INSTITUT JULES BORDET

ONCODISTINCT NETWORK

BSMO

12th Belgian Symposium on the Integration of Molecular Biology Advances into Oncology Clinical Practice and Post-MASCC

Liquid biopsy: ready for clinical practice?

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FNRS

SCIENTIA VINCERE TENEBRAS ULB

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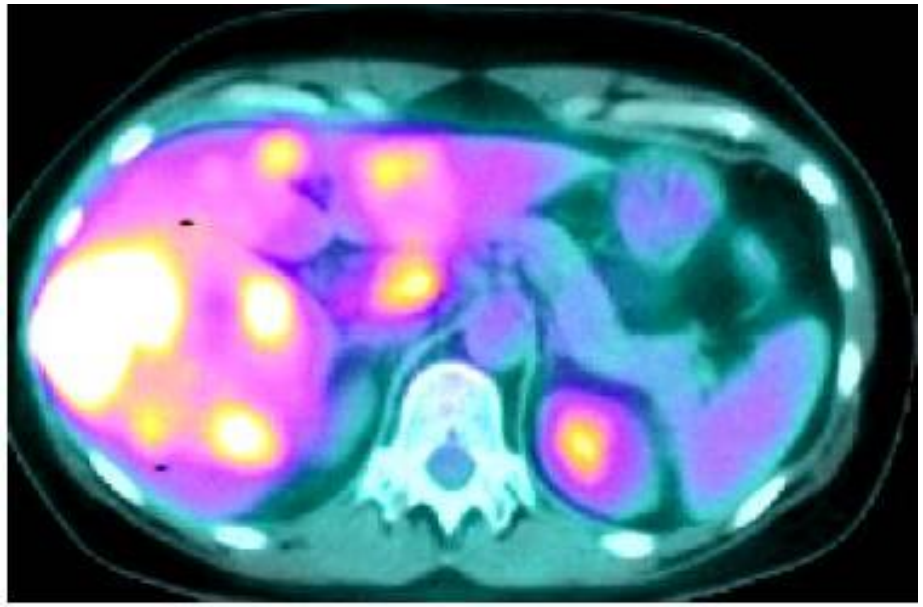
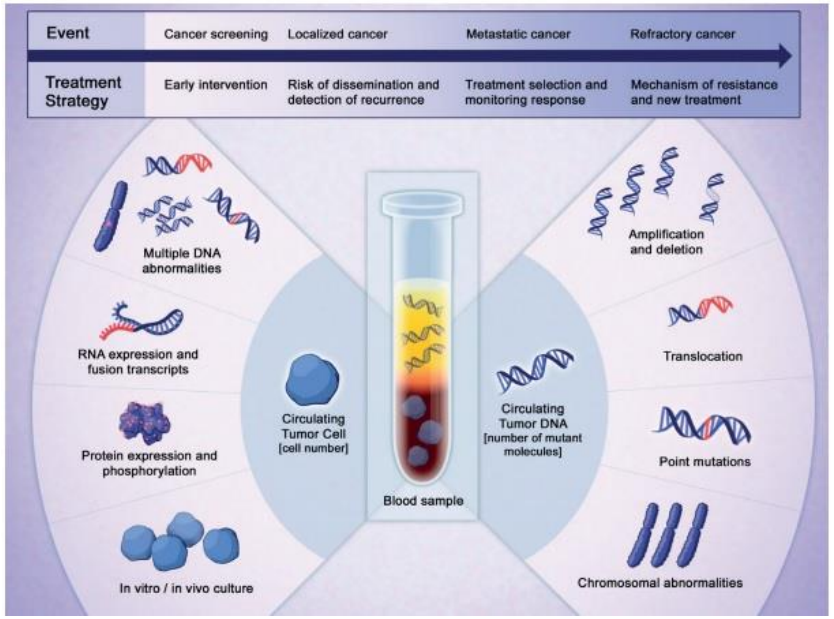
Imaging and liquid biopsy: complementary tools

Anatomical & Functional information

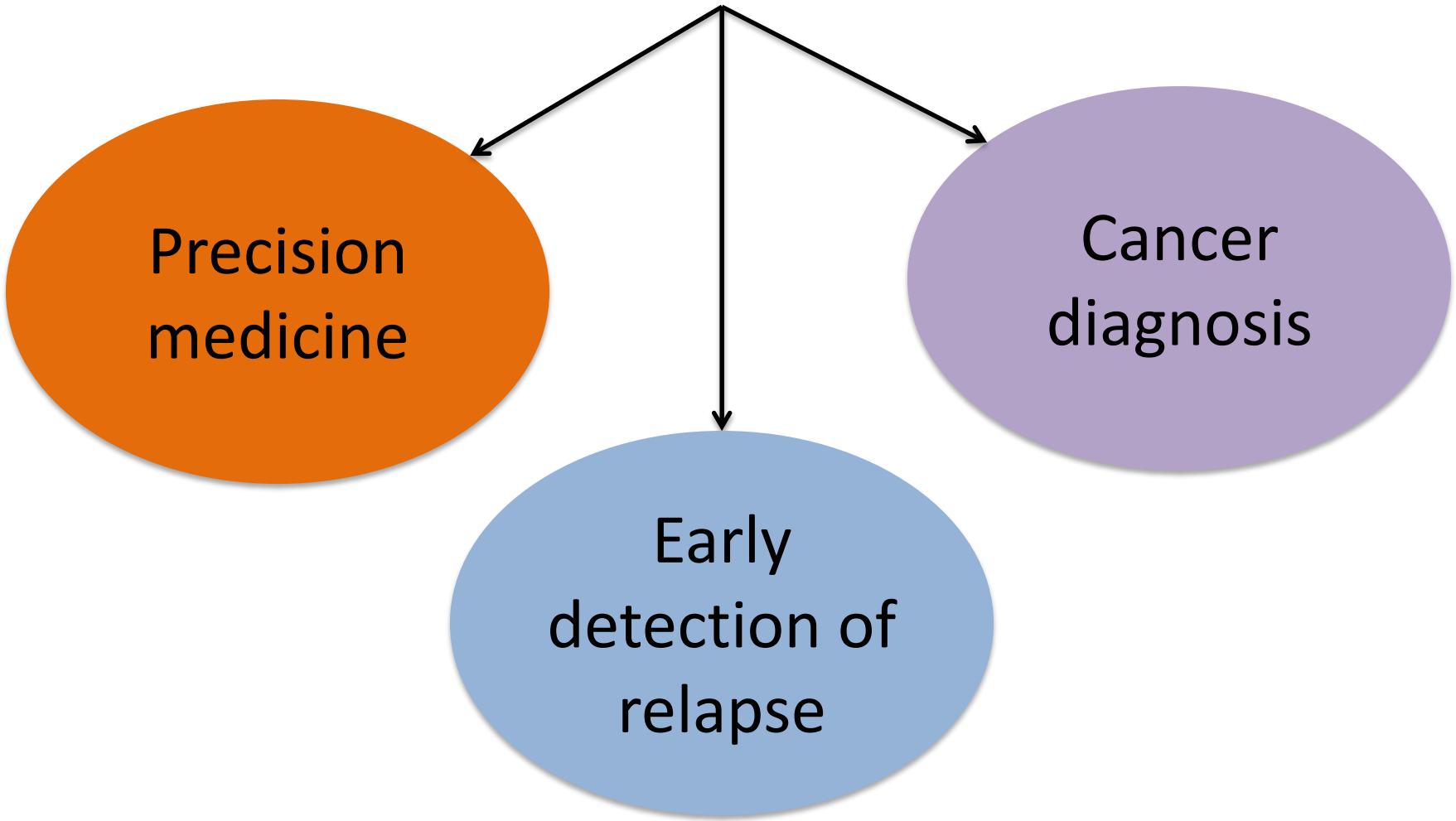


Genomic & Phenotypic information

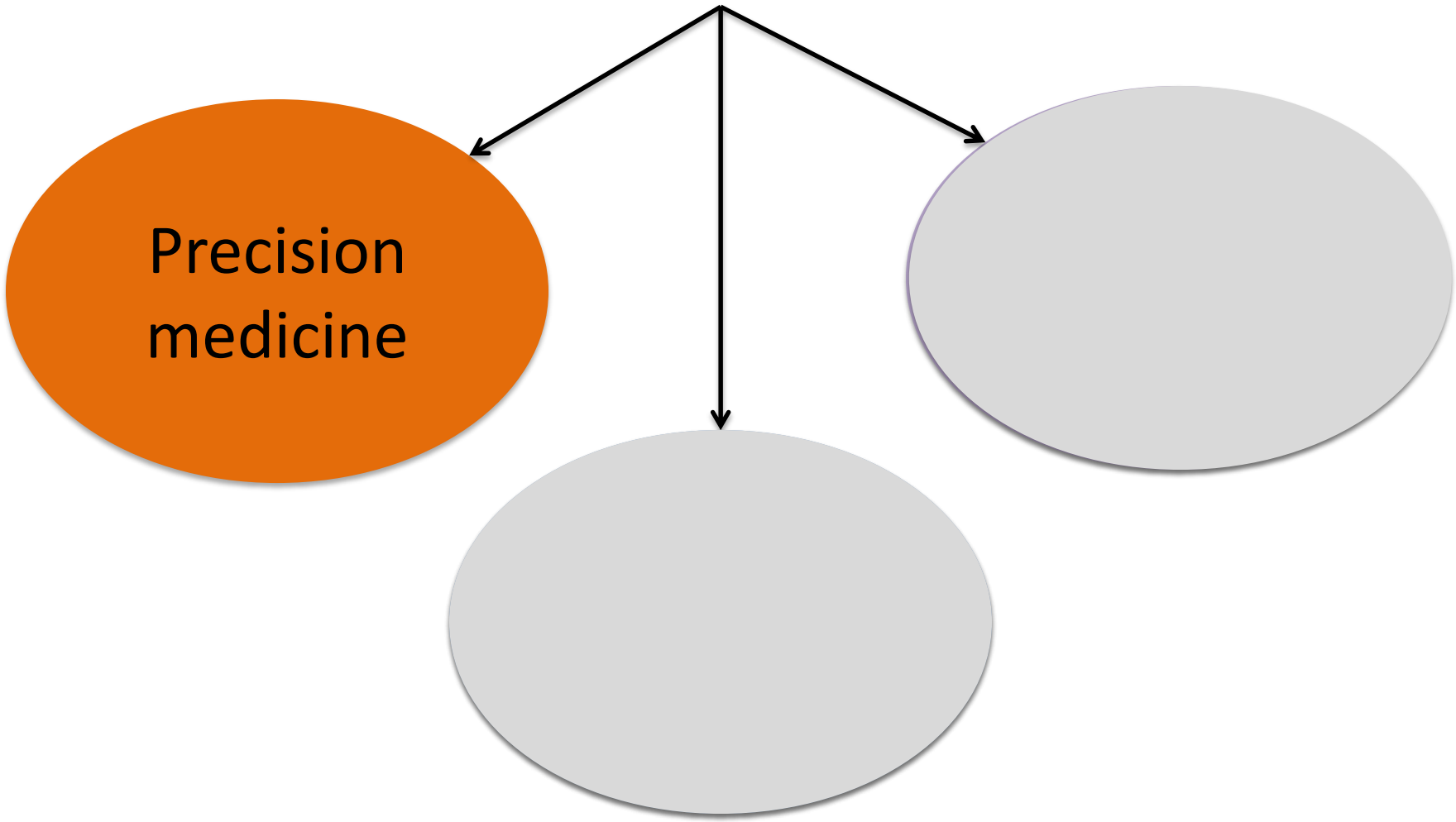


Precicion Medicine

Outline


Precision medicine
Cancer diagnosis
Early detection of relapse

Outline

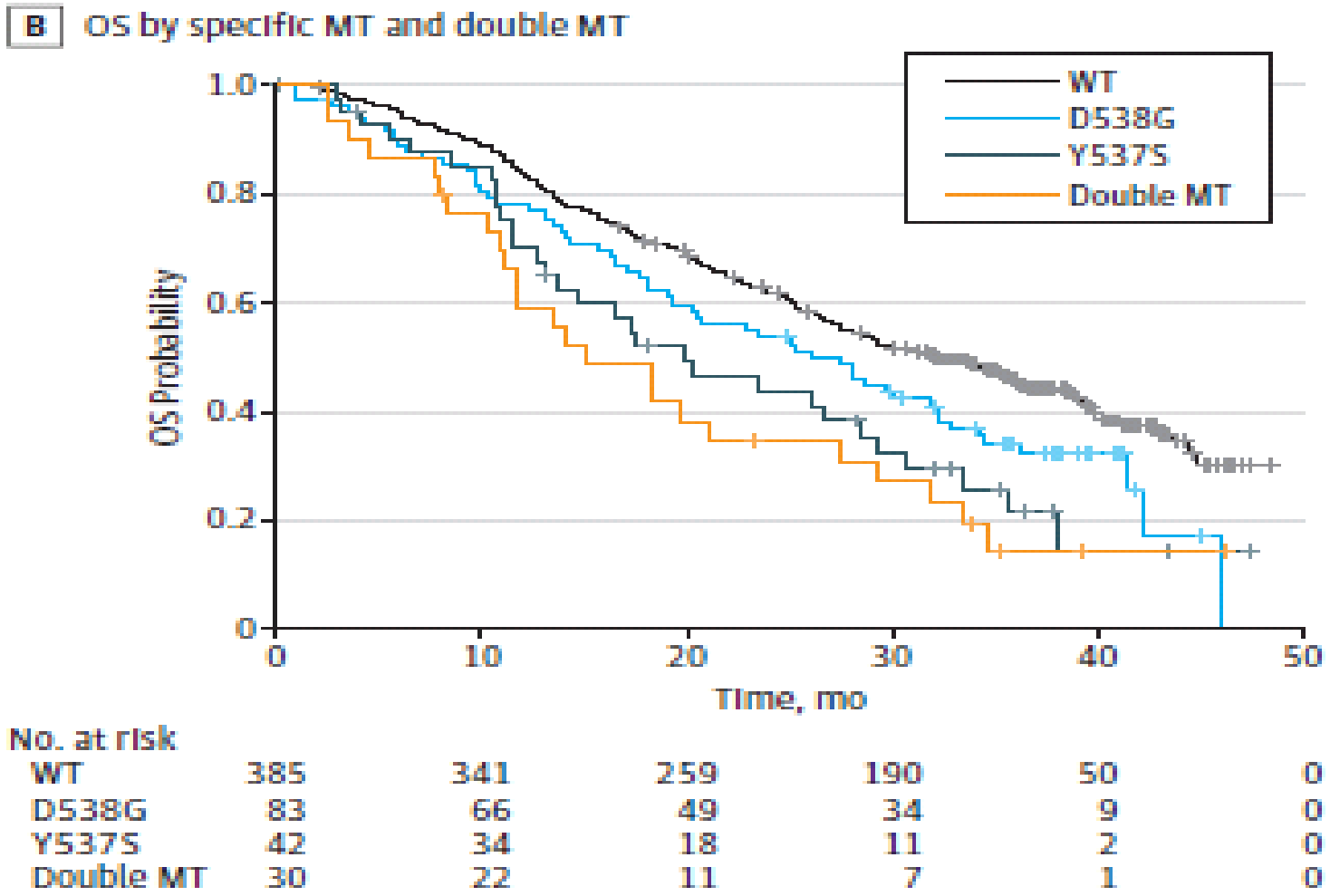


1st Liquid biopsy test approved

The **cobas**® EGFR Mutation Test v2 is a real-time PCR test for the qualitative detection of defined EGFR mutations of in NSCLC patients

Drug	FFPET	Plasma
TARCEVA® (erlotinib)	Exon 19 deletions and L858R	Exon 19 deletions and L858R
TAGRISSO™ (osimertinib)	T790M	T790M

ESR1 mutations worse OS (Bolero 2)

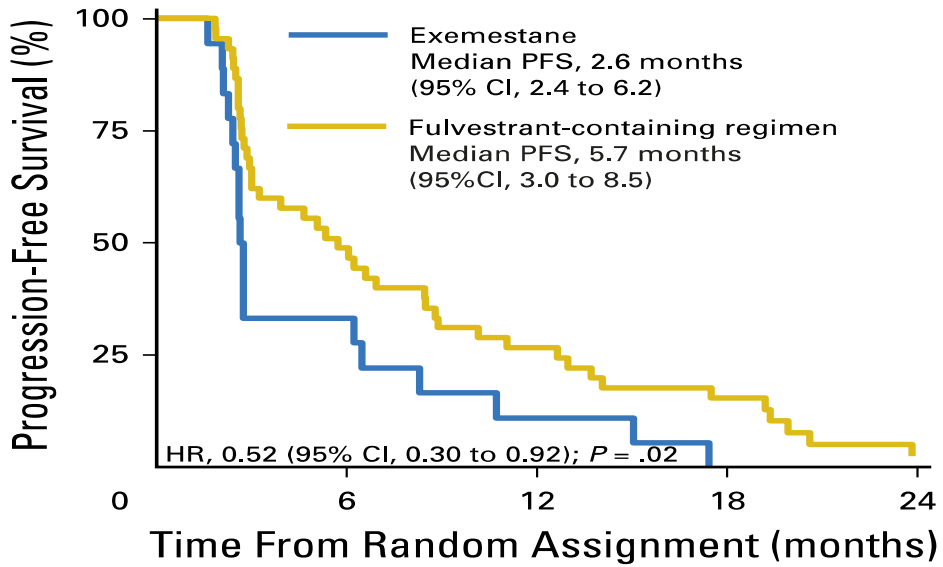


ESR1 mutations
33% post 1st line vs
11% starting 1st line

Chandarlapaty S et al, Jama Oncol 2016

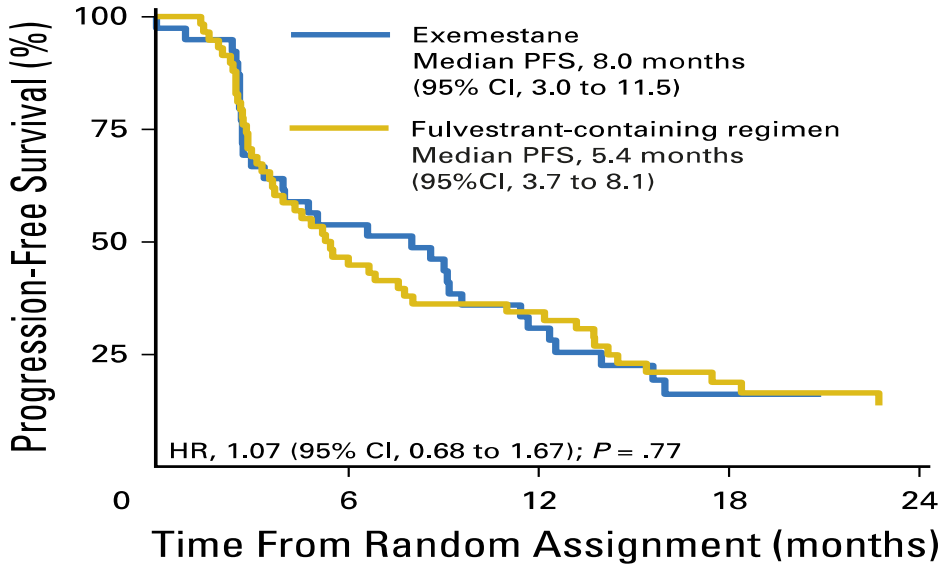
Fulvestrant better than exemestane in ESR1mut patients (Sofea)

PFS in *ESR1* mutant



No. at risk (events)									
Exemestane	18	(12)	6	(4)	2	(2)	0	(0)	0
Fulvestrant-containing	45	(23)	22	(10)	12	(5)	6	(5)	1

PFS in *ESR1* wild-type



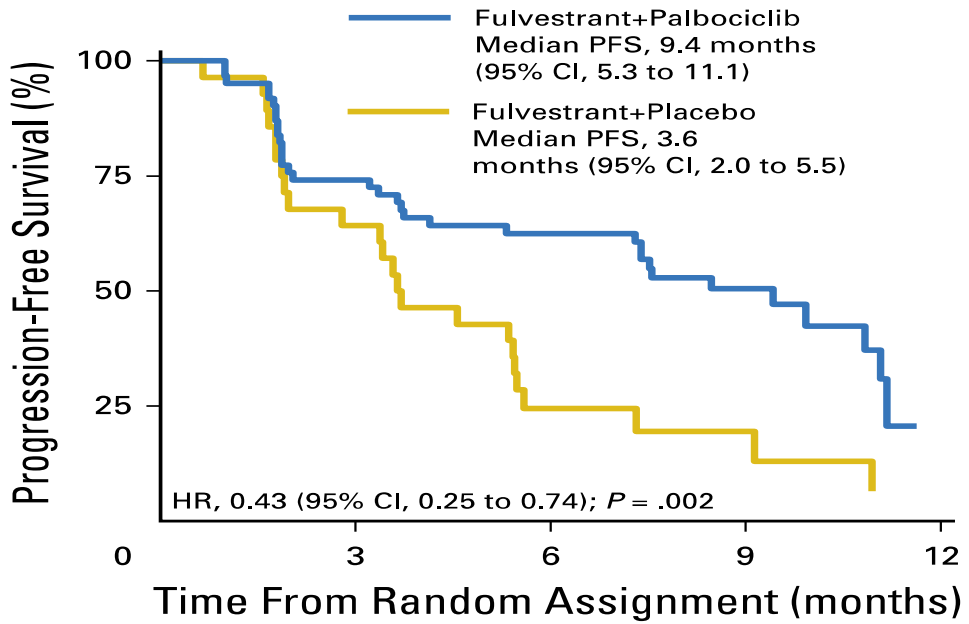
No. at risk (events)									
Exemestane	39	(18)	21	(9)	12	(5)	5	(0)	3
Fulvestrant-containing	59	(31)	27	(7)	19	(8)	8	(2)	5

Validation is needed!

Fribbens C et al, J Clin Oncol 2016

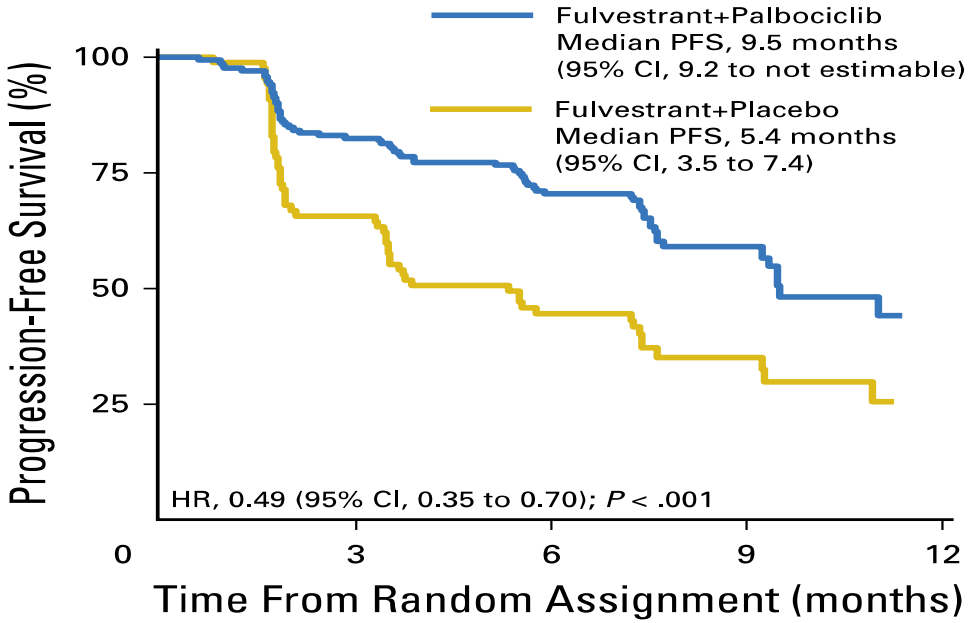
Palbo benefit irrespective of baseline *ESR1*mut status (Paloma 3)

PFS in *ESR1* mutant



No. at risk (events)									
Fulvestrant+Placebo	28	(10)	18	(11)	6	(1)	3	(2)	1
Fulvestrant+Palbociclib	63	(16)	45	(7)	36	(6)	22	(5)	0

PFS in *ESR1* wild-type

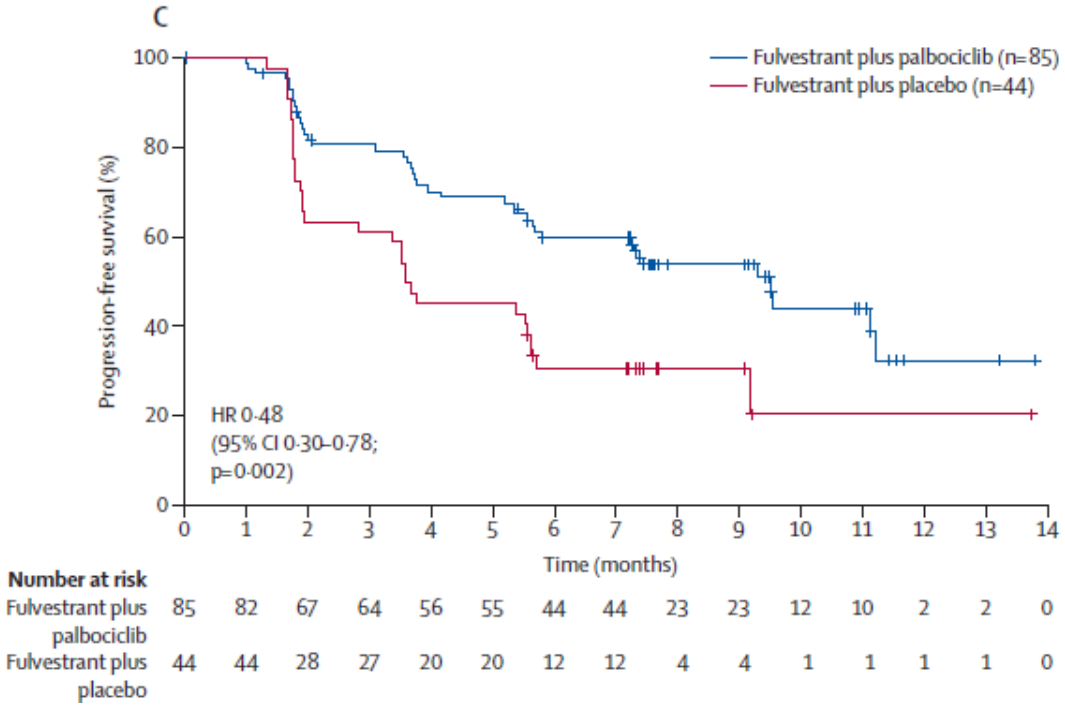


No. at risk (events)									
Fulvestrant+Placebo	92	(30)	57	(18)	35	(6)	16	(3)	0
Fulvestrant+Palbociclib	177	(30)	142	(20)	108	(13)	50	(7)	6

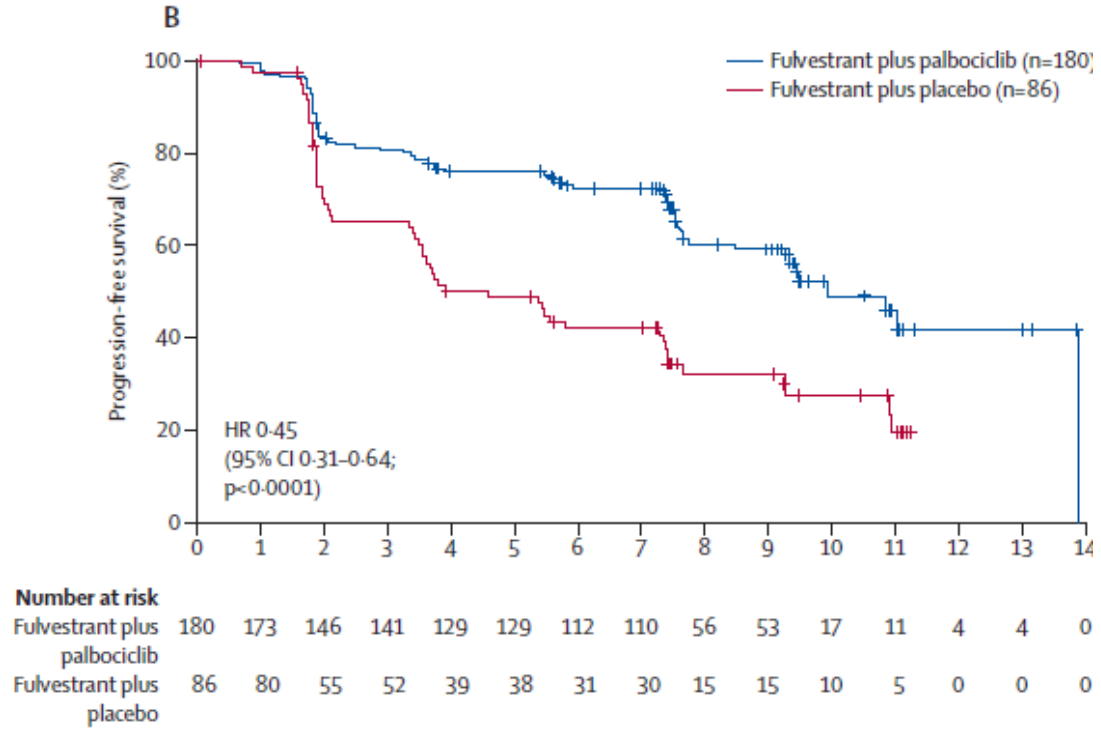
Fribbens C et al, J Clin Oncol 2016

Palbo benefit irrespective of baseline *PIK3CA*mut status (Paloma 3)

PFS in *PIK3CA* mutant



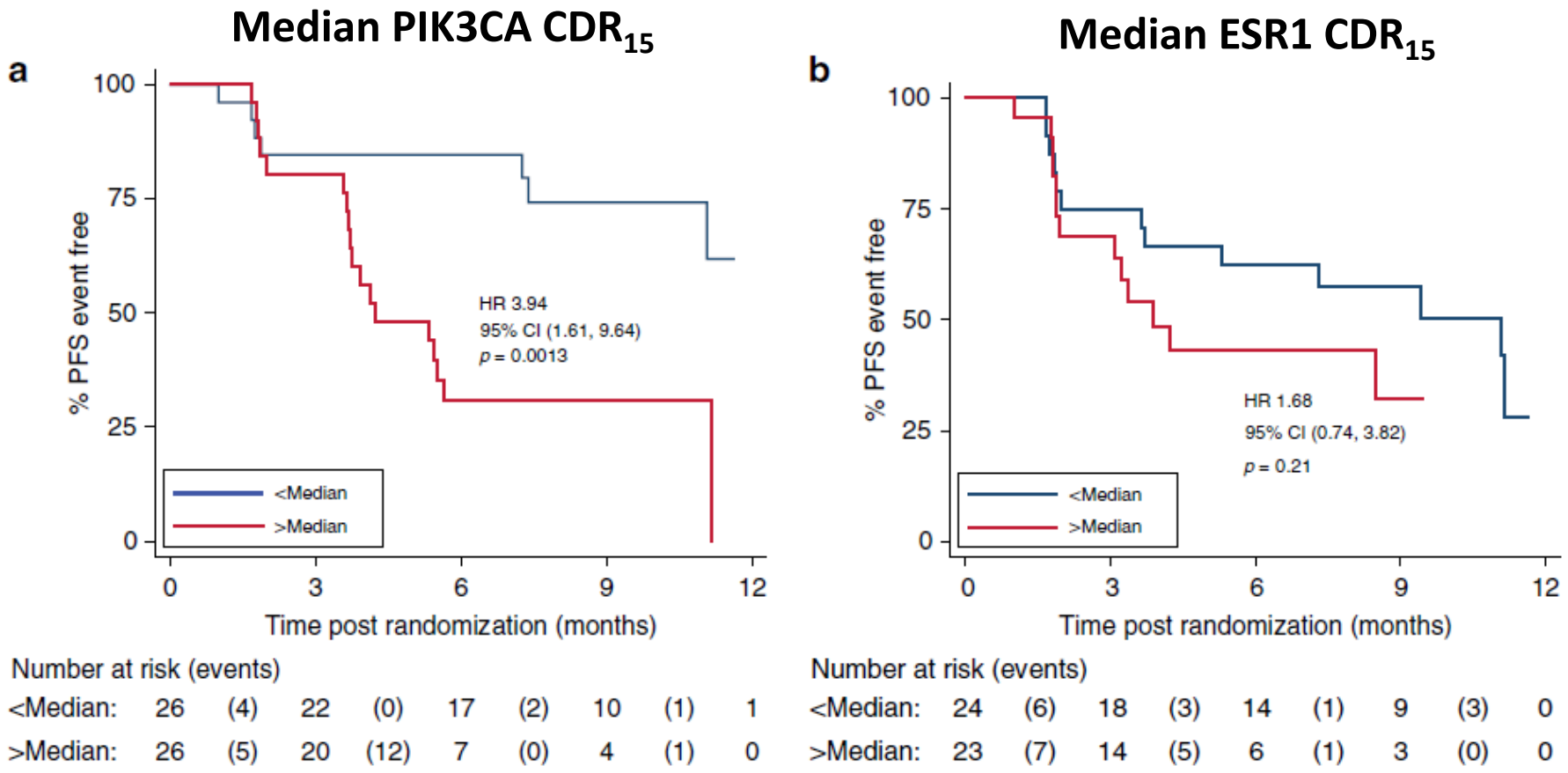
PFS in *PIK3CA* wild-type



Cristofanilli M et al, Lancet Oncol 2016

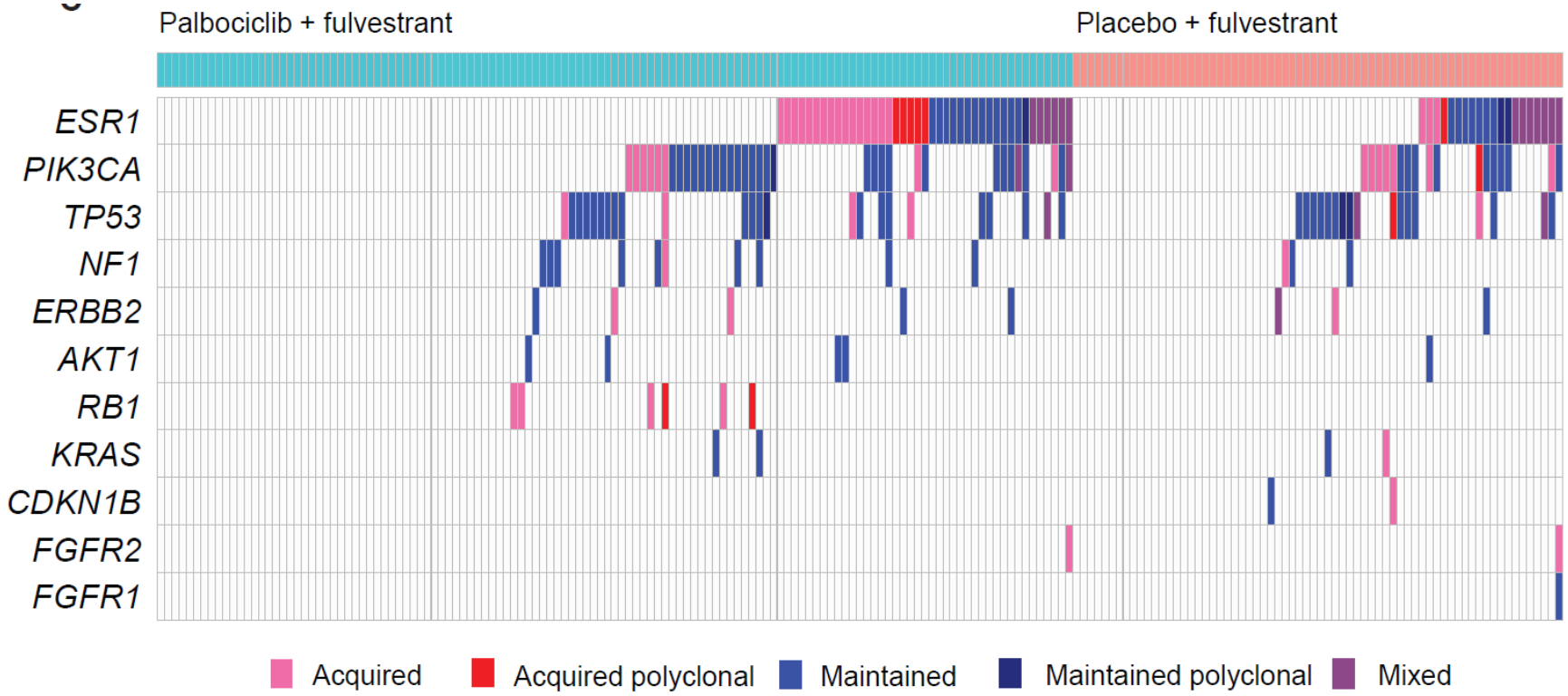
Early PIK3CA (clonal) but not ESR1 (subclonal) dynamics predict palbo benefit (Paloma 3)

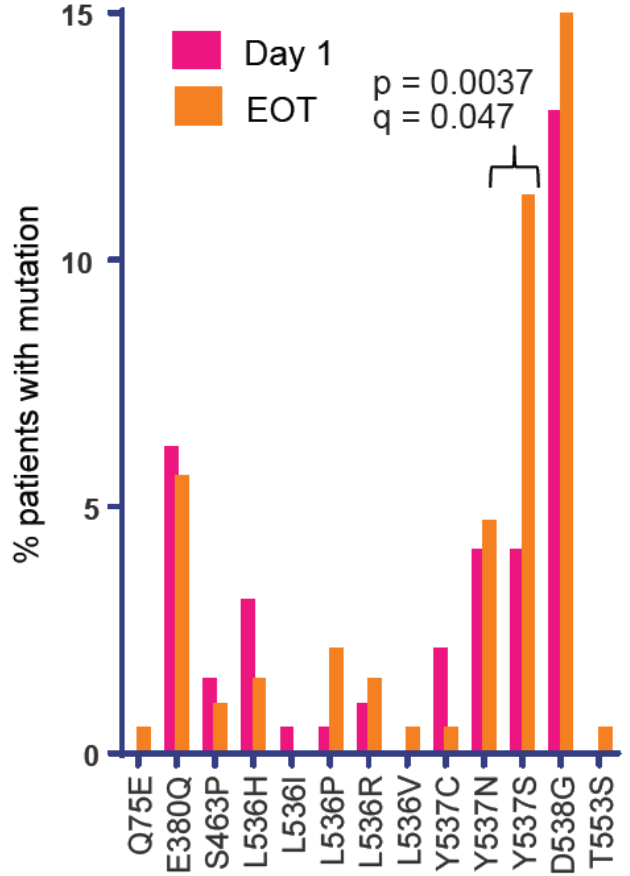
Circulating DNA ratio D15/D1 (CDR_{15}) in patients treated with fulvestrant and palbociclib



O'Leary B, et al, Nat Communications 2018

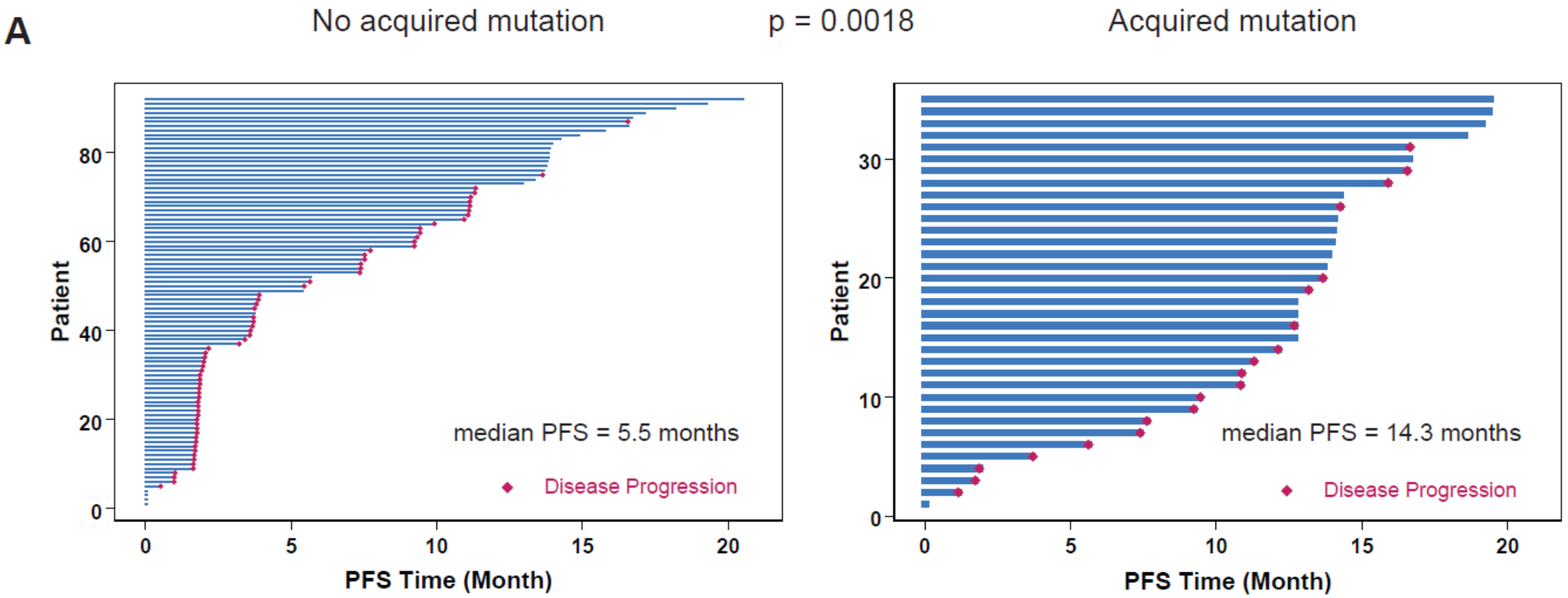
Acquired PIK3CA and ESR1 mutations (both arms) whereas acquired RB1 mutations (palbo arm)





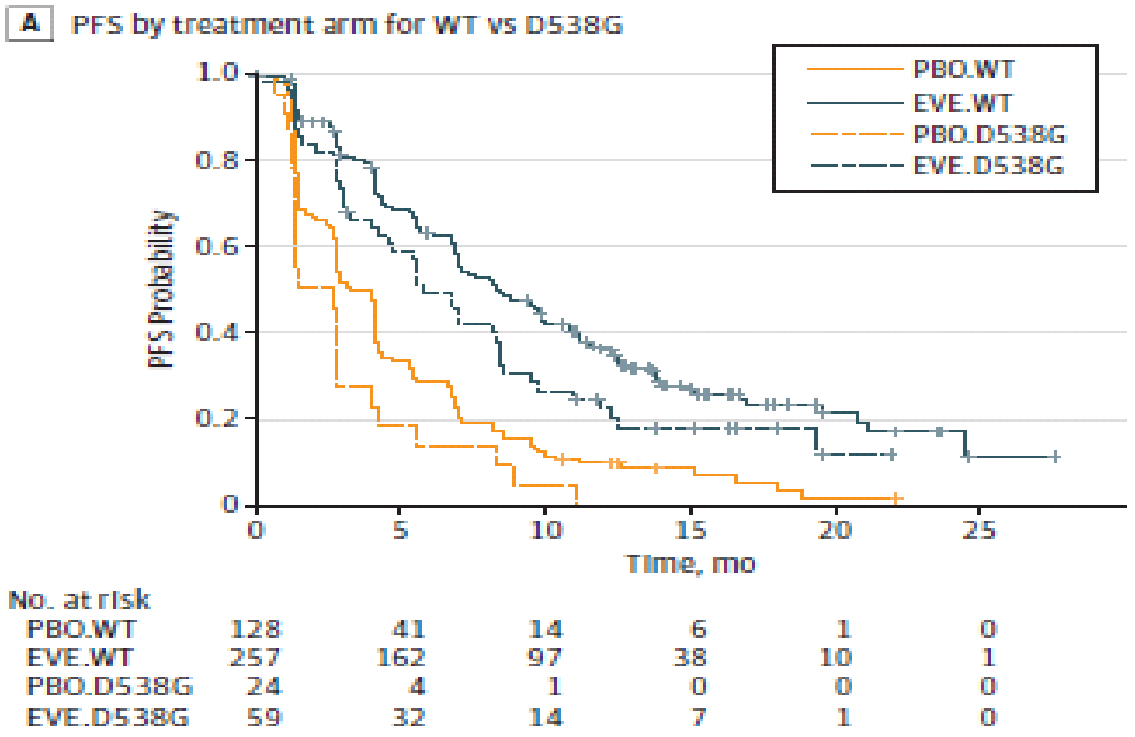
O'Leary et al, Cancer Disco 2018

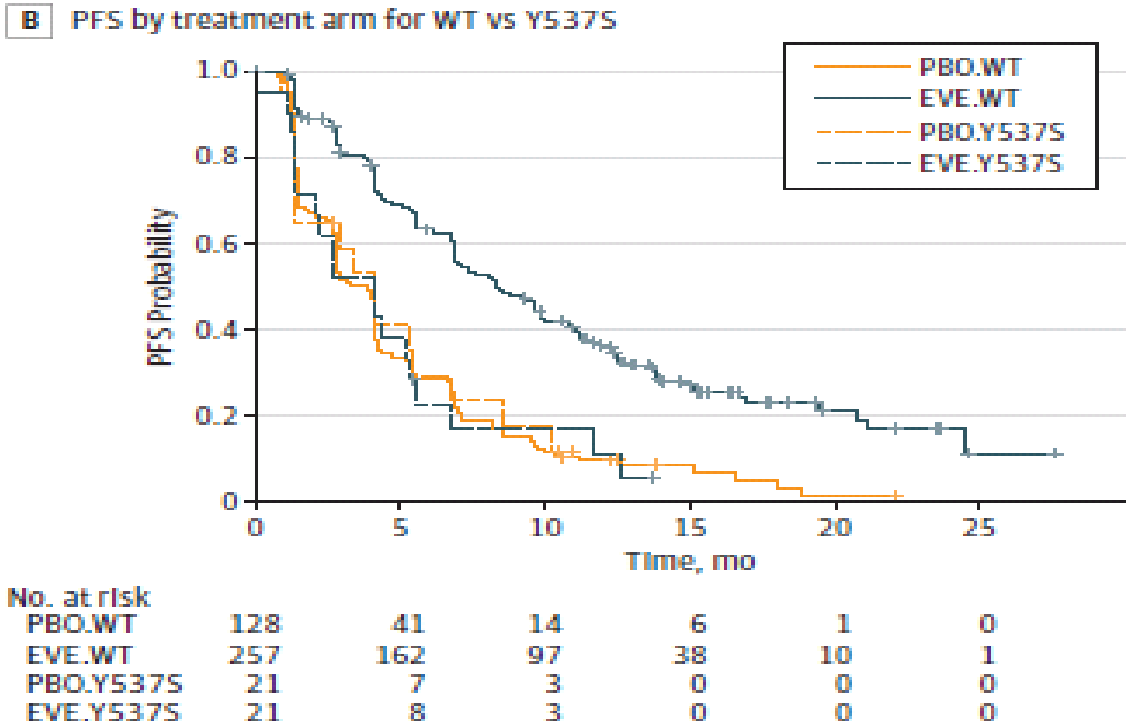
Early versus late resistance and acquired mutations at disease progression



O'Leary et al, Cancer Disco 2018

Benefit from adding everolimus to exemestane depend on ESR1 mut? (Bolero 2)

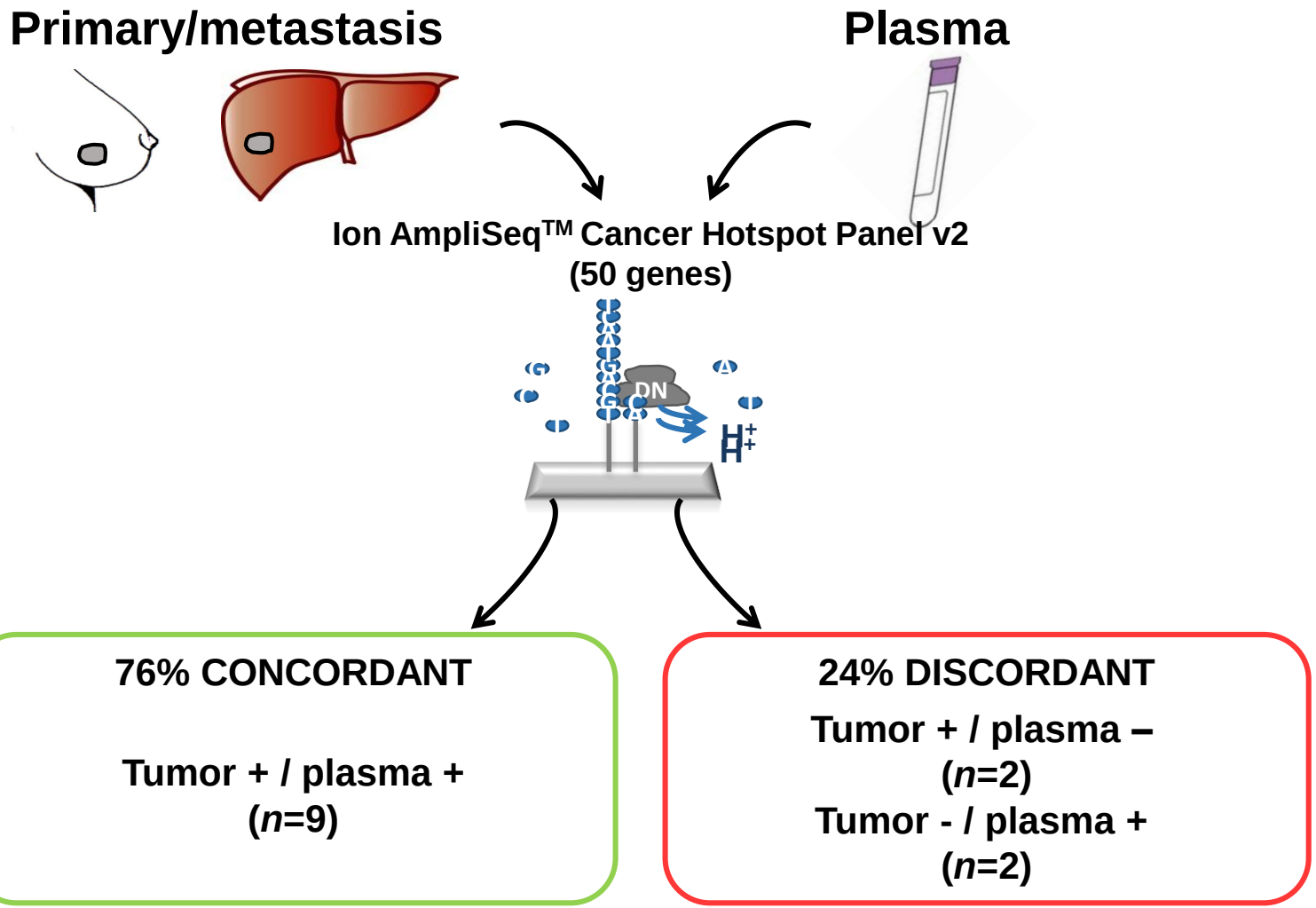




Validation is needed!

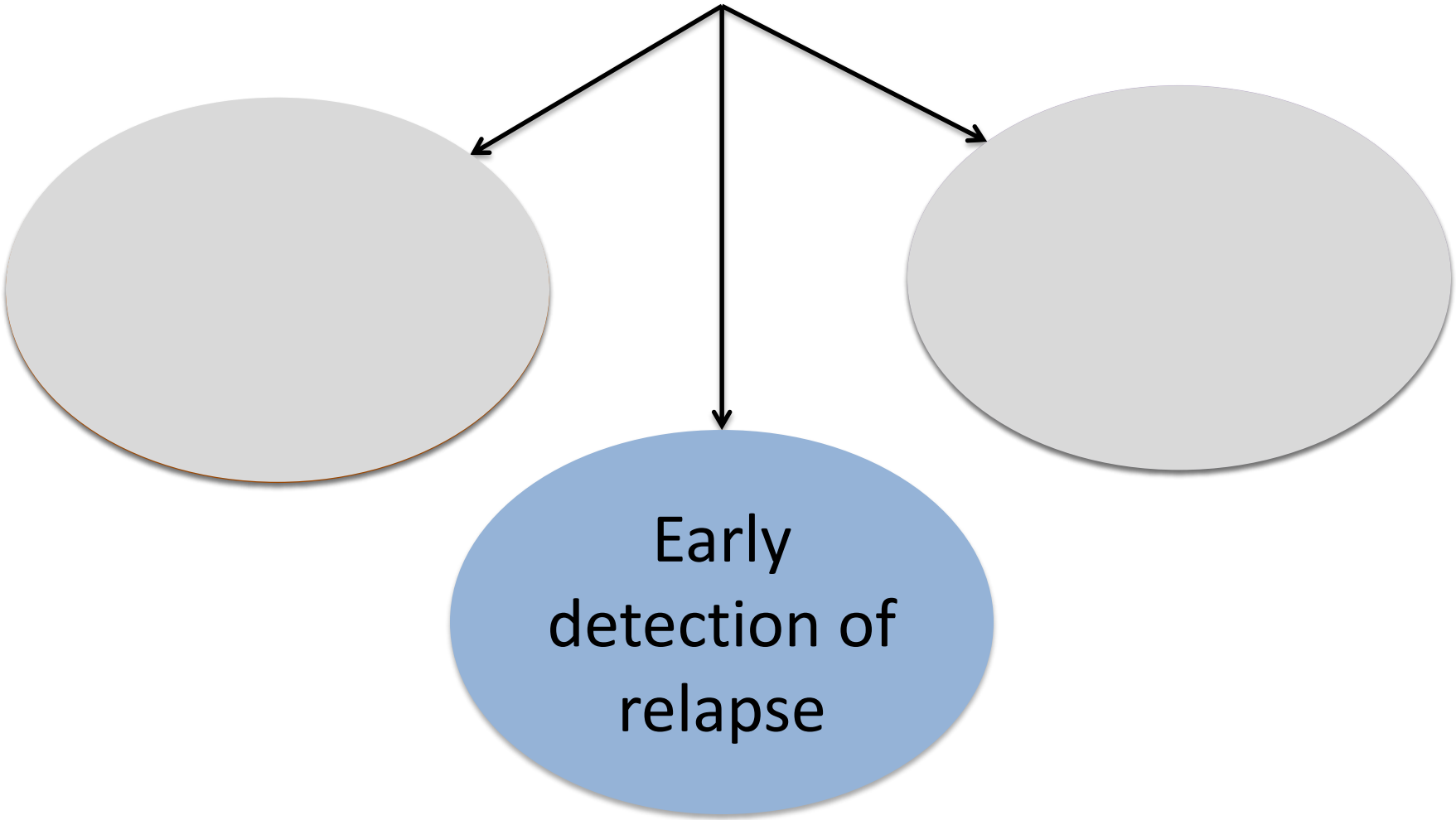
Chandarlapaty S et al, Jama Oncol 2016

Plasma ctDNA: an alternative to metastatic biopsy

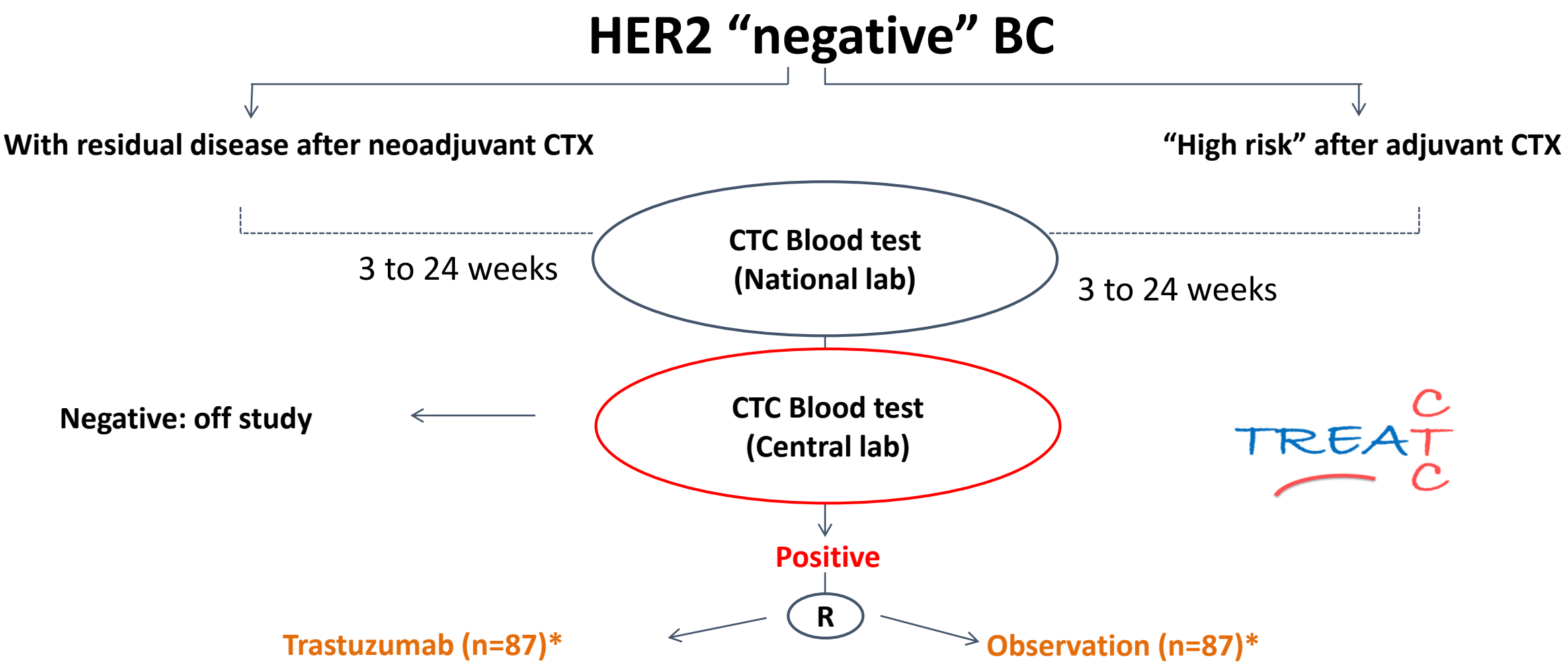


Rothé F et al. Ann Oncol 2014

Outline

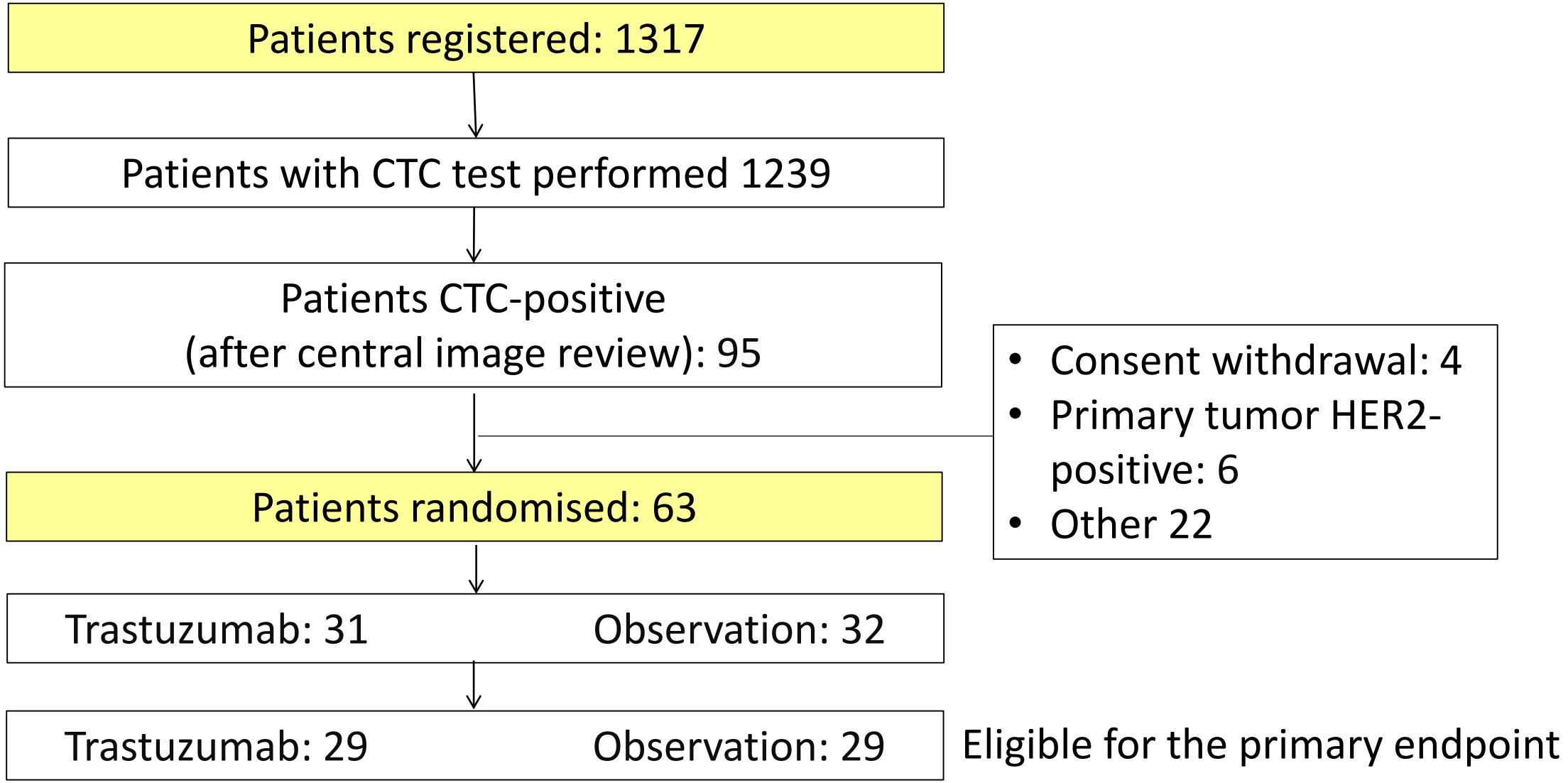


Treat CTC Trial



Ignatiadis M, et al. Eur J Cancer. 2016

Study flow chart



	Treatment arm		
	Trastuzumab (N=31)	Observation arm (N=32)	Total (N=63)
	N (%)	N (%)	N (%)
Age in years			
Median (range)	51.4 (31.9 - 69.4)	53.0 (31.4 - 68.6)	52.6 (31.4 - 69.4)
Pathological tumor size in mm			
Median (range)	25.0 (7.0 - 180.0)	24.0 (4.0 - 840.0)	24.0 (4.0 - 840.0)
Pathological lymph node status			
Negative	5 (16.1)	6 (18.8)	11 (17.5)
Positive	26 (83.9)	26 (81.3)	52 (82.5)
ER status			
Negative	9 (29.0)	11 (34.4)	20 (31.7)
Positive	22 (71.0)	21 (65.6)	43 (68.3)
Chemotherapy			
Neo-adjuvant	17 (54.8)	14 (43.8)	31 (49.2)
Adjuvant	14 (45.2)	18 (56.3)	32 (50.8)

Data are number of patients (%) or median (range).

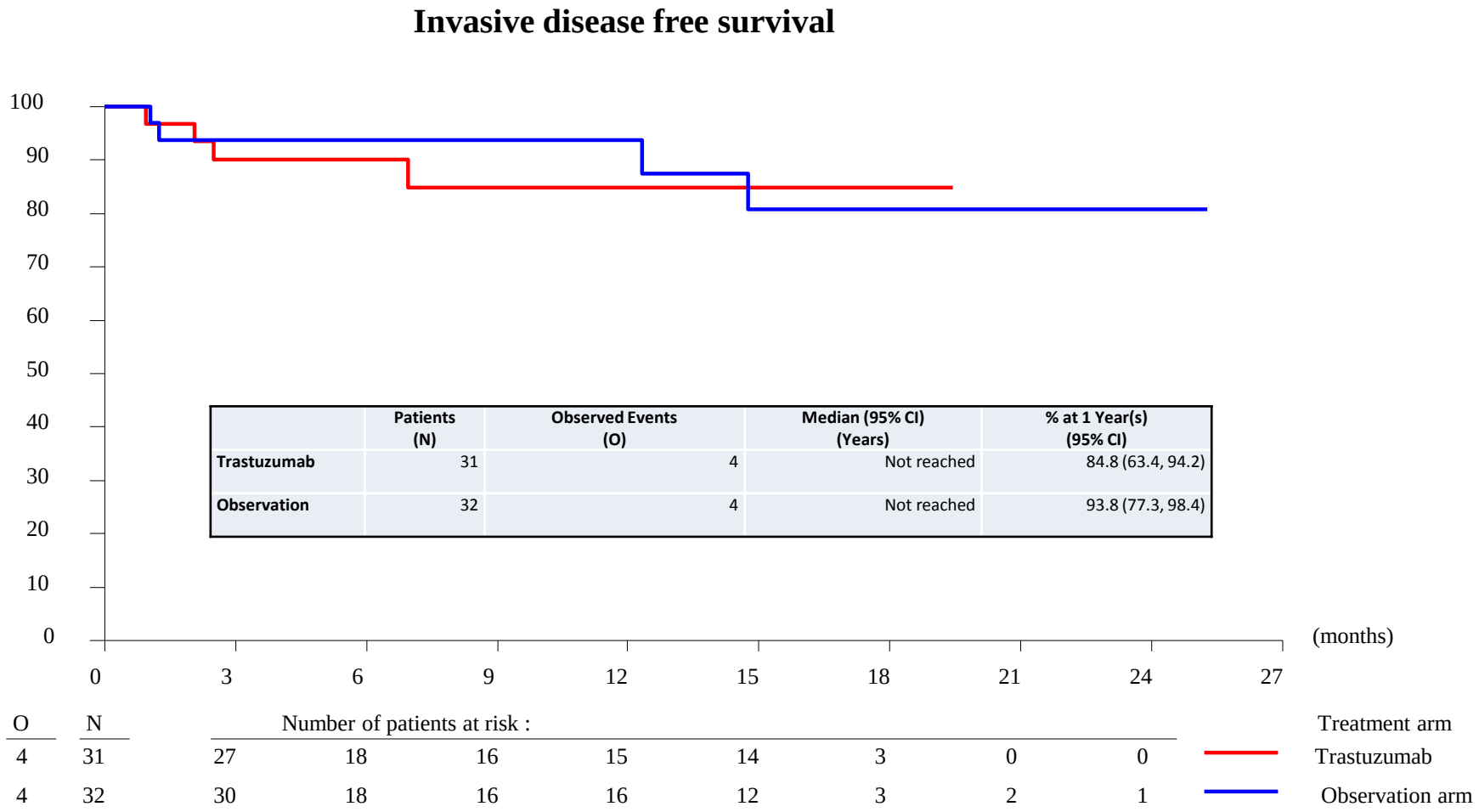
Ignatiadis M, et al. Ann Oncol 2018

Efficacy results for primary objective

Fifty-eight patients were evaluable for the primary endpoint, 29 in each arm. In 9 of the 58 patients, CTC(s) were still detected at week 18: 5 in the trastuzumab and 4 in the observation arm (one-sided Fisher exact test, p=0.765).

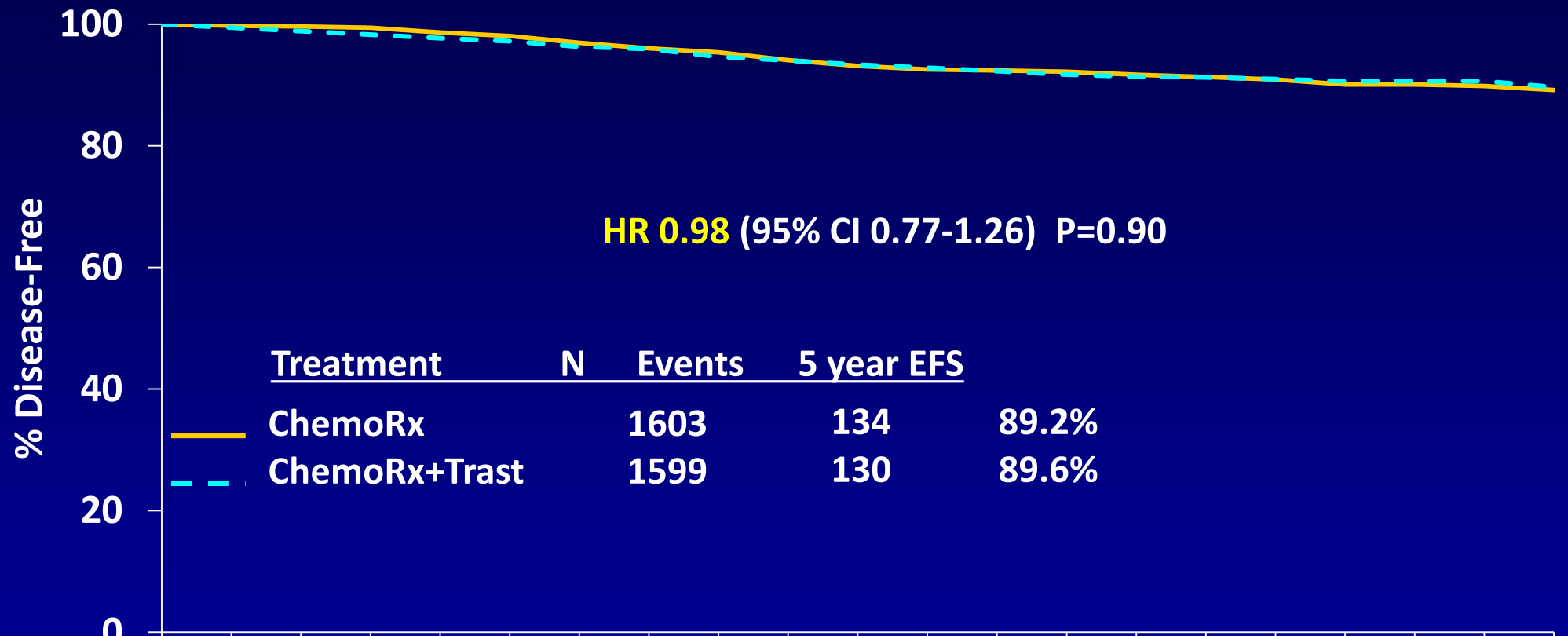
Ignatiadis M, et al. Ann Oncol 2018

Invasive Disease Free Survival



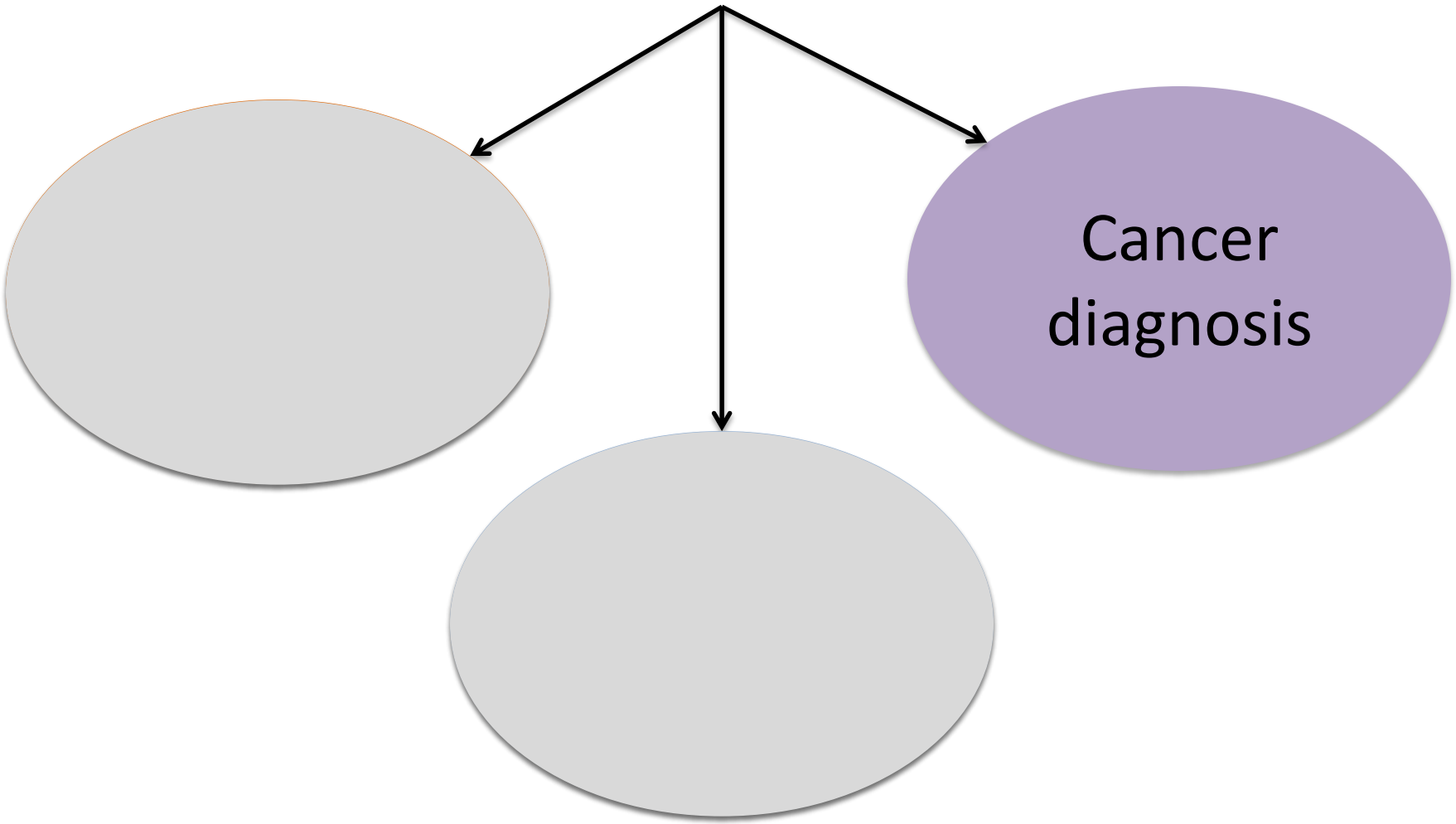
Ignatiadis M, et al. Ann Oncol 2018

B-47: Invasive Disease-Free Survival



No. at Risk						
ChemoRx	1603	1558	1423	1003	595	140
ChemoRx+Trast	1599	1528	1403	1009	591	117

Outline




GRAIL
A Revolution in Early
Cancer Detection

ctDNA for early diagnosis

HOPE

Diagnose cancer early on when still curable

CHALLENGE:

Sensitivity and specificity[1] of ctDNA for cancer diagnosis

[1] Mutations in cancer genes (e.g. p53 in 10% of non-cancer patients) occur even in individuals who will never develop cancer

(Lynnette Fernandez-Cuesta et al EBioMedicine 2016)

Challenges

- Physicians: Liquid biopsy in breast cancer is there for some time but no clinical utility have been demonstrated’
- Pharma: ‘Why use the liquid biopsy approach to give my drug to a small proportion of patients, if I can give it to all comers?’
- Regulators: ‘You need a clear pathway for drug approval based on ‘liquid biopsy’ test’

Opportunities

- Administer the right drug only to those that need it and for as long as they needed (dream of personalized medicine)

- Develop a new model for drug development

Acknowledgements

Les Amis de
l'Institut Bordet

Women with breast cancer