Breast Cancer Treatment Protocols: Systematic Review of the Last 35 Years

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Abstract: Breast cancer is the main leading type of cancer for women around the world and is responsible for 522,000 deaths per year worldwide. In order to reduce this number, clinicians and researchers are always looking for new strategies and protocols. However, the treatment for breast cancer is challenging and requires as much information as possible. To this end, we conducted a review of all protocols used for breast cancer treatment in the last 35 years with the objective to help clinicians to choose the best treatment possible available in their region. Many of the protocols are international references, and for that reason have been used in many countries like USA and Europe. The data, depicted in tables, may be helpful for clinicians worldwide and researchers to better understand the evolution of breast cancer protocols such as helping make daily routine decisions.

Keywords: Breast cancer, protocols, systematic review.

INTRODUCTION

Breast cancer in Western countries is a major cause of death among women. Statistics indicate a rise in frequency in developed and developing countries. According to the World Health Organization (WHO), in the 60s and 70s there was a 10-fold increase in incidence rates in the population-based cancer registries from different continents. Breast cancer is the second most common cancer worldwide (the first one is lung) and the most frequent type of cancer among women, with an estimated 1.67 million new cases of cancer diagnosed in 2012 (25% of all cancers worldwide), followed by colon & rectum, prostate and stomach. It is the most common cancer among women, with a different distribution between developed countries (794,000) and developing countries (883,000) [1]. This difference is due to access to a rapid and differential diagnosing exam. Breast cancer is ranked as the fifth leading cause of cancer deaths worldwide (522,000 deaths / year). In 2016, 1,685,210 new cancer cases and 595,690 cancer deaths were projected to occur in the United States [2]. Although considered to have relatively good prognosis if diagnosed and treated early, breast cancer mortality rates have remained high, most likely because the disease is still diagnosed in advanced stages. It is estimated that breast tumours may double in size every 3-4 months; this may represent a period of 10 years from its inception to a clinically palpable tumour. However, after the tumour becomes palpable, duplication is readily apparent. If left untreated, the tumour develops metastases, most commonly to the bones, lungs and liver and death may occur 3-4 years after palpation discovery of the tumour if not treated [3, 4].

This type of cancer does not have a single cause. Several factors are associated with increased risk of developing the disease, such as age, endocrine factors/reproductive history, behavioural/environmental factors and genetic/hereditary factors. About 5 to 10% of cases depend on the genetic component compared to 90% from external factors [5, 6]. Among the various external factors, the following should be highlighted:

1. Endocrine factors relating to reproductive history – These factors refer to stimulating the hormone oestrogen produced by the body itself or consumed through the continued use of substances with this hormone. These factors include: history of early menarche; late menopause (after 55 years); first pregnancy after age 30; nulliparity (not having children); and use of oral contraceptives and postmenopausal hormone replacement therapy, especially with long time use. The use of oral contraceptives is also considered a risk factor by the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO), although many studies on the subject have controversial results.

2. Behavioural or environmental factors – These factors include alcohol consumption, overweight

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and obesity after menopause and exposure to ionizing radiation (type of radiation present in radiotherapy and imaging tests such as X-ray, mammography and computed tomography). Smoking is a factor that has been studied over the years, with mixed results regarding the increased risk of breast cancer. Currently there is some evidence that it also increases the risk of this cancer.

3. Factors related to ionizing radiation – The risk is proportional to the dose and frequency of radiation. High or moderate doses of ionizing radiation (such as that which occurs in women exposed to radiation treatment in the chest at a young age) or low and frequent doses (such as that which occurs in women exposed to ten mammograms) increase the risk of development of breast cancer.

4. Genetic / hereditary factors – These factors are related to the presence of mutations in certain genes transmitted in the family, especially BRCA1 and BRCA2. Women with a history of breast cancer cases in blood relatives, may have a genetic predisposition and are considered to have a high risk for the disease. The following genetic factors beyond BRAC 1 and BRCA2 are also involved:

ATM

The ATM gene normally helps repair damaged DNA. The legacy of a copy of the abnormal gene has been associated with high breast cancer rates in some families.

TP53

The TP53 gene provides instructions for making the p53 protein that helps prevent the growth of abnormal cells. People with Li-Fraumeni syndrome are at increased risk of breast cancer as well as some other cancers, such as leukaemia, brain tumours and sarcomas. This mutation is a rare cause of breast cancer.

CHEK2

Mutations and/or changes in this gene can cause Li-Fraumeni syndrome, and therefore increase the chances of breast cancer. Importantly, if these mutations in CHEK2 gene do not cause the syndrome of Li-Fraumeni, it may double the risk of breast cancer.

PTEN

The PTEN gene normally helps regulate cell growth. The inherited mutations in the PTEN gene lead to Cowden syndrome and increase the chances of breast cancer.

CDH1

Women with mutations in this gene are at increased risk of lobular invasive breast cancer.

STK11

Defects in this gene can lead to Peutz-Jeghers syndrome. People affected by this disorder are at increased risk of breast cancer.

PALB2

The PALB2 gene is responsible for the production of a protein interaction with the protein produced by the BRCA2 gene. Mutations in this gene might lead to an increased risk of breast cancer. It is important to emphasise that there is no evidence that alterations of PLB2 have any influence in male breast cancer.

Breast cancer is highly heterogeneous, comprising distinct phenotypic and morphological profiles. These are characterised by three basic types according to their immunohistochemical properties. They can be classified as follows:

1. Hormone receptors positive breast cancer (HR positive breast cancer): are those which are present on the oestrogen receptor (ER) and progesterone receptor (PR). HR positive breast cancer can be further divided into two subtypes: luminal A and luminal B. Luminal A: Tumours tend to be ER + and/or PR + and HER-2 (human epithelial growth factor receptor positive type 2). Luminal B: Tumours tend to be ER + and/or PR + and HER-2 positive (or HER-2 with high Ki - 67).

2. Human Epithelial Growth Factor 2 positive breast cancer (HER-2 +): some breast cancer cells have a very high number of HER2 receptors. The extra HER2 receptors stimulate the cancer cells to divide and grow. When there are higher levels of the HER2 protein in breast cancer, it is called HER2 positive breast cancer.

3. Triple-negative breast cancer: refers to any type of breast cancer that does not express the genes for ER, PR, and HER-2 receptors.

Approximately 85% of all breast cancers are HR positive. About 20% of all breast cancers are HER-2 +. The triple-negative breast cancer, also called basal-like subtype, refers to any type of breast cancer that does not express the genes for ER, PR, and HER-2 receptors. The triple-negative breast cancers comprise about 15% of the entire population of breast cancer [7, 8].

The treatment for breast cancer is difficult and requires a lot of information regarding the tumour type (invasive or not, stage, gender, pregnancy). In general, the tumour treatment may be divided in two types: i) non-invasive breast cancer and invasive breast cancer.

In non-invasive breast cancer, the main protocol is chemotherapy, followed of surgery (mastectomy) with hormonal therapy. However, for invasive breast cancer, many factors may influence the decision about which protocol to use. In general, in early stages surgery followed by chemotherapy and radiotherapy are the main protocols. In advanced stages, chemotherapy with hormonal therapy will be used, and in some cases radiotherapy and surgery will be used in just a few cases [9-16].

SYSTEMATIC REVIEW METHODOLOGY

Literature Sources

A literature search was performed in databases including EMBASE, PubMed, and Cochrane Library, using the search terms like 'cancer protocol', 'treatment of cancer' 'breast cancer protocol'. The related articles function was used to extend the search. The last search date was December 2015. Two authors independently screened the titles and abstracts to determine potential eligibility for this systematic review. A third author checked the first two authors' work and finally the fourth author stratified the information. All discrepancies were analysed and after a consensus was achieved, it was either included or not included in the study.

Inclusion and Exclusion Criteria and Data Extraction

All available randomised controlled trials and observational studies that described a cancer treatment protocol were included. The language was restricted to Portuguese and English. Editorial comments, letters to editor, review studies, and case reports were included. Conference abstracts and experimental animal studies were excluded. Moreover, because of the different dose levels, Phase I and II trials were also excluded. Two authors independently extracted the following data from the selected articles: first author, year of publication, trial design, protocol used, outcome and statistics. In order to accurately select articles that met the inclusion criteria, two authors independently conducted the search work and evaluated each article and a third author checked the information.

Outcome

The primary outcome of this systematic review was to systematise all the protocols used for breast cancer treatment in the last 35 years worldwide.

RESULTS AND DISCUSSION

The results were depicted in Tables (**1-6**) in order to make the information more accessible and clear. The results were separated into periods of one decade in order to make the search easier. In the tables, the protocols were separated by adjuvant therapy, therapy for metastatic cancer (where the primary focus was breast cancer), combination regimens, and palliative therapy. In Table **6** we summarised the main drugs used and their mechanism (pharmacological). In all cases, the reference used is listed in the table as a cross reference tool.

DISCUSSION

The treatment of cancer is complex and demands a continuous updating of multiprofessional teams in the present day In this scenario, the development of new technological resources directed to the health sector, such as the increase in the number of therapeutic procedures for the same pathologies, has simply reshaped medical practice

Behavioral variability coupled with the exponential growth in the volume of published scientific information and the advent of Evidence-based Medicine have prompted the scientific community, hospitals and state-of-the-art diagnostic centers to seek uniformity in care delivery in order to reduce medical errors and improve the quality of services provided. In this stage the clinical protocol plays a prominent role.

Under the aegis of evidence-based medicine, clinical protocols have been developed and applied in a way that seeks to ensure minimal quality and ubiquitous access to treatment. Evidence-based clinical protocols are nothing more than therapeutic guidelines based on scientific evidence and consensus practices,

Table 1: Breast Cancer Protocols from 1970 to 1980

PROTOCOLS OF BREAST CANCER (1970-1980)								
ADJUVANT THERAPY								
TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
CMF classic	EORTC	Cyclophosphamide (C)	100	Oral	D1-14	The cycle is repeated every 28 days for a total of 12 cycles, but effective treatment has been observed for 6 months	In the study Tacini had no difference making 6 or 12 cycles	1
		Methotrexate (M)	40 (Bolus)	Intravenous	D1 and D8			
		5-Fluorouracil (F)	600 (Bolus)	Intravenous	D1 and D8			
THERAPY FOR METASTATIC TUMORS								
METASTATIC BREAST CANCER								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
CMF + Vincristine + Doxorrubicin	No information	Cyclophosphamide (C)	60	Oral	Daily	Weekly until progression	Metastatic	2
		Methotrexate (M)	15	Intravenous	Weekly			
		5-Fluorouracil (F)	300	Intravenous	Weekly			
		Vincristine	0,625	Intravenous	Weekly			
		Doxorrubicin (A)	60	Intravenous	Every 3 weeks			
COMBINATION REGIMENS FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
CMF classic	Bonadonna Regimen	Cyclophosphamide (C)	100	Oral	D1-14	The cycle is repeated every 28 days for a total of 12 cycles, but effective treatment has been observed for 6 months	No information	1
		Methotrexate (M)	40 (Bolus)	Intravenous	D1 and D8			
		5-Fluorouracil (F)	600 (Bolus)	Intravenous	D1 and D8			

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Table 2: Breast Cancer Protocols from 1981 to 1990

PROTOCOLS OF BREAST CANCER (1981-1990)								
NEOADJUVANT THERAPY								
TYPE HER2 UNKNOWN								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
CAF	No information	Cyclophosphamide (C)	100	Oral	D1-14	The cycle is repeated every 28 days until disease progression	Response rate of 61% in previously untreated patients	3
		Doxorrubicin (A)	30	Intravenous	D1 and D8			
		5-Fluorouracil (F)	500	Intravenous	D1 and D8			
ADJUVANT THERAPY								
TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
AC	NSABPB-15	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles	No information	4
		Cyclophosphamide (C)	600	Intravenous	D1			
CAF	No information	Cyclophosphamide (C)	600	Intravenous	D1	The cycle is repeated every 28 days for a total of 4 cycles	No information	5
		Doxorrubicin (A)	60	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			
CMFP	EORTC	Cyclophosphamide (C)	50	Oral	D1-14	The cycle is repeated every 28 days for a total of 12 cycles	No information	6
		Methotrexate (M)	15	Intravenous	D1 and D8			
		5-Fluorouracil (F)	350	Intravenous	D1 and D8			
		Prednisone (P)	20 mg (4x/day)	Intravenous	D1-7			
CMF	Toronto, Canada	5-Fluorouracil (F)	600	Intravenous	D1	The cycle is repeated every 21 days	No information	7
CMF	INT, Milan	Cyclophosphamide (C)	600	Intravenous	D1	The cycle is repeated every 21 days for a total of 12 cycles	No information	8
		Methotrexate (M)	40	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			
CMF	Regime IV	Cyclophosphamide (C)	600	Oral	D1	The cycle is repeated every 28 days for a total of 6 cycles	No information	5
		Methotrexate (M)	40	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			

THERAPY FOR METASTATIC TUMORS								
METASTATIC BREAST CANCER								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
CAF	No information	Cyclophosphamide (C)	100	Oral	D1-14	The cycle is repeated every 28 days until disease progression	Response rate of 61% in previously untreated patients	3
		Doxorrubicin (A)	30	Intravenous	D1 and D8			
		5-Fluorouracil (F)	500	Intravenous	D1 and D8			
FAC	No information	5-Fluorouracil (F)	500 (Bolus)	Intravenous	D1 and D8	The cycle is repeated every 21 days until disease progression	No information	9
		Doxorrubicin (A)	50 (Bolus)	Intravenous	D1			
		Cyclophosphamide (C)	500 (Bolus)	Intravenous	D1			
MMC-VBL	No information	Mitomycin (MMC)	10 (Bolus)	Intravenous	D1	The cycle is repeated every 28 days until disease progression	Response rate of 30% in patients previously treated and tolerable toxicity at doses at 4 week intervals mitomycin	10
		Vinblastine (VBL)	5 (Bolus)	Intravenous	D1 and D15			
VATH	No information	Vinblastine (V)	4,5 (Bolus)	Intravenous	D1	The cycle is repeated every 21 days for two cycles, assesses	Suitable for patients with previous therapy failed. Fluoxymesterone medicine is an anabolic unauthorized in Brazil	11
		Doxorrubicin (A)	45 (Bolus)	Intravenous	D1			
		Thiopeta (T)	12 (Bolus)	Intravenous	D1			
		Fluoxymesterone (H - Halotestin)	10 mg (3x/day)	Oral	Daily			

THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
AC	NSABP B15	Doxorrubicin (A)	60	Intravenous	D1	Repeating the cycle every 21 days to a maximum of 8 cycles	No information	4
		Cyclophosphamide (C)	600	Intravenous	D1			
CAF	No information	Cyclophosphamide (C)	600	Intravenous	D1	The cycle is repeated every 21 days	No information	5
		Doxorrubicin (A)	60	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			

THERAPY FOR METASTATIC TUMORS								
AGENTS OF REGIMENS ONLY								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Doxorrubicin	No information	Doxorrubicin (A)	20	Intravenous	D1	Repeat the cycle every 7 days	HER-2 Negative	12
Mitoxantrone	No information	Mitoxantrone (N)	12	Intravenous	D1	Repeat the cycle every 21 days	No information	13
PALLIATIVE THERAPY								
MONOTHERAPY								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Mitoxantrone	No information	Mitoxantrone (N)	12	Intravenous	D1	Repeat the cycle every 21 days	No information	13

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Table 3: Breast Cancer Protocols from 1991 to 200

PROTOCOLS OF BREAST CANCER (1991-2000)								
NEOADJUVANT THERAPY								
TYPE HER2 UNKNOWN								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Anastrozole	No information	Anastrozole	1 mg	Oral	Daily	Repeat daily for 4 to 6 months, up to 12 weeks	No information	14
Tamoxifen	No information	Tamoxifen	20 mg	Oral	Daily	Repeat daily for 4 to 6 months	No information	15
AC	NSABP B-18	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles	No information	16
		Cyclophosphamide (C)	600	Intravenous	D1			
EC	BCIRG B18	Epirubicin (E)	75	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles	No information	16
		Cyclophosphamide (C)	600	Intravenous	D1			
FAC	No information	5-Fluorouracil (F)	500	Intravenous	D1	The cycle is repeated every 21 days in total 4 to 6 cycles	No information	17
		Doxorrubicin (A)	50	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
FEC	No information	5-Fluorouracil (F)	500	Intravenous	D1	The cycle is repeated every 21 days in total 4 to 6 cycles	No information	17
		Epirubicin (E)	75-100	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
ADJUVANT THERAPY								
TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
CMF	No information	Cyclophosphamide (C)	600	Intravenous	D1	Repeat the cycle every 21 days for a total of 6 cycles	No information	18
		Methotrexate (M)	40	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			
FEC-100	No information	5-Fluorouracil (F)	500	Intravenous	D1	Repeat the cycle every 21 days for a total of 6 cycles	No information	19
		Epirubicin (E)	100	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			

ADJUVANT THERAPY								
TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
FEC	No information	5-Fluorouracil (F)	500	Intravenous	D1	The cycle is repeated every 21 days in total 4 to 6 cycles	No information	17
		Epirubicin (E)	75-100	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
TAC	No information	Docetaxel (T)	75	Intravenous	D1	Repeat the cycle every 21 days for a total of 6 cycles	No information	20
	BCIRG 0001	Doxorrubicin (A)	50	Intravenous	D1		Filgrastin: 300 µg subcutaneous in the D2-14 or Pegfilgrastin: 6 mg subcutaneous in single dose D2. Ciprofloxacin: 500 mg oral 12/12 hour in the D5-14.	23
		Cyclophosphamide (C)	500	Intravenous	D1			
ADJUVANT THERAPY								
COMBINATION REGIMENS OF DOSE-DENSE FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
A → T → C	No information	Doxorrubicin (A)	90	Intravenous	D1	The cycle is repeated every 2 weeks for a total of 3 cycles, followed by:	Filgrastin 5 µg/kg subcutaneous 3-10 days in every cycle	22
		Paclitaxel (T)	250 (24 h)	Intravenous	D1	The cycle is repeated every 2 weeks for a total of 3 cycles, followed by:		
		Cyclophosphamide (C)	3000 (1 h)	Intravenous	D1	The cycle is repeated every 2 weeks for a total of 3 cycles		

ADJUVANT THERAPY								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
AC	NSABP B-18	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles	No information	16
		Cyclophosphamide (C)	600	Intravenous	D1			
ADJUVANT THERAPY								
REGIMENS OF SOLE AGENTS (HORMONE THERAPY)								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Tamoxifen	NSABP B-14	Tamoxifen	20	Oral	Daily	Repeat daily for 5 years	ER positeve or ER unknown	23
ADJUVANT THERAPY								
TRANSPLANTATION OF AUTOLOGOUS PERIPHERAL BLOOD CELLS TRUNKS								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
CPB (Stamp I)	No information	Cyclophosphamide (C)	1875 (1h)	Intravenous	D-6,-5 and -4	Calculation of doses is the body surface area (BSA) by the equation = [(ideal BSA) + (current BSA)] / 2 for patients ≥ 120% of their ideal body weight.	Platelet transfusion is to minimize the risk of cardiac haemorrhagic necrosis. Continuous bladder irrigation on days D-6 and D-3.	24
		Cisplatin (P)	55 (24h)	Intravenous	D-6,-5 and -4			
		Carmustine (BCNU) ou (B)	600 (2h)	Intravenous	D-3			
		Transplante	-	Intravenous	D-1, 0 and+1			
		Bone marrow cells	-	Intravenous	D1			
		Platelet Transfusion	2 etapas	Intravenous	D-2			
CTCb (Stamp V)	No information	Cyclophosphamide (C)	1500 (24h - 4 doses)	Intravenous	D-7,-6,-5,-4 and -3	No information	Prophylaxis for hemorrhagic cystitis. Advanced disease.	25
		Thiopeta (T)	125 (24h - 4 doses)	Intravenous	D-7,-6,-5,-4 and -3			
		Carboplatin (Cb)	200 (24 h - 4 doses)	Intravenous	D-7,-6,-5,-4 and -3			
		Transplante	-	Intravenous	D0			
CTM	No information	Cyclophosphamide (C)	1500 (1h)	Intravenous	D-6,-5,-4 and -3	Calculation of doses is the body surface area (BSA) by the equation = [ideal kg + (0.25) (current ka - ideal Kg)]	Mitoxantrone dose of 10 mg/m^2/dose is for patients in stages II and IIIA. At doses of 10, 12.5 or 15 mg/m^2/dose patients IIIB and IV stages. Advanced disease.	26
		Thiopeta (T)	150 (2h)	Intravenous	D-6,-5,-4 and -3			
		Mitoxantrone (M)	10 a 15 (1h)	Intravenous	D-6,-5,-4 and -3			
		Transplante	-	Intravenous	D0			

THERAPY FOR METASTATIC TUMORS								
METASTATIC BREAST CANCER								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
CMF	Italian	Cyclophosphamide (C)	100	Oral	D1-14	No information	No information	27
		Methotrexate (M)	40	Intravenous	D1 and D8			
		5-Fluorouracil (F)	600	Intravenous	D1 and D8			
CMF	Italian	Cyclophosphamide (C)	600	Intravenous	D1-21	No information	No information	27
		Methotrexate (M)	40	Intravenous	D1-21			
		5-Fluorouracil (F)	600	Intravenous	D1-21			
FAC	No information	5-Fluorouracil (F)	500	Intravenous	D1	The cycle is repeated every 21 days	No information	28
		Doxorrubicin (A)	50	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
MMC-VNB	No information	Mitomycin (MMC)	15	Intravenous	D1 every 6 weeks	Repeat the cycle 6 times	Filgrastin: 5µg/kg/day in the D2-7	29
		Vinorelbine (VNB)	40-50	Intravenous	D1 every 3 weeks			
NFL	No information	Mitoxeastantrone (N)	10 (Bolus)	Intravenous	D1	The cycle is repeated every 21 days for two cycles, assesses	No significant toxicity in pretreated patients	30
		5-Fluorouracil (F)	1000 (24h)	Intravenous	D1-3			
		Leucovorin (folinic acid) (L)	100 (Bolus)	Intravenous	D1-3			
Vinorelbine + Cisplatin	Regime CIVIC	Vinorelbine (VNB)	6	Intravenous	D1-5	The cycle is repeated every 21 days	Patients pretreated with anthracyclines and taxanes	31
		Cisplatin	20	Intravenous	D1-5			
Vinorelbine + Doxorrubicin	Trials Group Study MA8	Vinorelbine (VNB)	25	Intravenous	D1 and D8	The cycle is repeated every 21 days	First line	32
		Doxorrubicin (A)	50	Intravenous	D1			
Vinorebilne + Paclitaxel	GOCS 08-BR-95	Vinorelbine (VNB)	30 (20 minutes)	Intravenous	D1 e D8	The cycle is repeated every 28 days	First line	33
		Paclitaxel (T)	135 (3 hour infusion started 1 hour after VNB)	Intravenous	D1			

THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Carboplatin + Paclitaxel	No information	Carboplatin	AUC of6	Intravenous	D1	The cycle is repeated every 21 days	No information	34
		Paclitaxel (T)	200 (3h)	Intravenous	D1			
CEF	No information	Cyclophosphamide (C)	75	Oral	D1-14	The cycle is repeated every 28 days	No information	35
		Epirubicin (E)	60	Intravenous	D1 and D8			
		5-Fluorouracil (F)	500	Intravenous	D1 and D8			
CMF (Modified)	10808	Cyclophosphamide (C)	600	Intravenous	D1	The cycle is repeated every 21 days	No information	36
		Methotrexate (M)	40	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			
Docetaxel + Doxorrubicin	No information	Docetaxel (T)	75	Intravenous	D1	Repeating the cycle every 21 days to a maximum of 8 cycles	Scheme myelotoxic enough, but induces rapid respons	37
		Doxorrubicin (A)	50	Intravenous	D1			
FEC-100	No information	5-Fluorouracil (F)	500	Intravenous	D1	The cycle is repeated every 21 days	No information	38
		Epirubicin (E)	100	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
FEC-75	French Eprubicin Study Group	5-Fluorouracil (F)	500	Intravenous	D1	The cycle is repeated every 21 days	No information	39
		Epirubicin (E)	75	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
FEC-50	No information	5-Fluorouracil (F)	500	Intravenous	D1	The cycle is repeated every 21 days	No information	39
		Epirubicin (E)	50	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
Gemcitabine + Cisplatin	No information	Gemcitabine (G)	750	Intravenous	D1 and D8	The cycle is repeated every 21 days	No information	40
		Cisplatin	30	Intravenous	D1 and D8			

THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Trastuzumab + Paclitaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	The cycle is repeated every 4 weeks	No information	41
		Paclitaxel (T)	80	Intravenous	Weekly			

THERAPY FOR METASTATIC TUMORS								
REGIMENS OF SOLE AGENTS								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Anastrozole	No information	Anastrozole	1 mg	Oral	Daily	No information	No information	42
Anastrozole	No information	Anastrozole	1 mg	Oral	Daily	To 5 years or undefined	First line in postmenopausal women	43
Capecitabine (Xeloda)	No information	Capecitabine (X)	1250 mg (2x/day) for 2 weeks followed by one week of rest	Oral	Daily	Repeating the cycle every 21 days. You can decrease the dose of capecitabine for 825-1000 mg/m^2(2x/day) orally on days 1-14 to reduce the risk of toxicity without compromising clinical efficacy.	HER-2 negative. Patients refractory to Paclitaxel	44
Docetaxel (Taxotere)	No information	Docetaxel (T)	60-100 mg/m^2 (1 a 24 h)	Intravenous	D1	Repeats the cycle every 21 days for 2 cycles, reassesses. Maximum of 5 cycles	Relapse after treatment with anthracyclines. Observe myelotoxicity	45
		Dexamethasone	8 mg (2x/day)	Oral	D1-5	Hypersensitivity reactions Prevention		

Docetaxel (Taxotere)	No information	Docetaxel (T)	100 mg/m^2	Intravenous	D1	The cycle is repeated every 21 days	Observe myelotoxicity	46
							HER-2 Negative	47
Docetaxel (Taxotere)	No information	Docetaxel (T)	35-40 mg/m^2	Intravenous	D1, D8, D15, D22, D29, D36 (6 weeks)	Weekly 14 days off, ie repeating cycles every 8 weeks	Observe myelotoxicity	48
Doxorrubicin	No information	Doxorrubicin (A)	75 mg/m^2	Intravenous	D1	Repeated every 21 days for a total of 4 cycles	No information	49
THERAPY FOR METASTATIC TUMORS								
REGIMENS OF SOLE AGENTS								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Doxorrubicin	No information	Doxorrubicin (A)	25	Intravenous	Weekly	12 cycles	No information	49
Liposomal Doxorrubicin	No information	Liposomal Doxorrubicin	45-60	Intravenous	D1	Repeats the cycle every 21-28 days	No information	50
Epirubicin	No information	Epirubicin	75	Intravenous	D1	Repeats the cycle every 21 days	No information	39
Etoposide	No information	Etoposide	50-100 mg	Intravenous	D1-21	Repeats the cycle every 28 days	Third or fourth line. Observe myelotoxicity.	51
Exemestane	No information	Exemestane	25	Intravenous	Daily	No information	Effective even after failure of aromatase inhibitors non-steroidal	52,53
Gemcitabine	No information	Gemcitabine	725	Intravenous	D1, D8 e D15	Repeats the cycle every 28 days	No information	54
Letrozole	No information	Letrozolee	2,5 mg	Intravenous	Daily	No information	No information	55
Megestrol	No information	Megestrol	40 mg	Intravenous	4x/dia (160 mg)	No information	Reserved for the fourth line hormonal	56
Paclitaxel (Taxol)	No information	Paclitaxel (T)	90 (1 h)	Intravenous	D1	Repeats the cycle every 7 days	Observe myelotoxicity.	57
Paclitaxel (Taxol)	No information	Paclitaxel (T)	175 (3 h)	Intravenous	D1	Repeats the cycle every 21 days	Observe myelotoxicity	58

Paclitaxel (Taxol)	No information	Paclitaxel (T)	80-100	Intravenous	Weekly for 3 weeks (D1, D8 e D15)	Repeats the cycle every 4 weeks	Observe myelotoxicity	59
							HER-2 Negative	60
Tamoxifen	No information	Tamoxifen	20 mg	Oral	Daily	No information	No information	61
Toremifine	No information	Toremifine	60 mg	Oral	Daily	No information	No information	62
Trastuzumab (Herceptin)	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	Repeat the cycle weekly for a total of 10 weeks. In the absence of disease progression continue the weekly maintenance dose of 2 mg / kg	HER-2 Positive	63
THERAPY FOR METASTATIC TUMORS								
REGIMENS OF SOLE AGENTS								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Vinorelbine (Navelbine)	No information	Vinorelbine (N)	25 - 30	Intravenous	D1	Repeats the cycle every 7 days	HER-2 Negative	64
Vinorelbine (Navelbine)	No information	Vinorelbine (N)	30	Intravenous	D1 and D8	Repeats the cycle every 21 days	First and second line. Well tolerated in elderly patients	65
PALLIATIVE THERAPY								
MONOTHERAPY								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Docetaxel (Taxotere)	No information	Docetaxel	60-75	Intravenous	D1	Repeats the cycle every 21 days	No information	66
Docetaxel (Taxotere)	No information	Docetaxel (T)	60-100 (1 to 24 h)	Intravenous	D1	Repeat cycles every 21 days for two cycles, then reevaluates	Relapse after treatment with anthracyclines	45
Doxorrubicin	No information	Doxorrubicin (A)	75	Intravenous	D1	Repeated every 21 days for a total of 4 cycles	Metastatic	49
Epirubicin	No information	Epirubicin	75	Intravenous	D1	Repeats the cycle every 21 days	Metastatic	39

Exemestane	No information	Exemestane	25 mg	Oral	Daily	No information	No information	52
Letrozole	No information	Letrozolee	2,5 mg	Oral	Daily	No information	No information	55
Megestrol	8741	Megestrol	160 mg	Oral	Daily	No information	No information	67
Paclitaxel (Taxol)	No information	Paclitaxel (T)	200 (3 h)	Intravenous	D1	Repeats the cycle every 21 days	Metastatic	68
Paclitaxel (Taxol)	No information	Paclitaxel (T)	80 (1 h)	Intravenous	D1	Repeats the cycle every 7 days	Metastatic	57
Tamoxifen	No information	Tamoxifen	20 mg	Oral	Daily	No information	No information	61
Vinorelbine (Navelbine)	No information	Vinorelbine (N)	25/30	Intravenous	D1 and D8	Repeats the cycle every 21 days	No information	65

PALLIATIVE THERAPY

COMBINATION REGIMENS

PROTOCOL	TRIAL	DRUGS NAMES	DOSAGE (mg/m^2)	ROUTE OF ADMINISTRATION	DAYS OF ADMINISTRATION	SCHEME THERAPEUTIC	COMMENTS	BIBLIOGRAPHIC REFERENCES
CMF	10808 / BR9601	Cyclophosphamide (C)	600	Intravenous	D1	Repeats the cycle every 21 days	No information	36
		Methotrexate (M)	40	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			
Gemcitabine + Cisplatin	No information	Gemcitabine	750	Intravenous	D1 and D8	Repeats the cycle every 21 days	No information	40
		Cisplatin (P)	30	Intravenous	D1 and D8			

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Table 4: Breast Cancer Protocols from 2001-2010

PROTOCOLS OF BREAST CANCER (2001-2010)								
NEOADJUVANT THERAPY								
TYPE HER2 UNKNOWN								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Letrozole	No information	Letrozole	2,5 mg	Oral	Daily	Repeat daily for 4 to 6 months	No information	69
AT → CMF	ECTO	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for 4 cycles followed by:	No information	70
		Paclitaxel (T)	200	Intravenous	D1			
		Cyclophosphamide (C)	600	Intravenous	D1 and D8	Repeat the CMF every 28 days for a total of 4 cycles		
		Methotrexate (M)	40	Intravenous	D1 and D8			
		5-Fluorouracil (F)	600	Intravenous	D1 and D8			
NEOADJUVANT THERAPY								
TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
AC → T	(NSABP B-27)	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for 4 cycles followed by:	At the end of the fourth cycle does not require surgery	71
		Cyclophosphamide (C)	600	Intravenous	D1			
		Docetaxel (T)	100	Intravenous	D1	Repeat the cycle every 21 days for a total of 4 cycles		
T → EC	No information	Paclitaxel (T)	175	Intravenous	D1	The cycle is repeated every 14 days for 4 cycles followed by:	No information	72
		Epirubicin (E)	90	Intravenous	D1	The cycle is repeated every 21 days for 4 cycles		
		Cyclophosphamide (C)	600	Intravenous	1			
NEOADJUVANT THERAPY								
TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
T → FEC	No information	Paclitaxel (T)	225 (24h) OR	Intravenous	D1	The cycle is repeated every 21 days for 4 cycles followed by:	Absence of data regarding the superiority of efficacy of continuous infusion regimen of paclitaxel infusions in shorter periods, such as 3h/ weekly also are accepted	73
			225 (24h) OR	Intravenous	D1			
			135 (3h) OR	Intravenous	Weekly			
		5-Fluorouracil (F)	80	Intravenous	D1 and D4	The cycle is repeated every 21 days for 4 cycles		
		Epirubicin (E)	500	Intravenous	D1			
		Cyclophosphamide (C)	75	Intravenous	D1			

T → FAC	No information	Paclitaxel (T)	500	Intravenous	D1	The cycle repeats every 7 days for 12 cycles, followed by:	No information	74
		5-Fluorouracil (F)	500	Intravenous	D1	Repeat the cycle every 21 days for a total of 6 cycles		
		Doxorrubicin (A)	50	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			

NEOADJUVANT THERAPY

TYPE HER2 POSITIVE

PROTOCOL	TRIAL	DRUGS NAMES	DOSAGE (mg/m^2)	ROUTE OF ADMINISTRATION	DAYS OF ADMINISTRATION	SCHEME THERAPEUTIC	COMMENTS	BIBLIOGRAPHIC REFERENCES
AC → TCH	No information	Doxorrubicin (A)	60	Intravenous	The cycle repeats every 3 weeks, followed by:	Repeat until you have completed 13 weeks	Filgrastrin	75
		Cyclophosphamide (C)	60					
		Paclitaxel (T)	80	Intravenous	Weekly			
		Carboplatin (C)	AUC de 2	Intravenous				
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous				
			Maintenance dose: 2 mg/kg					

NEOADJUVANT THERAPY

TYPE HER2 POSITIVE

PROTOCOL	TRIAL	DRUGS NAMES	DOSAGE (mg/m^2)	ROUTE OF ADMINISTRATION	DAYS OF ADMINISTRATION	SCHEME THERAPEUTIC	COMMENTS	BIBLIOGRAPHIC REFERENCES
AC dose-dense → TCH	No information	Doxorrubicin (A)	60	Intravenous	Every 2 weeks, followed by:	Repeat until you have completed 13 weeks	Filgrastrin	75
		Cyclophosphamide (C)	60					
		Paclitaxel (T)	80	Intravenous	Weekly			
		Carboplatin (C)	AUC of 2	Intravenous				
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous				
			Maintenance dose: 2 mg/kg					
AT → TH → CMFH	NOAH Trial	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for 3 cycles, followed by:	Emetogenic potential: high (during ATH), low (TH), moderate (CMFH). Anaphylactic potential: high (for paclitaxel). Trastuzumab full 52 weeks	76
		Paclitaxel (T)	150 (3 h)	Intravenous	D1			
		Paclitaxel (T)	175 (3 h)	Intravenous	D1	Repeat for another 4 cycles followed by:		
		Cyclophosphamide (C)	600	Intravenous	D1 and D8	Repeat CMF every 28 days, a total of 3 cycles		
		Methotrexate (M)	40	Intravenous	D1 and D8			

		5-Fluorouracil (F)	600	Intravenous	D1 and D8			
		Trastuzumab (H)	Loading dose: 8 mg/kg	Intravenous	Concomitant with all chemotherapy	Every 3 week until completing 1 year of therapy, or every 28 days when combined with CMF		
			Maintenance dose: 6 mg/kg					
Lapatinib + Paclitaxel	No information	Lapatinib	1500 mg/day	Oral	Daily	Repeat until you have completed 14 weeks	No information	77
		Paclitaxel (T)	80	Intravenous	Weekly	Repeat until you have completed 12 weeks		

NEOADJUVANT THERAPY

TYPE HER2 POSITIVE

PROTOCOL	TRIAL	DRUGS NAMES	DOSAGE (mg/m^2)	ROUTE OF ADMINISTRATION	DAYS OF ADMINISTRATION	SCHEME THERAPEUTIC	COMMENTS	BIBLIOGRAPHIC REFERENCES
Paclitaxel + FEC + Trastuzumab	No information	Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly	Repeats 24-week	No information	73
			Maintenance dose: 2 mg/kg					
		5-Fluorouracil (F)	600	Intravenous	Every 3 weeks	The cycle is repeated 4 times		
		Epirubicin (E)	75	Intravenous				
		Cyclophosphamide (C)	600	Intravenous				
		Paclitaxel (T)	225	Intravenous	Every 3 weeks			
TCH	No information	Docetaxel (T)	75	Intravenous	Every 3 weeks	Repeat until you have completed 18 weeks	No information	78
		Carboplatin (C)	AUC de 6	Intravenous	every 3 weeks			
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly			
			Maintenance dose: 2 mg/kg					
Trastuzumab + Capecitabine + Docetaxel	No information	Trastuzumab (H)	Loading dose: 8 mg/kg	Intravenous	every 3 weeks	The cycle is repeated 6 times	No information	79
			Maintenance dose: 6 mg/kg					
		Capecitabine (X)	900 (2x/day)	Oral	D1-14			
		Docetaxel (T)	36	Intravenous	D1			

NEOADJUVANT THERAPY								
TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
TH → FEC75 H	MDACC	Paclitaxel (T)	225 (24 h) OR	Intravenous	D1	Repeats every 21 days for a total of 4 cycles. Followed by:	The absence of data regarding the superiority of efficacy schema continuous infusion of paclitaxel infusions for shorter periods, such as 3h or weekly regimen are also accepted Emetogenic potential: high (during FEC) and low (for paclitaxel). Anaphylactic potential: high (for paclitaxel).	80
			135 (3 h) OR	Intravenous	D1			
			80	Intravenous	Weekly			
		5-Fluorouracil (F)	500	Intravenous	D1 and D4	Repeat the cycle (FEC) every 21 days for a total of 4 cycles		
		Epirubicin (E)	75	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
		Trastuzumab (H)	Loading dose: 4 mg/kg (90 min no D1)	Intravenous	Concomitant with any chemotherapy. Weekly, up to a total 24 weeks	Up to 24 weeks		
			Maintenance dose: 2 mg/kg (30 minutes)					
Trastuzumab + Docetaxel	JECBC 02 Trial	Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly	Repeat for 12 weeks	No information	81
			Maintenance dose: 2 mg/kg					
		Docetaxel (T)	70	Intravenous	Every 3 weeks	The cycle is repeated 4 times		
Trastuzumab + Docetaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly	Repeat until you have completed 12 weeks	No information	82,83
			Maintenance dose: 2 mg/kg					
		Docetaxel (T)	100	Intravenous	Every 3 weeks			
Trastuzumab + Docetaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly	Repeat until you have completed 14 weeks	No information	84
			Maintenance dose: 2 mg/kg					
		Docetaxel (T)	36	Intravenous	Every 3 weeks			
Trastuzumab + Docetaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly	Repeat for 18weeks	No information	85
			Maintenance dose: 2 mg/kg					
		Docetaxel (T)	100	Intravenous	Every 3 weeks	The cycle is repeated 6 times		

NEOADJUVANT THERAPY								
TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m²)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Trastuzumab + Docetaxel + Cisplatin	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	Repeat until you have completed 12 weeks	No information	86
		Docetaxel (T)	70	Intravenous	Every 3 weeks			
		Cisplatin	70	Intravenous	Every 3 weeks			
Trastuzumab + Docetaxel + Epirubicin	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	Repeat until you have completed 12 weeks	No information	87
		Docetaxel (T)	30	Intravenous	Weekly			
		Epirubicin (E)	35	Intravenous	Weekly			
Trastuzumab + Paclitaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	Repeat until you have completed 12 weeks	No information	88
		Paclitaxel (T)	175	Intravenous	Every 3 weeks			
Trastuzumab + Docetaxel + Vinorelbine	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	Repeat until you have completed 12 weeks	No information	89
		Docetaxel (T)	60	Intravenous	Every 2 weeks			
		Vinorelbine (N)	60	Intravenous	Every 2 weeks			
Trastuzumab + Vinorelbine	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	Repeat until you have completed 12 weeks	No information	90
		Vinorelbine (V)	25	Intravenous	Weekly			

NEOADJUVANT THERAPY								
TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m²)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Vinorelbine + Docetaxel + Trastuzumab → AC	No information	Vinorelbine (V)	45	Intravenous	D1	Repeat the cycle every 14 days for a total of 6 cycles	Surgery performed after completion of neoadjuvant chemotherapy. Necessary support with Filgrastim and Ciprofloxacin (quinolones)	91
		Docetaxel (T)	60	Intravenous	D1			
		Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	The cycle is repeated every 14 days for a total of 6 ciclos concomitante with neoadjuvant chemotherapy until completing 12 weeks, and following surgery:		
		Doxorrubicin (A)	60	Intravenous	D1	Repeats every 3 weeks for a total of 4 cycles		
		Cyclophosphamide (C)	600	Intravenous	D1			

ADJUVANT THERAPY								
TYPE HER2 POSITIVE OR NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
A → CMF	No information	Doxorrubicin (A)	75	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles, followed by:	No information	92
		Cyclophosphamide (C)	600	Intravenous	D1	The cycle (CMF) is repeated every 21 days for a total of 8 cycles		
		Methotrexate (M)	40	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			
AT → CMF	ECTO	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles, followed by:	No information	70
		Paclitaxel (T)	200	Intravenous	D1			
		Cyclophosphamide (C)	600	Intravenous	D1 e D8	The cycle (CMF) is repeated every 28 days for a total of 4 cycles		
		Methotrexate (M)	40	Intravenous	D1 e D8			
		5-Fluorouracil (F)	600	Intravenous	D1 e D8			

ADJUVANT THERAPY								
TYPE HER2 POSITIVE OR NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
AC → T	No information	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles, followed by:	No information	93
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	175	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles		
AC → T (WEEKLY)	E1199	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles, followed by:	No information	93
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	80	Intravenous	D1 (Weekly)	Repeat until you have completed 12 weeks		
AC → Docetaxel	E1199	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles, followed by:	No information	94
		Cyclophosphamide (C)	600	Intravenous	D1			
		Docetaxel (T)	100	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles		

AC → Docetaxel (WEEKLY)	No information	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles, followed by:	No information	93
		Cyclophosphamide (C)	600	Intravenous	D1			
		Docetaxel (T)	35	Intravenous	D1 (Weekly)	Repeat until you have completed 12 weeks		
Epirubicin → CMF	NEAT	Epirubicin (E)	100	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles, followed by:	No information	92
		Cyclophosphamide (C)	600	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles		
		Methotrexate (M)	40	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			
Epirubicin → CMF	No information	Epirubicin (E)	100	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles, followed by:	No information	92
		Cyclophosphamide (C)	750	Intravenous	D1	The cycle is repeated every 21 days for a total of 8 cycles		
		Methotrexate (M)	50	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			
ADJUVANT THERAPY								
TYPE HER2 POSITIVE OR NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
FAC	GEICAM	5-Fluorouracil (F)	500	Intravenous	D1	The cycle is repeated every 21 days for a total of 6 cycle	No information	95
		Doxorrubicin (A)	50	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
FEC → T	GEICAM 9906	5-Fluorouracil (F)	600	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles, followed by:	No information	96
		Epirubicin (E)	90	Intravenous	D1			
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	100	Intravenous	Weekly	Weekly for 8 weeks		
FEC → Docetaxel	PACS 01	5-Fluorouracil (F)	500	Intravenous	D1	Repeat the cycle every 21 days for a total of 6 cycles, followed by:	No information	97
		Epirubicin (E)	100	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
		Docetaxel (T)	100	Intravenous	D1	The cycle is repeated every 21 days for a total of 3 cycles		
TC	No information	Docetaxel (T)	75	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles	No information	21
	Trial 9735	Cyclophosphamide (C)	600	Intravenous	D1			98

ADJUVANT THERAPY								
COMBINATION REGIMENS OF DOSE-DENSE FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
AC → T	B 9741	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 14 days for a total of 4 cycles, followed by:	Administration of Pegfilgrastim subcutaneous on D2 for each cycle	99
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	175	Intravenous	D1	The cycle is repeated every 14 days for a total of 4 cycles		

ADJUVANT THERAPY								
COMBINATION REGIMENS OF DOSE-DENSE FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
A → T → C	CALGB 9741	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 2 weeks for a total of 4 cycles, followed by:	Administration of Filgrastin subcutaneously 5 µg/kg on days 3-10 every cycle	100
		Paclitaxel (T)	175	Intravenous	D1	The cycle is repeated every 2 weeks for a total of 4 cycles, followed by:		
		Cyclophosphamide (C)	600	Intravenous	D1	The cycle is repeated every 2 weeks for a total of 4 cycles		
AC → T	CALGB 9741	Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 14 days for a total of 4 cycles, followed by:	Administration of Filgrastin subcutaneously 300 µg on days 3-10 every cycle	100
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	175	Intravenous	D1	The cycle is repeated every 14 days for a total of 4 cycles		
AC → T	CALGB 9741	Doxorrubicin (A)	60	Intravenous	D1	Repeat the cycle every 14 days for a total of 4cycles, followed by:	Administration of Filgrastin subcutaneously 5 µg/kg on days 3-10 every cycle	100
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	80	Intravenous	D1	Weekly for 12 weeks		
AC → Docetaxel	No information	Doxorrubicin (A)	60	Intravenous	D1	Repeat the cycle every 14 days for a total of 4 cycles, followed by:	Administration of Pegfilgrastim subcutaneous on D2 for each cycle	101
		Cyclophosphamide (C)	600	Intravenous	D1			
		Docetaxel (T)	75	Intravenous	D1	The cycle is repeated every 14 days for a total of 4 cycles		

ADJUVANT THERAPY								
COMBINATION REGIMENS OF DOSE-DENSE FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
AC (Dose-densa) → T/H → H	No information	Doxorrubicin (A)	60	Intravenous	D1	Repeat the cycle every 14 days for a total of 4 cycles, followed by:	Administration of Pegfilgrastim subcutaneous on D2 for each cycle the first chemotherapy cycle	102
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	175	Intravenous	D1	The cycle is repeated every 14 days for a total of 4 cycles		
		Trastuzumab (H)	Loading dose: 4 mg/kg (hroughout the administration of Paclitaxel)	Intravenous	Weekly	Administered for 1 year		
			Maintenance dose: 2 mg/kg					
AC (Dose-densa) → T/H AC → H + Lapatinib	EGF10023	Doxorrubicin (A)	60	Intravenous	D1	Repeat the cycle every 14 days for a total of 4 cycles, followed by:	Administration of Pegfilgrastim subcutaneous on D2 for each cycle the first chemotherapy cycle	103
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	80	Intravenous	D1	Weekly repeated until completing 12 weeks, followed by:		
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly			
			Maintenance dose: 2 mg/kg					
		Lapatinib	1000 mg	Oral	Daily			
		Trastuzumab (H)	6 mg/kg	Intravenous	every 3 weeks	To complete 52 weeks (1 year)		
Docetaxel → AC	No information	Docetaxel (T)	75	Intravenous	D1	Repeat the cycle every 14 days for a total of 4 cycles, followed by:	Administration of Pegfilgrastim subcutaneous on D2 for each cycle	101
		Doxorrubicin (A)	60	Intravenous	D1	The cycle is repeated every 14 days for a total of 4 cycles		
		Cyclophosphamide (C)	600	Intravenous	D1			

ADJUVANT THERAPY								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
AC → T (WEEKLY)	NCT00004125	Doxorrubicin (A)	60	Intravenous	D1	Repeat the cycle every 14 days for a total of 4 cycles, followed by:	No information	93
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	80	Intravenous	D1 (weekly)	Repeat until you have completed 12 weeks		
AC → TH	NCCTG - N 9831	Doxorrubicin (A)	60	Intravenous	D1	Repeat the cycle every 14 days for a total of 4 cycles, followed by:	Totaling 52 weeks. Emetogenic potential: high (for AC) and low (for paclitaxel). PotentialAnafi Lactic: high (for paclitaxel).	104
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	80 (for 1 h)	Intravenous	D1	Repeats weekly cycle for 12 weeks, followed by:		
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly			
			Maintenance dose: 2 mg/kg					
		Trastuzumab (H)	2 mg/kg	Intravenous	Weekly	Repeat weekly for 40 weeks		
AC → TH	NCCTG - N 9831	Doxorrubicin (A)	60	Intravenous	D1	Repeat the cycle every 14 days for a total of 4 cycles, followed by:	Totaling 52 weeks. Emetogenic potential: high (for AC) and low (for paclitaxel). Potential Anafiactic: high (for paclitaxel).	104
		Cyclophosphamide (C)	600	Intravenous	D1			
		Paclitaxel (T)	175 (for 3 h)	Intravenous	D1	Repeating the cycle every 3 weeks for 4 cycles 12 weeks, followed by:		
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly			
			Maintenance dose: 2 mg/kg					
		Trastuzumab (H)	2 mg/kg	Intravenous	Weekly	Repeat weekly for 40 weeks		
CT	No information	Cyclophosphamide (C)	600	Intravenous	D1	The cycle is repeated every 21 days up to 4 cycles	No information	105
		Docetaxel (T)	75	Intravenous	D1			

ADJUVANT THERAPY								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m²)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
DH → FEC	FinHER	Docetaxel (T)	100	Intravenous	D1	Repeat the cycle every 21 days for a total of 3 cycles, followed by:	High potential emetogenic the FEC cycle	106
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly			
			Maintenance dose: 2 mg/kg					
		5-Fluorouracil (F)	600	Intravenous	D1	The cycle is repeated every 21 days for a total of 3 cycles		
		Epirubicin (E)	60	Intravenous	D1			
		Cyclophosphamide (C)	600	Intravenous	D1			
FAC	GEICAM	5-Fluorouracil (F)	500	Intravenous	D1	The cycle is repeated every 21 days for a total of 6 cycles	No information	95
		Doxorrubicin (A)	50	Intravenous	D1			
		Cyclophosphamide (C)	500	Intravenous	D1			
TCH	BCIRG 006	Docetaxel (T)	75	Intravenous	D1	Repeat the cycle every 21 days for a total of 6 cycles, followed by:	No information	107
		Carboplatin (C)	AUC of 6	Intravenous	D1			
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly			
			Maintenance dose: 2 mg/kg					
		Trastuzumab (H)	6 mg/kg	Intravenous	every 3 weeks	Repeat until you have completed 1 year		
VH → FEC	No information	Vinorelbine (V)	25	Intravenous	D1	Repeat the cycle every 21 days for a total of 4 cycles, followed by:	High potential emetogenic the FEC cycle	106
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	D1 weekly for 9 weeks			
			Maintenance dose: 2 mg/kg					
		5-Fluorouracil (F)	600	Intravenous	D1	The cycle is repeated every 21 days for a total of 4 cycles		
		Epirubicin (E)	60	Intravenous	D1			
		Cyclophosphamide (C)	600	Intravenous	D1			

ADJUVANT THERAPY								
REGIMENS OF SOLE AGENTS (HORMONE THERAPY)								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Anastrozole	ATAC Trial	Anastrozole	1	Oral	Daily	Daily repeated for 5 years	ER+ or ER- unknown	108
Exemestane	TEAM Trial	Exemestane	25	Oral	Daily	Daily repeated for 5 years	ER+ or ER- unknown	109
Goserelin (Zoladex)	ZEBRA	Goserelin	3,6	Subcutaneous	every 28 days	Repeats every month to 2 years. Proprietary adjuvant treatment.	Premenopausal women with hormone receptors (estrogen or progesterone) positive	110
Letrozole	No information	Letrozole	2,5	Oral	Daily	Daily repeated for 5 years	ER+ or ER unknown and metastatic	111
Tamoxifen + Anastrozole	ARNO 95 Study	Tamoxifen	20	Oral	Daily	Repeated daily for 2 to 3 years, followed by:	No information	112
		Anastrozole	1	Oral	Daily	Repeat daily for 2 to 3 years (SWITCH = Exchange)		
Tamoxifen + Exemestane	IES Trial	Tamoxifen	20	Oral	Daily	Repeated daily for 2 to 3 years, followed by:	No information	113
		Exemestane	25	Oral	Daily	Daily repeated for 5 years		
Tamoxifen + Letrozole	BIG 1-98	Tamoxifen	20	Oral	Daily	Repeated daily for 2 to 3 years, followed by:	The scheme can be started with Letrozole or Anastrozolee, and sequencing should be stopped at 5 years of therapy	114
		Letrozole	2,5	Oral	Daily	Repeated daily for 2 to 3 years		
Tamoxifen + Letrozole	NCIC CTG MA-17 Trial	Tamoxifen	20	Oral	Daily	Daily repeated for 5 years, followed by:	ER+	115
		Letrozole	2,5	Oral	Daily	Daily repeated for 5 years		

THERAPY FOR METASTATIC TUMORS								
METASTATIC BREAST CANCER								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
AT	10961	Doxorrubicin (A)	60 (Bolus)	Intravenous	D1	The cycle is repeated every 21 days for 6 cycles	No information	116
		Paclitaxel (T)	175 (3 h)	Intravenous	D1			
Gemcitabine + Capecitabine	No information	Gemcitabine	800	Intravenous	D1 and D8	The cycle is repeated every 21 days	No information	117
		Capecitabine (X)	750 (2x/day)	Oral	D1-14			
Gemcitabine + Capecitabine	No information	Gemcitabine	2000	Intravenous	D1	The cycle is repeated every 21 days	Patients pretreated with anthracyclines and taxanes	118
		Capecitabine (X)	1250 (2x/day)	Oral	D1-14			
Gemcitabine + Docetaxel	No information	Gemcitabine (G)	1200	Intravenous	D1 and D8	The cycle is repeated every 21 days	Patient pretreated with Anthracyclines and Taxanes. Observe myelotoxicity.	119
		Docetaxel (T)	75	Intravenous	D1			
Gemcitabine + Paclitaxel	No information	Gemcitabine (G)	1250	Intravenous	D1 and D8	The cycle is repeated every 21 days	No information	120
		Paclitaxel (T)	175	Intravenous	D1			
LHRH + Tamixifeno	No information	LHRH (luteinizing hormone-releasing hormone)	6,6 mg (Buserelin) OR 3,6 mg (Goserelin)	Subcutaneous	D1	The cycle is repeated every 6 weeks for the first 12 weeks and 8 weeks.	Woman premenopausal. Preferable negative HER.	121
		Tamoxifen	20 mg	Oral	Continuous			
Netronomic	No information	Cyclophosphamide (C)	50 mg/day	Intravenous	Continuous	Contínuo	Biweekly blood count	122
		Methotrexate (M)	2,5 mg/day	Intravenous	D1 and D2 every week			
Vinorelbine + Gemcitabine	GEICAM	Vinorelbine (VNB)	30	Intravenous	D1 and D8	The cycle is repeated every 21 days	Patient pretreated with Anthracyclines and Taxanes.	123
		Gemcitabine	1200	Intravenous	D1 and D8			
Vinorelbine + Gemcitabine	No information	Vinorelbine (VNB)	25	Intravenous	D1 and D15	Repeated every 2 weeks for at least 6 cycles	No information	124
		Gemcitabine (G)	1000	Intravenous	D1 and D15			

THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Anastrozole + Goserelin	No information	Anastrozole	1 mg	Oral	Daily	The cycle is repeated every 28 days until disease progression	Women premenopausal	125
		Goserelin	3,6 mg	Subcutaneous	every 28 days			
AT	E1193	Doxorrubicin (A)	50	Intravenous	D1	The cycle is repeated every 21 days	No information	126
		Paclitaxel (T)	150 (for 24 h)	Intravenous	D1			
A → T	E1193	Doxorrubicin (A)	60	Intravenous	D1	Repeat the cycle every 21 days, a maximum of 8 cycles, followed by:	No information	126
		Paclitaxel (T)	175	Intravenous	D1	The cycle is repeated every 21 days until disease progression		
T → A	E1193	Paclitaxel (T)	175	Intravenous	D1	The cycle is repeated every 21 days until disease progression, followed by:	No information	126
		Doxorrubicin (A)	60	Intravenous	D1	Repeat the cycle every 21 days, a maximum of 8 cycles		
AT	ERASME 3	Doxorrubicin (A)	50 (15 minutes)	Intravenous	D1	Repeat the cycle every 21 days, a maximum of 8 cycles	No information	127
		Paclitaxel (T)	150 (3 h)	Intravenous	D1			
Capecitabine + Bevacizumab	RIBBON 1	Capecitabine (X)	1000 (2x/day)	Oral	D1-14	The cycle is repeated every 21 days	Check recommendations for prevention of nausea and vomiting of oral agents.	128
		Bevacizumab (A)	15 mg/Kg	Intravenous	D1			
Carboplatin + Docetaxel	No information	Carboplatin (C)	AUC dof 6	Intravenous	D1	The cycle is repeated every 21 days	No information	129
		Docetaxel (T)	75	Intravenous	D1			
Carboplatin + Gemcitabine	No information	Carboplatin (C)	AUC of 5 (60 minutes)	Intravenous	D1	The cycle is repeated every 21 days	No information	130
		Gemcitabine (G)	1000 (30 minuntes)	Intravenous	D1 and D8			

THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Carboplatin + Paclitaxel	No information	Carboplatin (C)	AUC de 2 (30 a 60 minutes)	Intravenous	D1, D8 and D15	The cycle is repeated every 21 days	No information	131
		Paclitaxel (T)	100 – 135 (1 h)	Intravenous	D1, D8 and D15			
CMF (Modified)	BR9601	Cyclophosphamide (C)	750	Intravenous	D1	The cycle is repeated every 21 days for a total of 8 cycles	No information	92
		Methotrexate (M)	50	Intravenous	D1			
		5-Fluorouracil (F)	600	Intravenous	D1			
Cisplatin + Vinorelbine	No information	Cisplatin (P)	75	Intravenous	D1	The cycle is repeated every 21 days	No information	132
		Vinorelbine (N)	25	Intravenous	D1 and D8			
Docetaxel + Bevacizumab	AVADO Trial	Docetaxel (T)	100	Intravenous	D1	The cycle is repeated every 21 days	No information	133
		Bevacizumab (A)	15 mg/Kg	Intravenous	D1			
Docetaxel + Pegylated Liposomal Doxorubicin	No information	Docetaxel (T)	75	Intravenous	D2	The cycle is repeated every 21 days	No information	134
		Pegylated Liposomal Doxorubicin	30	Intravenous	D1			
Gemcitabine + Paclitaxel	No information	Gemcitabine (G)	1250	Intravenous	D1 and D8	The cycle is repeated every 21 days	No information	135,136
		Paclitaxel (T)	175	Intravenous	D1			
Paclitaxel + Bevacizumab	ECGO 2100	Paclitaxel (T)	90	Intravenous	D1, D8 and D15	The cycle is repeated every 28 days	No information	137
		Bevacizumab (A)	10 mg/Kg	Intravenous	D1 e D15			
XT	No information	Capecitabine (X)	1250 (2x/day)	Oral	D1-14	The cycle is repeated every 21 days	You can decrease the dose of Capecitabine for 825-1000mg/m^2 VO (2x/day) on days 1-14 to reduce the risk of toxicity without compromising the clinical efficacy.	138
		Docetaxel (T)	75	Intravenous	D1			

THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m²)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
XP	No information	Capecitabine (X)	825 (2x/day)	Oral	D1-14	The cycle is repeated every 21 days	No information	139
		Paclitaxel (P)	175	Intravenous	D1			
XN	No information	Capecitabine (X)	1000 (2x/day)	Oral	D1-14	The cycle is repeated every 21 days	No information	139
		Vinorelbine (N)	25	Intravenous	D1 and D8			
XI	No information	Capecitabine (X)	1000 (2x/day)	Oral	D1-14	The cycle is repeated every 21 days	No information	140
		Ixabepilone (I)	40	Intravenous	D1			
THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m²)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Capecitabine + Lapatinib	No information	Capecitabine (X)	1000 (2x/day)	Oral	D1-14	The cycle is repeated every 21 days	Check recommendations for prevention of nausea and vomiting of oral agents	141,142
		Lapatinib	1250	Oral	Daily			
Letrozole + Lapatinib	No information	Letrozole	2,5 mg	Oral	Daily	No information	Check recommendations for prevention of nausea and vomiting of oral agents. Women post menopause.	143
		Lapatinib	1500 mg	Oral	Daily			
TCH	No information	Paclitaxel (T)	175	Intravenous	D2	Repeat the cycle every 21 days for a total of 6 cycles	Emetogenic potential: moderate.Anaphylactic potential: high with paclitaxel	144
		Carboplatin (C)	AUC of 6	Intravenous	D2			
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	D1 of first week			
			Maintenance dose: 2 mg/kg		Weekly			
TCH	BCIRG 007	Docetaxel (T)	75	Intravenous	D1	Repeat the cycle every 21 days for a total of 8 cycles	No information	145
		Carboplatin (C)	AUC of 6	Intravenous	D1			
		Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	D1			
			Maintenance dose: 2 mg/kg	Intravenous	D8 e D15			

THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Trastuzumab + Anastrozole	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose:2 mg/Kg	Intravenous	Weekly	No information	Check recommendations for prevention of nausea and vomiting of oral agents	146
		Anastrozole	1 mg	Oral	Daily			
Trastuzumab + Capecitabine	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose:2 mg/kg	Intravenous	Weekly	The cycle is repeated every 21 days	No information	147
		Capecitabine (X)	1250 (2x/day)	Oral	D1-14			
Trastuzumab + Capecitabine	No information	Trastuzumab (H)	Loading dose: 8 mg/kg Maintenance dose:6 mg/kg	Intravenous	D1 all subsequent cycles	The cycle is repeated every 21 days	Check recommendations for prevention of nausea and vomiting of oral agents	148
		Capecitabine (X)	1250 (2x/dia)	Oral	D1-14			
Trastuzumab + Capecitabine + Docetaxel	No information	Trastuzumab (H)	Loading dose: 8 mg/kg Maintenance dose:6 mg/kg	Intravenous	Weekly	The cycle is repeated every 21 days	Check recommendations for prevention of nausea and vomiting of oral agents	149
		Capecitabine (X)	950 (2x/day)	Oral	D1-14			
		Docetaxel (T)	75	Intravenous	D1			
Trastuzumab + Docetaxel	M77001	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	Frist Step, repeat the cycle every 3 weeks for a total of 6 cycles. Followed by:	No information	150
		Docetaxel (T)	100	Intravenous	every 3 weeks			
		Trastuzumab (H)	2 mg/Kg	Intravenous	every 3 weeks	Repeat the cycle until completing one year		

THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Trastuzumab + Docetaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	D8 and D15	The first cycle is administered weekly for 3 weeks, 1 week rest. For subsequent cycles:	No information	151
		Docetaxel (T)	35	Intravenous	D1, D8 and D15			
		Trastuzumab (H)	2 mg/Kg	Intravenous	Weekly	The cycle is repeated every 4 weeks	No information	
		Docetaxel (T)	35	Intravenous	Weekly			
Trastuzumab + Gemcitabine	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	The cycle is repeated every 21 days	No information	152
		Gemcitabine	1200	Intravenous	Weekly for 2 weeks			
Trastuzumab + Lapatinib	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose:2 mg/kg	Intravenous	Weekly	Continued until progression of disease progression	Check recommendations for prevention of nausea and vomiting of oral agents	153,154
		Lapatinib	1000 mg	Oral	Daily			
Trastuzumab + Paclitaxel	No information	Trastuzumab (H)	Loading dose: 8 mg/kg Maintenance dose:6 mg/kg	Intravenous	Every 3 weeks	Frist Step, repeat the cycle every 3 weeks for a total of 6 cycles. Followed by:	No information	155
		Paclitaxel (T)	175	Intravenous	Every 3 weeks			
		Trastuzumab (H)	6 mg/Kg	Intravenous	Every 3 weeks until completing one year	After completion of chemotherapy or until disease progression		
Trastuzumab + Paclitaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose:2 mg/kg	Intravenous	Weekly	The cycle is repeated every 21 days	No information	156
		Paclitaxel (T)	175 (for 3h)	Intravenous	D1			

THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Trastuzumab + Paclitaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly	Weekly	No information	157
			Maintenance dose:2 mg/kg					
		Paclitaxel (T)	90	Intravenous	D1			
Trastuzumab + Vinorelbine	No information	Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly	Repeat the cycle weekly until disease progression	Good tolerance in older patients.	158,159
			Maintenance dose:2 mg/kg					
		Vinorelbine (N)	25	Intravenous	Weekly			

THERAPY FOR METASTATIC TUMORS								
REGIMENS OF SOLE AGENTS								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Abraxane (nanoparticles albumin-bound to paclitaxel)	No information	Abraxane	260	Intravenous	D1	Repeats the cycle every 21 days	No information	160
Abraxane (nanoparticles albumin-bound to paclitaxel)	No information	Abraxane	125	Intravenous	D1, D8 and D15	Repeats the cycle every 28 days	No information	161
Abraxane (nanoparticles albumin-bound to paclitaxel)	No information	Abraxane	260 (30 minnutes)	Intravenous	D1	Repeats the cycle every 21 days	HER-2 Negative	162
			100	Intravenous	D1, D8 e D15	Repeats the cycle every 28 days		
Pegylated Liposomal Doxorubicin	No information	Pegylated Liposomal Doxorubicin	50	Intravenous	D1	Repeats the cycle every 28 days	HER-2 Negative	163
Pegylated Liposomal Doxorubicin	No information	Pegylated Liposomal Doxorubicin	40	Intravenous	D1	Repeats the cycle every 28 days	No information	164
Fulvestrant	No information	Fulvestrant	250	Intramuscular	D1	Repeat administration every month	No information	165

THERAPY FOR METASTATIC TUMORS								
REGIMENS OF SOLE AGENTS								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Fulvestrant	EFECT	Fulvestrant	500mg loading dose D1, then 250mg on days D14 and D28	Intramuscular	Monthly	Repeat the monthly cycle until disease progression	No information	166
Fulvestrant	FIRST	Fulvestrant	500	Intramuscular	D0, D14 and D28	Repeats the cycle every 28 days	No information	167
Gemcitabine	No information	Gemcitabine	1200 (30 minnutes)	Intravenous	D1, D8 and D15	Repeats the cycle every 28 days	No information	168
Ixabepilone	No information	Ixabepilone	40	Intravenous	D1	Repeats the cycle every 21 days	No information	169,170
			40 (3 h)	Intravenous	D1		HER-2 Negative	
Letrozole	No information	Letrozole	2,5	Oral	Daily	Undefined	Metastatic (first line in post-menopausal women). HER2 negative	111
Trastuzumab (Herceptin)	No information	Trastuzumab (H)	Loading dose: 8 mg/kg	Intravenous	Repeat every 21 days	Continues at a dose of 6mg/kg to disease progression	HER-2 Positive	171
			Maintenance dose: 6 mg/kg					
Vinorelbine (Navelbine)	No information	Vinorelbine (N)	Loading dose: 80	Intravenous	Weekly	Weekly, at least 12 weeks	Metastatic (first line). Well tolerated in elderly patients	172
			Maintenance dose: 60				After 3 administration of maintenance dose, test myelotoxicity	
PALLIATIVE THERAPY								
MONOTHERAPY								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Capecitabine (Xeloda)	No information	Capecitabine (X)	1000 (2x/day) for 2 weeks	Oral	Daily	No information	No information	173
Dietilestilbestrol	No information	Dietilestilbestrol	6 mg	Oral	Daily	No information	No information	174
Fulvestrant	No information	Fulvestrant	250 mg	Intramuscular	D1	Repeat administration every 28 days	No information	165

Gemcitabine	No information	Gemcitabine	1200 mg/m^2 (30 minutes)	Intravenous	D1, D8 and D15	Repeat the cycles every 28 days	Metastatic	168
Trastuzumab (Herceptin)	NCT 00045032	Trastuzumab (H)	Loading dose: 8 mg/kg Maintenance dose: 6 mg/kg	Intravenous	Weekly	Repeat the cycles every 21 days	Continues at a dose of 6 mg/kg to disease progression	175
Trastuzumab (Herceptin)	HERA	Trastuzumab (H)	Loading dose: 8 mg/kg Maintenance dose: 6 mg/kg	Intravenous	Weekly	Repeats the cycle every 21 days up to 2 years	After adjuvant chemotherapy and / or radiotherapy	176

PALLIATIVE THERAPY

COMBINATION REGIMENS

PROTOCOL	TRIAL	DRUGS NAMES	DOSAGE (mg/m^2)	ROUTE OF ADMINISTRATION	DAYS OF ADMINISTRATION	SCHEME THERAPEUTIC	COMMENTS	BIBLIOGRAPHIC REFERENCES
Docetaxel + Doxorrubicin	No information	Docetaxel (T)	75	Intravenous	D1	Repeating the cycle every 21 days to a maximum of 8 cycles	Only in case of visceral metastasis whose need for responsefast supplant risk of toxicity	177
		Doxorrubicin (A)	50	Intravenous	D1			
Gemcitabine + Paclitaxel	No information	Gemcitabine (G)	1250	Intravenous	D1 and D8	The cycle is repeated every 21 days	No information	120
		Paclitaxel (T)	175	Intravenous	D1			
LHRH + Tamoxifen	No information	Goserelin	3,6 mg	Subcutaneous	D1	Even prohibitive toxicity	Woman premenopausal	178
		Tamoxifen	20 mg	Oral	Daily			
XT	No information	Capecitabine (X)	1250 (2x/day)	Oral	D1-14	The cycle is repeated every 21 days	Capecitabine can decrease the dose of 825-1000 mg/m^2 oral (2x/day) on days 1-14 to reduce the risk of toxicity without compromising clinical efficacy	138
		Docetaxel (T)	75	Intravenous	D1			

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Table 5: Breast Cancer Protocols from 2011 to 2015

PROTOCOLS OF BREAST CANCER (2011-2015)								
NEOADJUVANT THERAPY								
TYPE HER2 UNKNOWN								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
FAC → Docetaxel	No information	5-Fluorouracil (F)	500 (Bolus)	Intravenous	D1	The cycle is repeated every 21 days for 3 cycles, followed by:	No information	179
		Doxorrubicin (A)	50 (Bolus)	Intravenous	D1			
		Cyclophosphamide (C)	500 (Bolus)	Intravenous	D1			
		Docetaxel (T)	100	Intravenous	D1	The cycle is repeated every 21 days for a total of 3 cycles		
Anastrozolee + Goserelin	No information	Anastrozole	1 mg	Oral	Daily	Initiated 24 weeks before surgery until withdrawal criteria	Woman premenopausal	180
		Goserelin	3,6 mg	SC	every 28 days			

NEOADJUVANT THERAPY								
TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m²)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Docetaxel + Trastuzumab + Pertuzumab	NecSphere Trial (CLEOPATRA)	Trastuzumab (H)	Loading dose:8 mg/kg Maintenance dose: 6 mg/kg	Intravenous	D1	Repeat every 21 days	Emetogenic potential: Low.	181
		Pertuzumab	Loading dose: 840 mg Maintenance dose:420 mg	Intravenous	D1			
		Docetaxel (T)	75 – 100	Intravenous	D1			
Paclitaxel + Trastuzumab → Lapatinib	NecALTTO Trial	Lapatinib	750 mg/dia	Oral	D1	Repeat until a total of 6 cycles, followed by:	Emetogenic potential: Low. Check recommendations for prevention of nausea and vomiting of oral agents. Potential Anafi Lactic: high	182
		Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly			
		Paclitaxel (T)	80	Intravenous	Weekly	Repeat for 12 weeks		

NEOADJUVANT THERAPY								
TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m²)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
T → FEC + Trastuzumab + Lapatinib	CHER-LOB Study	Paclitaxel (T)	80 (1 h)	Intravenous	D1	Repeat the cycle every 7 days for a total of 12 cycles	Emetogenic potential: high. Check recommendations for prevention of nausea and vomiting of oral agents. Potential Anafi Lactic: high (for paclitaxel)	183
		5-Fluorouracil (F)	600	Intravenous	D1	Repeat the cycle (FEC) every 21 days		
		Epirrubicina (E)	75	Intravenous	D1			
		Cyclophosphamide (C)	600	Intravenous	D1			
		Trastuzumab (H)	Loading dose: 4 mg/kg (90 min on D1) Maintenance dose: 2 mg/kg (30 min)	Intravenous	Concomitant with any chemotherapy. Weekly up to 24 weeks	Repeat the cycle until you have completed 26 weeks		
		Lapatinib	1000 mg/day	Oral	Concomitant with any chemotherapy, from D1			

Trastuzumab + Docetaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	After local surgical treatment continue:	No information	179
		Docetaxel	No information	Intravenous	Weekly			
		Trastuzumab (H)	Loading dose: 8 mg/kg Maintenance dose: 6 mg/kg	Intravenous	Every 3 weeks	Repeat until you have completed 52 weeks		
Trastuzumab + Paclitaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg Maintenance dose: 2 mg/kg	Intravenous	Weekly	After local surgical treatment continue:	No information	179
		Paclitaxel (T)	No information	Intravenous	Weekly			
		Trastuzumab (H)	Loading dose: 8 mg/kg Maintenance dose: 6 mg/kg	Intravenous	Every 3 weeks	Repeat until you have completed 52 weeks		

ADJUVANT THERAPY

COMBINATION REGIMENS OF DOSE-DENSE FOR TYPE HER2 NEGATIVE

PROTOCOL	TRIAL	DRUGS NAMES	DOSAGE (mg/m^2)	ROUTE OF ADMINISTRATION	DAYS OF ADMINISTRATION	SCHEME THERAPEUTIC	COMMENTS	BIBLIOGRAPHIC REFERENCES
FAC → Docetaxel	No information	5-Fluorouracil (F)	500 (Bolus)	Intravenous	D1 and D8	The cycle is repeated every 21 days for 3 cycles, followed by:	No information	179
		Doxorrubicin (A)	50 (Bolus)	Intravenous	D1			
		Cyclophosphamide (C)	500 (Bolus)	Intravenous	D1			
		Docetaxel	100	Intravenous	D1	The cycle is repeated every 21 days for a total of 3 cycles		

ADJUVANT THERAPY								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
FAC → Docetaxel	No information	5-Fluorouracil (F)	500 (Bolus)	Intravenous	D1 e D8	The cycle is repeated every 21 days for 3 cycles, followed by:	No information	179
		Doxorrubicin (A)	50 (Bolus)	Intravenous	D1			
		Cyclophosphamide (C)	500 (Bolus)	Intravenous	D1			
		Docetaxel (T)	100	Intravenous	D1	The cycle is repeated every 21 days for a total of 3 cycles		
THERAPY FOR METASTATIC TUMORS								
METASTATIC BREAST CANCER								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGAPHIC REFERENCES**
Everolimus + Exemestane	BOLERO-2	Everolimus	10 mg	Oral	Daily	No information	After previous treatment with letrozole or anastrozole.	184
		Exemestane	25 mg	Oral	Daily			
THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 NEGATIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Liposomal Cisplatin + Vinorelbine	No information	Liposomal Cisplatin	120	Intravenous	D1, D8 and D15	The cycle is repeated every 21 days	No information	185
		Vinorelbine (N)	30	Intravenous	D1 and D8			
THERAPY FOR METASTATIC TUMORS								
COMBINATION REGIMENS FOR TYPE HER2 POSITIVE								
PROTOCOL	**TRIAL**	**DRUGS NAMES**	**DOSAGE (mg/m^2)**	**ROUTE OF ADMINISTRATION**	**DAYS OF ADMINISTRATION**	**SCHEME THERAPEUTIC**	**COMMENTS**	**BIBLIOGRAPHIC REFERENCES**
Trastuzumab + Paclitaxel	No information	Trastuzumab (H)	Loading dose: 4 mg/kg	Intravenous	Weekly	Weekly	No information	186
			Maintenance dose: 2 mg/kg					
		Paclitaxel (T)	90	Intravenous	Weeks 1 to 6, 8 to 13			

THERAPY FOR METASTATIC TUMORS								
REGIMENS OF SOLE AGENTS								
PROTOCOL	TRIAL	DRUGS NAMES	DOSAGE	ROUTE OF ADMINISTRATION	DAYS OF ADMINISTRATION	SCHEME THERAPEUTIC	COMMENTS	BIBLIOGRAPHIC REFERENCES
Eribulin (Halaven)	EMBRACE	Eribulin	1,4 mg/m^2	Intravenous	D1 and D8	Repeat every 21 days	Metastatic after phase two chemotherapeutic regimens for advanced cancer (Antracilcina and taxane)	187
T-DM1 (Kadcyla)	EMILIA Trial	Trastuzumab emtansine	3,6 mg/kg	Intravenous	Repeat every 21 days	No information	HER-2 Positive	188

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rationalized in their use and organized to make their application practical. Among the many advantages observed after the implementation of this model of care is the significant increase in the safety and quality of care, since it attenuates the variability of clinical behavior.

The diversity of procedures, especially the pharmacotherapeutics, available today for breast cancer, as well as the urgent need for transparent and rational communication with patients require the elaboration and adoption of tools that are simple and capable of expediting the provision of these services . Among them, the development of evidence-based clinical protocols is increasingly valued.

Protocols are considered an important tool for coping with various problems in service delivery and management. They focus on the standardization of clinical and surgical procedures in outpatient and hospital settings.

The results obtained in this review demonstrate the amount of information available for breast cancer treatment and the difficulty of summarizing it. However, it also demonstrates the relentless struggle of researchers to find a solution to breast cancer in a puerile attempt to overcome the disease.

In spite of the attempts and endless drugs used, what is perceived is that we are losing the fight, and contrary to every arsenal, millions of people die of cancer worldwide.

We hope that this review may help, in particular countries with low health resources, in the definition of efficient protocols and in accordance with the reality of each country. As well as setting a milestone in evidence-based search, helping the world in the fight against breast cancer.

DECLARATION OF CONFLICTS OF INTEREST

The authors state that do not have any conflicts of interest

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