NCCTG

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Country: USA

Group: North Central Cancer Treatment Group **(NCCTG)**

Chair: Edith A. Perez
Mayo Clinic
4500 San Pablo Road
JACKSONVILLE, FL 32224
USA
Email: perez.edith@mayo.edu

Other subgroup head/member: Kendrith Rowland
NCCTG Member Co-Chair

Website: http://ncctg.mayo.edu

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Title: N9831: Phase III trial of doxorubicin and cyclophosphamide (AC) followed by weekly paclitaxel with or without trastuzumab as adjuvant treatment for women with HER2 over-expressing or amplified node positive or high-risk node negative breast cancer.

Coordinator(s): Edith A. Perez
Mayo Clinic
4500 San Pablo Road
JACKSONVILLE, FL 32224
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: perez.edith@mayo.edu

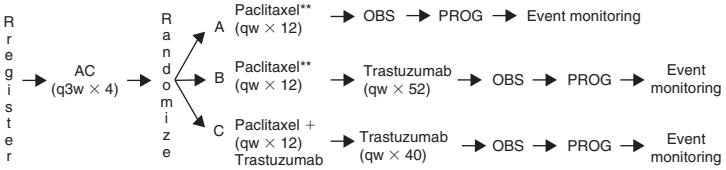
Summary:

- Study opened on 19 May 2000
- Study closed on 29 April 2005
- Final accrual: 3505 patients

Objectives:

- To pairwise compare the disease-free survival, overall survival, and cardiotoxicity of the three study regimens.

Scheme:



AC = doxorubicin/cyclophosphamide

Patients will be randomized if their tumor specimen on central review is confirmed as HER-2 amplified by FISH or 3+ by Hercep Test. If not confirmed, the patient will not receive any further study treatment and will go to event-monitoring phase; further adjuvant therapy will be as per investigator's discretion and the patient will be followed for disease free survival and overall survival.

** In April 2005, a joint interim analysis of the data from NSABP B-31 and NCCTG N9831 demonstrated that the addition of trastuzumab to paclitaxel following AC chemotherapy significantly prolonged disease-free survial. Following consultations with the NCCTG Data Monitoring Committee and NCI CTEP, patients randomized to Arm A who would complete or had completed paclitaxel on or after 25/10/2004, were offered the opportunity to receive trastuzumab (concurrently with paclitaxel, if patient was still receiving paclitaxel) and patients randomized to Arm B who were receiving paclitaxel on 25/04/2005, were offered the opportunity to receive trastuzumab concurrently with paclitaxel.

Update:

- Study closed on 29 April 2005. Joint analysis with NSABP B-31 was published in *New Engl J Med*. Final analysis is ongoing.

Related Publications: Perez EA, Suman VJ, Davidson NE, Kaufman PA, Martino S, Dakhil SR, Ingle JN, Rodeheffer RJ, Gersh BJ, Jaffe AS. Effect of doxorubicin plus cyclophosphamide on left ventricular ejection fraction

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in patients with breast cancer in the North Central Cancer Treatment Group N9831 Intergroup Adjuvant Trial. *J Clin Oncol* 2004; 22(18): 3700–3704.

Roche PC, Suman VJ, Jenkins RB, Davidson NE, Martino S, Kaufman PA, Addo FK, Murphy B, Ingle JN, Perez EA. Concordance between local and central laboratory HER2 testing in the breast intergroup trial N9831. *J Natl Cancer Inst* 2002; 94(11): 855–857.

Romond EH, Perez EA, Bryant J, Suman VJ, Geyer CE Jr, Davidson NE, Tan-Chiu E, Martino S, Paik S, Kaufman PA, Swain SM, Pisansky TM, Fehrenbacher L, Kutteh LA, Vogel VG, Visscher DW, Yothers G, Jenkins RB, Brown AM, Dakhil SR, Mamounas EP, Lingle WL, Klein PM, Ingle JN, Wolmark N. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *New Engl J Med* 2005; 353(16): 1673–1684.

Topics:

- Anthracyclines
- Cardiac function
- HER2 positive patients
- Taxanes
- Trastuzumab

Keywords: Phase III, breast cancer, adjuvant therapy, HER2+ , cyclophosphamide, doxorubicin, paclitaxel, trastuzumab, Cytoxan, Adriamycin, Taxol, Herceptin

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Title: N063D, BIG 2-06: Phase III Trial of Trastuzumab and/or Lapatinib in Patients with HER2+ Breast Cancer (Full title/acronym not available at time of publication).

Coordinator(s): Edith A. Perez
James N. Ingle
Mayo Clinic
200 First Street SW
ROCHESTER MN 55905
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: perez.edith@mayo.edu
ingle.james@mayo.edu

with Co-PI, Martine J. Piccart

Summary:

- Study scheduled to open January 2007
- Target accrual: 4000 in North America and 8000 total internationally

Objectives:

Treatment

- To compare disease-free survival (DFS) in patients with HER2 overexpressing and/or amplified breast cancer randomised to trastuzumab for 1 year versus lapatinib for 1 year versus a sequence of trastuzumab and lapatinib (1 year total) versus a combination of trastuzumab and lapatinib (1 year total).
- To compare overall survival (OS) in patients randomised to the four arms.
- To compare time to recurrence (TTR).
- To compare time to distant recurrence (TTDR).
- To evaluate the safety and tolerability of all four treatment groups.
- To compare the cumulative incidence of brain metastases as the first site of breast cancer recurrence.

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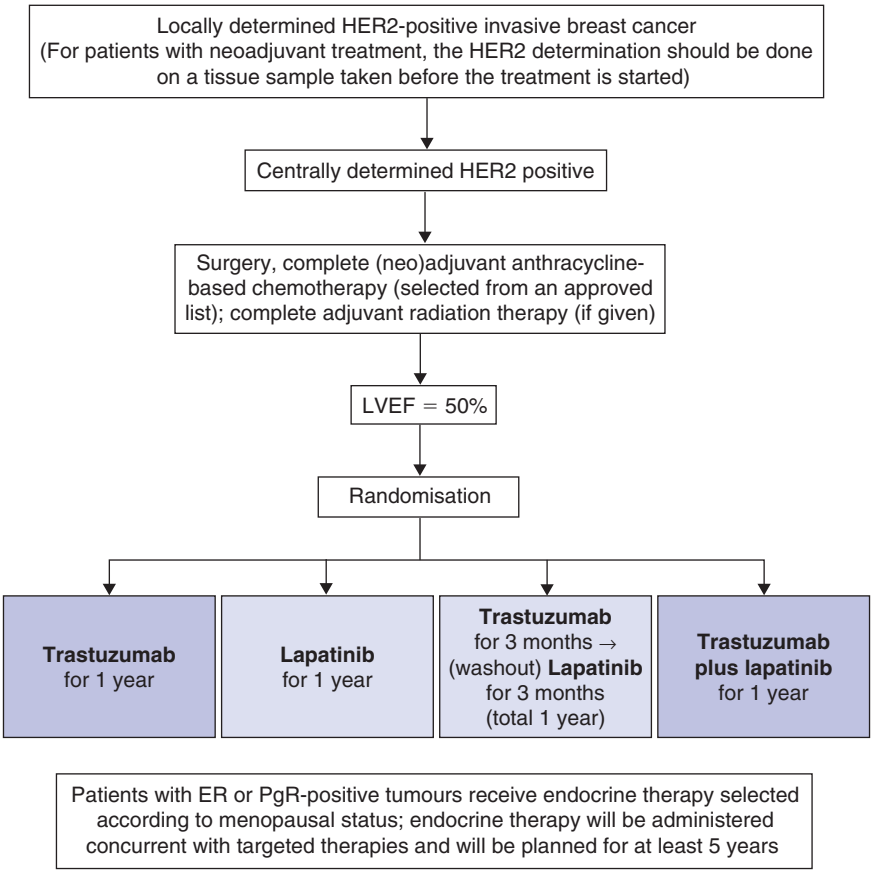
Scheme:



Update:
- Scheduled to open January 2007 with target accrual of 4000 patients in North America and 8000 patients total internationally

Related Publications: None available

Topics:
- Adjuvant HER2+breast cancer
- Blood markers

Keywords: Phase III, adjuvant breast cancer, HER2+, trastuzumab, lapatinib, herceptin, tykerb

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Title: N0537: Phase II Trial of VEGF Trap in Patients with Metastatic Breast Cancer Previously Treated with Anthracycline and/or Taxane

Coordinator(s): Edith A. Perez
Timothy J Hobday
Mayo Clinic
200 First Street SW
ROCHESTER MN 55905
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: perez.edith@mayo.edu
hobday.timothy@mayo.edu

Summary :

- Study scheduled to open November 2006
- Target accrual: 45

Objectives:

Treatment

- To assess anti-tumor activity (tumor response rate as defined by the RECIST criteria) of VEGF Trap in patients with metastatic breast cancer that have received =2 prior chemotherapy regimens for metastatic disease including taxane and/or anthracycline.
- To assess the 6-month progression-free survival rate of patients receiving VEGF Trap.
- To describe the adverse event profile (grade using the NCI CTCAE version 3.0) of VEGF Trap in patients with metastatic breast cancer previously treated with anthracycline and/or taxane.
- To describe the progression-free survival times of patients receiving VEGF Trap.
- To describe the overall survival of patients receiving VEGF Trap.
- To describe the duration of response in patients receiving VEGF Trap.

Translational

- To explore predictive markers of response to VEGF Trap based on pretreatment tumor characteristics as they relate to tumor angiogenesis, and to assess the effects of VEGF Trap on the patient's systemic angiogenic state, as measured by a novel plasma bioassay.
- Ascertain VEGF, VEGF-R, phosphoVEGF-R, HIF-1a, and/or tumor microvessel density levels pretreatment with VEGF Trap and posttreatment.
- To bank serum, plasma, genetic material, and tissue for future studies to identify biomarkers and correlates of response to treatment.

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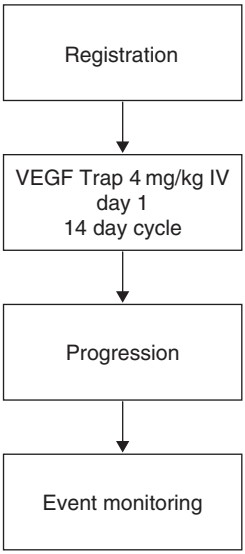
Scheme:



Update:

- Scheduled to open November 2006 with target accrual of 45

Related Publications:

Byrne AT, Ross L, Holash J, et al. Vascular endothelial growth factor-trap decreases tumor burden, inhibits ascites, and causes dramatic vascular remodeling in an ovarian cancer model. Clin Cancer Res 2003; 9:5721–5728.

Topics:

- Metastatic breast cancer
- Blood markers

Keywords:

Phase II, metastatic breast cancer, VEGF Trap

https://doi.org/10.1017/S1470903106009291 Published online by Cambridge University Press

Title: N0531: Phase II trial of weekly NAB (nanoparticle albumin bound)-paclitaxel (nab-paclitaxel) (abraxane) in combination with gemcitabine in patients with metastatic breast cancer.

Coordinator(s): Edith A. Perez
Mayo Clinic
4500 San Pablo Road
JACKSONVILLE, FL 32224
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: perez.edith@mayo.edu

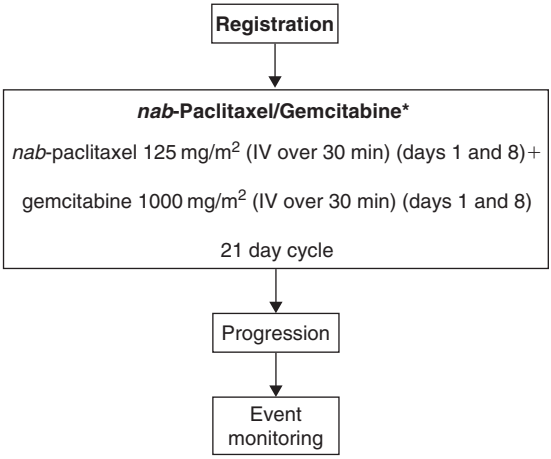
Summary:

- Study opened on 19 August 2005
- Target accrual: 43 patients

Objectives:

- The primary goal is to assess the anti-tumor activity (measured by response rates according to RECIST criteria) and adverse event profile (measured by the incidence and severity of observed adverse events graded by NCI CTCAE v3.0) of the regimen paclitaxel protein-bound particles for injectable suspension/gemcitabine for the treatment of patients with metastatic breast cancer.
- Secondary goals are to assess time to disease progression and survival in these patients with this regimen.
- Translational goal is to determine if there is a correlation between serum caveolin-1 levels and clinical outcome (response rate).

Scheme:



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Update:

- Study closed 26 May 2006 with total accrual of 50.

Related Publications:

Albain KS, Nag S, Calderillo-Ruiz G, Jordaan JP, Llombart A, Pluzanska A, Pawlicki M, Melemed AS, O'Shaughnessy J, Reyes JM. Global phase III study of gemcitabine plus paclitaxel (GT) vs. paclitaxel (T) as frontline therapy for metastatic breast cancer (MBC): First report of overall survival [Abstract 510]. *Proc Am Soc Clin Oncol (ASCO)* 2004; 22: 14S.

O'Shaughnessy J, Tjulandin S, Davidson N, *et al*. ABI-007 (ABRAXANE), a Nanoparticle Albumin-bound (nab) Paclitaxel Demonstrates Superior Efficacy vs Taxol in MBC: A Phase III Trial. *San Antonio Breast Cancer Symposium*, December 2003, San Antonio, TX, Latebreaker Abstract 44.

Topics:

- Metastatic breast cancer
- Gemcitabine
- Taxanes

Keywords:

Phase II, metastatic breast cancer, gemcitabine, Gemzar, nab-paclitaxel, abraxane, paclitaxel protein-bound particles for injectable suspension

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Title: N0437: Phase II trial of CT-2103 (Xyotax) with capecitabine as first-line chemotherapy for patients with metastatic breast cancer.

Coordinator(s): Edith A. Perez
Mayo Clinic
4500 San Pablo Road
JACKSONVILLE, FL 32224
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: perez.edith@mayo.edu

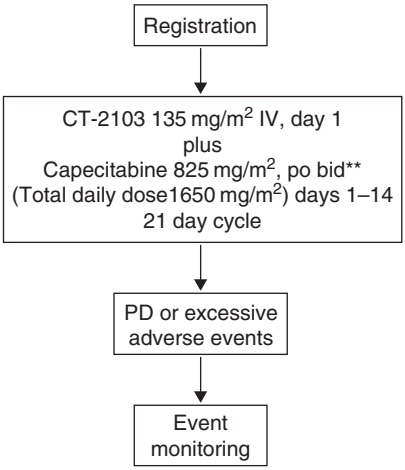
Summary:

- Study opened on 15 February 2006
- Target accrual: 45 patients

Objectives:

- To assess tumor response rate (RECIST criteria) and adverse event profile (NCI CTCAE v3.0) of CT-2103 in women or men with no prior chemotherapy for metastatic HER2 negative breast cancer.
- To examine the distributions of disease-free progression times and survival times.

Scheme:



** This dose is for patients with normal renal function (calculated creatinine clearance of ≥50 mL/min). Patients with moderate renal impairment (calculated creatinine clearance 30–50 mL/min) at base line require a dose reduction to 80% of the capecitabine starting dose or 660 mg/m^2 BID.

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Update:

- Study has accrued 15 patients as of October 2006.

Related Publications:

Gradishar WJ, Meza LA, Bipinkumar A, *et al*. Capecitabine plus paclitaxel as front-line therapy for metastatic breast cancer: a multicenter phase II study. *J Clin Oncol* 2004; 22: 2321–2327.

Xyotax (CT-2103) Investigator's Brochure, Cell Therapeutics, Feb 2004.

Topics:

- Metastatic breast cancer
- Capecitabine
- HER2 negative patients
- Taxanes

Keywords: Phase II, metastatic breast cancer, capecitabine, polyglutamate paclitaxel, Xeloda, Xyotax

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Title: N0436: Phase II trial of concurrent irinotecan plus cetuximab in patients with advanced breast cancer with prior anthracycline and/or taxane-containing therapy.

Coordinator(s): Timothy J. Hobday
Mayo Clinic
200 First Street, SW
ROCHESTER, MN 55905
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: hobday.timothy@mayo.edu

Summary:

- Study opened on 16 February 2006
- Target accrual: 62 patients

Objectives:

Treatment:

- To determine the anti-tumor activity by confirmed response rate of concurrent irinotecan and cetuximab in patients with advanced breast cancer with prior anthracycline and/or taxane-containing therapy.
- To estimate 6-month progression-free survival.
- To evaluate the adverse event profile of irinotecan in combination with cetuximab in patients with metastatic breast cancer.
- To obtain an estimated progression-free survival of patients.
- To obtain an estimated overall survival.

Translational Research:

- To evaluate markers of the EGFR pathway and related downstream pathways in relation to clinical activity.
- To explore the relationship between UGT1A1 genotype and both response and adverse events in patients treated with irinotecan and cetuximab.
- To explore the relationship of topoisomerase 1-alpha levels and clinical outcome for study patients.

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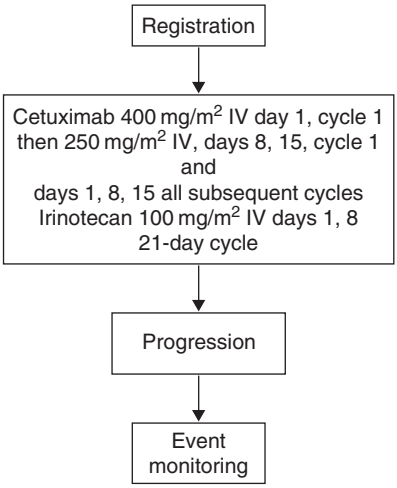
Scheme:



Update:

- Study temporarily closed as of October 2006; accrual is 21 as of 4 October 2006.

Related Publications:

Cunningham D, Humblet Y, Siena S, *et al*. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. *New Engl J Med* 2004; 351: 337–345.

Perez EA, Hillman DW, Mailliard JA, Ingle JN, Ryan JM, Fitch TR, Rowland KM, Kardinal CG, Krook JE, Kugler JW, Dakhil SR. Randomized phase II study of two irinotecan schedules for patients with metastatic breast cancer refractory to an anthracycline, a taxane, or both. *J Clin Oncol* 2004; 22(14): 2849–2855.

Topics:

- Metastatic breast cancer
- Blood markers

Keywords:

Phase II, metastatic breast cancer, cetuximab, irinotecan, Erbitux, Camptosar

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Title: N0434: The Association of Breast Density Changes, Plasma Hormone Changes, and Breast Cancer Recurrence: a companion study to NCIC CTG **MA.27.**

Coordinator(s): Celine M. Vachon
James Ingle
Mayo Clinic
200 First Str., SW
ROCHESTER, MN 55905
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: vachon.celine@mayo.edu; ingle.james@mayo.edu

Summary:

- Study opened on 8 December 2005, temporarily closed on 23 January 2006, will reopen April 2006.
- Target accrual: 550 patients

Objectives:

- To assess the change in percent breast density and dense area in response to aromatase inhibitor therapy from levels prior to the initiation of treatment through 2 years of therapy.
- To examine whether changes in percent breast density and dense area in response to aromatase inhibitor therapy from pre-treatment to 1-year correlate with changes in plasma hormones (estrone, estrone–sulfate, estradiol, SHBG) and drug levels (anastrozole or exemestane) over the same time period.
- To examine the associations of haplotype tagged SNPs in genes in the aromatase pathway identified through the Mayo Clinic and Indiana University Pharmacogenomics Research Network Projects with changes in percent and area density, plasma hormone levels, and 1-year drug levels.
- To determine if change over time in percent breast density and dense area (from pre-treatment to the time period prior to local recurrence) in the contralateral breast is associated with a local recurrence of breast cancer.
- To determine if change over time in percent breast density and dense area in the contralateral breast is associated with the development of contralateral breast cancer.
- To assess whether women with high pre-treatment percent density (upper tertile) experience greater decreases in percent breast density at 1 and 2 years of aromatase inhibitor therapy than women with low pre-treatment percent density (lower tertile).
- To assess whether women with high pre-treatment dense area (upper tertile) experience greater decreases in dense area at 1 and 2 years of

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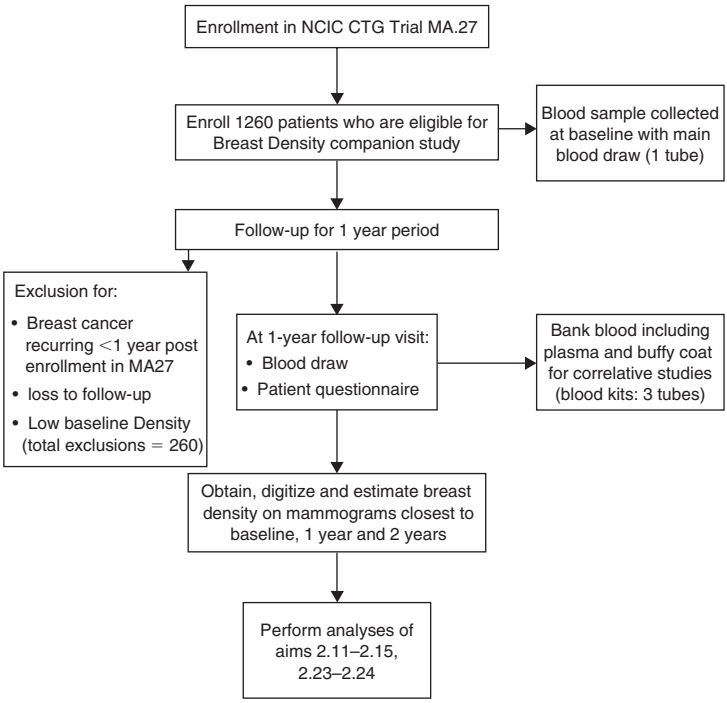
aromatase inhibitor therapy than women with low pre-treatment dense area (lower tertile).

Scheme:



Update:

- Study temporarily closed on 23 January 2006, due to suspension of parent protocol pending protocol changes. The study has accrued two patients.
- Protocol reopened 26 April 2006 and accrual as of 4 October 2006 is 359. [Note: Study is expected to reach full accrual prior to publication of this guide.]

Related Publications:

Wolfe JN. Breast patterns as an index for developing breast cancer. *Am J Roentgenol* 1976; 126: 1130–1137.

Vachon CM, Sellers TA, Pankratz VS, *et al*. Mammographic breast density, dense area and change in breast density with breast cancer risk: a matched case-control study using modern mammography. In *93rd Annual American Association for Cancer Research Meeting Proceedings* (2002). San Francisco, CA.

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Topics:

- Aromatase inhibitors
- Blood markers
- Hormone receptor positive breast cancer
- Postmenopausal patients

Keywords: Companion study (MA.27), hormone receptor positive breast cancer, postmenopausal patients, breast density, mammography

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Title: N0432: Phase II trial of docetaxel with capecitabine and bevacizumab as first-line chemotherapy for patients with metastatic breast cancer.

Coordinator(s): Edith A. Perez
Mayo Clinic
4500 San Pablo Road
JACKSONVILLE, FL 32224
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: perez.edith@mayo.edu

Summary:

- Study opened on 10 December 2004
- Study closed on 16 September 2005
- Final accrual: 46 patients

Objectives:

- Response rate (determined using the RECIST criteria).
- Time to disease progression.
- Survival time.
- Adverse event profile (adverse events graded using the NCI CTCAE v3.0).
- Duration of response.

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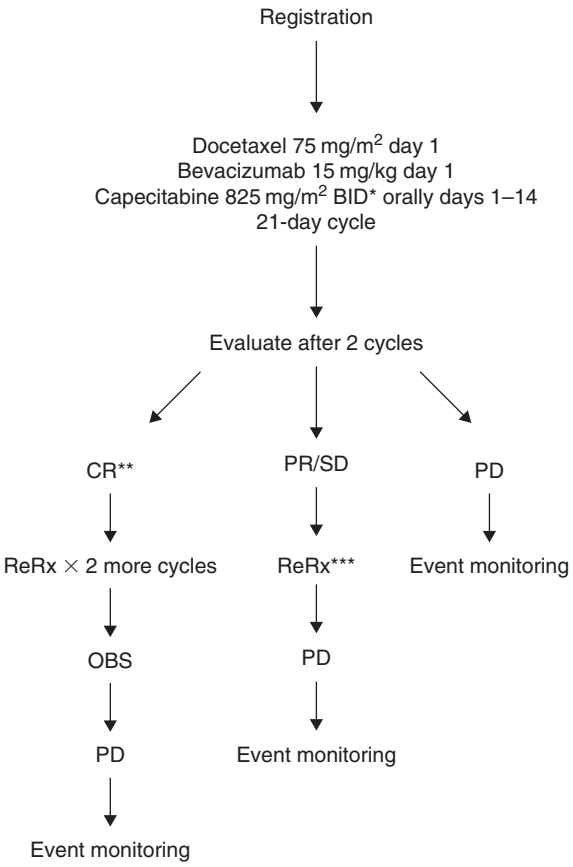
Scheme:



* Dose for normal renal function, calculated creatinine clearance of >50 mL/min. In patients with moderate renal impairment (calculated creatinine clearance 30–50 mL/min) at baseline, a dose reduction to 80% of the capecitabine starting dose or 660 mg/m^2 BID.
** A confirmed CR and then completion of an additional 2 cycles of treatment, but treatment may be continued at investigator's discretion.
*** Treatment may be continued until disease progression or intolerable toxicity at the investigator's discretion.

Update:

- Study closed on 16 September 2005, final accrual was 46 patients. Manuscript in preparation.

Related Publications:

Miller KD, Wang M, Gralow J, Dickler M, Cobleigh MA, Perez EA, Shenkier TN, Davidson NE. A randomized phase III trial of paclitaxel versus paclitaxel plus bevacizumab as first-line therapy for locally

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recurrent or metastatic breast cancer: a trial coordinated by the Eastern Cooperative Oncology Group (E2100). *San Antonio Breast Cancer Symposium*, December 2005, San Antonio, TX, Abstract 3.

Xeloda, Prescribing Information, Roche Laboratories, Inc., 2001.

Topics:

- Metastatic breast cancer
- Capecitabine
- Taxanes

Keywords: Phase II, metastatic breast cancer, docetaxel, bevacizumab, capecitabine, Taxotere, Avastin, Xeloda

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Title: N0338: Phase II trial of docetaxel and carboplatin administered every 2 weeks as induction therapy for stage II or III breast cancer.

Coordinator(s): Vivek Roy
Mayo Clinic
200 First Str., SW
ROCHESTER, MN 55905
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: roy.vivek@mayo.edu

Summary:

- Study opened on 5 August 2005, temporarily closed on 18 January 2006.
- Target accrual: 58 patients

Objectives:

Treatment:

- To determine the pathological complete response rate of a 2-month dose-dense, neoadjuvant regimen of docetaxel and carboplatin for women diagnosed with stage II/III breast cancer.
- To assess the adverse event profile of the dose-dense, neoadjuvant regimen for women diagnosed with stage II/III breast cancer.
- To determine the rate of breast conserving surgery.
- To determine the clinical response rate.
- To assess the feasibility of drug administration by determining the percent of planned dose actually administered per cycle.
- To determine the proportion of patients with negative pathologic lymph node status after the neoadjuvant regimen.
- To determine the proportion of patients with residual Ductal Carcinoma *in situ* after the neoadjuvant regimen.
- To compare the outcome profiles of the primary, Chevallier, and Sataloff classifications of pathological response.

Translational Research:

- To measure levels of COX-2 and EP1-4 G-protein coupled receptor expression of tumor before and after induction chemotherapy.
- To evaluate levels of PGE2 and VEGF, present in the plasma before and after induction chemotherapy.
- To evaluate T cell and dendritic cell phenotype and function before and after induction chemotherapy.

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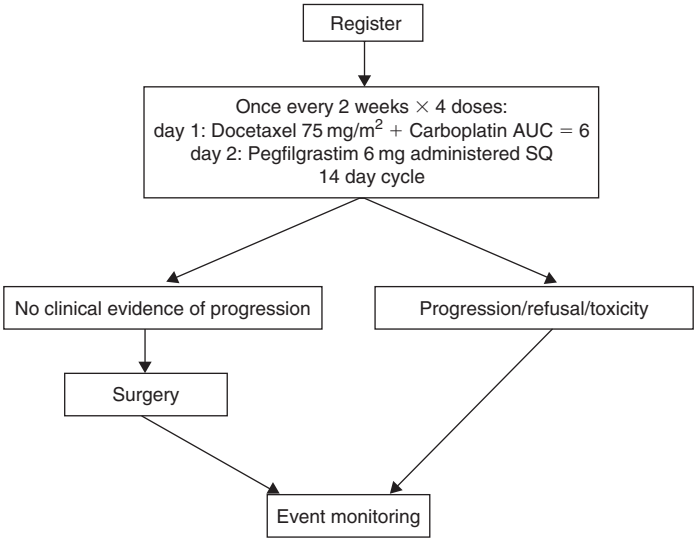
Scheme:



Update:

- Study reopened 9 June 2006 and accrual as of 4 October 2006 is 10.

Related Publications:

Chan S, Friedrichs K, Noel D, *et al*. Prospective randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer. The 303 Study Group. *J Clin Oncol* 1999; 17: 2341–2354.

Martin M, Diaz-Rubio E, Casado A, *et al*. Carboplatin: an active drug in metastatic breast cancer. *J Clin Oncol* 1992; 10: 433–437.

Nabholtz JM, Senn HJ, Bezwoda WR, *et al*. Prospective randomized trial of docetaxel versus mitomycin plus vinblastine in patients with metastatic breast cancer progressing despite previous anthracycline-containing chemotherapy. 304 Study Group. *J Clin Oncol 1999*; 17: 1413–1424.

O'Brien ME, Talbot DC, Smith IE. Carboplatin in the treatment of advanced breast cancer: a phase II study using a pharmacokinetically guided dose schedule. *J Clin Oncol* 1993; 11: 2112–2117.

Topics:

- Blood markers
- Dose densification
- Perioperative chemotherapy
- Taxanes

Keywords:

Phase II, breast cancer, neoadjuvant therapy, docetaxel, carboplatin, pegfilgrastim, Taxotere, Paraplatin, Neulasta

https://doi.org/10.1017/S1470903106009291 Published online by Cambridge University Press

Title: N0337: Phase II study of capecitabine in combination with vinorelbine and trastuzumab for the first- or second-line treatment of HER2+ metastatic breast cancer.

Coordinator(s): Winston W. Tan
Mayo Clinic
4500 San Pablo Road
JACKSONVILLE, FL 32224
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: tan.winston@mayo.edu

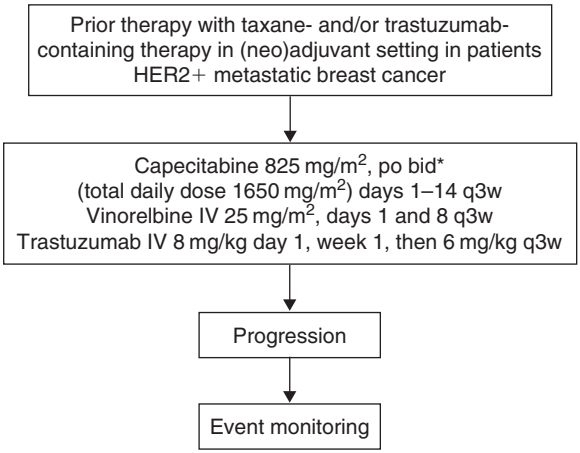
Summary:

- Study opened on 18 January 2005
- Target accrual: 47 patients

Objectives:

- To evaluate the overall response rate.
- To determine the time to progression, duration of response, and overall survival.
- To evaluate the safety profile of the combination of capecitabine, vinorelbine, and trastuzumab with the selected schedule using the NCI CTCAE v3.0.

Scheme:



* This dose is for patients with normal renal function (calculated creatinine clearance of ≥50 mL/min). For patients with moderate renal impairment (calculated creatinine clearance 30–50 mL/min) at baseline, required a dose reduction to 80% of the capecitabine starting dose or 660 mg/m^2 BID.

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Update:

- Study opened on 15 January 2005: accrual is 20 as of 4 October 2006.

Related Publications:

Bangemann N, Micheel S, *et al*. Capecitabine combined with trastuzumab in the therapy of intensively pretreated HER2 overexpressing metastatic breast cancer (MBC). *Proc ESMO* 2000, Abst 653 p.

Jahanzeb M, Mortimer JE, Yunus F, Irwin DH, Speyer J, Koletsky AJ, Klein P, Sabir T, Kronish L. Phase II trial of weekly vinorelbine and trastuzumab as first-line therapy in patients with HER2(+) metastatic breast cancer. *Oncologist* 2002; 7(5): 410–417.

Burstein HJ, Kuter I, Campos SM, *et al*. Clinical activity of trastuzumab and vinorelbine in women with HER2-overexpressing metastatic breast cancer. *J Clin Oncol* 2001; 19: 2722–2730.

Topics:

- Metastatic breast cancer
- HER2 positive patients
- Capecitabine
- Trastuzumab
- Vinorelbine
- Cardiac function

Keywords: Phase II, metastatic breast cancer, HER2+, capecitabine, vinorelbine, trastuzumab, Xeloda, Navelbine, Herceptin

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Title: N0336: Phase II trial of RAF kinase inhibitor BAY 43-9006 as single oral agent in patients with metastatic breast cancer previously exposed to anthracycline and/or taxane.

Coordinator(s): Edith A. Perez
Mayo Clinic
4500 San Pablo Road
JACKSONVILLE, FL 32224
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: perez.edith@mayo.edu

Summary:

- Study opened on 24 September 2004
- Study closed on 20 January 2006
- Final accrual: 24 patients

Objectives:

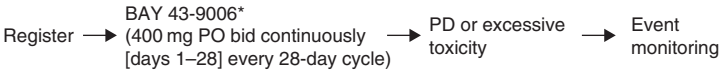
Treatment:

- To assess tumor response rate (determined using the RECIST criteria) and adverse event profile (adverse events graded using the NCI CTCAE v3.0) of BAY 43-9006 in women or men with metastatic breast cancer previously treated with anthracycline and/or taxane.
- To examine the distributions of disease progression times and survival times.

Translational Research:

- To examine the relationship between pre-treatment levels of activated ERK1/2 and tumor response to this regimen of BAY 43-9006.
- To examine changes in activated ERK1/2, phospho-AKT, and cleaved caspase 3 during the course of treatment.

Scheme:



*Tumor evaluation every 2 cycles

Update:

- The study was permanently closed on 20 January 2006, following first interim analysis. Patients are to be followed per protocol. Abstract reporting results of this study has been accepted at ASCO 2006.

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Related Publications: BAY 43-9006 Investigator's Brochure, versions 3 and 4.1. (2002 & 2003). Shah A, Lathia C, Heininger K, *et al*. (Eds.), Bayer Corporation, West Haven, CT.

Topics:
- Metastatic breast cancer
- Blood markers

Keywords: Phase II, metastatic breast cancer, RAF kinase inhibitor, sorafenib, Nexavar

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Title: N0332: Phase II trial of weekly irinotecan and docetaxel in refractory metastatic breast cancer.

Coordinator(s): Edith A. Perez
Mayo Clinic
4500 San Pablo Road
JACKSONVILLE, FL 32224
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: perez.edith@mayo.edu

Summary:

- Study opened on 9 April 2004
- Target accrual: 69 patients

Objectives:

- To assess the anti-tumor activity of a dose dense regimen of docetaxel and irinotecan for patients with refractory breast cancer.
- To assess the adverse event profile of the weekly dose dense combination of docetaxel and irinotecan.
- To obtain an estimate of the progression-free survival distribution.
- To obtain an estimate of the overall survival distribution.

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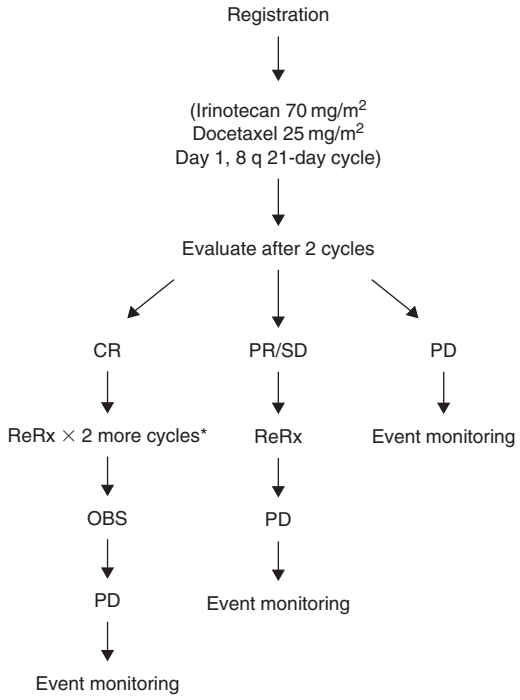
Scheme:



*Retreatment beyond 2 cycles may be done at physician discretion

Update:

- Accrual as of 4 October 2006 is 67. [Note: Study is expected to reach full accrual prior to publication of this guide.]

Related Publications:

Perez EA, Hillman DW, Mailliard JA, Ingle JN, Ryan JM, Fitch TR, Rowland KM, Kardinal CG, Krook JE, Kugler JW, Dakhil SR. Randomized phase II study of two irinotecan schedules for patients with metastatic breast cancer refractory to an anthracycline, a taxane, or both. *J Clin Oncol* 2004; 22(14): 2849–2855.

Topics:

- Metastatic breast cancer
- Dose densification
- Taxanes

Keywords:

Phase II, metastatic breast cancer, irinotecan, docetaxel, Camptosar, Taxotere

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Title: N0234: Phase II study of OSI-774 (Tarceva) and gemcitabine for patients with metastatic breast cancer.

Coordinator(s): Edith A. Perez
Mayo Clinic
4500 San Pablo Road
JACKSONVILLE, FL 32224
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: perez.edith@mayo.edu

Summary:

- Study opened on 8 August 2003
- Study closed on 8 July 2004
- Final accrual: 61 patients

Objectives:

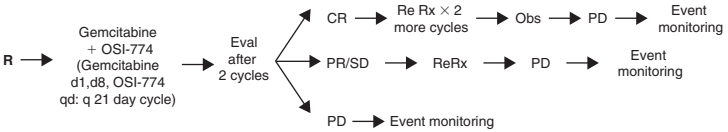
Treatment:

- To assess the anti-tumor activity of a combination of gemcitabine and OSI-774 for patients with metastatic breast cancer previously treated with anthracycline and/or taxane, in patients who have received either 0 or 1 prior chemotherapy regimen for metastatic disease.
- To assess the adverse event profile of gemcitabine in combination with OSI-774 in the treatment of patients with metastatic breast cancer.

Translational Research:

- To investigate the expression of EGFR and HER-2 receptors and their phosphorylated (active) forms, the amount of soluble EGFR in serum, TGFalpha, and the expression of several downstream signaling molecules in these pathways, including phospho-AKT, PTEN, myc, and PI-3 kinase, and pre- and post-treatment serum levels of soluble EGFR and HER-2 in terms of their impact on clinical response.
- Pharmacogenetic studies, if warranted following resequencing and functional analyses studies currently underway, will be performed to examine the impact of genetic differences in proteins involved in drug response (transport, metabolism, and mechanism of action) on clinical response and adverse events associated with gemcitabine.

Scheme:



* Retreatment beyond 2 cycles may be done at physician discreation.

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Update:

- Study closed on 8 July 2004, final accrual was 61 patients. Manuscript in preparation.

Related Publications:

Burch PA, Mailliard JA, Hillmen DW, Perez EA, Krook JE, Rowland KM, *et al*. Phase II study of gemcitabine and cisplatin in patients with metastatic breast cancer (MBC) and failure on prior chemotherapy: a North Central Cancer Treatment Group trial. *Breast Cancer Res Treat* 2000; 64: 81 abstr 322.

Colomer, R, Llombart A, Lluch A, Ojeda B, Barnadas A, Caranana V, *et al*. Paclitaxel/gemcitabine administered every two weeks in advanced breast cancer: preliminary results of a phase II trial. *Semin Oncol* 2000; 27(1)(suppl2): 20–24.

Fountzilas G, Nicolaides C, Bafaloukos D, Kalogera-Fountzila A, Kalofonos H, Samelis G, *et al*. Docetaxel and gemcitabine in anthracycline-resistant advanced breast cancer: a hellenic cooperative oncology group phase II study. *Cancer Invest* 2000; 18(6): 503–509.

Laufman LR, Spiridonidis CH, Carman L, Pritchard J, Roach R, Zangmeister J, *et al*. Secondline chemotherapy with weekly gemcitabine (GEM) and monthly docetaxel (DOC) in patients (pts) with metastatic breast cancer (MBC): a phase II study. *Proc Am Soc Clin Oncol* 2000; 19: 106a abstr 408.

Murad AM, Guimaraes RC, Aragao BC, Scalabrini-Neto AO, Rodrigues VH, Garcia R. Phase II trial of the use of paclitaxel and gemcitabine as a salvage treatment in metastatic breast cancer. *Am J Clin Oncol* 2001; 24(3): 264–268.

Sanchez P, Medina MB, Mohedano N, Jaen A, Porras I, González, *et al*. Results from a phase II study of gemcitabine in combination with paclitaxel in metastatic breast cancer. *Ann Oncol* 1998; 9(suppl 4):16 abstr 77P.

Topics:

- Metastatic breast cancer
- Blood markers

Keywords: Phase II, metastatic breast cancer, gemcitabine, erlotinib, Gemzar, Tarceva

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Title: N0032: Phase II trial of Faslodex in women with metastatic breast cancer and failure on aromatase inhibitor therapy.

Coordinator(s): James N. Ingle
Mayo Clinic
200 First Str., SW
ROCHESTER, MN 55905
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: ingle.james@mayo.edu

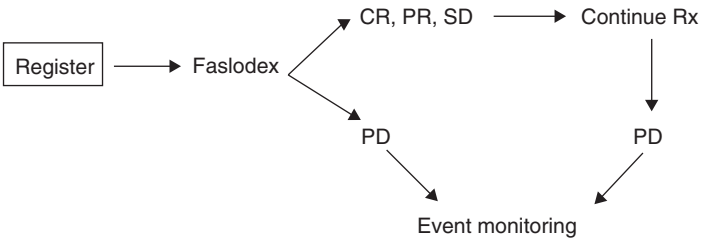
Summary:

- Study opened on 18 May 2001
- Study closed on 23 April 2004
- Final accrual: 80 patients

Objectives:

- To conduct a phase II trial of Faslodex in women with metastatic breast cancer who have disease progression following therapy with an aromatase inhibitor. The primary endpoint is objective response rate (complete response, partial response) and secondary endpoints are time to disease progression, overall survival, duration of response, and adverse events.
- To examine the effect of Faslodex on the insulin-like growth factor (IGF) system including IGF-I, total IGF-II, free IGF-I, IGFBP-1, IGFBP-3, IGFBP-4, and IGFBP-5.

Scheme:



Update:

- Study closed in April 2004. Results of this study have been published.

Related Publications: Ingle JN, Suman VJ, Rowland KM, Mirchandani D, Bernath AM, Camoriano JK, Fishkin PA, Nikcevich DA, Perez EA. North Central Cancer Treatment Group Trial N0032. Fulvestrant in women with advanced breast cancer after progression on prior aromatase inhibitor therapy: North Central Cancer Treatment Group Trial N0032. *J Clin Oncol* 2006; 24(7): 1052–1056.

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Topics:
- Metastatic breast cancer
- Hormone receptor positive breast cancer
- Hormonal therapy
- Postmenopausal patients

Keywords: Phase II, metastatic breast cancer, fulvestrant, Faslodex

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Title: N0031: A phase II study of topical ceramide lipids as treatment for cutaneous breast cancer.

Coordinator(s): Aminah Jatoi MD
Mayo Clinic
200 First Str., SW
ROCHESTER, MN 55905
USA
Tel: +1 507 284 1159
Fax: +1 507 284 5280
Email: jatoi.aminah@mayo.edu

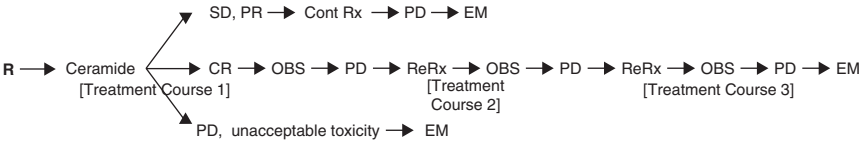
Summary:

- Study opened on 18 May 2001
- Study closed on 5 October 2001
- Final accrual: 26 patients

Objectives:

- The primary goal of this study is to evaluate the objective response rate of topical ceramides in patients with cutaneous breast cancer.
- A secondary goal is to evaluate time to progression of cutaneous disease and adverse events associated with topical ceramides.
- Another secondary goal is to assess disease-specific quality of life issues relevant to patients with cutaneous breast cancer.
- A final secondary goal is to explore the mechanism of action of ceramide lipids *in vivo*; we propose to determine whether apoptosis of tumor cells is the mechanism by which ceramide lipids might be working to induce tumor cell death.

Scheme:



Update

- Study closed in October 2001. Results of this study have been published.

Related Publications: Jatoi A, Suman VJ, Schaefer P, Block M, Loprinzi C, Roche P, Garneau S, Morton R, Stella PJ, Alberts SR, Pittelkow M, Sloan J, Pagano R. A phase II study of topical ceramides for cutaneous breast cancer. *Breast Cancer Res Treat* 2003; 80(1): 99–104.

Topics:

- Metastatic breast cancer

Keywords: Phase II, metastatic breast cancer, cutaneous breast cancer, topical ceramide

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