Stronger Together:
EGFR Resisters' Patient and Caregiver Summit

Access, Answers, and Action – Demystifying Clinical Trials

EGFR Patient & Caregiver Summit – Session 4

Recording Notice

Please be advised that this session and all general sessions of the *EGFR Resisters' Patient & Caregiver Summit* are being livestreamed and recorded.

Recordings will be made available on the EGFR Resisters website and accessible to the public.

By participating in this event, you consent to the recording and distribution of these sessions.

If you have any concerns, please speak with event staff.

Session Objectives

- Assess the fundamental value of clinical trials for driving therapeutic innovation and broadening horizons for people living with EGFRm lung cancer.

- Develop an improved understanding of what clinical trials are, how they work, and how to access them, including a high-level review of how to navigate ClinicalTrials.gov.

- Summarize ongoing EGFRm lung cancer clinical trials and practical strategies for discussing possible enrollment opportunities with care team members.

Session Speakers

Laura Book
Social Media Lead and Newsletter Editor
EGFR Resisters Board of Directors
Port Ludlow, WA

David P. Carbone, MD, PhD
Professor, College of Medicine
Barbara J. Bonner Chair in Lung Cancer Research
Director, James Thoracic Center
The Ohio State University
Columbus, OH

Hannah Johnson
Patient Advocate
Chicago, IL

Kristen Kimball, BS, MS
Caregiver Advocate
Boston, MA

Christine M. Lovly, MD, PhD, FASCO
Thoracic Medical Oncology
Currently transitioning between positions
Vanderbilt University Medical Center in Nashville, TN to
City of Hope Comprehensive Cancer Center in Duarte, CA

Koosha Paydary, MD, MPH, MSc
Assistant Professor of Medicine
Medical Oncologist
Rush University
Chicago, IL

Victoria Sherry, DNP, CRNP, ANP-BC, AOCNP
Adult Oncology NP for Thoracic Malignancies
Advanced Senior Lecturer
University of Pennsylvania
Philadelphia, PA

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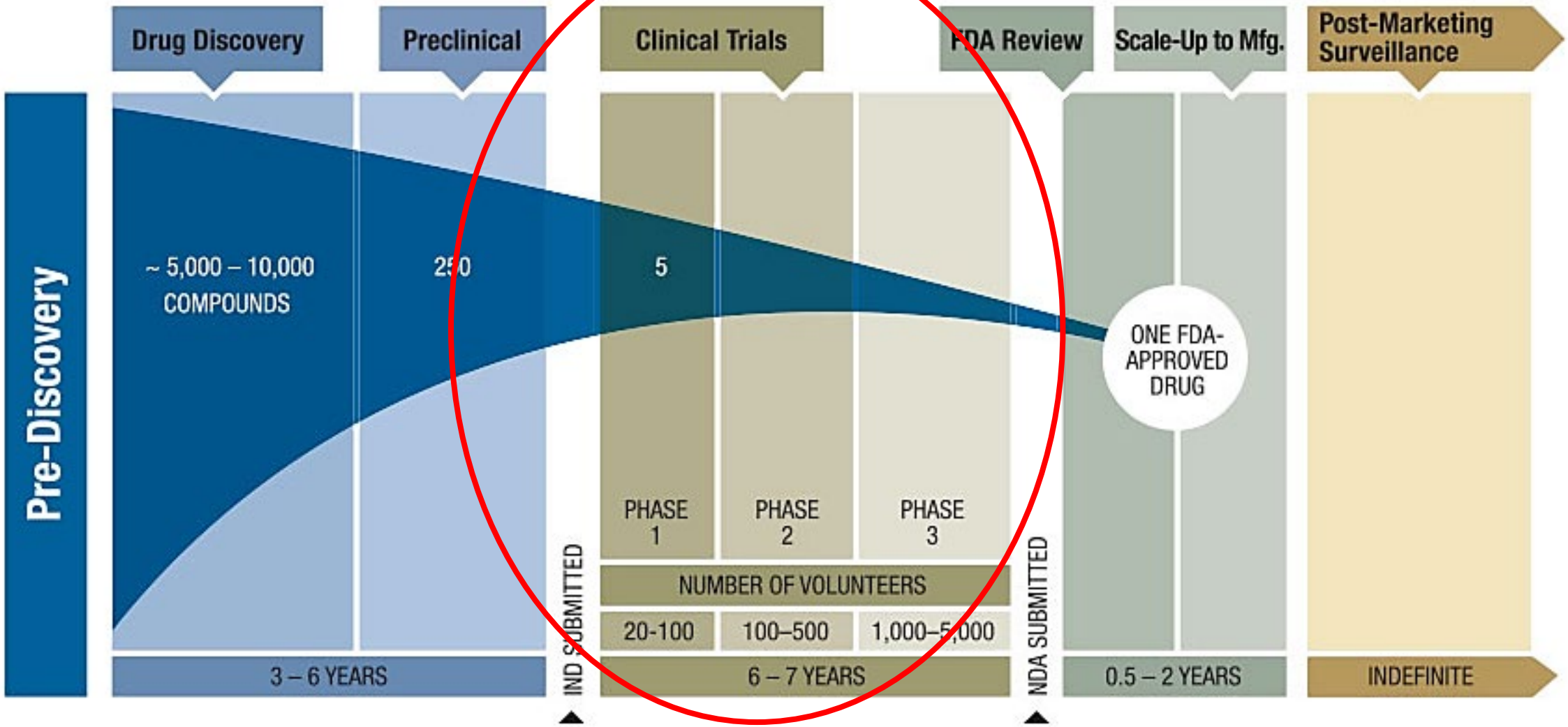
Overview of Clinical Trials and Drug Discovery in Medical Oncology

Koosha Paydary, MD, MPH, MSc

Drug Discovery Timeline



U.S. Food and Drug Administration

Drug Approval Process

What is a drug as defined by the FDA?

A drug is any product that is intended for use in the diagnosis, cure mitigation, treatment , or prevention of disease; and that tis intended to affect the structure or any function of the body.

PRE-CLINICAL

Drug Sponsor's Discovery and Screening Phase

Drug Developed

Drug sponsor develops a new drug compound and seeks to have it approved by FDA for sale in the United States.

1

Animals Tested

Sponsor must test new drug on animals for toxicity. Multiple species are used to gather basic information on the safety and efficacy of the compound being investigated/researched.

2

IND Application

The sponsor submits an Investigational New Drug (IND) application to FDA based on the results from intial testing that include, the drug's composition and manufacturing, and develops a plan for testing the drug on humans.

IND REVIEW

FDA reviews the IND to assure that the proposed studies, generally referred to as clinical trials, do not place human subjects at unreasonable risk of harm. FDA also verifies that there are adequate informed consent and human subject protection.

FDA's Center for Drug Evaluation and Research (CDER) evaluates new drugs before they can be sold.

The center's evaluation not only prevents quackery, but also provides doctors and patients the information they need to use medicines wisely. CDER ensures that drugs, both brand-name and generic, are effective and their health benefits outweigh their known risks.

CLINICAL

Drug Sponsor's Clinical Studies/Trials

3

PHASE 1

20-80

The typical number of healthy volunteers used in Phase 1; this phase emphasizes safety. The goal here in this phase is to determine what the drug's most frequent side effects are and, often, how the drug is metabolized and excreted.

4

PHASE 2

100's

The typical number of patients used in Phase 2; this phase emphasizes effectiveness. This goal is to obtain preliminary data on whether the drug works in people who have a certain disease or condition. For controlled trials, patients receiving the drug are compared with similar patients receiving a different treatment--usually a placebo, or a different drug. Safety continues to be evaluated, and short-term side effects are studied.

At the end of Phase 2, FDA and sponsors discuss how large-scale studies in Phase 3 will be done.

5

PHASE 3

1000's

The typical number of patients used in Phase 3. These studies gather more information about safety and effectiveness, study different populations and different dosages, and uses the drug in combination with other drugs.

Who reviews new drug submissions?

A team of CDER physicians, statisticians, chemists, pharmacologists, and other scientists review the drug sponsor's data and proposed labeling of drugs.

What other drug products are regulated by FDA?

Drugs include more than just medicines. For example, fluoride toothpastes, antiperspirants (not deodorant), dandruff shampoos, and sunscreens are all considered drugs.

NDA REVIEW

FDA's New Drug Application (NDA)Review

10

Drug Labeling

FDA reviews the drug's professional labeling and assures appropriate information is communicated to health care professionals and consumers.

8-9

Application Reviewed

After an NDA is received, FDA has 60 days to decide whether to file it so it can be reviewed. If FDA files the NDA, the FDA Review team is assigned to evaluate the sponsor's research on the drug's safety and effectiveness.

7

NDA Application

The drug sponsor formally asks FDA to approve a drug for marketing in the United States by submitting an NDA. An NDA includes all animal and human data and analyses of the data, as well as information about how the drug behaves in the body and how it is manufactured.

6

Review Meeting

FDA meets with a drug sponsor prior to submission of a New Drug Application.

11

Facility Inspection

FDA inspects the facilities where the drug will be manufactured.

12 FDA

Drug Approval

FDA reviewers will approve the application or issue a response letter.

FASTER APPROVALS

The **Accelerated Approval** program allows earlier approval of drugs that treat serious diseases and that fill an unmet medical need. The approval is faster because FDA can base the drug's effectiveness on a "surrogate endpoint," such as a blood test or X-ray result, rather than waiting for results from a clinical trial.

The **Fast Track** program helps reduce the time for FDA's review of products that treat serious or life-threatening diseases and those that have the potential to address an unmet medical need. Drug sponsors can submit portions of an application as the information becomes available ("rolling submission") instead of having to wait until all information is available.

POST-MARKETING

FDA's Post-Approval Risk Assessment Systems

PHASE 4

Because it's not possible to predict all of a drug's effects during clinical trials, monitoring safety issues after drugs get on the market is critical. The role of FDA's post-marketing safety system is to detect serious unexpected adverse events and take definitive action when needed.

Once FDA approves a drug, the post-marketing monitoring stage begins. The sponsor (typically the manufacturer) is required to submit periodic safety updates to FDA.

www.fda.gov/medwatch
(800) FDA-1088 (322-1088) phone
(800) FDA-0178 (322-0178) fax

MEDWATCH

FDA's MedWatch voluntary system makes it easier for physicians and consumers to report adverse events. Usually, when important new risks are uncovered, the risks are added to the drug's labeling and the public is informed of the new information through letters, public health advisories, and other education. In some cases, the use of the drug must be substantially limited. And in rare cases, the drug needs to be withdrawn from the market.

PDUFA

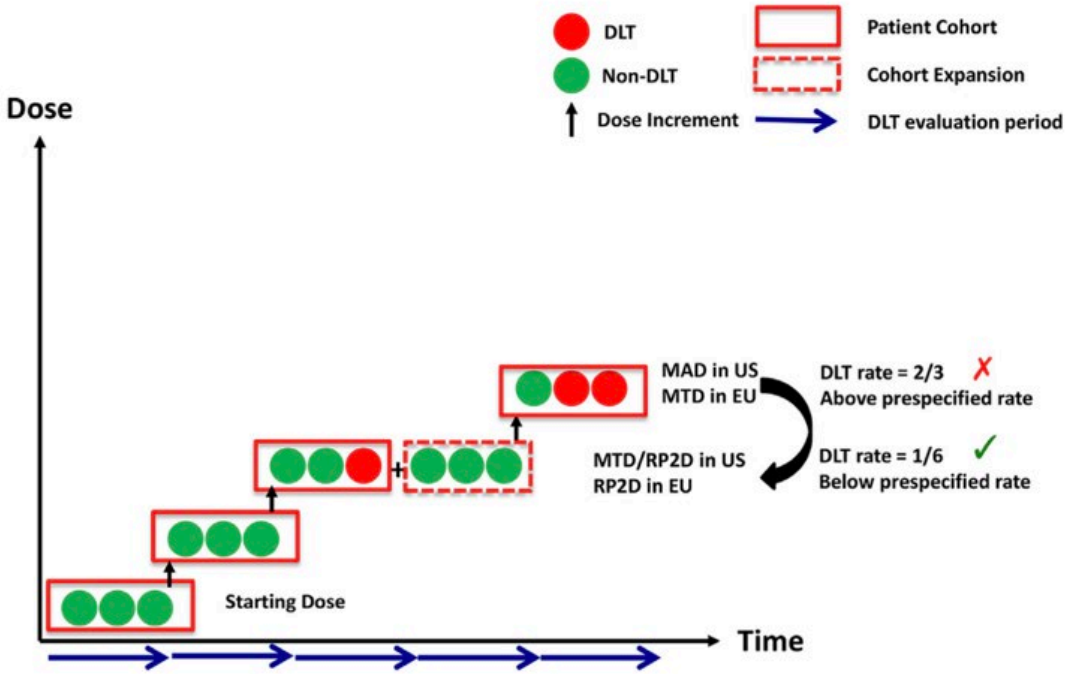
Prescription Drug User Fee Act

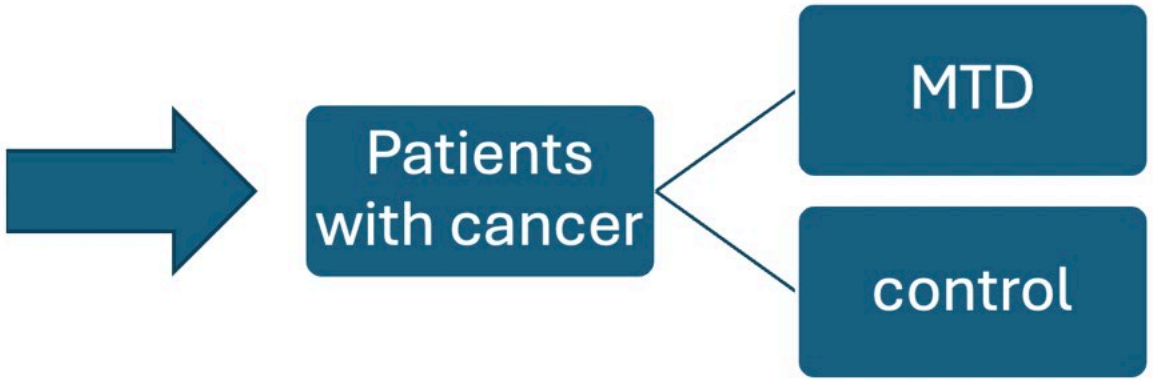
Since the PDUFA was passed in 1992, more than 1,000 drugs and biologics have come to the market, including new medicines to treat cancer, AIDS, cardiovascular disease, and life-threatening infections.

PDUFA has enabled the Food and Drug Administration to bring access to new drugs as fast or faster than anywhere in the world, all while maintaining the same thorough review process. Under PDUFA, drug companies agree to pay fees that boost FDA resources, and FDA agrees to time frames for its review of new drug applications.

Phase 1 Clinical Trials: Is the Treatment Safe?

- Proof-of-concept: Establish safety and possible efficacy signals
- Dose-limiting toxicity (DLT)
- Traditional dose finding of novel drugs in clinical trials





MTD: maximum tolerated dose; DLT: dose limiting toxicity; RP2D: recommended phase 2 dose

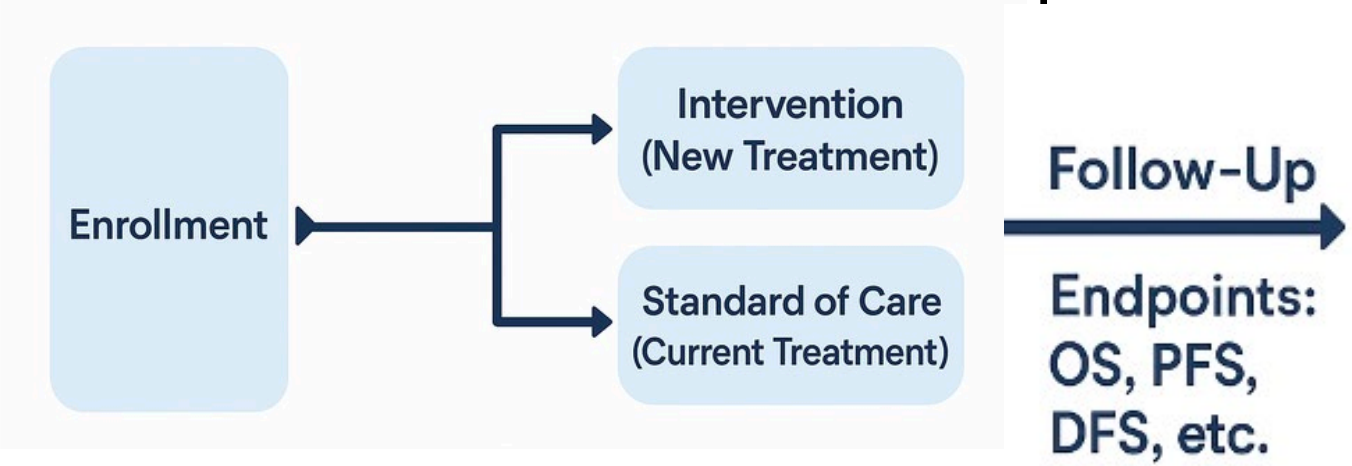
Cook N, et al. Early phase clinical trials to identify optimal dosing and safety. Molecular oncology (2015): 997-1007.

Phase 2 Clinical Trials: Does the Treatment Work?

- Compare intervention to control
- Can assess endpoints such as ORR, PFS, OS
  - **The cancer shrinks or disappears.**
  - **There's a longer period of time where the cancer doesn't get any bigger.**
  - **There's a longer time before the cancer comes back.**
  - **The treatment improves the quality of life of people who receive it.**
  - **People who get the treatment live longer than those who don't receive it.**

Phase 3 Clinical Trials: Is It Better than the Standard of Care?

- Compare the safety and effectiveness of new treatment to standard of care
- Often randomized
- *Blinded*
- Several hundreds-thousands of patients across many different locations



How to Evaluate Efficacy?

Statistical significance
AND
clinical meaningfulness

Mobocertinib withdrawal:

- Accelerated approval in 2021 for adults with locally advanced or metastatic NSCLC with EGFR exon 20 insertio mutations who had progressed after platinum chemotherap
- Phase 3 confirmatory trial (EXCLAIM-2) failed to show superior efficacy → withdrawn on July 15, 2024

Quick Word on Inclusion & Exclusion Criteria

- *Rules* in place by investigator that decide who can or cannot join the clinical trial to make sure study is safe, fair and focused on the right population.

- Inclusion criteria (who is allowed): type and stage of the cancer, age and performance status, specific labs

- Exclusion criteria (who is not allowed): other medical issues, prior treatments, certain medication use/allergies

Safety, fairness and scientific accuracy

Phase 4 Clinical Trials

- Postmarking surveillance trial
  - Safety surveillance (pharmacovigilance)
    - Involve thousands of people
    - Rare or long-term adverse events
    - May result in drug withdrawal or restricted to specific uses
  - Ongoing support after approval
    - Finding a new indication
    - Drug-drug interactions
    - Studies in special populations (pregnant women, pediatrics)

Resources

- https://www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials/things-to-consider.html
- https://www.fda.gov/patients
- https://clinicaltrials.gov/study-basics/patient-resources

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Overview of EGFR Resisters Clinical Trials Website

Laura Book and Mike Troy

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Panel Discussion

Key Themes, Questions, and Insights from Real-World Experiences

Hello

- About Us

Kris: The “Caregiver”

- Biologist/physiology
- Taught “A&P” at UCONN

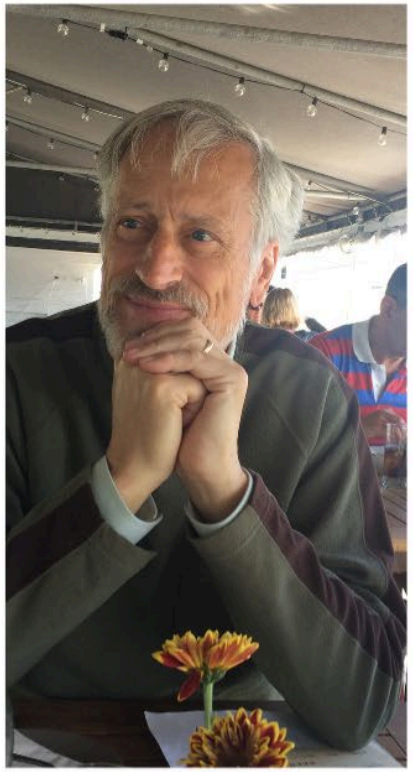
Dave: The “Patient”

- Engineer, communications software
- Hiker, rower, putterer, highly skilled woodworker, etc., etc.

Our family

- Three adult children, their spouses, the grandkids

- Our story
  - Healthy, fit 59-year-old rower without known risk factors. Married 35 years, children “launched”, trip!
    - Diagnosis (May 2012): Stage 4 lung cancer, EGFR+
      - Began SOC Tarceva (Erlotinib) at Yale

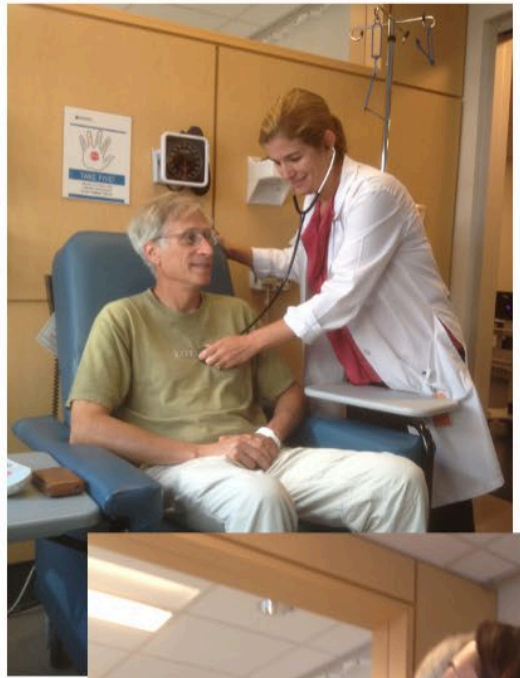


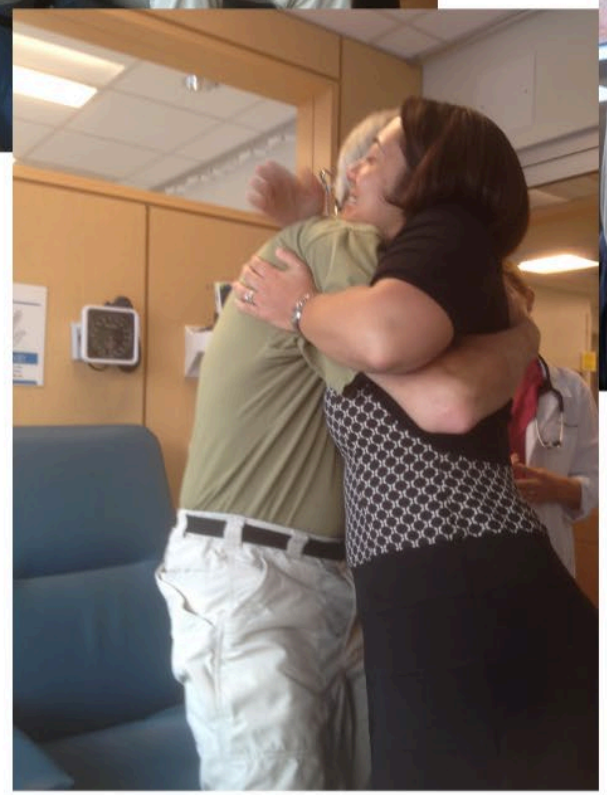
Worry, Scan, Treat, Repeat: The Cadence Of Living With Cancer

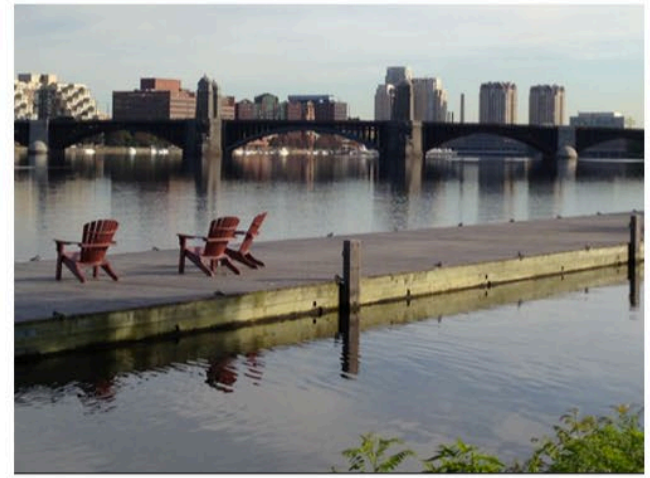
February 16, 2017 By David Kimball

David Kimball (Courtesy)

September 5, 2014:
Day 1 on AZD 9291







Last December, Mike was diagnosed on his 41st birthday after a brain met caused a seizure. Prior to his seizure, he was completely asymptomatic. He presented with mets to his brain, lymph nodes, liver, and peritoneum and was diagnosed with EGFR exon 19 NSCLC on Christmas Eve 2024.

He qualified for a NCI Study at Northwestern: Osimertinib With or Without Bevacizumab as Initial Treatment for Patients With EGFR-Mutant Lung Cancer. He was randomized into the study arm and had a complete metabolic response on his August 2025 PET.

He was an excellent candidate for consolidative surgery and we were preparing to exit his study so that he could have a segmentectomy to remove his primary tumor in early December.

Unfortunately, his recent CT has shown possible progression in his peritoneum so we are pivoting to a diagnostic laparoscopy this month. If the findings point to progression, he'll exit the study and add in carboplatin & pemetrexed.

We are so thankful to our team at Northwestern and to EGFR Resisters and the Young Lung Cancer Initiative for providing us hope and community.

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Q&A

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