



# Site Selection: Lessons from Cancer Clinical Trials

*Presentation by*  
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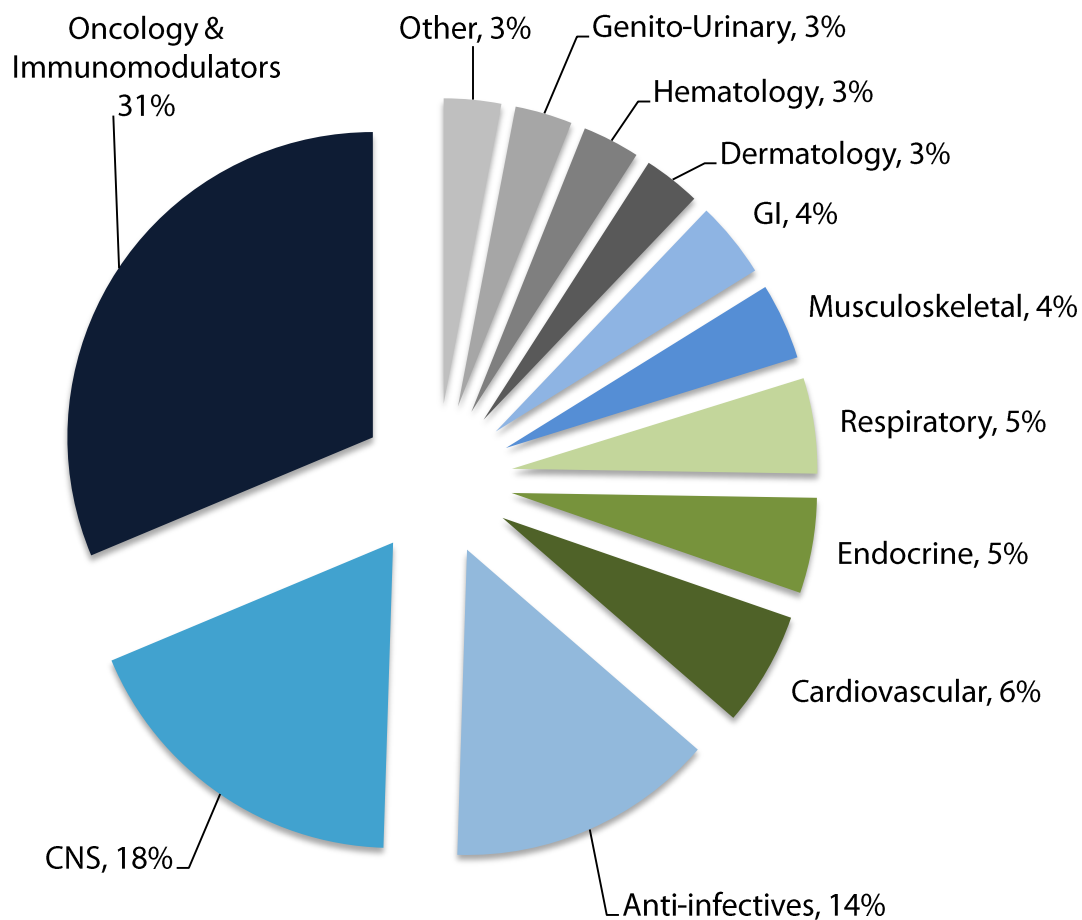
**DAVA Oncology, LP**  
...facilitating successful drug development<sup>SM</sup>

## Site Selection: Lessons from Cancer Clinical Trials

- Cancer clinical research
- Challenges to site selection
- Understanding sites and investigators
- Identifying the right site
- Case studies in site selection



## Oncology is the largest therapeutic area in clinical research



In 2010,  
31% of all compounds in  
clinical testing were  
oncology drugs or  
immunomodulators

# Multiple site selection challenges

*Site Selection is a critical step in the timely completion of a clinical study*

## Poor Site Performance

30% of sites enroll 70% of patients (Tufts CSDD/McKinsey)

50% of sites enroll 95% of patients (Tufts CSDD/McKinsey)

Difficult patient recruitment accounts for 85-95% of days lost in clinical trial delays (McKinsey/Lehman)

Each day a clinical trial is delayed can result in \$600,000 or more in lost sales (Cutting Edge)

Delays in approval of survival benefitting agents cause even higher losses for potential patients collectively as a group financially and socially (Philipson)

## Protocol Complexity

Comparing 2000-2003 to 2004-2007 (PhRMA)

49% increase in total procedures

54% increase in execution burden

58% increase in total eligibility criteria

Average trial has 2.3 protocol amendments resulting in average delay of 4 months (Getz)

Pathology requirements are more prevalent, require inter-practice coordination, and can delay start of treatment

## Investigator and Trial Demographics

Finite pool of clinical investigators and sites

Over one third of oncology investigators are new (Clinical Trial Magnifier)

Competition among sponsors for high performance sites

## Physician Perceptions

Physician knowledge of clinical trial data may be incomplete (Hoffman 2010)

Primary physicians may discourage patients from clinical trial participation (Hoffman 2005)

Patient interest in clinical trial participation is driven by physician

40-80% of cancer patients are unaware that clinical trials may be an option for them (NCI, Lara)

## What is required of a site?

- 1 Dedication to clinical research
- 2 GCP, ICH, and regulatory compliance
- 3 History of high patient enrollment
- 4 Commitment to an accelerated opening timeline
- 5 Excited by the study rationale
- 6 Significant patient population

*Although most oncology sites have very strong regulatory compliance and GCP, patient recruitment and data collection remain difficult*



## Significance of investigators in cancer clinical research

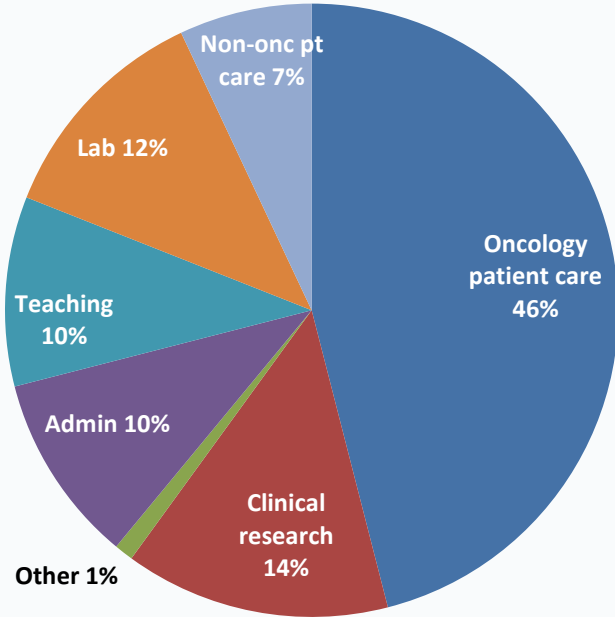
- Cancer is a life-threatening illness
- Cancer diagnoses often result in fear, uncertainty, and has emotional impact
- Oncologists are important sources of psychological support for patients
- Unique relationship between oncologist and patient
- Shared decision-making
- Patients' unmet need is information

- May not be life-threatening
- Less emotional impact on patients
- Specialty physicians may not be involved
- Patients may make decisions without consulting with their physician
- Individual decision-making
- Information easily accessible for patients in various media outlets

Other

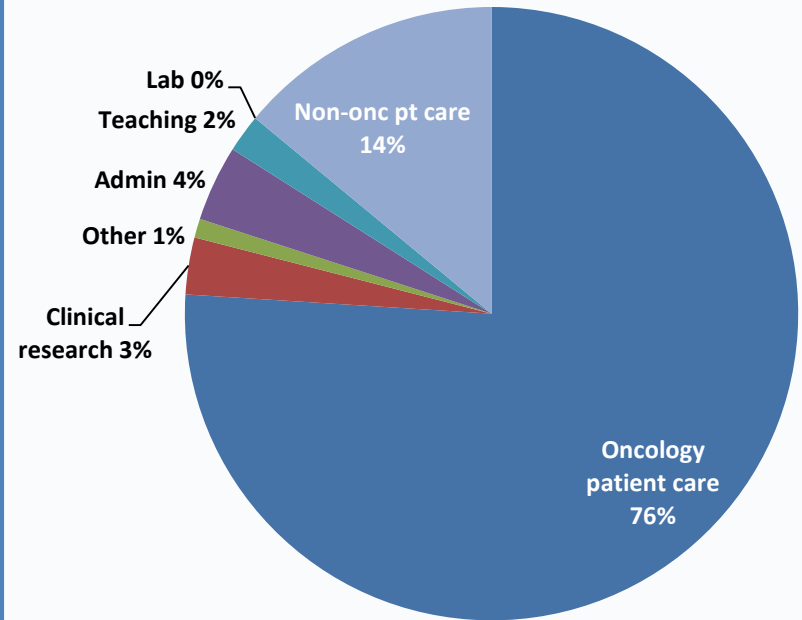
# Oncology physician profiles

## Academic Oncologists



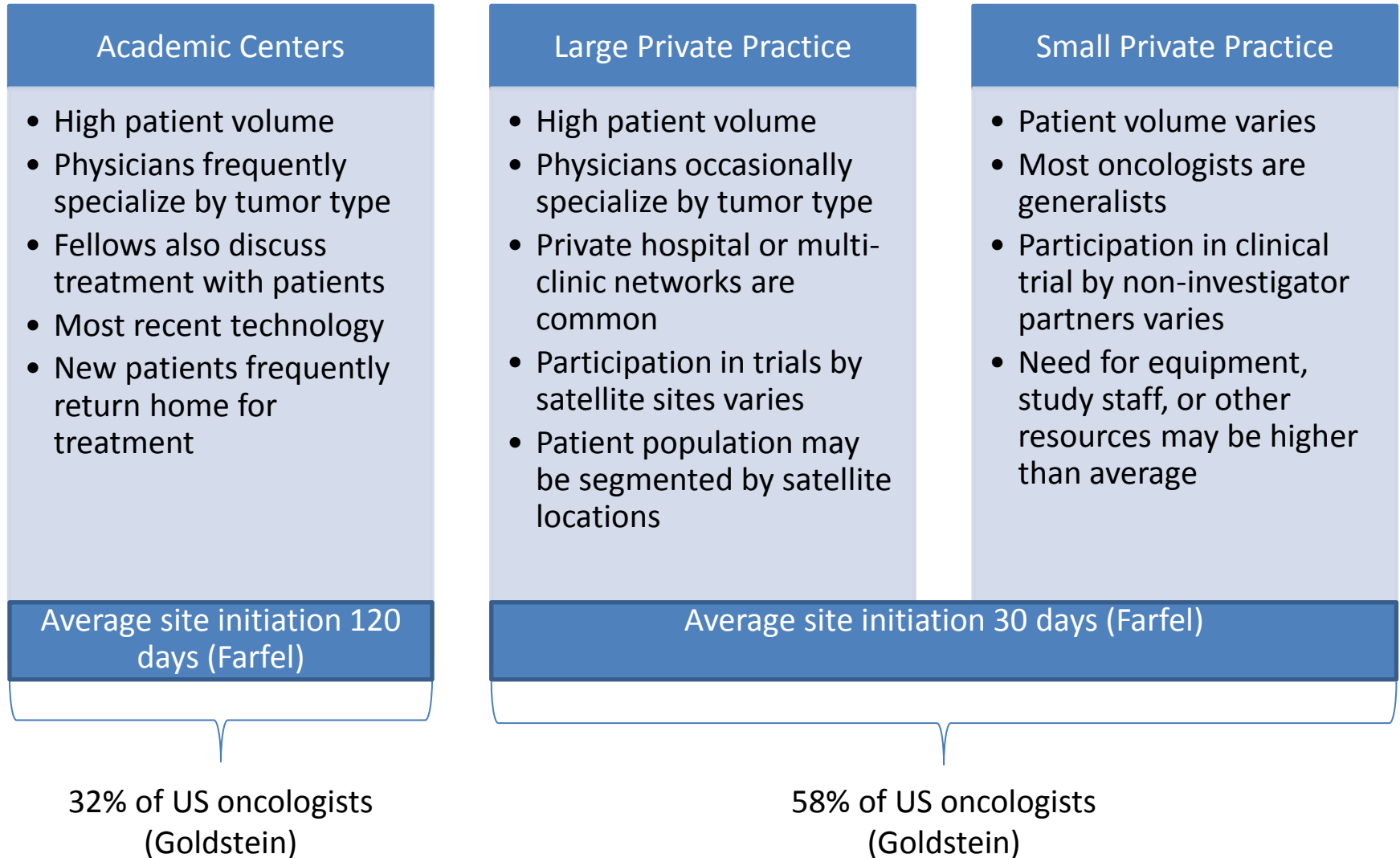
- 60% of time devoted to patient care or clinical research
- High prevalence of KOLs
- Principal investigator may travel frequently
- Sub-investigator, fellow, and research staff participation ideal

## Private Practice Oncologists



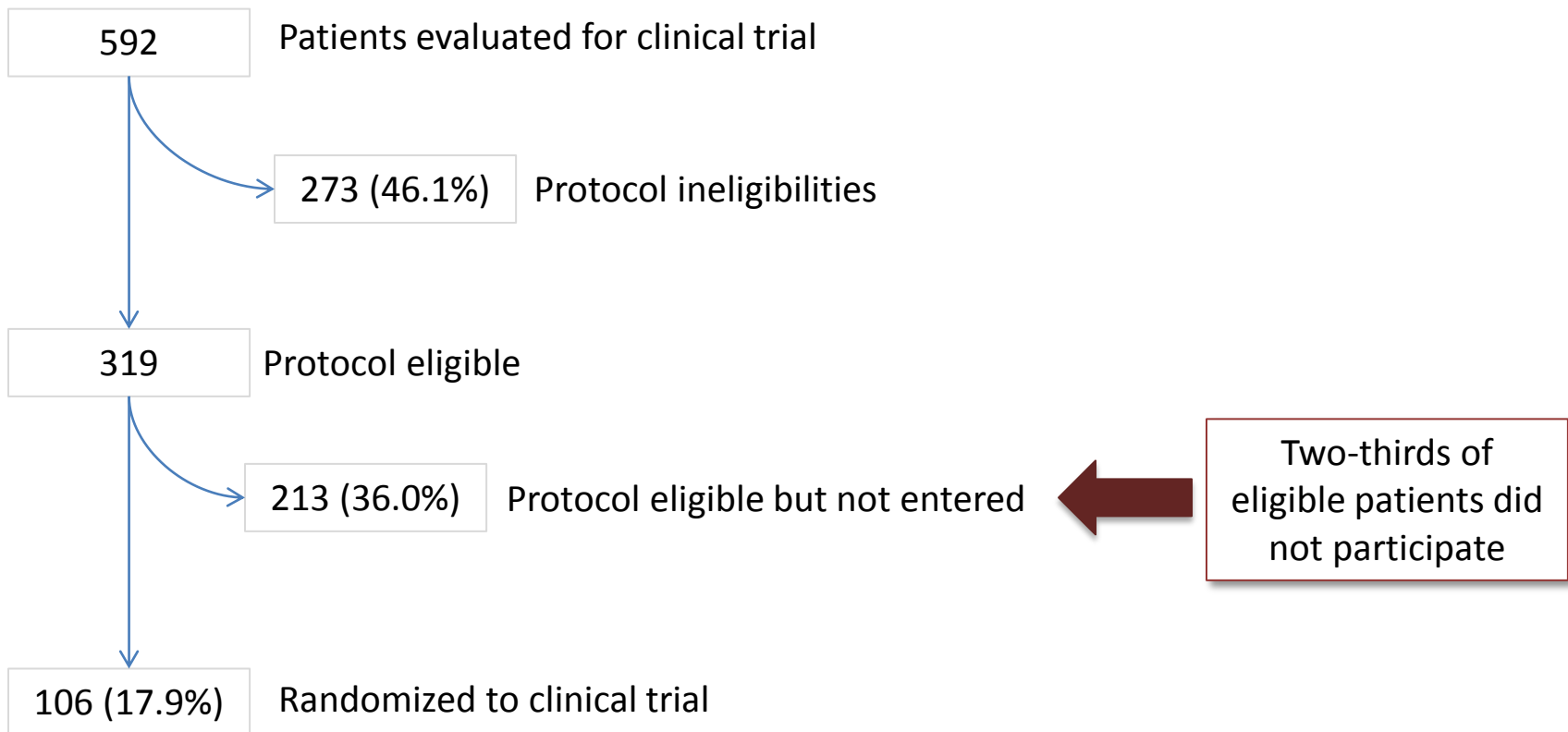
- 79% of time devoted to patient care or clinical research
- Sub-investigator, fellow, and research staff participation ideal

# Cancer trial site segmentation



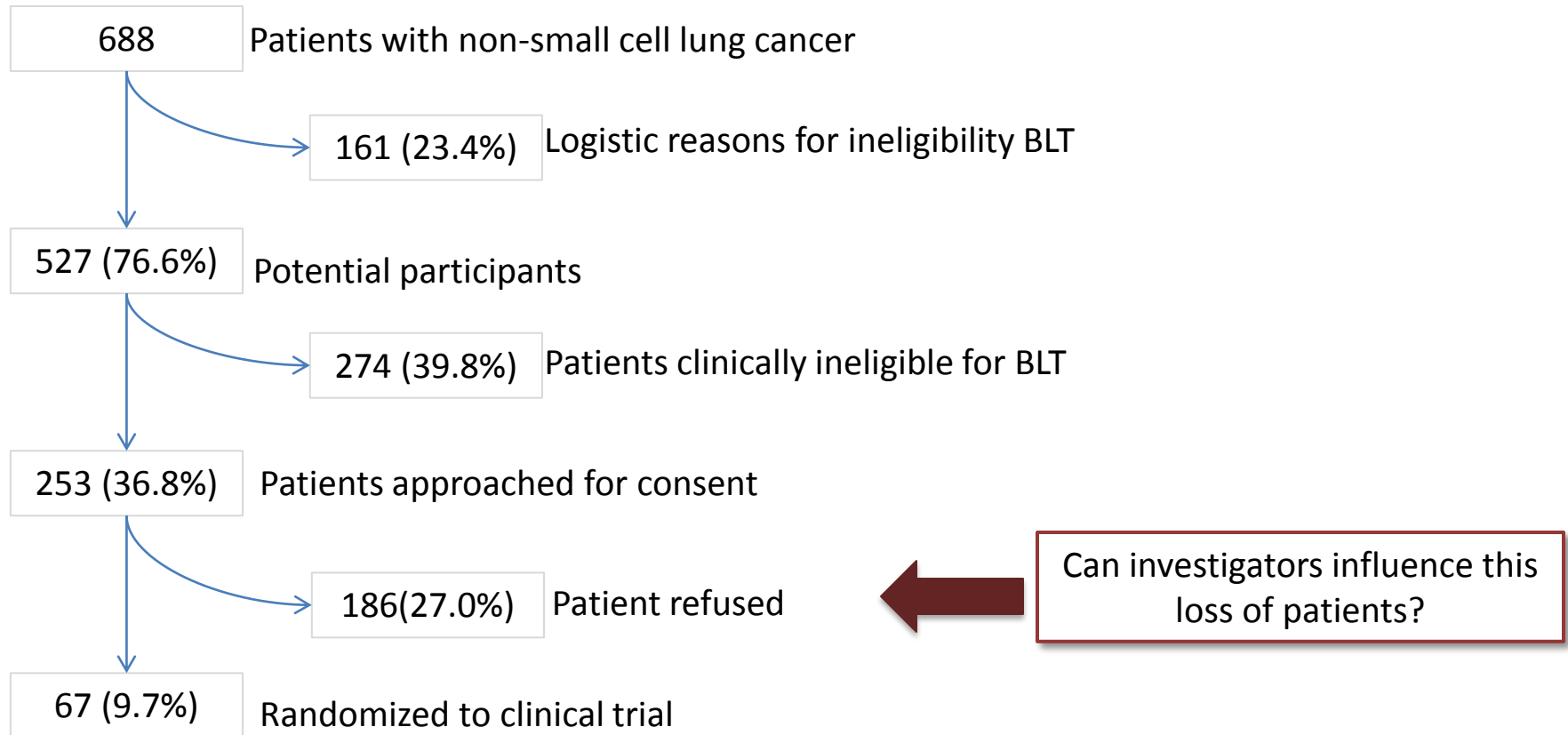
# Significant numbers of eligible patients are lost prior to enrollment

St. Michael's Hospital, Toronto, ON  
Breast Cancer Clinical Trials  
1984 – 1989 (prospective study, Kotwall)



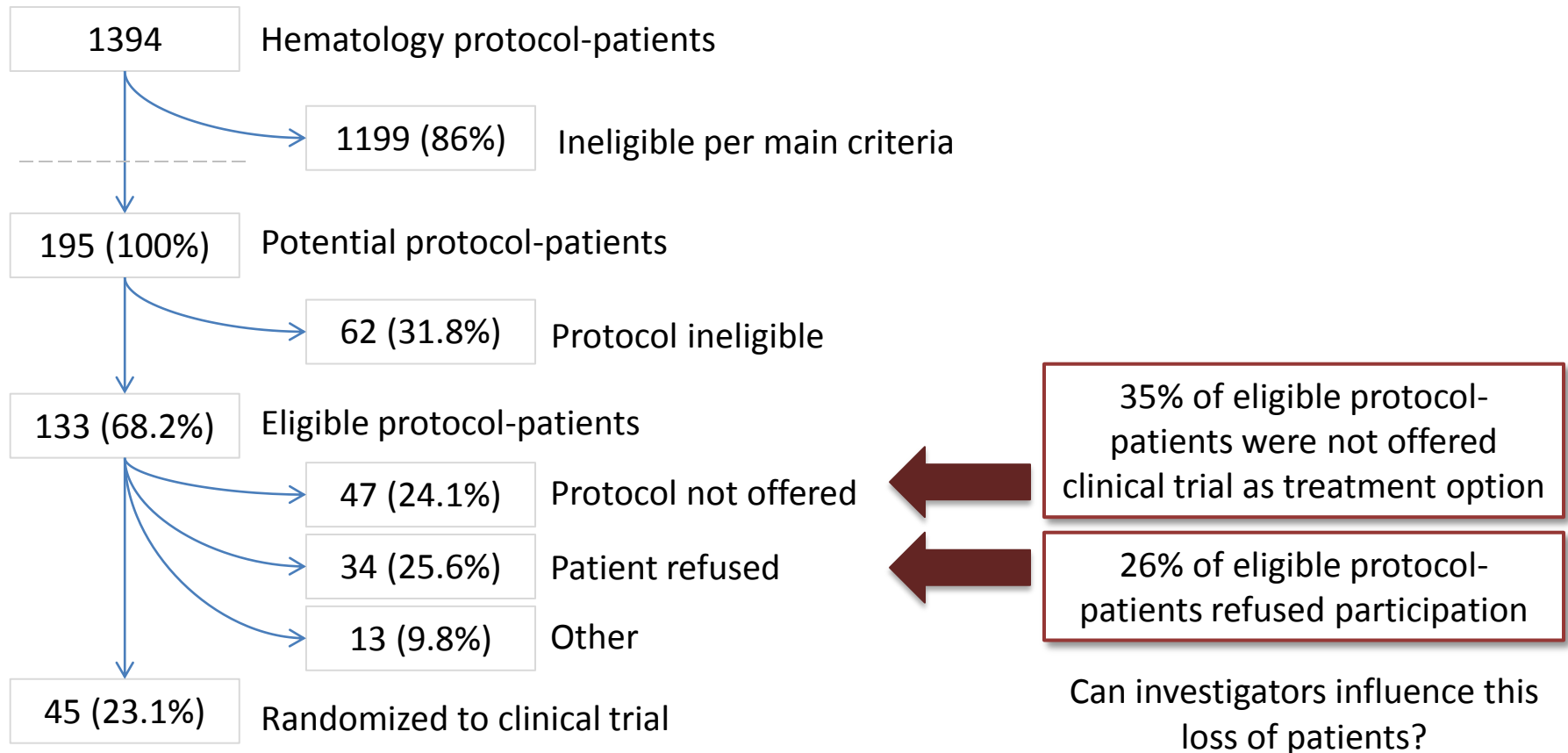
# Non-participation by patients can be due either to patient preference or investigator commitment

University College London Hospitals NHS Trust 1996-97  
 St Bartholomew's and The London NHS Trust 1995-98  
 Big Lung Trial (BLT): SOC +/- cisplatin based chemo  
 (Spiro, prospective study)



# Non-participation by patients can be due either to patient preference or investigator commitment

Centre hospitalier affilié universitaire de Québec 2002-2008  
17 hematology protocols (Lemieux, Retrospective study)



# Case 1: Academic Practice NSCLC Trial

Trial Design

- Age  $\geq$  18 years
- Inoperable metastatic NSCLC
- 1 prior platinum based regimen in the met. setting

**R**  
1:1

Arm A: docetaxel + NEW Drug

Arm B: docetaxel + placebo

Demographics

900 new NSCLC pts

300 - 2<sup>nd</sup> opinions only

600 - Treatment at institution

150 - Stage I-IIIa

450 - Stage IIIb-IV

75 - 2+ prior lines of therapy

375 - 0-1 prior lines of therapy

60 - single agent 1<sup>st</sup> line

315 - platinum doublet 1<sup>st</sup> line

105 - not candidates for 2<sup>nd</sup> line

210 - candidates for 2<sup>nd</sup> line therapy

3 investigators see 65% of NSCLC pts and put 30% on clinical trials

41 patients presented trial

15 investigators see 35% of NSCLC and put 10% on clinical trial

7 patients presented trial

48 patient presented trial information

24 patient refused any trial

18 patient went on institutional trial

6 patient went on trial

Standard of Care

Investigators

Patient Consent

**Site Profile:** Academic Center

## General Information

- 18,000 patients/yr., 25 medical oncologists
- 900 New NSCLC patients/yr.
- 2 institutional 2<sup>nd</sup> line metastatic NSCLC trials

## Data Coordinator

- 900 NSCLC - new or existing patient, staging, and progression rates provided

## Principal Investigator

- KOL for Lung cancer
- NSCLC standard of care pem/carbo or gem/carbo 1<sup>st</sup> line, erlotinib or docetaxel 2<sup>nd</sup> line
- Investigator segmentation of patient population based on patient's presentation and clinical goals

## Study Coordinator

- NSCLC treatment team membership
- Distribution of patients between PI, Sub-I, and non-study medical oncologists

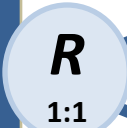
## Sub Investigators

- Awareness of study and relationship with study coordinator and principal investigator

# Case 1: Academic Practice NSCLC Trial

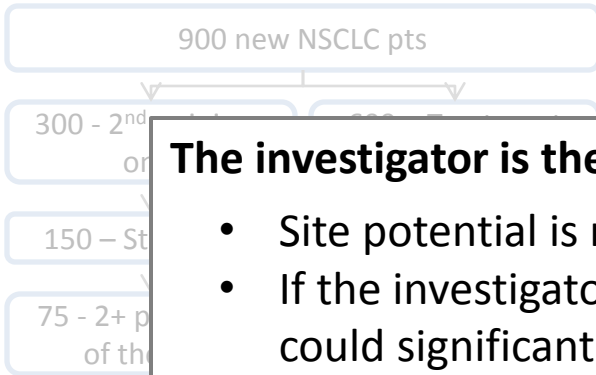
Trial Design

- Age ≥ 18 years
- Inoperable metastatic NSCLC
- 1 prior platinum based regimen in the met. setting



- Arm A: docetaxel + NEW Drug
- Arm B: docetaxel + placebo

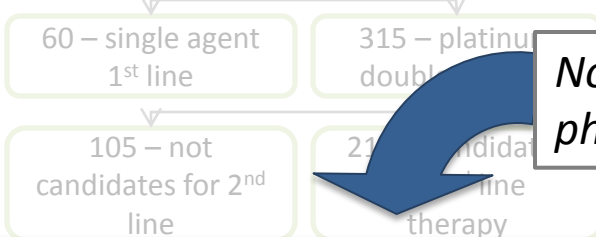
Demographics



**The investigator is the key to enrollment**

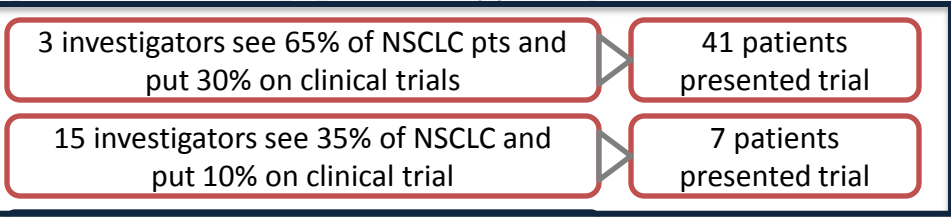
- Site potential is not the same as site performance
- If the investigators are motivated to enroll, this could significantly impact enrollment

Standard of Care

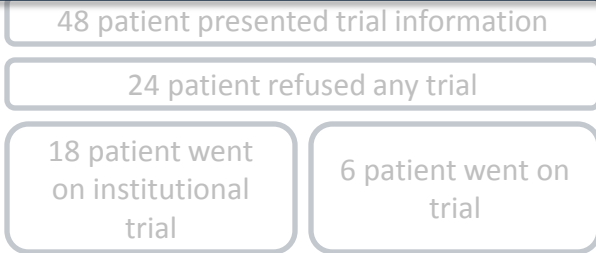


*Note the effect of increased physician engagement*

Investigators



Patient Consent



Site Profile: Academic Center

**General Information**

- 18,000 patients/yr., 25 medical oncologists
- 900 New NSCLC patients/yr.

2<sup>nd</sup> line metastatic NSCLC trials

**Data Coordinator**

Review or existing patient, staging, and test provided

**Principal Investigator**

Cancer  
Standard of care pem/carbo or gem/carbo 1<sup>st</sup> or docetaxel 2<sup>nd</sup> line

- Investigator segmentation of patient population based on patient's presentation and clinical goals

**Study Coordinator**

- NSCLC treatment team membership
- Distribution of patients between PI, Sub-I, and non-study medical oncologists

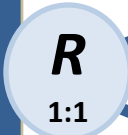
**Sub Investigators**

- Awareness of study and relationship with study coordinator and principal investigator

# Case 1: Academic Practice NSCLC Trial

Trial Design

- Age ≥ 18 years
- Inoperable metastatic NSCLC
- 1 prior platinum based regimen in the met. setting



- Arm A: docetaxel + NEW Drug
- Arm B: docetaxel + placebo

Site Profile: Academic Center

Demographics

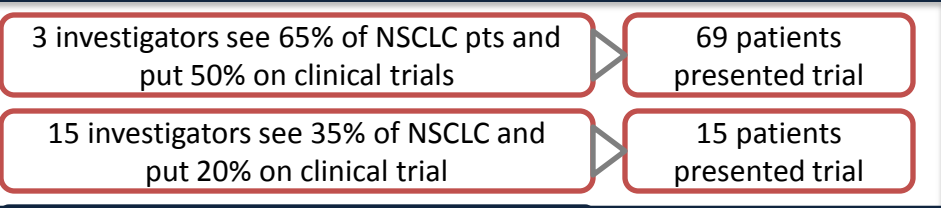
## The motivation for investigators

- Publication
- Patient benefit
- Access to new therapies
- Patient referral
- Scientific interest
- Financial benefit for research program

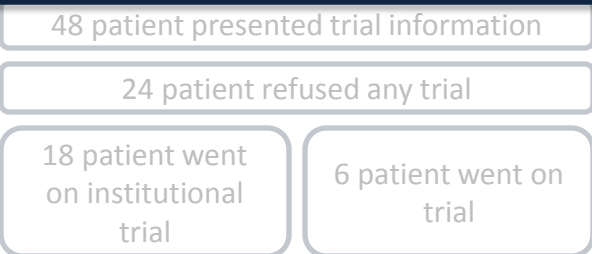
Standard of Care

*Increasing investigators' interest from 30 to 50% of patients approached and from 10 to 20% for other physicians increases patient participation 4-fold*

Investigators



Patient Consent



## General Information

logists

CLC trials

staging, and

on patient's presentation and clinical goals

## Study Coordinator

- NSCLC treatment team membership
- Distribution of patients between PI, Sub-I, and non-study medical oncologists

## Sub Investigators

- Awareness of study and relationship with study coordinator and principal investigator

# Case 2: Large Private Practice NSCLC Trial

Trial Design

- Age  $\geq$  18 years
- Inoperable metastatic NSCLC
- 1 prior platinum based regimen in the met. setting

**R**  
1:1

Arm A: docetaxel + NEW Drug

Arm B: docetaxel + placebo

Demographics

200 new NSCLC pts

50 – Stage I-IIIa

150 – Stage IIIb-IV

10 - 2+ prior lines of therapy

160 – 0-1 prior lines of therapy

30 – single agent 1st line

130 – platinum doublet 1st line

40 – not candidates for 2nd line

90 – candidates for 2nd line therapy

In community practices the engagement of sub investigators can have significant impact on trial accrual

5 investigators see 20% of NSCLC pts and put 30% on clinical trials

6 patients presented trial

20 investigators see 80% of NSCLC and put 5% on clinical trial

4 patients presented trial

10 patient presented trial information

5 patient refused any trial

5 patient went on trial

Standard of Care

Investigators

Patient Consent

Site Profile: Large Private Practice

## General Information

- 5,000 patients/yr., 25 medical oncologists
- 200 New NSCLC patients/yr.
- No 2<sup>nd</sup> line metastatic NSCLC trials

## Data Coordinator

- 200 NSCLC – new or existing patient, staging, and progression rates provided

## Principal Investigator

- In charge of the research program
- NSCLC standard of care pem/carbo +/- bev or gem/carbo 1<sup>st</sup> line, erlotinib or docetaxel 2<sup>nd</sup> line
- Switch maintenance in 20% of patients

## Study Coordinator

- Reviews all new patients to practice
- Distribution of patients between PI and Sub-I's is even

## Sub Investigators

- Awareness of study and relationship with study coordinator and principal investigator

# Case 3: Small Private Practice NSCLC Trial

Trial Design

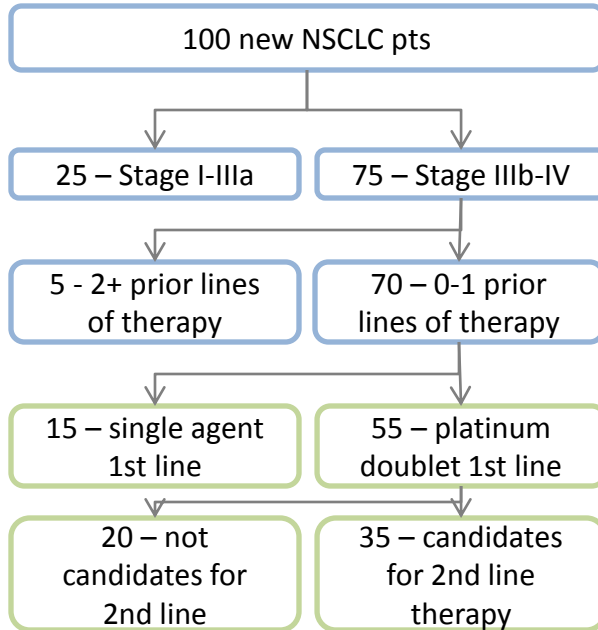
- Age  $\geq$  18 years
- Inoperable metastatic NSCLC
- 1 prior platinum based regimen in the met. setting

**R**  
1:1

Arm A: docetaxel + NEW Drug

Arm B: docetaxel + placebo

Demographics



Similarly in small practices, if most physicians are engaged the accrual can be as good as that of larger sites

Standard of Care

Investigators

Patient Consent

**Site Profile:** Small Private Practice

## General Information

- 2,500 patients/yr., 10 medical oncologists
- 100 New NSCLC patients/yr.
- No 2<sup>nd</sup> line metastatic NSCLC trials

## Data Coordinator

- 100 NSCLC – new or existing patient, staging, and progression rates provided

## Principal Investigator

- In charge of the research program
- NSCLC standard of care pem/carbo +/- bev or gem/carbo 1<sup>st</sup> line, erlotinib or docetaxel 2<sup>nd</sup> line
- Switch maintenance in 20% of patients

## Study Coordinator

- Reviews all new patients to practice
- Distribution of patients between PI and Sub-I's is even

## Sub Investigators

- Awareness of study and relationship with study coordinator and principal investigator

4 investigators see 40% of NSCLC pts and put 35% on clinical trials

5 patients presented trial

6 investigators see 60% of NSCLC and put 5% on clinical trial

1 patients presented trial

6 patient presented trial information

3 patient refused any trial

3 patient went on trial

# Choosing the Right Sites & Investigators

## Identification

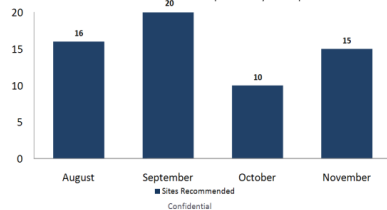
Use DAVA physician database to generate comprehensive potential site list based upon study criteria, our experience with the sites and DAVA MD relationships

## Analysis

DAVA MDs analyze sites and evaluate their qualifications, capabilities and potential enrollment through site specific questions. DAVA MD contacts site MDs to discuss study rationale and any potential hurdles to the protocol

### Site Recommendation Performance

- DAVA Involvement**
- July 2010 – December 2010
  - 48% of the 69 selected sites have been recommended by DAVA
- Sites Recommended**
- 20 Sites DAVA recommended had previously declined
  - 17 Sites DAVA recommended were previously unresponsive






## Recommendation

DAVA MDs obtain site interest. Once interest is expressed, Clinical Trial Specialists contact sites to complete site documents. DAVA gains commitment from qualified sites and discusses recommended sites with the sponsor



## Case study: 70% increase in site commitment

- Sponsor requested DAVA to re-engage sites regarding participation in clinical trial
- DAVA recommended 47 uncommitted sites out of 67 total sites previously contacted by sponsor.
- Personal medical oncology calls and visits with PI's and research staff were the most effective means of enlisting support for the trial

Recruited Sites	
 Previously unresponsive to sponsor	22 (46.8%)
 Previously declined to sponsor	22 (46.8%)
 Were not contacted by sponsor	3 (6.4%)

### DAVA Site Recommendations

Utilizing a direct physician-to-physician approach to engage potential investigators is effective in generating interest and commitment at the site level. This model reflects a finding by Coomis et al (J Onc Prac. 2009; 5: p50) that 73% of overall clinical trial awareness was generated by physicians' interest in the scientific rationale of the study.

*White Paper 2011*



## Lessons in Cancer Site Selection

- Protocol designed to work within standard of care
- Significant patient population
- History of high accrual
- Investigator understands study rationale and challenges from discussion with study affiliated medical oncologist or other clinical expert
- Investigator is excited by study
- Site meets all GCP/ICH and FDA guidelines
- Site has appropriate facilities, staff, equipment and technology to complete study





# Thank you for your participation!

Join us for our next presentation!  
**Recruiting Patients for Cancer Trials:  
Focus on the Physicians!**

February 8, 2012

4:05 pm - 4:20 pm

Symphony Ballroom II

If you have any questions, please contact me!

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