BIOVICA

Nye værktøjer til monitorering af brystcancer

Helle Fisker – Commercial VP Europe

MSc Biotechnology, Immunology (DTU)

Executive MBA (CBS)

Commercial Experience

- Launches
  - +30 treatments and vaccines in Denmark
  - 350 medical device products worldwide
- Marketing and sales:
  - Pharma (Lilly, GSK)
  - Diagnostics (Dako, Leica)
  - Start Ups (ViroGates, Visiopharm)
- Diagnostics market industry consultant
  - Sysmex
  - AGFA Healthcare
  - Diaceutics
  - Tieto …

Lives in Rungsted, Denmark – husband and a daughter

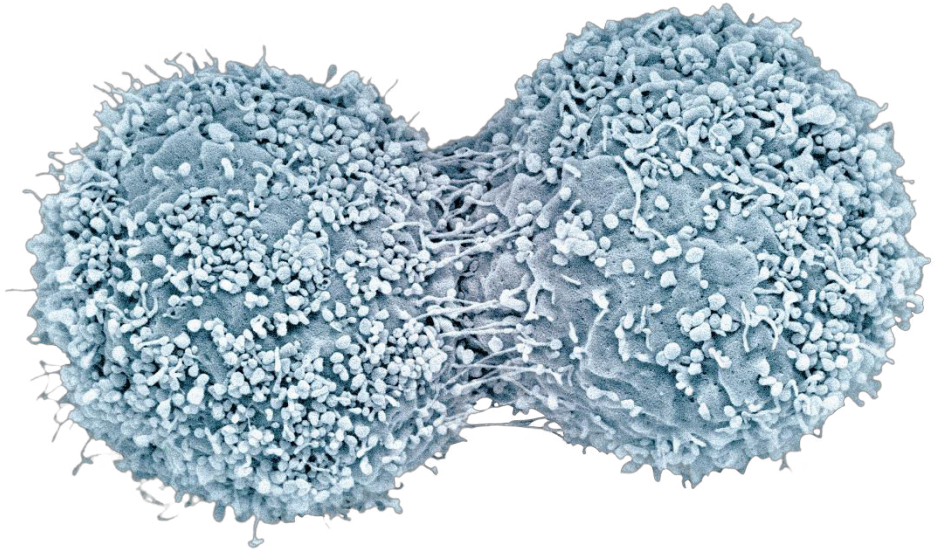
Future trends in oncology and diagnostics

- Personalized Therapy
- Easy to use
- Cellular level
- IVD-R
- Automation/Digitalization

On the Cellular level

Cell division activity is central tumor information

- Activity on the cellular level
- Measured on the protein level
- Can help guide personalized treatment choices in adjunction to other biomarkers



Can you measure cellular activity for all solid tumors in the blood?

- In a simple blood test Thymidine Kinase Activity (Tka) can be measured
- Metastatic tumours – breast, HR+, HER2-
- Automated
- Time to result – 1 day
- It is a measure of activity level (DuA)

TK - Scientific Rationale for Efficacy Evaluation of Cell Cycle Regulating Drugs

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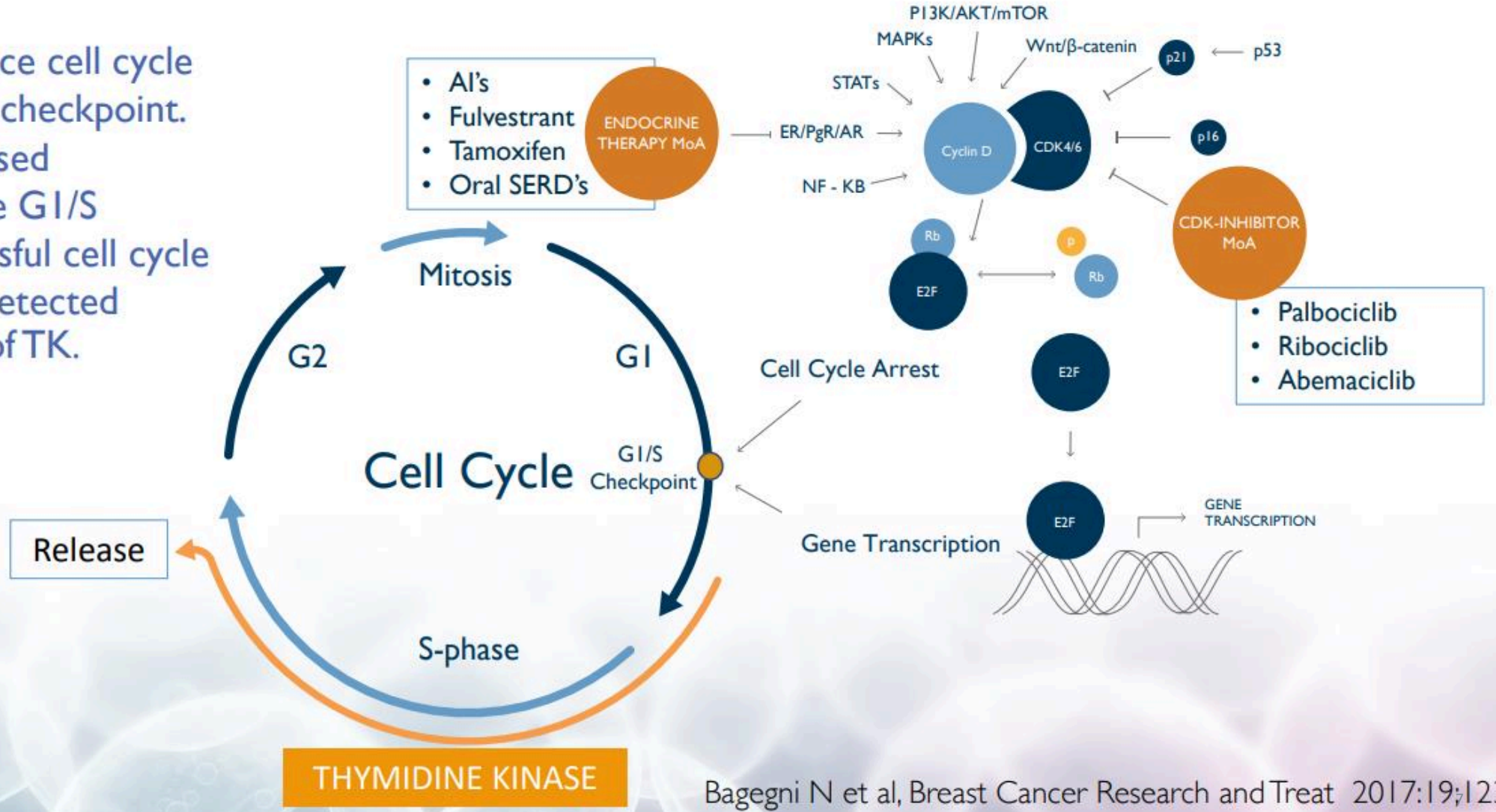
Specific drugs induce cell cycle arrest at the G1/S checkpoint. Since TK is expressed downstream of the G1/S checkpoint, successful cell cycle inhibition can be detected as changed levels of TK.



TK=Thymidine Kinase

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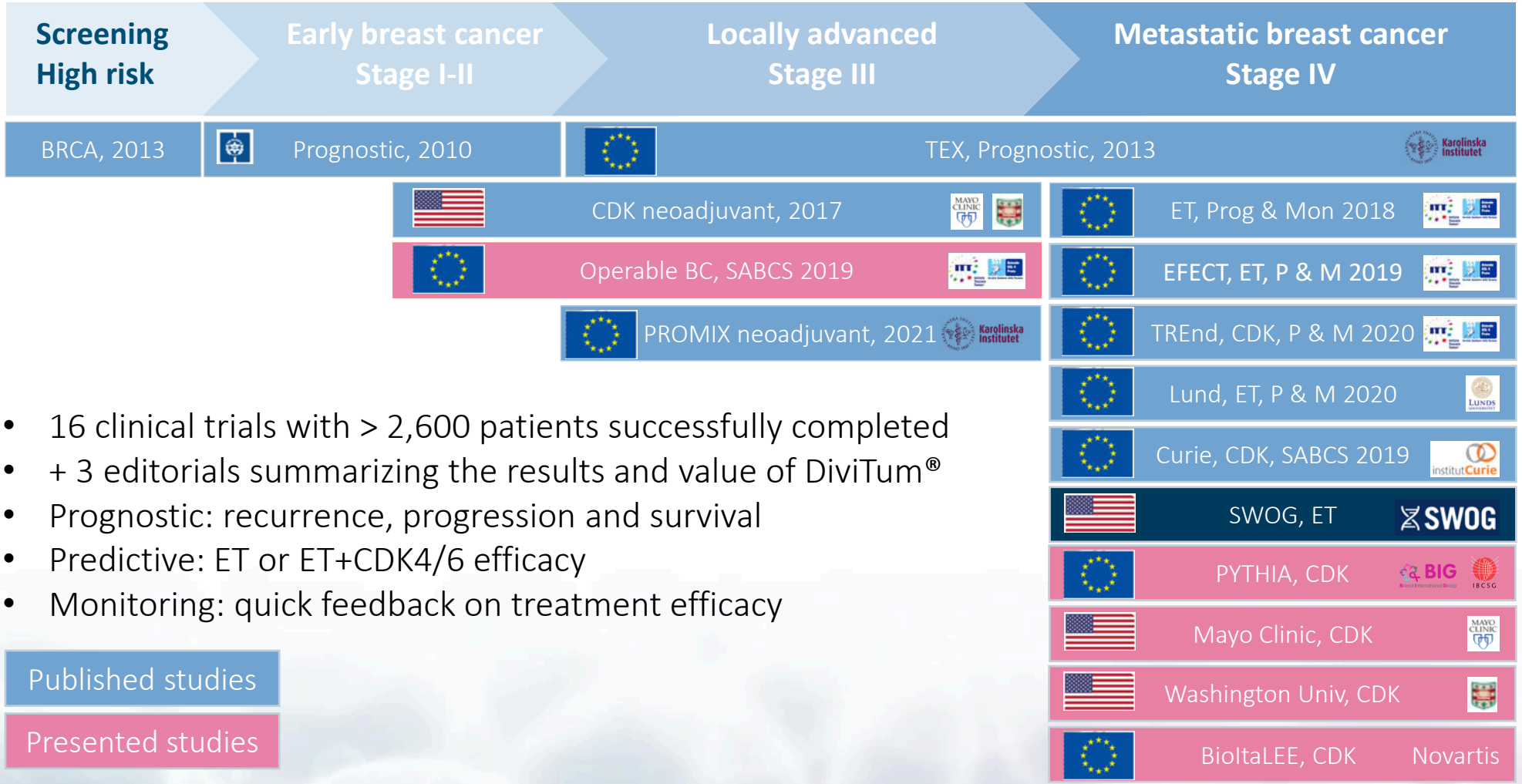
Bagegni N et al, Breast Cancer Research and Treat 2017:19;123

DiviTum® Tka – Finalized Breast Cancer Studies



- 16 clinical trials with > 2,600 patients successfully completed
- + 3 editorials summarizing the results and value of DiviTum®
- Prognostic: recurrence, progression and survival
- Predictive: ET or ET+CDK4/6 efficacy
- Monitoring: quick feedback on treatment efficacy

Key Opinion Leader Collaborators
– key success factor for clinical acceptance

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Matthew P. Goetz
M.D
Mayo Clinic

Daniel F. Hayes
M.D, Professor
University of Michigan
Ex. ASCO President
SWOG Transl. Med.

Vered Stearns
M.D & Professor
Johns Hopkins

Geoffrey Shapiro
M.D, Ph.D
Dana Farber

Matthew J. Ellis
M.D, Professor
Baylor Collage

William Gradishar
M.D, Professor
Northwestern Med.

Richard Finn
M.D, Ass. Professor
UCLA

Cynthia X. Ma
M.D, Professor
Washington University

Angelo Di Leo
M.D, Ph.D
Hospital of Prato
IBCSG Exec. Committee
BIG against BC Exec Board
ESMO Lifetime Achievement

Martine J. Piccart
M.D, Professor
Université Libre de Bruxelles
Founder Big against BC
Ex. ESMO President

Jonas Bergh
M.D, Professor
Karolinska Institutet
ESMO BC Award
Ex Chairman SweBCG
EMA Advisory Group
Member Nobel Assembly

Luca Malorni
M.D, Ass. Professor
Hospital of Prato
Baylor Collage

Thomas Hatschek
M.D, PhD
Karolinska Institutet

Samuel Rotstein
M.D, PhD
Karolinska Sjukhuset

Henrik Lindman
M.D, Ass. Professor
Uppsala Universitet
Vice Chairman SweBCG

Sacha Howell
M.D, PhD
Senior Lecturer and Honorary
Consultant in Medical Oncology
The Christie NHS Foundation Trust

The MBC HR+, HER2- patient can feel safe the next 30 days

DiviTum®TKa blood test

- Assures patients that their tumor will not progress within the next 30 days
- Indicates the current treatment is working
- Requires min. 1 mL venous blood per test – no extra radiation for the patient

Progression within 30 days during treatment

	n	Cases	Specificity	NPV
	1164	63	81%	97%

Data on file from SWOG S0226 Trial, submitted to the FDA 2021

Is availability of radiologist an issue?

Can a blood-based biomarker test complement Radiology Imaging?

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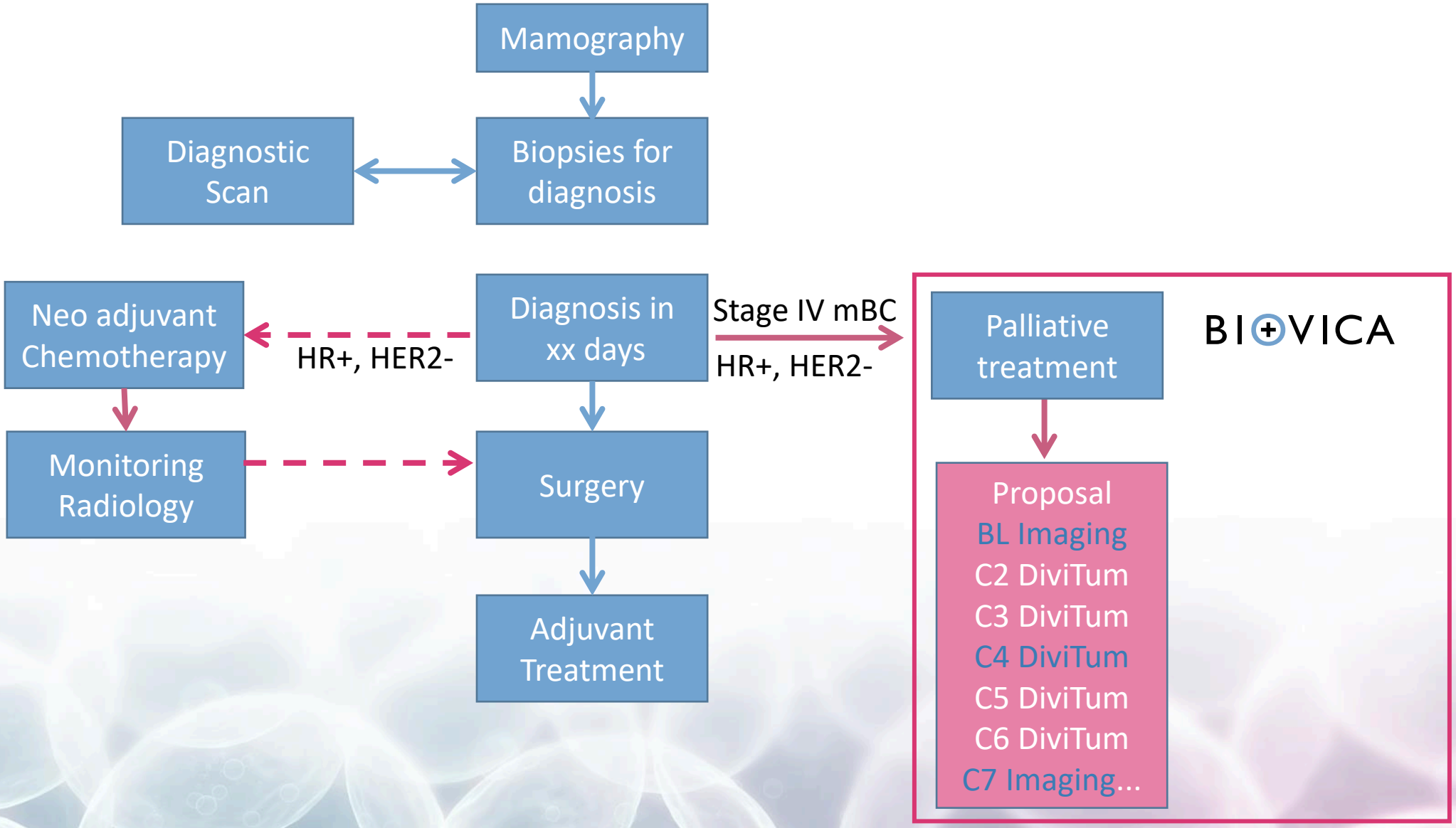


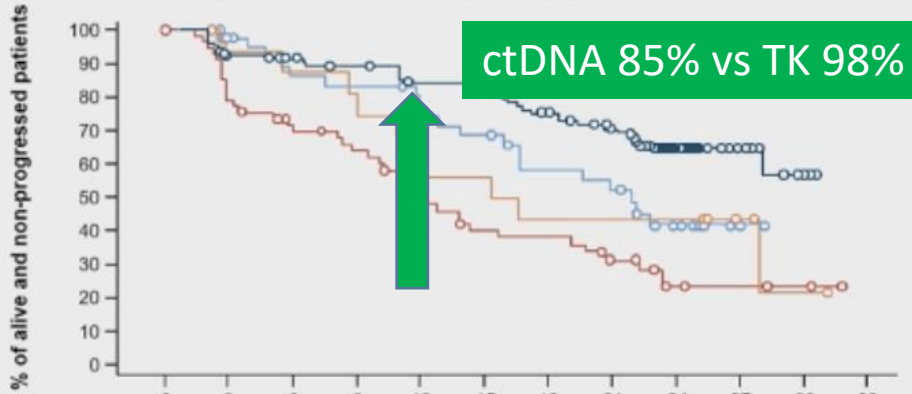
DiviTum®Tka vs. ctDNA – SABCS 2021

San Antonio Breast Cancer Symposium®, December 7–10, 2021

PFS by combining detection of mutation at baseline and D15

VAF status	mPFS (95% CI)
WT at BL, WT at D15 (n=115)	NE (28.09,NE)
WT at BL, Mut at D15 (n=19)	15.93 (9.03,NE)
Mut at BL, WT at D15 (n=44)	21.85 (15.93,NE)
Mut at BL, Mut at D15 (n=60)	12.32 (8.80,19.09)

Kaplan-Meier Curve of PFS (months) by status at BL and D15



ctDNA 85% vs TK 98%

Pre-treatment baseline (mutation vs no mutation) and D15 (mutation vs no mutation) ctDNA assessment provide independent information

	HR (95% CI)*	P value
Status at screening *WT vs Mut*	0.57 (0.35,0.91)	0.0194
Status at D15 *Not Mut at D15 vs Mut at D15*	0.53 (0.33,0.86)	0.0097

Cox models evaluating PFS by presence or absence of mutation at baseline and C1D15 adjusted for main clinical variables

*Analysis on patients with valid liquid biopsy sample at screening and at D15 (n=224).
BL, baseline; CI, confidence interval; ctDNA, circulating tumor DNA; D, day; HR, hazard ratio; mPFS, median progression-free survival; Mut, mutated; NE, not estimable; VAF, variant allele frequency; WT, wild type.

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CDK4/6 Inhibitors in Breast Cancer

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- Almost ALL HR+ mBC patients will be prescribed a CDK4/6 inhibitor at some point during their course of therapy
- If given in the first line metastatic setting, most patients will remain on a CDK4/6i based therapy for 2-3^{+} years
- Other than ER/PR positivity, there is no biomarker that can predict benefit for a CDK4/6 inhibitor
- The identification of a biomarker of response and resistance to CDK4/6 inhibition remains an important yet unmet need in oncology.
- Biovica has very strong data suggesting that DiviTum®TKa can serve as a biomarker of CDK4/6i response

BioItaLEE Data Shows 3 Patterns of TKa levels

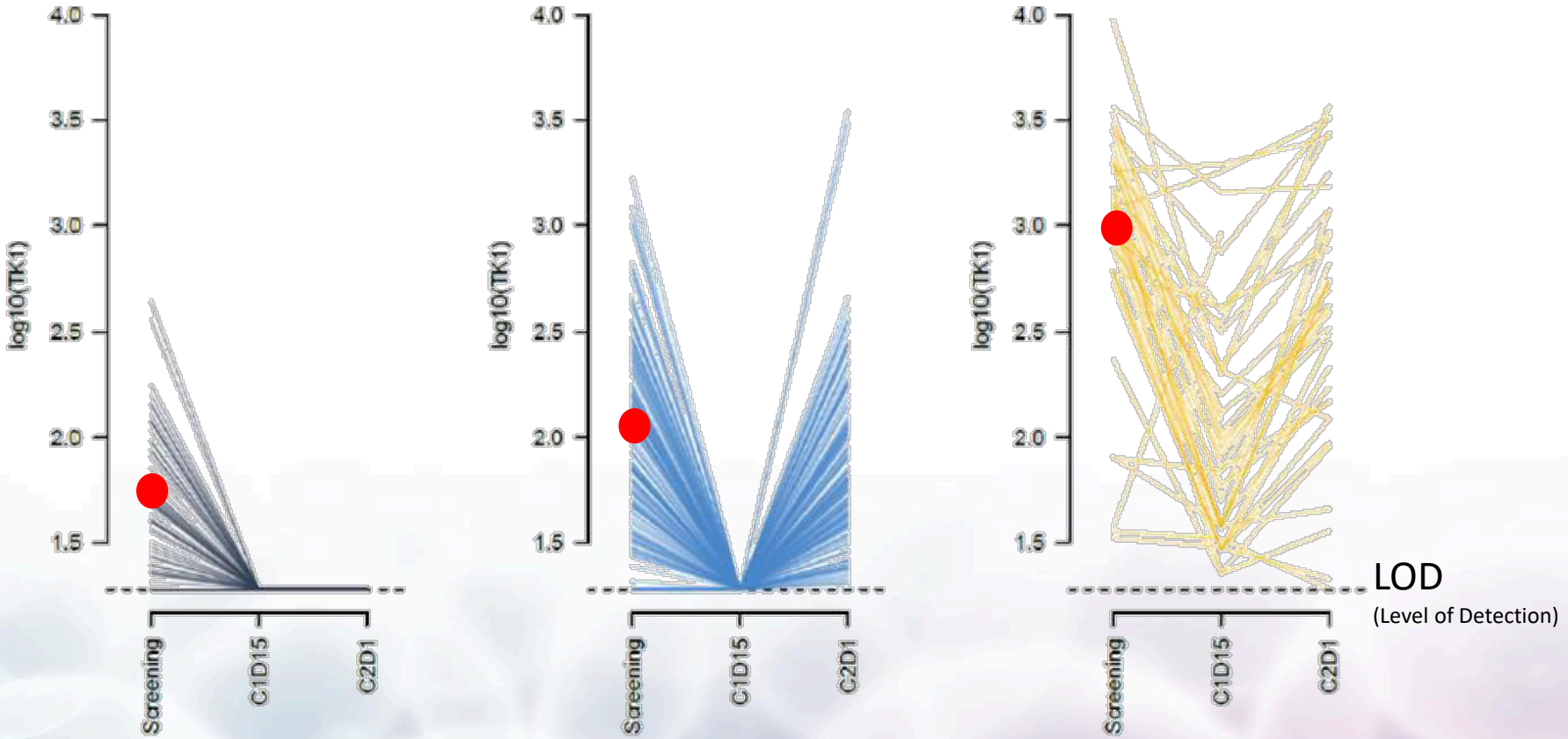
- 287 HR+ Her2- mBC patients
- 1st line therapy with ribociclib + letrozole
- TKa analyzed at BL, C1D15, C2D1, the on-treatment TKa values were used to identify patterns

● = median BL TKa

PATTERN 1 (n=62)
TKa<LOD atC1D15 and at C2D1

PATTERN 2 (n=135)
TKa<LOD at C1D15 and >LOD at C2D1

PATTERN 3 (n=37)
TKa>LOD at C1D15



26% **58%** **16%**

Malorni et al, ESMO 2021 poster 292P

TKa Patterns Correlate with Patient Outcome

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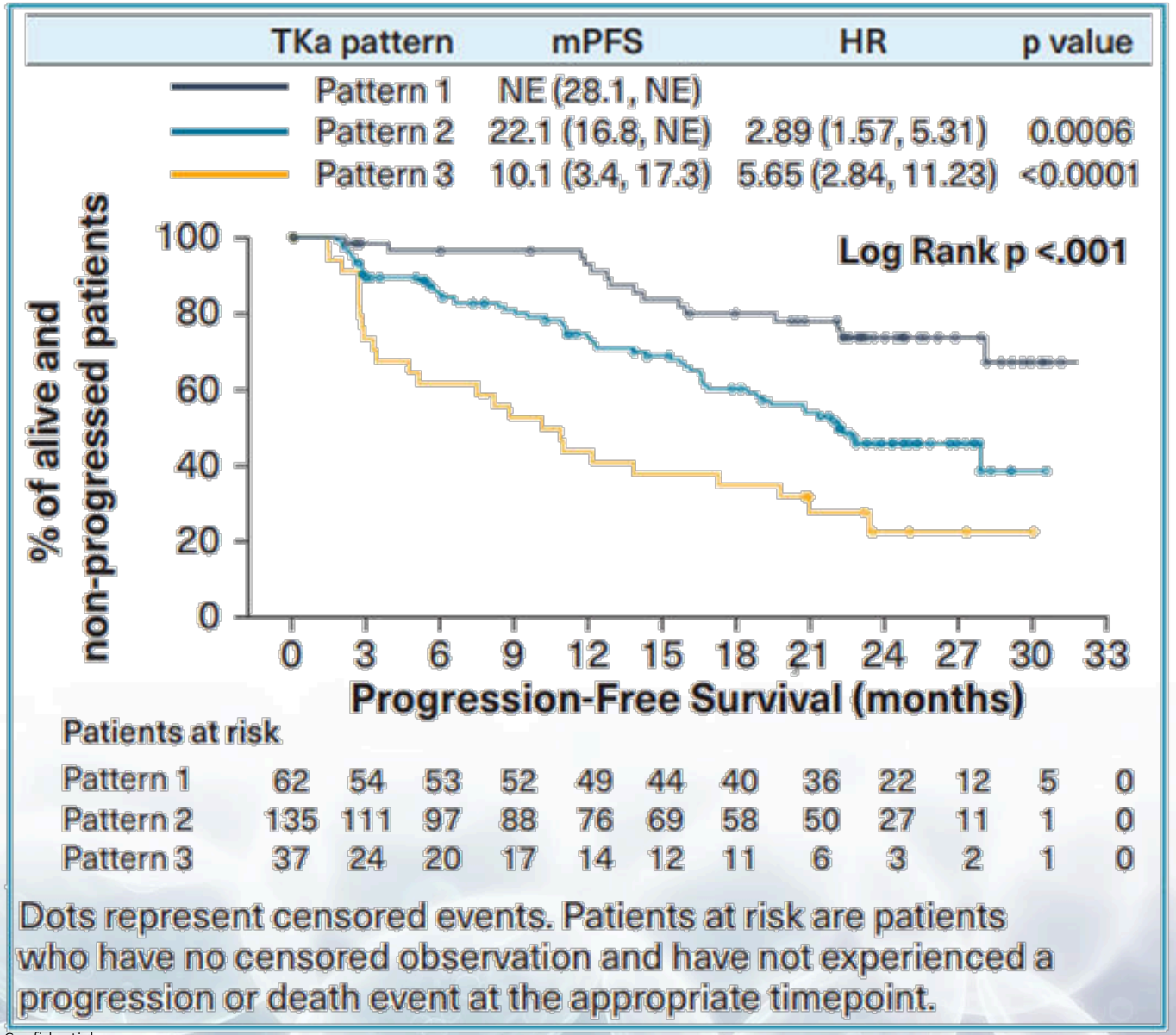


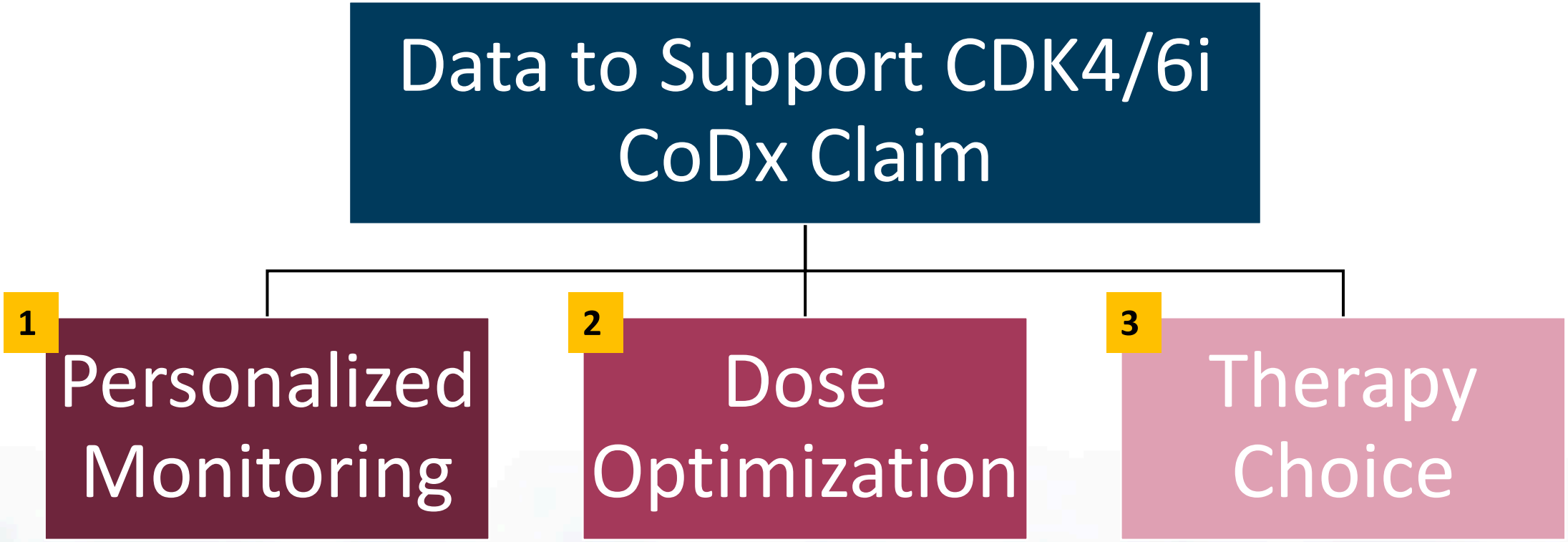
Pattern 1: TKa <LOD at D15 and C2D1

Pattern 2: TKa <LOD at D15 and >LOD at C2D1

Pattern 3: TKa >LOD at D15 and C2D1

Malorni et al, ESMO 2021 poster 292P

Highest Priority Clinical Activity



DiviTum-TKa: A Complementary Diagnostic for HR+ mBC Patients Prescribed a CDK4/6 Inhibitor

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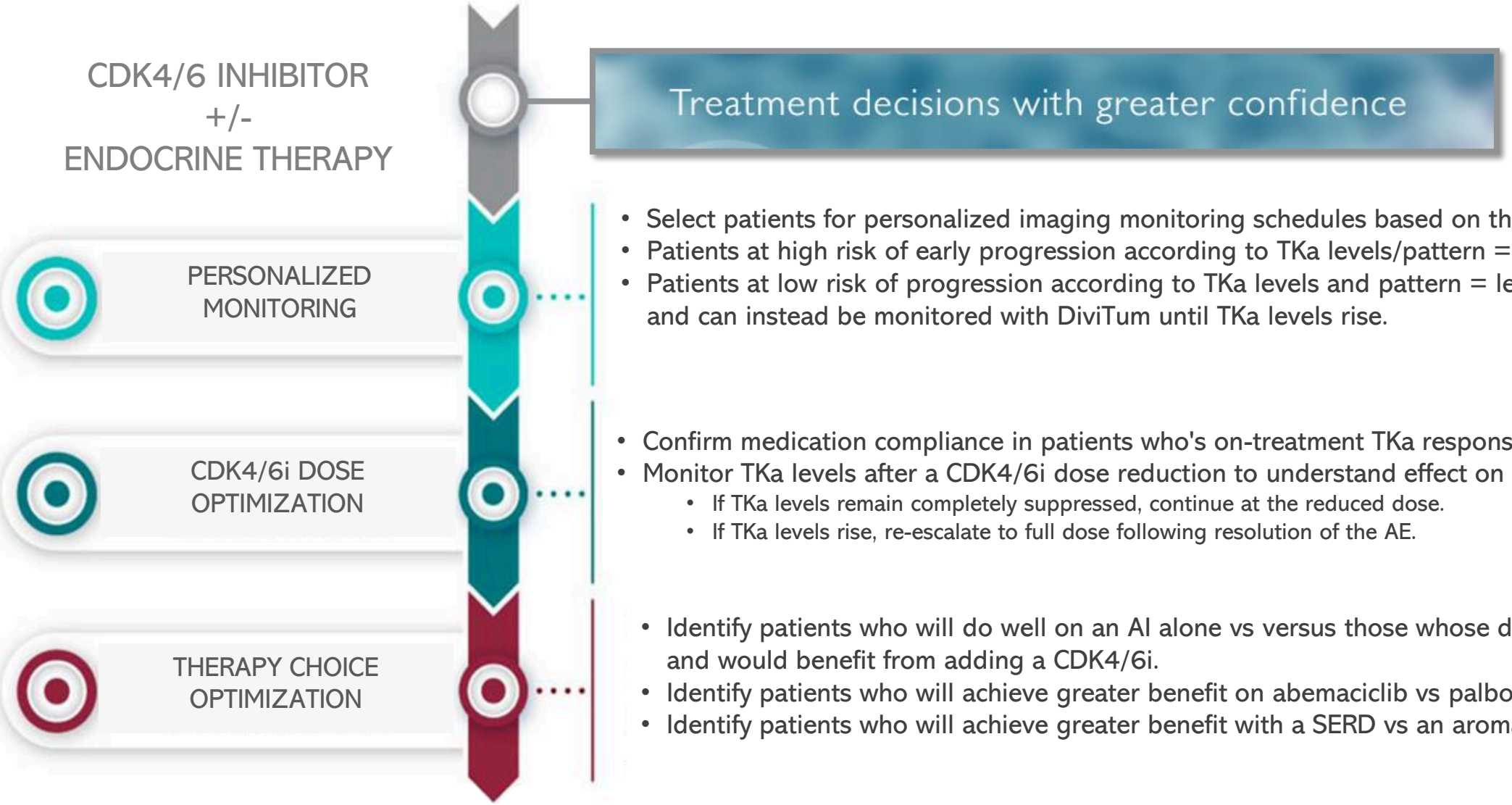


- Select patients for personalized imaging monitoring schedules based on their TKa profiles.
- Patients at high risk of early progression according to TKa levels/pattern = closer monitoring.
- Patients at low risk of progression according to TKa levels and pattern = less frequent imaging and can instead be monitored with DiviTum until TKa levels rise.

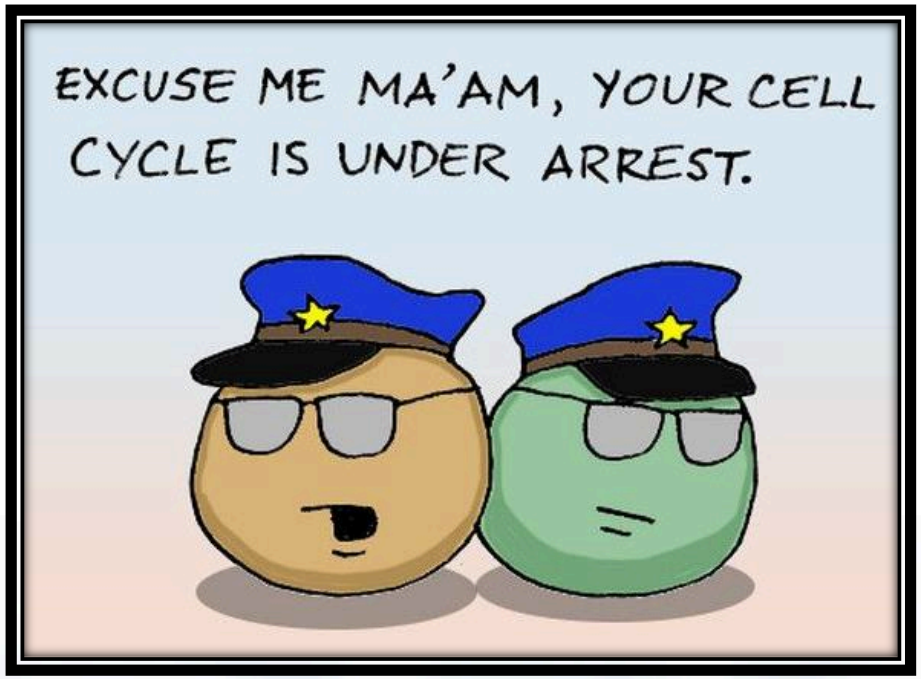
- Confirm medication compliance in patients who's on-treatment TKa response is not optimal
- Monitor TKa levels after a CDK4/6i dose reduction to understand effect on proliferation
  - If TKa levels remain completely suppressed, continue at the reduced dose.
  - If TKa levels rise, re-escalate to full dose following resolution of the AE.

- Identify patients who will do well on an AI alone vs versus those whose disease is more proliferative and would benefit from adding a CDK4/6i.
- Identify patients who will achieve greater benefit on abemaciclib vs palbo/ribociclib
- Identify patients who will achieve greater benefit with a SERD vs an aromatase inhibitor

What does DiviTum® Tka mean for the patient?

- Can be used for MBC, HR+, HER2- monitoring
- Monthly vs. quarterly with Radiology
- 1-3 mL venous blood is sufficient

DiviTum® Tka tells you how your patient *IS* responding to treatment



- Thymidine kinase activity is directly linked to cell cycle progression
- DiviTum®TKa provides ON-TREATMENT readouts of thymidine kinase activity


Thank You!