Public Meeting on Breast Cancer Patient-Focused Drug Development

April 2, 2015

U.S. Food and Drug Administration
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Welcome

Soujanya Giambone, MBA
Office of Strategic Programs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

April 2, 2015

Agenda

- **Setting the context**
  - Opening Remarks
  - Overview of FDA's Patient-Focused Drug Development Initiative
  - Background on Breast Cancer and Therapeutic Options
  - Overview of Discussion Format

- **Discussion Topic 1**: Disease symptoms and daily impacts that matter most to patients

- **Discussion Topic 2**: Patients' perspectives on current approaches to treating breast cancer

- **Open Public Comment**

- **Closing Remarks**

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Opening Remarks

Amna Ibrahim, MD

Deputy Director, Division of Oncology Products I (DOP I)
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

April 2, 2015

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FDA's Patient-Focused Drug Development Initiative

Theresa Mullin, PhD
Director, Office of Strategic Program
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

April 2, 2015

Patient-Focused Drug Development under PDUFA V

- **FDA is developing a more systematic way of gathering patient perspective on their condition and available treatment options**
  - Patient perspective helps inform our understanding of the context for the assessment of benefit-risk and decision making for new drugs
  - Input can inform FDA's oversight both during drug development and during our review of a marketing application

- **Patient-Focused Drug Development is part of FDA commitments under the fifth reauthorization of the Prescription Drug User Fee Act (PDUFA V)**
  - FDA will convene at least 20 meetings on specific disease areas over the next five years
  - Meetings will help develop a systematic approach to gathering patient input

Identifying Disease Areas for the Patient-Focused Meetings

- **In September 2012, FDA announced a preliminary set of diseases as potential meeting candidates**
  - Public input on these nominations was collected. FDA carefully considered these public comments and the perspectives of our drug review divisions at FDA

- **FDA identified a set of 16 diseases to be the focus of meetings for fiscal years 2013-2015**
  - Another public process has been initiated to determine the disease set for fiscal years 2016-2017

Disease Areas to be the focus of meetings for FY 2013-2015

FY 2013

- Chronic fatigue syndrome
- HIV
- Lung cancer
- Narcolepsy

FY 2014

- Sickle cell disease
- Fibromyalgia
- Pulmonary arterial hypertension
- Inborn errors of metabolism
- Hemophilia A, Hemophilia B, von Willebrand disease, and other heritable bleeding disorders
- Idiopathic pulmonary fibrosis

FY 2015

- Female sexual dysfunction (October 27-28)
- **Breast cancer**
- Chagas disease (April 28, 2015)
- Functional gastrointestinal disorders (May 11, 2015)
- Alpha-1 antitrypsin deficiency
- Parkinson's disease and Huntington's disease

Tailoring Each Patient-Focused Meeting

- **Each meeting focuses on a set of questions that aim to elicit patients' perspectives on their disease and on treatment approaches**
  - We start with a set of questions that could apply to any disease area; these questions are taken from FDA's benefit-risk framework and represent important considerations in our decision-making
  - We then further tailor the questions to the disease area of the meeting (e.g., current state of drug development, specific interests of the FDA review division, and the needs of the patient population)
- **Focus on relevant current topics in drug development for the disease at each meeting**
  - E.g., focus on HIV patient perspectives on potential "cure research"
- **We've learned that active patient involvement and participation is key to the success of these meetings.**

"Voice of the Patient" Reports

- Following each meeting, FDA publishes a Voice of the Patient report that summarizes the patient testimony at the meeting, perspectives shared in written docket comments, as well as any unique views provided by those who joined the meeting webcast.
- These reports serve an important function in communicating to both FDA review staff and the regulated industry what improvements patients would most like to see in their daily life.
- FDA believes that the long run impact of this program will be a better, more informed understanding of how we might find ways to develop new treatments for these diseases.

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Background on Breast Cancer and Therapeutic Options

Suparna Wedam, MD

Medical Officer, DOP I/Breast Cancer Oncology Group
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

April 2, 2015

Introduction

- Second leading cause of cancer-related death among women.
- In the United States for 2015 an estimated:
  - 231,840 women will be diagnosed with breast cancer
  - 40,290 will die from the disease

American Cancer Society www.cancer.org

Risk Factors

- Gender
- Age
- Genetic Risk Factors
- Personal/Family History
- Dense Breast Tissue
- Certain breast conditions
- Menarche/Menopause
- Nulliparity
- Birth control
- Hormone replacement
- Breastfeeding
- Alcohol use
- Obesity
- Physical activity

Diagnosis

- Symptoms (which prompt imaging)
  - Early stage: Often asymptomatic; may have palpable breast mass
  - Late stage: Also may be asymptomatic. May have constitutional (fatigue, weight loss, decreased appetite) or localized symptoms (bone, abdominal)

Diagnosis

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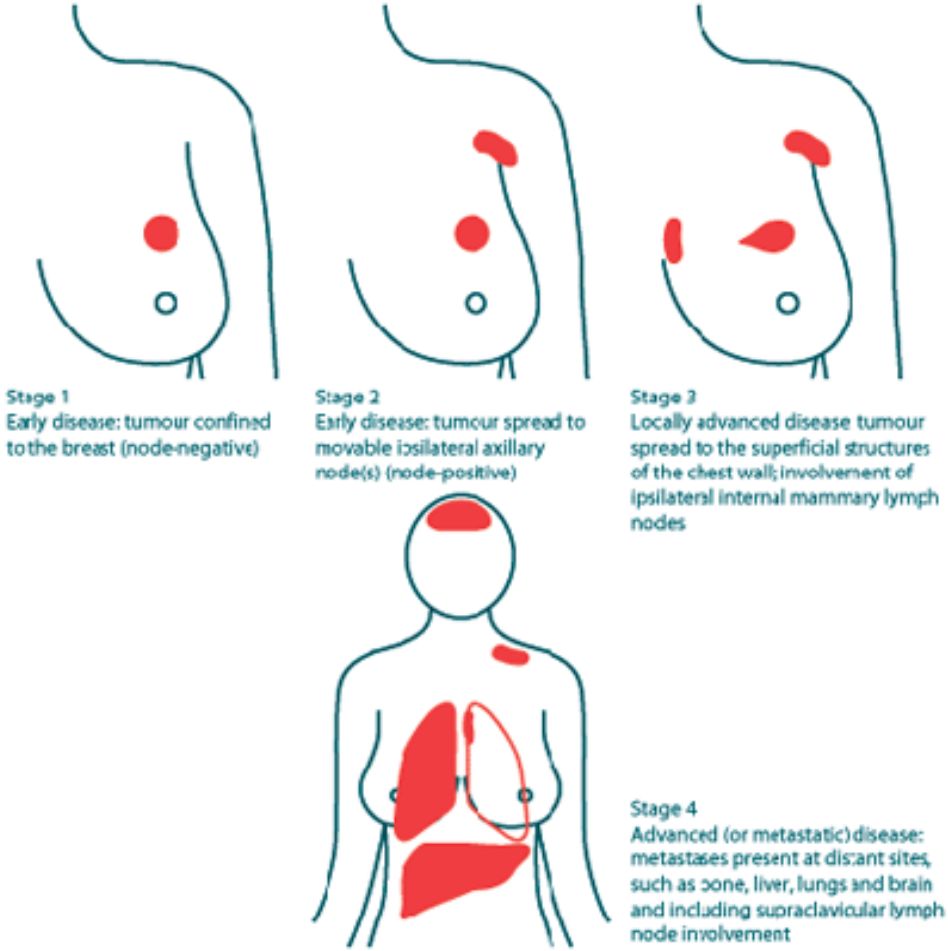
- Tissue confirmation

Diagnosis

- Symptoms
  - Early stage: Often asymptomatic
  - Late stage: Also may be asymptomatic. May have constitutional (fatigue, weight loss, decreased appetite) or localized symptoms (bone, abdominal)
- Tissue confirmation
- Stage the cancer
  - Based on TNM (tumor, node, metastasis)
  - Stage I, II, III (treat for curative intent)
  - Stage IV

Staging of Breast Cancer



Stage 1
Early disease: tumour confined to the breast (node-negative)

Stage 2
Early disease: tumour spread to movable ipsilateral axillary node(s) (node-positive)

Stage 3
Locally advanced disease tumour spread to the superficial structures of the chest wall; involvement of ipsilateral internal mammary lymph nodes

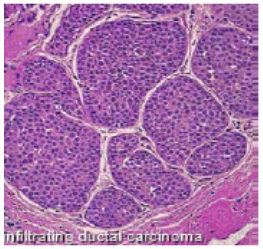
Stage 4
Advanced (or metastatic) disease: metastases present at distant sites, such as bone, liver, lungs and brain and including supraclavicular lymph node involvement

Formulate treatment plan

- Stage
- Invasive vs noninvasive (in situ)
- Tumor histology (ductal, lobular, etc)
- ER, PR and HER2 status
- Histologic grade of tumor
- Genomic testing (Oncotype DX, Mammaprint, etc)
- Age, comorbidities

Evolution in Cancer Classification

Tumor Histological Subtypes

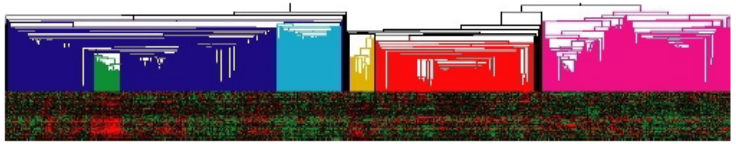


Clinical Subtypes

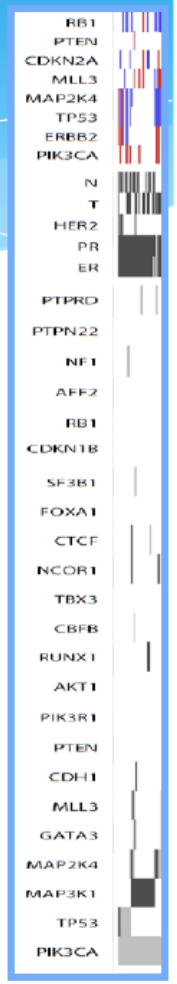
HR, HER2

Molecular Subtypes

Normal Breast
Luminal A
Luminal B
Claudin-low
Basal-like
HER2-enriched



Multiple Genomic Subsets



Common Side Effects of Treatment

Surgery	Radiotherapy	Chemotherapy	"Targeted" therapy
• Pain • Weakness • Fatigue • Lymphedema • Risk of infection or bleeding	• Fatigue • Localized skin irritation • Cognitive impairment with brain irradiation • Lung injury (radiation pneumonitis) • Heart injury	• Fatigue • Nausea/vomiting • Nerve damage • Mouth sores • Hair loss • Increased risk of bleeding and infection	• Rash • Diarrhea • Fatigue • Heart injury • Infusion reactions • Lung injury • Liver injury

Approved Therapies

Hormonal Therapy	Chemotherapy	"Targeted" therapy
• Tamoxifen • Anastrozole • Goserelin • Letrozole • Exemestane • Fulvestrant	• Methotrexate • Cyclophosphamide • Doxorubicin • Paclitaxel • Docetaxel • Capecitabine • Epirubicin • Abraxane • Ixabepilone • Eribulin	• Trastuzumab • Lapatinib • Pertuzumab • TDM-1

FDA Drug Approval

Requires substantial evidence from adequate and well-controlled clinical trials

Clinical benefit

Improvement in how one **feels** or **functions** or prolongation of **survival**

A validated surrogate for one of the above

FDA Guidance
Patient-Reported Outcomes (PROs)

- PROs can represent direct measures of treatment benefit (feel/function)
- PROs highlight patients' unique ability to contribute to the field of drug development
- FDA encourages the development of well-defined and reliable PRO instruments that capture clinical benefit concepts that are important to patients

Thank You

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Overview of Discussion Format

Soujanya Giambone, MBA
Office of Strategic Programs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

April 2, 2015

Discussion Overview

Topic 1: The symptoms that matter most to you

- Which symptoms have the most significant impact on your life?
- How do these symptoms affect your ability to do specific activities?
- How have your symptoms changed?

Topic 2: Current approaches to treating breast cancer

- What are you doing to treat breast cancer?
- What are the biggest downsides to your treatments?
- What would you look for in an “ideal” treatment?

Discussion Format

- **We will first hear from a panel of patients and caregivers**
  - The purpose is to set a good foundation for our discussion
  - They reflect a range of experiences with breast cancer

- **We will then broaden the dialogue to include patients and patient representatives in the audience**
  - The purpose is to build on the experiences shared by the panel
  - We will ask questions and invite you to raise your hand to respond
  - Please state your name before answering

Discussion Format, continued

- **You'll have a chance to answer "polling" questions**
  - Their purpose is to aid our discussion
  - In-person participants, use the "clickers" to respond
  - Web participants, answer the questions through the webcast
  - Patients and patient representatives only, please

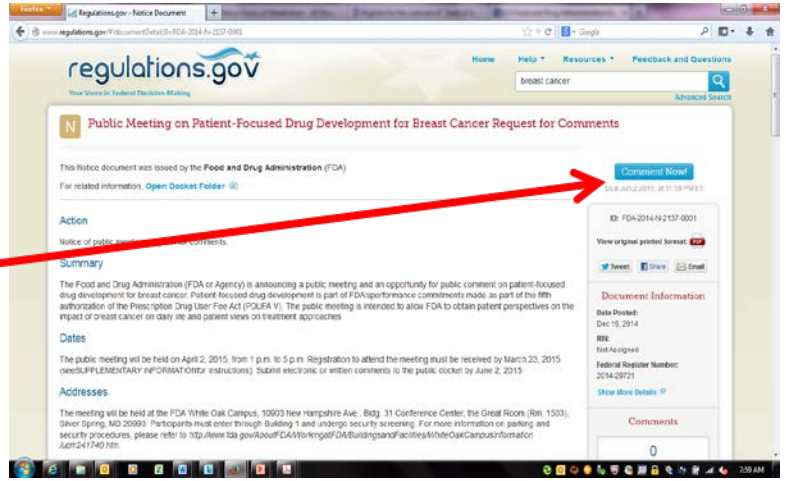
- **Web participants can add comments through the webcast**
  - Although they may not all be read or summarized today, your comments will be incorporated into our summary report
  - We'll occasionally go to the phones to give you another opportunity to contribute

Send us your comments!

- **You can send us comments through the "public docket"**
  - The docket will be open until June 2, 2015
  - Share your experience, or expand upon something discussed today
  - Comments will be incorporated into our summary report
  - Anyone is welcome to comment

Visit:
http://www.regulations.gov/#!documentDetail;D=FDA-2014-N-2137-0001

Click Comment Now!



Resources at FDA

- FDA Office of Health and Constituent Affairs
  - Contact: PatientNetwork@fda.hhs.gov, (301) 796-8460
  - Liaison between FDA and stakeholder organizations
  - Runs the Patient Representative Program
    - Patient Representatives advise FDA at Advisory Committee meetings
- CDER Office of Center Director
  - Professional Affairs and Stakeholder Engagement (PASE)
  - Contact: Francis Kalush, francis.kalush@fda.hhs.gov, (240) 402-6506
  - Facilitates communication and collaboration between CDER and patient and healthcare professional stakeholders and others on issues concerning drug development, drug review and drug safety.

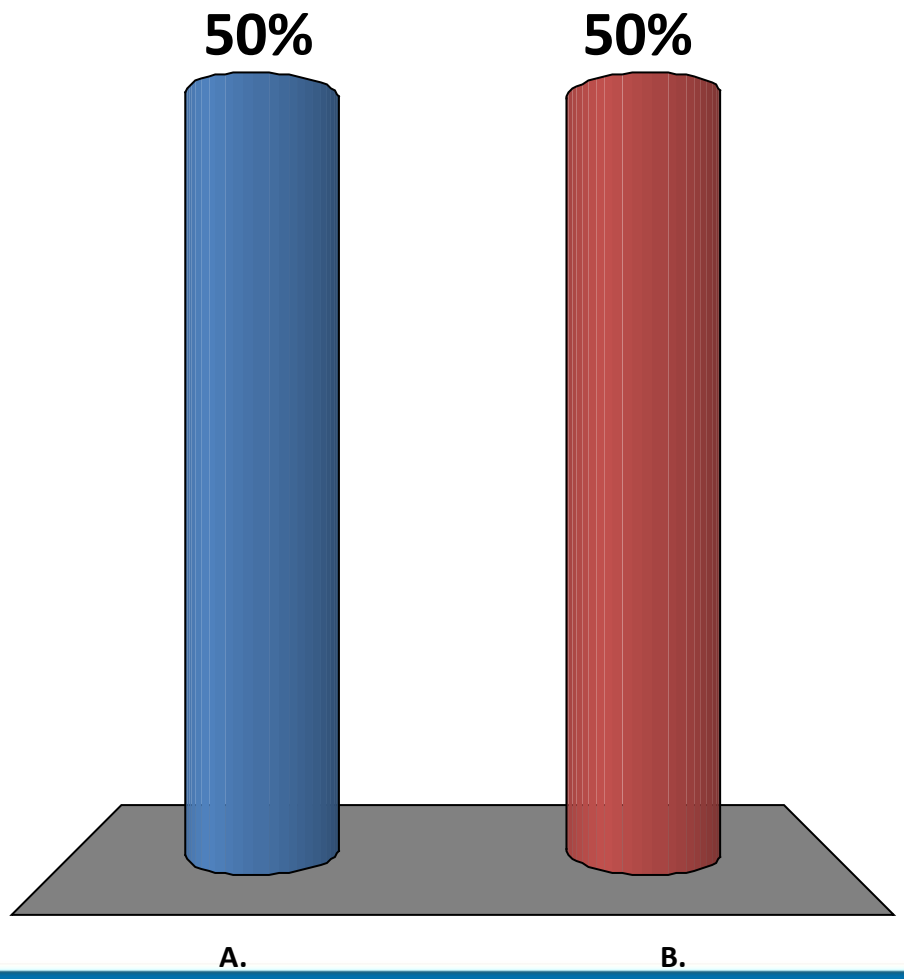
Discussion Ground Rules

- We encourage patients to contribute to the dialogue– caregivers and advocates are welcome too
- FDA is here to listen
- Discussion will focus on symptoms and treatments
  - Open Public Comment Period is available to comment on other topics
- The views expressed today are personal opinions
- Respect for one another is paramount
- Let us know how the meeting went today; evaluations at registration desk

Where do you live?

A. Within Washington, D.C. metropolitan area (including the Virginia and Maryland suburbs)

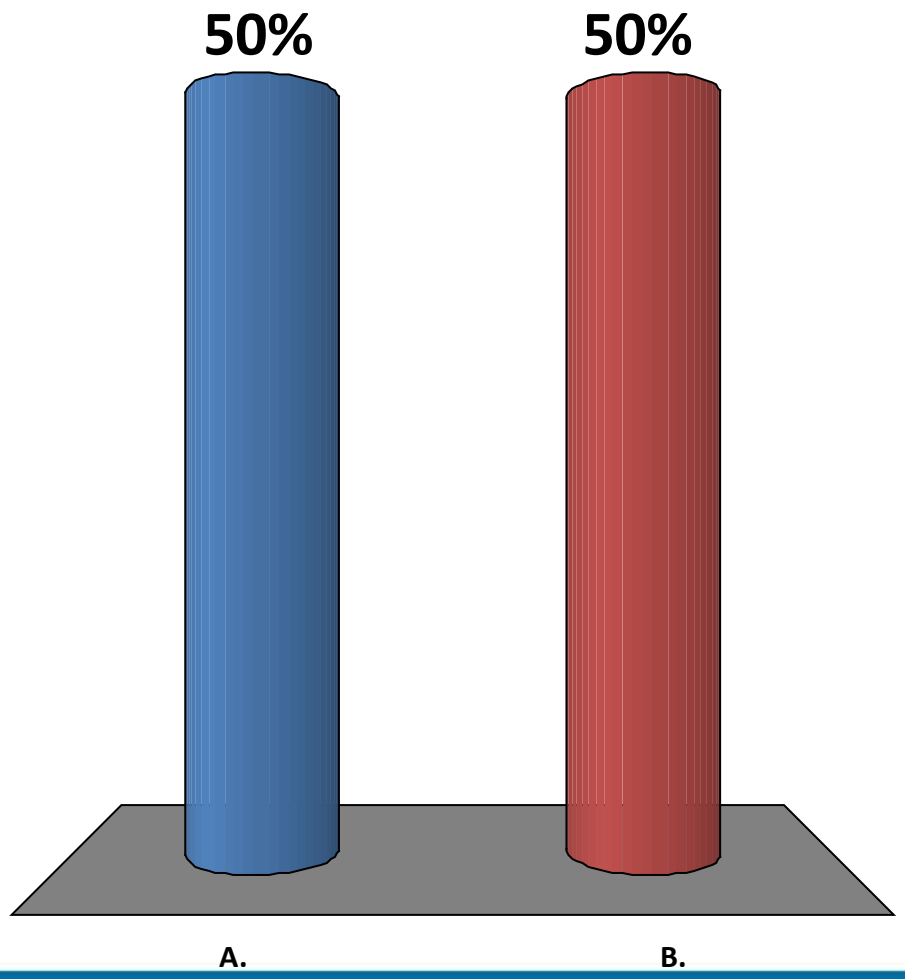
B. Outside of the Washington, D.C. metropolitan area



Have you ever been diagnosed as having breast cancer?

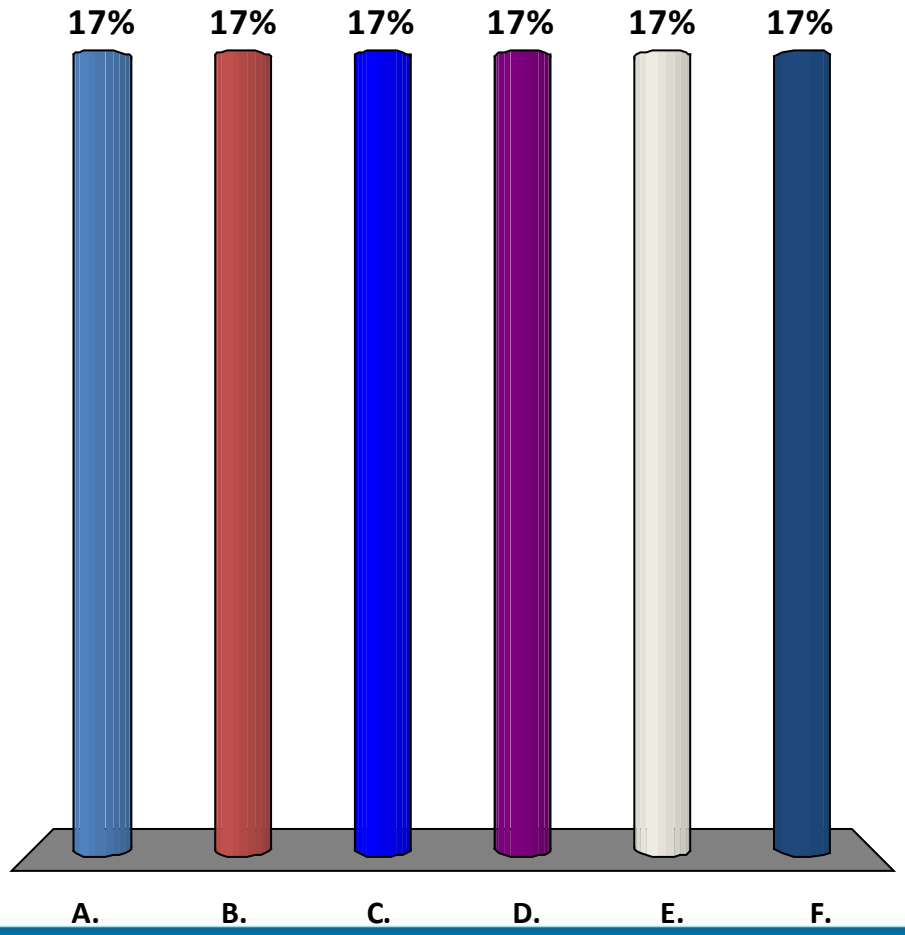
A. Yes

B. No



What is your age / your loved one's age?

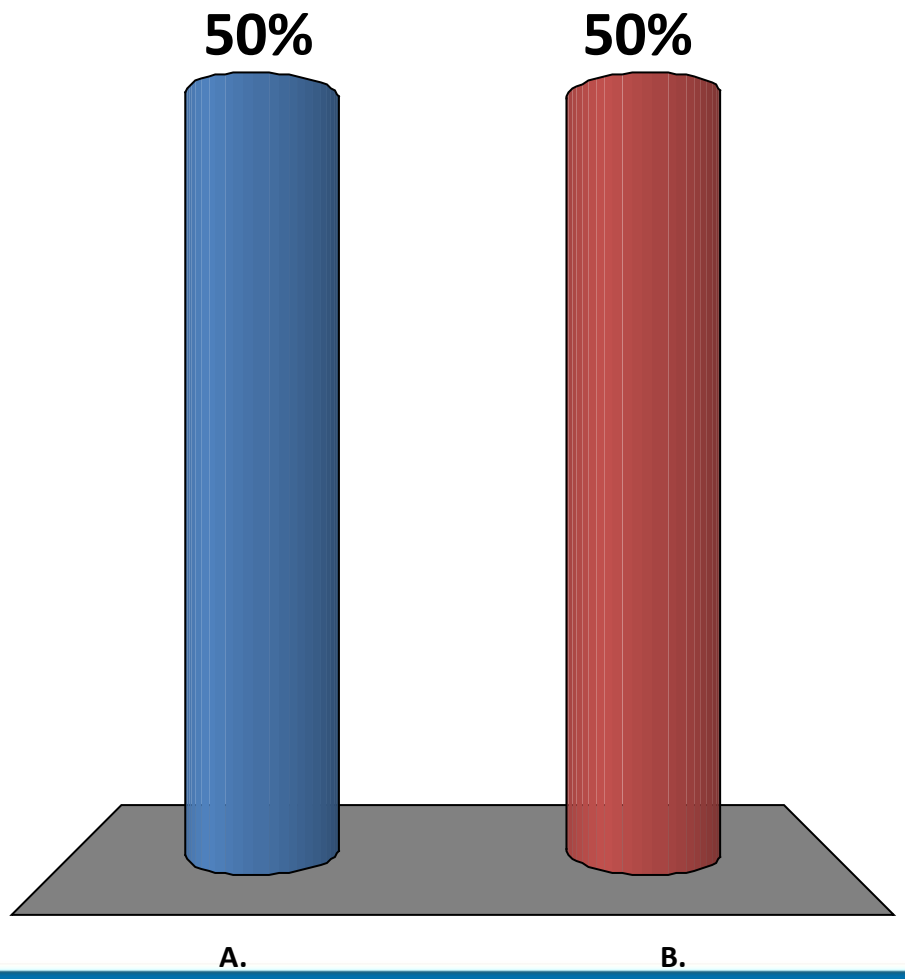
A. Younger than 30
B. 31 – 40
C. 41 – 50
D. 51 – 60
E. 61 – 70
F. 71 or greater



Are you:

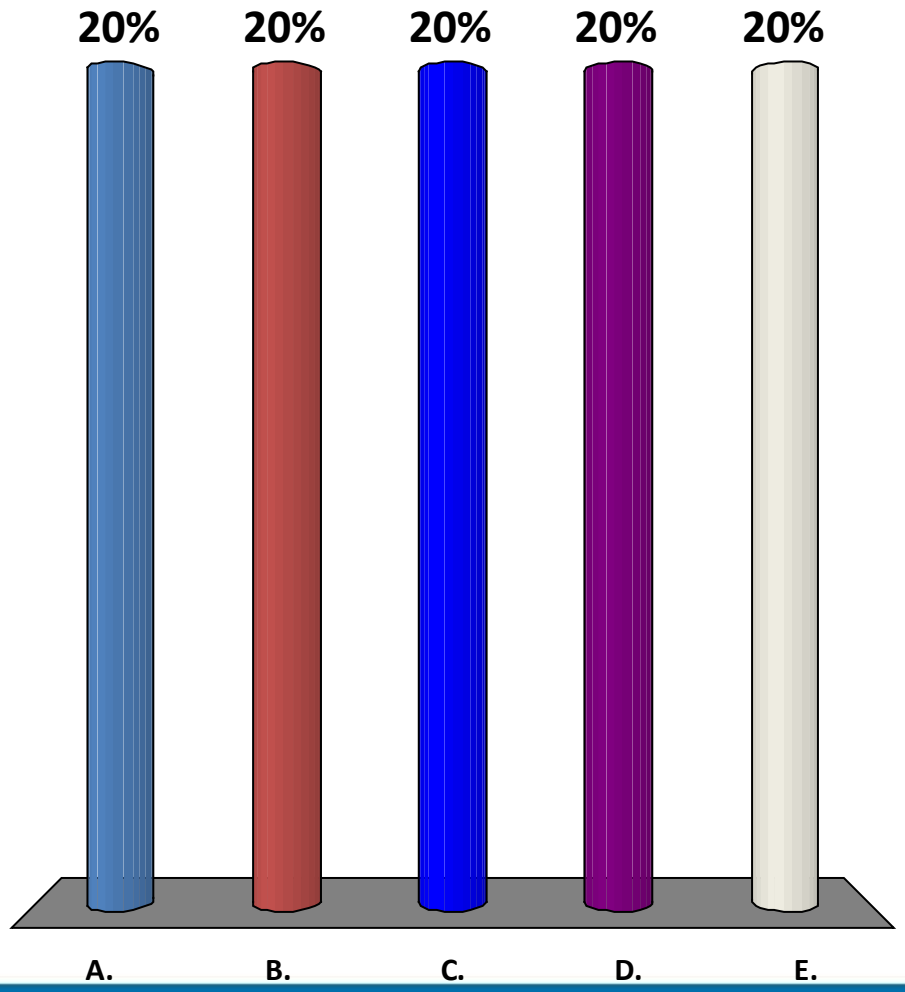
A. Male

B. Female



What is the length of time since your diagnosis?

A. Less than 1 year ago
B. 1 year ago to 2 years ago
C. 2 years ago to 5 years ago
D. More than 5 years ago
E. I'm not sure



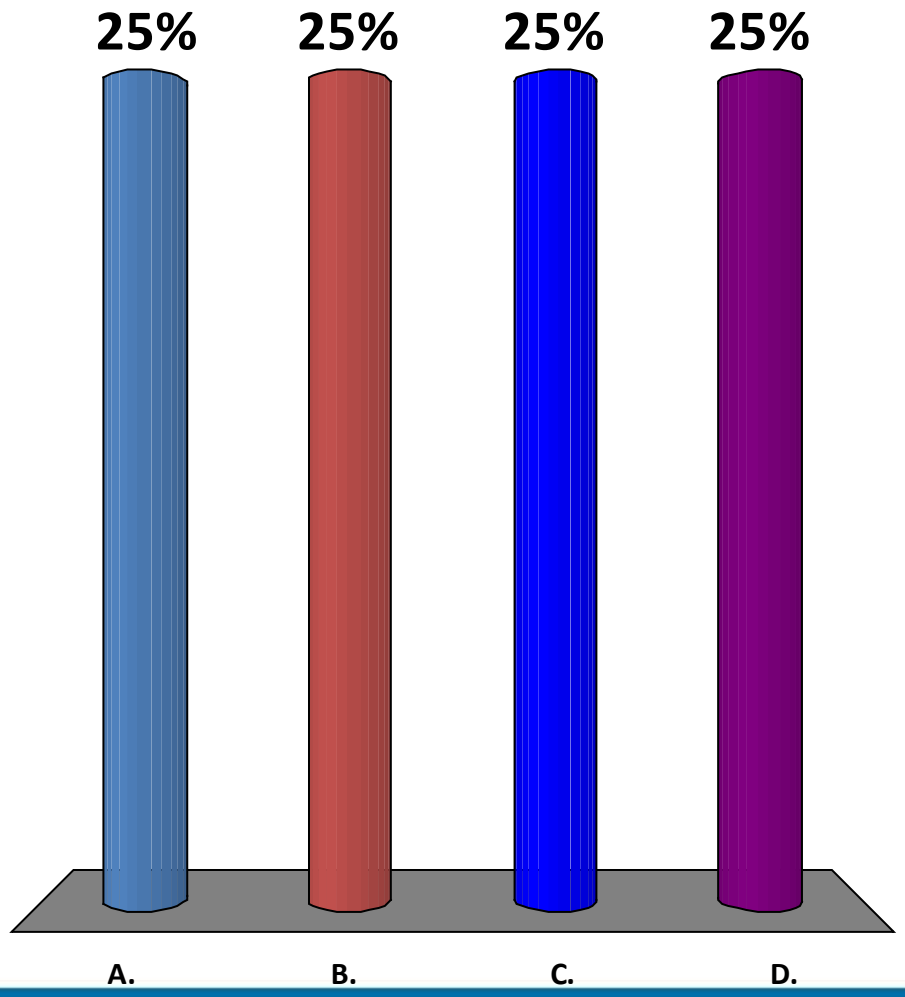
Which of the following best describes your current condition?

A. My cancer is localized and has not spread outside my breasts and/or local lymph nodes

B. My cancer has spread (metastasized) to the rest of my body

C. I have been treated for my cancer and currently have no evidence of disease

D. I'm not sure



Discussion Topic 1

Disease symptoms and daily impacts that matter most to patients

Soujanya Giambone
Facilitator

Topic 1 Panel Participants

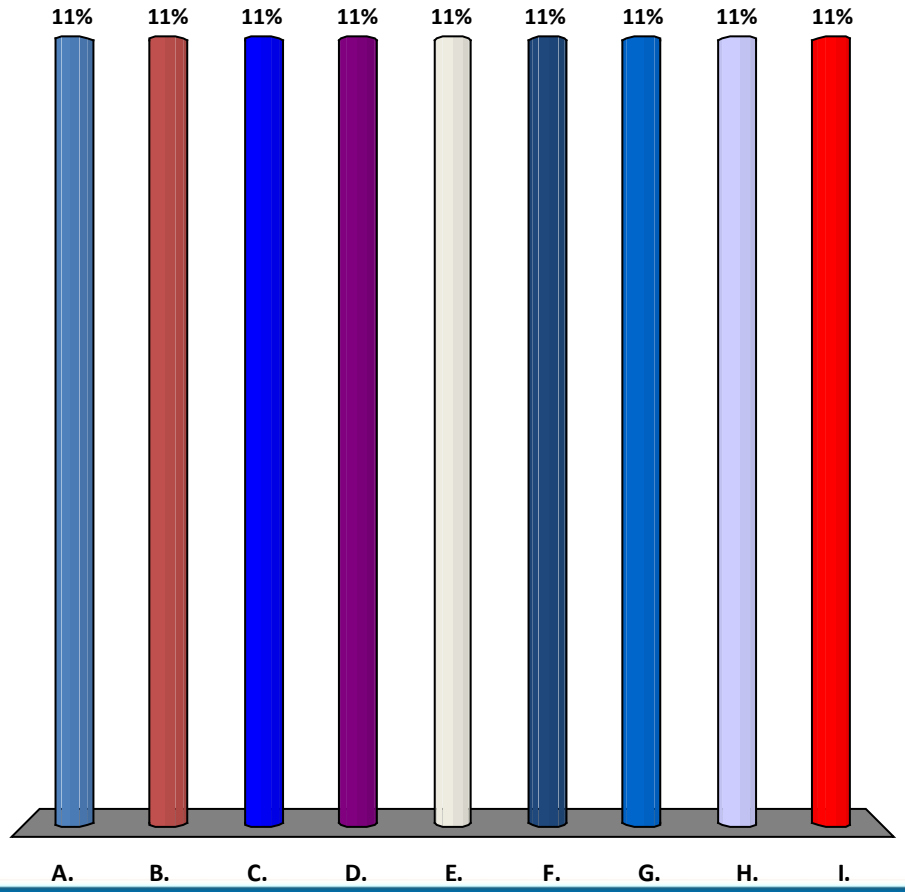
- Karen Durham
- Katy McRae
- Debbie Dunne
- Sandy Finestone

Topic 1 Discussion: Disease symptoms and daily impacts that matter most to patients

- How long ago was your diagnosis of breast cancer? Is your cancer currently in only one area or has it spread to other parts of the breast or lymph nodes or outside of the breast?
- Of all the symptoms that you experience because of your breast cancer, which 1-3 symptoms have the most significant impact on your daily life?
- Are there specific activities that are important to you but that you cannot do at all, or as fully as you would like, because of breast cancer?

Of all the symptoms you have experienced because of breast cancer, which do you consider to have the most significant impact on your daily life? **Please choose up to three symptoms.**

A. Pain, such as breast pain, or bone pain
B. Swelling
C. Fatigue or lack of energy
D. Depression or anxiety
E. Cognitive dysfunction, such as memory loss
F. Numbness/tingling in hands and/or feet
G. Fertility issues
H. Menopausal symptoms
I. Other symptoms/side effects of cancer treatments not mentioned



BREAK

Discussion Topic 2

Patients' perspectives on current approaches to treating Breast Cancer

Soujanya Giambone
Facilitator

Topic 2 Panel Participants

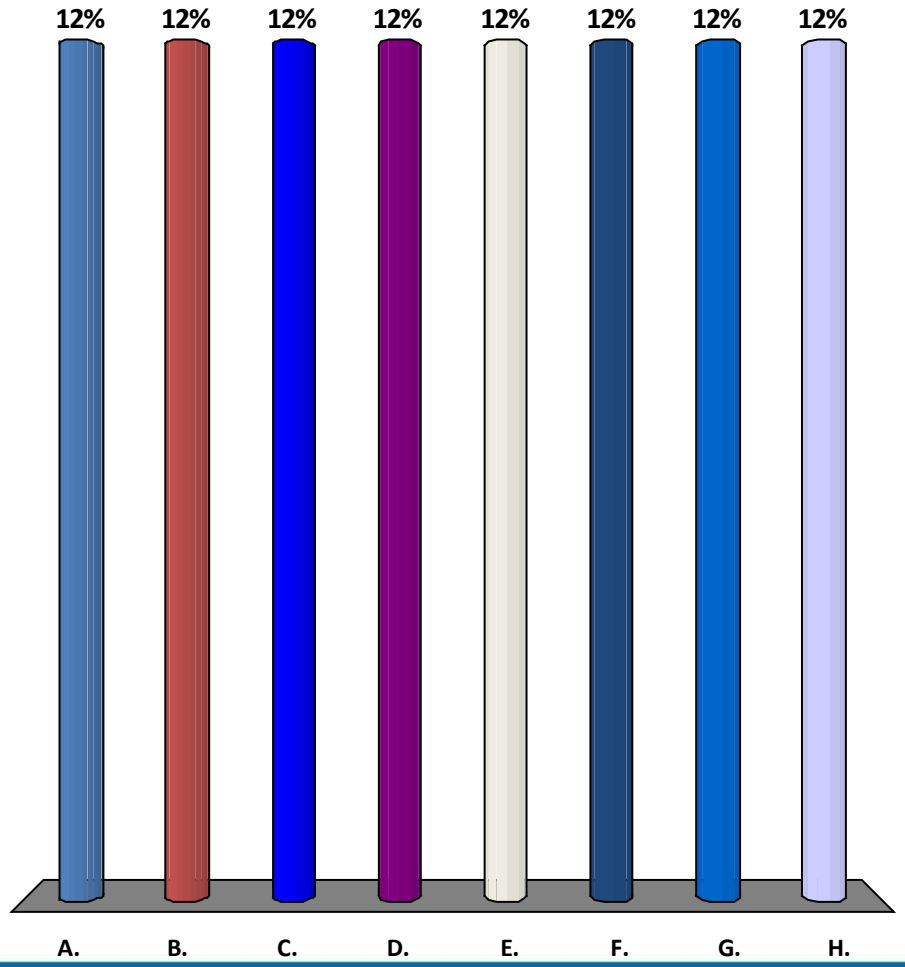
- Colleen Duffey
- Susan Faris
- Elizabeth Cappel
- Shirley Mertz

Topic 2 Discussion: Patients' perspectives on current approaches to treating breast cancer

- Are you currently undergoing any cancer treatments to help reduce or control the spread of your breast cancer?
- What supportive care treatments are you taking to help improve or manage your symptoms?
- When thinking about your overall goals for treatment, how do you weigh the importance of prolonging your life versus improving your symptoms?
- What factors do you take into account when making decisions about using treatments to help reduce or control the spread of your breast cancer?

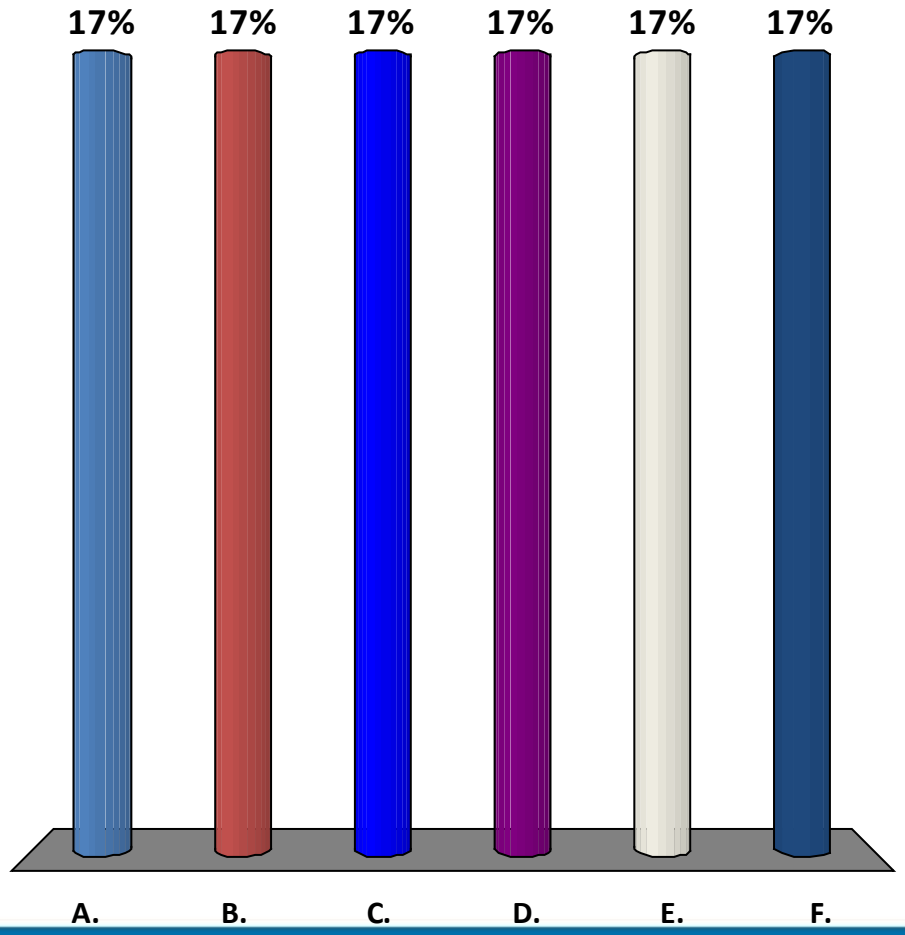
Have you ever used any of the following cancer treatments to help reduce or control the spread of your breast cancer? Include any current treatment

A. Chemotherapy
B. Radiation therapy
C. Surgery to remove the tumor(s) or any part of the breast
D. Targeted drug therapy
E. Hormone therapy
F. Other
G. I have not undergone any cancer treatments
H. I'm not sure



Besides your cancer treatments, what therapies have you taken to help manage any symptoms you have experienced because of your breast cancer or your breast cancer medication? Check all that apply.

A. Pain medications
B. Dietary supplements or diet changes
C. Complementary or alternative therapies, such as massage, acupuncture
D. Herbal remedies, such as soy supplements
E. Other therapies
F. I am not doing or taking any therapies to treat symptoms



Scenario

What thoughts and questions come to mind?

- Drug X is a chemotherapy drug being developed for patients with breast cancer
  - It was studied in a clinical trial comparing "standard of care" chemotherapy plus Drug X versus standard of care alone

- Clinical trial results showed that:
  - The addition of Drug X **prolonged survival on average 2 months longer** (median survival was 12 months on Drug X + standard of care, versus 10 months on standard of care alone)
  - In addition to toxicities related to standard of care chemotherapy, patients treated with Drug X had **more diarrhea and rash**, and had **more rare but serious toxicities** such as liver injury and lung inflammation

Of the following factors, which two would you rank as most important to your decisions about using treatments to help reduce or control the spread of your breast cancer? Please select up to two responses.

A. Whether the treatment is expected to help relieve the symptoms I experience because of my cancer

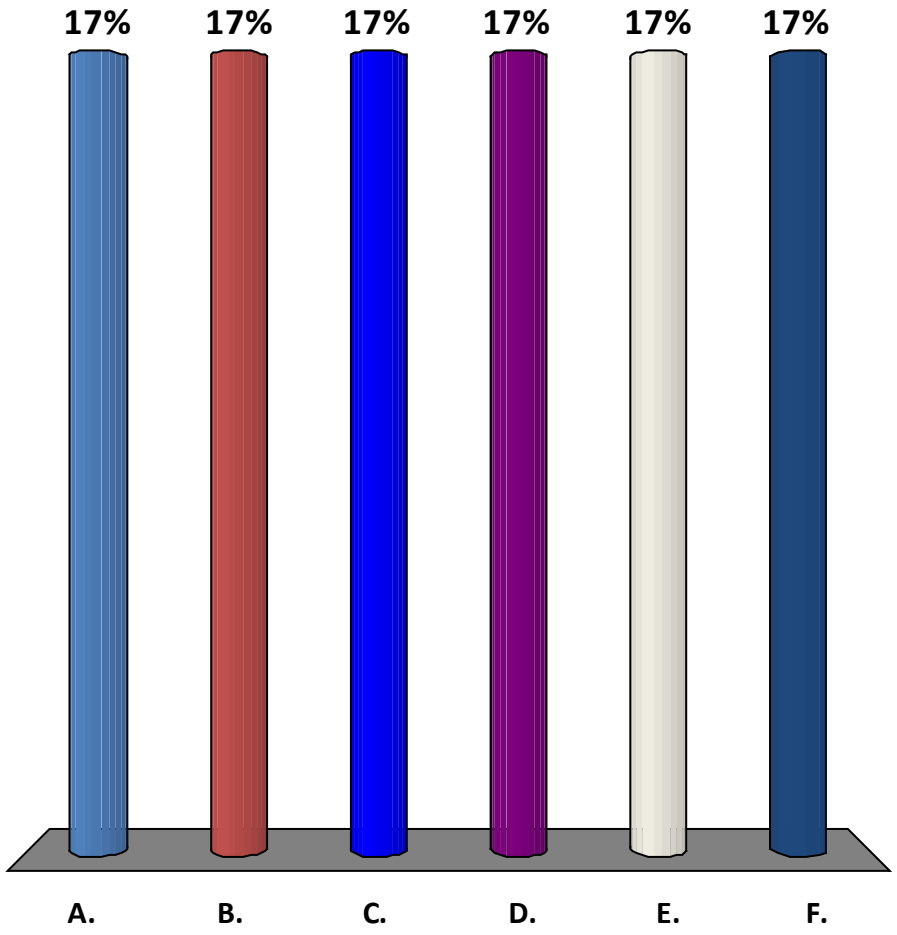
B. The small but significant risk of serious side effects associated with treatment, such as blood clots or kidney failure

C. How long the treatment would *probably* prolong my life

D. How long the treatment could *possibly* prolong my life (for longer than expected)

E. The expected side effects of the treatment, such as nausea, loss of appetite, etc.

F. How the treatment is administered, such as how long the treatment takes, whether it requires hospitalization, required doctor visits, etc.



Of the following factors, which one would you rank as least important to your decisions about using treatments to help reduce or control the spread of your breast cancer?

A. Whether the treatment is expected to help relieve the symptoms I experience because of my cancer

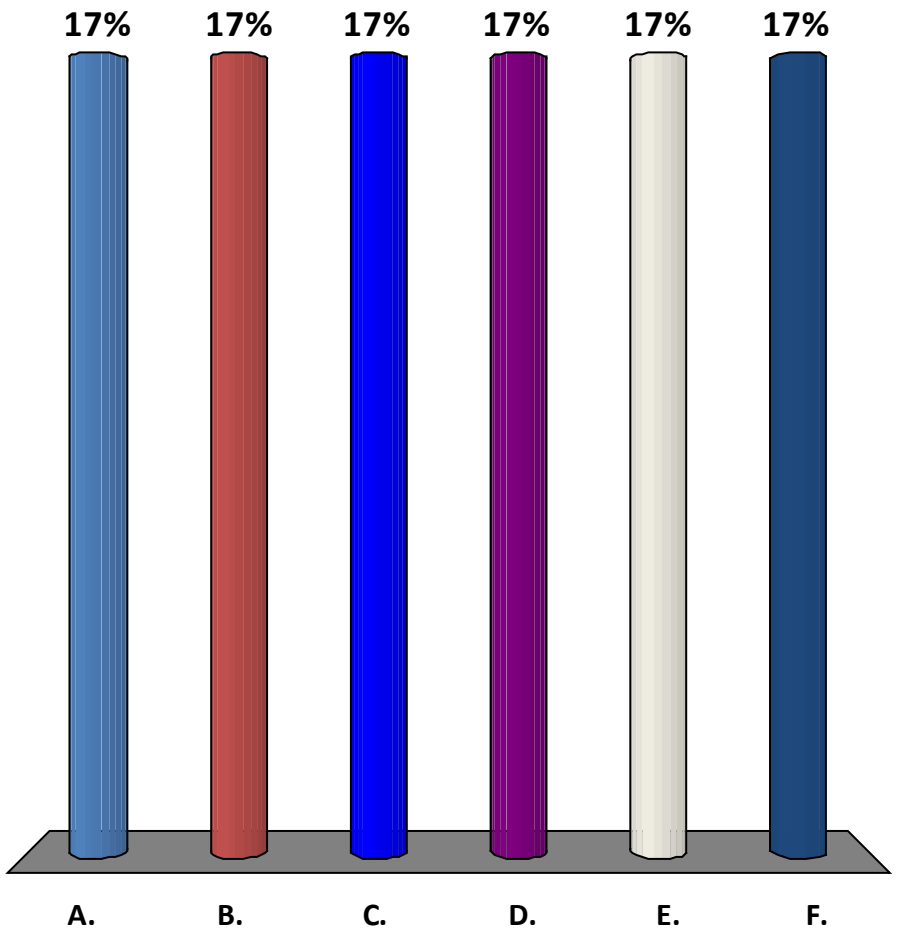
B. The small but significant risk of serious side effects, such as blood clots or kidney failure

C. How long the treatment would *probably* prolong my life

D. How long the treatment could possibly prolong my life (for longer than expected)

E. The expected side effects of the treatment, such as nausea, loss of appetite, etc.

F. How the treatment is administered, such as how long the treatment takes, whether it requires hospitalization, required doctor visits, etc.



Open Public Comment Period

Closing Remarks

Amy McKee, MD

Medical Officer, DOP I
Center for Drug Evaluation and Research
U.S. Food and Drug Administration