CARDIOTOSSICITÀ E SCOMPENSO

IL PARERE DELL'ONCOLOGO

Unit of Investigative Clinical Oncology (INCO)
Fondazione del Piemonte per l'Oncologia
Candiolo Cancer Institute (IRCCs)

Dott.ssa Rossella Martinello

Quali sono i farmaci oncologici che possono causare disfunzione miocardica e scompenso cardiaco?

Agenti antitumorali causa di disfunzione miocardica

Incidence of left ventricular dysfunction associated with chemotherapy drugs

Chemotherapy agents	Incidence (%)
Anthracyclines (dose dependent)	
Doxorubicin (Adriamycin) 400 mg/m² 550 mg/m² 700 mg/m²	 3–5 7–26 18–48
Idarubicin (>90 mg/m²)	5–18
Epirubicin (>900 mg/m²)	0.9–11.4
Mitoxanthone >120 mg/m²	2.6
Liposomal anthracyclines (>900 mg/m²)	2
Alkylating agents	
Cyclophosphamide	7–28
Ifosfamide <10 g/m² 12.5–16 g/m²	 0.5 17
Antimetabolites	
Clofarabine	27
Antimicrotubule agents	
Docetaxel	2.3–13
Paclitaxel	<1

Chemotherapy agents	Incidence (%)
Monoclonal antibodies	
Trastuzumab	1.7–20.1
Bevacizumab	1.6–4
Pertuzumab	0.7–1.2
Small molecule tyrosine kinase inhibitors	
Sunitinib	2.7–19
Pazopanib	7–11
Sorafenib	4–8
Dasatinib	2–4
Imatinib mesylate	0.2–2.7
Lapatinib	0.2–1.5
Nilotinib	1
Proteasome inhibitors	
Carfilzomib	11–25
Bortezomib	2–5
Miscellanous	
Everolimus	<1
Temsirolimus	<1

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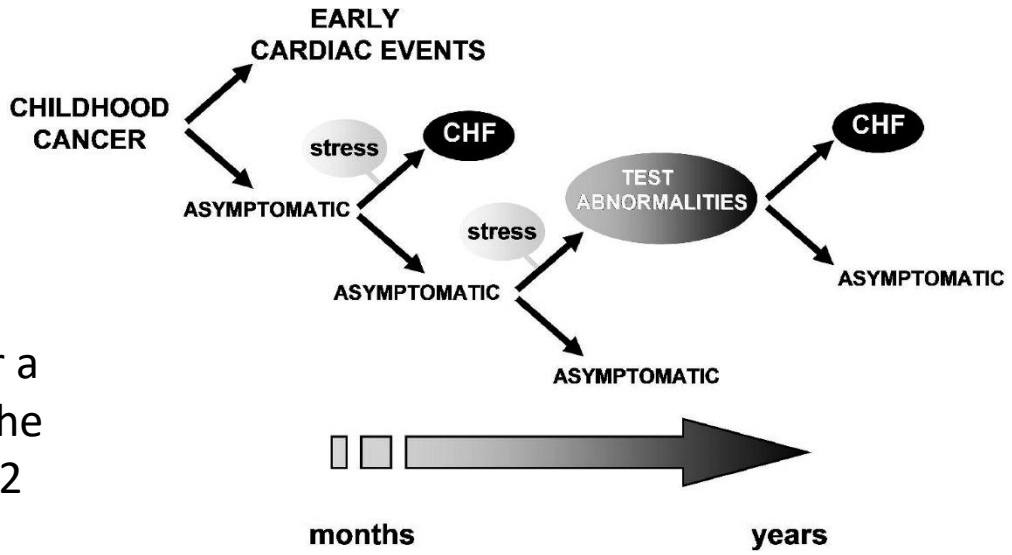
European Heart Journal (2016) 37, 2768–2801

Antracicline

- Le antracicline, antibiotici glicosidici, rappresentano una classe chemioterapici efficaci nel trattamento di un ampio spettro di tumori solidi ed ematologici
- Lo sviluppo di cardiotossicità ne limita il potenziale terapeutico andando ad impattare sulla prognosi

Tipi di Neoplasia	Schedule
Linfomi	ABVD, BEACOPP, CHOP
Leucemie	CVAD
Mammella	FEC, FAC, EC, AC, TAC
Esofago e stomaco	ECF, ECX, EOF, EOX
Sarcomi dei tessuti molli	AD, AIM, MAID
Mieloma multiplo	DT-PACE, VDT-PACE, Bortezomib/Doxorubicina/Desametasone

Cardiotossicità da Antracicline



- **Acute**: occurring after a single dose, or a single course, of anthracyclines, with the onset of clinical manifestations within 2 weeks from the end of treatment
- **Early-onset chronic**: developing within 1 year
- **Late-onset chronic**: developing years, or even decades, after the end of chemotherapy

Drug	Relative cardiotoxicity	Incidence of HF rises to >5% when cumulative dose exceeds (mg/m^2)
Doxorubicin rapid infusion	1	400
Epirubicin	0.7	900
Daunorubicin	~0.75	800
Idarubicin	0.53	150

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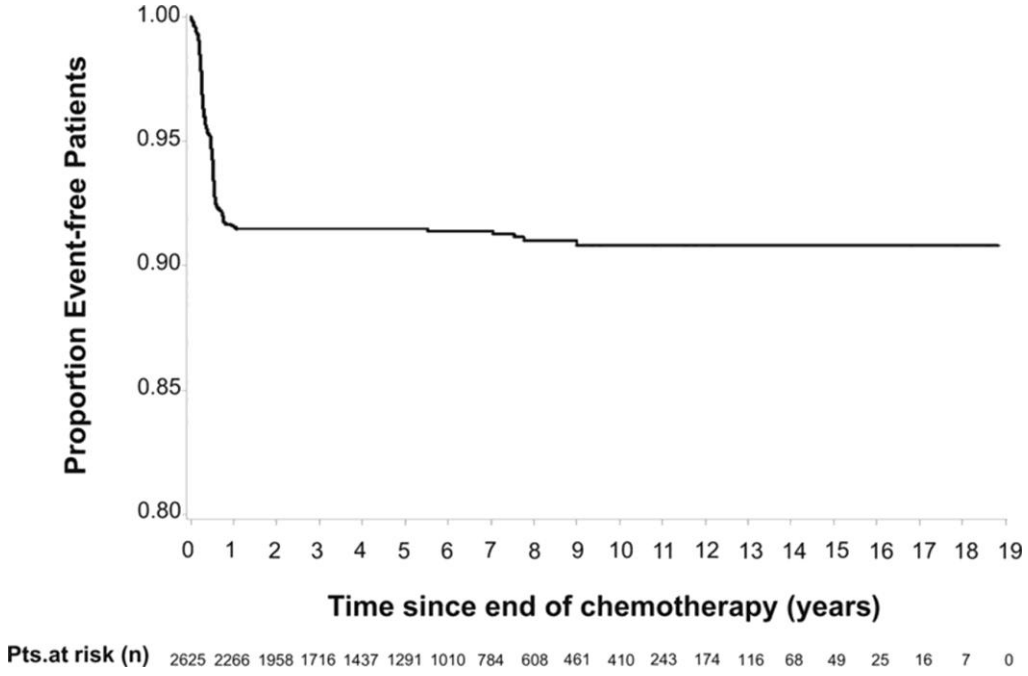
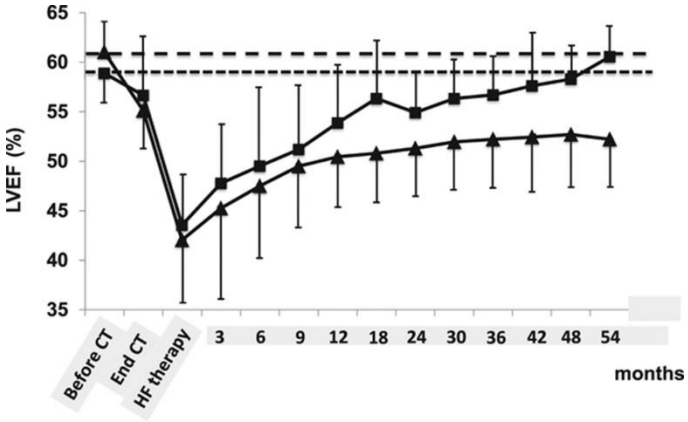
Early Detection of Anthracycline Cardiotoxicity and Improvement With Heart Failure Therapy

Cardinale D. et al. Circulation. 2015;131:1981-1988

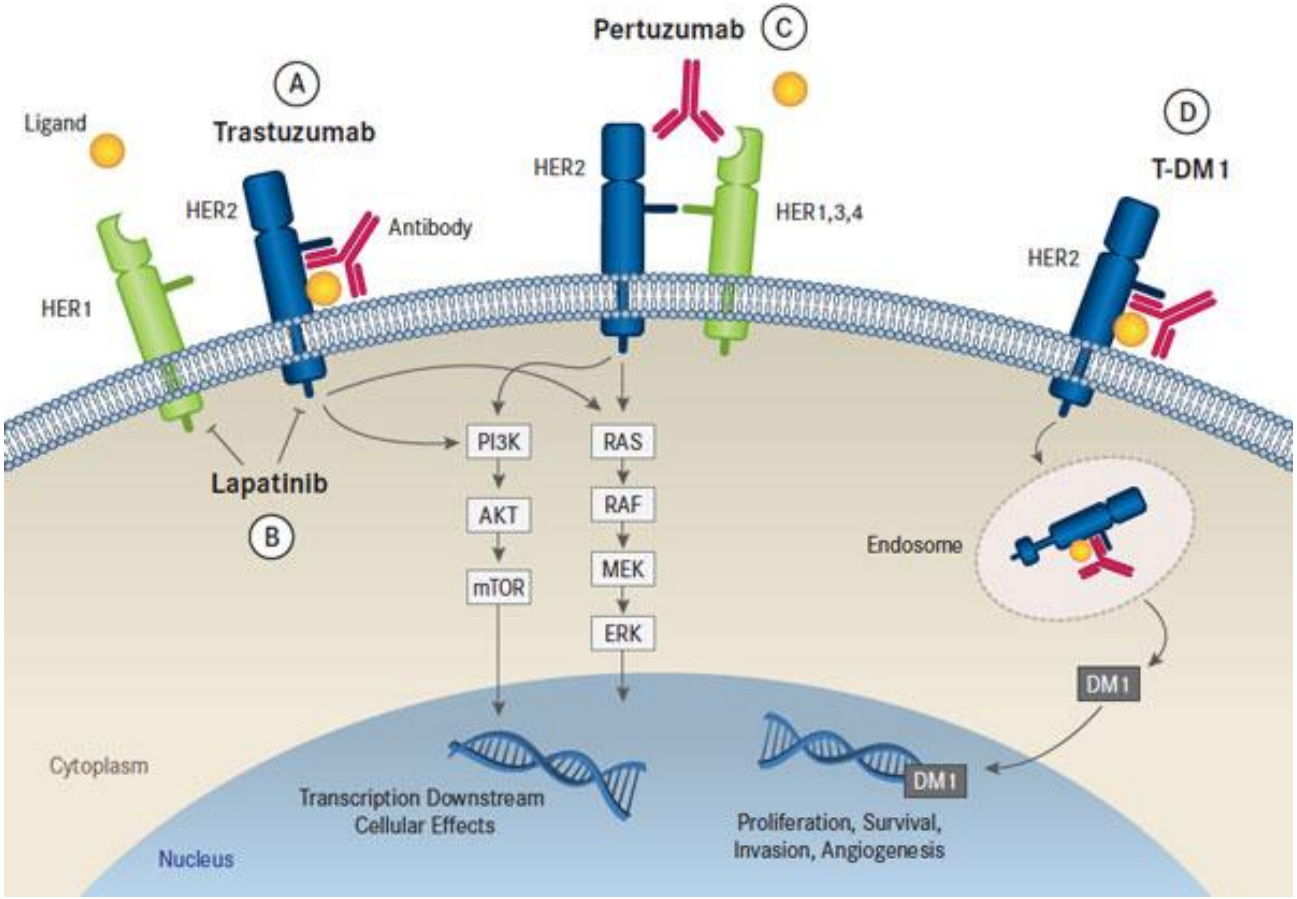


Kaplan–Meier curve showing the cumulative incidence of cardiotoxicity in the study population.



Left ventricular ejection fraction (LVEF) in patients with cardiotoxicity and with partial (triangle) or full (square) recovery with heart failure therapy

Anti HER2



Teplinsky E. 2014 http://www.onclive.com

Table 2 Trastuzumab-associated cardiotoxicity in clinical trials

Author (year)	Setting	Study design	Treatment arms	Number of patients	Any LVEF drop Number (%)	Any CHF Number (%)
Slamon *et al* (2001)[4]	MBC first line	Phase 3	AC+trastuzumab	143	Not reported	39 (27.2)
			AC	135		11 (8.1)
			Paclitaxel+trastuzumab	91		12 (13.2)
			Paclitaxel	95		1 (1.1)
Marty *et al* (2005)[22]	MBC first line	Phase 2	Docetaxel+trastuzumab	86	16 (18)	2
			Docetaxel	76	7 (8)	0
Gasparini *et al* (2007)[23]	MBC first line	Phase 2	Paclitaxel+trastuzumab	28	Not reported	0
			Paclitaxel	40	Not reported	0
Von Minckwitz *et al* (2011, 2009)[24 38]	MBC beyond first line	Phase 3	Capecitabine	78	0	0
			Capecitabine+trastuzumab	78	1 (1.28)	1 (1.28)
Kaufman *et al* (2009)[25] (Tandem)	MBC first line	Phase 3	Anastrozole+trastuzumab	103	1 (0.97)	1 (0.97)
			Anastrozole	104	0	0
Buzdar *et al* (2007)[26]	Neoadjuvant	Phase 2	FEC+paclitaxel+trastuzumab (concomitant)	45	Not reported	1
			FEC+paclitaxel	19	1	0
Gianni *et al* (2010)[27]	Neoadjuvant	Phase 3	A+paclitaxel+CMF+trastuzumab	117	30 (27)	2 (1.7)
			A+paclitaxel+CMF	217	33 (15)	0
Untch *et al* (2010)[28] (Gepar quattro)	Neoadjuvant	Phase 3	Chemotherapy+trastuzumab	445	4 (0.89)	1 (0.22)
			Chemotherapy	1050	0	2 (0.19)
Buzdar *et al* (2013)[29]	Neoadjuvant	Phase 3	FEC+paclitaxel+trastuzumab (concomitant)	142	35 (24.6)	1 (0.7)
			FEC+paclitaxel+trastuzumab (sequential)	138	21 (15.2)	0
de Azambuja *et al* (2014)[30] (HERA)	Adjuvant	Phase 3	Chemotherapy+trastuzumab 1 year	1682	120 (7.2)	19 (0.8)
			Chemotherapy+trastuzumab 2 years	1673	69 (4.1)	14 (0.8)
			Chemotherapy	1744	15 (0.9)	0
Romond *et al* (2012)[31] (NSABP-B31)	Adjuvant	Phase 3	AC+paclitaxel	743	Not reported	9 (1.2)
			AC+paclitaxel+trastuzumab	947	114 (12)	36 (3.8)
Advani *et al* (2016)[32] (N9831)	Adjuvant	Phase 3	AC+paclitaxel	664	64 (9.6)	6 (0.9)
			AC+paclitaxel+trastuzumab	710	119 (16.7)	19 (2.6)
			AC+paclitaxel/trastuzumab	570	136 (23.8)	20 (3.5)
Slamon *et al* (2011, 2015)[33 39]	Adjuvant	Phase 3	AC+docetaxel	1073	114 (11.2)	8 (0.8)
			AC+docetaxel+trastuzumab	1074	206 (19.1)	21 (2.0)
			Docetaxel+carboplatin+trastuzumab	1075	97 (9.4)	4 (0.4)
Spielman *et al* (2009)[34]	Adjuvant	Phase 3	FEC/ED	268	7 (2.6)	1 (0.37)
			EC/ED+trastuzumab	260	29 (11.1)	4 (1.5)
Joensu *et al* (2006)[35]	Adjuvant	Phase 3	Docetaxel/vinorelbine+FEC	116	0	2 (1.72)
			Docetaxel/vinorelbine+trastuzumab+FEC	115	0	1 (0.86)
Pivot *et al* (2015)[36]	Adjuvant	Phase 3	Chemotherapy+trastuzumab 6 months	1690	45 (2.7)	9 (0.53)
			Chemotherapy+trastuzumab 1 year	1690	70 (4.1)	11 (0.65)
Tolaney *et al* (2015)[37]	Adjuvant	Phase 2	Paclitaxel+trastuzumab	406	13 (3.2)	2 (0.5)

A, doxorubicin; AC, doxorubicin, cyclophosphamide; CHF, cardiac heart failure; CMF, cyclophosphamide, methotrexate, 5-fluorouracil; EC, epirubicin, cyclophosphamide; ED, epirubicin, docetaxel; FEC, 5-fluorouracil, epirubicin, cyclophosphamide; HERA, herceptin adjuvant; LVEF, left ventricular ejection fraction; MBC, metastatic breast cancer.

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Cardiotossicità da Trastuzumab

	Tipo I	Tipo II
Agenti responsabili	**Doxorubicina**	**Trastuzumab**
Tipo di decorso e risposta alla terapia cardioprotettrice	Il danno è permanente e irreversibile. C'è possibilità di stabilizzazione, ma può recidivare anche a distanza di anni	Con l'interruzione del trattamento possibilità di recupero
Dose-effetto	Dose effetto-correlata e cumulativa	Non dose effetto-correlata
Rechallenge	Alta probabilità di una disfunzione ricorrente, progressiva, che può esitare in un intrattabile scompenso cardiaco e morte	Sono necessari dati maggiori per poter valutare la possibilità di rechallenge
Danni ultrastrutturali	Vacuolizzazione, disarrangiamenti e dispersione delle miofibrille; necrosi	Non apparenti danni ultrastrutturali

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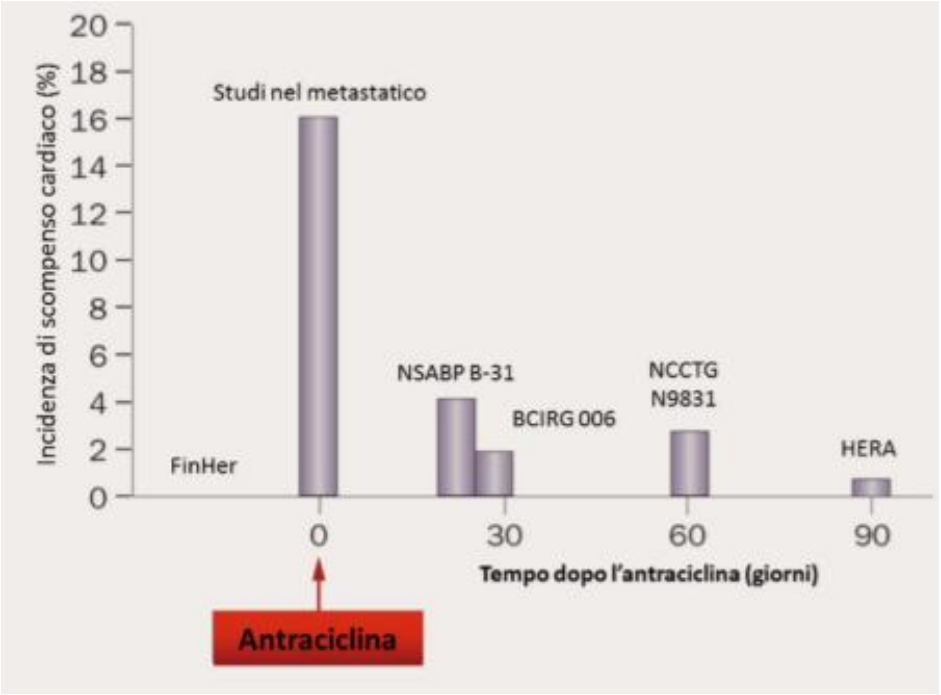
Interazioni tra antracicline e trastuzumab nel danno cardiaco



Cardiotossicità da Trastuzumab nella pratica clinica

Study	N° of pts	Age	Setting	Cardiac event	CHF
Guarneri JCO 2006	173	Median 50 y	MBC	28.3%	10.3%
Aiello Bowles J Natl Cancer Inst 2012	554	82% < 65y 18% >65 y	Adj	-	3.6-4.1%*
Chavez-MacGregor JCO 2013	2203	Median 71 y	Adj	-	29.4%
Bonifazi The Oncologist 2013	2046	68% < 60 y 32% > 60 y	Adj	2.6%**	1.4%**
Fried Breast Cancer Res Treat 2013	124	Median 51 y	Adj	22.4%	3.2%
Serrano Annals of Oncology 2012	45	Median 75.9 y	Adj and MBC	26.6%	8.9%
Tarantini J Cardiac Fail 2012	449	Median 55 y	Adj	27%	3%
ICARO Network Ann Oncol 2012	499	339 pts < 60 y 160 pts > 60 y	Adj	23% 33%	2% 6%
Farolfi Heart 2013	179	54	Adj	44%	2%

*≥1 primary discharge diagnosis, T only and T+ anthracyclines respectively
**requiring hospitalization

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Cardiac Monitoring During Adjuvant Trastuzumab-Based Chemotherapy Among Older Patients With Breast Cancer

Mariana Chavez-MacGregor, Jiangong Niu, Ning Zhang, Linda S. Elting, Benjamin D. Smith, Jose Banchs, Gabriel N. Hortobagyi, and Sharon H. Giordano

RESULTS

A total of 2,203 patients were included in this study, and the median age of the cohort was 72 years. Baseline cardiac evaluation was performed in 78.8% (n = 1,734) of the patients; 68.2% (n = 1,502) had a test within the first 4 months of trastuzumab therapy. However, subsequent monitoring (one cardiac evaluation at least every 4 months during trastuzumab therapy) was performed in 42.6% (n = 939). In the entire cohort, only 36% of the patients (n = 730) had adequate cardiac monitoring according to our definition and current guidelines (baseline test and monitoring during therapy). The pattern of moni-

Variable	Univariable		Multivariable	
	Crude OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Patients variables				
Age, years				
66-70	Reference		Reference	
71-75	0.83 (0.68 to 1.01)	.06	0.96 (0.78 to 1.18)	.68
76-80	0.61 (0.48 to 0.79)	< .001	0.78 (0.60 to 1.01)	.06
> 80	0.75 (0.56 to 1.01)	.05	0.87 (0.62 to 1.23)	.43
Year of diagnosis				
2005	Reference		Reference	
2006	1.14 (0.87 to 1.50)	.34	1.19 (0.91 to 1.56)	.2
2007	1.35 (1.01 to 1.79)	.04	1.42 (1.07 to 1.88)	.01
2008	1.52 (1.13 to 2.05)	.006	1.65 (1.21 to 2.27)	.001
2009	1.54 (1.14 to 2.06)	.004	1.83 (1.32 to 2.54)	< .001
Comorbidity				
0	Reference		Reference	
1	1.00 (0.81 to 1.24)	.99	1.18 (0.94 to 1.48)	.15
2+	0.84 (0.60 to 1.18)	.32	1.13 (0.80 to 1.60)	.49
Anthracycline				
No	Reference		Reference	
Yes	1.28 (1.08 to 1.53)	.005	1.39 (1.14 to 1.71)	.001
Hypertension				
No	Reference		Reference	
Yes	0.96 (0.81 to 1.14)	.64	0.99 (0.81 to 1.20)	.89
CAD				
No	Reference		Reference	
Yes	0.75 (0.53 to 1.06)	.10	0.86 (0.61 to 1.22)	.40
Physician variables				
Decade of graduation				
Prior to 1980	Reference		Reference	
1980-1989	1.2 (0.94 to 1.52)	.45	1.21 (0.95 to 1.55)	.12
After 1990	1.93 (1.53 to 2.44)	< .001	1.66 (1.29 to 2.12)	< .001
Sex of physician				
Male	Reference		Reference	
Female	1.75 (1.42 to 2.16)	< .001	1.37 (1.10 to 1.70)	.005

Table 3 Cardiotoxicity in the main phase 3 clinical trials with the use of anti-HER2 targeted agents other than trastuzumab

Author	Setting	Treatment arms	Number of patients	LVEF drop (≥10 points and <50%) N (%)	CHF N (%)
Pertuzumab					
Swain *et al*[49]	MBC, first-line	Docetaxel+trastuzumab +placebo	396	27 (6.6)	13 (3.3)
		Docetaxel+trastuzumab +pertuzumab	408	27 (6.6)	6 (1.5)
T-DM1					
Verma *et al*[67]	MBC, first-line and beyond first-line	T-DM1	495	8 (1.7)	1 (0.2)
		Lapatinib+capecitabine	496	7 (1.6)	0 (0.0)
Krop *et al*[68]	MBC, beyond first-line	T-DM1	404	6 (1.0)	0 (0.0)
		Treatment of physician's choice	198	2 (1.0)	0 (0.0)
Lapatinib					
Geyer *et al*[69]	MBC, beyond first-line	Lapatinib+capecitabine	163	4 (2.5)	0 (0.0)
Cameron *et al*[70]		Capecitabine	161	4 (2.5)	0 (0.0)
de Azambuja *et al*[71]	Neoadjuvant setting	Lapatinib+paclitaxel	154	2 (1.3)	1 (0.6)
		Trastuzumab+paclitaxel	149	2 (1.3)	0 (0.0)
		Lapatinib+trastuzumab +paclitaxel	152	7 (4.6)	2 (1.3)
Piccart-Gebhart *et al*[72]	Adjuvant setting	CT+trastuzumab	2097	97 (4.6)	53 (2.5)
		CT+lapatinib	2100	63 (3.0)	37 (1.8)
		CT+trastuzumab → lapatinib	2091	57 (2.7)	37 (1.8)
		CT+trastuzumab +lapatinib	2093	103 (4.9)	68 (3.2)
Neratinib and afatinib					
Harbeck *et al*[73]	MBC, first-line and beyond first-line	Afatinib+vinorelbine	332	1 (0.3)	0 (0.0)
		Trastuzumab+vinorelbine	168	3 (1.8)	2 (1.2)
Awada *et al*[74]	MBC, first-line	Neratinib+paclitaxel	242	Not reported 3 (1.3%)*	Not reported
		Trastuzumab+paclitaxel	237	Not reported 7 (3.0)*	Not reported
Chan *et al*[75]	Adjuvant setting	Neratinib	1420	4 (0.3)	1 (0.1)
		Placebo	1420	2 (0.1)	0 (0.0)

*Defined as CHF, decreased LVEF, LVSD and peripheral oedema.
CHF, cardiac heart failure; CT, chemotherapy; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic dysfunction; MBC, metastatic breast cancer; T-DM1, trastuzumab-emtansine.

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Cardiotossicità da anti-HER2

Come prevenire lo scompenso cardiaco da farmaci antitumorali?

Strategie di prevenzione

- Individuare i pazienti a rischio di sviluppare scompenso cardiaco
  - Riconoscimento dei fattori di rischio
  - Correzione dei fattori di rischio modificabili
  - Educazione del paziente
  - Identificazione delle comorbidità cardiovascolari preesistenti
  - Adeguamento della terapia cardiologica
- Adeguare il trattamento antitumorale
  - Utilizzo delle antracicline liposomiali
  - Schemi non contenenti antracicline
  - Sistemi di cardioprotezione
- Appropriato monitoraggio
  - Imaging cardiaco seriato
  - Marker predittivi di disfunzione ventricolare

Strategie di prevenzione

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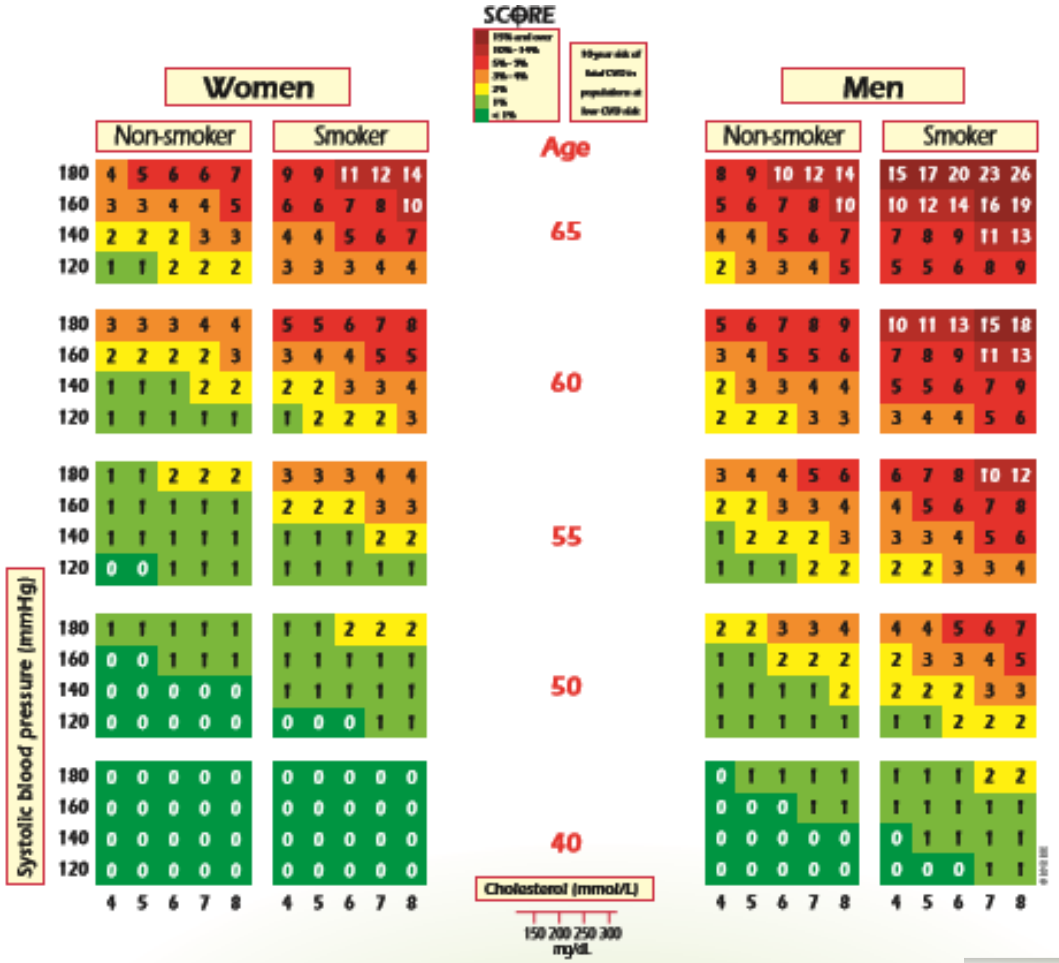
Rischio cardiovascolare nella popolazione generale



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Source: European Guidelines on CVD Prevention in Clinical Practice (2012)
European Heart Journal (2012) 33, 1635–1701 - doi:10.1093/eurheartj/ehs092

Rischio cardiovascolare nella popolazione trattata

Factors associated with risk of cardiotoxicity following treatment with anthracyclines

Risk factors

- Cumulative dose
- Female sex
- Age
  - >65 years old
  - Paediatric population (<18 years)
- Renal failure
- Concomitant or previous radiation therapy involving the heart
- Concomitant chemotherapy
  - alkylating or antimicrotubule agents
  - immuno- and targeted therapies
- Pre-existing conditions
  - Cardiac diseases associating increased wall stress
  - Arterial hypertension
  - Genetic factors

Factors associated with risk of cardiotoxicity following anti HER2compounds and VEGF inhibitors

Agent	Risk factors
Anti-HER2 compounds	
– Antibodies - Trastuzumab - Pertuzumab - T-DM1 – Tyrosine kinase inhibitor - Lapatinib	• Previous or concomitant anthracycline treatment *(short time between anthracycline and anti-HER2 treatment)* • Age (>65 years) • High BMI >30 kg/mg^2 • Previous LV dysfunction • Arterial hypertension • Previous radiation therapy
VEGF inhibitors	
– Antibodies - Bevacizumab - Ramucirumab	Pre-existing HF, significant CAD or left side VHD (e.g. mitral regurgitation), chronic ischaemic cardiomyopathy • Previous anthracycline
– Tyrosine kinase inhibitors - Sunitinib - Pazopanib - Axitinib - Neratinib - Afatinib - Sorafenib - Dasatinib	• Arterial hypertension • Pre-existing cardiac disease

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European Heart Journal (2016) 37, 2768–2801

Strategie di prevenzione

- Individuare i pazienti a rischio di sviluppare scompenso cardiaco
  - Riconoscimento dei fattori di rischio
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  - Imaging cardiaco seriato
  - Marker predittivi di disfunzione ventricolare

Schedule di trattamento prive di Antracicline

Adjuvant docetaxel and cyclophosphamide plus trastuzumab in patients with *HER2*-amplified early stage breast cancer: a single-group, open-label, phase 2 study

Stephen E Jones, Rufus Collea, Devchand Paul, Scot Sedlacek, Anne M Favret, Ira Gore Jr, Deborah L Lindquist, Frankie Ann Holmes, Mary Ann K Allison, Barry D Brooks, Raul M Portillo, Svetislava J Vukelja, Michael S Steinberg, Christopher Stokoe, Maria W Crockett, Yunfei Wang, Lina Asmar, Nicholas J Robert, Joyce O'Shaughnessy Lancet Oncol 2013; 14: 1121–28

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JOURNAL OF CLINICAL ONCOLOGY

Docetaxel With Cyclophosphamide Is Associated With an Overall Survival Benefit Compared With Doxorubicin and Cyclophosphamide: 7-Year Follow-Up of US Oncology Research Trial 9735

Stephen Jones, Frankie Ann Holmes, Joyce O'Shaughnessy, Joanne L. Blum, Svetislava J. Vukelja, Kristi J. McIntyre, John E. Pippen, James H. Bordelon, Robert L. Kirby, John Sandbach, William J. Hyman, Donald A. Richards, Robert G. Mennel, Kristi A. Boehm, Wally G. Meyer, Lina Asmar, Daniel Mackey, Stefan Riedel, Hyman Muss, and Michael A. Savin

The NEW ENGLAND JOURNAL of MEDICINE

Adjuvant Paclitaxel and Trastuzumab for Node-Negative, HER2-Positive Breast Cancer

Sara M. Tolaney, M.D., M.P.H., William T. Barry, Ph.D., Chau T. Dang, M.D., Denise A. Yardley, M.D., Beverly Moy, M.D., M.P.H., P. Kelly Marcom, M.D., Kathy S. Albain, M.D., Hope S. Rugo, M.D., Matthew Ellis, M.B., B.Chir., Ph.D., Iuliana Shapira, M.D., Antonio C. Wolff, M.D., Lisa A. Carey, M.D., Beth A. Overmoyer, M.D., Ann H. Partridge, M.D., M.P.H., Hao Guo, M.S., Clifford A. Hudis, M.D., Ian E. Krop, M.D., Ph.D., Harold J. Burstein, M.D., Ph.D., and Eric P. Winer, M.D.

Cardioprevenzione_Studio MANTICORE 101

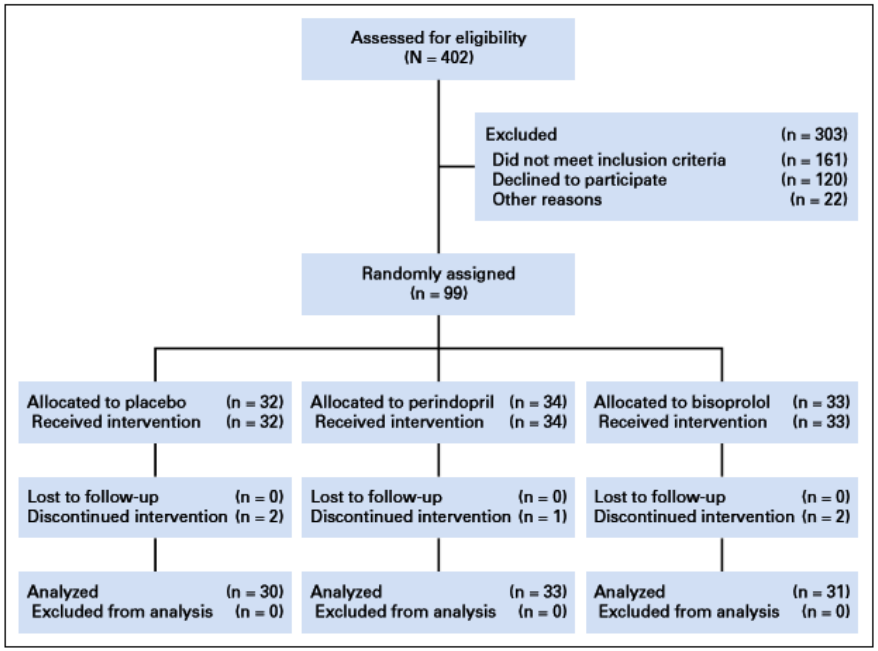


Table 4. Multivariable Model for Contributors to the Change in LVEDVi and LVEF

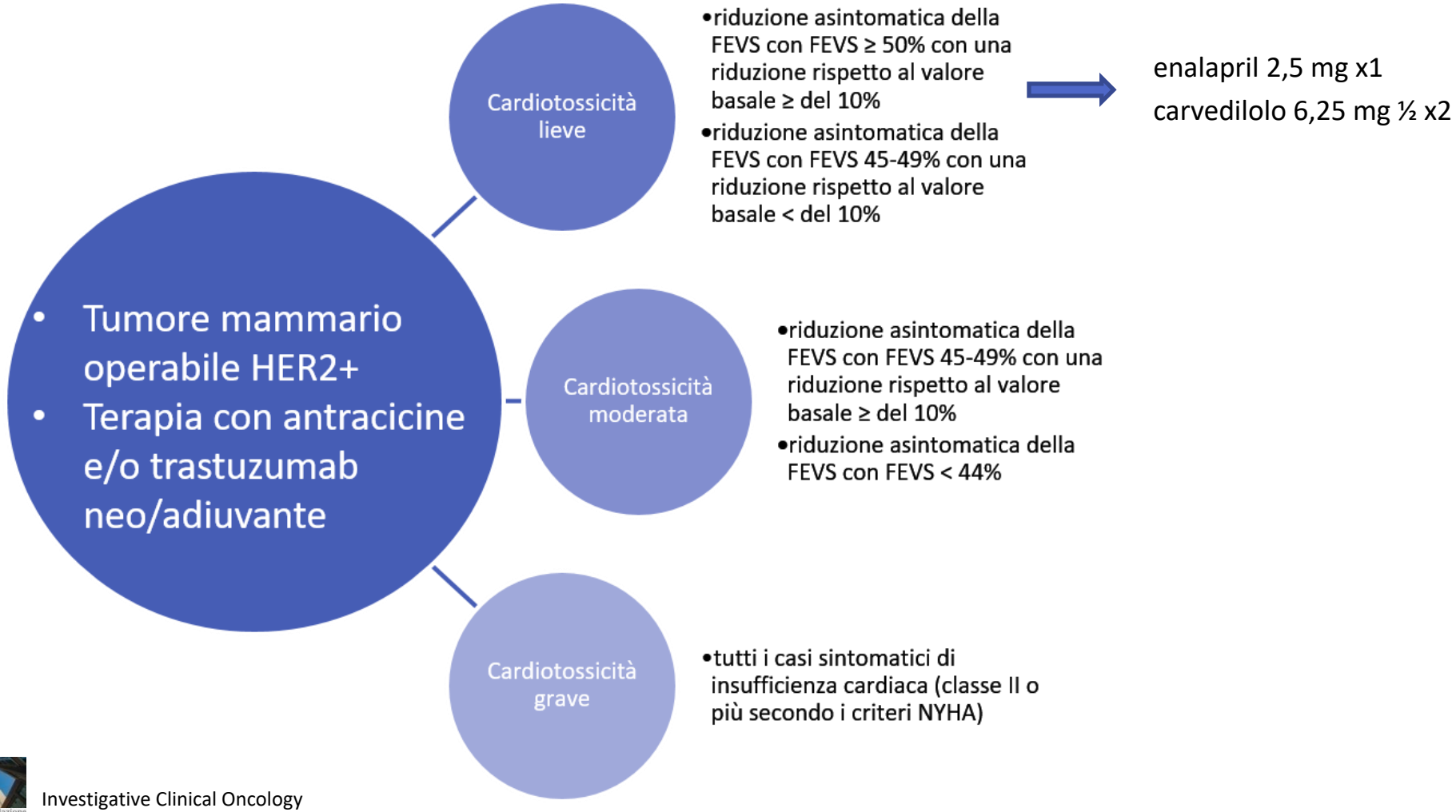
Characteristic by Outcome Variable	β	95% CI	*P*
ΔLVEDVi			
Treatment group			
Perindopril	.892	−5.040 to 6.824	.766
Bisoprolol	1.580	−4.198 to 7.357	.588
Age	−.103	−0.401 to 0.194	.492
Baseline LVEDVi	−.528	−0.880 to −0.175	.004
Baseline LVESVi	.358	−0.278 to 0.994	.266
Baseline LV MASSi	.144	−0.254 to 0.543	.473
Anthracycline chemotherapy	−2.135	−7.958 to 3.689	.468
Left chest irradiation	3.605	−1.140 to 8.350	.135
ΔLVEF			
Treatment group			
Perindopril	2.594	0.495 to 4.693	.016
Bisoprolol	4.560	2.440 to 6.680	< .001
Age	.085	−0.018 to 0.188	.103
Baseline LVEF	−.561	−0.749 to −0.374	< .001
Anthracycline chemotherapy	−.364	−2.487 to 1.759	.734
Left chest irradiation	.703	−1.062 to 2.467	.431

Abbreviations: LVEDVi, indexed left ventricular end diastolic volume; LVEF, left ventricular ejection fraction; LVESVi, indexed left ventricular end systolic volume; LV MASSi, indexed left ventricular mass.

Interruptions in trastuzumab therapy as a result of LV dysfunction were fewer among the perindopril-treated (3 of 33 patients) and bisoprolol-treated (3 of 31 patients) groups compared with placebo (9 of 30 patients; P=.03).

Pituskin E. et al. J Clin Oncol 2016

CARDIORETE_trial in corso



Strategie di prevenzione

- Individuare i pazienti a rischio di sviluppare scompenso cardiaco
  - Riconoscimento dei fattori di rischio
  - Correzione dei fattori di rischio modificabili
  - Educazione del paziente
  - Identificazione delle comorbidità cardiovascolari preesistenti
  - Adeguamento della terapia cardiologica
- Adeguare il trattamento antitumorale
  - Utilizzo delle antracicline liposomiali
  - Schemi non contenenti antracicline
  - Sistemi di cardioprotezione
- Appropriato monitoraggio
  - Imaging cardiaco seriato
  - Marker predittivi di disfunzione ventricolare

Cardio-Onco-Hematology in Clinical Practice. Position Paper and Recommendations

Lopez-Fernandez et al.Rev Esp Cardiol. 2017

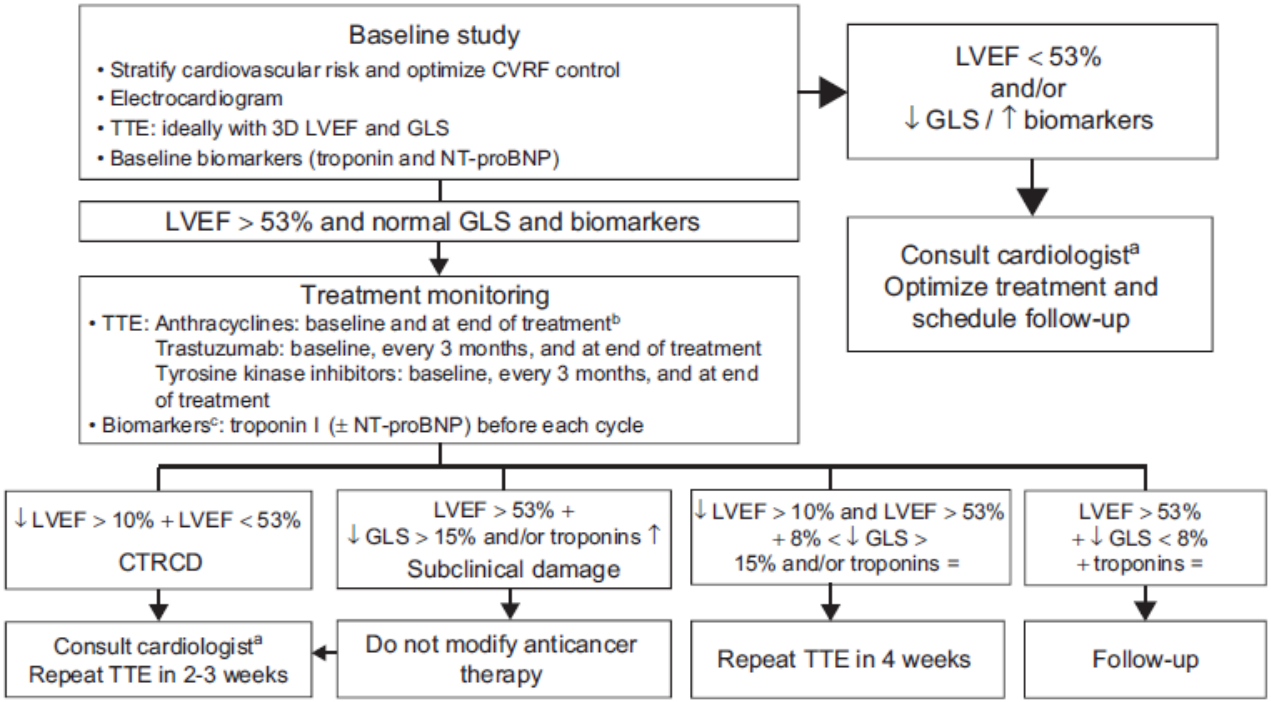


Figure 2. Monitoring algorithm for anticancer drug therapy.[14] 3D, 3-dimensional; CTRCD, cancer therapeutics-related cardiac dysfunction; CVRFs, cardiovascular risk factors; GLS, global longitudinal strain; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B type natriuretic peptide; TTE, transthoracic echocardiography. [a]Ideally, a specialist cardio-onco-hematology clinic. [b]Reevaluation of LVEF is recommended before treatment completion if the cumulative dose exceeds 240 mg/m^2. In these patients, the LVEF should be regularly monitored until the end of treatment. [c]In patients with low cardiovascular risk and without history of cardiotoxic treatment, determination of troponin levels before each cycle reduces the number of echocardiograms required and limits their use to symptomatic patients or those with troponin elevation.

Cosa fare in caso di insorgenza di disfunzione miocardica o scompenso cardiaco da farmaci antitumorali?

Gestione della disfunzione miocardica e dello scompenso cardiaco iatrogeni

- Sospensione temporanea/interruzione definitiva del trattamento
- Terapia cardiologica

Gestione della disfunzione miocardica e dello scompenso cardiaco iatrogeni

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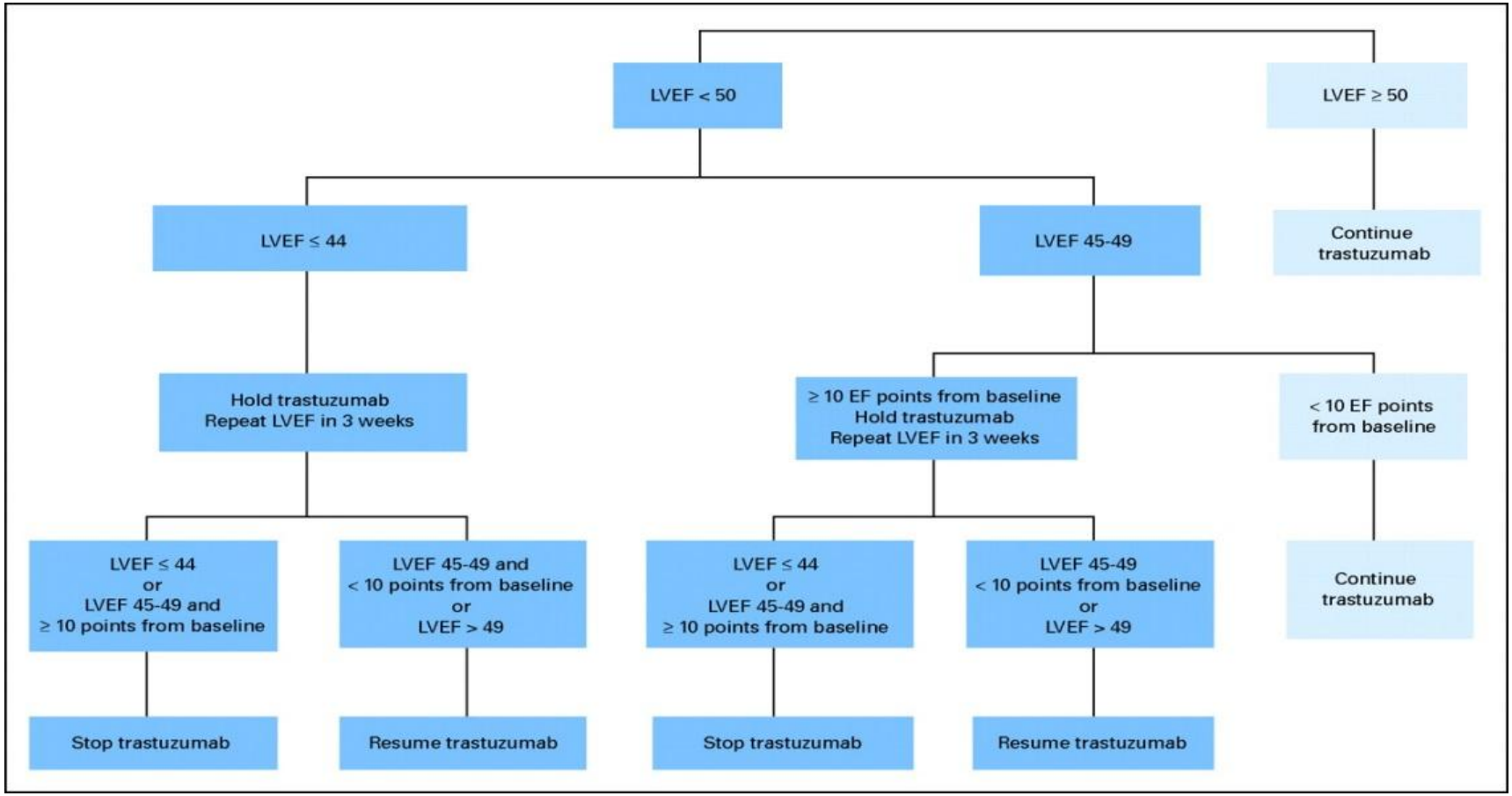
Algoritmo per l'interruzione e la ripresa del trastuzumab basato sui livelli di FEVS



Algoritmi per la sospensione del trattamento antitumorale

Treatment and monitoring of patients receiving cardiotoxic agents and with a LVEF < 53%.

Anthracyclines	Trastuzumab	Antiangiogenics*
• ↓ LVEF < 10%, maintain anticancer therapy • ↓ LVEF > 10% or LVEF < 45%, interrupt for 1 month and reevaluate • Restart if LVEF > 45%	• ↓ LVEF < 15%, maintain anticancer therapy • ↓ LVEF > 15% or LVEF < 40%, interrupt for 1 month and reevaluate • Restart if LVEF > 40%	• Optimize HT treatment • LVEF < 40%, interrupt for 1 month and reevaluate • Restart if LVEF > 40%

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Quali controlli effettuare nei pazienti trattati con farmaci antitumorali cardiotossici?

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Rev Esp Cardiol. 2017

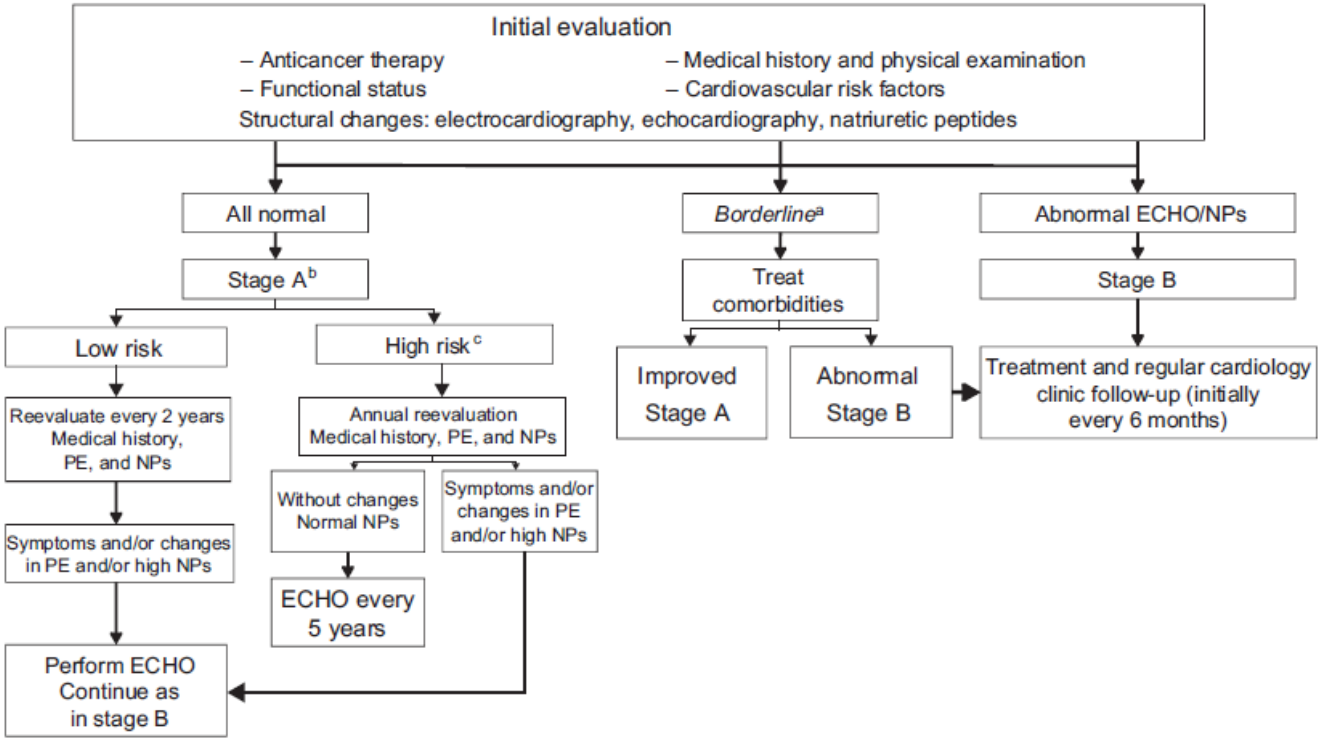

Figure 10. Follow-up algorithm for patients with prolonged survival, modified from Carver et al.[82] ECG, electrocardiography; ECHO, echocardiography; HF, heart failure; LVEF, left ventricular ejection fraction; NPs; natriuretic peptides; PE, physical examination. [a]Minor alterations in the ECG or intraventricular conduction disorder, nonsustained arrhythmias, or LVEF between 50% and 55%. [b]Patients with HF risk. [c]Any of the following conditions: age during treatment < 15 or > 65 years, female sex, any cardiac symptom or physical examination abnormality, cardiovascular risk factors, left ventricular dysfunction or previous heart disease, anthracyclines > 350 mg/m^2, chest radiation ≥ 35 Gy, combined treatment with anthracyclines and radiotherapy, premodern-era radiotherapy, follow-up > 10 years after treatment.

Quali sono in breve le raccomandazioni dell'Oncologo?

Conclusioni

- Molti farmaci oncologici possono determinare SC
  - Antracicline
  - Anti HER2
  - Antiangiogenetici
- Prevenire l'insorgenza della tossicità cardiaca
  - Identificazione dei pazienti a rischio
  - Fattori di rischio modificabili
  - Indicazioni oncologiche
  - Monitoraggio
- Corretta gestione dell'AE
  - Sospensione/interruzione del farmaco
  - Terapia cardiologica
- Adeguato follow-up
  - Selezionare l'intensità caso per caso

GRAZIE DI…