

Enrollment of older adults in Cancer clinical trials : US Food and Drug Administration Experience

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Enrollment of Older Adults in Cancer Clinical Trials- A Continuing Conversation



SPECIAL ARTICLE

A Correction Has Been Published >

Group Cancer
Cancer Site

Underrepresentation of Patients 65 Years of Age or Older in Cancer-Treatment Trials

Laura F. Hutchins, M.D., [CLINICAL TRIALS](#)

Albain, M.D.

N Engl J Med 1999; 341:2

74:2208-14.

Key words: neoplasm; incidence rates.

The U. S. population is increasing steadily, and the number of older adults is increasing. In current studies, one in five patients aged 65 or older is enrolled in trials. This is a significant decrease from 1990, when one in three patients aged 65 or older was enrolled in trials. The elderly, therefore, increasingly have become one of the most important groups targeted for future cancer treatment trials. It is necessary better to understand the causes of, treatment of, and response to treatment of cancer in old age.

Within the past decade, enrollment in clinical trials designed to assess the efficacy and toxicity of new cancer treatments has risen. The results of large, collaborative intervention studies have provided important data on patient demographics, treatment response, clinical

Participation of Patients 65 Years of Age or Older in Cancer Clinical Trials

Joy H. Lewis, Meredith L. Kilgore, Dan J. Montello...

Original Contribution

June 9, 2004

Lung	61.1
Breast	47.7
Colorectal	74.1
Ovarian	46.1
Pancreas	74.1
Total	56.1

Participation in Cancer Clinical Trials by Race-, Sex-, and Age-Based Disparities

Vivek H. Murthy, MD, MBA; Harlan M. Krumholz, MD, SM; Cary P. Gross, MD

> Author Affiliations

JAMA. 2004;291(22):2720-2726. doi:10.1001/jama.291.22.2720

	P value
	<0.001
	0.007
	<0.001
	0.001
	0.001
	0.001
	0.001
	0.001
	0.001

In 1990, the five leading causes of death among patients aged 65 and older were cancer of the lung, colon and rectum, and leukemia. In 1999, the five leading causes of death among women in this age group, the five leading causes of death were carcinomas of the lung, breast, colon and rectum, pancreas, and ovary. To determine the representation of the elderly in clinical trials, the 1992 accrual of the National Cancer Institute (NCI)-sponsored Clinical Cooperative Group treatment trials (which included more than 8000 elderly patients) for the aforementioned sites was compared with the 1990 incidence data from the NCI's Surveillance, Epidemiology, and End Results program. Of the male patients enrolled in the trials, an average of 39% were older than 65 (47.3% lung, 78.5% prostate, 47.5% colorectal, 45.6% pancreas, and 9.6% leukemia); whereas 25.9% of all women enrolled in trials were 65 or older (43.6% lung, 17.3% breast, 46.2% colorectal, 59.6% pancreas, and 35.4% ovary). With respect to incidence, older patients generally are underrepresented in cancer treatment trials. With the exception of the data on prostate cancer, each of the comparisons using the Z statistic gave probability values of less than 0.01. The most significant discrepancies between incidence and participation in cancer treatment protocols were noted for leukemia in males and breast cancer in females.

Possible explanations for these findings include (1) a research focus on aggressive therapy, which may be unacceptably toxic to the elderly; (2) presence of comorbidity in the elderly; (3) fewer trials available specifically aimed at older patients; (4) limited expectations for long term benefits on the part of physicians, relatives, and the patients themselves; and (5) a lack of financial, logistic, and social support for the participation of elderly patients in clinical trials.

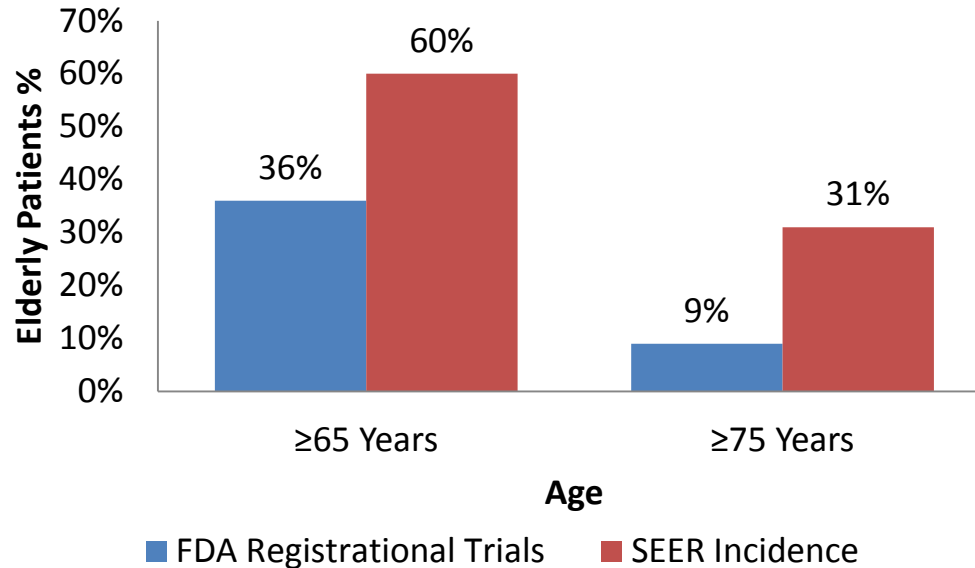
Recognizing this situation, NCI recently sponsored a

FDA Guidance & Perspectives



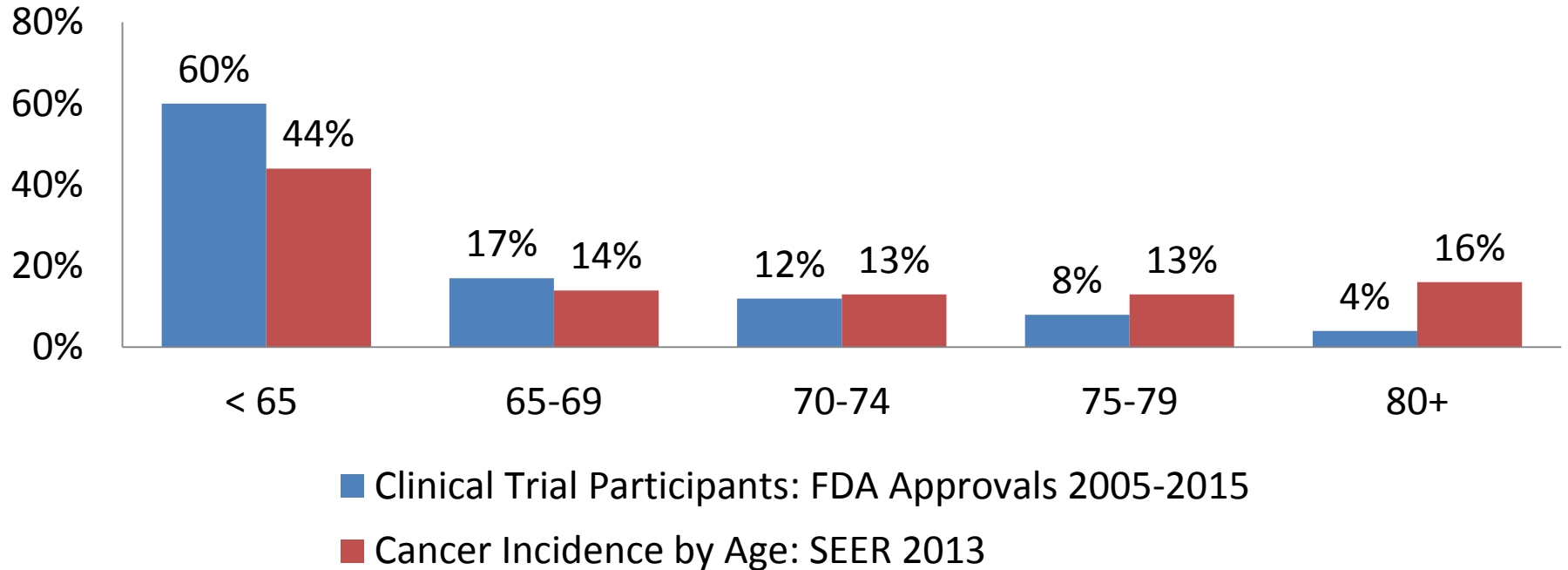
Year	
1989	Guidance for the Study of Drugs Likely to Be Used in the Elderly (FDA)
1994 2012	Guidance for Industry: E7 Studies in Support of Special Populations (FDA)
2016	Evaluation and Reporting of Age, Race, and Ethnicity Data in Medical Device Clinical Studies (FDA)
2016	Enrollment of Older Adults on Oncology Trials: an FDA Perspective (Journal of Geriatric Oncology)

Enrollment of Older Adults in Cancer Clinical Trials- U.S Food and Drug Administration Experience



Modified from Fig 1. Enrollment of Elderly Patients in Clinical Trials for Cancer Drug Registration: A 7-Year Experience by the US Food and Drug Administration [Lilia Talarico](#), [Gang Chen](#), [Richard Pazdur](#)

Elderly Cancer Patients Enrolled on Clinical Trials Supporting FDA Approval Compared with SEER Cancer Incidence by Age Group



Tumor Type/ Indication*

Advanced Solid Tumors
 - early phase clinical trials
 - multiple tumor types

Hematologic Malignancies

Head and Neck Cancer

Lung Cancer

Melanoma

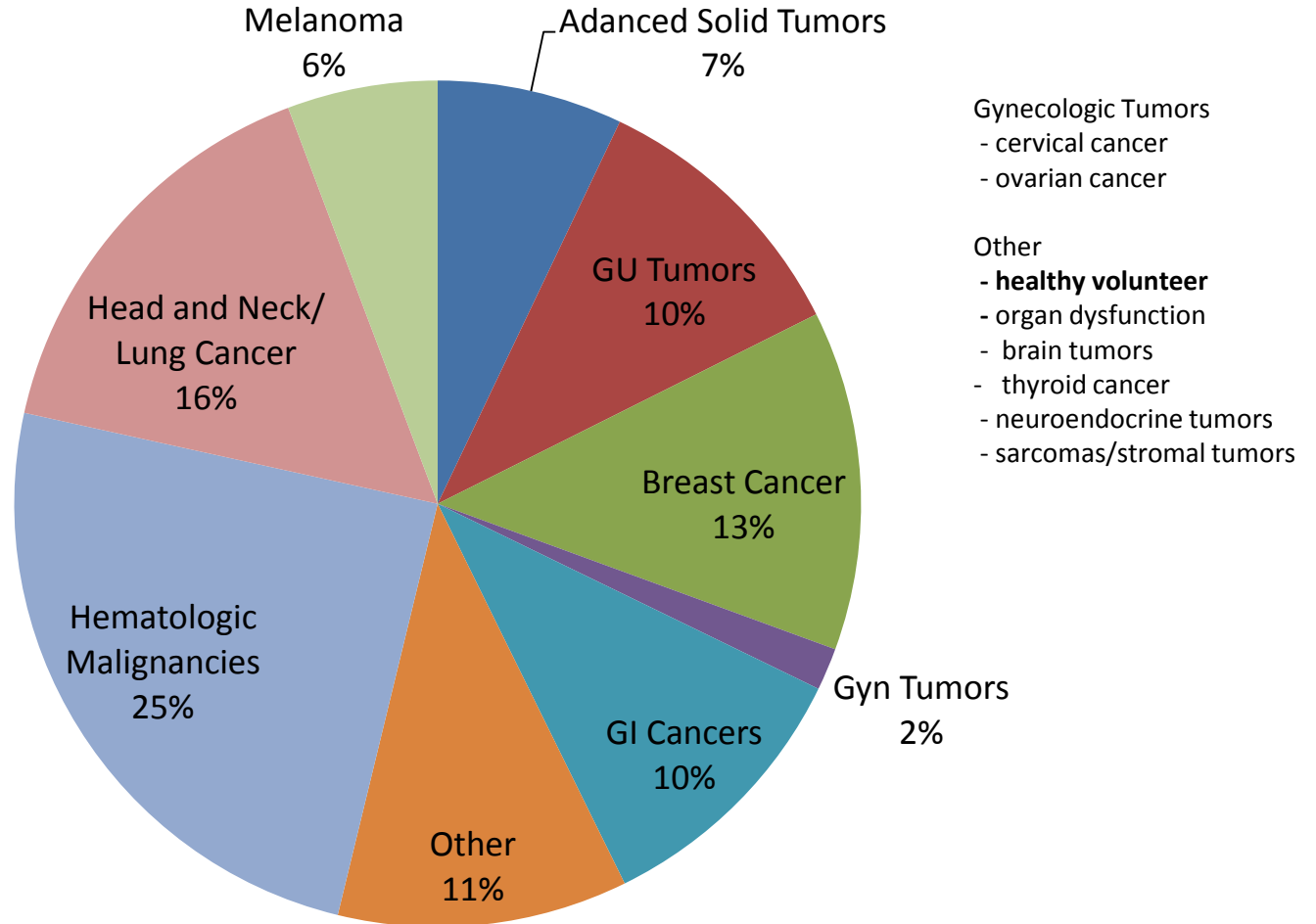
Genitourinary Malignancies

- **prostate cancer**
 - urothelial carcinoma
 - renal cell carcinoma

Gastrointestinal Malignancies

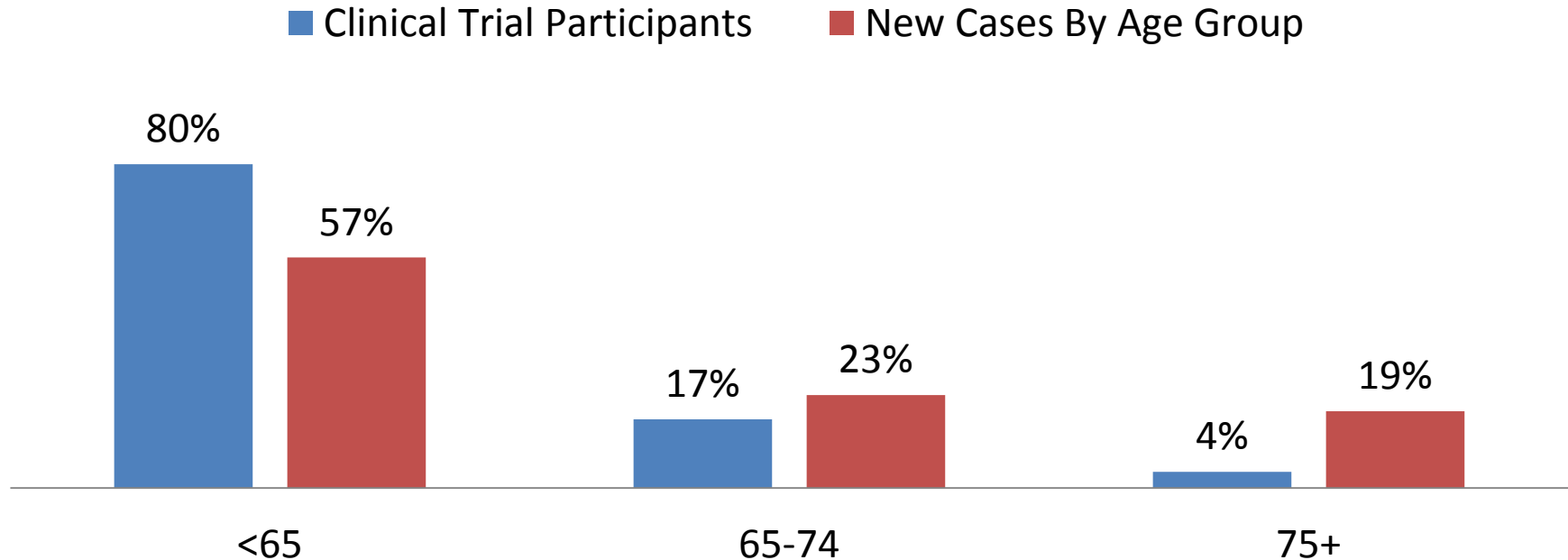
- **colorectal cancer**
 - hepatocellular carcinoma
 - pancreatic cancer
 - gastric cancer

Breast Cancer



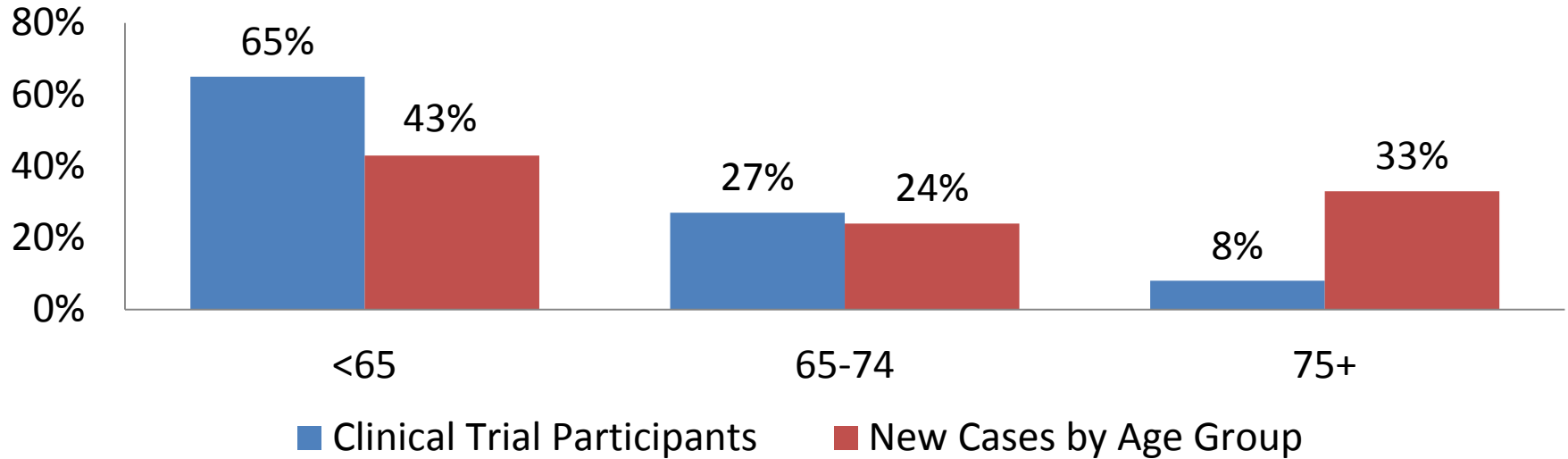
*Excludes pediatric studies included to support adult indications, biosimilars, supportive medications (n=176598)

Elderly Patients with Breast Cancer Enrolled on FDA Trials Compared with New Cases by Age Group

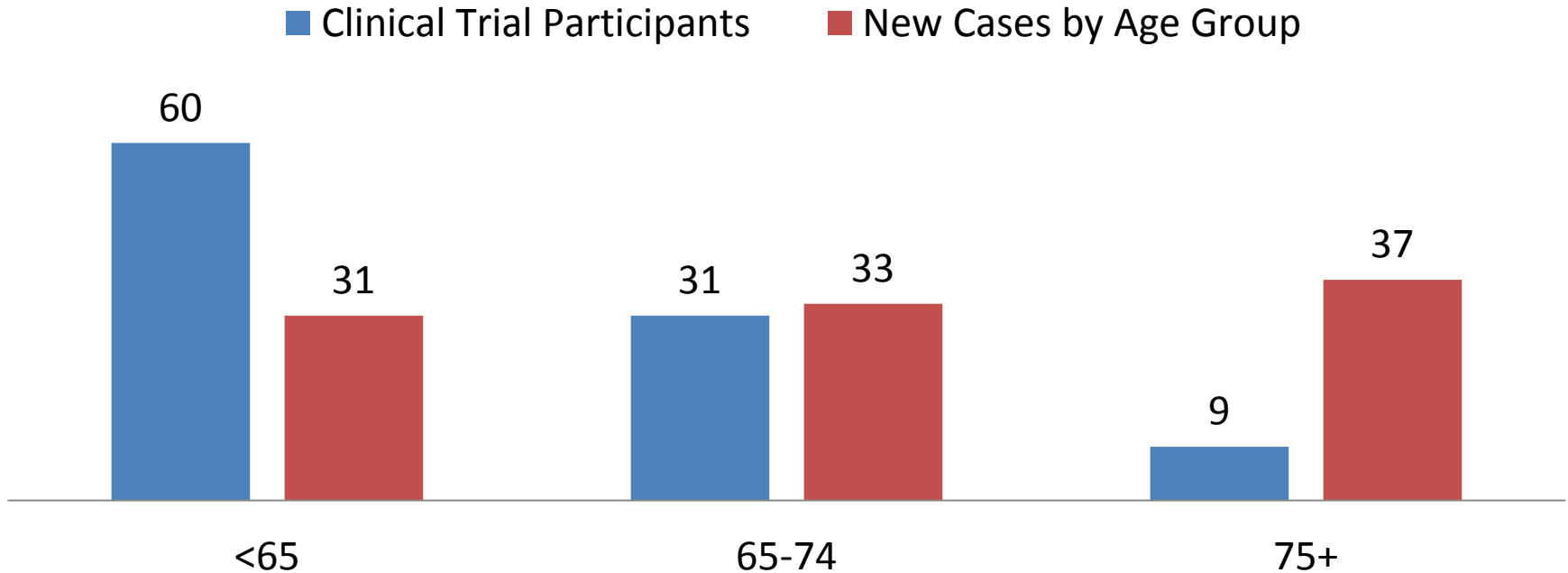


FDA Registration Trials 2005-2015
SEER 18 2010-2014, All Races, Females

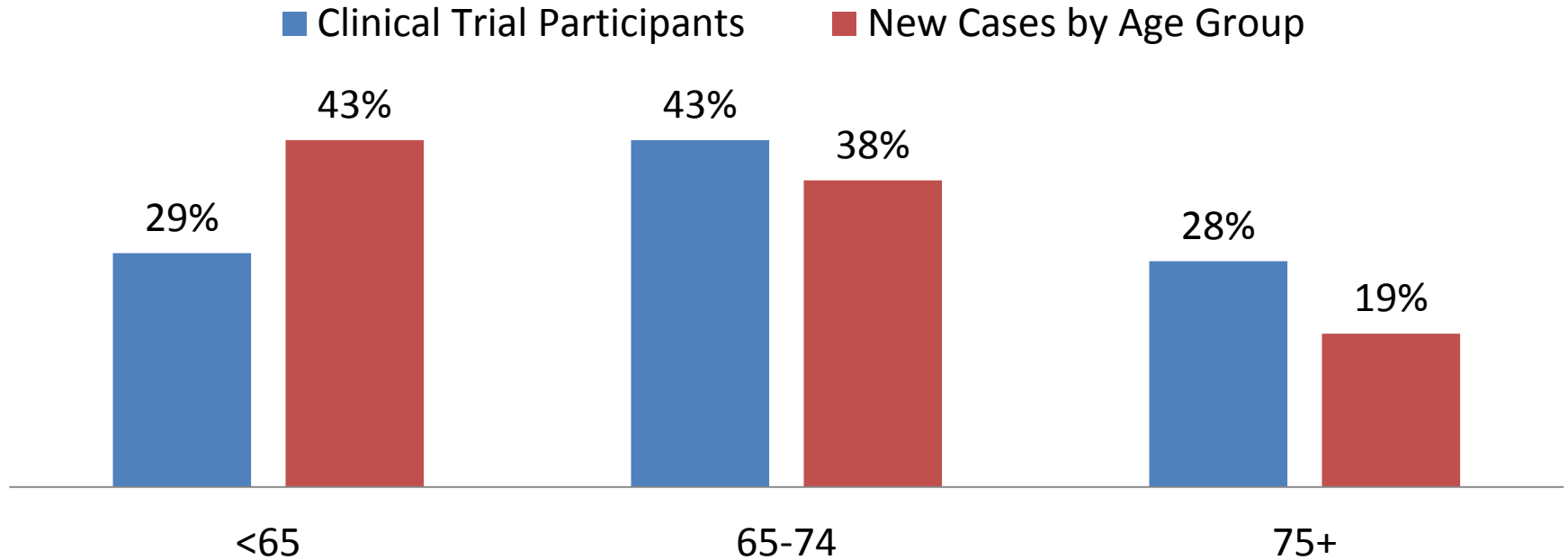
Elderly Patients with Colorectal Cancer Enrolled on FDA Trials Compared with New Cases by Age Group



Elderly Patients with Lung Cancer Enrolled on FDA Trials Compared with New Cases by Age Group



Elderly Patients with Prostate Cancer Enrolled on FDA Trials Compared with New Cases by Age Group



Labeling – Geriatric Use Section

- Interest in including the most critical safety and efficacy information for older patients
 - descriptive information to better characterize drug and biological product use in older patients

Example #1 – Urothelial Carcinoma

Of the 119 cisplatin-ineligible patients with urothelial carcinoma treated with Drug X in Study 4, 83% were 65 years or older and 41% were 75 years or older. The overall response rate in patients 65 years or older was 23% (23/99) and in patients 75 years or older was 29% (14/49). Grade 3 or 4 adverse reactions occurred in 53% (52/99) of patients 65 years or older and 51% (25/49) of patients 75 years or older. No overall differences in safety or efficacy were observed between patients ≥ 75 years of age and younger patients.

Example #2 – Hematologic malignancies

Of the 905 patients in clinical studies of Drug X, 62% were ≥ 65 years of age, while 21% were ≥ 75 years of age. No overall differences in effectiveness were observed between younger and older patients. Anemia (all grades) and Grade 3 or higher pneumonia occurred more frequently among older patients treated with Drug X.

Example #3 – Melanoma



Of the 559 patients with melanoma randomized to receive Drug X plus Drug Y in Study 1, 24% were aged 65 years and older and 6% patients aged 75 years and older. No overall differences in the effectiveness of Drug X were observed in elderly patients as compared to younger patients. The incidences of peripheral edema (26% vs. 12%) and anorexia (21% vs. 9%) were increased in elderly patients as compared to younger patients.

fda.gov/drug trials snapshot



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Drugs

Home > Drugs > Drug Approvals and Databases

Drug Approvals and Databases

- Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book)
- Bioresearch Monitoring Information System (BMIS)
- Clinical Investigator Inspection List (CLIL)

Drug Trials Snapshot

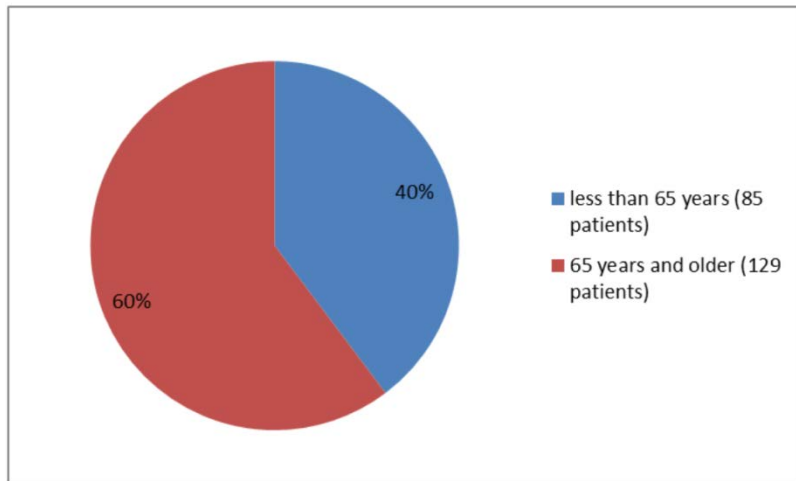
WHAT IS THE PURPOSE OF DRUG TRIALS SNAPSHOT?

The FDA has developed Drug Trials Snapshots to provide information to the public about who participated in the clinical trials for new FDA approved drugs. Drug Trials Snapshot is part of a pilot project to provide information about the sex, age, race and ethnicity of clinical participants for a small group of recently approved drugs. In addition to information about who participates in the trial, each Snapshot also includes information on how the study was designed, results of the efficacy and safety studies and, if known, differences in efficacy and side effects among sex, race and age (referred to as subgroups).

Drug Snapshot Example- IDHIFA



Baseline Demographics by Age



Age Categories, n(%)	
Age (years) Median (Min, Max)	68 (19, 100)
≤ 65 years	85 (40)
>65 years	129 (60)
≥75 years	51 (24)

Subgroup Analyses of Complete Response Rate by Age

Age		
≤ 65 years	7/76 (7.4)	3.8, 18.1
>65 years	30/123 (24.4)	17.1, 33.0

Subgroup Analyses of Adverse Events

Age Group (n)		
<65 years, (85)	85 (100)	72 (85)
>=65 years, (129)	129 (100)	93 (72)

Conclusions

- Older cancer patients continue to be underrepresented in cancer clinical trials
- Most striking in ≥ 75 age groups
- Product Label/clinical reviews/Drug Snapshots include information on safety and effectiveness in older adults

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