COMET Trial for low-risk DCIS

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

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COMET
A DCIS STUDY
Expanding Knowledge & Options

Sponsors: PCORI and Alliance Foundation Trials (AFT)

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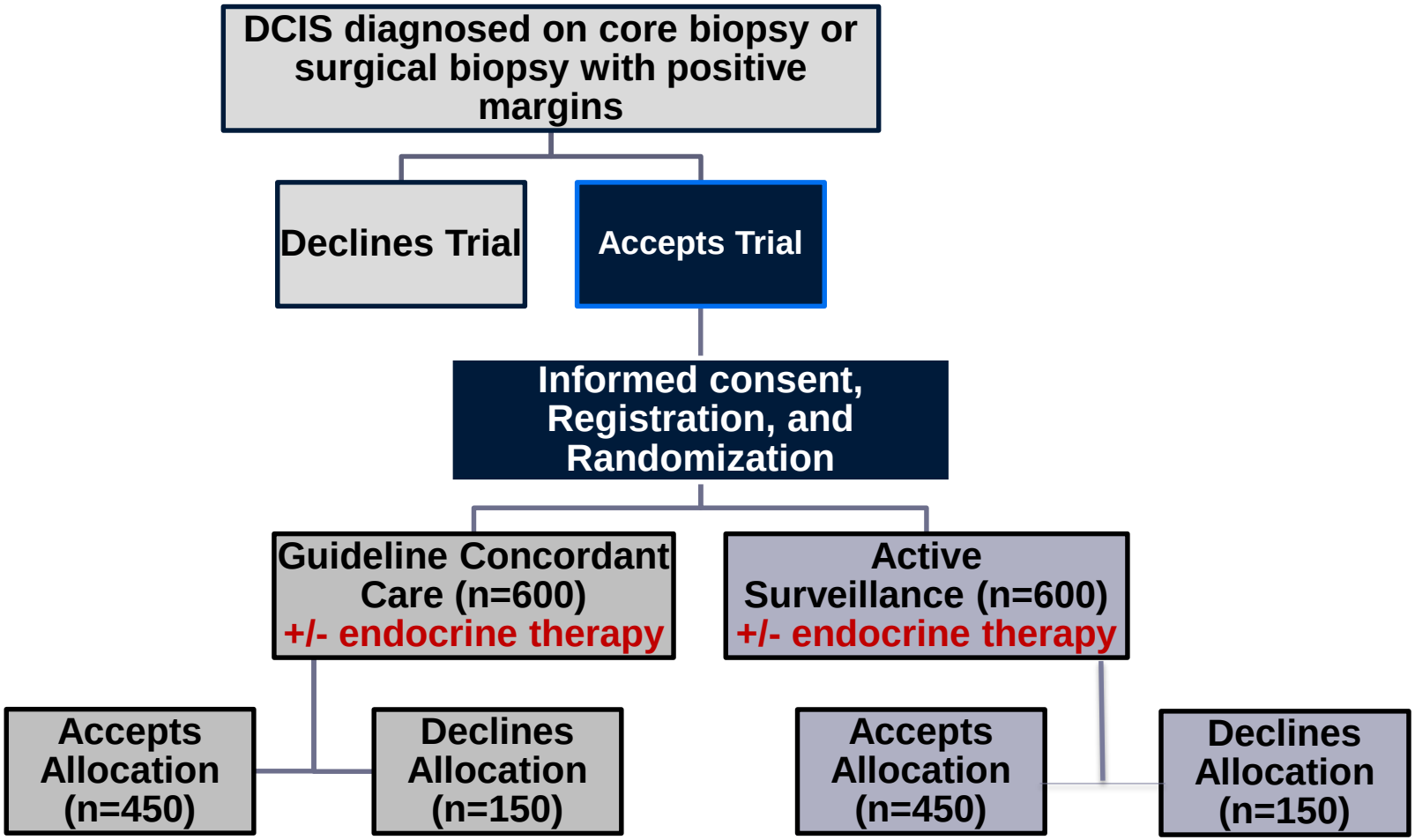
Introduction and Welcome
Study Design and Study Update

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

Study Flow Diagram



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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

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Analysis Plan

- **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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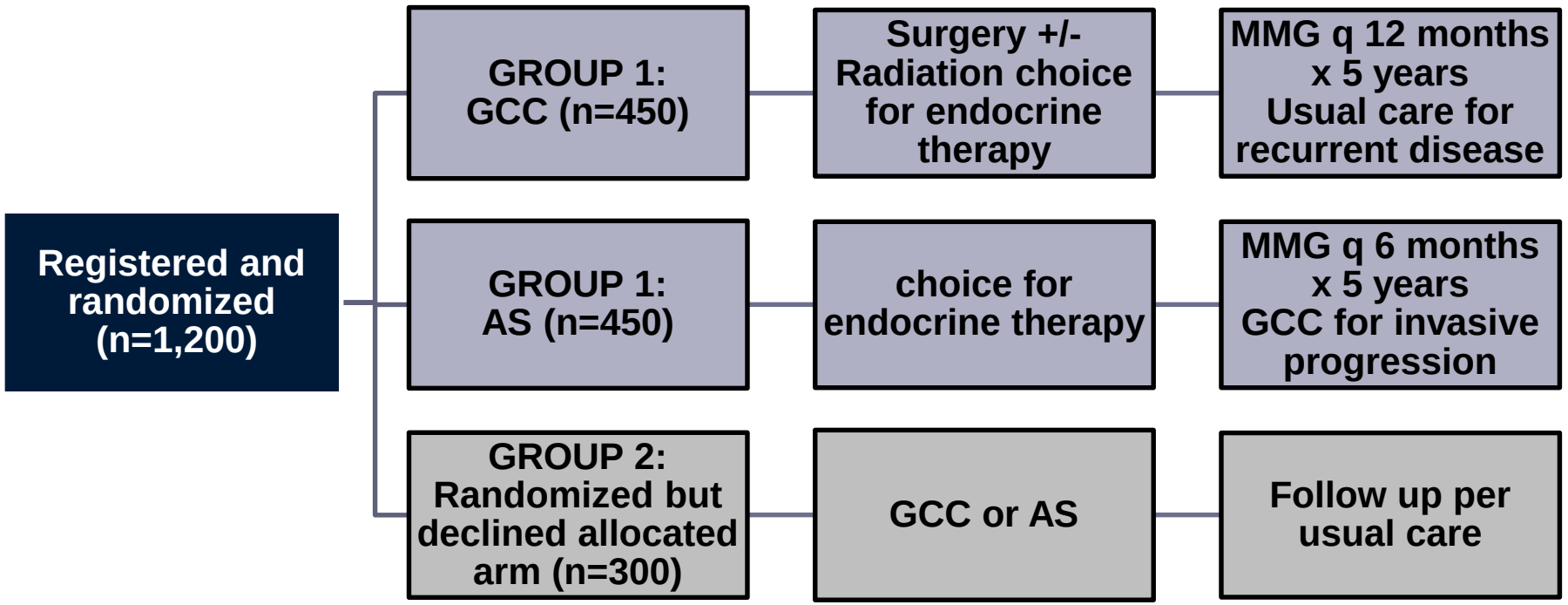
Trial Schema



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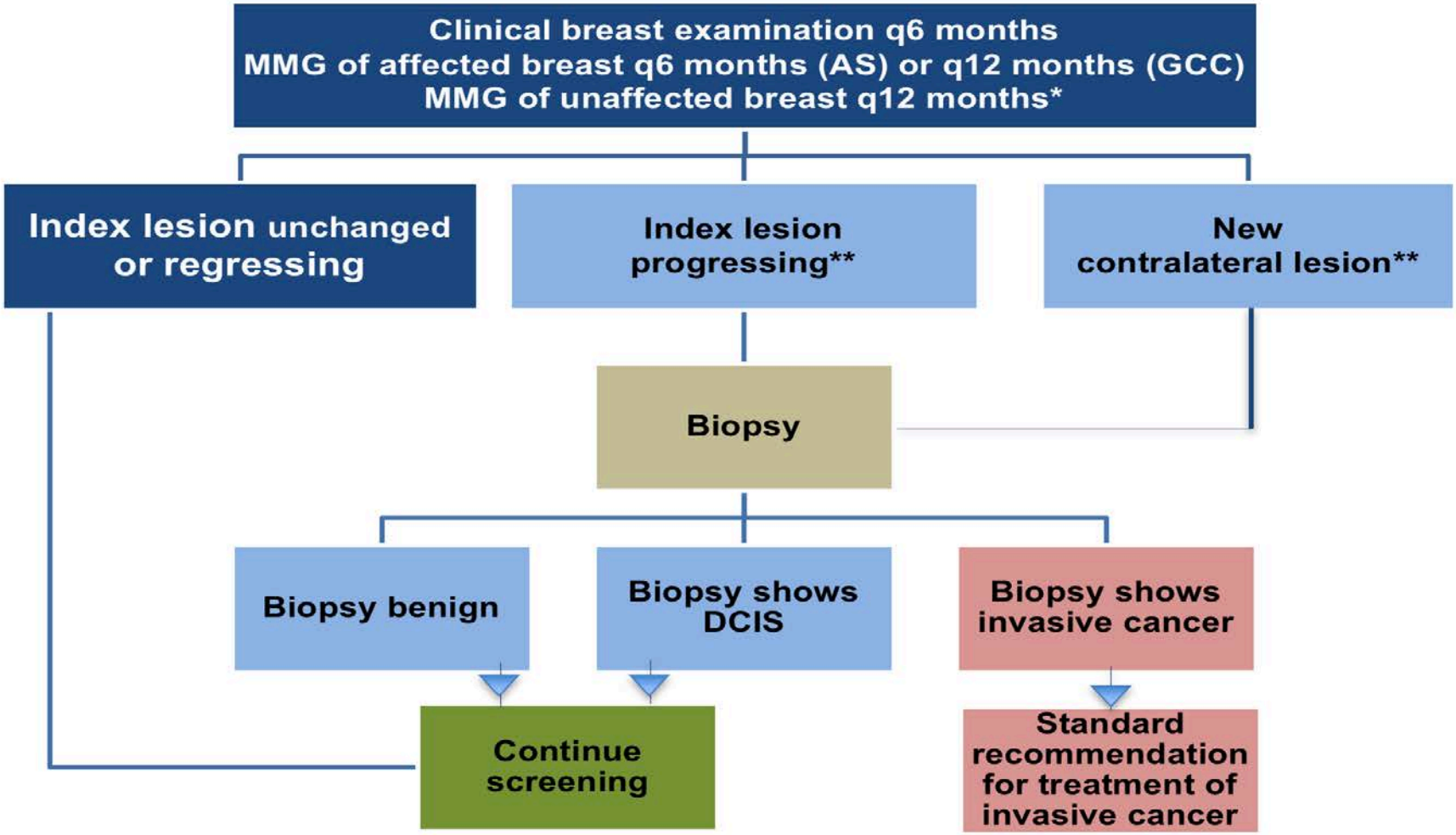
Active Surveillance Protocol



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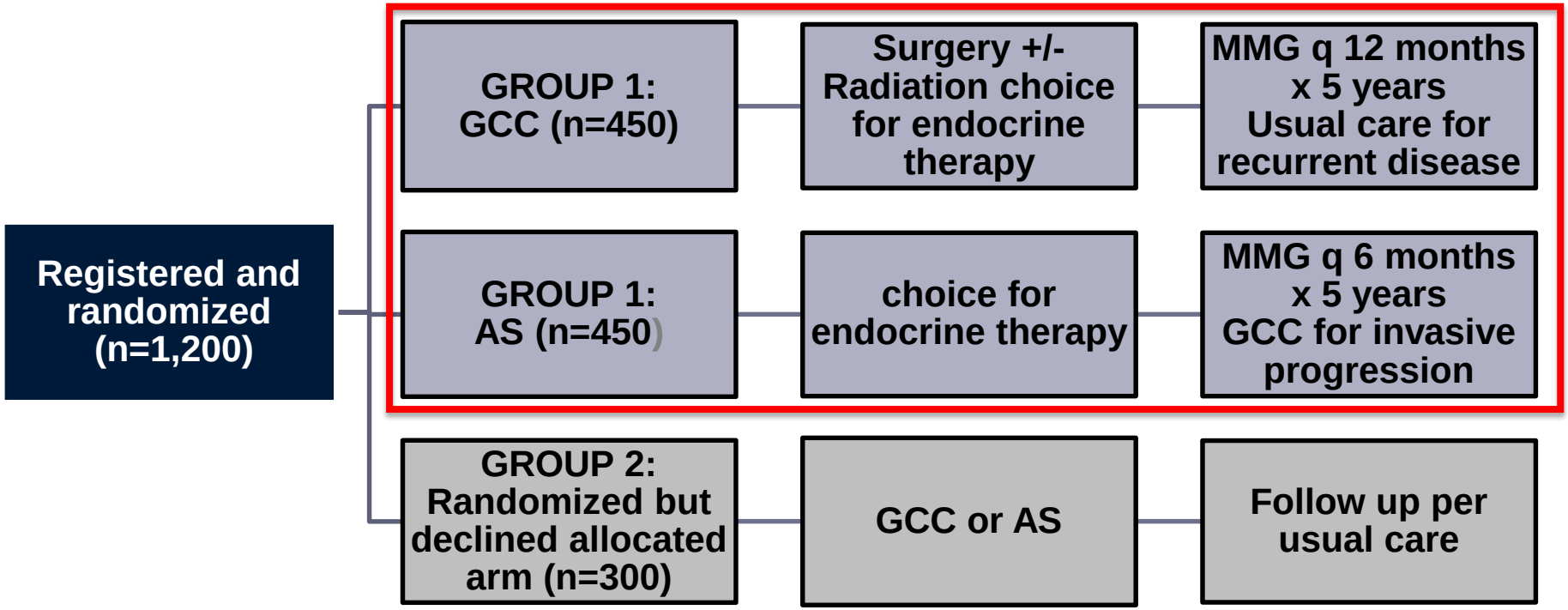
Trial Schema



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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

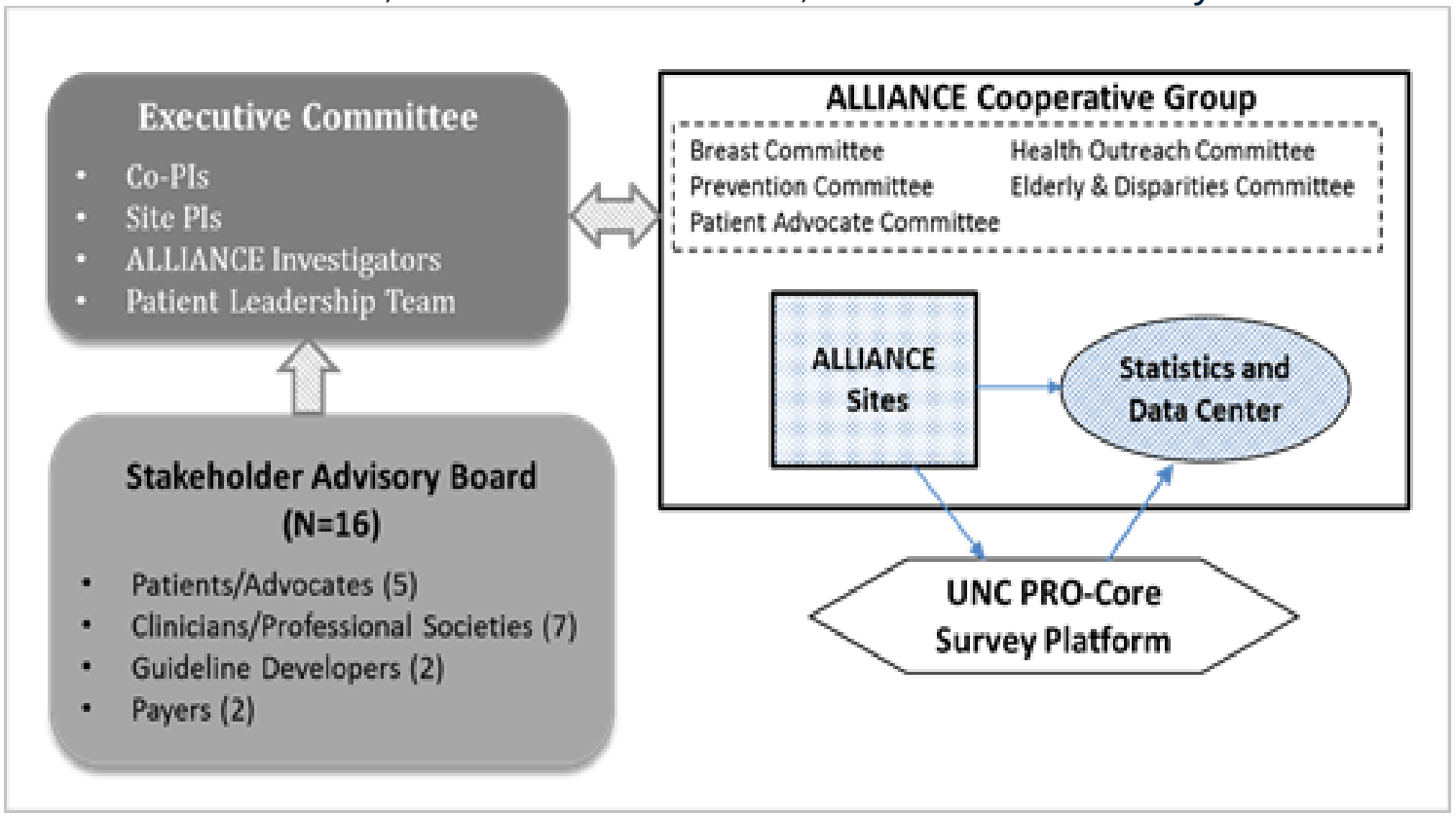
Liz Frank, Deborah Collyar, Desiree Basila, Donna Pinto

(COMET Patient Leadership Team)

PLT Engagement

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



Patient/Provider Letters from PLT

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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 dcisoptions.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 (PCS-1505-30497).

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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 trial will find clear, honest communication, easy to understand resources, and expert guidance throughout the 5-year study.

What is The COMET Study?
COMET stands for "Comparison of Operative to Monitoring and Endocrine Therapy for low risk DCIS." The study will enroll 1200 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 to 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.

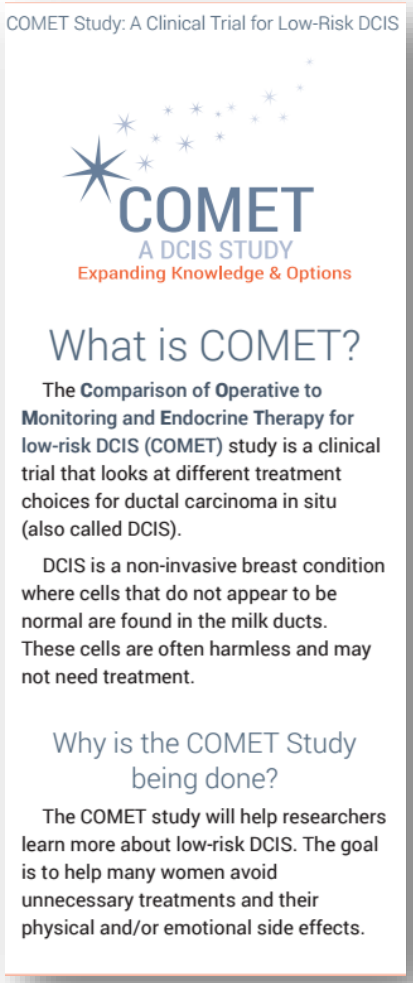
Please join us in finding a better way to care for women with low risk DCIS.

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@duke.edu) or visit dcisoptions.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 (PCS-1505-30497).

Patient Card/Brochure


COMET Study: A Clinical Trial for Low-Risk DCIS

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What is COMET?

The **C**omparison of **O**perative to **M**onitoring and **E**ndocrine **T**herapy 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.


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 vist www.dcisoptions.org.

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

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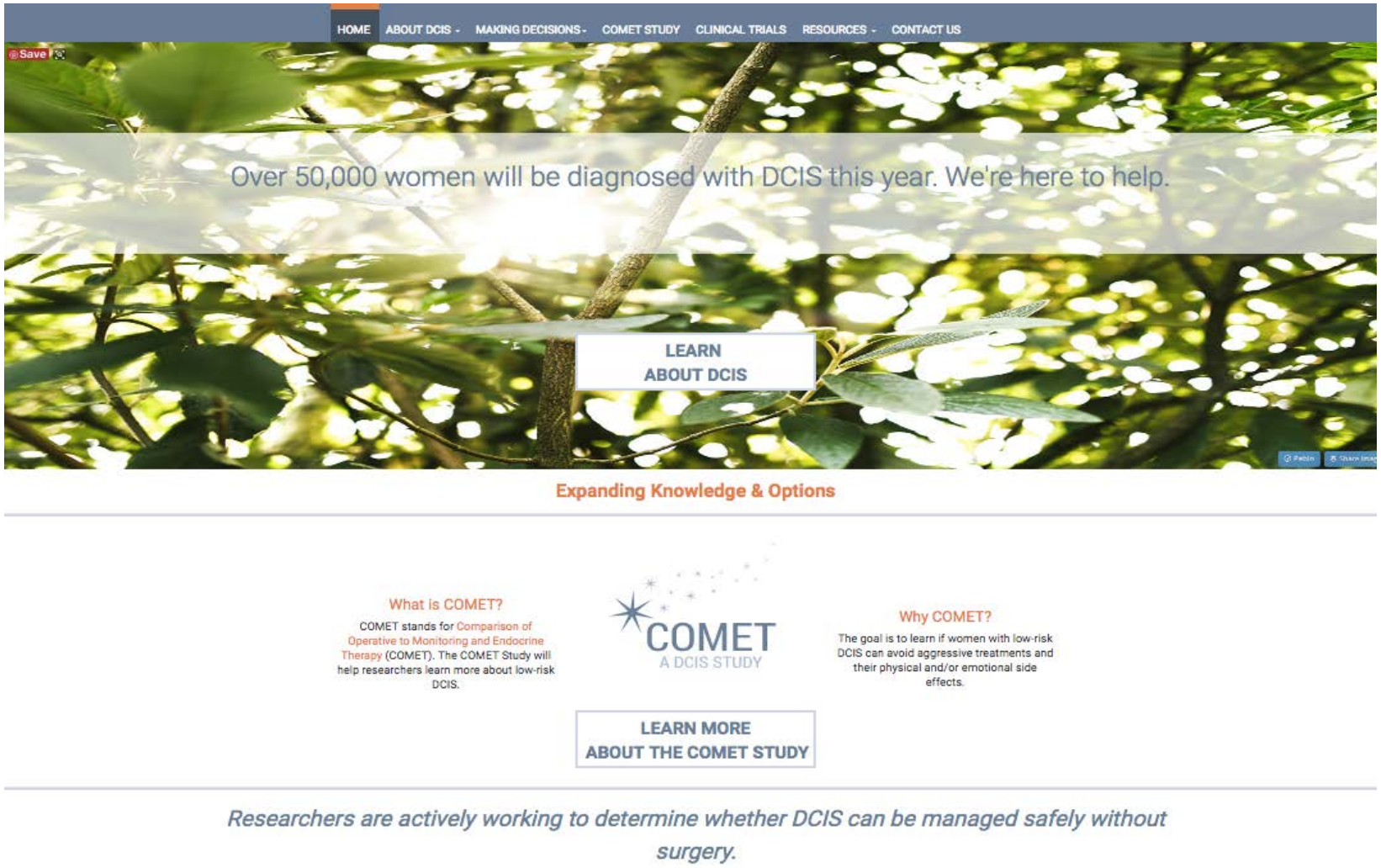
COMET Website – DCISoptions.org



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
  http://myfox8.com/2017/10/09/breast-cancer-comet-study/
- 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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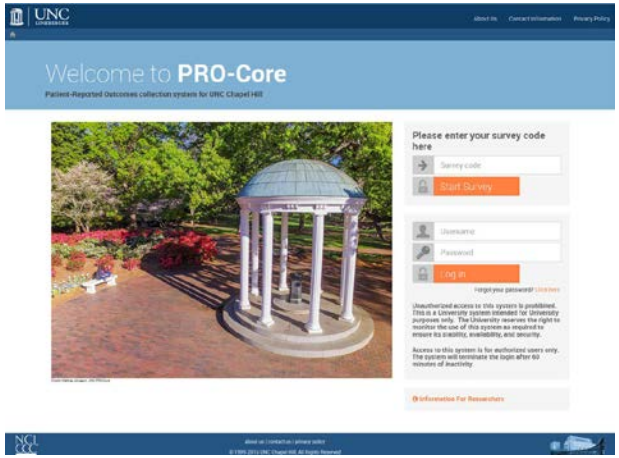
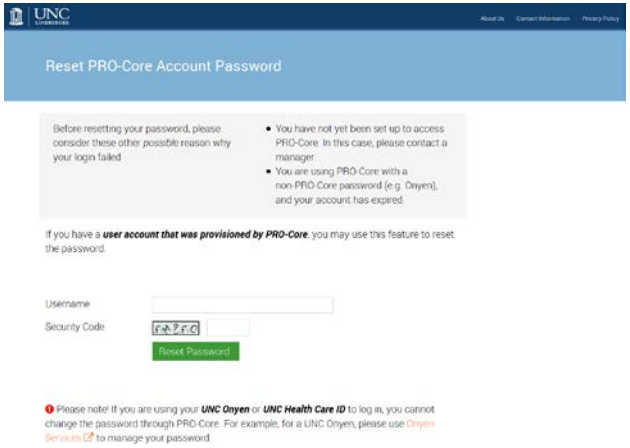
PRO-CORE Update

Antonia Bennett (University of North Carolina)

PRO-Core – first-time access

- 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





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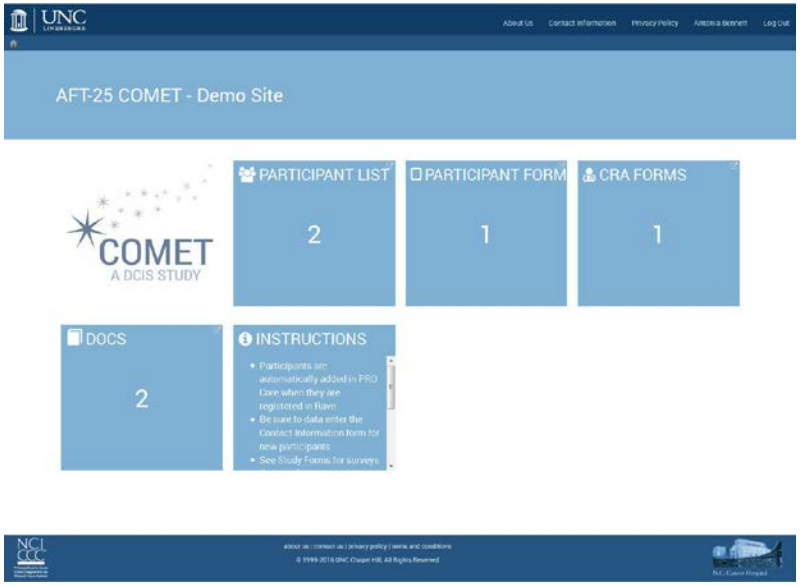
PRO-Core – Contact Information

- 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)

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How would you discuss the COMET study with a patient?

Interactive discussion (All)

DCIS language considerations

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

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

DCIS language: concepts

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

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Next steps and closing remarks

Shelley Hwang (Duke University)