The background of the slide features a white surface with several bright orange, round pills. A cluster of about a dozen pills is in the upper left, blurred to create a sense of depth. A single pill is in sharp focus in the lower right quadrant. The pills are set against a white background that transitions into a blue curved banner at the top of the slide.

Public Meeting on Pulmonary Arterial Hypertension Patient-Focused Drug Development

May 13, 2014



Welcome

Soujanya Giambone, MBA

Office of Strategic Programs

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

May 13, 2014

Agenda

- **Setting the context**
 - Opening Remarks
 - Overview of FDA's Patient-Focused Drug Development Initiative
 - Background on Pulmonary Arterial Hypertension 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 pulmonary arterial hypertension
- **Open Public Comment**
- **Closing Remarks**



Opening Remarks

Ellis Unger, MD

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

May 13, 2014



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

May 13, 2014

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 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 selected a set of 16 diseases selected to be the focus of meetings for fiscal years 2013-2015**
 - 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 2013-2015

FY 2013

- Chronic fatigue syndrome
- HIV
- Lung cancer
- Narcolepsy

FY 2014

- Sickle cell disease
- Fibromyalgia
- **Pulmonary arterial hypertension**
- Inborn errors of metabolism

FY 2014 – 2015

- Alpha-1 antitrypsin deficiency
- Breast cancer
- Chronic Chagas disease
- Female sexual dysfunction
- Hemophilia A, Hemophilia B, von Willebrand disease, and other heritable bleeding disorders
- Idiopathic pulmonary fibrosis
- Irritable bowel syndrome, gastroparesis, and gastroesophageal reflux disease
- 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 topic 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 Pulmonary Arterial Hypertension and Therapeutic Options

Shari Targum, MD

Division of Cardiovascular and Renal Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

May 13, 2014

Background on Rare Diseases

- Pulmonary arterial hypertension is the 3rd rare disease being featured in our series of Patient-Focused Drug Development meetings
- Rare disease / orphan drug definition:
 - A disease or condition affecting less than 200,000 people in the US
 - Approximately 7,000 different rare diseases have been defined, affecting approximately 30 million Americans
 - So, almost 1 in 10 Americans suffer from rare diseases

Rare Disease Resources at FDA

- FDA Office of Health and Constituent Affairs (OHCA)
 - Serves as a liaison between FDA and patients
 - Refer to the Patient Network website, a one-stop shop for patients:
<http://www.patientnetwork.fda.gov/>
 - Contact OHCA at PatientNetwork@fda.hhs.gov
- FDA Office of Orphan Products Development
 - Advances the evaluation and development of products that demonstrate promise for diagnosis or treatment of rare diseases
 - Provides incentives for sponsors to develop products for rare diseases
- CDER Office of New Drugs Rare Disease Program
 - Supports the research, development, regulation, and approval of products for the treatment of rare disorders

Introduction

- Pulmonary arterial hypertension (PAH) is a rare, under-diagnosed, progressive condition defined by mean elevated arterial pressure
- In patients with PAH, the average pulmonary arterial pressure is 25 mm Hg or greater at rest (compared with 15 mm Hg in patients without PAH)

Types of PAH

- There are 3 types of PAH:
 - **Idiopathic PAH:** PAH from an unknown cause
 - **Familial PAH:** PAH inherited from family
 - **Associated PAH:** the most common type – PAH associated with the use of certain drugs or with having specific conditions. These include:
 - Congenital heart disease
 - Connective tissue disease
 - Sickle cell disease
 - Thyroid disease
 - Liver disease
 - Human immunodeficiency virus (HIV)
 - Conditions that affect the veins and small blood vessels of the lungs.

Symptoms

- Patients may experience symptoms including:
 - Chest pain, usually in the front of the chest
 - Dizziness
 - Fainting
 - Fatigue
 - Leg swelling
 - Light-headedness during exercise
 - Shortness of breath during routine activity
 - Weakness

Diagnostic Criteria

- PAH can be difficult for doctors to diagnose for the following reasons:
 - **The symptoms of PAH are similar to those of other, more common, heart and lung problems**, including asthma, pneumonia, chronic obstructive pulmonary disease (COPD), and coronary disease.
 - **A physical exam in the early stages may be normal or almost normal.** A doctor who suspects a patient may have PAH usually runs a series of tests to measure blood pressure in the pulmonary arteries, decide how well the heart and lungs are working, and rule out other diseases.

Diagnostic Criteria (Cont'd)

- Tests include:
 - Chest X-Ray (of the heart and lungs)
 - Electrocardiogram (an electrical measure of your heart rate and how regularly your heart is beating)
 - Echocardiogram (an ultrasound picture of the heart to help determine how well it is working)
 - Right-heart catheterization (a special device that the doctor threads through a vein into the heart and arteries of the lungs to measure pressure in the arteries and test how well the heart is pumping)
 - Pulmonary function tests (breathing tests that measure lung function)
 - Perfusion lung scan (an image that shows blood flow through the lungs)
 - Six-minute walk test (a measure of the patient's ability to do exercise)

Treatment Options

- There are several treatment options that aim to reduce symptoms, improve quality of life, or slow down how quickly the disease progresses.
- Treatment options include:
 - Medications
 - Surgery (heart-lung transplantation, atrial septostomy)
 - Lifestyle changes (weight loss, light exercise, emotional support, healthy diet)

Treatment Options

- Treatments to ease symptoms include:
 - Endothelin receptor antagonists (ERAs), such as bosentan and ambrisentan, to stop the harmful effects of endothelin, a hormone that helps control blood flow and cell growth in blood vessels.
 - Phosphodiesterase-5 inhibitors (PDEI), such as sildenafil, to relax the muscles and reduce abnormal cell growth in blood vessels.
 - Prostacyclins to relax blood vessels, reduce abnormal cell growth, and help prevent blood clots.
 - Inhaled oxygen to reduce shortness of breath

Patient-Reported Outcomes

- In conditions like PAH, which are not fully understood, input from patients is especially important
- Patient-reported outcomes (PROs) can represent direct measures of treatment benefit – how a patient feels or functions
 - 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

A background image showing several orange, round pills scattered across a white surface. One pill is in sharp focus in the lower right foreground, while others are blurred in the background.

Overview of Discussion Format

Soujanya Giambone, MBA

Office of Strategic Programs

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

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?
- Can you compare an average day of symptoms to your worse day?

Topic 2: Current approaches to treating PAH

- What are you doing to treat your PAH?
- How well do your treatments work for you?
- What are their biggest downsides?
- What would you look for in an “ideal” treatment?

Discussion Format

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

- **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 July 14, 2014
 - 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-
2012-N-0967-0592](http://www.regulations.gov/#!documentDetail;D=FDA-2012-N-0967-0592)

Click Comment Now!

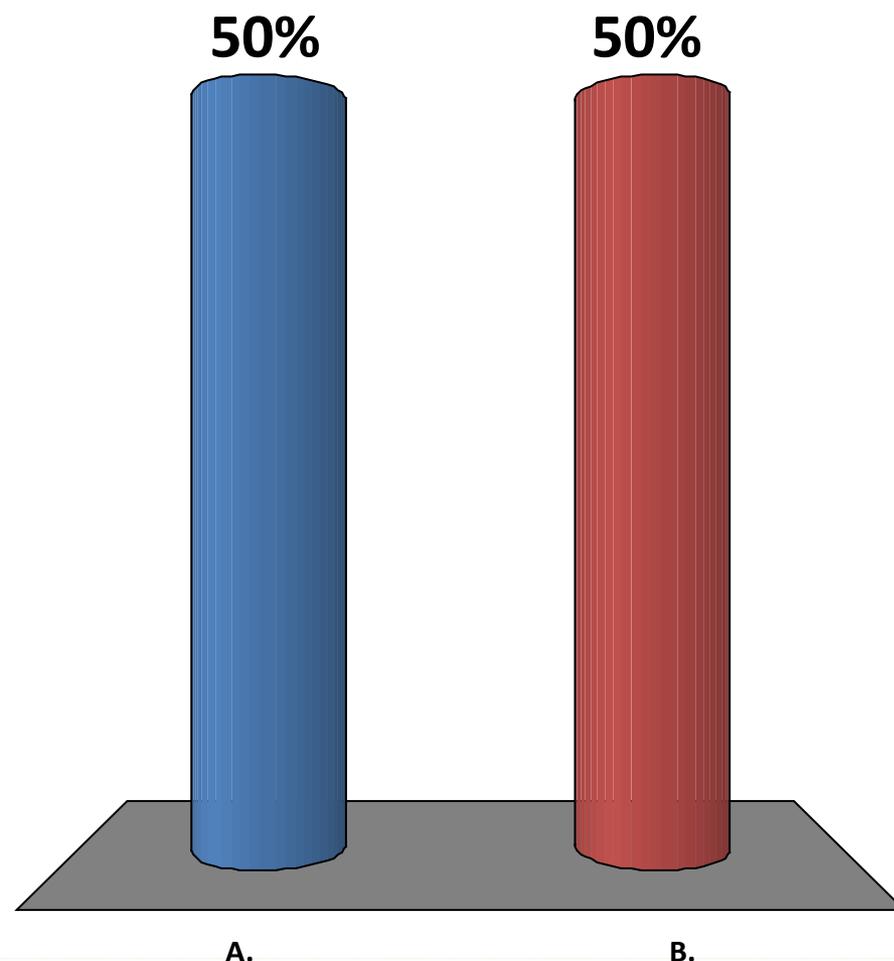
The screenshot shows the 'regulations.gov' website interface. The main heading is 'Pulmonary Arterial Hypertension Public Meeting on Patient-Focused Drug Development'. Below the heading, there is a 'Comment Now!' button. A red arrow originates from the text 'Click Comment Now!' on the left and points directly to this button. The page also displays various sections like 'Action', 'Summary', 'Dates', and 'Addresses', along with a 'Document Information' sidebar on the right.

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

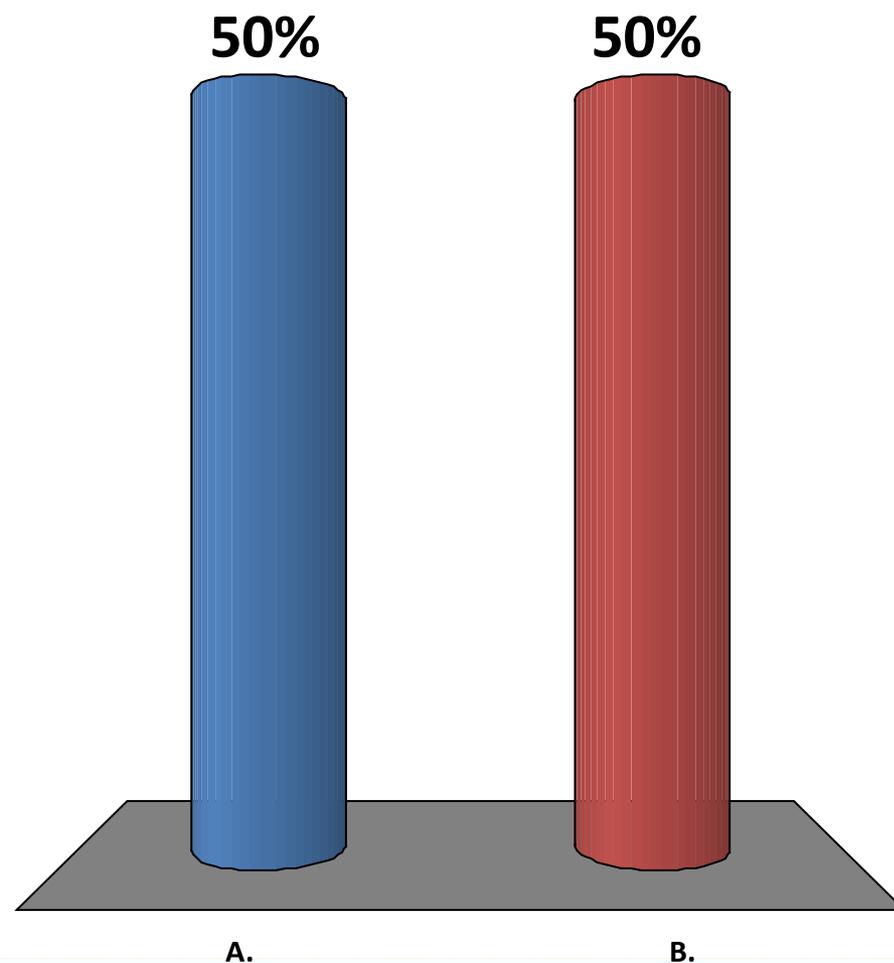
Where do you live?

- A. Within the Washington, D.C. metropolitan area (including the VA and MD suburbs)
- B. Outside of the Washington, D.C. metropolitan area



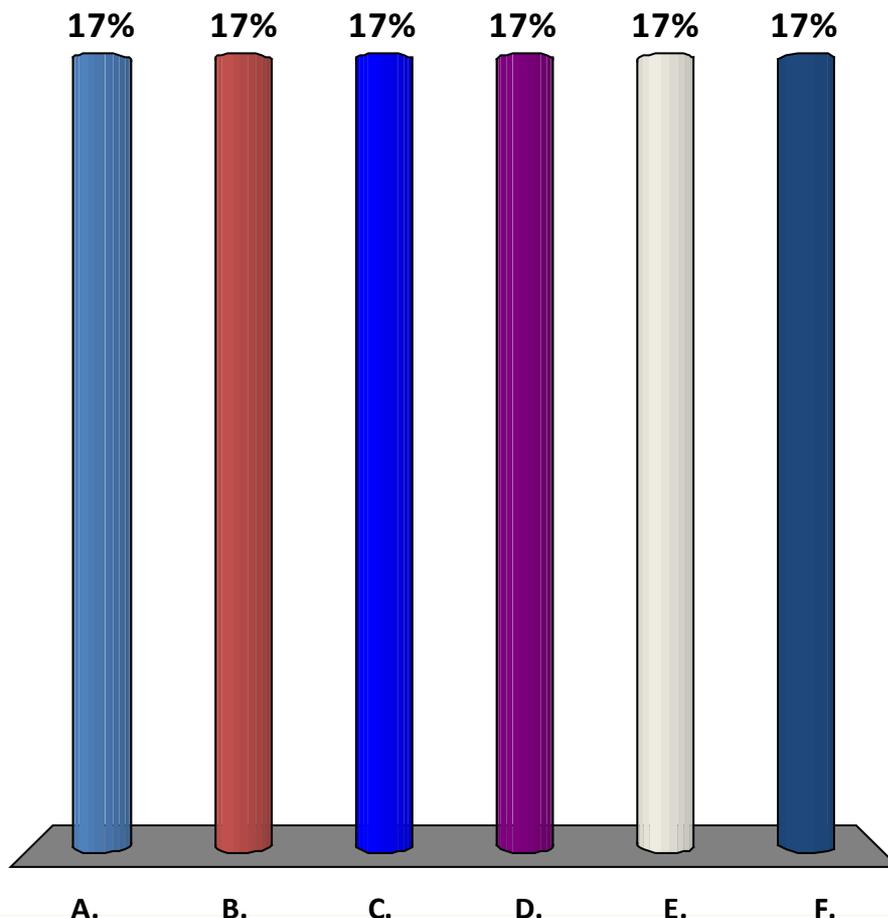
Have you ever been diagnosed as having pulmonary arterial hypertension?

- A. Yes
- B. No



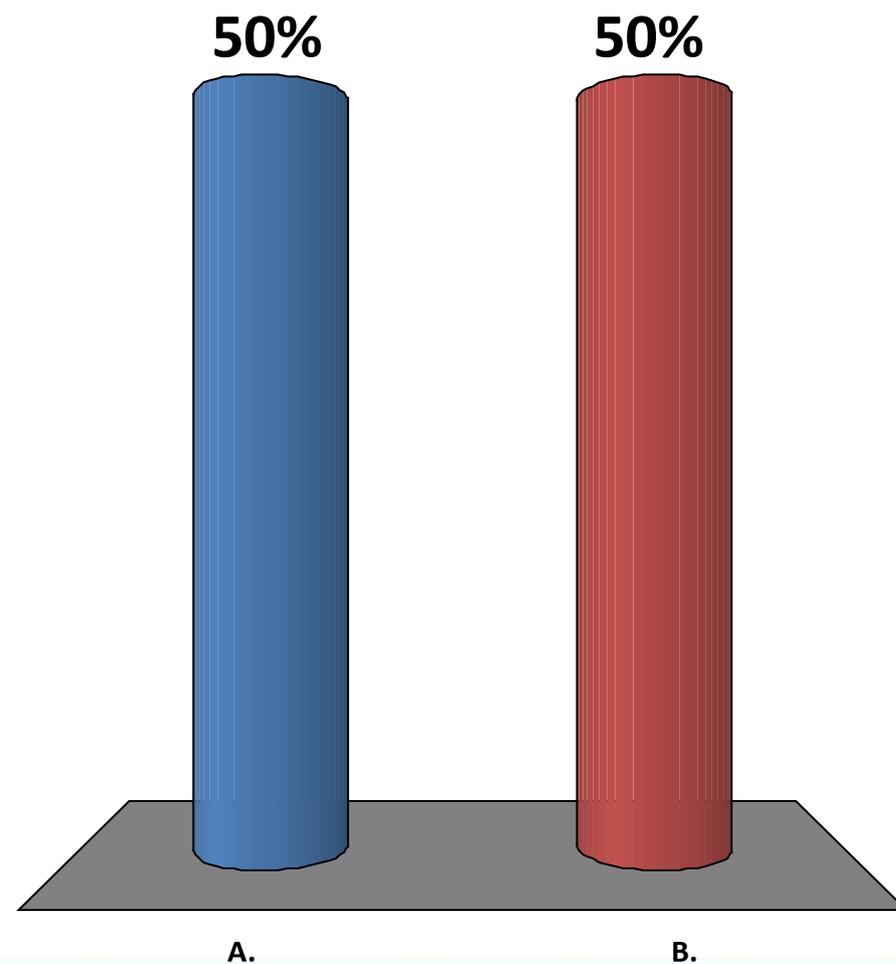
What is your age?

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



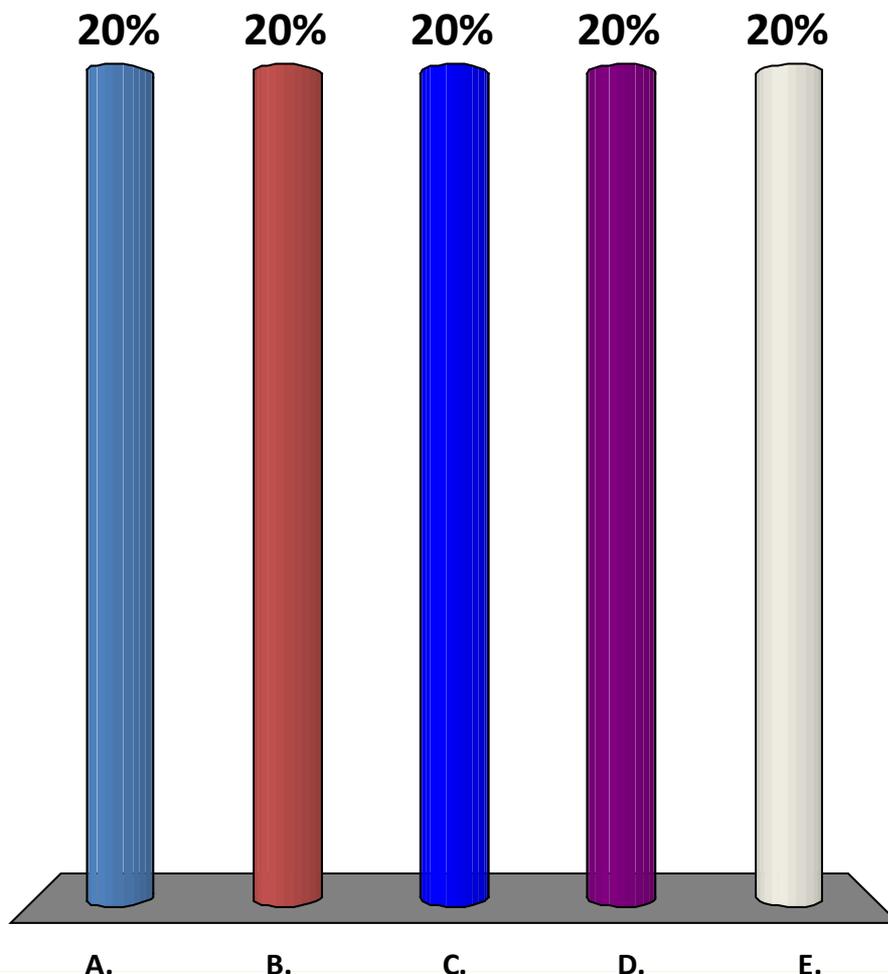
Are you:

- A. Male
- B. Female



What is the length of time since your diagnosis?

- A. Less than 5 years
- B. 5 – 10 years
- C. 10 – 20 years
- D. More than 20 years





Discussion Topic 1

Disease symptoms and daily impacts that matter most to patients

Soujanya Giambone

Facilitator

Topic 1 Panel Participants

Alex Flipse

Kevin Paskawych

Nicole Matthews

Holly Tissue-Thompson

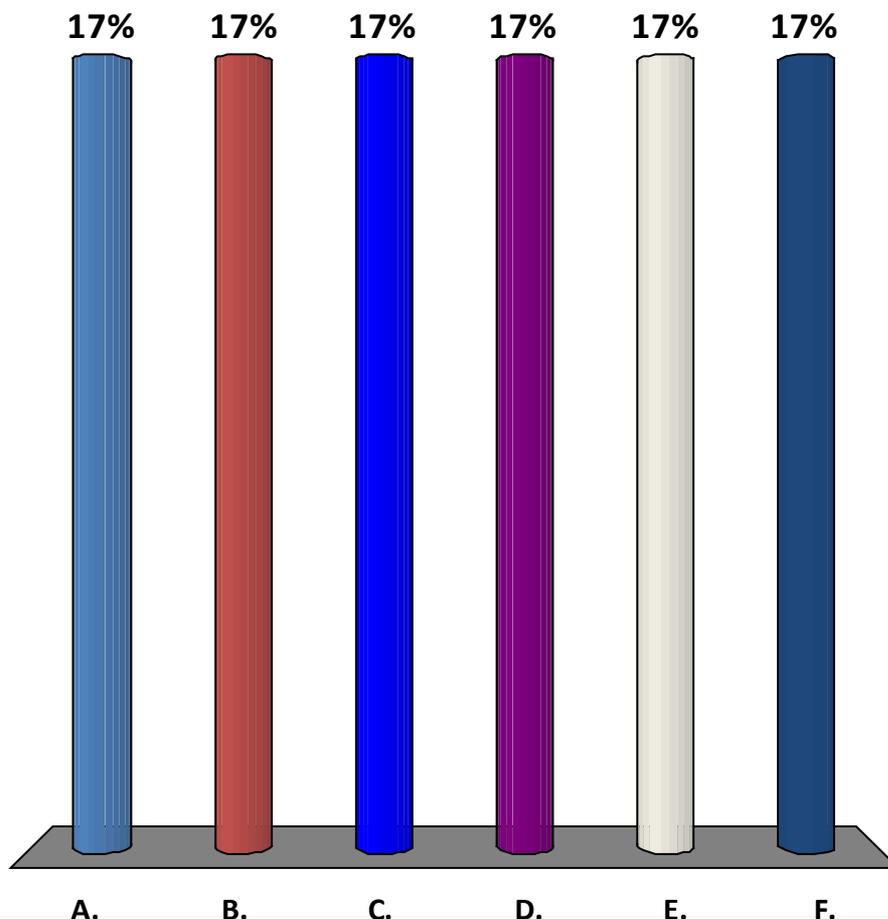
Colleen Connor

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

- Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your 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 your condition?
- How have your condition and its symptoms changed over time?

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

- A. Pain, such as chest pain
- B. Shortness of breath, wheezing or other breathing difficulties
- C. Dizziness, fainting or lightheadedness
- D. Fatigue
- E. Swelling, such as swollen ankles or legs
- F. Other symptoms not mentioned



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

- Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your 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 your condition?
- How have your condition and its symptoms changed over time?



BREAK



Discussion Topic 2

Patients' perspectives on current approaches to treating pulmonary arterial hypertension

Soujanya Giambone

Facilitator

Topic 2 Panel Participants

Lucille Monko

Colleen Brunetti

Katie Tobias

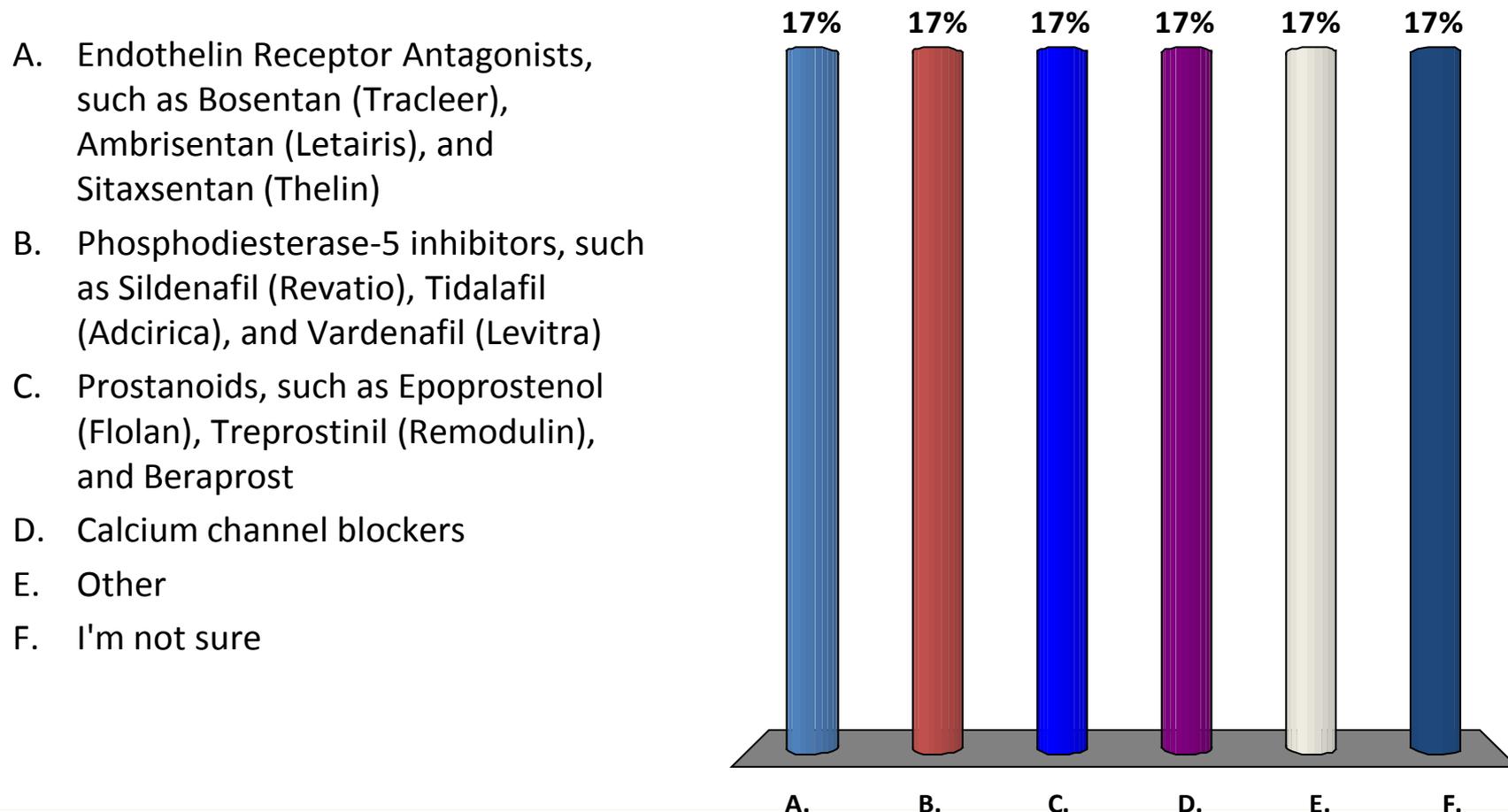
Stacey Gausling

Tamera Pixler

Topic 2 Discussion: Patients' perspectives on current approaches to treating pulmonary arterial hypertension

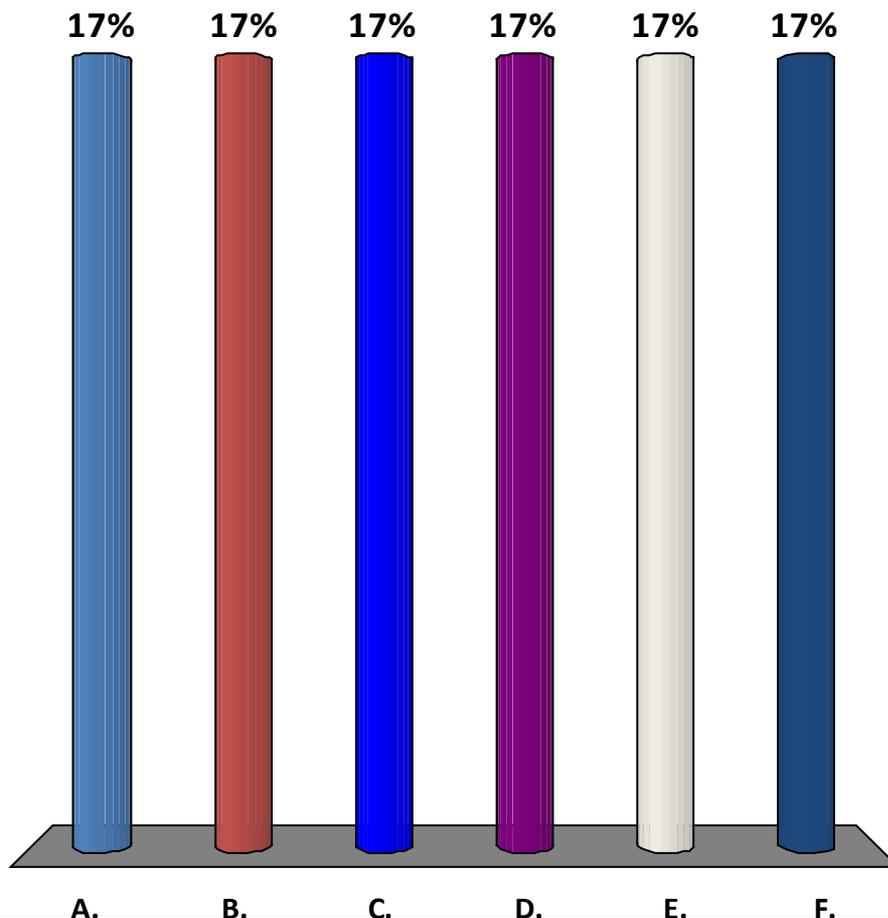
- What are you currently doing to help treat your condition or its symptoms?
- Have the medications for pulmonary arterial hypertension made a difference to you? If so, in what ways?
- What are the most significant downsides to your current treatments, and how do they affect your daily life?
- What specific things would you look for in an ideal treatment for your condition?

Have you ever used any of the following drug therapies to help reduce the symptoms of pulmonary arterial hypertension? Check all that apply



What else are you doing to help reduce your symptoms of PAH? **Check all that apply**

- A. Other drugs, such as blood thinners
- B. Supplemental oxygen
- C. Surgery, such as lung or heart-lung transplantation, and atrial septostomy
- D. Lifestyle changes, such as limit activity or changes in your home
- E. Other therapies not mentioned
- F. I am not doing or taking any therapies to treat symptoms



Topic 2 Discussion: Patients' perspectives on current approaches to treating pulmonary arterial hypertension

- What are you currently doing to help treat your condition or its symptoms?
- Have the medications for pulmonary arterial hypertension made a difference to you? If so, in what ways?
- What are the most significant downsides to your current treatments, and how do they affect your daily life?
- What specific things would you look for in an ideal treatment for your condition?



Open Public Comment Period

A background image showing a cluster of orange, round pills in the upper left corner, with a single pill in sharp focus in the lower right corner. The pills are set against a white background with a blue curved border at the top.

Closing Remarks

Norman Stockbridge, MD, PhD

Director, Division of Cardiovascular and Renal Products

Center for Drug Evaluation and Research

U.S. Food and Drug Administration