

# **Lung Cancer Basic Overview**

## ***Patient Forum: 2020***

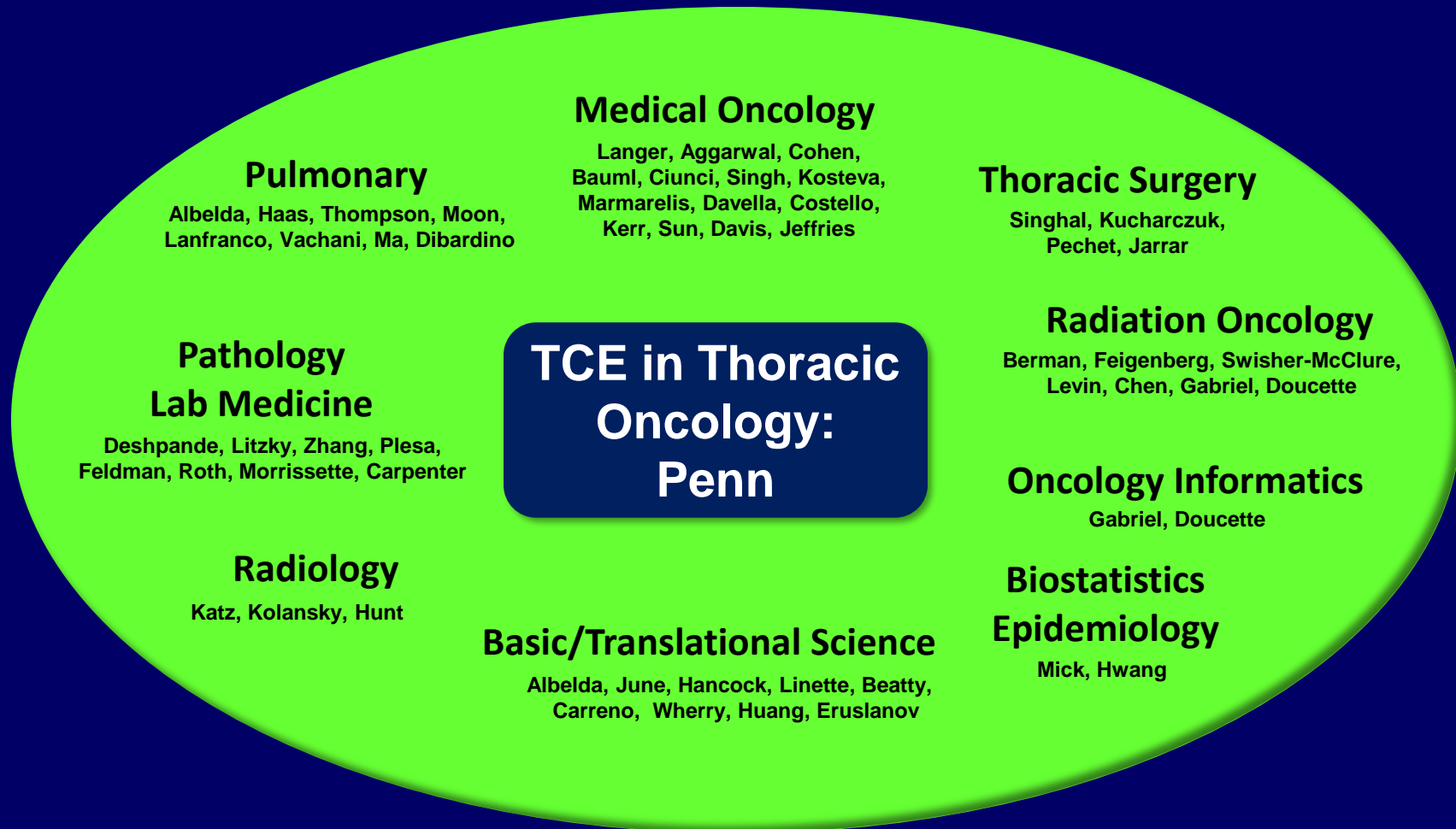
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**Corey J Langer MD, FACP**  
**Director of Thoracic Oncology**  
**Abramson Cancer Center**  
**Professor of Medicine**  
**University of Pennsylvania**  
**Philadelphia, PA 19104**

# What everyone should know about Lung Cancer

- World-wide Epidemic
- It is a largely preventable illness
  - Eliminating smoking could prevent ~150,000 cases annually in the US – in 20-40 years time
- Increasing percentage of those diagnosed are non-smokers or remote former smokers (> 20%)
  - Different biology and clinical behavior; higher incidence of mutations and other molecular markers
- Cure rates remain disappointing, although we've seen major improvements over the past 30 yrs, especially the past 5-10 years thanks to screening, targeted therapy and immunotherapy
- Pro-active, supportive care may yield as much survival benefit as toxic, systemic therapy
- Clinical and translational research is the key to improving survival rates
- Best outcomes occur in the setting of a multi-disciplinary, collaborative partnership with good logistical access

# Multidisciplinary approach: Penn



# Multidisciplinary approach: Penn

*It Takes a Village!!!*

## Pulmonary

Albelda, Haas, Thompson, Moon,  
Lanfranco, Vachani, Ma, Dibardino

## Medical Oncology

Langer, Aggarwal, Cohen,  
Bauml, Ciunci, Singh, K  
Marmarelis, Sun, Dav

## Pathology Lab Medicine

Deshpande, Litzky, Z  
Feldman, Roth, Mc

## Radiation Oncology

Berman, Feigenberg, Swisher-McClure,  
Levin, Chen, Gabriel, Doucette

## Oncology Informatics

Gabriel, Doucette

## Biostatistics Epidemiology

Mick, Hwang

## Basic/Translational Science

Albelda, June, Hancock, Linette, Beatty,  
Carreno, Wherry, Huang, Eruslanov

# Lung Cancer: Overview

- Research is underfunded (compared to other cancers, e.g. breast cancer)
- Early detection makes a difference
  - The NLST proved this
    - In at risk individuals, low dose spiral CTs detected lung cancers earlier than conventional CXRs, when they were more curable; this led to a decrease in lung cancer mortality
    - NELSON trial from Europe proved confirmatory
- Types of lung cancer have changed over past 40 years
  - Non-small cell lung cancer (NSCLC): 75% → 87%
  - Small cell lung cancer (SCLC): 25% → 13%

# Lung Cancer: Other Truisms

- Surgery remains the major curative approach, especially in early stage lung cancer
  - Techniques have improved
  - Complications have diminished, and hospital stays have shortened
  - Short-course adjuvant chemotherapy provides a clear benefit in Stage II/IIIA node (+) NSCLC and in pts with tumors > 4 cm
- Locally advanced NSCLC is responsive to combined chemoradiation, with improvement in cure rates from 5-7% to ~ 30% over the past 25 years
  - Immunotherapy after definitive chemo and XRT delays recurrence and improves survival rates (NEJM 2017, 2018)
  - Can we harness new technology (protons, SBRT) to our biologic understanding of lung cancer?

# Advanced NSCLC

- We have witnessed major improvements in outcome over the past 25 yrs
- Our prior monolithic, “one size fits all” approach no longer works
- Treatment is now individualized based on
  - Histology (appearance under the microscopic)
  - Molecular markers (EGFR, ALK, ROS-1, BRAF, **cMET, RET, KRAS (G12C)** etc)
  - Immune markers (PDL1, others??)
- Immunotherapy has made major inroads, both 2<sup>nd</sup> and 1<sup>st</sup> line,
  - Marked increase in response rates and survival rates, particularly in combination with chemo
  - **Similar benefits now seen in extensive stage SCLC**
- Treatment goals identical
  - Improve Duration of life
  - Improve Quality of life

# NSCLC: STANDARD AGENTS

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## OLD (pre 1990)

- Cisplatin → Carboplatin
- Etoposide
- Vinblastine
- Ifosfamide
- Mitomycin-C

## NEWER (post 1990)

- Paclitaxel
- Docetaxel
- Gemcitabine
- Vinorelbine
- Irinotecan

## LATEST (post 2000)

- Pemetrexed; Nab-paclitaxel
- Erlotinib; Afatinib; Gefitinib; Dacomitinib → Osimertinib
- Crizotinib → Ceritinib, Alectinib, Brigatinib, Lorlatinib
- Dabrafenib and Tremetinib
- Entrectinib, Larotrectinib
- Salpercatinib; Prasetinib
- Capmatinib
- Bevacizumab, Ramucirumab
- Cetuximab, Necitumumab
- Nivolumab, Pembrolizumab, Atezolizumab, Durvalumab



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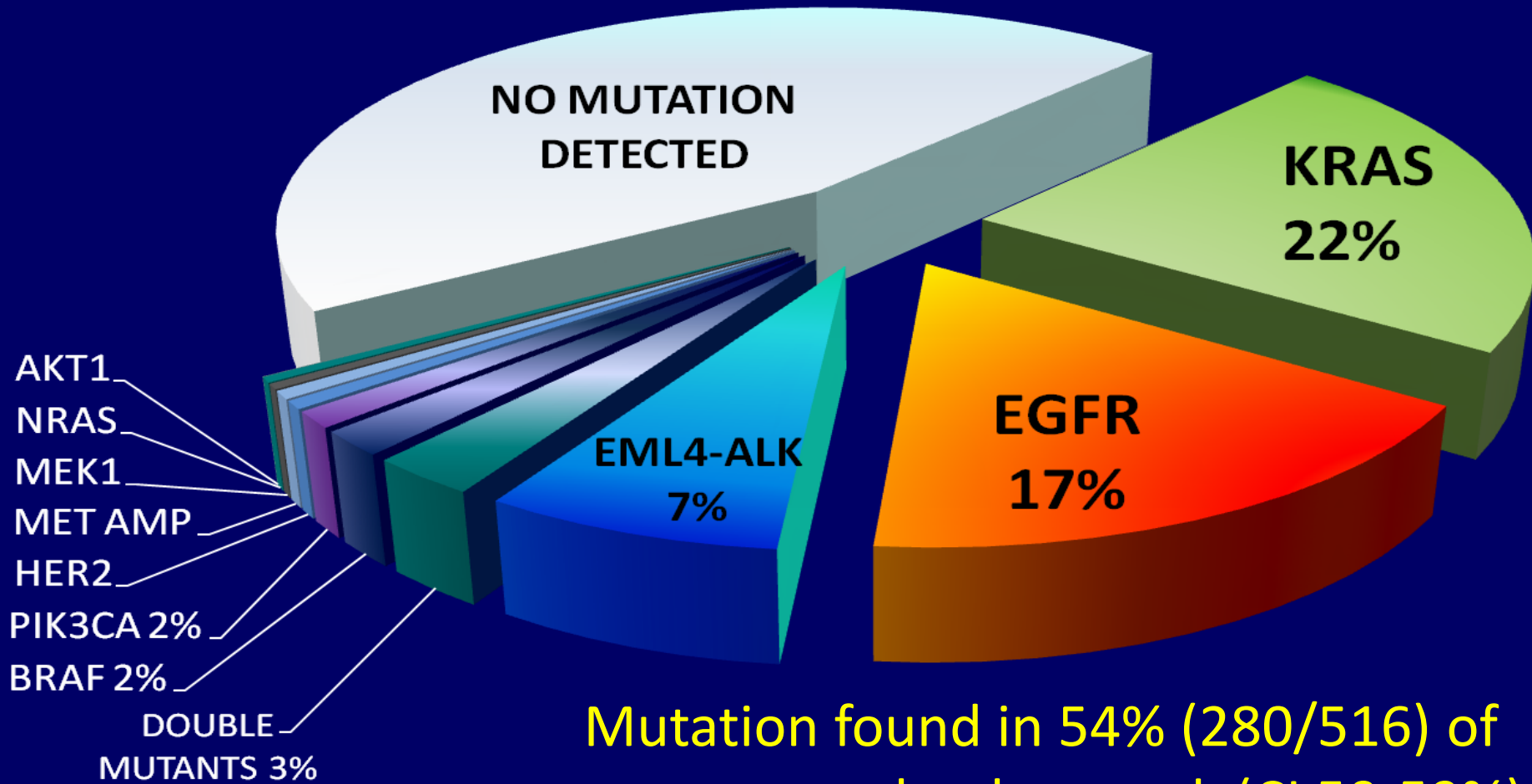
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- Cetuximab, Necitumumab
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# Incidence of Mutations Detected



**Mutation found in 54% (280/516) of tumors completely tested (CI 50-59%)**

# NSCLC Pt Treated With an EGFR Inhibitor



6 FEB 2002

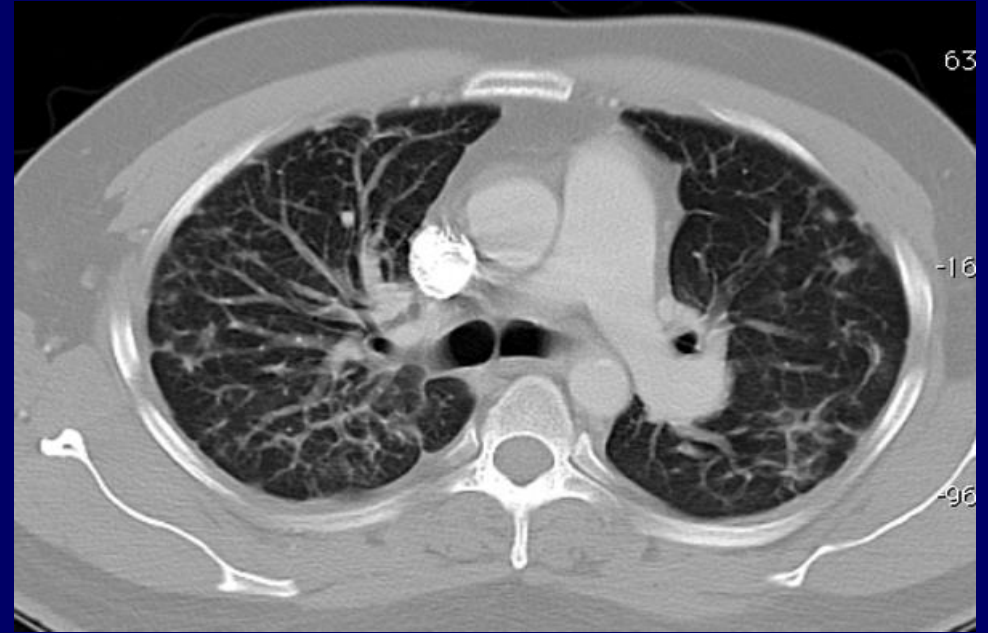


11 FEB 2002

# Response to Crizotinib

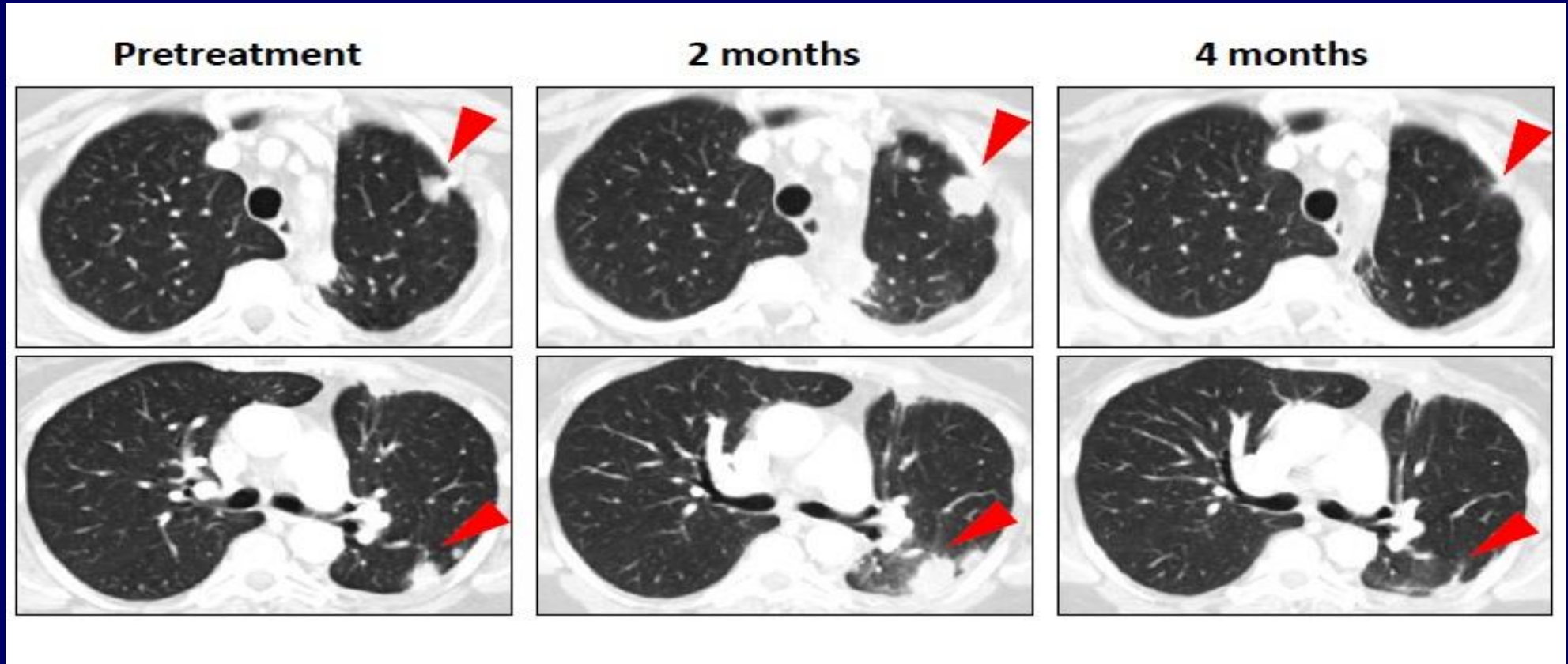


Pre-Treatment



Crizotinib x 12 weeks

# Response of Metastatic NSCLC (Nivolumab)



- Initial progression in pulmonary lesions of a NSCLC patient with non-squamous histology was followed by regression
- Dx '04, EGFR mutation +; Rx Gem/carbo, erlotinib, erlotinib + LBH589 (trial for T790 mutation), and lastly pemetrexed

# Synopsis: Current TCE

- The lung cancer field, despite recent modest gains, urgently needs scientific and conceptual breakthroughs.
- Leveraging existing and unique scientific strengths at Penn, **the centerpiece of our strategy is the immunobiology and immunotherapy of lung cancer, but we are now expanding back to molecular/genetic pathways and to all stages of lung cancer**



# CLINICAL TRIAL HIERARCHY

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- **PHASE I (EXPERIMENTAL)**

- New agent(s) or new combination of established agents
- Establish top, safe dose (MTD ~ maximally tolerated dose) or OBD
- *May* require tumor biopsies or frequent blood draws (PKs)
- Usually reserved for tumors for which no standard treatment exists or after “standard” treatments have been exhausted

- **PHASE II**

- Systemic agent(s) applied to multiple patients with a specific disease type
- Gauge side effects (toxicity); feasibility
- Determine activity (response rate); freedom from progression; survival

- **PHASE III**

- Randomized comparison of standard established treatment (control arm) vs. new(er) promising regimen (investigational arm)
- Computerized coin toss (neither patient nor physician chooses)
- Placebo controls used only if observation is standard

# IMPEDIMENTS TO CLINICAL TRIALS

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- **TIME** (labor-intensive)
- **FUNDING** (third party payer)
- **PERCEPTION**: physician; patient



# WHAT PATIENTS (and CLINICIANS) SHOULD KNOW ABOUT CLINICAL TRIALS

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1. Carefully conducted protocols mandate IRB approval, intensive monitoring, and close follow-up.
2. Informed consent is required.
3. Alternative options must be discussed. You cannot be coerced.
4. Total accrual is limited; statisticians oversee results/analysis.
5. Serious adverse events (AEs) are reported to IRB. Excessive AEs can result in a trial's early closure or major amendment(s).
6. All clinical trials subject to FDA audit.
7. Enrollees on clinical trials do as well, if not better, than patients treated off protocol or empirically; costs are  $\leq 10\%$  higher than standard care.
8. You are not a guinea pig; you can opt out of clinical trial at will, at any time without compromise to subsequent care.
9. Your physician may halt your participation if you are not benefiting, if superior therapies emerge, or if toxicity proves intolerable.

# 10 QUESTIONS to ASK YOUR HEALTH CARE TEAM

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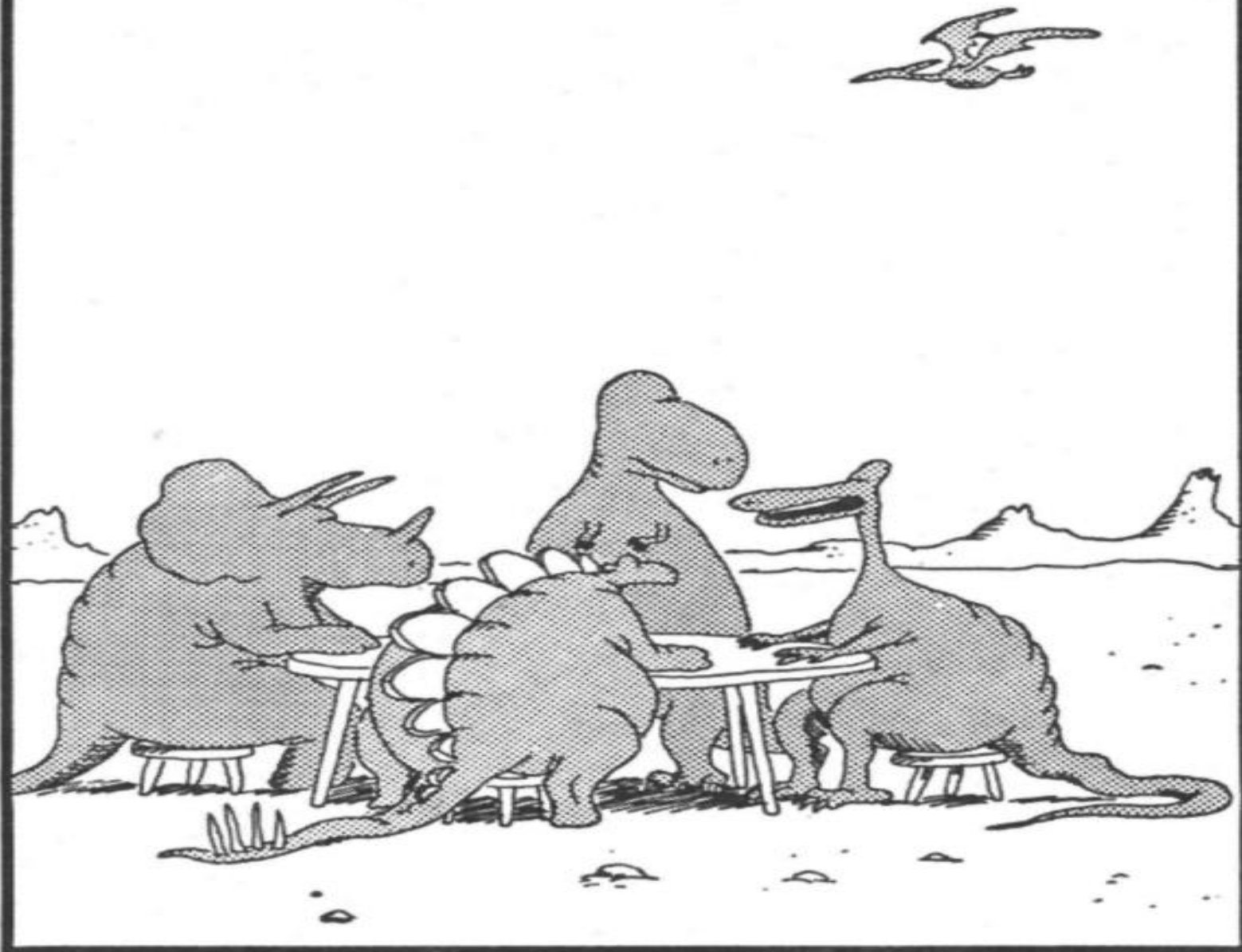
1. What are the most common side effects of my treatment?
2. What causes the side effects?
3. How can I prevent or minimize the side effects?
4. Do you have any printed material on the treatment?
5. Can I take other medicines while I am receiving treatment?
6. How will I know if my treatment is working?
7. Can I speak with someone on a one-to-one basis who has had a similar treatment experience?
8. What other options do I have regarding therapy? What are my options if treatment stops working?
9. Can I get financial assistance with medications or transportation?
10. How can I help other patients once I've completed my own treatment?

... Adapted from SPIRIT Project

# Lung Cancer: Ongoing Dilemmas

- Improving Funding
- Research Access
- Combating Stigma
- Prognostic Uncertainty; “Scanxiety”
- Disease Complexity
  - Staging
  - Histologic
  - Molecular
- Elderly outreach
- Managing Expectations

Fanson



“Well, time for our weekly brain-stem-storming session.”