Taxanes
- **Paclitaxel**
- **Docetaxel**
- **Nab-paclitaxel**

Vinca alkaloids
- **Vinorelbine**

Other anti-tubule
- **Eribulin**

Antimetabolites
- **Methotrexate**
- **5-FU**
- **Capecitabine**
- **Gemcitabine**

Alkylating agents
- **Cyclophosphamide**
- **Platinum agents**

Epothilones
- **Ixabepilone**

Alone or in combinations

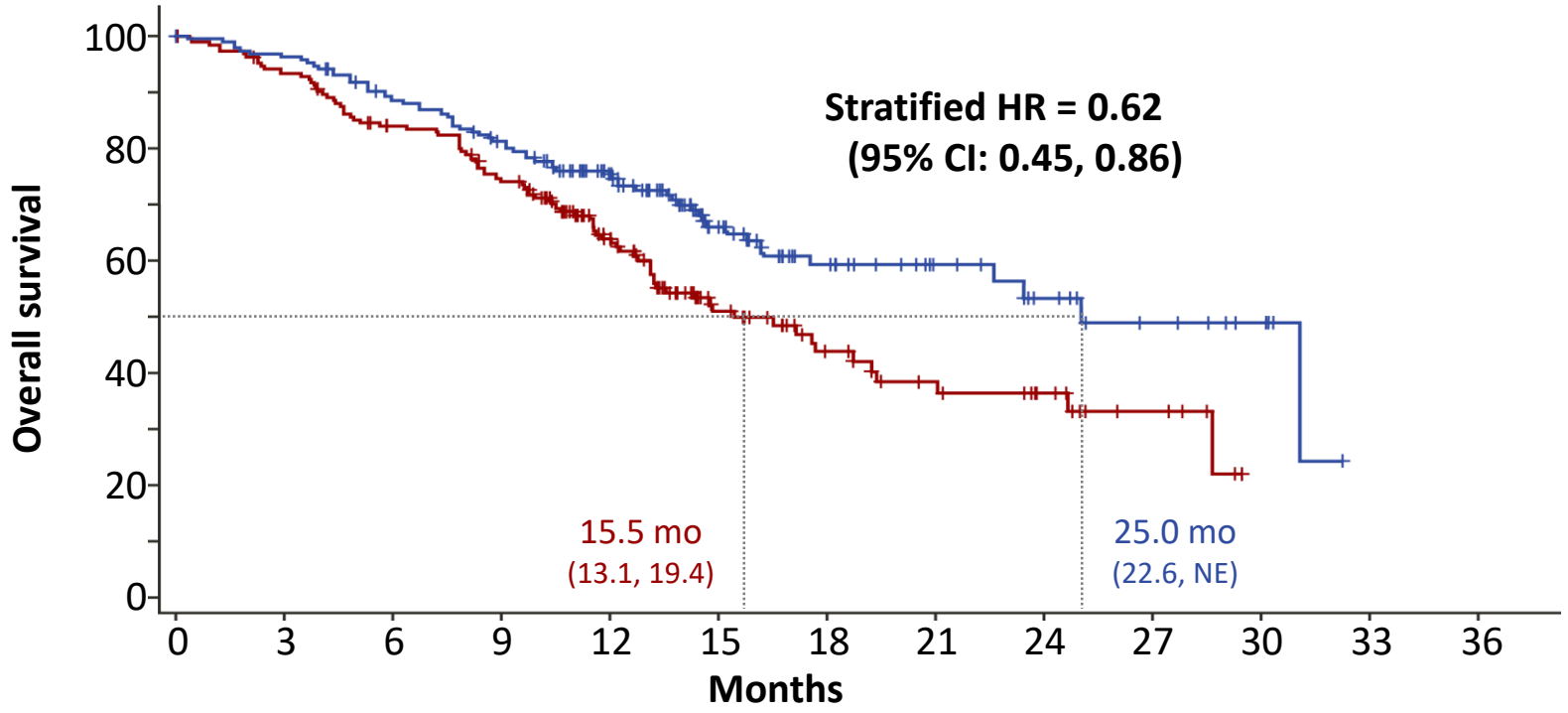
General principles TNBC:
- Taxanes = platinums 1st-line
  - If PDL1+, use nab paclitaxel + atezolizumab immunoRx
- Combination chemo more toxic but higher response

General principles ET-refractory:
- Same
- + oral agent (cape) good transition drug

Overall Survival in PD-L1+ Tumors with ImmunoRx added to Chemo

Impassion 130
1st-line TNBC

	Atezo + nab-P (n = 185)	Plac + nab-P (n = 184)
OS events, n	64	88
2-year OS (95% CI), %	54% (42, 65)	37% (26, 47)



- 1st line setting – first immunotherapy approval in breast cancer
- Many many trials pending
- Less tractable than melanoma, NSCLC, etc.
- Effect markedly lower in pretreated patients

Schmid et al, NEJM 2019

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Summary

- **Nonmetastatic breast cancer is common and curable. Mainstays of therapy = chemotherapy, endocrine therapy, anti-HER2 depending on risk and type of cancer.**
  - Challenges – tailoring therapy, identifying if agents active in metastatic disease help reduce risk of recurrence if used (neo)adjuvantly.

- **Metastatic breast cancer is 40,000 women per year in U.S. Longevity after diagnosis increasing, now ~ 3y overall, but not curable.**
  - Challenges – reducing toxicity, improving targeted therapies, role of immunotherapy

Thank you!

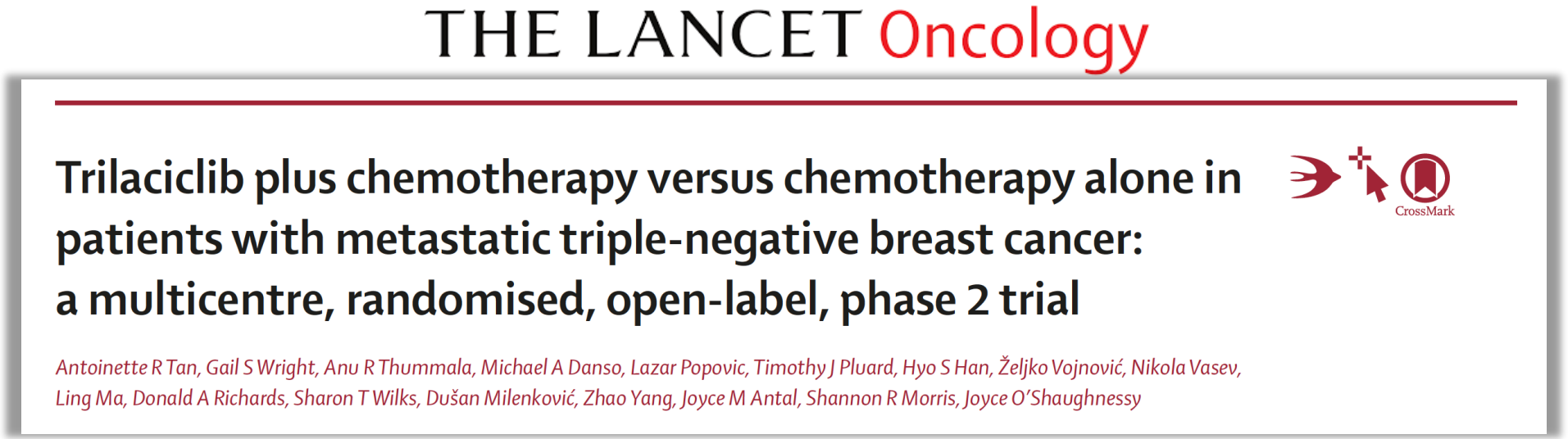
ESMO Data Review: Trilaciclib and G1T48

Raj Malik, M.D.

Chief Medical Officer and Senior Vice President, R&D

Trilaciclib mTNBC randomized Phase 2 trial: key findings

- 102-patient three-arm trial; all groups received gemcitabine/carboplatin (GC), a single-day regimen
  - Group 1 – GC only
  - Group 2 – GC + trilaciclib on day of GC
  - Group 3 – GC + trilaciclib on day prior to and day of GC
- ***Both trilaciclib arms showed significant OS improvement compared to control***
- Endpoints for myelopreservation were not achieved in this trial
- Trilaciclib was well tolerated with improvement in anemia-related PRO measures


THE LANCET Oncology

Trilaciclib plus chemotherapy versus chemotherapy alone in patients with metastatic triple-negative breast cancer: a multicentre, randomised, open-label, phase 2 trial

Antoinette R Tan, Gail S Wright, Anu R Thummala, Michael A Danso, Lazar Popovic, Timothy J Pluard, Hyo S Han, Željko Vojnović, Nikola Vasev, Ling Ma, Donald A Richards, Sharon T Wilks, Dušan Milenković, Zhao Yang, Joyce M Antal, Shannon R Morris, Joyce O'Shaughnessy

Lancet Oncol 2019; September 28, 2019
http://dx.doi.org/10.1016/S1470-2045(19)30616-3
Now **Online First** at TheLancet.com: 10.15 CEST, September 28, 2019

ESMO 2019: Trilaciclib improves overall survival when given with gemcitabine/carboplatin (GC) in patients with metastatic triple negative breast cancer (mTNBC) in a randomized Phase 2 trial; Abstract #6255

Significant overall survival benefit with trilaciclib

ITT population	Control (GC only) (Group 1)	Trilaciclib + GC (Group 2)	Trilaciclib + GC (Group 3)	Trilaciclib + GC (Group 2+3)
	N = 34	N = 33	N = 35	N = 68
Median OS (months)	12.6	20.1	17.8	20.1
HR		0.33	0.34	0.36
p-value		0.028	0.0023	0.0015
Median PFS (months)	5.7	9.4	7.3	8.8
HR		0.60	0.59	0.59
p-value		0.13	0.12	0.063

Overall Response Rate (ORR): 33% (Group 1), 50% (Group 2), 37% (Group 3)

Patients with death - Group 1: 20/34 (58.8%); Group 2: 11/33 (33.3%); Group 3: 14/35 (40.0%)

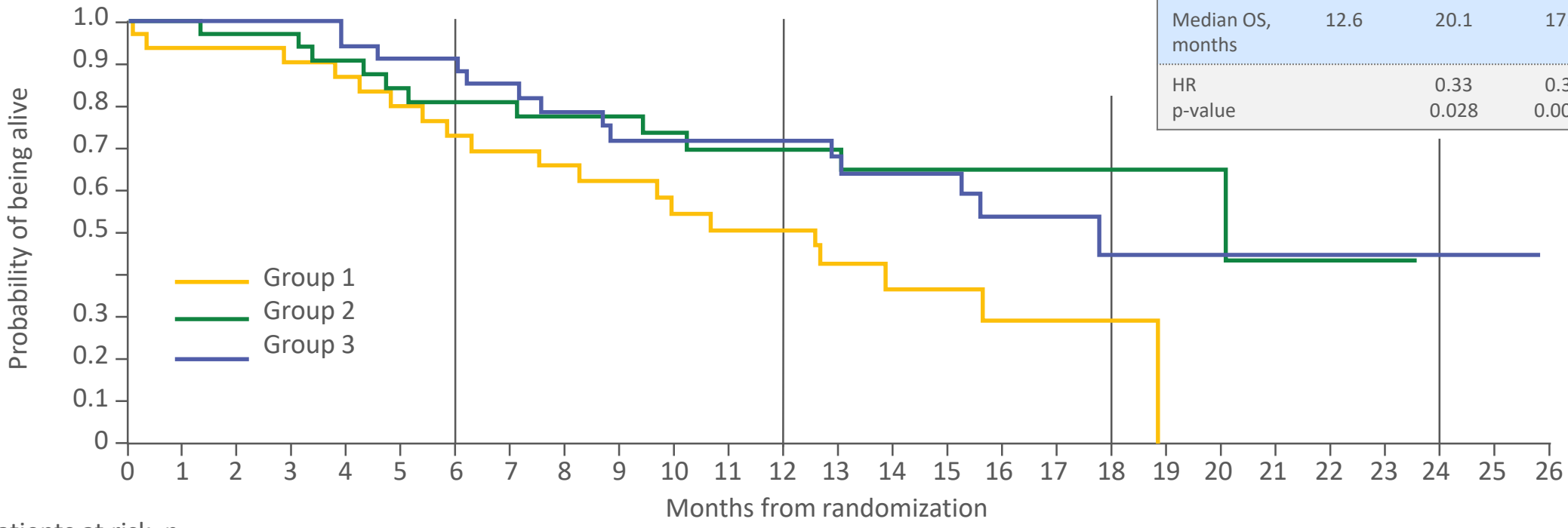
Group 1: GC only (Day 1/8) (n=34); Group 2: trilaciclib + GC (Day 1/8) (n=33); Group 3: trilaciclib + GC (Day 1/2/8/9) (n=35)

ESMO 2019: Trilaciclib improves overall survival when given with gemcitabine/carboplatin (GC) in patients with metastatic triple negative breast cancer (mTNBC) in a randomized Phase 2 trial; Abstract #6255

Results published concurrently in *The Lancet Oncology*

Significant overall survival benefit with trilaciclib

	Group 1	Group 2	Group 3
Median OS, months	12.6	20.1	17.8
HR		0.33	0.34
p-value		0.028	0.0023



Patients at risk, n

Group 1	34	27	27	26	25	23	21	19	18	16	14	13	13	9	6	6	3	2	1	0	0	0	0	0	0	0
Group 2	33	33	32	31	28	26	24	22	20	20	19	17	17	15	13	13	12	10	8	5	3	2	1	1	0	0
Group 3	35	35	35	35	32	31	30	26	23	21	21	20	19	17	13	13	9	8	5	3	3	1	1	1	1	0

OS benefit greater than PFS suggests immune-mediated effect

Based on data as of 17 May 2019

Group 1: GC only (Day 1/8) (n=34); Group 2: trilaciclib + GC (Day 1/8) (n=33); Group 3: trilaciclib + GC (Day 1/2/8/9) (n=35)

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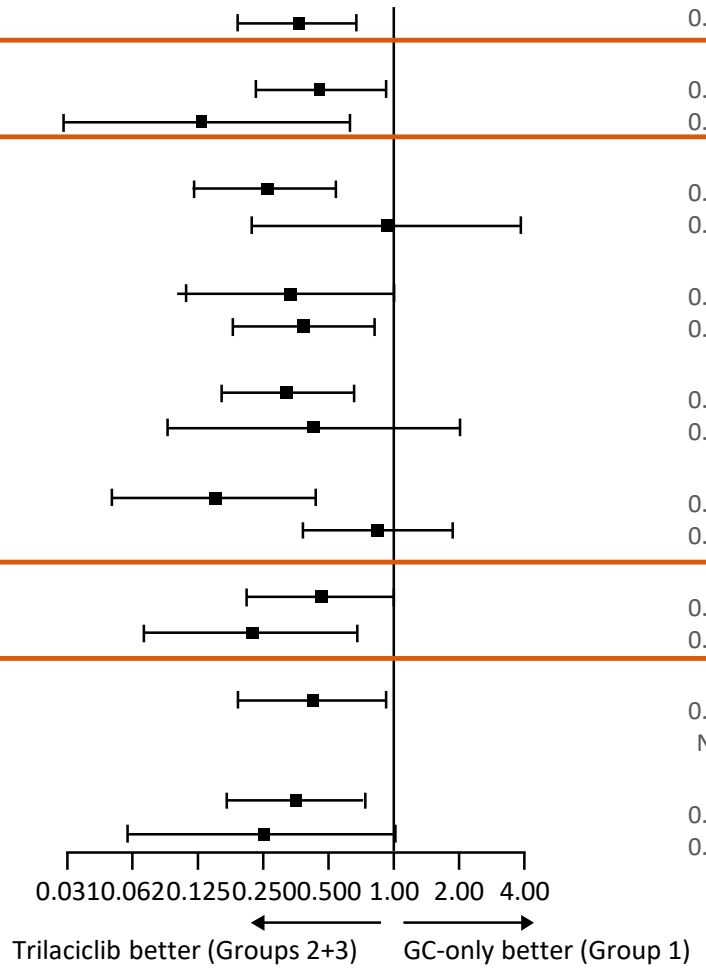
Results published concurrently in *The Lancet Oncology*

OS benefit across all subgroups

Pre-specified subgroup analyses

Subgroup	No. of patients	No. of events	HR	95% CI
Overall (ITT)	102 (100)	45	0.36	(0·19–0·67)
Age				
<65 years	76 (74·5)	36	0.45	(0·23–0.91)
≥65 years	26 (25·5)	9	0.13	(0·03–0·63)
Race				
White	78 (76·5)	33	0.26	(0·12–0·54)
Non-white	24 (23·5)	12	0.92	(0·22–3·84)
Liver involvement				
Yes	26 (25·5)	17	0.33	(0·11–1·01)
No	76 (74·5)	28	0.38	(0·18–0·81)
Region				
USA	83 (81·4)	37	0.32	(0·16–0·65)
Ex-USA	19 (18·6)	8	0.42	(0·09–2·02)
ECOG PS				
0	53 (52)	18	0.15	(0·05–0·44)
1	49 (48)	27	0.72	(0·33–1·61)
Number of prior lines therapy				
0	64 (62·7)	28	0.46	(0·21–0.99)
1 or 2	38 (37·3)	17	0.22	(0·07–0·67)
BRCA classification				
Unknown	66 (64·7)	28	0.42	(0·19–0.92)
Positive	8 (7·8)	3	NE	(NE–NE)
Histological TNBC classification				
Always	71 (69·6)	31	0.35	(0·17–0·74)
Acquired	25 (24·5)	12	0.25	(0·06–1·02)



Based on data as of 17 May 2019 • Group 1: GC (Day 1/8) (n=34); Group 2: GC + trilaciclib (Day 1/8) (n=33); Group 3: GC + trilaciclib (Day 1/2/8/9) (n=35)
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; ITT, intention-to-treat; NE, not estimable
ESMO 2019: Trilaciclib improves overall survival when given with gemcitabine/carboplatin (GC) in patients with metastatic triple negative breast cancer (mTNBC) in a randomized Phase 2 trial; Abstract #6255
Results published concurrently in *The Lancet Oncology*

G1T48 (Oral SERD) Update

G1T48 Phase 1 trial: key findings

✓Well tolerated; favorable safety profile at all dose levels

✓No dose-limiting toxicities observed; maximum tolerated dose not reached

✓AEs mostly Grade 1

✓^{18}F-FES PET scans – ER occupancy ≥ 80% in doses ≥ 400 mg

✓Preliminary evidence of anti-tumor activity in heavily pre-treated population

✓Phase 1 completed; 600 mg and 1,000 mg dose expansion cohorts enrolling

Dose-escalation study of G1T48, an oral selective estrogen receptor degrader (SERD), in postmenopausal women with ER+/HER2- locally advanced or metastatic breast cancer (ABC); Abstract #3587

Favorable tolerability and safety profile; AEs mostly Grade 1

Drug-related adverse event	Grade 1	Grade 2	Grade 3	Grade 4	Total (N=26)
Fatigue	6 (23.1%)	1 (3.8%)	1 (3.8%)	0	8 (30.8%)
Hot flush	5 (19.2%)	2 (7.7%)	0	0	7 (26.9%)
Diarrhea	6 (23.1%)	1 (3.8%)	0	0	7 (26.9%)
Headache	4 (15.4%)	0	0	0	4 (15.4%)
Nausea	4 (15.4%)	0	0	0	4 (15.4%)
Muscle spasms	2 (7.7%)	1 (3.8%)	0	0	3 (11.5%)
Myalgia	3 (11.5%)	0	0	0	3 (11.5%)
Abdominal distension	1 (3.8%)	1 (3.8%)	0	0	2 (7.7%)
Musculoskeletal stiffness	1 (3.8%)	1 (3.8%)	0	0	2 (7.7%)
Cough	0	1 (3.8%)	0	0	1 (3.8%)
Hypoglycemia	0	1 (3.8%)	0	0	1 (3.8%)
Lymphopenia	0	1 (3.8%)	0	0	1 (3.8%)
Pain (musculoskeletal chest)	0	1 (3.8%)	0	0	1 (3.8%)

AEs occurring in ≥3 patients or ≥CTCAE Grade 2; All TEAEs; AEs regardless of causality

Data cut: 12 August 2019

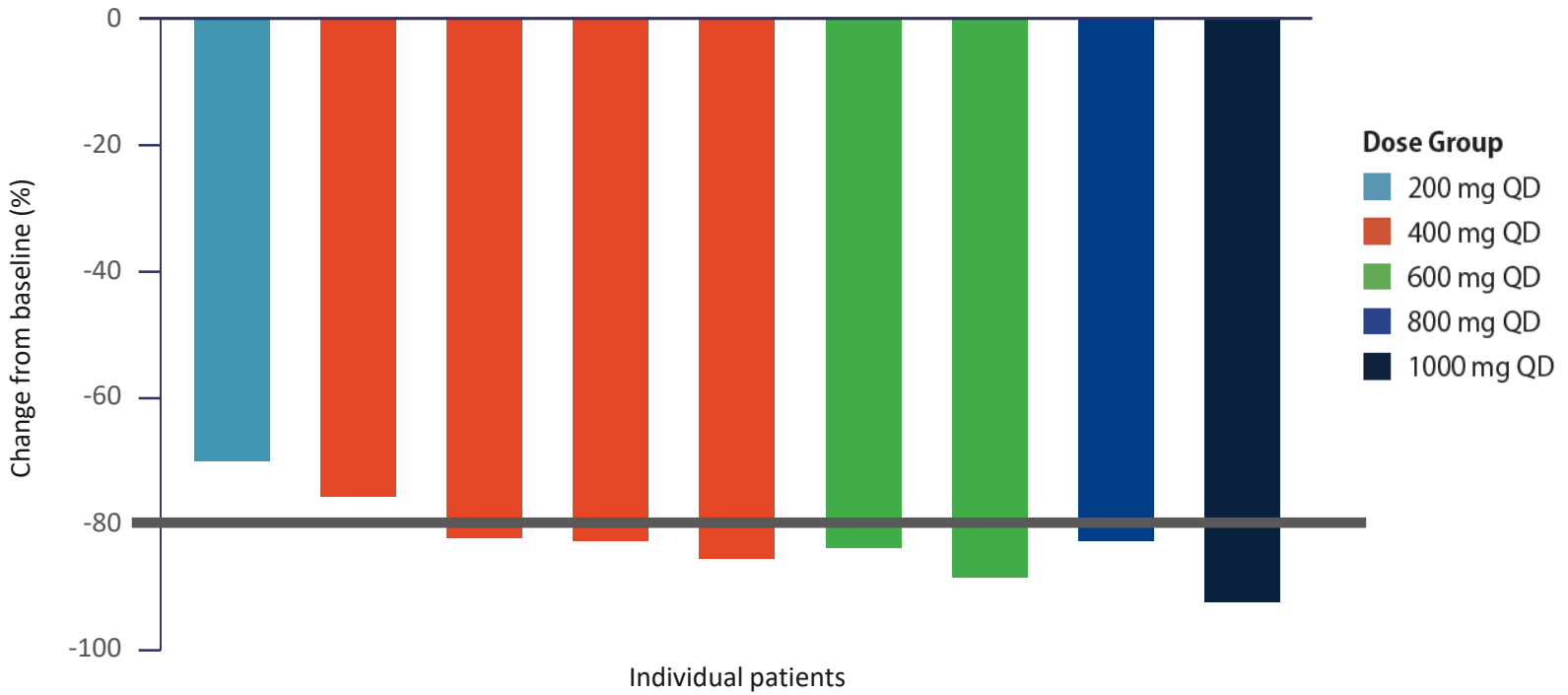
Dose-escalation study of G1T48, an oral selective estrogen receptor degrader (SERD), in postmenopausal women with ER+/HER2- locally advanced or metastatic breast cancer (ABC); Abstract #3587

PK/PD profile: robust target engagement

PK summary

- Generally dose-dependent increases in exposure
- Food decreased variability and increases exposure
- Patients in expansion cohorts being dosed with food

PD: ^{18}F-FES PET uptake in tumors



≥ 80% decrease in uptake at doses ≥ 400 mg

Dose-escalation study of G1T48, an oral selective estrogen receptor degrader (SERD), in postmenopausal women with ER+/HER2- locally advanced or metastatic breast cancer (ABC); Abstract #3587

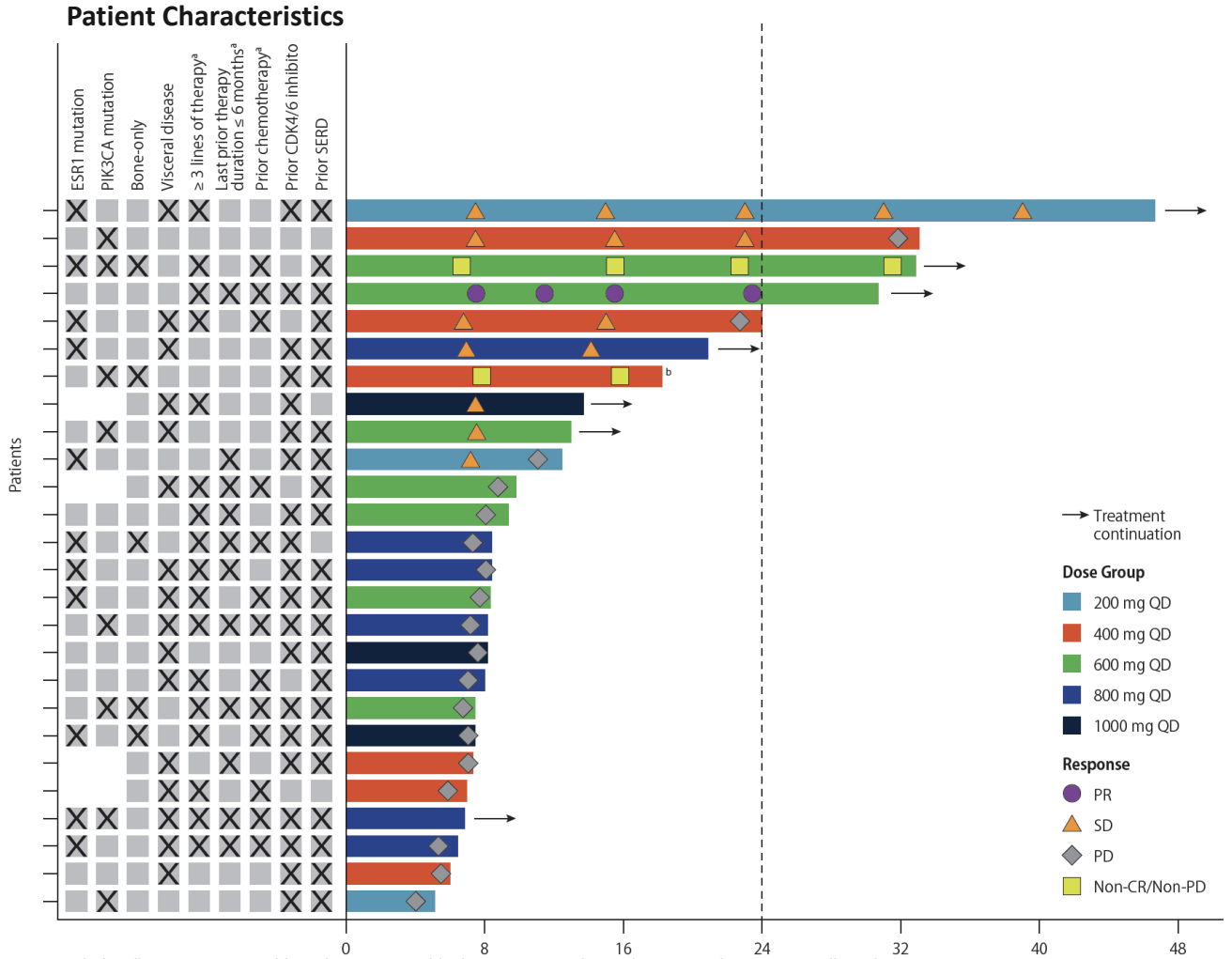
Heavily pre-treated patient population

N = 26	Patients	%
Prior fulvestrant	22	84.6%
Prior CDK4/6 inhibitor	20	76.9%
Prior chemotherapy	13	50.0%
Last prior therapy duration ≤ 6mos	11	42.3%
≥ 3 lines of therapy	17	65.4%
Visceral disease	16	61.5%

~85% of patients had prior fulvestrant therapy
~65% of patients had received at least three lines of therapy

Dose-escalation study of G1T48, an oral selective estrogen receptor degrader (SERD), in postmenopausal women with ER+/HER2- locally advanced or metastatic breast cancer (ABC); Abstract #3587

Efficacy demonstrated in heavily pre-treated population



Includes all patients (measurable and non-measurable disease). No grey box indicates samples were not collected.
[a] In advanced/metastatic setting; [b] One patient discontinued treatment due to Grade 2 gastrointestinal symptoms.
CDK, cyclin-dependent kinase; CR, complete response; ESR1, estrogen receptor 1; PD, progressive disease; PIK3CA, phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha; PR, partial response; QD, once daily; SD, stable disease; SERD, selective estrogen receptor degrader.

Response evaluable pts (N=19)	
ORR	1 (5.3%)
CBR	3 (15.8%)

ORR=(CR+PR); CBR=(CR+PR+SD≥24 weeks)

- Patient characteristics associated with PD by 8 weeks:
  - Visceral disease
  - ≥ 3 lines of prior therapy
  - ≤ 6 months on most recent prior therapy
  - Prior chemotherapy in metastatic setting

Dose-escalation study of G1T48, an oral selective estrogen receptor degrader (SERD), in postmenopausal women with ER+/HER2- locally advanced or metastatic breast cancer (ABC); Abstract #3587

ESMO 2019: key findings

Trilaciclib: mTNBC

- Trilaciclib improved overall survival when added to GC regimen
- Well tolerated with improvement in anemia-related PRO measures
- Phase 3 trial beginning in 2H20

G1T48

- Favorable safety and tolerability profile
- Evidence of anti-tumor efficacy in heavily pre-treated population
- Phase 3 trial beginning in 2H20

Q&A

Dr. Carey, Dr. Malik & Dr. Velleca

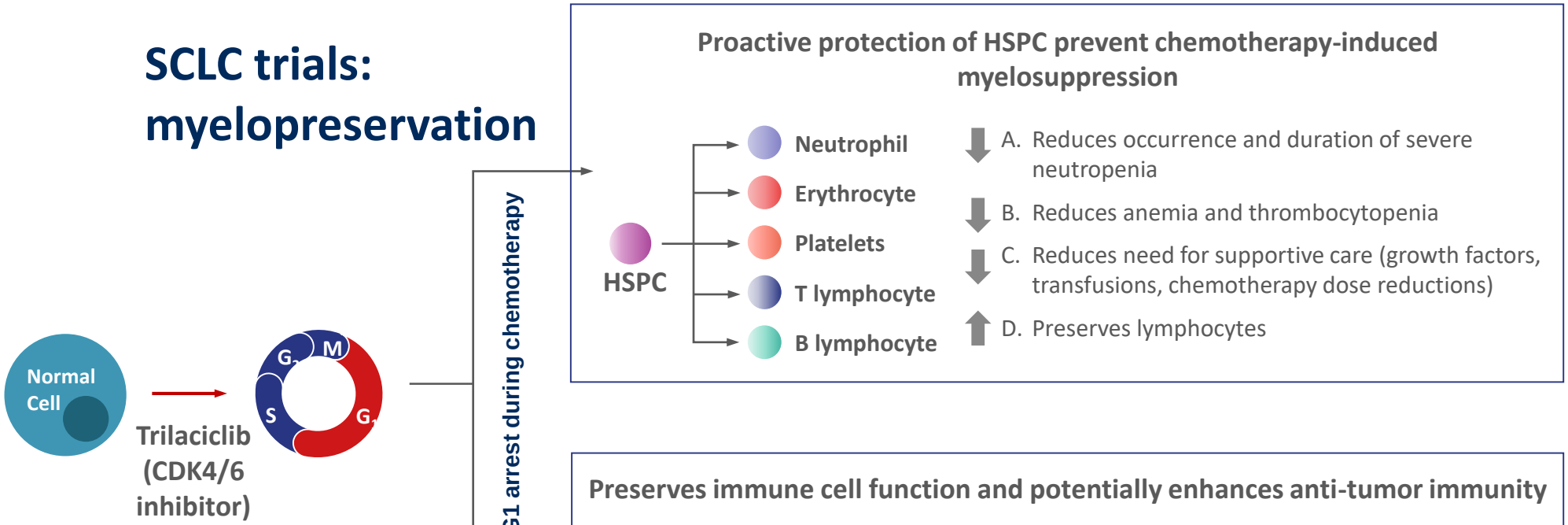
Pipeline Development Strategy and Regulatory Milestones

Raj Malik, M.D.

Chief Medical Officer and Senior Vice President, R&D

Trilaciclib: context-dependent efficacy

SCLC trials: myelopreservation



Weiss et al, Annals of Oncology 2019
He et al, Science Translational Medicine 2017
Bisi et al, Mol Cancer Ther., 2016

TNBC trial: OS improvement

Tan et al, Lancet Oncology 2019
Zhang et al, Nature 2018
Jerby-Arnon et al, Cell 2018
Goel et al, Nature 2017
Deng et al, Cancer Discovery 2017

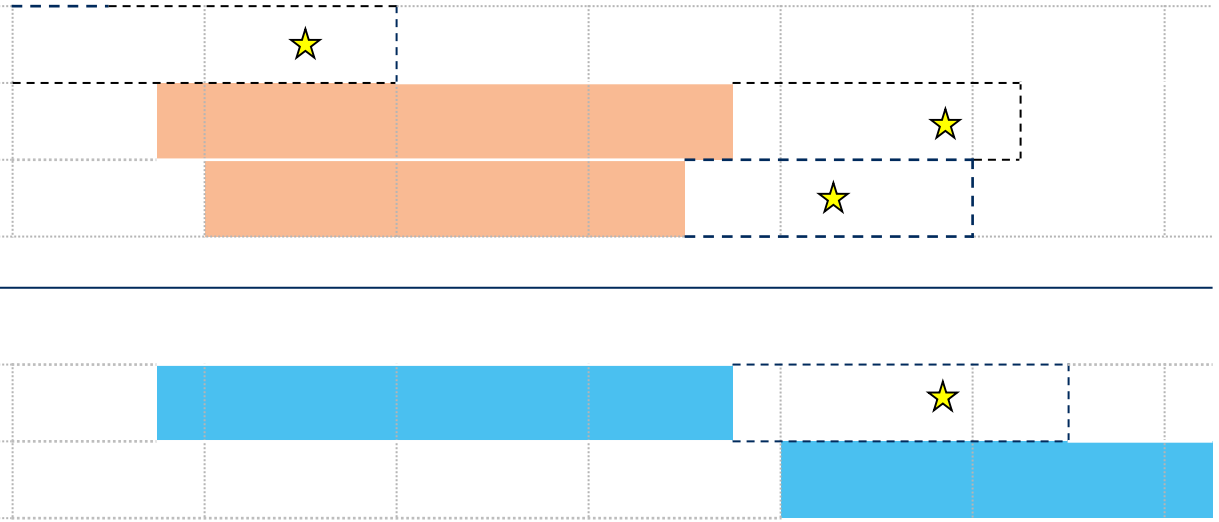
Trilaciclib benefits linked to setting

	Primary Benefit: Myelopreservation	Primary Benefit: Anti-Tumor Efficacy
Chemotherapy schedule	Multi-day regimens	Single-day regimens
Tumor type	---	Tumor microenvironments more favorable to immune modulation
Settings/indications:	✓ **SCLC (etoposide + platinum, topotecan)** ✓ **1L mCRC (5-FU regimens)** ✓ **Neoadjuvant TNBC (doxorubicin + cyclophosphamide + taxane)**	✓ **1L mTNBC (TBD +/- anti-PD-L1)** ✓ **1L mBC (taxane)**

Two-pronged development strategy: myelopreservation and anti-tumor efficacy

Development plan targets broad myelopreservation label and anti-tumor efficacy label for specific tumors

DISEASE OF INTEREST	CHEMO REGIMENS
Myelopreservation	
1L SCLC	Etoposide + platinum, topotecan
1L mCRC	5-FU regimens
Neoadj TNBC	Doxo + cyclo + taxane
Anti-tumor efficacy	
1L mTNBC	TBD +/- anti-PD-L1
1L mBC	Taxane

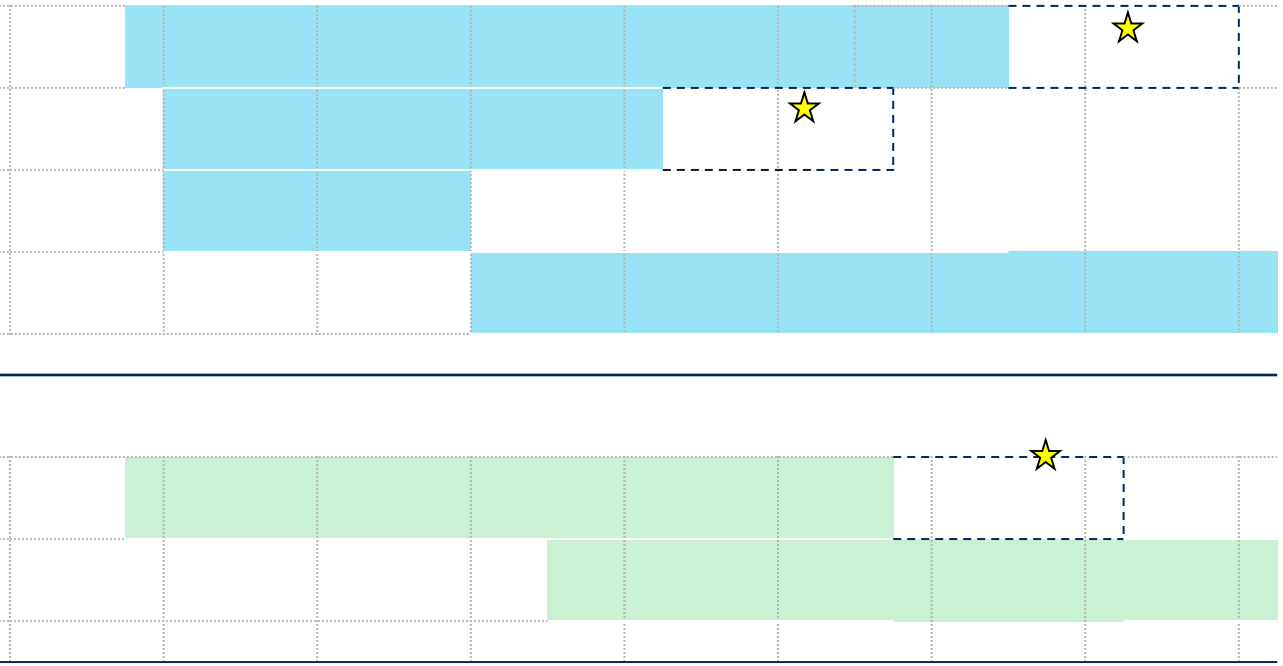


Partnering to enable expansion in other tumor types: e.g. NSCLC

☆ Denotes timing for completion of FDA review and potential U.S. approval; RoW is ~2Q later for all indications except SCLC. End of shading highlights data readout; dashed box indicates preparing, filing and regulatory review period.

Lerociclib and G1T48: improving patient care in advanced/metastatic and adjuvant settings

DISEASE OF INTEREST	COMBO DRUG
G1T48	
1L ER+ mBC	CDK4/6i
2L ER+ mBC	Everolimus
Neoadjuvant BC*	N/A
Adjuvant ER+ BC	NA
lerociclib	
1L ER+ mBC	Fulvestrant
Adjuvant ER+ BC	Aromatase inhibitor



G1T48 and lerociclib partnering to enable expansion in other indications

★ Denotes timing for completion of FDA review and potential U.S. approval; RoW is ~2Q later for all indications. End of shading highlights data readout; dashed box indicates preparing, filing and regulatory review period.
* Neoadjuvant trial enables adjuvant trial

Commercial Opportunity and Strategy

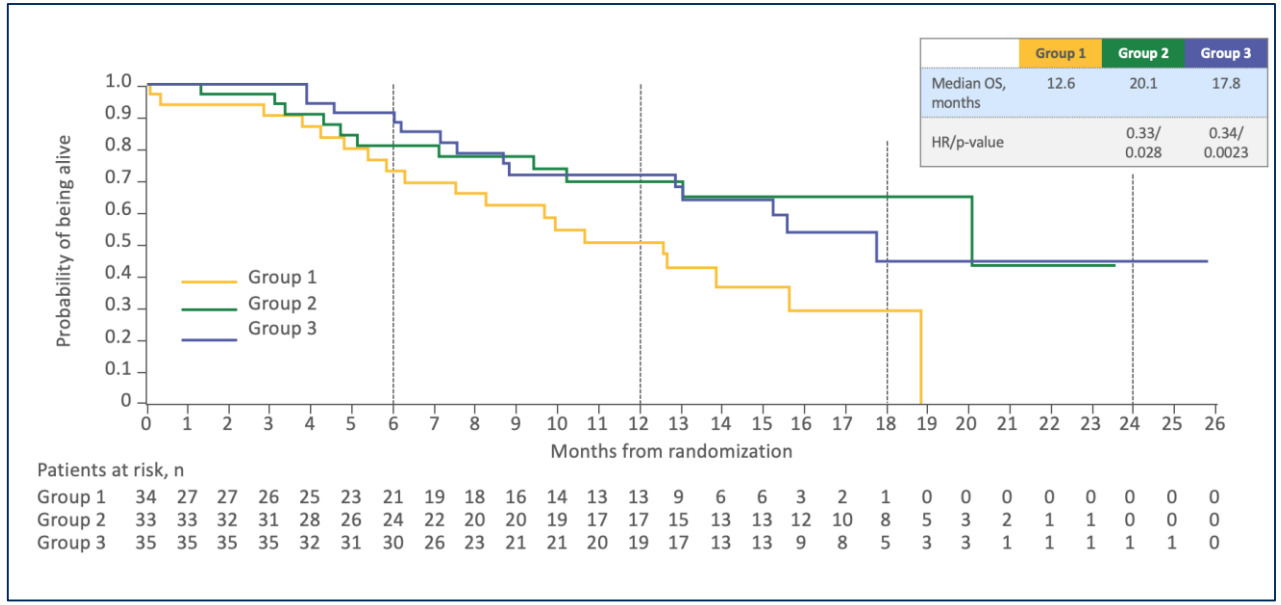
John Demaree
Chief Commercial Officer

Trilaciclib provides context-dependent efficacy: myelopreservation or improved survival

SCLC: Myelopreservation

	PLACEBO + CHEMOTHERAPY	TRILACICLIB + CHEMOTHERAPY	
Patients (intent-to-treat population)	120	125	P-VALUE[+]
Mean duration (in days) of severe neutropenia in cycle 1 (SD)	4 (5.2)	1 (2.3)	**<0.0001**
Occurrence of severe neutropenia	64 (53.3%)	16 (12.8%)	**<0.0001**
Occurrence of RBC transfusions on/after 5 weeks	32 (26.7%)	19 (15.2%)	**0.0207**
Cumulative incidence RBC transfusions on/after 5 wks: event rate per 100 wks	3.2	1.5	**0.0020**
Occurrence of Grade 3/4 anemia	39 (32.5%)	26 (20.8%)	**0.0188**
Occurrence of Grade 3/4 thrombocytopenia	44 (36.7%)	26 (20.8%)	**0.0081**

TNBC: OS Improvement

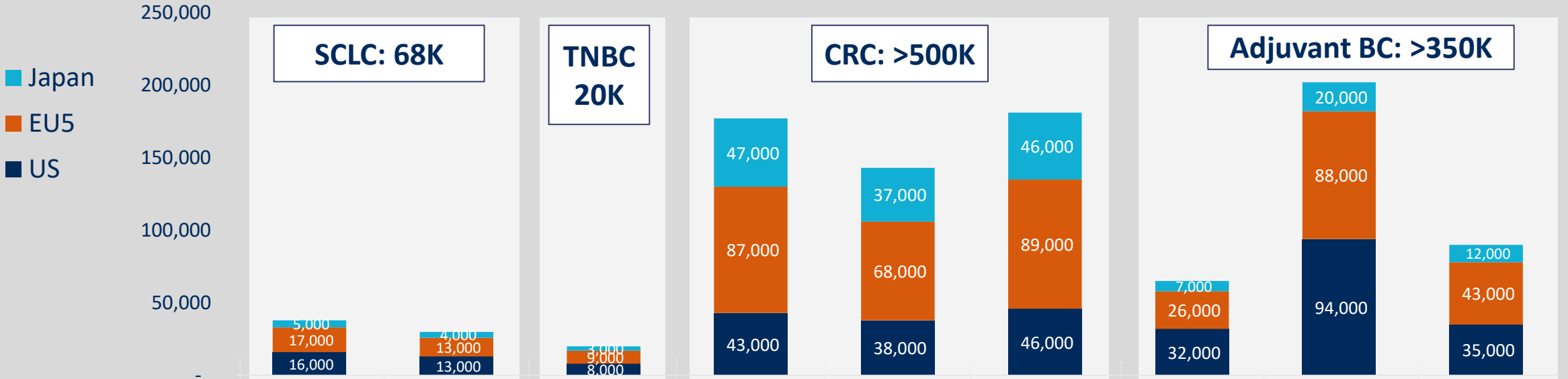


Improved patient experience

- Trilaciclib is a first-in-class investigational therapy designed to improve outcomes for people with cancer treated with chemotherapy
- G1 market research suggests substantial share uptake in all indicated patients

~1 million chemo-treated patients in planned indications

Global Chemotherapy Treated Incident Patients (G7)*



	1L SCLC	2/3L SCLC	1L TNBC	1L CRC	2/3L CRC	Adjuvant CRC	Adjuvant TNBC	Adjuvant HR+/HER2- BC	Adjuvant HER2+ BC
% currently treated with eligible chemo regimen**	~100% (EP)	50% (topotecan or EP)	55% (GC, taxane or IO + chemo)	80% (5-FU)	70% (5-FU)	50% (5-FU)	65% (AC)	50% (AC)	40% (AC)
Estimated mean # of cycles***	4-6	3-4	7-8	11-23	4-12	12	8	8	8

Potential to be used for myelopreservation in the same patient across multiple lines of therapy

*Source: Secondary epi sources, 2027 estimates

**EP refers to any regimen that includes etoposide + platinum; GC refers to gemcitabine/carboplatin; AC refers to any regimen that includes Adriamycin and cyclophosphamide; 5-FU refers to any regimen that includes fluorouracil (e.g., FOLFOX). In addition to CRC, pancreatic cancer, gastroesophageal cancer and squamous cell carcinoma of the head and neck (SCCHN) are also treated with 5-FU regimens (% currently treated with 5-FU regimens varies by tumor type and region)

***Source: SCLC and TNBC: G1 Therapeutics' completed trials; CRC and Adjuvant BC: number of cycles for eligible chemo regimens from Decision Resources Group Treatment Landscape and Forecast Assumptions 2018 Reports (CRC and BC)

Trilaciclib go-to-market strategy

Capabilities

- ✓ Hired experienced key functional talent at G1
- ✓ Utilizing contractors for initial functional-level buildouts, including sales
- ✓ Maintaining strategic agility to scale as needed for future launches

Planning

- ✓ Comprehensive launch plans across all functions
- ✓ All milestones on schedule
- ✓ Trilaciclib supply will be available at approval

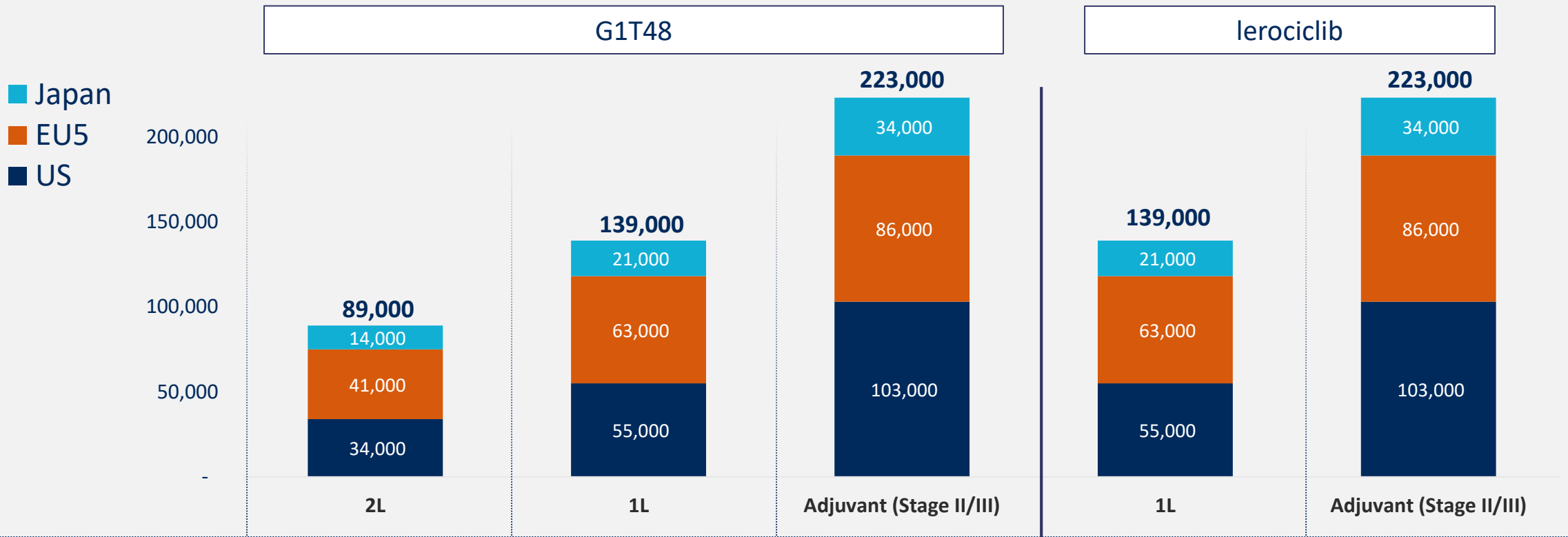
Partner

- Leverage partner's capabilities and scale to maximize uptake and expand development
- G1 partner to commercialize ex-US
- G1 intends to maintain a significant US role

Commercial team: significant oncology launch experience (XTANDI, Tagrisso, Tecentriq, Femara)

G1T48 and lerociclib: >350,000 1L and adjuvant BC patients

Global HR+/HER2- Breast Cancer Treated Incident Patients (G7)*



Duration**	14 months	33 months	60 months	25 months	60 months

Adjuvant use: long treatment duration requires well tolerated profile

*Source: Secondary epi sources, 2027 estimates
**Duration estimates based on similar trial results in the same or similar patient populations as planned trials

Q&A

Dr. Malik, Mr. Demaree & Dr. Velleca

Upcoming Catalysts and Closing Remarks

Mark Velleca, M.D., Ph.D.
Chief Executive Officer

Catalysts across all programs in 2019/2020

	INDICATION/COMBO	4Q19	1H20	2H20
trilaciclib IV - CDK4/6i	1st-line SCLC (+ etop/carbo)	Begin rolling NDA submission for SCLC	Complete NDA submission for SCLC	MAA filing for SCLC
	1st-line SCLC (+ etop/carbo/Tecentriq)			
	2nd/3rd-line SCLC (+ topotecan)			
	Metastatic TNBC (+ gem/carbo)			Initiate Phase 3 TNBC trial
	Metastatic CRC (5-FU regimens)			Initiate Phase 3 mCRC trial
lerociclib Oral - CDK4/6i	ER+, HER2- BC (+ Faslodex)	Present additional Phase 1b/2a data		Initiate Phase 3 BC trial
	EGFRm NSCLC (+ Tagrisso)			
G1T48 Oral - SERD	ER+, HER2- BC			Initiate Phase 3 CDK4/6i combination trial + Present additional data

Well funded with $325M cash at end of 2Q19; anticipate 2019 YE cash of $260-270M

Lisa Carey, M.D., FASCO

Chief of Hematology/Oncology and Physician-in-Chief, N.C. Cancer Hospital

Associate Director of Clinical Sciences, Lineberger Comprehensive Cancer Center

Lisa A. Carey, M.D., FASCO is the Richardson and Marilyn Jacobs Preyer Distinguished Professor in Breast Cancer Research in the Department of Medicine at the University of North Carolina (UNC). She graduated from Wellesley College, then received her medical degree from the Johns Hopkins University School of Medicine where she remained for her residency in Internal Medicine followed by a fellowship in Medical Oncology and an advanced degree in Clinical Investigations. Dr. Carey joined the UNC faculty and Lineberger Comprehensive Cancer Center in 1998. Currently she is the Chief of the Division of Hematology and Oncology and Physician-in-Chief of the North Carolina Cancer Hospital. In addition, she has a role at Lineberger Comprehensive Cancer Center as the Associate Director for Clinical Sciences.

Dr. Carey has a longstanding research interest in the clinical application of laboratory findings in breast cancer, with a particular interest in the clinical implications of different molecular subtypes of breast cancer. She designs and leads clinical trials of novel drugs and approaches, and is a close collaborator with several laboratory investigators and epidemiologists. Dr. Carey has served in many roles for the American Society of Clinical Oncology (ASCO), the American Association for Cancer Research (AACR) and the NCI. She was awarded the Doris Duke Clinician Scientist Award in 1999, a Career Development Award from the National Cancer Institute (NCI) in 2000, was inducted into the Johns Hopkins Society of Scholars in 2008, was awarded the NCI Director's Service Award in 2011, and was named co-chair of the Alliance National Cooperative Group Breast Committee in 2016. Dr. Carey was honored to become a member of the Komen Scientific Advisory Board as of April 2018 and in June 2019 earned the distinction of Fellow of the American Society of Clinical Oncology (FASCO).

G1 THERAPEUTICS

INVESTOR CONTACT:

Jeff Macdonald

919.907.1944

jmacdonald@g1therapeutics.com

www.g1therapeutics.com

Nasdaq: GTHX