Any news in ABC in young women?

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Director, Breast Unit, Champalimaud Clinical Center, Lisbon, Portugal

ESMO Board of Directors & NR Committee Chair

ESO Breast Cancer Program Coordinator

EORTC Breast Group Chair

DISCLOSURES

Consultant/Ad Board:

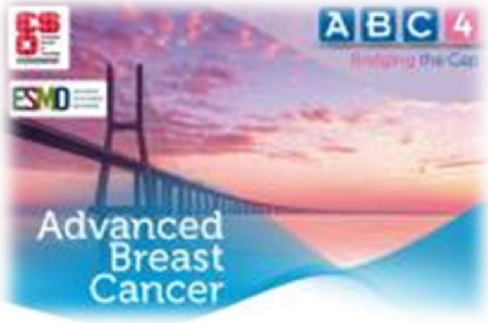
Astellas/Medivation, AstraZeneca, Celgene, Daiichi-Sankyo, Eisai, GE Oncology, Genentech, GlaxoSmithKline, Merck-Sharp, Merus BV, Novartis, Pfizer, Pierre-Fabre, Roche, Sanofi, Teva

BCY3

1.200 participants
84 countries

1070 participants
71 countries

800 participants
64 countries



Access to the report is available online

Pfizer Oncology

European School of Oncology
learning to care

www.breastcancervision.com

ABC3 www.abc-lisbon.org

GLOBAL STATUS OF mBC DECADE REPORT

here & now

Here & Now is a pan-European ABC awareness initiative from Novartis Oncology.
The campaign aims to improve understanding of the high degree of unmet need, including the social and psychological impact of ABC, ultimately to improve support and care for patients across Europe.

Campaign ambassadors

NOVARTIS
ONCOLOGY

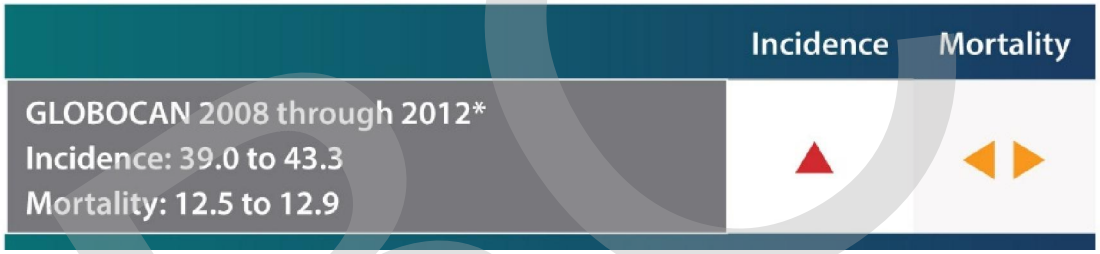
THE MAGNITUDE OF THE PROBLEM

BCY3

Breast Cancer remains a global health issue

- Breast cancer represents a significant public health burden across the globe with **increasing incidence rates**
- **Mortality rates**, predominantly due to mBC, have **remained stable at best but the absolute number of deaths is rising**
  - Wide variations exist in country specific trends
  - Approximately 20% -30% of eBC patients recur with mBC

Trends in Breast Cancer Incidence and Mortality Rates [1-3]

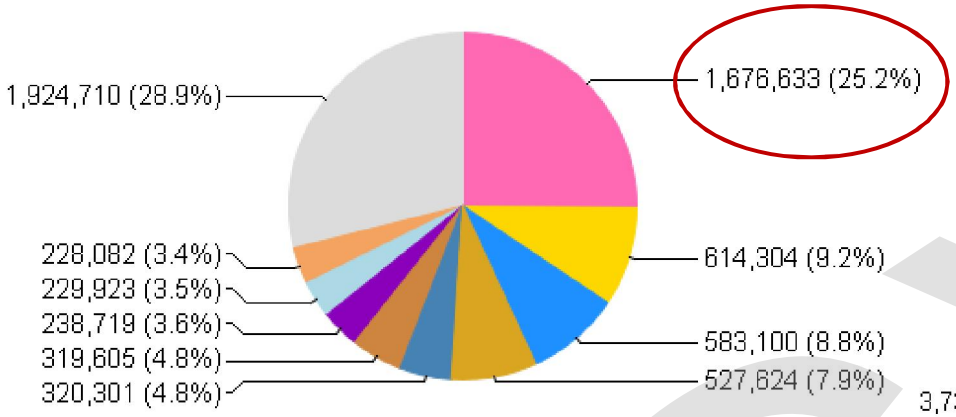


There will be an estimated **561,334 deaths** worldwide in 2015 and an estimated **805,116 by 2030**, representing a 43% increase in absolute number of deaths from BC[4]

GLOBAL STATUS OF mBC DECADE REPORT

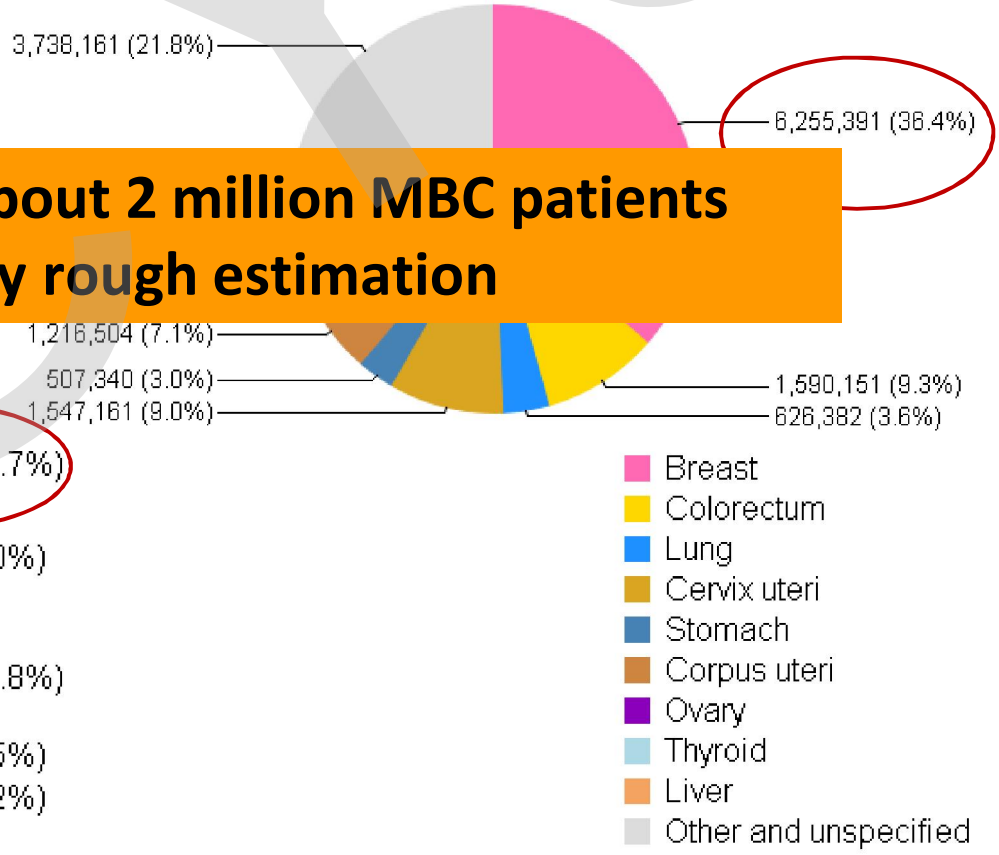
HOW MANY ABC PATIENTS EXIST?

Incidence



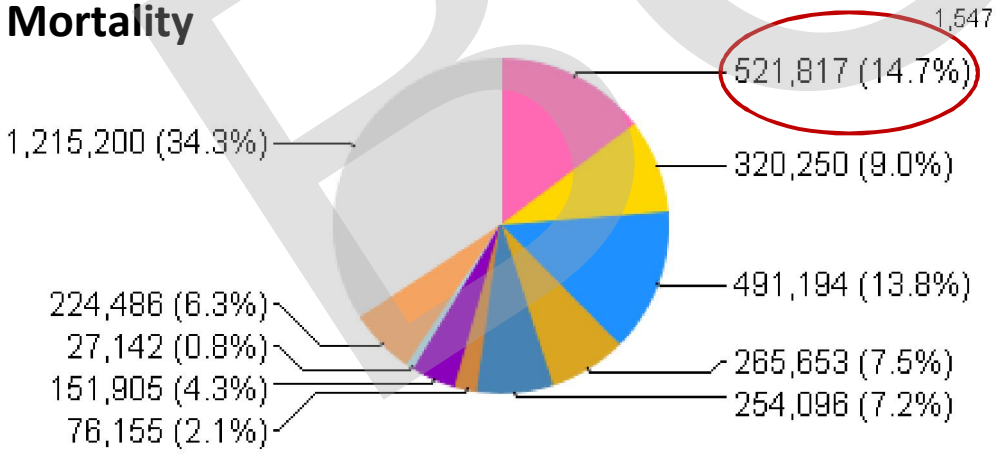
GLOBOCAN 2012 data

5-Year PREVALENCE



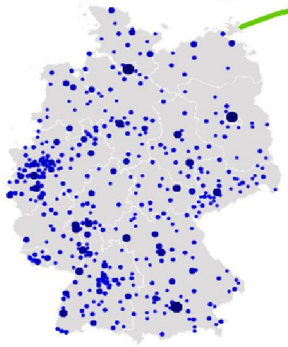
If 1 third would be MBC: about 2 million MBC patients
BUT it is just a very rough estimation

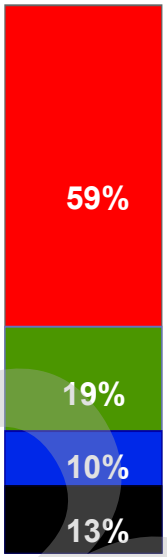
Mortality



Overall survival and sequential treatment of patients with MBC

- 134 sites, 298 oncologists, all over Germany
- > 3,700 pts/1409 ABC pts
- (goal: 4,500 BC pts/2250 ABC pts by end 2015)





HR pos
HER2 neg

HR pos
HER2 pos

HR neg
HER2 pos

triple neg

BUT
NO SUBGROUP OF YOUNG PATIENTS!

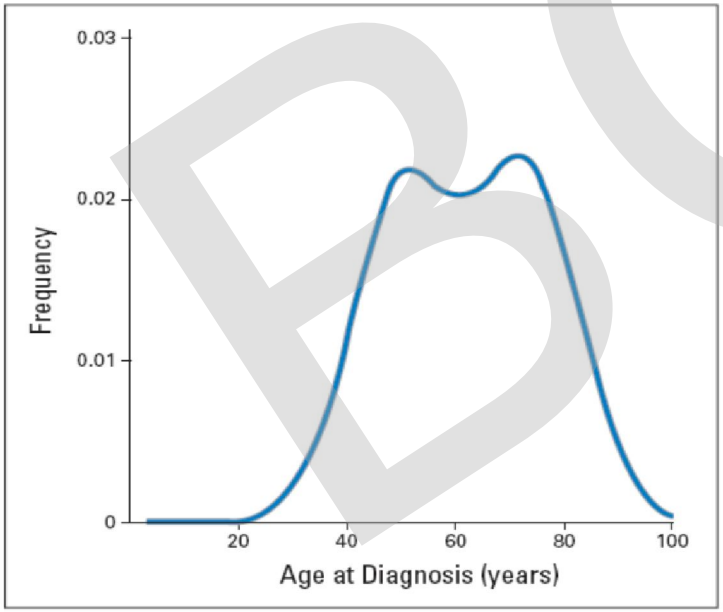
BCY3

ABC in YOUNG

DEFINITION: ABC diagnosed < 40 years

INCIDENCE (difficult to ascertain… but:)

- **Higher %** of young patients have **STAGE IV AT PRESENTATION** (~30%-35% for < 35 and ~20%-25% for < 40)
- **Higher %** of young patients with **ER neg & TNBC**
- **Worse prognosis** of EBC in very young women. Overall, 1/3 of EBC will relapse; probably higher % in young



Age	Annual incidence/100 000 women
<20	0.1
20-24	1.4
25-29	8.1
30-34	24.8
35-39	58.4
40-44	116.1
45-49	198.5

BCY3

ABC in YOUNG: OUTCOME DATA

Once it is metastatic is the outcome different?

BC Cancer Agency Survivorship Cohort (Canada)

1529 ABC patients

- Diagnosed between 01 Jan 1970 and 31 Dec 2008 inclusive
- Age at diagnosis >17 at first diagnosis
- Females only
- invasive cases only
- BC resident at first diagnosis

Exclusions:

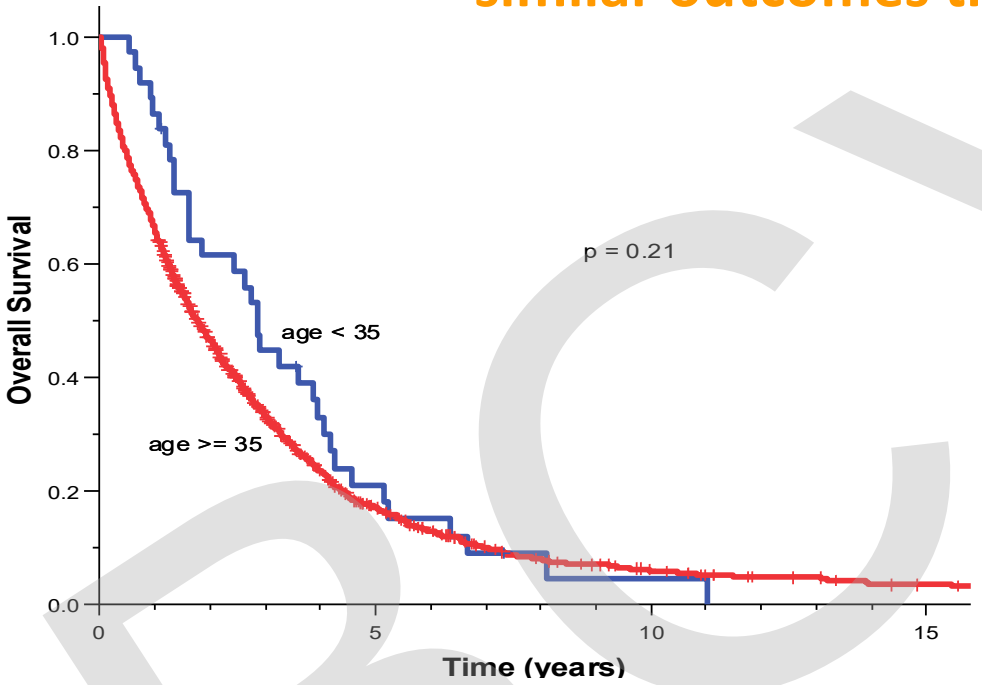
- Pts with a prior or synchronous invasive non-breast cancer with the exception of an invasive non-melanoma skin (synchronous defined as a dx of another primary cancer within 6 months of the index breast cancer)
- Stage I-III & stage unknown cases
- Stage IV cases with site of distant mets = supraclavicular nodes in cases staged with the 4th or 5th TNM version
- Cases with diagnosis date = death date

K. Gelmon, ABC 1

BCYS

OS all Stage IV pts using ≤ or > 35 years of age

Small number < 35 but apparently similar outcomes than older pts with ABC

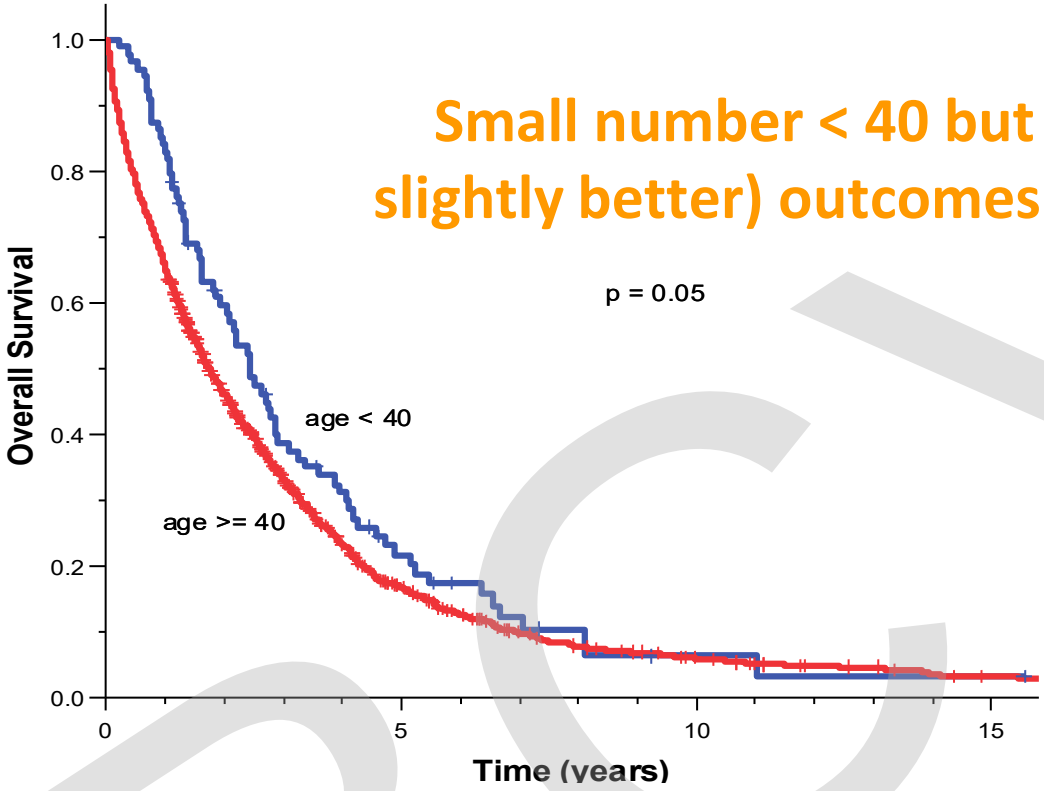


	n	3 year OS	5 year OS
Age < 35 at diagnosis	**37**	44.7 (28.2, 59.9)	20.9 (9.4, 35.7)
Age ≥ 35 at diagnosis	**1492**	33.1 (30.7, 35.6)	16.9 (14.9, 19.0)

K. Gelmon, ABC 1

BCYS

OS all Stage IV pts using 40 years of age as cut-off



Small number < 40 but apparently similar (or slightly better) outcomes than older pts with ABC

	n	3 year overall survival & 95% confidence intervals	5 year overall survival & 95% confidence intervals	p=value
Age < 40 at diagnosis	88	38.7 (28.3, 48.9)	21.6 (13.3, 31.3)	0.05
Age ≥ 40 at diagnosis	1441	33.1 (30.6, 35.6)	16.7 (14.7, 18.8)	

K. Gelmon, ABC 1

BCYS

THE BEST ENDPOINT(S)

BCY3

Strong consideration should be given to the use of validated PROMs (patient-reported outcome measures) for patients to record the symptoms of disease and side effects of treatment experienced as a regular part of clinical care.

These PROMs should be simple, and user-friendly to facilitate their use in clinical practice, and thought needs to be given to the easiest collection platform e.g iPad or smart phones.

Systematic monitoring would facilitate communication between patients and their treatment teams by better characterizing the toxicities of all anticancer therapies. This would permit early intervention of supportive care services enhancing QoL.

(LoE: I C) (87%)

BCYS

Which is/are best endpoint(s) for advanced cancer?

DOES PFS BENEFIT MATTER IF NOT ASSOCIATED WITH OS BENEFIT?

Depends!

- **on the type of disease:**
- **PD not always linked to symptoms (ovarian ≠ breast)**
- **Available therapies**

- **on the type of drug:**
- **Toxicity / QoL**
- **Affordability**

BCYS

Which is/are best endpoint(s) for MBC?

OS

Pros: 1) The most objective endpoint
2) The most desired endpoint (both for patients & physician)

Cons: 1) May be influenced by subsequent therapies
2) Needs longer follow-up

COMPOSITE ENDPOINTS
PATIENT-REPORTED OUTCOMES

Pros: 1) Less influenced by subsequent therapies
2) Obtained faster

Cons: 1) Is not a good surrogate for OS benefit
2) Not always associated with clinically meaningful benefit (only when associated with symptom control and/or low toxicity)
3) More subjective endpoint (specially in situations where response assessment is difficult (e.g. bone disease))

BOX3

We strongly recommend the use of objective scales, such as the ESMO Magnitude of Clinical Benefit Scale or the ASCO Value Framework, to evaluate the real magnitude of benefit provided by a new treatment and help prioritize funding, particularly in countries with limited resources.

(LoE: Expert opinion) (88%)

Previous statement about cost also continues approved:

The medical community is aware of the problems raised by the cost of ABC treatment. Balanced decisions should be made in all instances; patients' well being, length of life and patient's preference should always guide decisions.

(LoE: Expert opinion) (100%)

BCYB

European Society for Medical Oncology

ESMO Magnitude of Clinical Benefit Scale

BCY3

JOURNAL OF CLINICAL ONCOLOGY

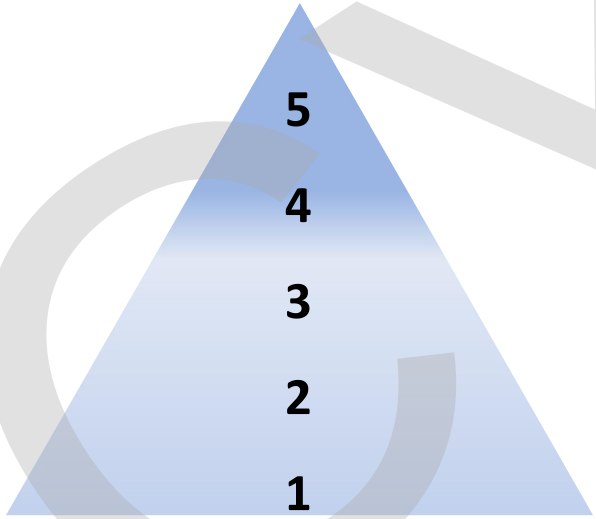
ASCO SPECIAL ARTICLE

American Society of Clinical Oncology Statement: A Conceptual Framework to Assess the Value of Cancer Treatment Options

Lowell E. Schnipper, Nancy E. Davidson, Dana S. Wollins, Courtney Tyne, Douglas W. Blayney, Diane Blum, Adam P. Dicker, Patricia A. Ganz, J. Russell Hoverman, Robert Langdon, Gary H. Lyman, Neal J. Meropol, Therese Mulvey, Lee Newcomer, Jeffrey Peppercorn, Blase Polite, Derek Raghavan, Gregory Rossi, Leonard Saltz, Deborah Schrag, Thomas J. Smith, Peter P. Yu, Clifford A. Hudis, and Richard L. Schilsky

ESMO Magnitude of Clinical Benefit Scale for new anticancer drugs

Non-curative setting



Only approved drugs & published data
Score evaluates a drug in a given setting
PFS results only (no score 5!)

BOY3

Annals of Oncology 26: 1547–1573, 2015

Evaluation form 2b: treatments with non-curative intent, primary endpoint **PFS or TTP**

Preliminary magnitude of clinical benefit grade
(highest grade scored)

3	2	1

Toxicity and QoL adjustment when only a PFS improvement

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Annals of Oncology 26: 1547–1573, 2015

BCY3

The ABC community strongly calls for clinical trials addressing important unanswered clinical questions in this setting, and not just for regulatory purposes.
Clinical trials should continue to be performed, even after approval of a new treatment, to provide real world data on its performance, efficacy and toxicity.

(LoE: Expert opinion) (100%)

BCYS

GENERAL RECOMMENDATIONS

BCY3

General recommendations

Many specific issues in the treatment of young women with BC, both in the early and in the advanced settings, still lack definitive proven standards.

Therefore, well-designed, independent, prospective randomized trials should be a global research priority

EVEN MORE TRUE FOR ABC!

General recommendations

The care of all young patients with breast cancer (either early stage, EBC, or advanced disease, ABC) should be **discussed within a multidisciplinary team before any treatment decision-making, and provided in specialized breast clinics.**

Here & Now research

here & now

96% of HCPs agree that a multidisciplinary team approach improves the level of care for patients with ABC[10]

BUT…

Over a quarter (26%) of the HCPs surveyed do not work as part of a multidisciplinary team[10]

BCN13

NOVARTIS ONCOLOGY

Advanced Breast Cancer (ABC)

(i.e. metastatic disease diagnosed before the age of 40)

MAIN MESSAGE!

Also in the metastatic setting, age alone is not a reason to prescribe more aggressive therapy and International Consensus Guidelines for management of advanced breast cancer must be applied (ABC (ESO-ESMO) and NCCN guidelines).

TREATMENT - GENERAL

The age of the patient should not be the sole reason to withhold effective therapy (in elderly patients) nor to overtreat (in young patients). Age alone should not determine the intensity of treatment. (LoE: 1 B) (100%)

The Breast 26 (2016) 87–99

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Second international consensus guidelines for breast cancer in young women (BCY2)

Shani Paluch-Shimon [a, 1], Olivia Pagani [b, 1], Ann H. Partridge [c], Eran Bar-Meir [d], Lesley Fallowfield [e], Deborah Fenlon [f], Eitan Friedman [a], Karen Gelmon [g], Oreste Gentilini [h], James Geraghty [i], Nadia Harbeck [j], Stephen Higgins [k], Sibylle Loibl [l], Elizabeth Moser [m], Fedro Peccatori [n], Hila Raanani [a], Bella Kaufman [a, 2], Fatima Cardoso [m, o, *, 2]

Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA)

Lancet Oncol 2012; 13: e148–60

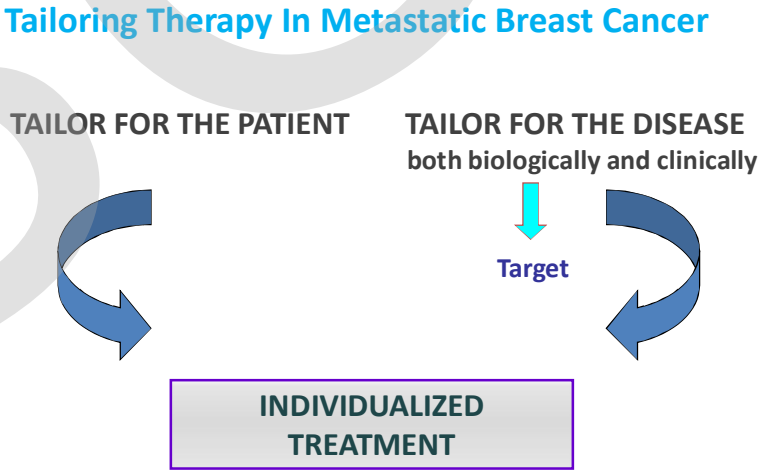
Laura Biganzoli, Hans Wildiers, Catherine Oakman, Lorenza Marotti, Sibylle Loibl, Ian Kunkler, Malcolm Reed, Stefano Ciatto, Adri C Voogd, Etienne Brain, Bruno Cutuli, Catherine Terret, Margot Gosney, Matti Aapro, Riccardo Audisio

TREATMENT - GENERAL

Treatment choice should take into account at least these factors:

HR & HER-2 status,
previous therapies and their toxicities, disease-free interval,
tumor burden (defined as number and site of metastases),
biological age, performance status, co-morbidities (including organ dysfunctions),
menopausal status (for ET),
need for a rapid disease/symptom control,
socio-economic and psychological factors,
available therapies in the patient's country
and patient preference.

(LoE: Expert opinion) (100%)



BCY3

GENERAL RECOMMENDATIONS

Following a thorough assessment and confirmation of MBC, the potential treatment goals of care should be discussed. Patients should be told that MBC is incurable but treatable, and that some patients can live with MBC for extended periods of time (many years in some circumstances).

This conversation should be conducted in accessible language, respecting patient privacy and cultural differences, and whenever possible, written information should be provided.

(LoE: Expert opinion) (97%)

BCYS

Patients with mBC need realistic, compassionate and individualized **communication**

Of 582 surveyed oncologists and other healthcare practitioners in the U.S., Europe, Latin America and Australia…

Less than 50% of healthcare professionals report having **received training** on how to bring bad news to patients and families

There is a need for patients to proactively seek involvement in decision making

Healthcare professionals reported that **only half** their **patients voice their treatment goals**

Earlier discussion on end-of-life is needed to prepare patients

In **65%** of cases, **end-of-life discussions are held too late** - first arising after multiple changes in treatment have already occurred

Breast Cancer Center Survey. Sponsored by Pfizer Oncology. August 2015

Societal attitudes towards mBC have an impact on the patient experience

48–76% of the general public **believe** that **advanced/metastatic breast cancer is curable**

- Research results confirmed that **attitudes** about mBC, particularly in developing countries, are still **extreme**
  - Diagnosis is seen as either a hopeless situation or something that can be beaten and cured
  - As a result, patients with mBC either ignore the views of the wider community or limit contact with people outside of their support network

The Challenges of Extreme Societal Opinions about mBC

Death sentence ← **mBC Attitudes** → *Curable*

Some believe people with mBC will die very soon	Others overly positive, thinking people can "beat" mBC
Driven by perception that all cancer is terrible / imminently fatal	Typically driven by visibility of success stories in eBC
Or by perception that once cancer spreads, end of life must be close	Patients themselves may believe their mBC can be cured – in some cases, the medical team appears to have painted an overly positive picture

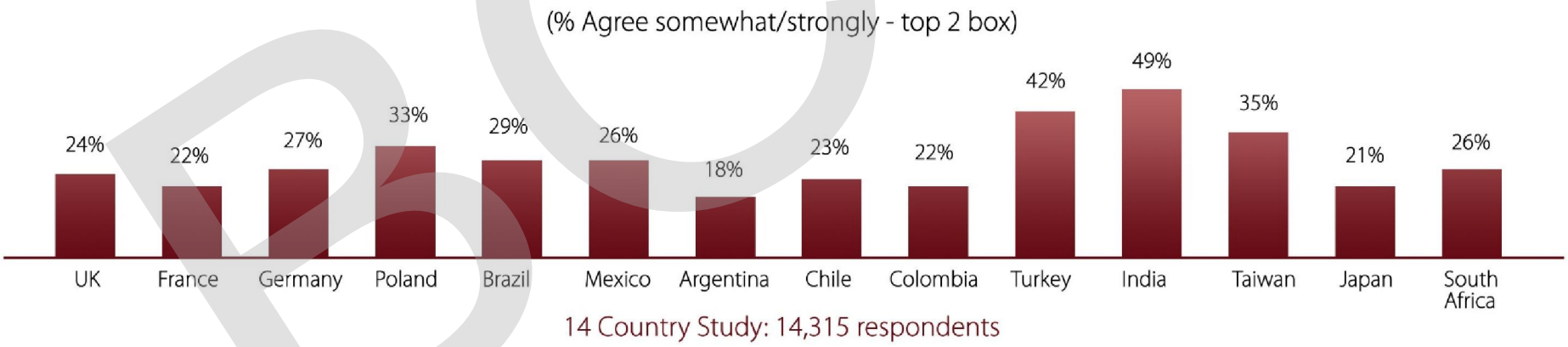
1. mBC Patient and Caregiver Qualitative Research, commissioned by Pfizer. January 2016.

BCK3

Public perceptions may perpetuate the **stigma and isolation** for mBC patients

On average, **28%** of the general population indicated that patients with mBC should **keep it a secret** and **not discuss it** with anyone other than their physician

Percentage of respondents that felt people with advanced or metastatic breast cancer should not talk about it with anyone other than their physician



GLOBAL STATUS OF mBC DECADE REPORT

mBC General Population Survey, commissioned by Pfizer. August 2015

Here & Now research

here & now

Over half of women with ABC felt they were perceived negatively by society[9]

37% of patients stated they have lost confidence or a sense of personal identity since their ABC diagnosis[9]

BCIB

NOVARTIS ONCOLOGY

SURVIVORSHIP ISSUES

ABC patients who desire to work or need to work for financial reasons should have the opportunity to do so, with needed and reasonable flexibility in their working schedules to accommodate continuous treatment and hospital visits.

(LoE: Expert opinion) (100%)

BCY3

Here & Now research

here & now

Approximately **half** of the women in employment had to change their work situation due to ABC[9]

37% of them have to give up work temporarily and or gave up work altogether[9]

56% of patients experienced a decline in household income as a result of ABC[9]

BCIS

NOVARTIS ONCOLOGY

mBC patients that return to work face immediate and long-term challenges

Many women with mBC want to work, yet in some countries, they experience **stress due to lack of job security, access to employer benefits or the effect of being unable to meet contractual commitments**[1]

Many **employers and health care providers** are **not educated** about the **impact of mBC on work**

43% to 93% of breast cancer patients **re-enter the workplace** after diagnosis, however, challenges remain. In one international study, **half of respondents with mBC who returned to work left within 1 year**[2]

Maintaining employment provides psychological, economic and societal benefits to patients with cancer or their caregivers

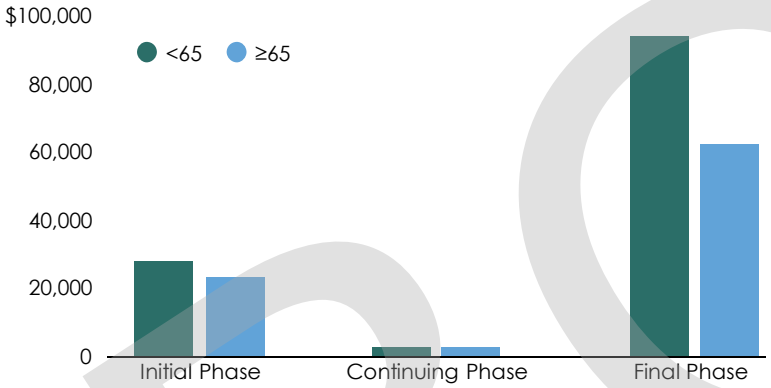
BCK

1. Canadian Breast Cancer Network. Breast Cancer: Economic Impact and Labour Force Re-Entry. 2010. 2. Corneliussen-James D. International survey identifies key support and lifestyle needs of metastatic breast cancer (mBC) patients. The Breast. 2011;20:S12-S55.

The **indirect cost burden** of mBC can be seen at **patient/family level, healthcare system and societal level**

The **costs** associated with **treating mBC** effectively are **greater than** those incurred whilst **managing early stages of breast cancer**[2]

Annualized Treatment Cost Trend for Managing BC in 2010[1]



Initial Phase = 12 months following diagnosis; continuing phase = the period between initial and final phase shown as cost per year; final phase = last 12 months of life

Disease Stage	Disability-adjusted Life Year (DALY) Averted	
	Africa/Asia	North America
Stage I,II or III	<$390	$6,550
Stage IV	>$3,500	$70,400

The **indirect costs** of mBC can account for **more than 50% of the total cost of care**[3]

1. Lidgren M, Wilking N, Jönsson B, Rehnberg C. Resource use and costs associated with different states of breast cancer. Int J Technol Assess Health Care. 2007;23(2):223-231.
2. Groot MT, Baltussen R, Uyl-de Groot C, Anderson BO, Hortobágyi GN. Costs and health effects of breast cancer interventions in epidemiologically different regions of Africa, North American, and Asia. Breast J. 2006;12(Suppl 1):s81–S90.
3. Spence D, Morstyn L, Wells K. The support and information needs of women with secondary breast cancer. Breast Cancer Network Australia (BCNA). 2015.

GLOBAL STATUS OF mBC DECADE REPORT

BCNA

SPECIFIC RECOMMENDATIONS

BCY3

ER POSITIVE / HER-2 NEGATIVE MBC

Endocrine therapy (ET) is the preferred option for hormone receptor positive disease, even in the presence of visceral disease, unless there is visceral crisis or concern/proof of endocrine resistance. (LoE: 1 A) (93%)

BCY3

VISCERAL CRISIS is defined as **severe organ dysfunction** as assessed by signs and symptoms, laboratory studies, and **rapid progression of disease.**

Visceral crisis **is not the mere presence of visceral metastases** but implies important visceral compromise leading to a clinical indication for a more rapidly efficacious therapy, particularly since another treatment option at progression will probably not be possible.

(LoE: Expert opinion) (95%)

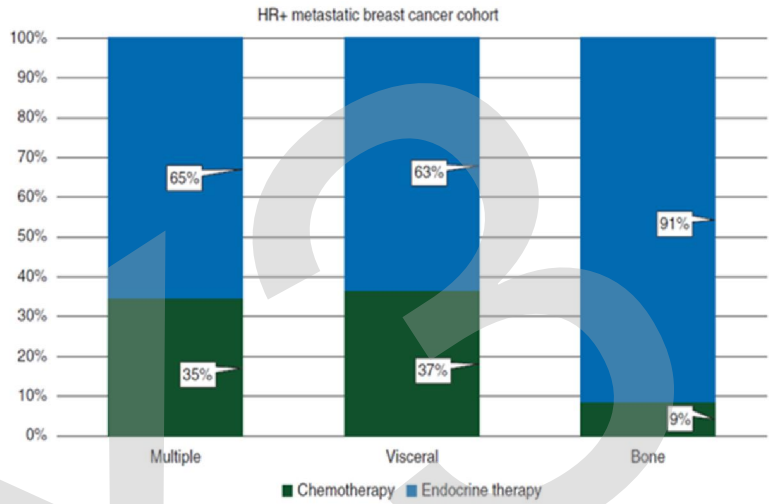
BCY3

In real life, one-quarter of patients with hormone receptor-positive metastatic breast cancer receive chemotherapy as initial palliative therapy: a study of the Southeast Netherlands Breast Cancer Consortium

D. J. A. Lobbezoo[1,2], R. J. W. van Kampen[1], A. C. Voogd[1,3], M. W. Dercksen[2], F. van den Berkmortel[4], T. J. Smilde[5], A. J. van de Wouw[6], F. P. J. Peters[7], J. M. G. H. van Riel[8], N. A. J. B. Peters[9], M. de Boer[1], P. G. M. Peer[10] & V. C. G. Tjan-Heijnen[1*]

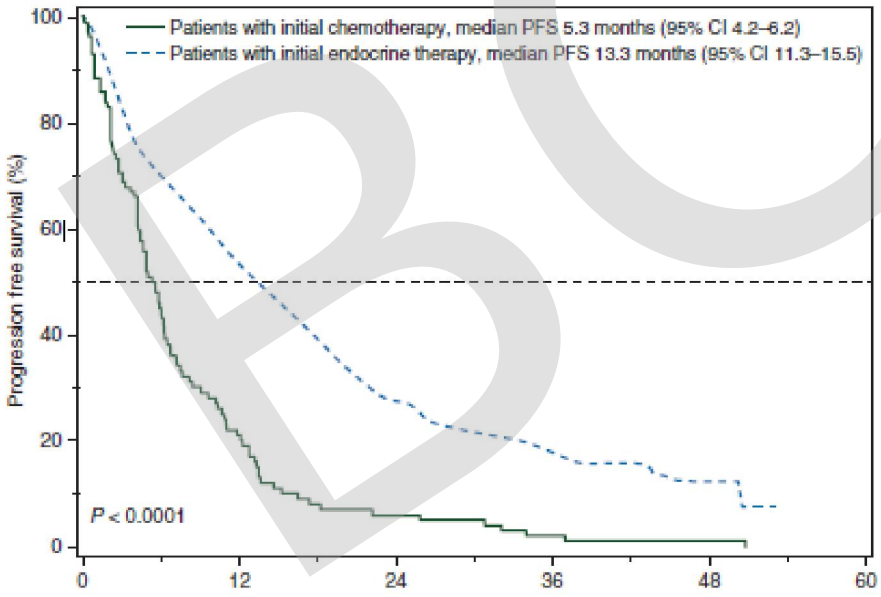
[1]GROW—School for Oncology and Developmental Biology, Maastricht University Medical Center, Maastricht; [2]Department of Internal Medicine, Máxima Medical Center, Veldhoven; [3]Netherlands Comprehensive Cancer Organisation, Utrecht; [4]Department of Internal Medicine, Atrium-Orbis Heerlen, Heerlen; [5]Department of Medical Oncology, Jeroen Bosch Hospital, Den Bosch; [6]Department of Internal Medicine, VieCuri Medical Center, Venlo; [7]Department of Internal Medicine, Atrium-Orbis Sittard, Sittard; [8]Department of Internal Medicine, St Elisabeth Hospital, Tilburg; [9]Department of Internal Medicine, St Jans Hospital, Weert; [10]Department for Health Evidence, Radboud University Medical Center, Nijmegen, The Netherlands

Received 24 May 2015; revised 28 August 2015 and 14 October 2015; accepted 26 October 2015

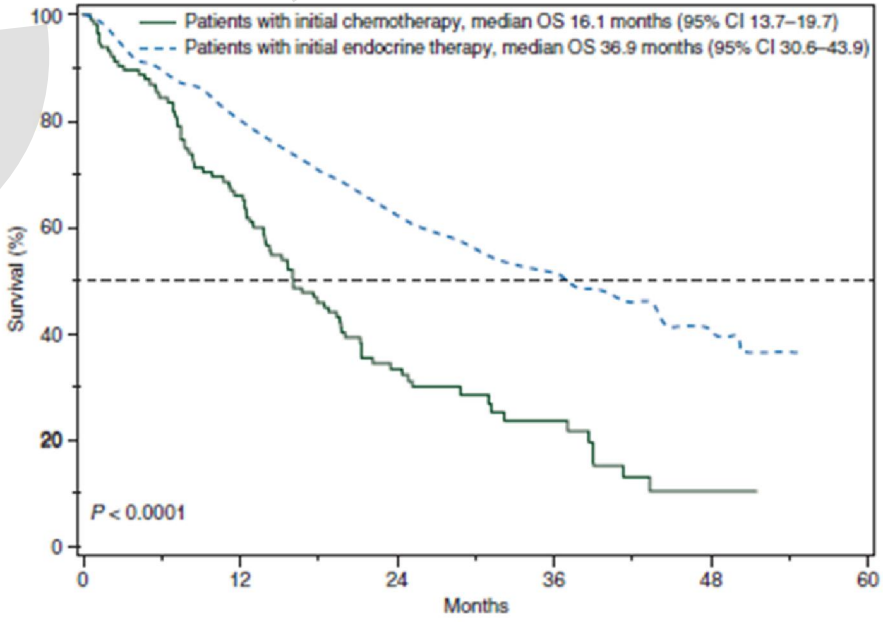


Starting with ET vs. Starting with CT

PFS



OS



BCYB

ER POSITIVE / HER-2 NEGATIVE MBC

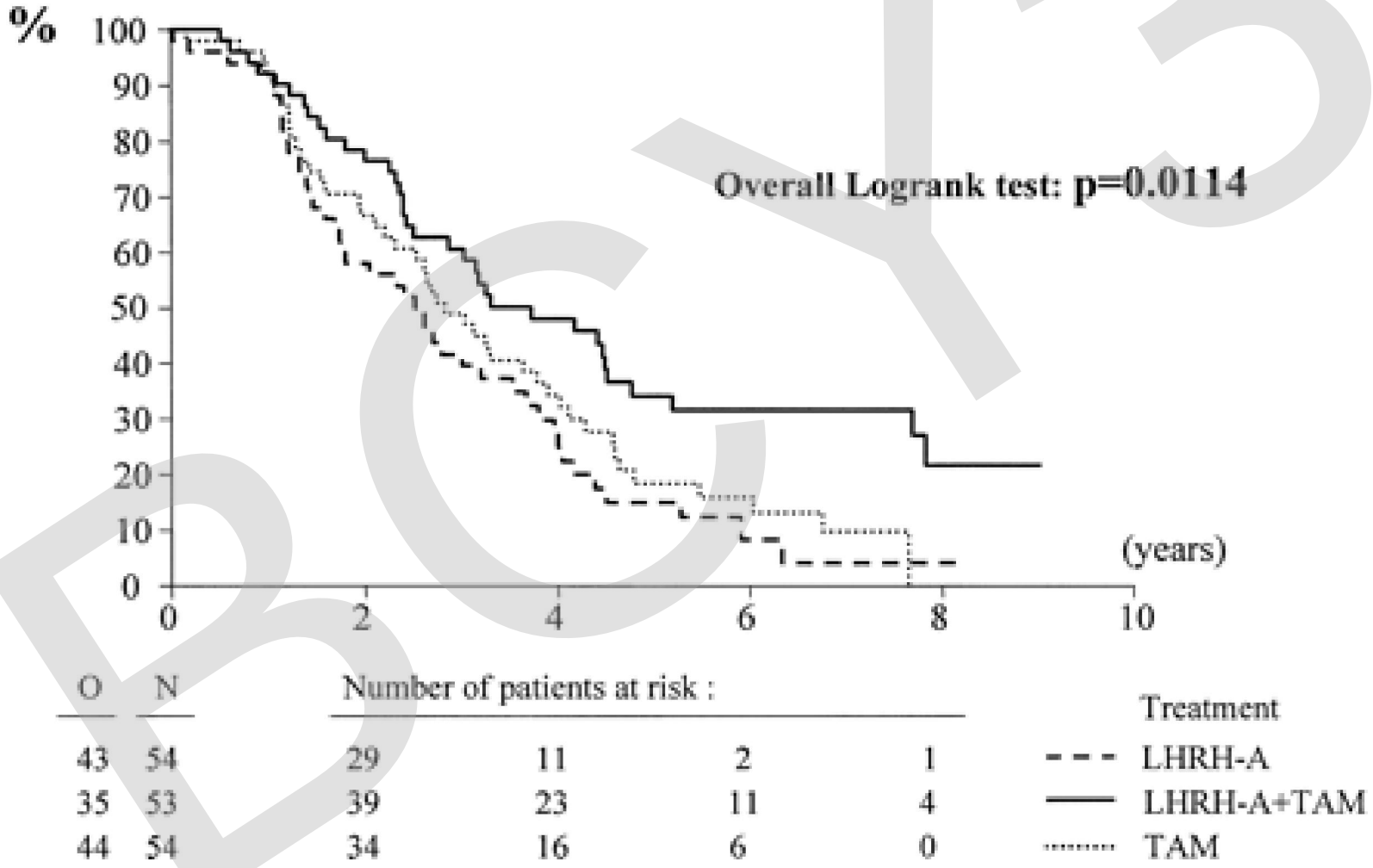
For pre-menopausal women, for whom ET was decided, ovarian suppression/ablation combined with additional endocrine therapy is the preferred choice. (LoE: 1 B) (93%)

For pre-menopausal women, the additional endocrine agent can be AI or tamoxifen, according to type and duration of prior adjuvant endocrine therapy but AI absolutely mandates the use of ovarian suppression/ablation. (LoE: 1 B) (95%)

Fulvestrant is also a valuable option, but for the moment also mandates the use of ovarian suppression/ablation. (LoE: 1 C) (95%)

BCY3

Adding OS to tamoxifen improves survival in premenopausal women with advanced disease



BCY3

(Klijn, *et al. JNCI* 2000)

PRIMARY ENDOCRINE RESISTANCE is defined as:

Relapse while on the first 2 years of adjuvant ET, or

PD within first 6 months of 1st line ET for MBC, while on ET

SECONDARY (ACQUIRED) ENDOCRINE RESISTANCE is defined as:

Relapse while on adjuvant ET but after the first 2 years, or

Relapse within 12 months of completing adjuvant ET, or

PD ≥ 6 months after initiating ET for MBC, while on ET

(LoE: Expert opinion) (67%)

Note: resistance is a continuum and these definitions help mainly clinical trials and not necessarily clinical practice

ABC3

ER POSITIVE / HER-2 NEGATIVE MBC

The addition of everolimus to an AI is a valid option for some post-menopausal patients with disease progression after a non-steroidal AI, since it significantly prolongs PFS, albeit without OS benefit.
The decision to treat must take into account the individual relevant toxicities associated with this combination and should be made on a case by case basis. (LoE: 1 B) (85%)
Tamoxifen can also be combined with everolimus. (LoE: 2 B) (85%)

MAJOR ISSUE: ALL PATIENTS INCLUDED IN TRIALS WERE POST-MENOPAUSAL

BCY3

ER POSITIVE / HER-2 NEGATIVE MBC

The addition of the CDK4/6 inhibitor palbociclib to an aromatase inhibitor, as 1st line therapy, for post-menopausal patients (except patients relapsing < 12 months from the end of adjuvant AI), provided a significant improvement in PFS (10 months), with an acceptable toxicity profile, and is therefore one of the preferred treatment options, where available. OS results are still awaited.

LoE: 1A (92%)

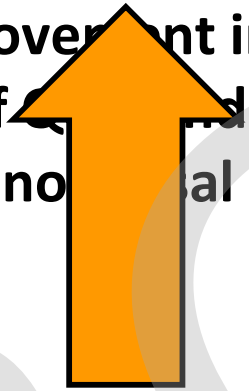
Same problem:
ALL PTS ENROLLED WERE POST-MENOPAUSAL

Statement revised after SABCS & ASCO

BCYB

ER POSITIVE / HER-2 NEGATIVE MBC

The addition of CDK4/6 inhibitor palbociclib to Fulvestrant, beyond 1st line therapy, for pre/peri/post-menopausal patients, provided significant improvement in PFS (about 5 months) as well as improvement of OS, is a treatment option. OS results are awaited. For pre/peri-menopausal pts, an LHRH-agonist must also be used.
(LoE: 1 B) (86%)



At present, no predictive biomarker other than hormone receptor status exists to identify patients who will benefit from these type of agents and research efforts must continue.

BCY3

ESMO Guidelines for the Use of First-Line Endocrine Therapy in Postmenopausal HR+ ABC

ENDOCRINE TREATMENT STRATEGY

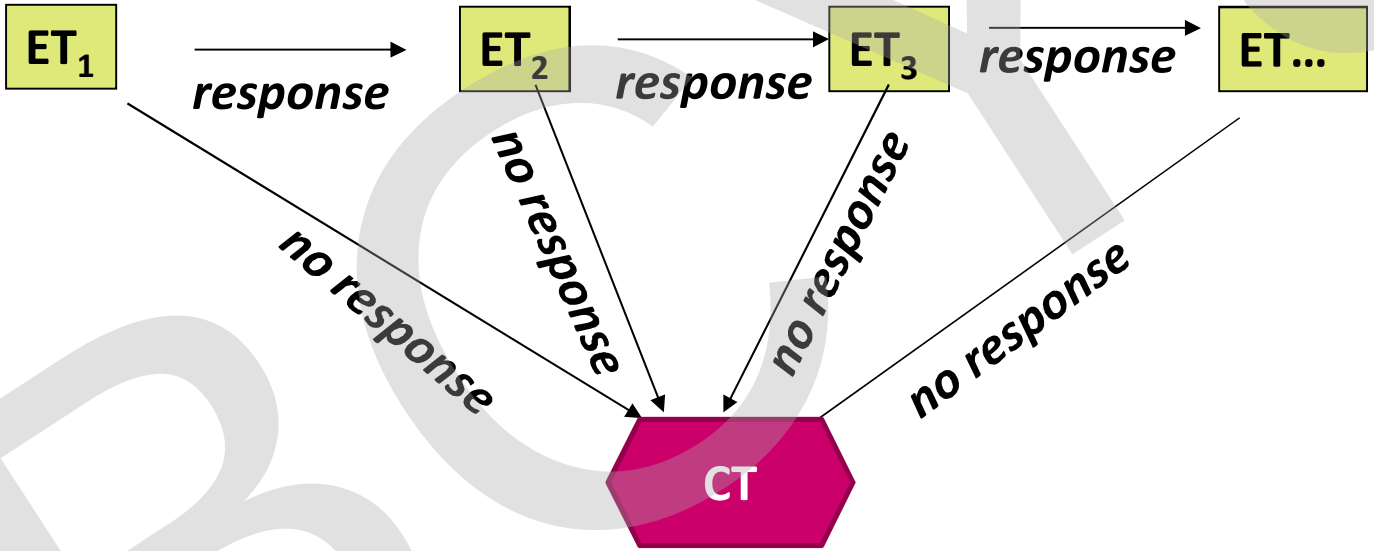


Image adapted from Senkus & Cardoso F, et al. *Ann Oncol*. 2013, ESMO GUIDELINES

BCY3

CHEMOTHERAPY (general)

Both combination and sequential single agent CT are reasonable options. Based on the available data, we recommend sequential monotherapy as the preferred choice for MBC.

Combination CT should be reserved for patients with rapid clinical progression, life-threatening visceral metastases, or need for rapid symptom and/or disease control.

(LoE: 1 B). (96%)

Please see also Cardoso et al, JNCI 2009; 101: 1174–1181

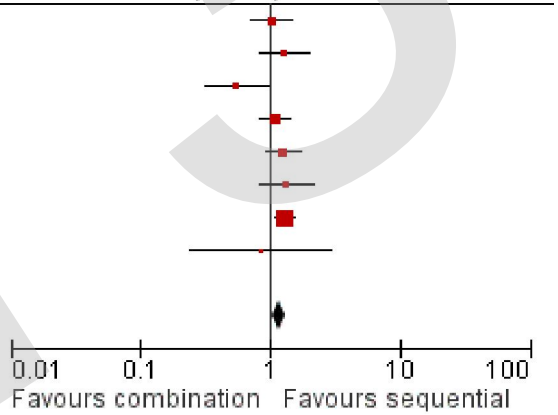
BCY3

Cochrane meta-analysis of Combination vs. Sequential monoCT for ABC

Progression-free survival (all trials)

Study or Subgroup	log[Hazard Ratio]	SE	Combination Total	Sequential Total	Weight	Hazard Ratio IV, Fixed, 95% CI
Alba 2004	0.0296	0.1827	69	75	10.7%	1.03 [0.72, 1.47]
Baker 1974	0.239	0.2295	46	30	6.8%	1.27 [0.81, 1.99]
Beslija 2006	-0.6033	0.2865	50	50	4.3%	0.55 [0.31, 0.96]
Conte 2004	0.0862	0.139	106	92	18.5%	1.09 [0.83, 1.43]
Fountzilas 2001	0.2151	0.1579	90	93	14.3%	1.24 [0.91, 1.69]
Park 2010	0.2776	0.2429	41	40	6.0%	1.32 [0.82, 2.12]
Sledge 2003	0.2469	0.0962	230	453	38.5%	1.28 [1.06, 1.55]
Tomova 2010	-0.1625	0.6415	46	53	0.9%	0.85 [0.24, 2.99]
Total (95% CI)			**678**	**886**	**100.0%**	**1.16 [1.03, 1.31]**

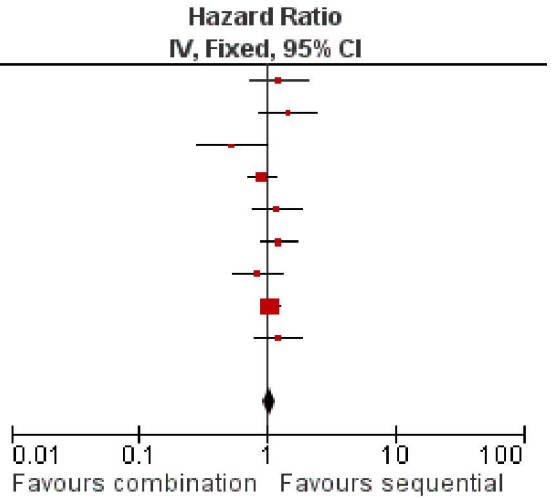
Heterogeneity: Chi² = 9.41, df = 7 (P = 0.22); I² = 26%
Test for overall effect: Z = 2.52 (P = 0.01)



Overall survival (all trials)

Study or Subgroup	log[Hazard Ratio]	SE	Combination Total	Sequential Total	Weight	Hazard Ratio IV, Fixed, 95% CI
Alba 2004	0.2151	0.2634	69	75	4.5%	1.24 [0.74, 2.08]
Baker 1974	0.3716	0.2606	46	30	4.6%	1.45 [0.87, 2.42]
Beslija 2006	-0.6387	0.3182	50	50	3.1%	0.53 [0.28, 0.99]
Chlebowski 1989	-0.1054	0.1282	129	93	19.2%	0.90 [0.70, 1.16]
Conte 2004	0.174	0.2355	106	92	5.7%	1.19 [0.75, 1.89]
Fountzilas 2001	0.1989	0.1667	90	93	11.3%	1.22 [0.88, 1.69]
Park 2010	-0.1744	0.235	41	40	5.7%	0.84 [0.53, 1.33]
Sledge 2003	0.0488	0.0901	230	453	38.8%	1.05 [0.88, 1.25]
Tomova 2010	0.1989	0.211	46	53	7.1%	1.22 [0.81, 1.84]
Total (95% CI)			**807**	**979**	**100.0%**	**1.04 [0.93, 1.16]**

Heterogeneity: Chi² = 10.54, df = 8 (P = 0.23); I² = 24%
Test for overall effect: Z = 0.76 (P = 0.45)



Dear RF et al. Combination vs. sequential single agent CT for MBC (Review) 2013

HER-2 POSITIVE MBC

NO SPECIFIC RECOMMENDATIONS FOR YOUNG WOMEN
THE SAME FOR ALL AGES!

BCY3

HER-2 POSITIVE MBC

In patients achieving a complete remission, the optimal duration of maintenance anti-HER2 therapy is unknown and needs to be balanced against treatment toxicity, logistical burden and cost.

Stopping anti-HER2 therapy, after several years of sustained complete remission, may be considered in some patients, particularly if treatment re-challenge is available in case of progression.
(LoE: Expert Opinion) (93%)

BCYB

Advanced breast cancer

Although young age has been associated with an increased risk of CNS METASTASES, surveillance and therapeutic recommendations should not differ from those for older women with the same disease characteristics and extent, since clinical and pathologic characteristics predicting for CNS recurrence often overlap with factors that indicate increased risk for general metastatic dissemination (i.e. young age, ER- and PR-negativity, HER-2 overexpression, high proliferation, and genomic instability).

TRIPLE NEGATIVE ABC

For non-BRCA-associated triple negative ABC, there are no data supporting different or specific CT recommendations. Therefore, all CT recommendations for HER-2 negative disease also apply for triple negative ABC.
(LoE: 1 A) (98%)

BCY3

TRIPLE NEGATIVE ABC

In triple-negative ABC patients (regardless of BRCA status), previously treated with anthracyclines with or without taxanes in the (neo)adjuvant setting, carboplatin demonstrated comparable efficacy and a more favorable toxicity profile, compared to docetaxel, and is therefore an important treatment option.

(LoE: 1 A) (91%)

BCY3

BRCA-associated MBC

In patients with BRCA-associated triple negative or endocrine-resistant MBC *previously treated with an anthracycline with or without a taxane* (in the adjuvant and/or metastatic setting), a platinum regimen is the preferred option, if not previously administered and no suitable clinical trial is available.

(LoE: 1 A) (86%)

All other treatment recommendations are similar to sporadic MBC.

BCY3

BRCA-associated MBC

In patients with TN or Luminal MBC, genetic counseling and possibly BRCA testing should be discussed with the patient, if the results can impact on treatment decisions and/or on clinical trials entry.

(LoE: Expert Opinion) (91%)

BC 3

Metronomic chemotherapy is a reasonable treatment option, for patients not requiring rapid tumor response.
(LoE: 1 B) (88%)

The better studied regimen is CM (low dose oral cyclophosphamide and methotrexate); other regimens are being evaluated (including capecitabine and vinorelbine).

Randomized trials are needed to accurately compare metronomic CT with standard dosing regimens.

BCY3

- **AGE-RELATED QoL issues & SUPPORTIVE INTERVENTIONS**

- **PALLIATIVE CARE: problems are different & should be addressed specifically (ex: (young) children and spouse)**

BCY3

VISION

To improve the lives of women and men living with advanced breast cancer and fight for a cure for this disease.

MISSION

The Advanced Breast Cancer (ABC) Global Alliance provides all involved partners (patient support groups, health professionals, advocates, pharmaceutical and diagnostic companies, research groups, societies, organizations and individuals) **a platform to work together in common projects** designed to improve the lives of advanced breast cancer patients worldwide.

It will also **raise awareness and lobby worldwide** for the improvement of the lives of ABC patients.

ABC GlobAlliance

All ABC Global Alliance partners commit to:

1. Develop, implement and promote **research projects** dedicated to advanced breast cancer.
2. Develop, implement and promote **education and awareness projects**, with a global, national or regional reach, aiming at improving the survival and quality of life for ABC patients.
3. Fight and work for **equal access to the best cancer care** for ABC patients, which must involve care by **multidisciplinary and specialized teams**.
4. Work for the worldwide **implementation of high quality guideline**s for the management of advanced breast cancer so that every ABC patient is treated according to these guidelines.
5. Fight and work for implementation of polices that facilitate better and equal access to care for all ABC patients, including access to the **WHO essential medicines**, access to **high quality and specialized radiation therapy** and **access to high quality palliative and supportive care, in particular pain control.**

BCY3

All ABC Global Alliance partners commit to:

6. Fight for the **implementation of polices that facilitate the right to work** for ABC patients.
7. **Raise public awareness** about ABC and the specific needs of ABC patients.
8. Fight for **access to needed services for caregivers**, including socio-economic support.
9. Enhance **education of ABC patients and health care professionals**.
10. Fight and lobby for changes in **work-related laws, clinical trials laws, and other laws** that directly affect ABC patients around the world.

BCY3

A **global Call-to-Action** is being developed, with tangible objectives for the next decade, in the various areas that impact on the lives of ABC patients.

To achieve these objectives **several projects** must be developed and implemented around the world.

The ABC Global Alliance is the platform.
The partners will run the projects (**no duplication!).**
Experienced partners mentoring/helping less experienced…Joint projects … Joint lobbying …

BCY3

PLEASE JOIN US

Patient organizations, Cancer Organizations, Pharma and Diagnostic Companies, Institutions, Foundations, Individuals, … SPARC grantees

ABCglobalalliance@eso.net

BCA3

Bridging the Gap

ABC4

European School of Oncology

learning to care

Advanced Breast Cancer

2-4 November 2017 • Lisbon, Portugal

Fourth International Consensus Conference

SAVE THE DATE

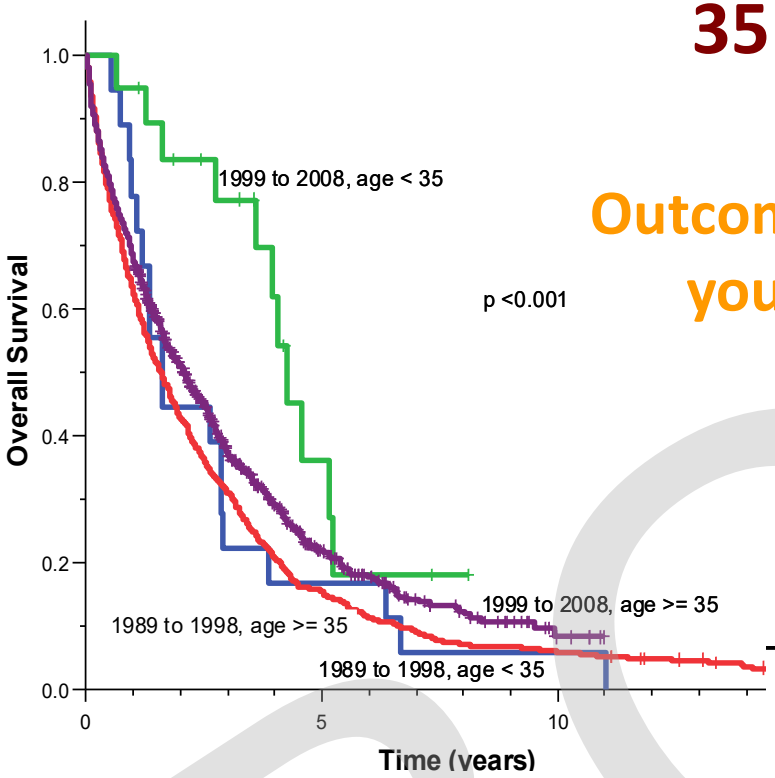
RECEIVE UPDATES AT: WWW.ABC-LISBON.ORG • #ABClisbon

BCY3

BACK-UP

BCY3

OS stage IV patients by Diagnosis Era age ≤ 35 or > 35 years of age



Outcome seems to have improved more for younger ABC pts than for older ones

… but too small numbers

Group 1 vs. group 2	-	0.88
Group 1 vs. group 3	-	0.02
Group 1 vs. group 4	-	0.67
Group 2 vs. group 3	-	0.003
Group 2 vs. group 4	-	<0.001
Group 3 vs. group 4	-	0.03

	n	3 year overall survival & 95% confidence intervals	5 year overall survival & 95% confidence intervals	p=value
1989 – 1998, age < 35 at dx (grp 1)	18	22.2 (6.9, 42.9)	16.7 (4.1, 36.5)	<0.001
1989 – 1998, age ≥ 35 at dx (grp 2)	604	31.0 (27.3, 34.7)	15.2 (12.5, 18.2)	
1999 – 2008, age < 35 at dx (grp 3)	19	77.2 (49.7, 90.8)	36.0 (12.1, 61.0)	
1999 – 2008, age ≥ 35 at dx (grp 4)	888	37.3 (34.0, 40.7)	21.9 (18.8, 25.2)	

BCY3

What is in the Literature

- There are some studies reporting young women with early breast cancer and outcomes
- Little literature about metastatic cancer and outcomes
- Small series in a variety of journals
- Many are older series
- There are nursing and quality of life papers but they are also scarce
- The biggest source of information about very young women with metastatic breast cancer are breast cancer blogs and websites

Courtesy K. Gelmon, ABC 1

BCYC