Early Drug Development:
The Point of View of an Experienced Principal Investigator

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Next Oncology

San Antonio TX

I Hope You Will Come Away From This Meeting

1. Energized about Early Drug Development

2. Learn Clinical drug development Problem Solving
    a. Practical Protocol Development
    b. Solutions for everyday puzzling clinical study results

3. Understand the Responsibility of Being a PI

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Drug Development is the Most Exciting Part of Oncology!

You will witness the future of oncology agents early

You will learn the biology of the disease alongside the therapies

You will witness diseases once “incurable” become treatable

You will transform lives

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Being Principle Investigator:
Great Career, Greater Responsibility

- In all aspects of the conduct of the study you are responsible

- More than “signing” a form (1572)
  - Legal responsibilities with consequences

  - Delegation log merely means you are responsible for actions of others

  - Documentation is key

We Perform Phase I Studies to Determine Safety

This is not a perfunctory step

- Necessary for our patients now and in our future patients
- This may be the only opportunity to get dose right

Documentation is Key

- Must understand NCI CTC, and document ***without bias***
- Do not leave this to the junior or ill trained staff

Phase I is a Specialization:
Not Everyone Can Do It Well

Similar to Bone Marrow Transplantation-Subspecialization

- Concept accepted in Hematology Oncology
- Avoid “anyone can do Phase I” mentality
- Not a “ticket” to Phase 2 and late-stage studies
- Create infrastructure and culture to support Phase I investigators

As a PI…
You Must Remain Neutral and Non-Proprietary

This is not “your” drug/therapy

- Good Science requires dispassionate observation and analysis

Honest documentation of the adverse events, and reporting to the sponsor

- If the drug fails, due to poor tolerability, poor PK, ineffective target inhibition, it is not your failure!

Remember:

We Are Developing the Medicines Our Children and Grandchildren Will Inherit!

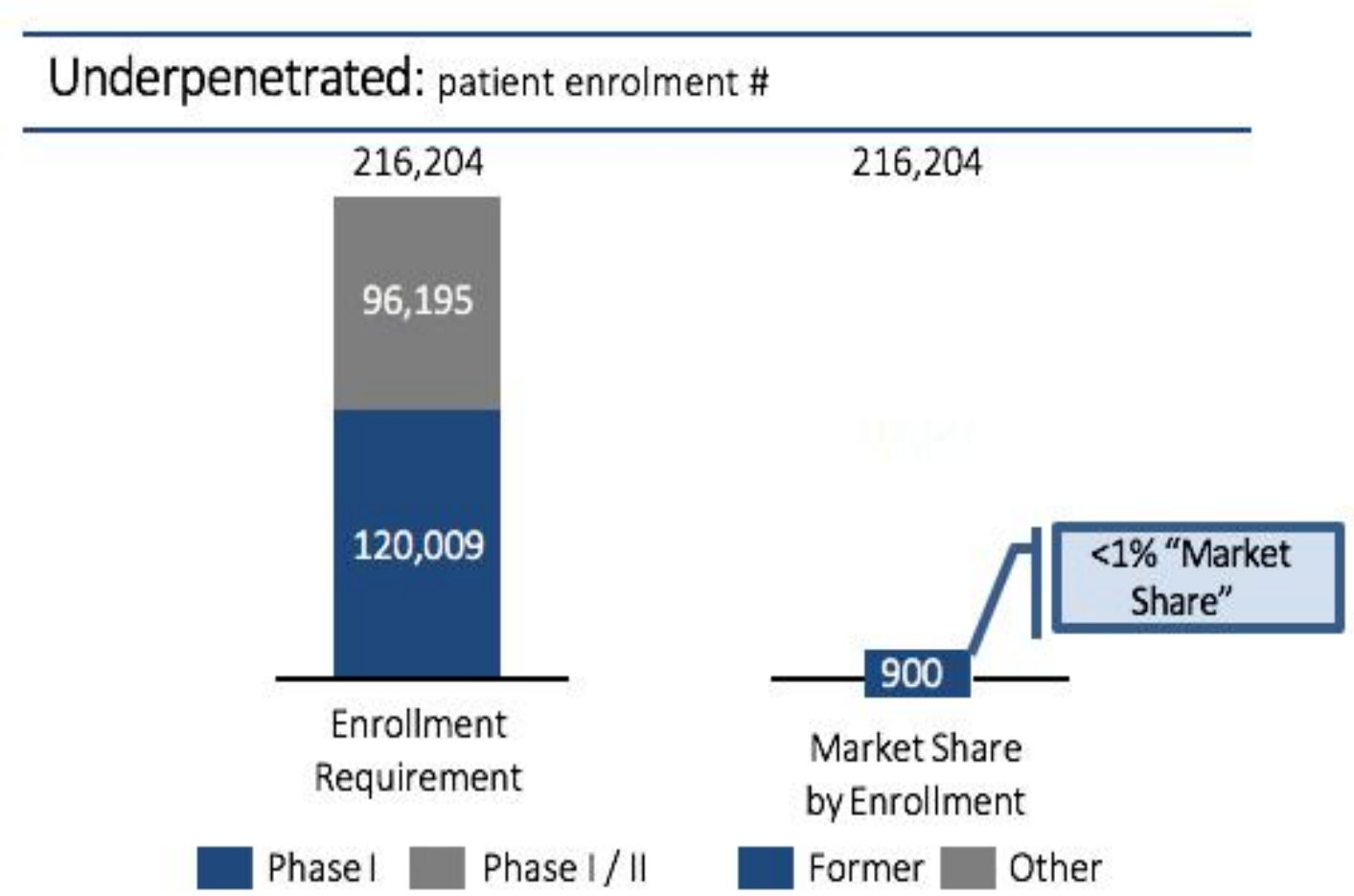
Phase I is Changing

Dose Escalation followed by Expansion Cohorts are common

Alternate dose escalation schemes, and statistical methods

Creating Infrastructure to Support Phase I

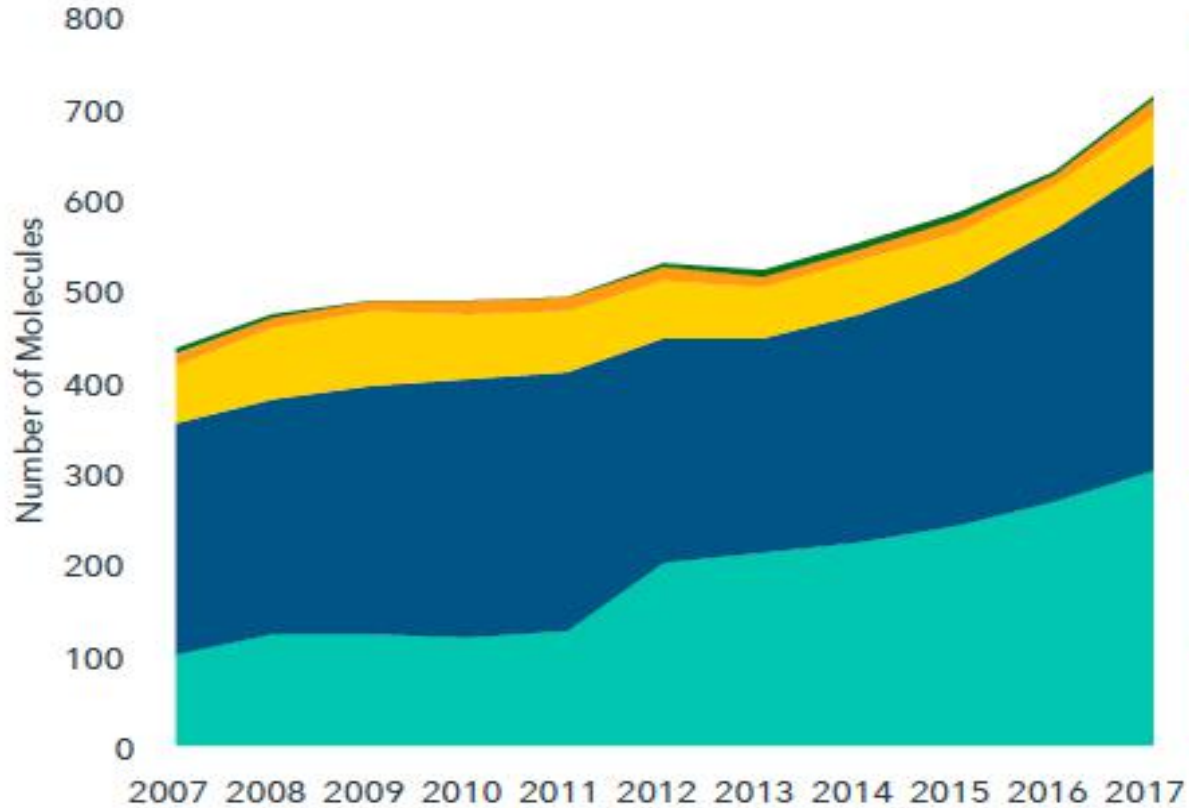
More Phase I Sites Needed
More Phase I Investigators Need Training



Source: IMS Institute for Healthcare Informatics, Clinicaltrials.gov

The pipeline of new medicines in late phase development exceeded 700 molecules, an increase of over 60% since 2007

Chart 29: The Pipeline of Late Phase Oncology Molecules, 2007-2017



Year	2007 (434)	2017 (710)
Radiotherapies	0.9% (4)	0.4% (3)
Hormonals	3% (14)	2% (17)
Cytotoxics	15% (63)	8% (54)
Targeted Small Molecule	59% (254)	47% (335)
Targeted Biologics	23% (99)	42% (301)

Source: IQVIA, ARK R&D Intelligence, Dec 2017; IQVIA Institute, Mar 2018

Education of the Next Generation of PIs

This must be viewed as a priority

- In the US, many phase I programs are in decline
- Loss of Clinical Pharmacology training
  - Fewer grants
  - Fewer PK labs in university cancer centers
    - Move to CROs as more cost effective
  - Need separate education avenues