COMET Trial for low-risk DCIS

Comparison of Operative to Monitoring and Endocrine Therapy for Low Risk DCIS: COMET

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E. Shelley Hwang
Ann Partridge
Alastair Thompson
Advocate Lead: Liz Frank

Project Manager: Thomas Lynch

Sponsors: PCORI and Alliance Foundation Trials (AFT)
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Introduction and Welcome
Study Design and Study Update

Shelley Hwang (Duke University)
Active Surveillance Trials for DCIS

- UK (LORIS) and EORTC (LORD) trials have been initiated
- Newly diagnosed clinically “low risk” DCIS
- Primary outcome: ipsilateral invasive cancer-free survival
- Randomization: usual care (surgery and/or RT) vs. active surveillance
- Regular surveillance with imaging
- Intervene if evidence of progression to invasive cancer
DCIS diagnosed on core biopsy or surgical biopsy with positive margins

- Declines Trial
- Accepts Trial

- Informed consent, Registration, and Randomization

- Guideline Concordant Care (n=600) +/- endocrine therapy
  - Accepts Allocation (n=450)
  - Declines Allocation (n=150)

- Active Surveillance (n=600) +/- endocrine therapy
  - Accepts Allocation (n=450)
  - Declines Allocation (n=150)
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*Eligibility Criteria*

- Age >40 at diagnosis; agree to randomization
- Pathologic confirmation of grade I/II DCIS without invasion by 2 local pathologists (microinvasion not allowed)
- ER ≥ 10%; HER2-negative (0, 1+, or 2+ if testing performed)
- No evidence of other breast disease on physical examination and breast imaging within 6 months of registration
- Available for follow up examinations
- Ability to read, understand and evaluate study materials
- Speaks Spanish or English
Hypothesis:

- 2, 5-year rate of invasive cancer diagnosis is not inferior in the AS group compared to the GCC group

Sample size considerations:

- 2-group test of non-inferiority of proportions, with the 2-year invasive cancer rate in the GCC group assumed to be 0.10 with a non-inferiority margin of 0.05.
- Sample size of n=446 per group will have 80% power to detect the specified non-inferiority margin.
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**Trial Schema**

Registered and randomized (n=1,200)

- GROUP 1: GCC (n=450)
  - Surgery +/- Radiation choice for endocrine therapy
  - MMG q 12 months x 5 years
  - Usual care for recurrent disease

- GROUP 1: AS (n=450)
  - choice for endocrine therapy
  - MMG q 6 months x 5 years
  - GCC for invasive progression

- GROUP 2: Randomized but declined allocated arm (n=300)
  - GCC or AS
  - Follow up per usual care
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Active Surveillance Protocol

Clinical breast examination q6 months
MMG of affected breast q6 months (AS) or q12 months (GCC)
MMG of unaffected breast q12 months*

Index lesion unchanged or regressing

Index lesion progressing**

New contralateral lesion**

Biopsy

Biopsy benign

Biopsy shows DCIS

Biopsy shows invasive cancer

Continue screening

Standard recommendation for treatment of invasive cancer

ALLIANCE FOUNDATION TRIALS, LLC
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**Analysis Plan**

- **Analysis 1:** ITT per protocol component

- **Analysis 2:** pragmatic component based upon treatment received for patients who are randomized and decline participation in the assigned arm (**crossover**):
  - any switch **from AS to GCC** if any breast surgery on the affected breast in the absence of invasive cancer when randomized to AS
  - cross-over **from GCC to AS** if the patient refuses surgery when randomized to GCC
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Study Update

- July 2016: NOA
- Enrollment over 4 years
- June 2017: First site open
- **34** Alliance sites are currently active
- **65** Alliance sites are working towards activation
- **13** Alliance sites have recruited a patient
  - **8** Alliance sites have recruited one patient
  - **5** Alliance sites have recruited more than one patient
- **21** patients have been randomized
- Seeking to open to enrollment through NCORP sites
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Questions?
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Overview of Engagement Activities

Liz Frank, Deborah Collyar, Desiree Basila, Donna Pinto
(COMET Patient Leadership Team)
Patient Leadership Team (PLT)

- Communicate and coordinate all patient engagement activities
- Ensure all patient participation aligned
  - i.e. Intl Committee, Executive Committee, Stakeholder Advisory Board
Hello!

As dedicated patient advocates, we have kept patients at the center of the AFT-25 COMET Study. We would like to welcome you to learn about the study, and explain why you might want to consider participating.

Why do we believe this clinical trial is so important?

For many years, different types and grades of DCIS were treated all the same – with immediate surgery (with or without radiation), and perhaps hormonal therapy. However, recent studies have led researchers to question whether some women with low risk DCIS would do just as well if carefully monitored by their physician. This way of managing DCIS is called “active surveillance” or “active monitoring.”

The COMET Study will compare the outcomes of women on active surveillance to those who have immediate surgery. The results will help researchers, doctors and patients alike know more about the nature of certain types of DCIS and if active surveillance is a reasonable and safe management choice. If you decide to participate in the COMET Study, you will find a supportive experience; clear, honest communication; easy to understand resources; and expert guidance. Your health will be carefully monitored over the course of the 5-year study.

Importantly, you will make an invaluable contribution to the understanding of DCIS and its management, which will benefit women like you for years to come. By completing the patient survey at the start of the study (and then at regular periods throughout), you will share important parts of your experience that doctors are not always aware of. This information will aid other women like you when they face a DCIS diagnosis. Please visit dispositions.org

The COMET Study website will have information on health and lifestyle that we hope will be of interest to you and others on the study. We will also feature interviews with different members of the COMET Study project team to keep you informed about new developments in DCIS management and research. Please discuss the COMET Study with your doctor.

There is also a list of commonly asked questions on the COMET website that may be helpful. Thank you for considering being a part of this important study. We look forward to learning more with you!

Best wishes,

Donna Pinto, Desiree Basila, Deborah Collyar, Liz Frank
Patient Leadership Team of the COMET Study

This work is supported through a Patient-Centered Outcomes Research Institute (PCORI) Award (PC5-1505-30497).

Comet A DCIS Study

Is there a better way to care for women with low risk DCIS?
The AFT-25 COMET Study hopes to answer this question.

Dear Healthcare Provider:

As dedicated patient advocates, we have kept patients at the center of the COMET Study. We hope you will talk with your patients about the study. Women who seek information about, or participate in the study will find clear, honest communication, easy to understand resources, and expert guidance throughout the 5-year study.

How is the COMET Study?

COMET stands for “Comparison of Operative to Monitoring and Endocrine Therapy for Low Risk DCIS.” This study will enroll 1,200 patients diagnosed with low-risk DCIS from 100 cancer centers throughout the U.S. Women who participate will be randomized to receive one of two treatment approaches:

1. Current standard of care (surgery, radiation therapy and/or endocrine therapy of choice)
2. Careful monitoring with mammograms and physical exams every 6 months, and possibly endocrine therapy based on your shared-decision making discussions

Why is the COMET Study urgently needed?

- There is a growing concern that low risk DCIS is being over-treated.
- Retrospective trials indicate that up to 80% of DCIS cases may be “low-risk” and may never develop into invasive cancer or a future DCIS occurrence if left untreated and carefully monitored.
- Current uncertainty and disagreement in the medical community about DCIS contributes to patient confusion, fear, and anxiety.
- Results of this study may help more physicians feel confident in offering patients active surveillance as a safe treatment choice for low-risk DCIS.
- Patients may experience a better quality of life knowing that they are being monitored carefully while avoiding potentially unnecessary physical, emotional, and financial burdens.

Without evidence from the COMET Study, physicians and patients will never learn if active surveillance is a reasonable and safe option. Given that low risk DCIS is not life-threatening, we believe this study will help women make confident, informed treatment decisions that align with their personal preferences.

Please join us in finding a better way to care for women with low risk DCIS.

Thank you for sharing this opportunity with women who may be eligible by providing them with the accompanying patient letter. We believe both patients and providers who participate in the COMET Study will make a major contribution to the understanding of DCIS and its management. For more information about the study, please contact Tom Lynch (thomas.lynch2@dulican.org) or visit dispositions.org

Donna Pinto, Deborah Collyar, Desiree Basila, Liz Frank
Patient Leadership Team, COMET Study

This work is supported through a Patient-Centered Outcomes Research Institute (PCORI) Award (PC5-1505-30497).
What is COMET?

The Comparison of Operative to Monitoring and Endocrine Therapy for low-risk DCIS (COMET) study is a clinical trial that looks at different treatment choices for ductal carcinoma in situ (also called DCIS).

DCIS is a non-invasive breast condition where cells that do not appear to be normal are found in the milk ducts. These cells are often harmless and may not need treatment.

Why is the COMET Study being done?

The COMET study will help researchers learn more about low-risk DCIS. The goal is to help many women avoid unnecessary treatments and their physical and/or emotional side effects.

Low-risk DCIS is not a threat to a woman’s life.

Why would women join the COMET study?

→ Low-risk DCIS is not a threat to a woman’s life.
→ Some women may want to avoid or delay surgery while being closely watched by their doctors.
→ Close monitoring of low-risk DCIS may result in the same excellent outcomes as the standard treatments of surgery and radiation, but with none of the physical and/or emotional side effects that many women experience.
→ Participation in this trial is valuable and appreciated. This study helps patients, researchers and doctors learn more about DCIS.
→ Joining this trial is a chance for DCIS patients to improve the lives of future generations of women diagnosed with DCIS.

You may be eligible to join the COMET study.

To learn more about this study or see if you may be eligible, talk to your doctor or visit www.dcисoptions.org.
Over 50,000 women will be diagnosed with DCIS this year. We're here to help.

What is COMET?
COMET stands for Comparison of Operative to Monitoring and Endocrine Therapy (COMET). The COMET Study will help researchers learn more about low-risk DCIS.

Why COMET?
The goal is to learn if women with low-risk DCIS can avoid aggressive treatments and their physical and/or emotional side effects.

Researchers are actively working to determine whether DCIS can be managed safely without surgery.
Future Documents (IRB Review)

- Tips and Talking Points for Providers
- Frequently Asked Questions for Patients, Friends and Family
- DCIS language considerations
  - Separating DCIS terms from breast cancer terms
Future Resources

• Videos and Webinars
  • Discussions with patients (for providers)
  • Information for COMET participants

• Participant Engagement Plan

• Expanded Website section
  • How to think about risk
  • Resources for patients
  • COMET in the media/news page
Outreach Strategies

• Goal: spread awareness and on-going news about COMET

• Leverage TV news interviews w/site investigators

• Email campaign: email 1x month to activated and interested sites, nonprofit orgs, stakeholders

• NEWS/MEDIA page on DCISoptions.org
  • Feature links to TV news, articles, podcasts
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PRO-CORE Update

Antonia Bennett (University of North Carolina)
Go to pro.unc.edu and click on link “Forgot your password?” (below login button)

Enter your email address in the “Username” box

- Enter security code that appears on the screen/click “Reset Password”

- Follow instructions to reset your password

- Read and click agree to Terms and Conditions to gain access to your COMET study site folders
PRO-Core – Contact Information

- Step-by-step training slides are located in the DOCS folder of PRO Core (accessed from the main screen) and on SiteZone
- If site staff have other questions about PRO Core, email questions to: COMET_procore@unc.edu
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AFT systems/logistics Update

Stephanie Moine (Alliance)
Vance Erese (Alliance)
How would you discuss the COMET study with a patient?

*Interactive discussion (All)*
Using language to promote patient understanding of DCIS and COMET.

Aims:

- Reduce fear & confusion
- Encourage a sense of calm & agency
- Support positive patient experiences
## DCIS language: terms

<table>
<thead>
<tr>
<th>Current term</th>
<th>Suggested term</th>
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</thead>
<tbody>
<tr>
<td>Co-morbidity</td>
<td>Other health condition</td>
</tr>
<tr>
<td>DCIS (too general)</td>
<td>‘Low-risk’ DCIS (low or intermediate grade DCIS) and ‘higher risk’ DCIS (high grade DCIS)</td>
</tr>
<tr>
<td>Cancer/pre-cancer/</td>
<td>Abnormal cells, low risk of becoming invasive</td>
</tr>
<tr>
<td>Pre-invasive/non-invasive/pre-cursor</td>
<td></td>
</tr>
<tr>
<td>Disease</td>
<td>Condition</td>
</tr>
<tr>
<td>Endocrine therapy</td>
<td>Endocrine (Hormone-blocking therapy)</td>
</tr>
<tr>
<td>Mortality/death</td>
<td>Survival (most survive)</td>
</tr>
<tr>
<td>Morbidity</td>
<td>Side effects</td>
</tr>
<tr>
<td>Option</td>
<td>Choice</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>Radiation treatment</td>
</tr>
<tr>
<td>Recurrence</td>
<td>Future breast occurrence, residual (remaining) DCIS</td>
</tr>
<tr>
<td>Risk</td>
<td>Chance, odds</td>
</tr>
<tr>
<td>Stage 0 breast cancer</td>
<td>Condition/low-risk DCIS/higher-risk DCIS</td>
</tr>
<tr>
<td>Survivor</td>
<td>Person diagnosed with low-risk/higher risk DCIS</td>
</tr>
<tr>
<td>Tools</td>
<td>Aids/support/materials</td>
</tr>
<tr>
<td>Tumor</td>
<td>Growth/lump/lesion/mass you can feel (palpable)</td>
</tr>
<tr>
<td>Watchful waiting (too passive)</td>
<td>Active surveillance/careful monitoring</td>
</tr>
</tbody>
</table>
# DCIS language: concepts

<table>
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<tr>
<th>Current concept</th>
<th>Suggested concept</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCIS as a single condition</td>
<td>Different kinds of DCIS have different levels of risk</td>
</tr>
<tr>
<td>DCIS as a well understood condition</td>
<td>DCIS is a condition that is not well understood, and many questions remain</td>
</tr>
<tr>
<td>Relative risk (for populations)</td>
<td>Absolute risk (how risk affects a person over a given period of time)</td>
</tr>
<tr>
<td>Lack of toxicity associated with standard of care</td>
<td>Standard treatment has risks and complications (surgery, side effects, changes to look and feel of the breast)</td>
</tr>
<tr>
<td>treatment</td>
<td></td>
</tr>
<tr>
<td>Standard of care means you must be treated</td>
<td>Active Surveillance may be a choice for some, clinical trials will find out</td>
</tr>
<tr>
<td>Urgent, emergency, ticking time bomb</td>
<td>Not an emergency, take time to understand and make informed decisions</td>
</tr>
</tbody>
</table>
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Next steps and closing remarks

Shelley Hwang (Duke University)