YOUNG RESEARCHERS
ROUND TABLE BREAKFAST
Hearing the Metastatic Voice

FINDING SOLUTIONS
RESEARCH SERIES

Pfizer Oncology
The Presentation Portion of Today’s Program will be Broadcast on Facebook Live!

@KomenNCTriangletotheCoast
Welcome

Dr. Katherine Hoadley
Assistant Professor, Department of Genetics
UNC Lineberger Comprehensive Cancer Center

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Thank You to Our Presenting Sponsor!

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HEAR MY VOICE

MBC Community hospitals need to be part of the Clinical trials Solution. How do we make this happen?

Keep talking about MBC. Every chance given!
We Heard Your Voice!

Here is what Komen NCTC is doing:

– Metastatic Breast Cancer Support Group

Research Overviews

Dr. Katherine Hoadley
UNC Lineberger Comprehensive Cancer Center
Research Overviews

Dr. Susana Garcia Recio
The University of North Carolina at Chapel Hill
Research Overviews

Linnea Olsson
The University of North Carolina At Chapel Hill
Research Overviews

Hamzah Kharabsheh
Komen Graduate Training in Disparities Research Trainee
North Carolina Central University

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Research Overviews

Taylor Krebs
Komen Research Scholar
Duke University

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New Metastatic Breast Cancer Therapies

Dr. Charles Perou
The May Goldman Shaw Distinguished Professor of Molecular Oncology
UNC Lineberger Comprehensive Cancer Center

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New Therapies for the Treatment of Metastatic Breast Cancers
~200,000 women in the USA are living with metastatic breast cancer

2015- original breast cancer

2019 - metastasis in liver, brain

We have the 2015 tumor for testing and “precision medicine”

However...
The 2015 tumor is not the problem, the 2019 tumors are.

Slide courtesy of Lisa Carey
Cancers Evolve over time and space

Normal breast cells (orange)  Cancer cells (green)

Diagnosis  First metastasis  Later metastasis

These are not the same, They differ by a few genetic markers (mutations, amp, delete)
65 patients at UNC participated so far
Detailed genetics (DNA) and genomics (RNA expression) on the primary tumor and multiple metastases.

Key Findings:
• Many cancers include multiple “subcancers / subclones”.
• Polyclonal seeding by multiple subclones is common
• Each subclone has some different genetic alterations.
• Which alterations are genetic drivers?
• Which alterations to therapeutically target?
Primary goal

- To identify the molecular features responsible for the development and progression of metastatic breast cancer, including the development of resistance to therapy

Multi-platform genomic analysis of 250 metastatic breast cancer pairs (i.e. primary tumor and metastasis from the same patient) in a two tiered approach

- Retrospective Study (n=50)
  - Already banked, clinically annotated biospecimens with appropriate consent and high quality materials
  - Patients with multiple metastases of particular focus

- Prospective Study (n=200)
  - Prospectively enrolled patients with serially collected biospecimens with appropriate consent and follow up
  - Return of genomic results
Clinical Treatment Groups for MBC Patients

- **Estrogen Receptor and/or Progesterone Receptor positive**
  - Subtypes = LumA/B
  - Biomarkers = IHC
  - Drugs = tamoxifen and/or aromatase inhibitors

- **Triple-Negative (TNBC)**
  - Subtypes = ~75% Basal-like
  - Biomarkers = IHC x3
  - Drugs = multi-agent chemotherapy

- **HER2 positive**
  - Subtypes = ~66% HER2-E
  - Biomarkers = IHC or FISH
  - Drugs = trastuzumab, pertuzumab, tDM1
Therapies for ER+/HER2- Metastatic Breast Cancers

- **CDK4/6 Inhibitors** = (abemaciclib, palbociclib, or ribociclib) = Approved
  - First line in combination with an aromatase inhibitor or fulvestrant
  - MONALEESA-7 and MONARCH2 showed OS benefit

- **PIK3CA Inhibitor** = (alpelisib) = Approved
  - First line in combination with fulvestrant for PIK3CA-mutated tumors
  - Approved May 2019 based on results of the SOLAR-1 trial

- **mTOR inhibitor** = (everolimus) = Approved
  - Second line in combination with exemestane after progression on letrozole or anastrozole.

- **Selective Estrogen Receptor Degrader (SERDs)** = Approved, and more in development
  - Cause degradation of ER protein, and thus may target ESR1-mutants (~30-40% of AI treated MBCs)
  - Fulvestrant is approved, others in development (brilanestrant, elacestrant, more)

- **AKT Inhibitors** (capivasertib) = in testing, not yet approved
  - 10% of ER+ tumors have a somatic mutation in AKT1
  - ORR, PFS and OS benefit in phase II FAKTION trial

- **HDAC inhibitor** (entinostat) = = in testing, not yet approved
  - Showed PFS and OS benefit in Phase II trial ENCORE301
  - In Phase III testing (E2112)

- **Immune Checkpoint Inhibitors** = (pembrolizumab, durvalumab, atezolizumab) = none yet approved
  - PD-1 inhibitor (avelumab + palbociclib + fulvestrant, PACE Trial)
  - Very low response rates to date
Therapies for HER2+ Metastatic Breast Cancer

TARGETING HER2
• Lapatinib + capecitabine (approved 2007)
• Ado-trastuzumab emtansine (TDM1) (approved 2013)

• Neratinib + capecitabene approved for brain metastases and seeking FDA approval in the metastatic setting based on NALA trial results
• Neratinib is approved in extended adjuvant therapy after completion of 1 year of trastuzumab + pertuzumab
• Neratinib + TDM1 in clinical trials

• Tucatinib + trastuzumab + capecitabine (HER2Climb trial) = not yet approved

NON-HER2 TARGETING
• Immune checkpoint inhibitors = many in testing
  • atezolizumab/trastuzumab/pertuzumab/ in clinical trials
• CDK4/6 Inhibitors = in testing
Therapies for Metastatic Triple Negative Breast Cancer

- **Immune Checkpoint Inhibitors** (*Atezolizumab*): approved March 2019
  - atezolizumab + nab-paclitaxel improves PFS and OS in PD-L1 positive metastatic TNBC (IMpassion130 trial)
  - MANY immune therapy trials underway!

- **PARP inhibitors** (targeting DNA repair in a unique way)
  - Olaparib for germline BRCA-mutated metastatic HER2-negative breast cancer (OlympiAD): approved January 2018
  - Talazoparib for germline BRCA-mutated metastatic breast cancer (EMBRACA trial): approved October 2018
  - Somatic mutations in BRCA1/2 being tested as biomarkers for PARPi (TBCRC 048)

- **Sacituzumab Govitecan** (*IMMU-132*): an antibody-drug conjugate (ADC) targeting the protein TROP-2 and delivering SN-38 (active metabolite of irinotecan), in Phase III testing

- **Combination Therapies**
  - pembrolizumab + niraparib (Immune therapy + PARPi) (TOPACIO trial)
  - durvalumab + olaparib (Immune therapy + PARPi) (MEDIOLA trial)
  - Pembrolizumab + cyclophosphamide (LCCC 1525)
There are many basic research studies being performed using model systems to identify the key genes/proteins that mediate metastasis. We need to continue to support basic research so that we can experimentally study the metastatic process, which is complex and mediated by cell-cell interactions.

There are a number of translational initiatives, like AURORA US, being performed to identify the genetic and genomic ‘drivers’ of metastasis. These studies are critical to perform as they are based upon actual metastatic tumor specimens.

There is a growing number of approved drugs for MBC patients (CDK4/6 inhibitors, TDM1, Atezolizumab, PARPi, PIK3CAi), and many more in Phase II and Phase III testing.

Conclusions
Roundtable Discussion
Palliative Care in Oncology

Dr. Anthony Galanos, MA, MD
Palliative Medicine Specialist
Duke Cancer Institute

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Palliative Care in Oncology

The Data Support the Marriage

Anthony Nicholas Galanos, MA MD
Professor of Medicine
Duke Palliative Care
Komen Early Career Researchers Breakfast
October 4, 2019
Durham North Carolina
Outline

• A brief introduction to Palliative Care

We just have 10 minutes! 😊
“Oncodoxes”: The catch 22’s of oncology

(Mintzer. JCO. 2013; 31:393-394)

• Be optimistic/ be honest
• Be aggressive /Be careful
• Prolong survival/ Refer to hospice sooner

“It is easy for the those working in hospice and palliative medicine to criticize the oncologist for continuing with chemotherapy. They are not the ones who have to make the call.”

Palliative Care: What it is not

- End of life care only
- Hospice
- Abdication of the patient
Palliative Care: What it is

• Symptom management

• Unbound by point in the trajectory, eg, from time of diagnosis to bereavement

• Communication: goals of care

• “And/with” and NOT “either/or”
What is Palliative Care?

• Specialized medical care for people with serious illness

• Relief from symptoms, pain and stress – *whatever the diagnosis*

• Improve quality of life for both patient and family

• A team that provides an *extra layer of support*

• Appropriate at any age and at any stage of illness – *Can be provided together with curative treatment*

- The Domains of Care in the Palliative care model are congruent with the American Society of Clinical Oncology Statement: physical, psychological, social and spiritual consequences of cancer.

- “There is a need to change the paradigm for advanced cancer care to include an earlier and more thorough assessment of patients’ options, goals, and preferences, and to tailor the care that we deliver to those individual needs throughout the continuum of care.”
Is a marriage possible between Oncology and PC?

“By all means marry:
If you get a good wife, you will become happy.
If you get a bad one, you will become a philosopher.”

Socrates (c. 470-399 BC)
Landmark Study

- 151 patients
- Newly dx met NSCLC
- Randomized
  - Standard oncologic care (SOC)
  - SOC + early palliative care
- Primary outcome: QOL
Palliative Care Improves Survival

Integration and Impact of Palliative Care on an Oncology Inpatient Ward: The Duke 9300 Experience

Medicine Grand Rounds
September 5, 2014

Richard F. Riedel, MD
Kim M. Slusser, MSN, RN, CHPN
Anthony N. Galanos, MD

- Retrospective cohort study at Duke. Pre and post intervention patients admitted to the solid tumor inpatient service
- Cancer dx and stage; LOS; ICU transfer rate; discharge dispo; time to readmit: 7 and 30d. Nursing and MD satisfaction surveys.
- Lower LOS and 7 day readmission rates
- Increasing hospice referrals and 15% decrease in ICU transfers.
- Physicians and nurses universally favored the model.
Reasons for Palliative Care Consultation

- Communication
- Symptom
- Dispo
- EOL
Manage the Symptoms First

“No man can be rendered pain free whilst he still wrestles with his faith. No man can come to terms with his God when every waking moment is taken up with pain or vomiting.”

“Words are, of course, the most powerful drug used by mankind.”

Rudyard Kipling

1865-1936
Patient-Clinician Communication: American Society of Clinical Oncology Consensus Guideline


ABSTRACT

Purpose
To provide guidance to oncology clinicians on how to use effective communication to optimize the patient-clinician relationship, patient and clinician well-being, and family well-being.

Methods
ASCO convened a multidisciplinary panel of medical oncology, psychiatry, nursing, hospice and palliative medicine, communication skills, health disparities, and advocacy experts to produce recommendations. Guideline development involved a systematic review of the literature and a formal consensus process. The systematic review focused on guidelines, systematic reviews and meta-analyses, and randomized controlled trials published from 2006 through October 1, 2016.

Results
The systematic review included 47 publications. With the exception of clinician training in communication skills, evidence for many of the clinical questions was limited. Draft recommendations underwent two rounds of consensus voting before being finalized.

Recommendations
In addition to providing guidance regarding core communication skills and tasks that apply across the continuum of cancer care, recommendations address specific topics, such as discussion of goals of care and prognosis, treatment selection, end-of-life care, facilitating family involvement in care, and clinician training in communication skills. Recommendations are accompanied by suggested strategies for implementation. Additional information is available at www.asco.org/supportive-care-guidelines and www.asco.org/guidelineswiki.

J Clin Oncol 35:3618-3632. © 2017 by American Society of Clinical Oncology
What patients (families) want

Fogarty, et al. “Can 40 Seconds of Compassion Reduce Patient Anxiety?”
J Clin Onc, 1999

• They want compassion and empathy

  – Study design: RCT of videotaped intervention, with pre and post-test anxiety inventory and rating of MD
    • 123 breast cancer survivors and 87 healthy volunteers,
    • video of oncologist consultation …scripted but varied on degree of compassion demonstrated

  – Results: viewing the “enhanced compassion” video was associated with significantly decreased anxiety
    • Also a/w higher rating of physician on non-emotional topics
Here’s the “intervention”

• It’s only 40 seconds long!

  • Segment 1: “I know this is a tough experience to go through and I want you to know that I am here with you. Some of the things that I say to you today may be difficult to understand, so I want you to feel comfortable in stopping me if something I say is confusing or doesn’t make sense. We are here together, and we will go through this together.”

  • Segment 2: I know this is a tough time for you and I want to emphasize again that we are in this together. I will be with you each step along the way.

What we do...we tend to...

• **...miss or ignore opportunities for empathy**
  
  (Suchman et al. *JAMA*. 1997;277: 678-82. A model of empathic communication....

  – **Study design:** audio-recorded clinic visits
    • 290 pts with advanced cancer, 51 oncologists
    • coded for the presence of empathic opportunities

  – **Results:** 37% of conversations contained at least one empathic opportunity
    • **oncologists responded empathically only 22% of time**
      – responses more prevalent among younger oncologists and those self-rated as “more socioemotional than technical”
Integration of Palliative Care Into Standard Oncology Care: American Society of Clinical Oncology Clinical Practice Guideline Update


Abstract

Purpose
To provide evidence-based recommendations to oncology clinicians, patients, family and friend caregivers, and palliative care specialists to update the 2012 American Society of Clinical Oncology (ASCO) provisional clinical opinion (PCO) on the integration of palliative care into standard oncology care for all patients diagnosed with cancer.

Methods
ASCO convened an Expert Panel of members of the ASCO Ad Hoc Palliative Care Expert Panel to develop an update. The 2012 PCO was based on a review of a randomized controlled trial (RCT) by the National Cancer Institute Physicians Data Query and additional trials. The panel conducted an updated systematic review seeking randomized clinical trials, systematic reviews, and meta-analyses, as well as secondary analyses of RCTs in the 2012 PCO, published from March 2010 to January 2016.

Results
The guideline update reflects changes in evidence since the previous guideline. Nine RCTs, one quasirandomized trial, and five secondary analyses from RCTs in the 2012 PCO on providing palliative care services to patients with cancer and/or their caregivers, including family caregivers, were found to inform the update.

Recommendations
Inpatients and outpatients with advanced cancer should receive dedicated palliative care services, early in the disease course, concurrent with active treatment. Referral of patients to interdisciplinary palliative care teams is optimal, and services may complement existing programs. Providers may refer family and friend caregivers of patients with early or advanced cancer to palliative care services.

Hospital Based Palliative Care

“Palliative care is not a way out but a way through...

Hospitals are a place of miracles and cures, but when that can not be the outcome, we

‘...palliate often and comfort always.’ ”

Carey K. Anders, MD

Roundtable Discussion

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Exploring the Patient and Doctor Relationship

Dr. Sarah Sammons, MD
Duke Cancer Institute / Duke University

Elizabeth Levene, executive director at Helps Education Foundation and Living with MBC

Facilitated by:
Katrina Cooke, Advocate and Living with MBC
Roundtable Discussion And Report Out
Carey K. Anders, MD

Closing Remarks

Pam Kohl, executive director

Living with Metastatic Breast Cancer

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