‘ASK YOUR DOCTOR (ONCOLOGIST) ABOUT CLINICAL TRIALS!’

ALL ABOUT RESEARCH IN ADVANCED BREAST CANCER

Alison Conlin, MD, MPH
Director, Breast Cancer Oncology

Nikki Moxon, OCN, RN
Lead Research Nurse

Providence Cancer Center
IN THIS TALK YOU WILL LEARN.....

What is a clinical trial or study?
Why would I/my loved one go on a clinical trial?
How do I/my loved one go on a clinical trial?
Great stories.....
DEFINITIONS: WHAT IS A CLINICAL TRIAL?

NIH Definition of a Clinical Trial

A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Randomized: assigned to treatment side by flip of coin (you do not get to chose)

Arm: one side of a clinical study

Blinded: the people involved do not know the assignment

Placebo: a substance or procedure with no therapeutic effect
WHAT TYPES OF STUDIES ARE THERE?

Interventions to prevent or treat a disease. Some examples are:

• Medical products, such as drugs or devices; procedures
• Changes to participants’ behavior, such as diet or exercise intervention
• Compare new idea vs. ‘standard of care’ medical approaches
• Drug development in phases, Phase 1-4
Phase 1, safety and dosing
- Goal is usually dose finding and side effect profile
- Not necessarily efficacy
- Sometimes it is first in human testing
- Approximately 70% of drugs move onto next phase
- Takes weeks to months

Phase 2
- Efficacy and side effects
- Gives us a good idea how well it may work
- Approximately 33% of drugs move onto the next phase.
- Takes months
PHASE OF CLINICAL TRIALS

Phase 3, Efficacy in a specific situation
- Goal is often to compare to standard of care and make better
- LARGE studies so looking for other uncommon side effects
- Approximately 25% of drugs move onto next phase which is approval
- Takes years

Phase 4, post-market monitoring
- Already approved, watching it for anything unexpected
- For years after approval
WHAT TYPES OF STUDIES ARE THERE?

Categories:

- Treatment trials
- Cancer Control trials
- Imaging and surveillance trials
- Tissue collection/ Biospecimen trials
- Cancer Control Delivery Research
- Registry
EXAMPLES OF OPEN STUDIES AT PROVIDENCE

Currently Open Study Types

- Therapeutic: 88%
- Other: 6%
- Cancer Control/Prevention: 3%
- Registry: 3%
- Observational: 0%
WHERE DO THE IDEAS FOR STUDIES COME FROM?

Categories:

- **Large cooperative group organizations sponsored by the NCI: SWOG, Alliance, ECOG, NRG:**
  - This is groups of doctors with shared interests, ‘thought leaders’

- **Pharma (pharmaceutical company sponsored):**
  - Company has a question about how their drug/ideas fit in

- **Investigator initiated study:**
  - An idea by a doctor who has some research focus
WHO SPONSORS (PAYS FOR) CLINICAL STUDIES?

- Pharmaceutical companies
- Investigators
- Academic and medical centers
- Federal agencies: NIH, US Dept. Veterans Affairs, National Cancer Institute, Oregon Health Authority
OUR CLINICAL RESEARCH GOALS

- Improve prevention, early diagnosis and treatment of cancer
- Discover whether a particular drug or medical treatment is safe and effective
- Advance the state of scientific and medical knowledge
- Measure and improve the quality of life for patients and their families
OUR CLINICAL RESEARCH GOALS ARE NOT:

- Try new things on people who don’t know any better
- Use patients as a ‘guinea pig’
- Harm patients
- Do studies to get more funding for other studies
- Make money
WHO CONDUCTS CLINICAL TRIALS/STUDIES?

Investigators, medical doctors are the lead
- Principal investigator is the study lead doctor, either locally or nationally.
- Co-investigators are doctors working with patients on the study

Clinical studies also have a research team that may include doctors, nurses, social workers, and other health care professionals.
- Research nurses often spend most time with patients on study
WHERE ARE STUDIES CONDUCTED?

Hospitals both university and community

Community event (biospecimen collection)

Mostly in the outpatient clinics:
- Oncology and Hematology Care Clinic – Eastside, Westside, Southeast, Newberg
- Not all studies are available everywhere!
  - In fact it takes a LOT OF WORK to open, keep open and monitor a study so most places are VERY selective
WHO CAN PARTICIPATE?
THIS IS KEY!

Eligibility (Inclusion/Exclusion criteria)
- This defines who can go on a study and can be very LENGTHY

Factors such as:
- age, gender
- the type and stage of a disease
- previous treatment history
- other medical conditions
HOW ARE PARTICIPANTS PROTECTED?

- Informed consent
- IRB – Institutional Review Board
- Monitoring Committees
- Federal Agencies: Office of Human Subjects Research Protection and FDA
HOW DO WE EVALUATE PATIENTS ON STUDY?

- Clinical exam at specific time points
- Labs
- Other testing like EKGs
- Specific imaging to follow the progress (or better regress) of cancer areas
  - RECIST criteria
HOW DO WE EVALUATE PATIENTS ON STUDY?

RECIST 1.1 Criteria
3.1.1. Measurable Tumour lesions:

Must be accurately measured in at least one dimension (longest diameter in the plane of measurement is to be recorded) with a minimum size of:

- 10 mm by CT scan (CT scan slice thickness no greater than 5 mm; see Appendix II on imaging guidance).
- 10 mm caliper measurement by clinical exam (lesions which cannot be accurately measured with calipers should be recorded as non-measurable).
- 20 mm by chest X-ray.
HOW DO WE EVALUATE PATIENTS ON STUDY?

RECIST 1.1 Criteria

Malignant lymph nodes: To be considered pathologically enlarged and measurable, a lymph node must be 15 mm in short axis when assessed by CT scan (CT scan slice thickness recommended to be no greater than 5 mm). At baseline and in follow-up, only the short axis will be measured and followed.
HOW DO WE EVALUATE PATIENTS ON STUDY?

RECIST 1.1 Criteria

All other lesions, including small lesions (longest diameter <10 mm or pathological lymph nodes 10 to <15 mm short axis) as well as truly non-measurable lesions. Lesions considered truly non-measurable include:

1) Leptomeningeal disease
2) Ascites
3) Pleural or pericardial effusion
4) Inflammatory breast disease
5) Lymphangitic involvement of skin or lung
6) Abdominal masses/abdominal organomegaly identified by physical exam that is not measurable by reproducible imaging techniques.
HOW DO WE EVALUATE PATIENTS ON STUDY?

RECIST 1.1 Criteria

1) Total of 5 target lesions
2) Maximum 2 per organ
3) Bone lesions not considered measurable (unless there is a soft tissue component that meets other criteria for target lesions).
4) ...
HOW WOULD YOU PICK AN AREA HERE?
WHY WOULD I/MY LOVED ONE GO ON A CLINICAL STUDY?

To get access to new treatments
To have better chance of success with your condition
To help us learn and advance science

We do not have all the answers
QUESTIONS TO ASK

- How often will I have to visit the hospital or clinic?
- How long will the study last?
- What are the costs? Does the study pay for anything?
- What type of long-term follow-up care is part of this trial?
- If I benefit from the intervention, will I be allowed to continue receiving it after the trial ends?
- Will results of the study be provided to me?
HOW DO I/MY LOVED ONE GO ON A CLINICAL STUDY?

Usually you have to be offered by your doctor
You can search www.clinicaltrials.gov
Second opinion at a center that does a lot of studies
Look online at websites of where you are going

ASK YOUR DOCTOR ABOUT CLINICAL TRIALS
ADVANCED BREAST CANCER TRIALS

- Typically each trial is offered to patients with specific markers:
  - Estrogen and/or progesterone receptor positive vs. negative
  - Her2-neu positive vs. negative

- Will often require specific kinds of previous treatment (or lack thereof) for breast cancer to be eligible for trial.

- Size and location of advanced or metastatic disease can also be a factor for enrollment.

- Require treatment and interventions on the study to follow protocol specified schedule.
EXAMPLES OF ADVANCED BREAST CANCER STUDIES

Wide variety of treatment types being tested alone and in new combinations:

- Endocrine therapy combinations (CDK 4/6 inhibitors with new drugs)
- Immunotherapy (Anti-PD1 with chemotherapy or hormone therapy)
- Targeted therapies (Oral targeted lesions)
GREAT STORY #1....

MJC is a 68 year old Korean woman who presented with chest pain and left breast redness in September of 2013.

She was due for a mammogram and had that with a new mass and abnormal lymph nodes.

A biopsy in the breast and lymph node showed estrogen positive and Her-2-neu over-expressed breast cancer.

She was having a lot of hip pain and continued chest pain (normal heart tests) and so PET/CT done and had many bones with breast cancer in it.

She started on standard of care first chemotherapy with docetaxel and trastuzumab (Herceptin) and pertuzumab (Perjeta). She did this for 6 cycles and then stayed on just trastuzumab and pertuzumab for 1 year (December 2014).

She had significant shrinkage in her breast and lymph node on this. Pain went away with some radiation and some treatment.
GREAT STORY #1....

One year later on this combination her tumor markers started to rise.

The PET/CT in December 2014 showed more intense and new bone areas of cancer spread.

She was offered standard 2nd line treatment with T-DM1 (Kadcyla).

She was also offered a new clinical trial with an oral, targeted therapy called ONT-380 (Tucatinib). This was a phase 1 study of the combination of standard therapy (T-DM1) and new oral pill.

She consented and went on study.
GREAT STORY #1....

Initially she had some treatments held for lab abnormalities.
She was able to stay on study.
She was on IV treatment with T-DM1 (standard of care) and oral ONT-380 for 30 cycles or from December 2014 to October 2016.
She then had growth on PET/CT in new bones.
This is the longest she has been on any treatment during her advanced breast cancer.
She is still alive, feeling really well and on 5th line of treatment.
ONT-380 is now known as tucatinib and is in phase 3 study for approval in coming year(s).

MJC benefited from the study and ALSO contributed to our advancement for many other women.

MJC has had 3 grandchildren born while under my care.
KML is a 64 year old woman who in 1992 (age 38), had stage 2 breast cancer, estrogen positive, treated with chemotherapy and lumpectomy and radiation. She took 5 years of tamoxifen.

In 2010 (age 57), had new lump near her chest bone and imaging and biopsy proven recurrence, stage 4, of her breast cancer to bone. It was still estrogen positive and Her-2-neu negative.

From April 2010 to February 2013 she took oral anti-estrogen letrozole. Then she took injection anti-estrogen fulvestrant from February 2013 to June 2013.

Her chest bone mass was rapidly growing at this time.

I met her as she was about to start oral chemotherapy for this.
GREAT STORY #2....

I gave her options and instead started her on tamoxifen pills in late June 2013.

KML was on tamoxifen when a new phase 1 study opened at Providence over 1 year later in August 2014.

The study was looking at various combinations of a new oral CDK 4/6 inhibitor with different endocrine therapies.

It required many blood draws on 1\textsuperscript{st} and 2\textsuperscript{nd} day called PKs.

This oral CDK4/6 inhibitor is called \textbf{LY2835219}. In July 2013, no oral CDK4/6 inhibitors were approved.

She consented to the study requirements.

She added study drug this TO her tamoxifen in August 2014.

Her chest bone (sternal) tumor shrunk and has been stable since then.
GREAT STORY #2....

KML is on cycle #46 of treatment, over 3 ½ years on study.

The drug (LY2835219) she is on has been approved as Verzenio (abemaciclib) either with fulvestrant or alone. It is not yet approved with tamoxifen.

KML has traveled to Hawaii more times than I can count, has 2 new grandchildren and is very active on her large property at home.
GREAT STORY #3....

EJ is a 71 year old woman, who had stage 3 triple negative breast cancer in 2012 treated with mastectomy and chemotherapy.

Then in July 2015 she had new worsening shortness of breath and anemia and was found to have large mass in lining of lungs (pleural mass) with fluid (pleural effusion) as well as bone abnormalities.

She had biopsy of lung mass and it showed ER- PR- Her2-neu negative breast cancer. She was seen by my colleague in Newberg, Dr. Perlewitz, who knew about a study we had open but did not have it open there.

EJ came to see me and started on a phase 3 study in August 2015.
EJ enrolled on a randomized, blinded, placebo-controlled phase 3 study, Roche WO29522.

This was of standard chemotherapy as first line treatment, weekly nab-paclitaxel (Abraxane) with or without anti-PDL1 (atezolizumab).

EJ is still on study, cycle 33 for 2 ½ years with stage 4 triple negative breast cancer.

The study will be done soon but EJ can continue, although we aren’t sure what she is getting.

EJ goes to the Shakespeare festival in Ashland every year.
GREAT STORY #3...
QUESTIONS?

We are the center of hope.