



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

[www.fda.gov](http://www.fda.gov)



## Public Meeting on Lung Cancer Patient-Focused Drug Development

June 28, 2013



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

[www.fda.gov](http://www.fda.gov)



## Welcome

**Patricia Keegan, MD**

Director, Division of Oncology Products 2  
Office of New Drugs  
Center for Drug Evaluation and Research  
U.S. Food and Drug Administration

## Agenda Overview

- **Setting the Context:**
  - Welcome (Patricia Keegan)
  - Patient-Focused Drug Development (Theresa Mullin)
  - Background on Lung Cancer and Treatment Options (Sean Khozin)
  - Discussion Format (Sara Eggers)
- **Discussion Topic 1:** Most significant symptoms of lung cancer and their impact on daily life
- **Discussion Topic 2:** Patient perspective on lung cancer treatment options
- **Open Public Comment Period**



## FDA's Patient-Focused Drug Development Initiative

Theresa Mullin, PhD

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

## Basic Observations

- Patients are uniquely positioned to inform FDA understanding of the clinical context
- FDA could benefit from a more systematic method of obtaining patients' point of view on the severity of a condition, and its impact on daily life, and their assessments of available treatment options
- Current mechanisms for obtaining patient input are often limited to discussions related to specific applications under review, such as Advisory Committee meetings

## 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 analysis both during and outside of review
- **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 input

## Which Disease Areas would be the Focus of PDUFA V Meetings? Criteria for Nomination

- Disease areas that are chronic, symptomatic, and affect functioning and activities of daily living
- Disease areas for which important aspects of that disease are not formally captured in clinical trials
- Disease areas for which there are currently no therapies or very few therapies, or the available therapies do not directly affect how a patient feels, functions, or survives
- Disease areas that reflect a range of severity
- Disease areas that have a severe impact on identifiable sub-populations (such as children or the elderly)
- Disease areas that represent a broad range in terms of size of the affected population

## 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 through an online docket and at a public meeting held in October 2012
  - Over 4,500 comments were submitted, which addressed over 90 disease areas
  - FDA carefully considered these public comments and the perspectives of our drug review divisions at FDA
- **FDA selected a set of 16 diseases selected to be the focus of meetings for fiscal years 2013-2015; this set was published in the Federal Register in April 2013**
  - Another public process will be initiated in 2015 to determine the set for fiscal years 2016-2017

## Disease Areas to be the focus of meetings for FY 2013

### FY 2013

1. Chronic fatigue syndrome – April 25
2. HIV – June 14
- 3. Lung cancer – June 28**
4. Narcolepsy – September

## Disease Areas to be the focus of meetings for FY 2014-2015

### FY 2014 – 2015

1. Alpha-1 antitrypsin deficiency
2. Breast cancer
3. Chronic Chagas disease
4. Female sexual dysfunction
5. Fibromyalgia
6. Hemophilia A, Hemophilia B, von Willebrand disease, and other heritable bleeding disorders
7. Idiopathic pulmonary fibrosis
8. Irritable bowel syndrome, gastroparesis, and gastroesophageal reflux disease with persistent regurgitation symptoms on proton-pump inhibitors
9. Neurological manifestations of inborn errors of metabolism
10. Parkinson's disease and Huntington's disease
11. Pulmonary arterial hypertension
12. Sickle cell disease

## Tailoring Each Patient-Focused Meeting

- **In planning the format and questions we consider unique characteristics of the disease context**
  - E.g., Current state of drug development, specific interests of the FDA review division, and the needs of the patient population
  - Each meeting focuses on a set of questions that aim to elicit patients' perspectives on their disease and on treatment approaches
- **Two meetings to date: CFS/ME and HIV**
  - CFS/ME Focus: Impact of disease on patients' daily lives and experience with current treatments
  - HIV Focus: Patients' experience with current treatments and perspectives on potential "cure research"
  - Common to both meetings:
    - Patient, caretaker, and patient advocate perspectives were powerful and insightful
    - Patient stakeholder involvement was key to the success of past meetings
- **We've been exploring different methods of gathering input: polling questions and interactive webcast options**

## Product of Patient-Focused Meetings

- **Each meeting will result in a short meeting report that will be shared with FDA reviewers and posted on the FDA website**
  - The patient perspectives captured in these reports will provide helpful insights for FDA reviewers conducting benefit-risk assessment for drugs to treat that disease



## Background on Lung Cancer and Therapeutic Options

Sean Khozin, MD, MPH

Division of Oncology Products 2  
Office of Hematology and Oncology Products  
Center for Drug Evaluation and Research  
U.S. Food and Drug Administration



## Introduction

Lung cancer is the leading cause of cancer deaths in the United States

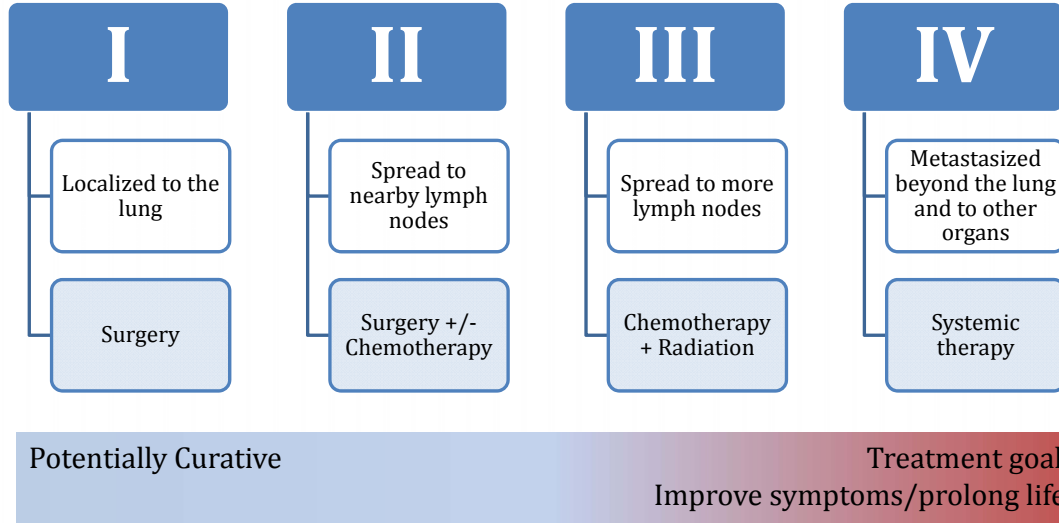
- More than 200,000 diagnoses each year
- About 160,000 deaths

There are two general types of lung cancer

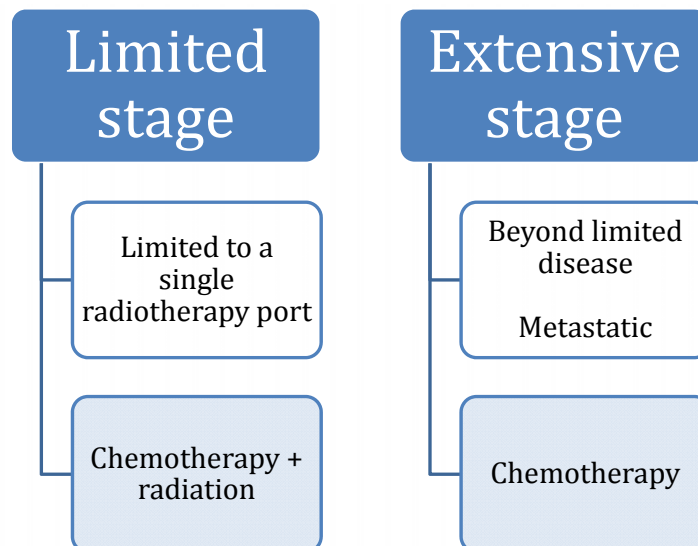
- Small cell lung cancer (15%)
- Non-small cell lung cancer (85%)
  - Includes squamous cell carcinoma, adenocarcinoma, and large cell carcinoma



## Non-Small Cell Lung Cancer



## Small Cell Lung Cancer





## Symptoms

Early symptoms of lung cancer can be difficult to detect until the cancer is advanced

Respiratory and constitutional symptoms may include

- Cough
- Shortness of breath
- Pain
- Loss of appetite
- Weight loss
- General sense of fatigue or feeling unwell

## Radiation Therapy

High-energy radiation to reduce tumors and kill cancer cells

Used in both small and non-small cell lung cancer

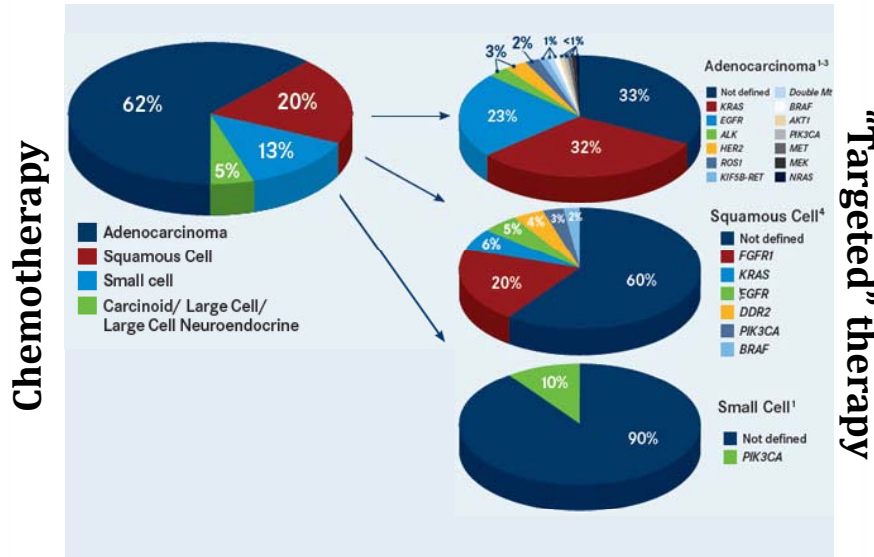
Can be used

- to support or replace surgery
- concurrently with chemotherapy
- to reduce tumor size and symptoms

# Systemic Therapy

**Traditional:** Based on histology

**Molecular:** Based on genetic profile



# Common Side Effects of Treatment

Surgery	Radiotherapy	Chemotherapy	"Targeted" therapy
<ul style="list-style-type: none"> <li>• Pain</li> <li>• Weakness</li> <li>• Fatigue</li> <li>• Shortness of breath</li> <li>• Risk of infection or bleeding</li> </ul>	<ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Localized skin irritation</li> <li>• Sore throat</li> <li>• Difficulty swallowing</li> <li>• Cognitive impairment with brain irradiation</li> <li>• 5-15% lung injury (radiation pneumonitis)</li> </ul>	<ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Nausea/vomiting</li> <li>• Nerve damage</li> <li>• Mouth sores</li> <li>• Hair loss</li> <li>• Increased risk of bleeding and infection</li> </ul>	<ul style="list-style-type: none"> <li>• Rash</li> <li>• Diarrhea</li> <li>• Fatigue</li> <li>• High blood pressure</li> <li>• Increased risk of bleeding</li> <li>• Visual changes</li> <li>• Lung injury</li> <li>• Liver injury</li> </ul>

## 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 Drug Approval

### Standard review

- Review time within 10-12 months

### Expedited programs

- Major advances to treat serious conditions
- Review time within 6-8 months

## FDA's Expedited Programs

	Fast Track (1988)	Breakthrough (2012)	Priority (1992)	Accelerated Approval (1992)
Eligibility	<ul style="list-style-type: none"> <li>- Serious condition</li> <li>- Nonclinical/clinical data demonstrate potential to address unmet medical need</li> </ul>	<ul style="list-style-type: none"> <li>- Serious condition</li> <li>- Preliminary clinical evidence indicating drug represents substantial improvement over available therapies</li> </ul>	<ul style="list-style-type: none"> <li>- Major advances in treatment over existing therapies or provides a treatment where no adequate therapy exists</li> </ul>	<ul style="list-style-type: none"> <li>- Serious condition</li> <li>- Meaningful therapeutic benefit over existing therapies or no adequate therapies exist</li> </ul>
NDA/BLA Review	Rolling review	Likely abbreviated review time	Abbreviated review time	Approval based on surrogate endpoints reasonably likely to predict clinical benefit

## FDA drug approvals in lung cancer (partial list)

### Chemotherapy

Cisplatin

Paclitaxel

Gemcitabine

Docetaxel

Pemetrexed

### "Targeted" therapy

Crizotinib

- For patients with ALK-rearrangements

Erlotinib

- For patients with certain EGFR mutations

Bevacizumab

## FDA Guidance

### Patient-Reported Outcomes (PROs)

PROs can represent direct measures of treatment benefit (feel/function)

- All measurements need to be evaluated in well-conducted, placebo-controlled or double-blinded, randomized trials

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



## Overview of Discussion Format

Sara Eggers, PhD

Office of Program and Strategic Analysis  
Office of Strategic Programs  
Center for Drug Evaluation and Research  
U.S. Food and Drug Administration



## Discussion Format

- **We will first hear from a panel of patients and representatives**
  - The purpose is to set a good foundation for our discussion
  - Panel members include patients and advocates
  - They reflect a range of experiences with lung cancer
- **We will then broaden the discussion to include other patients and patient representatives in the audience**
  - The purpose is to build on the experiences shared by the panel
  - The facilitator will ask follow up questions, inviting participants to raise hands to comment

## Discussion Format, continued

- **Periodically, we will invite in-person and web participants to respond to specific questions**
  - The purpose is to aid discussion by seeing how many participants share a particular perspective
  - In-person participants can use the “clickers” to respond to a question
  - Web participants can respond to the poll through the webcast
  - Patients and patient representatives only, please
- **Those participating by live webcast can add additional comments through the webcast comment box**
  - Although they may not be read or summarized today, they will be considered part of the public record

## Discussion Ground Rules

- We encourage patients, caregivers and other patient representatives to contribute to the dialogue
- FDA staff is here to listen
- Our discussion will focus on understanding the common ground regarding lung cancer and its treatment
- Participant feedback on the meeting is important
- Respect for one another is paramount



## **Where do you live?**

1. Within Washington DC metropolitan area (including the Virginia and Maryland suburbs)
2. Outside the Washington DC metropolitan area

## **Have you ever been diagnosed as having lung cancer?**

1. Yes
2. No

## What is your age?

1. Younger than 30
2. 31 – 40
3. 41 – 50
4. 51 – 60
5. 61 – 70
6. 71 or greater

## Are you?

1. Male
2. Female

## What is the length of time since your diagnosis?

1. Less than 1 year ago
2. 1 - 2 years ago
3. 2 - 5 years ago
4. More than 5 years ago
5. I'm not sure

## Which of the following best describes your current condition?

1. My cancer is localized and has not spread outside my lungs
2. My cancer has spread (metastasized) to the rest of my body
3. My cancer is currently in remission
4. I'm not sure



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

[www.fda.gov](http://www.fda.gov)



## Discussion Topic 1



### Disease symptoms and daily impacts that matter most to patients

Sara Eggers, PhD  
Facilitator



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

[www.fda.gov](http://www.fda.gov)

## Topic 1 Panel Participants

- Kathleen Skambis
- Susan Warmerdam
- Lorren Sandt (Caring Ambassadors Program)
- Sheila Ross (Lung Cancer Alliance)

## Discussion: Most Significant Symptoms

- How long ago was your diagnosis of lung cancer? Is your cancer currently in only one area of the lung or has it spread to other parts of the lung or outside of the lungs?
- Of all the symptoms that you experience because of your lung cancer, which 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 lung cancer?

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

1. Pain, such as chest pain or shoulder pain.
2. Shortness of breath, wheezing or other breathing difficulties
3. Coughing, or coughing up blood or phlegm
4. Loss of appetite or weight loss
5. Voice hoarseness or difficulty speaking
6. Fatigue or lack of energy
7. Depression or anxiety
8. Other side effects of cancer treatments
9. Other symptoms not mentioned

## Discussion: Most Significant Symptoms

- How long ago was your diagnosis of lung cancer? Is your cancer currently in only one area of the lung or has it spread to other parts of the lung or outside of the lungs?
- Of all the symptoms that you experience because of your lung cancer, which 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 lung cancer?

**BREAK**



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

[www.fda.gov](http://www.fda.gov)



## Discussion Topic 2



### Patients' perspectives on current approaches to treating lung cancer

Sara Eggers, PhD  
Facilitator



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

[www.fda.gov](http://www.fda.gov)

## Topic 2 Panel Participants

- Denise Hogan
- Stephanie Haney
- John Ryan
- Karen Arscott
- Shelley Fuld Nasso (National Coalition for Cancer Survivorship)



## Discussion on Lung Cancer Treatments

- Are you currently undergoing any cancer treatments to help reduce or control the spread of your lung 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 lung cancer?

**Have you ever undergone any of the following cancer treatments to help reduce or control the spread of your lung cancer? Include any current treatment.**

1. Chemotherapy
2. Radiation Therapy
3. Surgery to remove the tumor(s)  
or any part of the lung
4. Targeted drug therapy
5. Other
6. I have not undergone any cancer treatments
7. I'm not sure

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

1. Pain medications
2. Steroids
3. Supplemental oxygen
4. Breathing, exercise or relaxation techniques
5. Dietary supplements or diet changes
6. Complementary or alternative therapies, such as massage, acupuncture.
7. Other therapies
8. I'm not taking or doing any therapies to treat symptoms

## Discussion on Lung Cancer Treatments

- Are you currently undergoing any cancer treatments to help reduce or control the spread of your lung 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 lung cancer?

**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 lung cancer? Please select up to two responses.**

1. Whether the treatment is expected to help relieve the symptoms I experience because of my cancer
2. The small but significant risk of serious side effects, such as blood clots or kidney failure
3. How long the treatment would probably prolong my life
4. How long the treatment could possibly prolong my life (for longer than expected)
5. The expected side effects of the treatment, such as nausea, loss of appetite etc.
6. How the treatment is administered, such as how long the treatment takes, whether it requires hospitalization, requires 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 lung cancer?**

1. Whether the treatment is expected to help relieve the symptoms I experience because of my cancer
2. The small but significant risk of serious side effects, such as blood clots or kidney failure
3. How long the treatment would probably prolong my life
4. How long the treatment could possibly prolong my life (for longer than expected)
5. The expected side effects of the treatment, such as nausea, loss of appetite etc.
6. How the treatment is administered, such as how long the treatment takes, whether it requires hospitalization, requires doctor visits, etc.

## Discussion on Lung Cancer Treatments

- Are you currently undergoing any cancer treatments to help reduce or control the spread of your lung 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 lung cancer?

### Scenario 1

## What thoughts and questions come to mind?

- Drug X is a chemotherapy drug being developed for patients with metastatic non-small cell lung 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



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

[www.fda.gov](http://www.fda.gov)



## Open Public Comment Period



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

[www.fda.gov](http://www.fda.gov)



## Closing Remarks

**Theresa Mullin, PhD**

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