Lectures for training: Discussione

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Research Article

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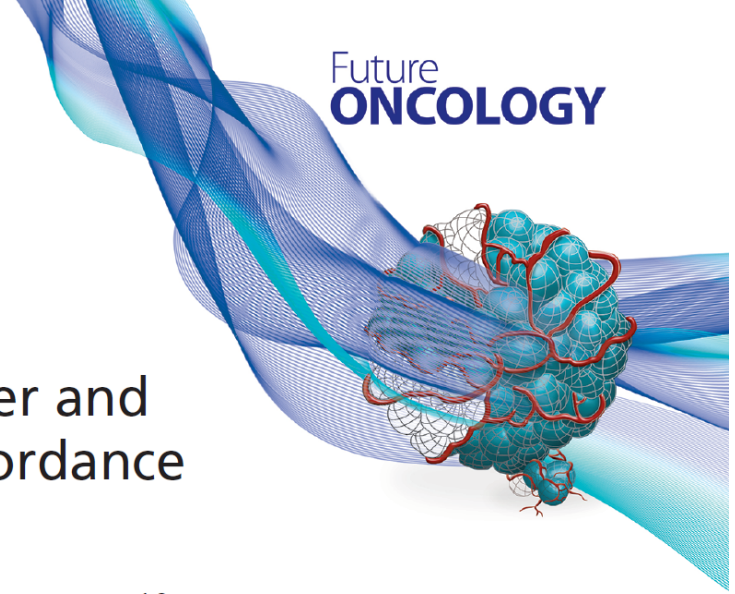


Comparison of primary breast cancer and paired metastases: biomarkers discordance influence on outcome and therapy

Elena Ongaro[1,2], Lorenzo Gerratana*[,1,3], Marika Cinausero[1,2], Giacomo Pelizzari[1,3], Elena Poletto[1], Manuela Giangreco[3,4], Claudia Andreetta[1], Stefano Pizzolitto[5], Carla Di Loreto[3,6], Alessandro Marco Minisini[1], Mauro Mansutti[1], Stefania Russo[1], Gianpiero Fasola[1] & Fabio Puglisi[3,7]

Original Study

Determinants of Last-line Treatment in Metastatic Breast Cancer

Marika Cinausero,[1,2] Lorenzo Gerratana,[1,2] Elisa De Carlo,[1,2] Donatella Iacono,[1,2] Marta Bonotto,[1,2] Valentina Fanotto,[1,2] Vanessa Buoro,[1,2] Debora Basile,[1,2] Maria Grazia Vitale,[1,2] Karim Rihawi,[3] Gianpiero Fasola,[2] Fabio Puglisi[1,4]

Comparison of primary BC and paired metastasis: summary

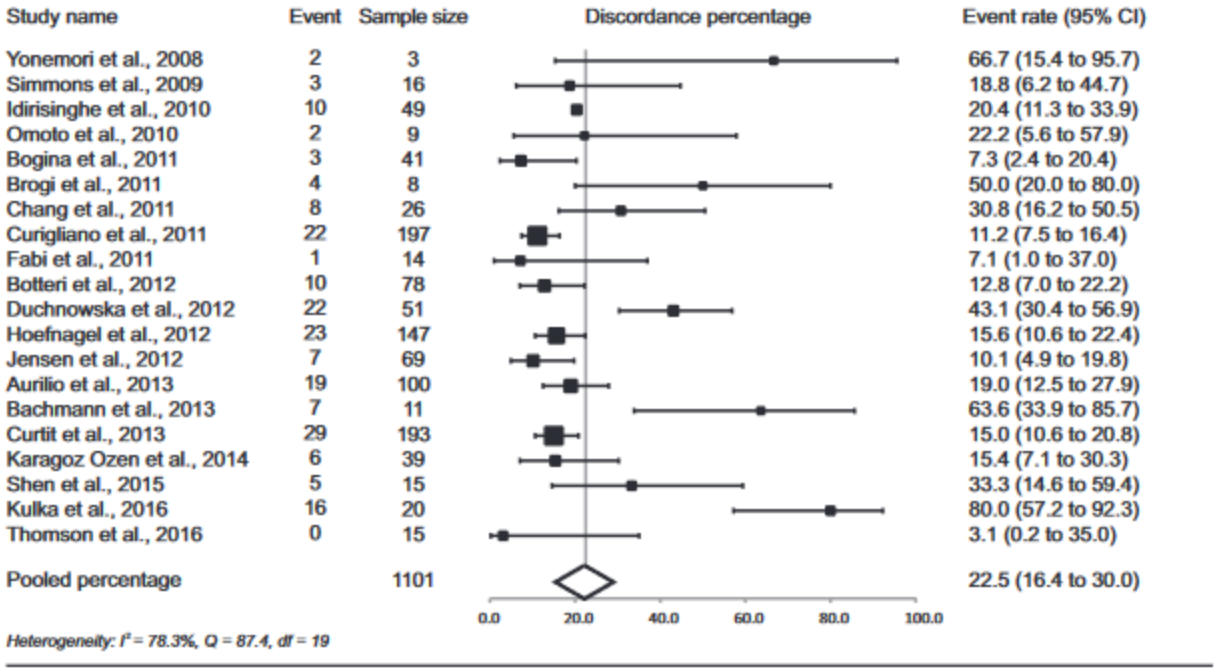
- Retrospective cohort of 232 mBC patients with matched tumor samples
- Conversion rate: ER→12.7% (loss>gain); PgR→49.7% (loss>gain), Ki67→35% (gain>loss)
- Tumor phenotype discordance: 22%, shift to more aggressive subtype was more common, enrichment in LumB and TN on metastates
- Prior tax or anthra associated with PgR loss (not endocrine Tx)
- Prior tax or AI associated with ER reduction
- Prognostic impact: concordant ER+>Loss ER>Concordant ER-

Ongaro E et al, Future Oncol 2018

ER conversion from primary to metastasis

ER+ → ER-: 22.5%

ERα conversion: positive to negative

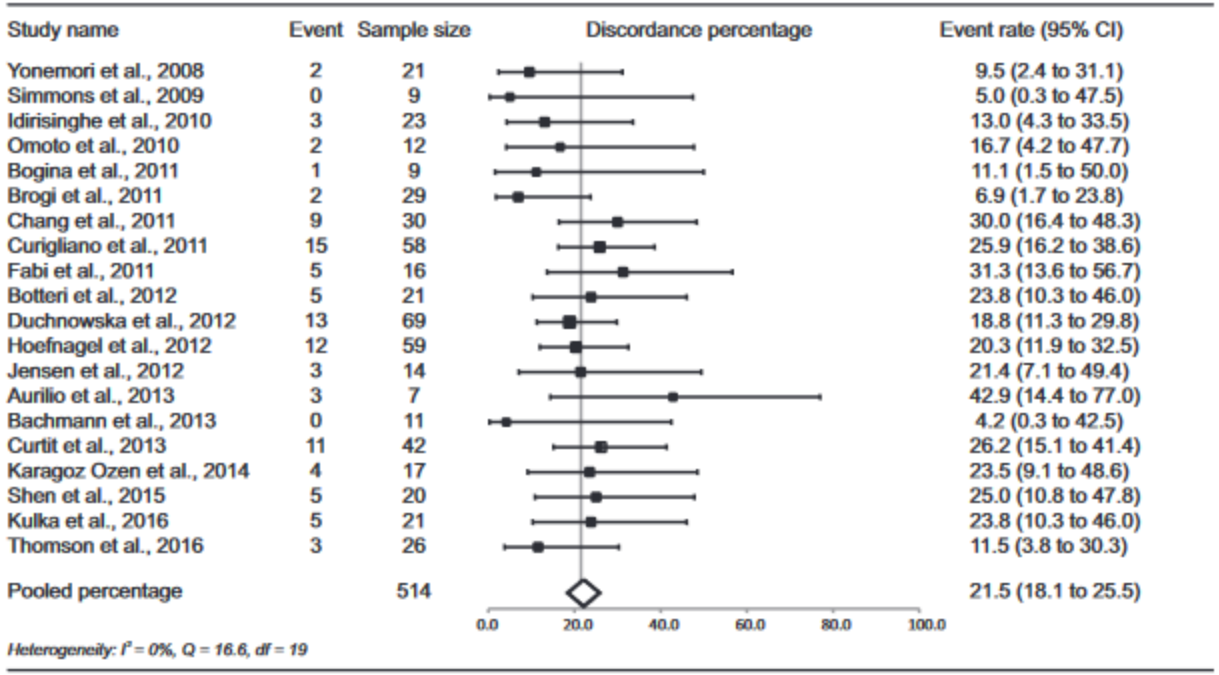


Study name	Event	Sample size	Event rate (95% CI)
Yonemori et al., 2008	2	3	66.7 (15.4 to 95.7)
Simmons et al., 2009	3	16	18.8 (6.2 to 44.7)
Idirisinghe et al., 2010	10	49	20.4 (11.3 to 33.9)
Omoto et al., 2010	2	9	22.2 (5.6 to 57.9)
Bogina et al., 2011	3	41	7.3 (2.4 to 20.4)
Brogi et al., 2011	4	8	50.0 (20.0 to 80.0)
Chang et al., 2011	8	26	30.8 (16.2 to 50.5)
Curigliano et al., 2011	22	197	11.2 (7.5 to 16.4)
Fabi et al., 2011	1	14	7.1 (1.0 to 37.0)
Botteri et al., 2012	10	78	12.8 (7.0 to 22.2)
Duchnowska et al., 2012	22	51	43.1 (30.4 to 56.9)
Hoefnagel et al., 2012	23	147	15.6 (10.6 to 22.4)
Jensen et al., 2012	7	69	10.1 (4.9 to 19.8)
Aurilio et al., 2013	19	100	19.0 (12.5 to 27.9)
Bachmann et al., 2013	7	11	63.6 (33.9 to 85.7)
Curtit et al., 2013	29	193	15.0 (10.6 to 20.8)
Karagoz Ozen et al., 2014	6	39	15.4 (7.1 to 30.3)
Shen et al., 2015	5	15	33.3 (14.6 to 59.4)
Kulka et al., 2016	16	20	80.0 (57.2 to 92.3)
Thomson et al., 2016	0	15	3.1 (0.2 to 35.0)
Pooled percentage		1101	22.5 (16.4 to 30.0)

Heterogeneity: I^2 = 78.3%, Q = 87.4, df = 19

ER- → ER+: 21.5%

ERα conversion: negative to positive



Study name	Event	Sample size	Event rate (95% CI)
Yonemori et al., 2008	2	21	9.5 (2.4 to 31.1)
Simmons et al., 2009	0	9	5.0 (0.3 to 47.5)
Idirisinghe et al., 2010	3	23	13.0 (4.3 to 33.5)
Omoto et al., 2010	2	12	16.7 (4.2 to 47.7)
Bogina et al., 2011	1	9	11.1 (1.5 to 50.0)
Brogi et al., 2011	2	29	6.9 (1.7 to 23.8)
Chang et al., 2011	9	30	30.0 (16.4 to 48.3)
Curigliano et al., 2011	15	58	25.9 (16.2 to 38.6)
Fabi et al., 2011	5	16	31.3 (13.6 to 56.7)
Botteri et al., 2012	5	21	23.8 (10.3 to 46.0)
Duchnowska et al., 2012	13	69	18.8 (11.3 to 29.8)
Hoefnagel et al., 2012	12	59	20.3 (11.9 to 32.5)
Jensen et al., 2012	3	14	21.4 (7.1 to 49.4)
Aurilio et al., 2013	3	7	42.9 (14.4 to 77.0)
Bachmann et al., 2013	0	11	4.2 (0.3 to 42.5)
Curtit et al., 2013	11	42	26.2 (15.1 to 41.4)
Karagoz Ozen et al., 2014	4	17	23.5 (9.1 to 48.6)
Shen et al., 2015	5	20	25.0 (10.8 to 47.8)
Kulka et al., 2016	5	21	23.8 (10.3 to 46.0)
Thomson et al., 2016	3	26	11.5 (3.8 to 30.3)
Pooled percentage		514	21.5 (18.1 to 25.5)

Heterogeneity: I^2 = 0%, Q = 16.6, df = 19

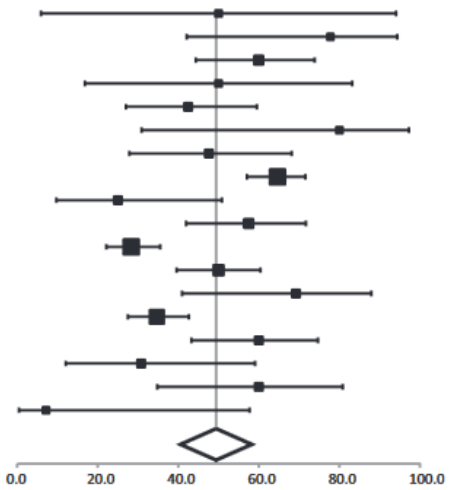
Schrijver ,JNCI 208

PgR conversion from primary to metastasis

PgR+ → PgR-: 49.4%

PR conversion: positive to negative

Study name	Event	Sample size	Event rate 95% CI
Yonemori et al., 2008	1	2	50.0 (5.9 to 94.1)
Simmons et al., 2009	7	9	77.8 (42.1 to 94.4)
Idirisinghe et al., 2010	24	40	60.0 (44.3 to 73.8)
Omoto et al., 2010	3	6	50.0 (16.8 to 83.2)
Bogina et al., 2011	14	33	42.4 (27.0 to 59.5)
Brogi et al., 2011	4	5	80.0 (30.9 to 97.3)
Chang et al., 2011	10	21	47.6 (27.9 to 68.2)
Curigliano et al., 2011	106	164	64.6 (57.0 to 71.6)
Fabi et al., 2011	4	16	25.0 (9.7 to 50.8)
Duchnowska et al., 2012	23	40	57.5 (42.0 to 71.7)
Hoefnagel et al., 2012	49	173	28.3 (22.1 to 35.5)
Aurilio et al., 2013	43	86	50.0 (39.6 to 60.4)
Bachmann et al., 2013	9	13	69.2 (40.9 to 88.0)
Curtit et al., 2013	52	150	34.7 (27.5 to 42.6)
Karagoz Ozen et al., 2014	21	35	60.0 (43.3 to 74.7)
Shen et al., 2015	4	13	30.8 (12.0 to 59.1)
Kulka et al., 2016	9	15	60.0 (34.8 to 80.8)
Thomson et al., 2016	0	6	7.1 (0.4 to 57.7)
Pooled percentage		827	49.4 (40.5 to 58.2)

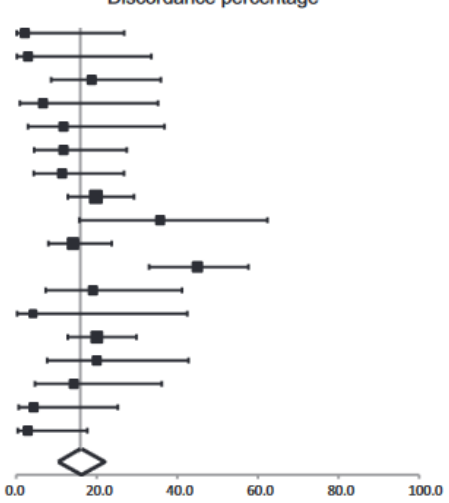


Heterogeneity: I^2 = 77.0%, Q = 73.9, df = 17

PgR- → PgR+: 15.9%

PR conversion: negative to positive

Study name	Event	Sample size	Event rate 95% CI
Yonemori et al., 2008	0	22	2.2 (0.1 to 26.8)
Simmons et al., 2009	0	16	2.9 (0.2 to 33.6)
Idirisinghe et al., 2010	6	32	18.8 (8.7 to 35.9)
Omoto et al., 2010	1	15	6.7 (0.9 to 35.2)
Bogina et al., 2011	2	17	11.8 (3.0 to 36.8)
Brogi et al., 2011	4	34	11.8 (4.5 to 27.5)
Chang et al., 2011	4	35	11.4 (4.4 to 26.8)
Curigliano et al., 2011	18	91	19.8 (12.8 to 29.2)
Fabi et al., 2011	5	14	35.7 (15.7 to 62.4)
Duchnowska et al., 2012	11	78	14.1 (8.0 to 23.7)
Hoefnagel et al., 2012	27	60	45.0 (33.0 to 57.6)
Aurilio et al., 2013	4	21	19.0 (7.3 to 41.2)
Bachmann et al., 2013	0	11	4.2 (0.3 to 42.5)
Curtit et al., 2013	17	85	20.0 (12.8 to 29.8)
Karagoz Ozen et al., 2014	4	20	20.0 (7.7 to 42.8)
Shen et al., 2015	3	21	14.3 (4.7 to 36.1)
Kulka et al., 2016	1	23	4.3 (0.6 to 25.2)
Thomson et al., 2016	1	35	2.9 (0.4 to 17.7)
Pooled percentage		630	15.9 (11.3 to 22.0)



Heterogeneity: I^2 = 61.3%, Q = 43.9, df = 17

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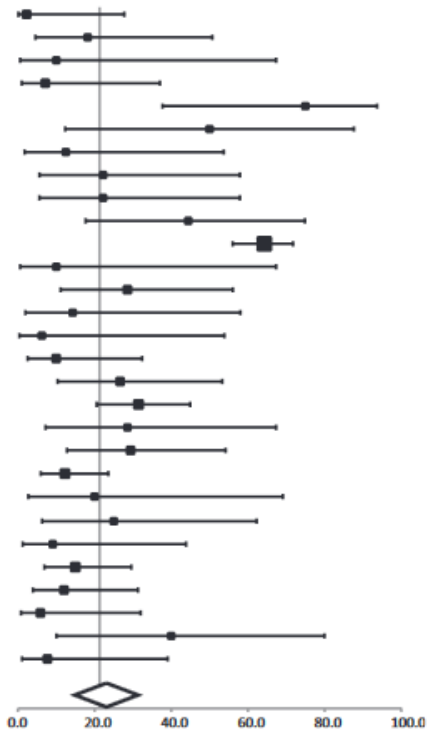
HER2 conversion from primary to metastasis

HER2+ → HER2-: 21.3%

HER2 conversion: positive to negative

Study name	Event	Sample size	Event rate (95% CI)
Gancberg et al., 2002	0	21	2.3 (0.1 to 27.7)
Vincent-Salomon et al., 2002	2	11	18.2 (4.6 to 50.7)
Regitnig et al., 2004	0	4	10.0 (0.6 to 67.4)
Zidan et al., 2005	1	14	7.1 (1.0 to 37.0)
Fuchs et al., 2006	6	8	75.0 (37.7 to 93.7)
Lorincz et al., 2006	2	4	50.0 (12.3 to 87.7)
Gaedcke et al., 2007	1	8	12.5 (1.7 to 53.7)
Santinelli et al., 2008	2	9	22.2 (5.6 to 57.9)
Yonemori et al., 2008	2	9	22.2 (5.6 to 57.9)
Cabioglu et al., 2009	4	9	44.4 (17.7 to 74.9)
Lower et al., 2009	90	140	64.3 (56.0 to 71.8)
Simmons et al., 2009	0	4	10.0 (0.6 to 67.4)
Idirisinghe et al., 2010	4	14	28.6 (11.1 to 56.1)
Omoto et al., 2010	1	7	14.3 (2.0 to 58.1)
Bogina et al., 2011	0	7	6.3 (0.4 to 53.9)
Brogi et al., 2011	2	20	10.0 (2.5 to 32.4)
Chang et al., 2011	4	15	26.7 (10.4 to 53.3)
Curigliano et al., 2011	17	54	31.5 (20.6 to 44.9)
Fabi et al., 2011	2	7	28.6 (7.2 to 67.3)
Botteri et al., 2012	5	17	29.4 (12.8 to 54.2)
Duchnowska et al., 2012	7	57	12.3 (6.0 to 23.6)
Jensen et al., 2012	1	5	20.0 (2.7 to 69.1)
Aurilio et al., 2013	2	8	25.0 (6.3 to 62.3)
Bachmann et al., 2013	1	11	9.1 (1.3 to 43.9)
Curtit et al., 2013	6	40	15.0 (6.9 to 29.6)
Nakamura et al., 2013	3	25	12.0 (3.9 to 31.3)
Shen et al., 2015	1	17	5.9 (0.8 to 32.0)
Kulka et al., 2016	2	5	40.0 (10.0 to 80.0)
Thomson et al., 2016	1	13	7.7 (1.1 to 39.1)
Pooled percentage		563	21.3 (14.3 to 30.5)

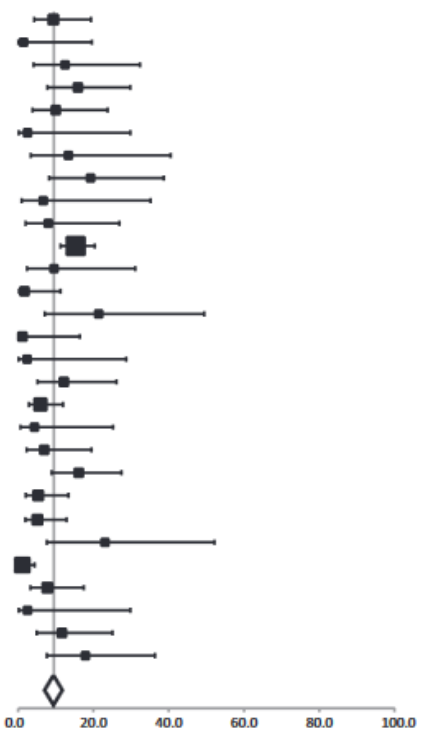


Heterogeneity: I^2 = 74.4%, Q = 109.2, df = 28

HER2- → HER2+: 9.5%

HER2 conversion: negative to positive

Study name	Event	Sample size	Event rate (95% CI)
Gancberg et al., 2002	6	64	9.4 (4.3 to 19.3)
Vincent-Salomon et al., 2002	0	33	1.5 (0.1 to 19.6)
Regitnig et al., 2004	3	24	12.5 (4.1 to 32.4)
Zidan et al., 2005	7	44	15.9 (7.8 to 29.8)
Fuchs et al., 2006	4	40	10.0 (3.8 to 23.8)
Lorincz et al., 2006	0	19	2.5 (0.2 to 29.8)
Gaedcke et al., 2007	2	15	13.3 (3.4 to 40.5)
Santinelli et al., 2008	5	26	19.2 (8.2 to 38.7)
Yonemori et al., 2008	1	15	6.7 (0.9 to 35.2)
Cabioglu et al., 2009	2	25	8.0 (2.0 to 26.9)
Lower et al., 2009	37	242	15.3 (11.3 to 20.4)
Simmons et al., 2009	2	21	9.5 (2.4 to 31.1)
Idirisinghe et al., 2010	1	58	1.7 (0.2 to 11.2)
Omoto et al., 2010	3	14	21.4 (7.1 to 49.4)
Bogina et al., 2011	0	41	1.2 (0.1 to 16.4)
Brogi et al., 2011	0	20	2.4 (0.1 to 28.7)
Chang et al., 2011	5	41	12.2 (5.2 to 26.1)
Curigliano et al., 2011	7	118	5.9 (2.9 to 11.9)
Fabi et al., 2011	1	23	4.3 (0.6 to 25.2)
Botteri et al., 2012	3	43	7.0 (2.3 to 19.5)
Duchnowska et al., 2012	10	62	16.1 (8.9 to 27.5)
Jensen et al., 2012	4	75	5.3 (2.0 to 13.4)
Aurilio et al., 2013	4	78	5.1 (1.9 to 12.9)
Bachmann et al., 2013	3	13	23.1 (7.6 to 52.2)
Curtit et al., 2013	2	178	1.1 (0.3 to 4.4)
Nakamura et al., 2013	5	64	7.8 (3.3 to 17.4)
Shen et al., 2015	0	19	2.5 (0.2 to 29.8)
Kulka et al., 2016	5	43	11.6 (4.9 to 25.1)
Thomson et al., 2016	5	28	17.9 (7.6 to 36.4)
Pooled percentage		1486	9.5 (7.4 to 12.1)



Heterogeneity: I^2 = 42.1%, Q = 48.3, df = 28

Schrijver ,JNCI 208

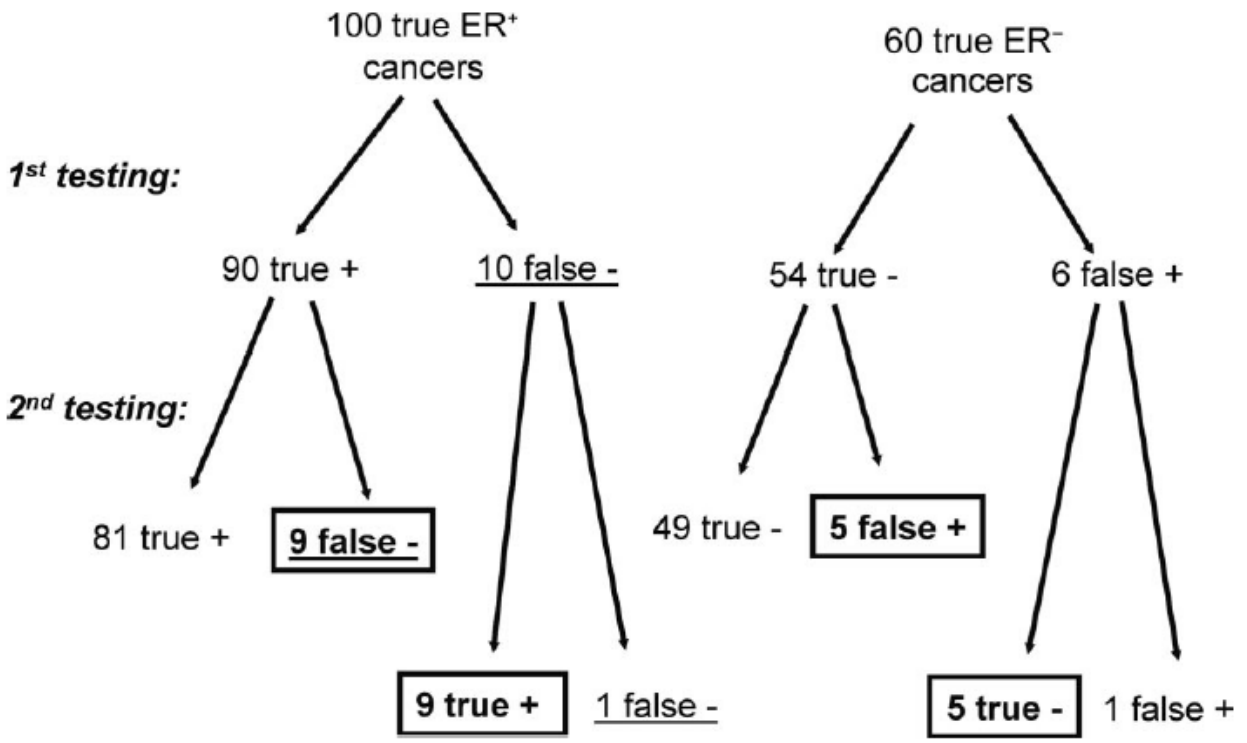
Sources of HER2 testing variations

- Preanalytic
  - Time to fixation
  - Method of tissue processing
  - Time of fixation
  - Type of fixation
- Analytic
  - Assay validation
  - Equipment calibration
  - Use of standardized laboratory procedures
  - Training and competency assessment of staff
  - Type of antigen retrieval
  - Test reagents
  - Use of standardized control materials
  - Use of automated laboratory methods
- Postanalytic
  - Interpretation criteria
  - Use of image analysis
  - Reporting elements
  - Quality assurance procedures
    - Laboratory accreditation
    - Proficiency testing
    - Pathologist competency assessment

Wolff AC et al, J Clin Oncol 25:118-145 , 2007

Estrogen and HER-2 Receptor Discordance Between Primary Breast Cancer and Metastasis

LAJOS PUSZTAI,[a] GIUSEPPE VIALE,[b] CATHERINE M. KELLY,[a] CLIFFORD A. HUDIS[c]



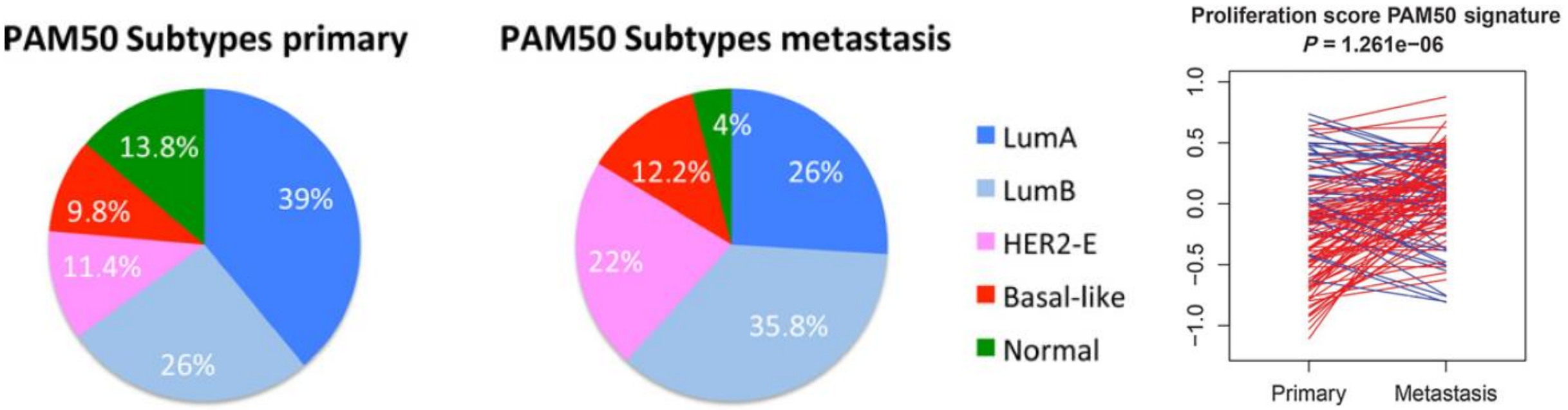
The Oncologist® Breast Cancer

Genomic alterations associated with discordant HR expression from primary to metastasis

- Metastasis samples
  - HR+→TN vs concordant HR+: ↑TP53 mut, ↑CDKNB2 and RB1 del
- Primary tumor samples
  - HR+→TN vs concordant HR+: ↑TP53 mut,↓PIK3CA mut, ↑alterations in DNA repair pathways, ↑TMB

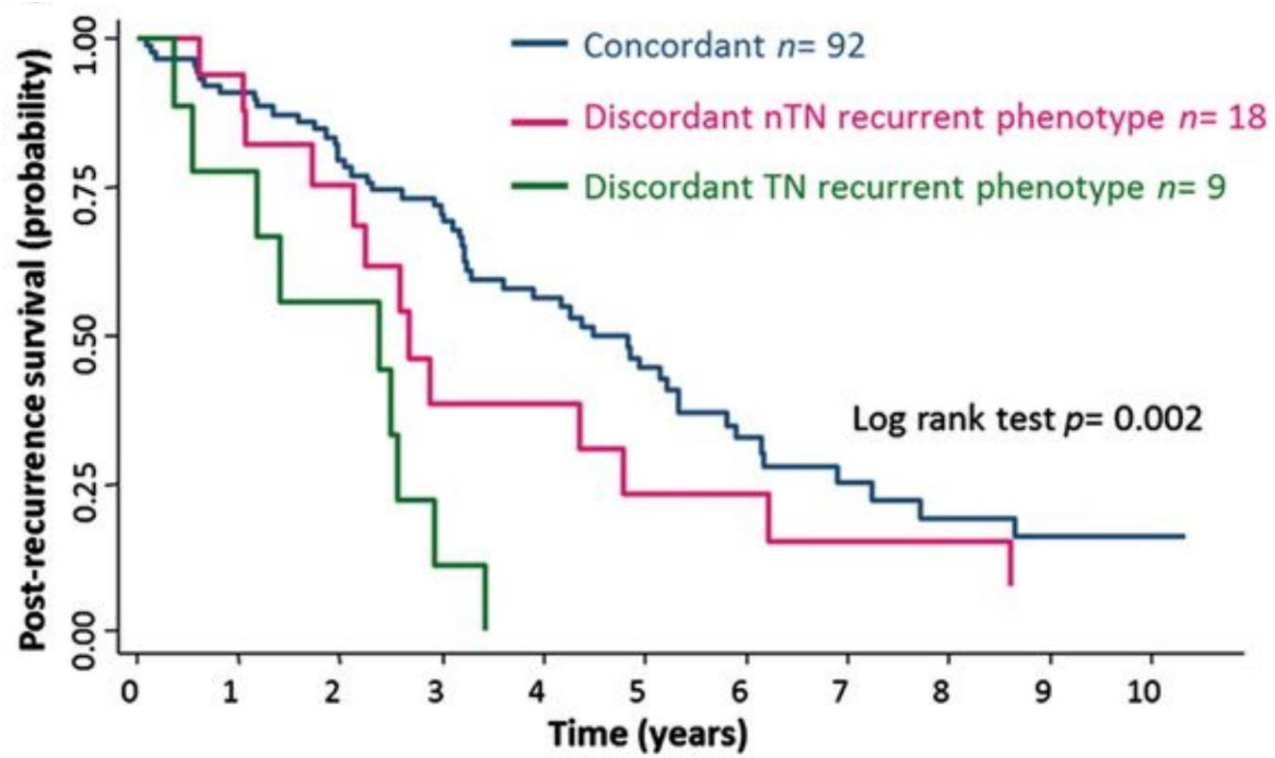
Garrido-Castro A, SABCS 2018

PAM50 subtype in primary and matched metastatic BC samples



Cejalvo JM et al, Clin Cancer Res 2017

Tumor phenotype discordance



Dieci MV, Ann Oncol 2013

Tumor phenotype discordance during progression

- Biopsy of recurrence is suggested whenever possible, mostly when the clinical course of disease is not coherent with the known primary tumor phenotype
  - It can allow to diagnose second non-BC primary tumors
  - It may offer the opportunity for a more personalized treatment
  - It may allow the possibility to enroll patients in clinical trials

Determinants of last-line treatment in mBC: summary

- Retrospective cohort of 410 mBC died because of disease progression
- LumA 14%, LumB 53%, LumB HER2+ 8%, HER2+ 10%, TN 15%
- Median n° of lines = 3; last-line CT 68%, last-line ET 32.4%
- Median LLS = 100 days; 15% died <30d, 48% died <90d

Cinausero M, Clin Breast Cancer 2017

Limiting active anticancer treatment in the end of life period: ASCO Top-Five list in Oncology

"In reality, only 2 major reasons exist for administering chemotherapy to most patients with metastatic cancer: to help them live longer and/or to help them live better." ***Blanke CD & Fromme EK, JAMA Oncol 2015***

Top-Five list in Oncology (ASCO)

1- Don't use cancer-directed therapy for solid tumor patients with the following characteristics: PS 3-4, no benefit from prior evidence-based interventions, not eligible for a clinical trial, and no strong evidence supporting the clinical value of further anti-cancer treatment.

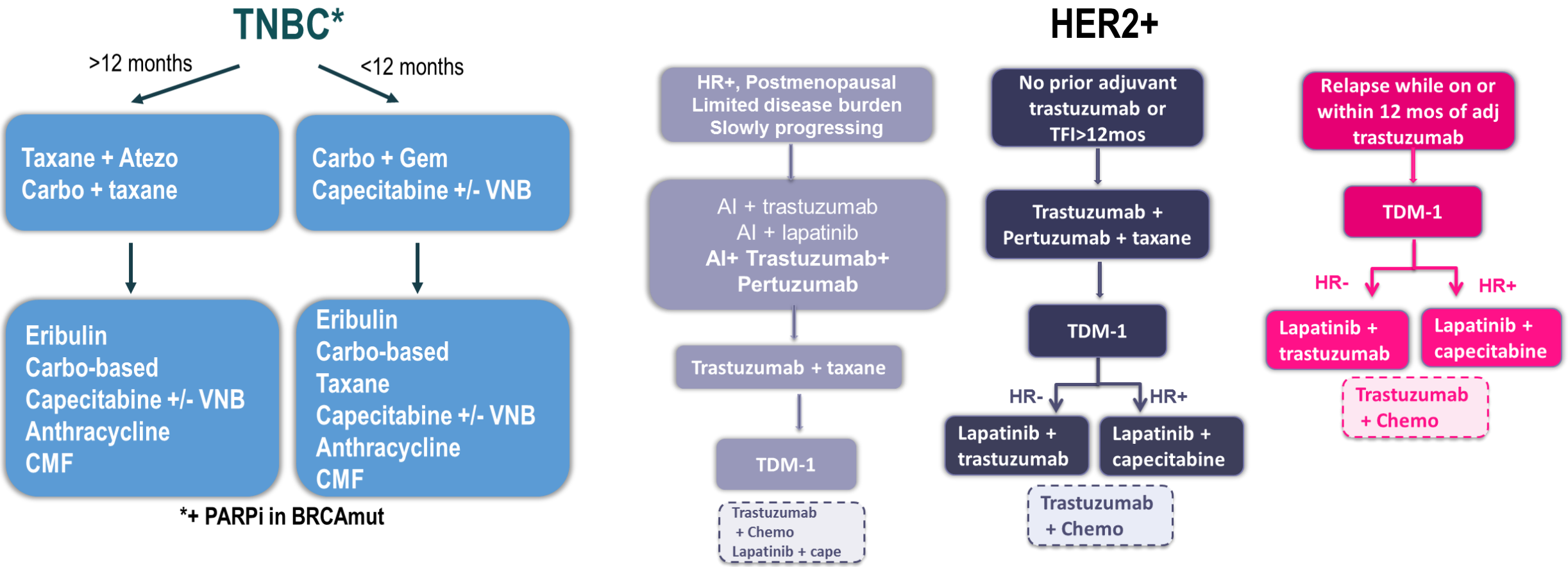
Schnipper LE et al, JCO 2012

Why is it so difficult?

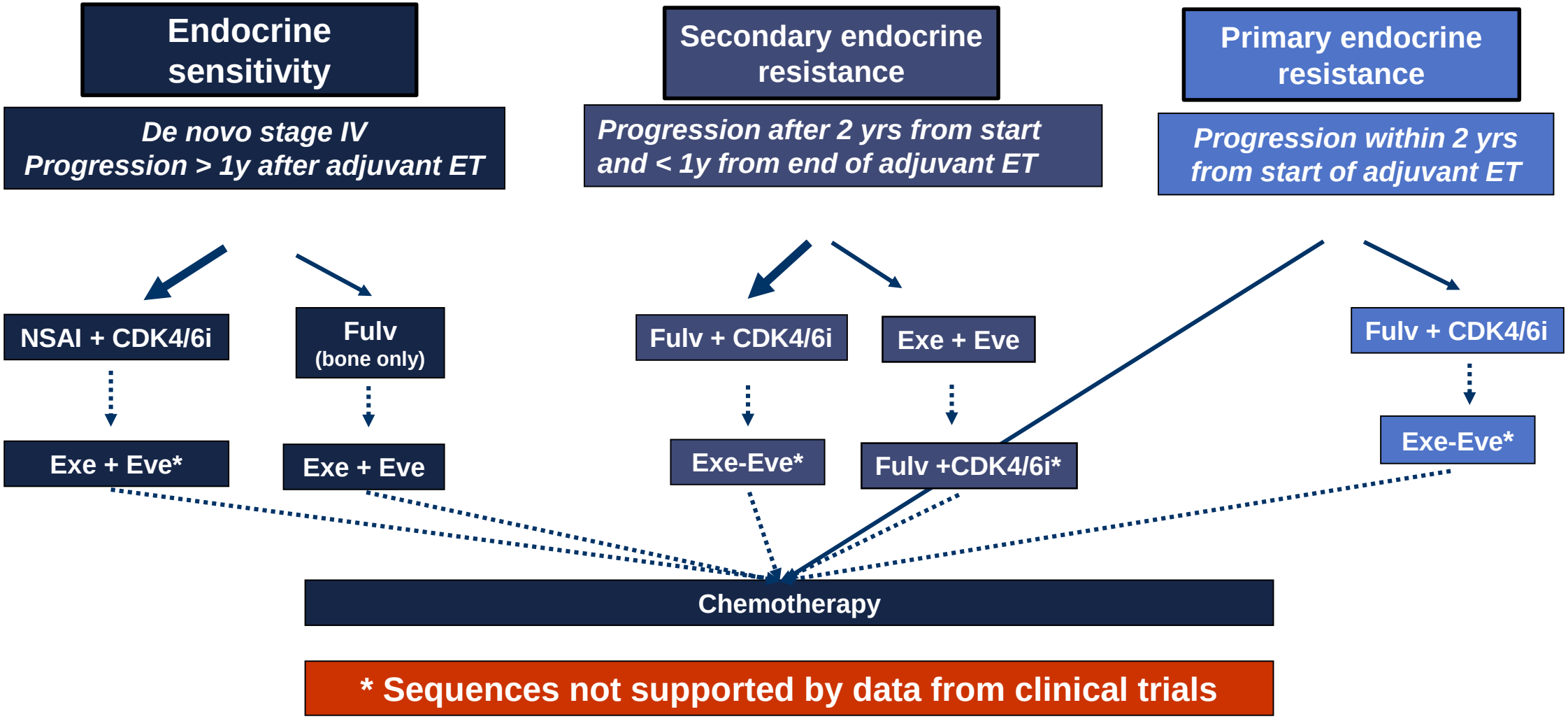
- **How are decisions made?**
  - Decision-making was shared and ongoing, including stopping, starting and trying different treatments. Oncologists often experienced **'professional role dissonance' between their self-perception as 'treaters', and talking about end of life care.**
- **Why are decisions made?**
  - Clinical factors: disease progression, worsening functional status, treatment side-effects. Non-clinical factors: physicians' personal experience, values, emotions. **Some patients continued treatment to maintain 'hope', often reflecting limited understanding of palliative goals**.
- **When are decisions made?**
  - Limited evidence reveals patients' decisions based upon quality of life benefits. **Clinicians found timing withdrawal particularly challenging.**
- **Who makes the decisions?**
  - Decisions were based **within physician-patient interaction.**

Clarke et al., BMC Cancer 2015

Do you always know this will be the last? The evolving scenario of mBC treatment



Do you always know this will be the last? The evolving scenario of mBC treatment



PIK3CA (and ESR1) mutational status on tumor tissue/ctDNA likely to have a role in treatment sequencing

Do you always know this will be the last?

Table 1 Patient and Disease Characteristics

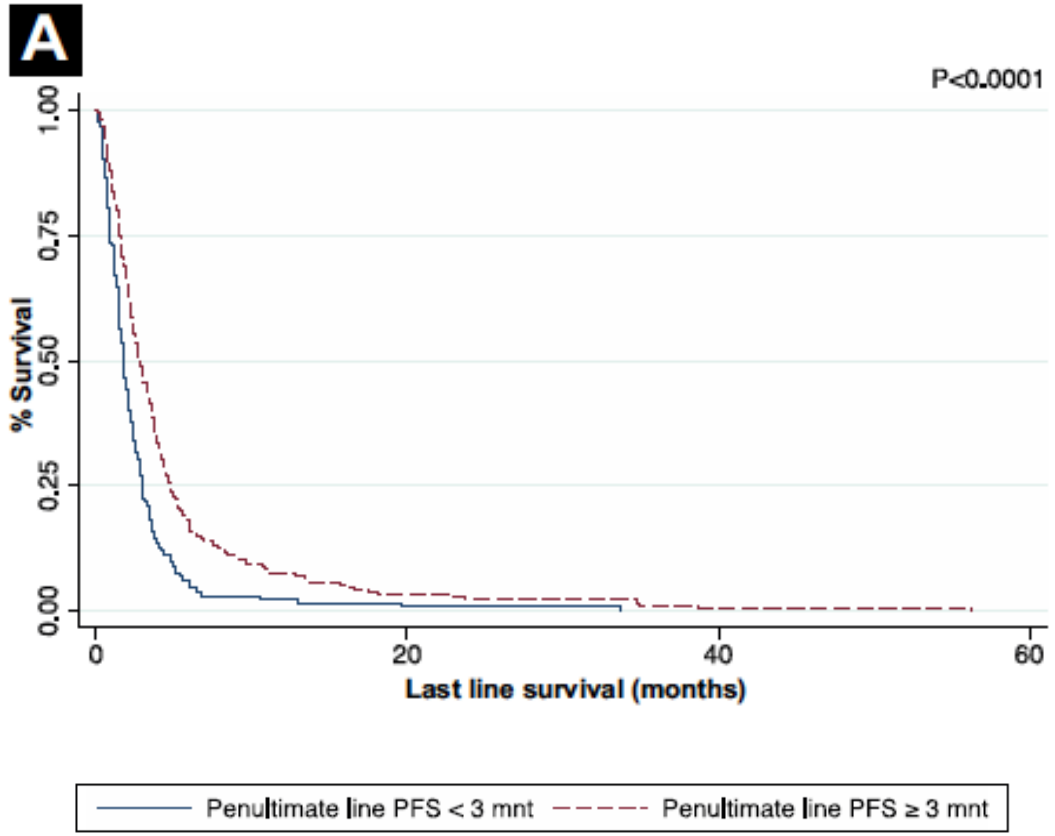
Variable	Total Population	Lightly Pretreated[a]	Heavily Pretreated[a]	*P* Value[b]
Primary tumor histotype (n = 404)				.333
Ductal	75.99 (307)	76.23 (170)	75.69 (137)	
Lobular	17.57 (71)	18.83 (42)	16.02 (29)	
NOS	6.44 (26)	4.93 (11)	8.29 (15)	
ER status (n = 378)				.002
Negative	24.07 (91)	30.24 (62)	16.76 (29)	
Positive	75.93 (287)	69.76 (143)	83.24 (144)	
PR status (n = 379)				<.0001
Negative	39.31 (149)	48.31 (100)	28.49 (49)	
Positive	60.69 (230)	51.69 (107)	71.51 (123)	
HR status (n = 410)				<.0001
Negative	29.02 (119)	36.12 (82)	20.22 (37)	
Positive	70.98 (291)	63.88 (145)	79.78 (146)	
Ki-67 (n = 308)				.483
<14%	27.92 (86)	26.32 (45)	29.93 (41)	
≥14%	72.08 (222)	73.68 (126)	70.07 (96)	
HER2 status (n = 371)				.469
Negative	82.21 (305)	81.37 (166)	84.24 (139)	
Positive	17.25 (64)	18.63 (38)	15.76 (26)	
Luminal type (n = 330)				.0379
Luminal A-like	13.64 (45)	11.41 (21)	16.44 (24)	
Luminal B-like, HER2$^-$	53.03 (175)	49.46 (91)	57.53 (84)	
Luminal B-like, HER2$^+$	7.88 (26)	7.07 (13)	8.90 (13)	
HER2$^+$, nonluminal	10.30 (34)	12.50 (23)	7.53 (11)	
Triple negative	15.15 (50)	19.57 (36)	9.59 (14)	
Asthenia (n = 326)				.0564
No	47.55 (155)	52.69 (88)	42.14 (67)	
Yes	52.45 (171)	47.31 (79)	57.86 (92)	
Dyspnea (n = 341)				.6828
No	71.26 (243)	70.29 (123)	72.29 (120)	
Yes	28.74 (98)	29.71 (52)	27.71 (46)	
Anemia (n = 281)				.1254
No	57.30 (161)	61.64 (90)	52.59 (71)	
Yes	42.70 (120)	38.36 (56)	47.41 (64)	
Jaundice (n = 325)				.9913
No	96.31 (313)	96.32 (157)	96.30 (156)	
Yes	3.69 (12)	3.68 (6)	3.70 (6)	
Ascites (n = 322)				.7438
No	91.30 (294)	90.80 (148)	91.82 (146)	
Yes	8.70 (28)	9.20 (15)	8.18 (13)	
Pain (n = 352)				.8366
No	38.92 (137)	39.44 (71)	38.37 (66)	
Yes	61.08 (215)	60.56 (109)	61.63 (106)	
Anorexia, weight loss, cachexia (n = 337)				.4024
No	73.29 (247)	75.29 (128)	71.26 (119)	
Yes	26.71 (90)	24.71 (42)	28.74 (48)	
Liver function impairment (n = 278)				.6914
No	86.33 (240)	85.51 (118)	85.51 (122)	
Yes	13.67 (38)	14.49 (20)	12.86 (18)	
Edema (n = 319)				.2448
No	88.40 (282)	86.34 (139)	90.51 (143)	
Yes	11.60 (37)	13.66 (22)	9.49 (15)	
Pleural effusion (n = 317)				.1612
No	84.86 (269)	82.10 (133)	87.74 (136)	
Yes	15.14 (48)	17.90 (29)	12.26 (19)	
Neurologic symptoms (n = 330)				<.0001
No	74.24 (245)	84.24 (139)	64.24 (106)	
Yes	25.76 (85)	15.76 (26)	35.76 (59)	
CNS symptoms (n = 158)				.352
No	85.44 (135)	88.16 (67)	82.93 (68)	
Yes	14.56 (23)	11.84 (9)	17.07 (14)	
Pathologic fractures (n = 300)				.2625
No	95.33 (286)	93.96 (140)	96.69 (146)	
Yes	4.67 (14)	6.04 (9)	3.31 (5)	
ECOG PS at last line (n = 404)				.6321
0-1	65.35 (264)	66.37 (148)	64.09 (116)	
2-3	34.65 (140)	33.63 (75)	35.91 (65)	
Age at last line (n = 410)				.0029
<70 y	58.05 (238)	51.54 (117)	66.12 (121)	
≥70 y	41.95 (172)	48.46 (110)	33.88 (62)	

Determinants of last-line treatment in mBC: summary

	PS>1	Jaundice	Impaired liver function	Anorexia/ cachexia	Non-BC specialist
All					
<30d	X	X			
<90d	X				
Lightly pretreated					
<30d	X				
<90d			X		
Heavily pretreated					
<30d	X		X		X
<90d	X			X	

Cinausero M, Clin Breast Cancer 2017

Benefit from prior Tx line influences outcome with subsequent Tx



	Univariate analysis		Multivariate analysis	
	RR [IC 95%]	*P*	RR [IC 95%]	*P*
Prognostic factors of TDC 2				
Hormonal receptors: Negative/Positive	1.17 [1.02–1.33]	0.0208	1.23 [0.98–1.34]	0.0733
Adjuvant chemo.: No/Yes	0.86 [0.77–0.96]	0.009	0.87 [0.75–1.00]	0.0597
Metastatic site: Others/liver	0.89 [0.81–0.98]	0.022	0.83 [0.73–0.96]	0.0133
DFI: <2/≥2 years	1.24 [1.07–1.43]	0.0038	1.19 [1.03–1.37]	0.0142
TDC 1: <9/≥9 months	1.21 [1.09–1.33]	0.0002	1.17 [1.02–1.34]	0.0243
Response no/yes	1.44 [1.31–1.60]	<0.0001	1.75 [0.77–4.84]	0.1889
Prognostic factors of TDC 3				
Hormonal receptors: Negative/Positive	1.24 [1.03–1.47]	0.0223	1.19 [0.98–1.43]	0.0796
Metastatic site: Others/liver	0.85 [0.75–0.97]	0.0203	0.84 [0.71–0.98]	0.0360
TDC 2 <6/≥6 months	1.31 [1.15–1.49]	<0.0001	1.30 [1.1–1.55]	0.0024
Response no/yes	1.47 [1.26–1.72]	<0.0001	1.52 [1.25–1.87]	<0.0001
Prognostic factors of TDC 4				
TDC 3: <6/≥6 months	1.32 [1.09–1.61]	0.0054	1.31 [1.05–1.63]	0.016
Response no/yes	1.54 [1.21–2.03]	0.0004	1.50 [1.17–1.98]	0.0011
Prognostic factors of TDC 5				
TDC 4: <6/≥6 months	1.31 [0.96–1.82]	0.0883	1.15 [0.81–1.64]	0.4377
Response no/yes	1.99 [1.29–3.32]	0.0011	1.93 [1.24–3.24]	0.0029

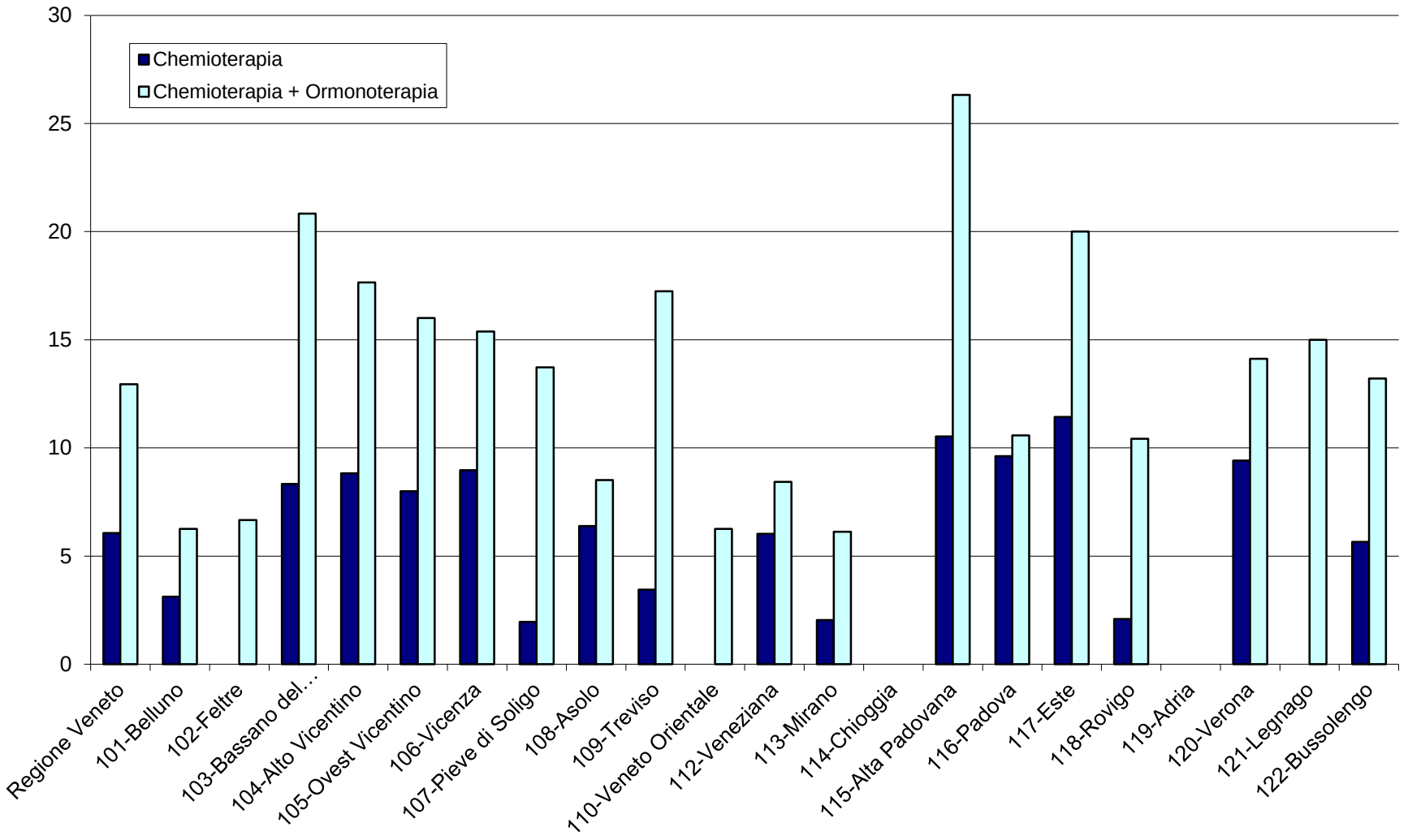
Cinausero M, Clin Breast Cancer 2017

Dufresne A, Breast Cancer Res Treat 2008

Misurazione degli Indicatori PDTA Rete Oncologica Veneta

Proporzione di pazienti che hanno ricevuto trattamento oncologico attivo 30 giorni prima del decesso

Benchmark < 10% (60/989)



Dati Rete Oncologica Veneta, anno 2016

QUESITO GRADE n.6: Cure palliative precoci

QUESITO CLINICO n. 20 (RIFERIRSI AL quesito GRADE n. 6)

Nei pazienti con carcinoma avanzato/metastatico, è raccomandabile l'integrazione delle cure palliative precoci con il trattamento oncologico rispetto al "solo practice model"?

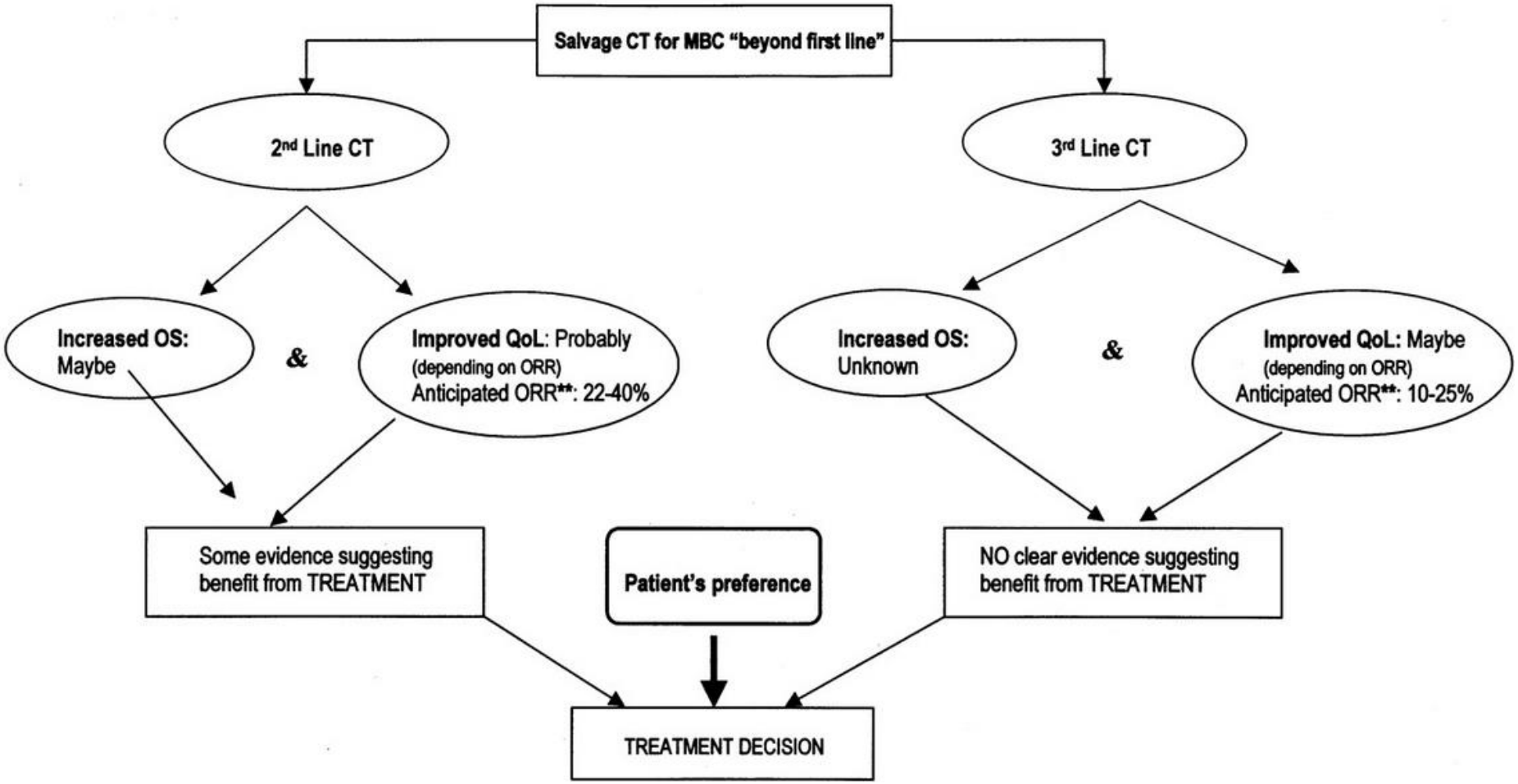
Qualità Globale delle evidenze GRADE	Raccomandazione clinica	Forza della raccomandazione clinica
Molto bassa	Nei pazienti con carcinoma avanzato/metastatico, è raccomandabile l'integrazione delle cure palliative precoci con il trattamento oncologico rispetto al "solo practice model"?	**Positiva forte (ove disponibile un team di cure pallaitive)** **Positiva debole (ove non disponibile un team di cure palliative)**

Raccomandazioni prodotte secondo metodologia GRADE

Fare riferimento all' Allegato 1 per il razionale, la sintesi delle evidenze e i dettagli alla raccomandazione

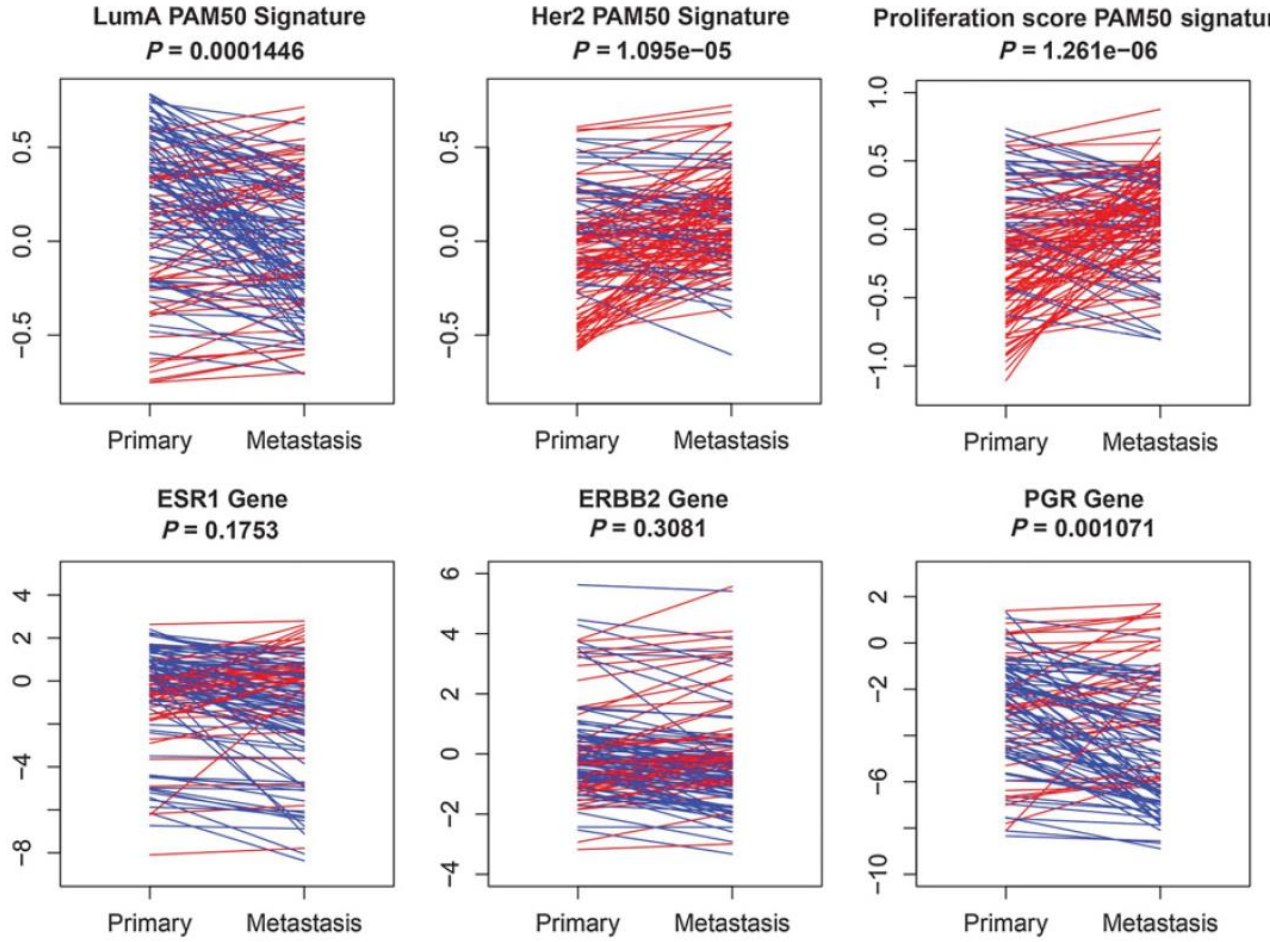
- Quesito elaborato dal WG AIOM «Cure Palliative Precoci»
- Inserito in capitolo dedicato (capitolo 13)

The scenario of mBC treatment (CT) in 2002



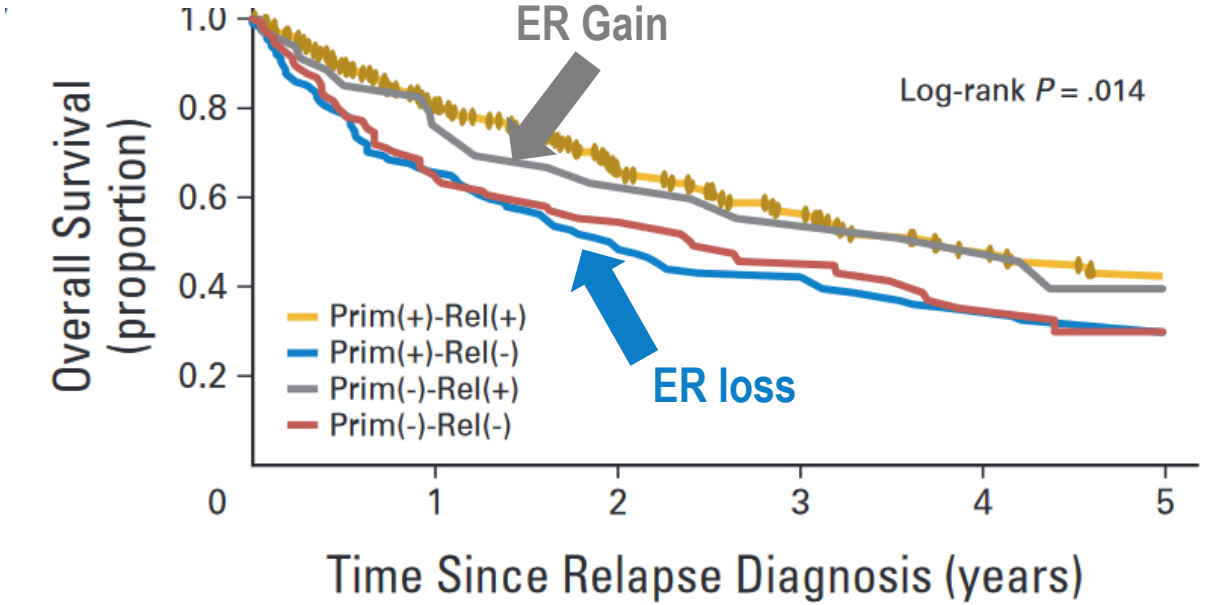
Cardoso F, Ann Oncol 2002

Gene expression in primary and matched metastatic BC samples



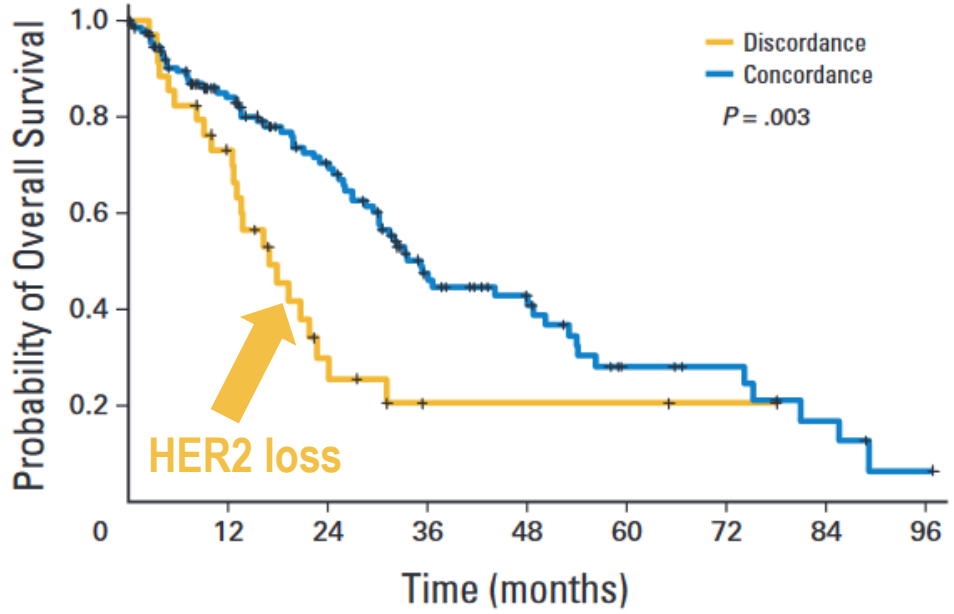
Cejalvo JM et al, Clin Cancer Res 2017

Discordance in receptor expression from primary to MBC



No. at risk						
Prim(+)-Rel(+)	216	161	112	82	59	41
Prim(+)-Rel(-)	113	69	47	35	27	17
Prim(-)-Rel(+)	36	24	19	12	10	2
Prim(-)-Rel(-)	94	55	41	29	15	10

Lindstrom LS, J Clin Oncol 2012



Discordance									
N	35	22	7	2	2	2	1	0	0
Deaths	0	9	12	2	0	0	0	0	0
Concordance									
N	133	87	63	33	22	10	8	4	1
Deaths	0	19	13	19	3	7	0	3	2

Niikura N, J Clin Oncol 2012