

Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation Trial

## Essentials of AL TTO

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 Fran M Palmieri, RN MSN OCN CCRP - Nursing  
 Kristen Perkins, Protocol Specialist - Protocol Office

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## Essentials of AL TTO

- What is AL TTO
- Enrollment Update
- Pathology Submission
- Helpful Items Available to Order from CTSU
- Forms and Submission (including reimbursement)
- NCCTG Study Team - We're here to help!
- Overview of Treatment
- Management of Treatment Effects
- Adverse Events




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## Essentials of AL TTO

### N063D/BIG2-06/EGF106708

Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation®

A randomised, multi-centre, open-label, phase III study of adjuvant lapatinib, trastuzumab, their sequence and their combination in patients with HER2/ErbB2 positive primary breast cancer




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## ALTTO: World Tour An International Collaboration

### Two Study Co-Chairs:

- Edith A Perez MD – NCCTG - USA
- Martine Piccart MD – Breast International Group (BIG) – Belgium




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## ALTTO: World Tour An International Collaboration

### Statistical Center

- Frontier Science – USA and Scotland

### Data Center

- Breast European Adjuvant Study Team (BrEAST) - Belgium




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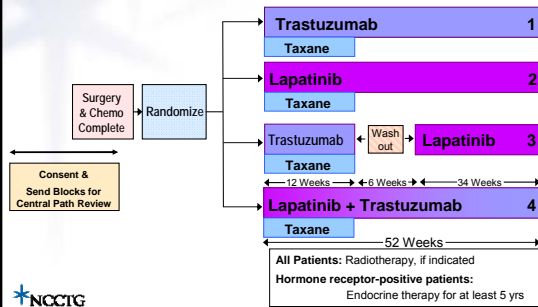
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## Essentials of ALTTO Study Design: Design 2 Schema




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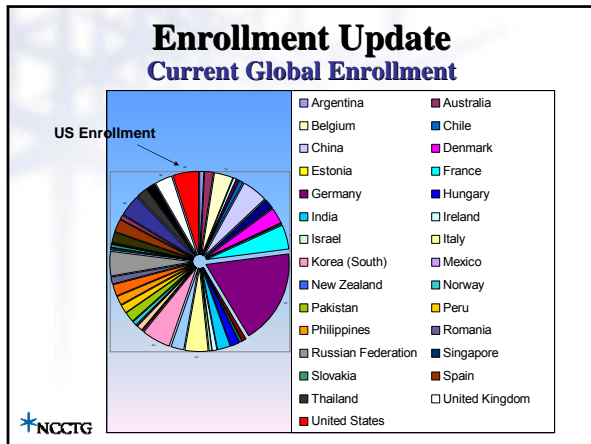
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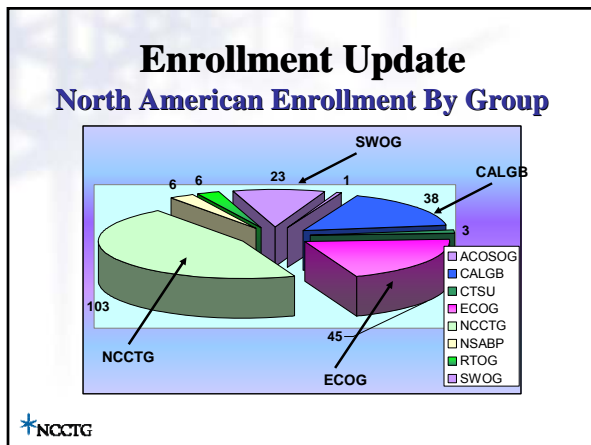
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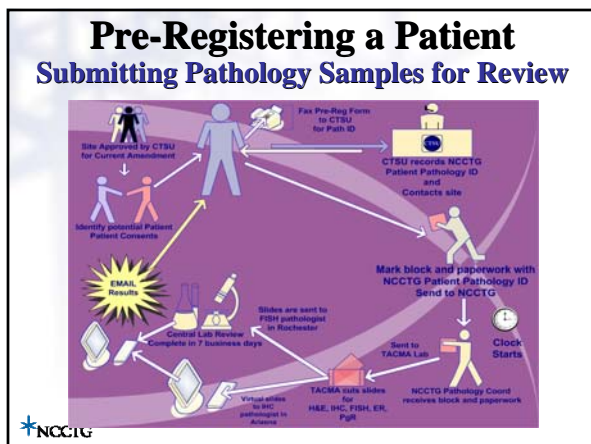
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## Helpful Items Available Order from CTSU



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## Reimbursement Available

### Remember to Send in Your Form to NCCTG

Reimbursement available

- Reimbursement payments of up to \$11,997 US per patient (divided into four payment time points).
- The first reimbursement can be requested as soon as a patient is randomized and the Screening CRF is submitted.

Enrollment: • \$3,600  
Year 1: • \$3,600  
Year 2: • \$2,400  
Year 5: • \$2,397



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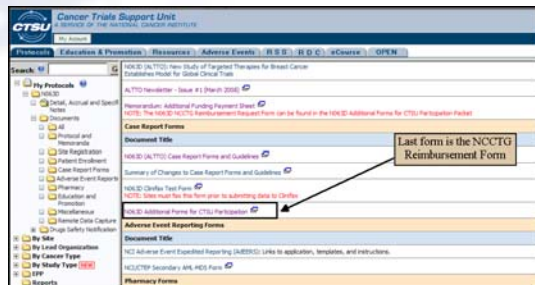
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## Where do I find the Form?

### Remember to Send in Your Form to NCCTG



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## Paperwork and Specimens

Where does all this stuff go?

### Fax to CTSU:

- Requests for Central Pathology ID
- Requests for randomization

### Send to NCCTG:

- Tissue & Blood specimens with corresponding paperwork
- QOL Booklets
- All related forms listed in **Appendix 6** - North American Procedures

### Fax to BrEAST (CliniFax):

- ALTTO Case Report Forms

### Send to AdEERS:

- All SAEs as usual



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## The ALTTO Study Team

We're Here to Answer Your Questions!



Did you know that there's a toll-free Patient Information Hotline (just for patients)?

- Phone: (888) 313-5689



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## The ALTTO Study Team

We're Here to Answer Your Questions!

### Any Questions About ALTTO

- Send an email to: [alto@mayo.edu](mailto:alto@mayo.edu)

### Central Pathology Review Submission:

Tabitha K Hanson

- Phone: (507) 284-8666
- email: [hanson.tabitha@mayo.edu](mailto:hanson.tabitha@mayo.edu)

### Patient Eligibility & Treatment:

Barb Mulhern

- Phone: (507) 538-0269
- email: [mulhern.barbara@mayo.edu](mailto:mulhern.barbara@mayo.edu)



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**The ALTTO Study Team**  
**We're Here to Answer Your Questions!**

**Study Related Documents:**  
 Lynn Flickinger  
 • Phone: (507) 538-7034  
 • email: [flickinger.lynn@mayo.edu](mailto:flickinger.lynn@mayo.edu)

Kristen Perkins  
 • Phone: (507) 266-0209  
 • email: [perkins.kristen@mayo.edu](mailto:perkins.kristen@mayo.edu)

**Adverse Event Submission:**  
 Pat McNamara  
 • Phone: (507) 266-3028  
 • email: [mcnamara.patricia@mayo.edu](mailto:mcnamara.patricia@mayo.edu)

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**ALTTO: Overview of Treatment Effects**

*Fran M Palmieri RN MSN OCN®  
 Clinical Nurse Specialist  
 NCCTG Breast Program Nurse  
 Resource  
 Manager, Breast Clinic and Breast Cancer Program, Mayo-Clinic  
 Jacksonville*

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**80-85% of Women are Disease-Free at 4 years with Trastuzumab**  
**Can we improve upon these results?**

- Lapatinib inhibits growth of breast cancer cell lines that acquire resistance to trastuzumab
- Lapatinib in combination with trastuzumab is synergistic in HER2+ breast cancer cell lines
- Offers more complete blockade of HER signaling
- Effective eradicator of tumorigenic "stem cells" when given alone to women with HER2 positive breast cancer
- Decreased proliferation (Ki67/p-MAPK )
- Documented activity in the refractory and 1<sup>st</sup>-line MBC setting, as well as preoperative Rx

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## Expected Therapies

- **Taxanes**
  - Paclitaxel (Taxol®)
  - Docetaxel (Taxotere®)
- **Trastuzumab (Herceptin®)**
  - FDA approved for MBC September 1998 and for EBC in November 2006
- **Lapatinib (Tykerb®)**
  - FDA approved for MBC March 2007
- **TCHL (docetaxel-carboplatin) regimen**
  - Safety data in collection now

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## Potential Adverse Events

	Taxanes	Trastuzumab	Lapatinib
Hematologic	▲ Anemia, neutropenia	▲ Neutropenia, febrile neutropenia, anemia	▲ Anemia, thrombocytopenia
Diarrhea	▲	▲	▲
Peripheral Neuropathy	▲		
Arthralgia	▲	▲	
Fatigue	▲	▲	▲
Nausea/vomiting		▲	▲
Cardiac dysfunction	▲	▲	▲
Skin rash	▲	▲	▲
Infusion reactions	▲	▲	
Adherence Issues	▲	▲	▲

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## Lapatinib GI Effects

- **Diarrhea**
  - Take 1 hour before or after food intake
    - Combination with food ↑ risk
  - Assess/grade severity
    - Soft frequent stool vs. watery diarrhea
  - Pharmacological intervention with ↑ stool frequency, watery stools or discomfort (cramping)
    - Loperamide (Imodium®),  
Diphenoxylate w/atropine (Lomotil®)
  - Dietary modifications

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## Lapatinib GI Effects

- **Nausea/vomiting**
  - Infrequent, manage conservatively
    - Dietary changes; prochlorperazine usually sufficient
    - May need 5-HT3 inhibitor if refractory to prochlorperazine (occasional)
- **Stomatitis/mucositis**
  - Generally mild, Grade 1-2, resolves in 5-6 days

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## Lapatinib Dermatologic Effects

- **Rash**
  - Characteristic pustular/papular appearance
    - Face, head, scalp, upper torso with pruritus, dry skin, erythema common
  - Secondary infections
    - Yellow exudate, crusty surface
    - Pustules, warmth, pain
    - Tetracycline or clindamycin recommended
  - See NCCN Rash Guidelines 2009

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## Rash Assessment & Management



### Rash Management

- Moisturizer/emollients to alleviate dryness
- Use makeup
- Remove makeup with mild liquid cleanser - Dove®, Neutrogena®, Ivory Skin Cleansing Liqui-Gel®
- Use sunscreen (SPF30)

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Images courtesy of Susan Moore

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## Other Lapatinib Issues

### Congestive Heart Failure (CHF)

- Incidence of ~3% in N9831 (trastuzumab)
- Low cardiotoxic potential seen in 3689 patients
  - Any cardiac event 1.6%, symptomatic in 0.2%
  - Follow stringent cardiac monitoring and reporting
- Drug Administration
  - Avoid concomitant strong CYP3A4 inhibitors including grapefruit /juice
  - All tabs are taken as one dose each day

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## Treatment Related Fatigue

- Reported as one of the most problematic side effects related to many therapies, and the disease itself
  - Diminishing quality of life/ability to manage self-care
- Symptoms may include
  - Lethargy – weakness or total lack of energy, malaise
  - Sleeplessness
  - Anxiety
  - Difficulty with concentration, thinking clearly, making decisions

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## Treatment Related Fatigue

- Interventions that help alleviate fatigue
  - Regular exercise (Evidence Based)
  - Correct known causes of fatigue
    - Anemia, nutritional deficits, sleep disorders
  - Anti-depressant and anti-anxiety medications
  - Other lifestyle modifications
    - Attention-restoring activities
  - Psychological counseling, physical therapy
  - Medications to relieve pain experienced with myalgia/arthritis

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## Patient Care Thoughts

- Timely reporting is essential
- Adverse events should be manageable
  - Help patients determine reportable issues
  - Stress the importance of diarrhea reporting
- Dose modification and treatment interruption should be made per protocol
  - Always use good medical judgment – but communicate with us
- Utilize supportive care strategies
- Carefully consider long term adherence issues

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## The ALTTO Study Team Come Meet Us!

- Stop by our ALTTO Information Table Thursday or Friday
  - Fran, Lynn, Kristen and Cathie
  - Examples of **ALTTO Trial ToolKit**
    - Staff and Patient Education Materials

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## Questions

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