FLORIDA CANCER SPECIALISTS & Research Institute

Clinical Trials

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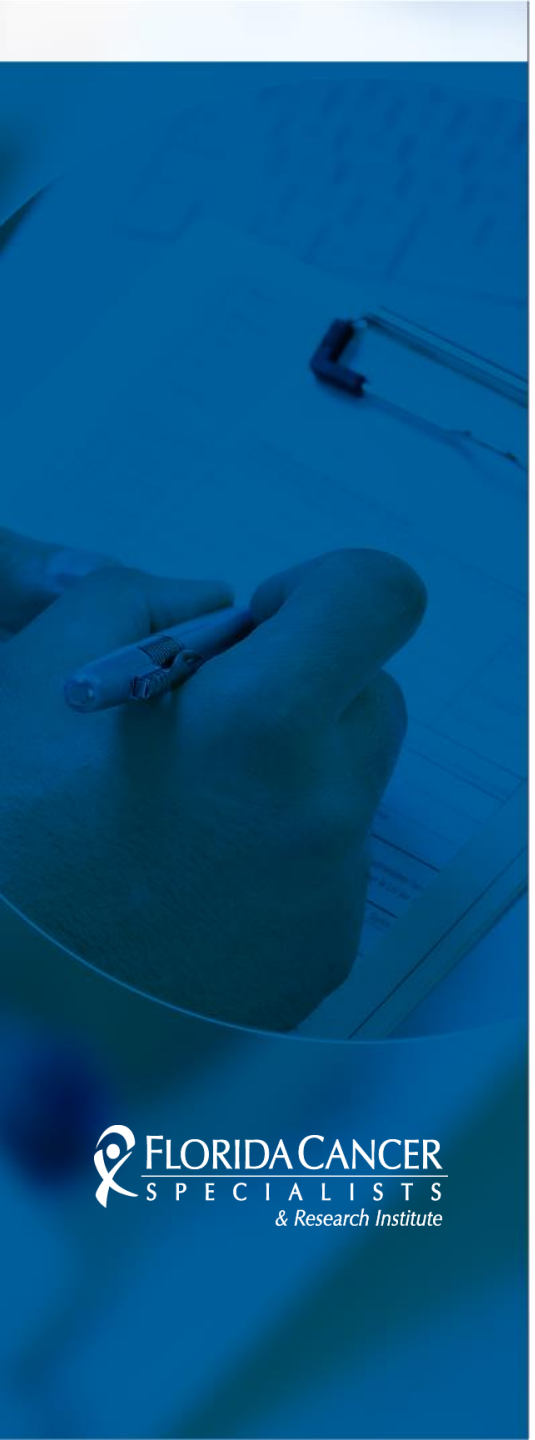
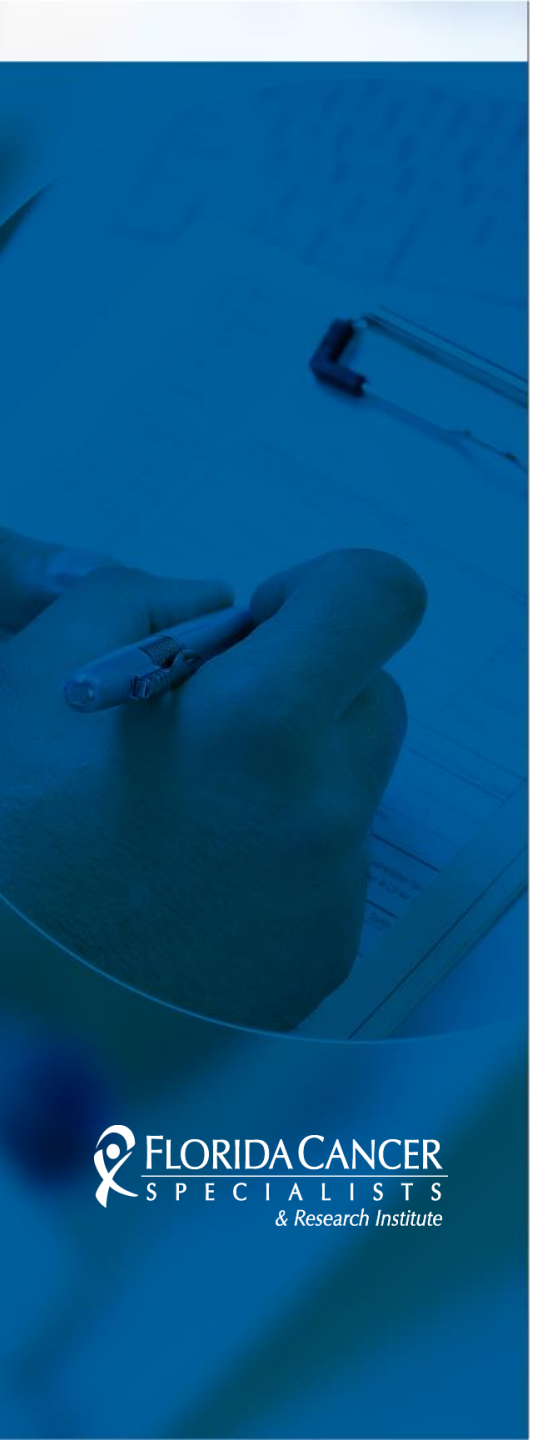
Florida Cancer Specialists
“Great Strides Together”



Utilizing a team approach to provide the best care to the patient in oncology clinical trials



Outline

- Importance of Clinical Trials
- Oncology Progress
- Clinical Trial Model
- Clinical Trial Team
- Challenges
- Hope for the future

Importance of Clinical Trials

- In 2019 in the US, estimated
  - 1,762,450 new cases of cancer
  - 606,880 people will die from cancer
- In 2019 in Florida, estimated:
  - 131,470 new cases
  - 45,000 deaths

Clinical trials are the key to making progress

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2019 Estimates

Estimated New Cases

Male			Female		
Prostate	174,650	20%	Breast	268,600	30%
Lung & bronchus	116,440	13%	Lung & bronchus	111,710	13%
Colon & rectum	78,500	9%	Colon & rectum	67,100	7%
Urinary bladder	61,700	7%	Uterine corpus	61,880	7%
Melanoma of the skin	57,220	7%	Melanoma of the skin	39,260	5%
Kidney & renal pelvis	44,120	5%	Thyroid	37,810	4%
Non-Hodgkin lymphoma	41,090	5%	Non-Hodgkin lymphoma	33,110	4%
Oral cavity & pharynx	38,140	4%	Kidney & renal pelvis	29,700	3%
Leukemia	35,920	4%	Pancreas	26,830	3%
Pancreas	29,940	3%	Leukemia	25,860	3%
All sites	**870,970**		**All sites**	**891,480**	

Estimated Deaths

Male			Female		
Lung & bronchus	76,650	24%	Lung & bronchus	66,020	23%
Prostate	31,620	10%	Breast	41,760	15%
Colon & rectum	27,640	9%	Colon & rectum	23,380	8%
Pancreas	23,800	7%	Pancreas	21,950	8%
Liver & intrahepatic bile duct	21,600	7%	Ovary	13,980	5%
Leukemia	13,150	4%	Uterine corpus	12,160	4%
Esophagus	13,020	4%	Liver & intrahepatic bile duct	10,180	4%
Urinary bladder	12,870	4%	Leukemia	9,690	3%
Non-Hodgkin lymphoma	11,510	4%	Non-Hodgkin lymphoma	8,460	3%
Brain & other nervous system	9,910	3%	Brain & other nervous system	7,850	3%
All sites	**321,670**		**All sites**	**285,210**	

Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

Importance of Clinical Trials

- Death rate from cancer in US has declined steadily over past 2 decades (American Cancer Society).
- Death rate in 2015 was 26% less than it was in 1991.

Importance of Clinical Trials

- Today people are living longer due to improvements in
  - Cancer Treatment
    - Safer and more effective due to clinical trials studying
      - Drugs, Vaccines, Surgery, XRT, immunotherapy
  - Cancer Detection
    - Improved screening
  - Cancer Prevention
    - Tobacco, Obesity
  - Supportive Care

Summary of Historical Progress in Oncology

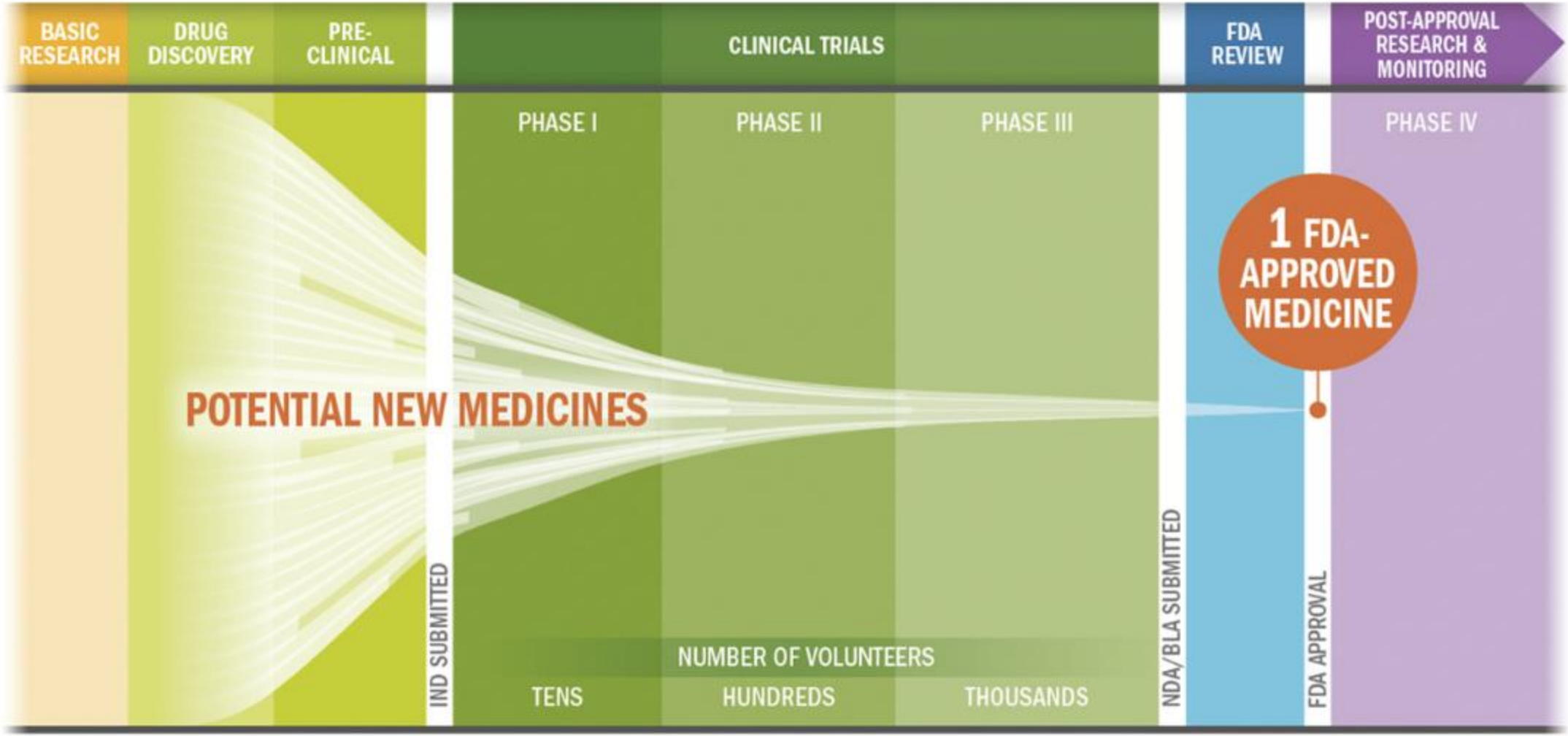
- 1846: Advent of general anesthesia opens door for modern cancer surgery
- 1884: Radical Mastectomy
- 1903: Radiation Therapy to Treat Cancer
- 1940s: Pap test, First chemotherapy drug
- 1960s: Philadelphia Chromosome, MOPP cures 50% Hodgkin Lymphoma, and FOBT for colorectal cancer screen
- 1970s: CT scan first used, CMF/mammogram
- 1980s: PSA, Tamoxifen, Procrit, Neupogen
- 1990s: laparoscopy, anti-emetics, Taxanes, Rituxan, Herceptin
- 2000s: Gleevec, Human Genome Project, EGFR agents, Avastin, Erbitux, Vectibix, Gardasil
- 2010s: Immunotherapy, AIs, CLL therapy, PD-1 and PDL-1, CDK, CAR-T

Practice Changing Clinical Trials at FCS in Breast Cancer

- ATAC Trial
  - Arimidex, Tamoxifen, Alone or in Combination
- NSABP trastuzamab
  - Adjuvant therapy for HER2+ breast cancer
- APHINITY
  - Adding pertuzumab to trastuzumab after surgery for HER2+ breast cancer
- Impassion 130
  - Immunotherapy + chemo in metastatic triple negative breast cancer

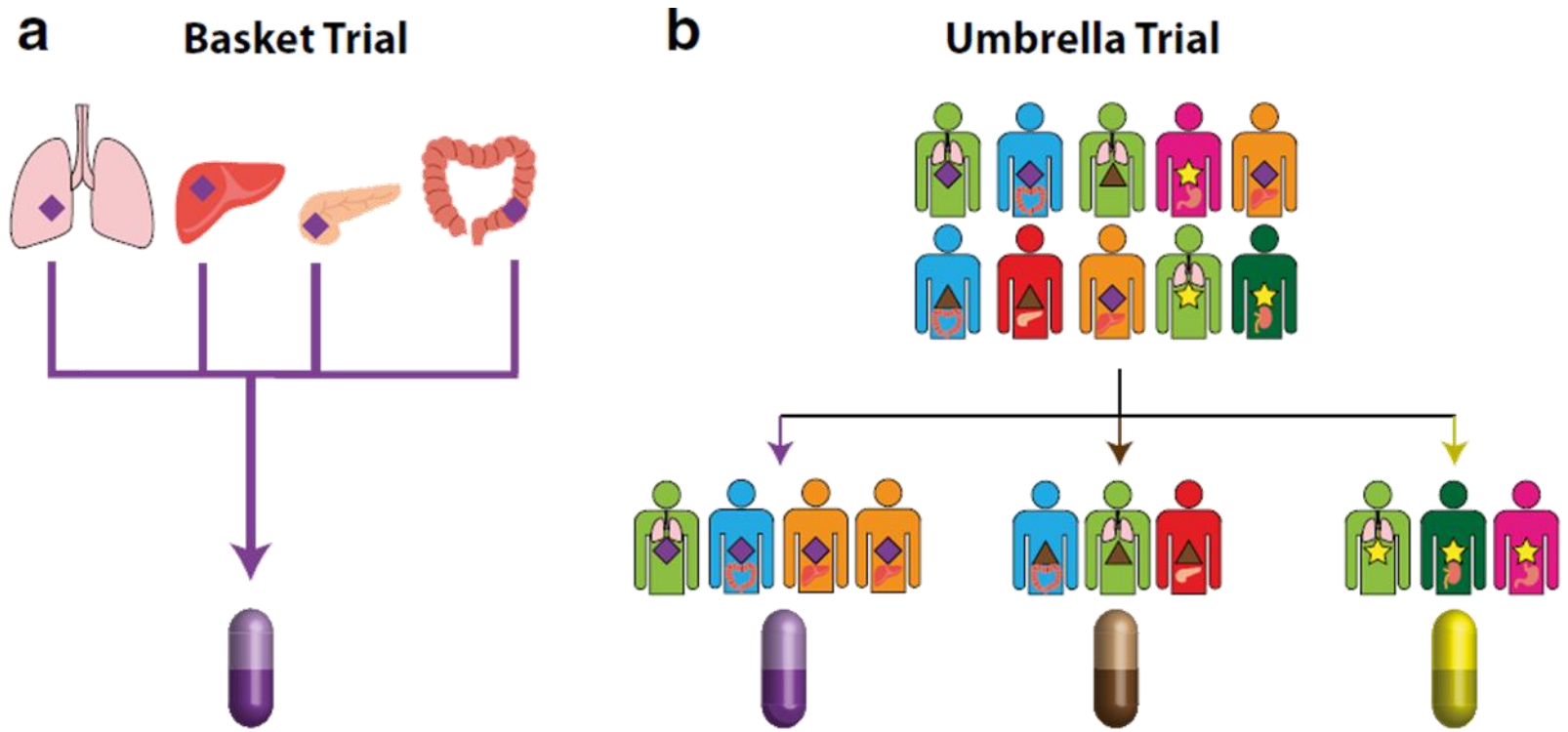
Clinical Trial Steps

- Phase I
  - Find a safe dose (MTD and DLT)
  - How should treatment be given
  - Unknown whether drug will be effective
- Phase II
  - To determine if new treatment has an effect on certain cancer
  - Using maximum tolerated dose and dose limited toxicities
- Phase III
  - Current standard against promising alternative

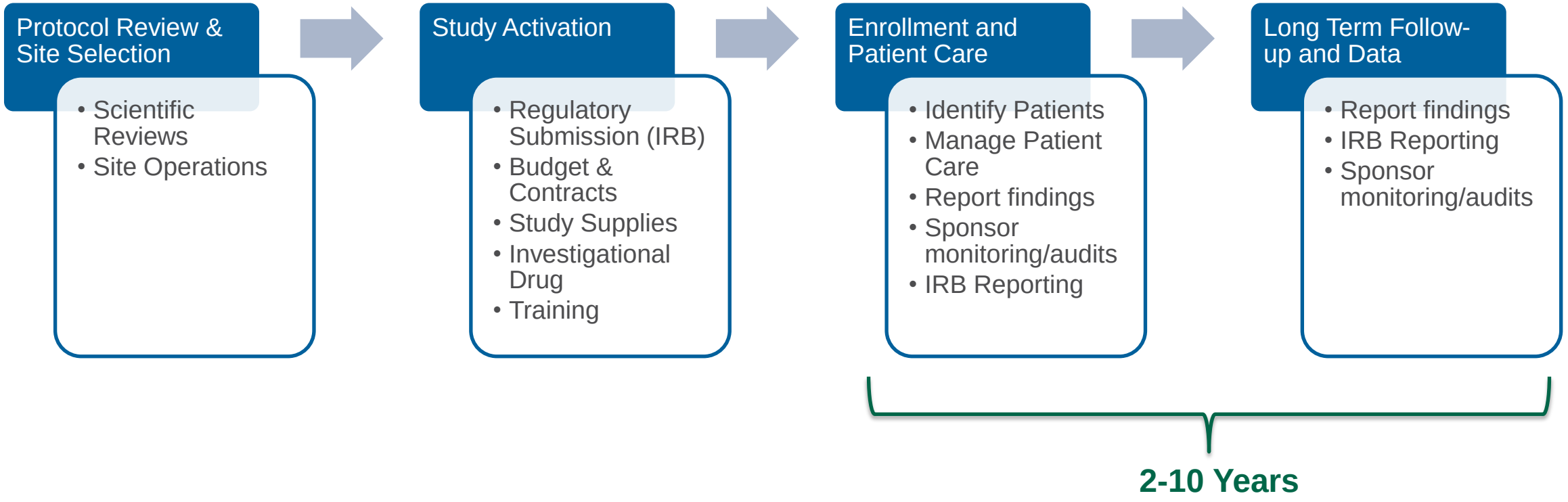


Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

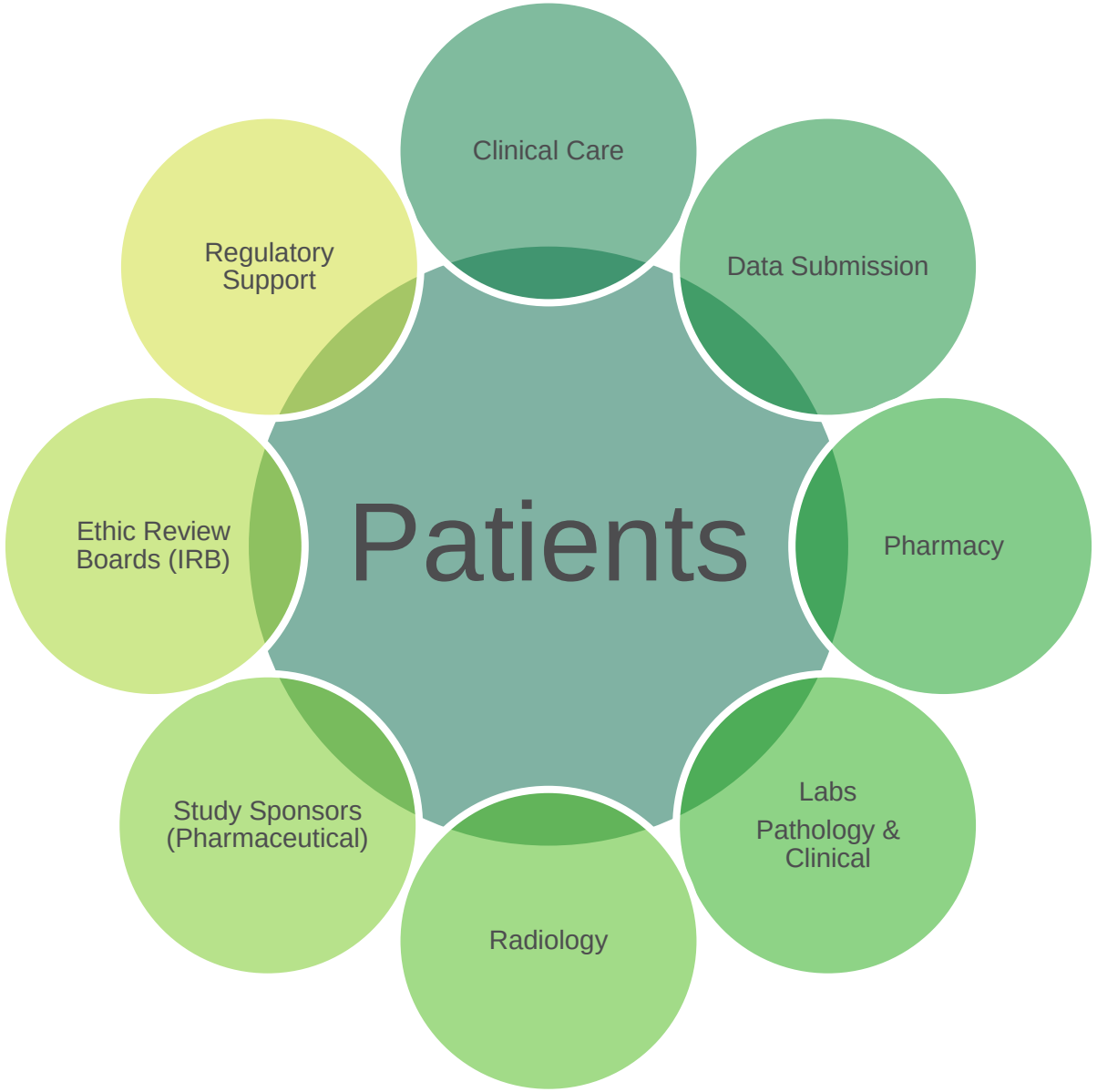
Innovative Trial Design & Increasing Complexity For Targeted Therapy



Opening and Managing Clinical Trials



Research Team



Clinical Trial Team

- Principal investigator (PI)
- Sub Investigator (Sub-I)
- Pharmacists
- Clinical Research Coordinator
- Regulatory Specialist
- Data Manager
- Contract & Budget Specialists
- Quality & Education

Clinical Trial Team: Principal Investigator

- An individual who conducts a clinical investigation
- Responsible leader of team
  - Ensures investigation is conducted according to signed investigator statement, investigational plan, and regulations
  - Protects rights, safety, welfare, of subjects
  - Protects control of drugs under investigation
- Responsibilities
  - Protocol compliance
  - Informed consent
  - Record Keeping and Retention
  - Control of investigational drug
  - IRB review and approval
  - Adverse event reporting
  - Integrity of date / inspection of records

Clinical Trial Team: Sub-investigator

- Research team member designated and supervised by Principal Investigator to perform critical study-related procedures and/or to make important study-related decisions
  - FDA regards sub-investigators as those individuals authorized to make medical judgements and decisions regarding study subjects
    - Facilitate consent process
    - Educate patients about research medication and adverse events
    - Assess and monitor adverse events
    - Provide direct patient care

Clinical Trial Team: Clinical Research Coordinator

- Manages and conducts day-to-day study activities in accordance with protocol, applicable regulations and GCP requirements
  - Proper consenting of subjects
  - Coordination of clinical treatment, study visits, and follow-up
  - Subject screening, recruitment, enrollment,
  - Maintenance of study source documents
  - Proper reporting of adverse effects

Clinical Trial Team: Regulatory Specialist

- Maintains regulatory submissions to IRB

Clinical Trial Team: Data Manager

- Abstract research data from patient's medical record/source documents to the case report form and enter data into database
- Conduct self-audits to ensure data quality
- Provide periodic reports from database
- Assist in preparation for audits/monitoring visits

Clinical Trial Team

- Appropriate skills and training
- Good Clinical Practice standard
- Follow protocol standards
- Adheres to site Standard Operating Procedures

Challenges in Clinical Trials

- Fewer than 1 in 20 adult cancer patients enroll in clinical trials
- Why?
- What can we do to improve this and get new treatments to our patients more quickly?

Challenges in Clinical Trials

- Structural challenges
- Clinical challenges
- Awareness
- Attitudes
- Demographic/Socioeconomic

Challenges to Clinical Trials

- Structural Challenges
  - Transportation, travel costs, access to insurance, child care
  - Access

- Clinical Challenges
  - Ineligibility to available protocols
  - Narrow eligibility criteria.
    - Comorbidities and Performance Status restrictions
      - Sacrificing generalizability.

Challenges to Clinical Trials

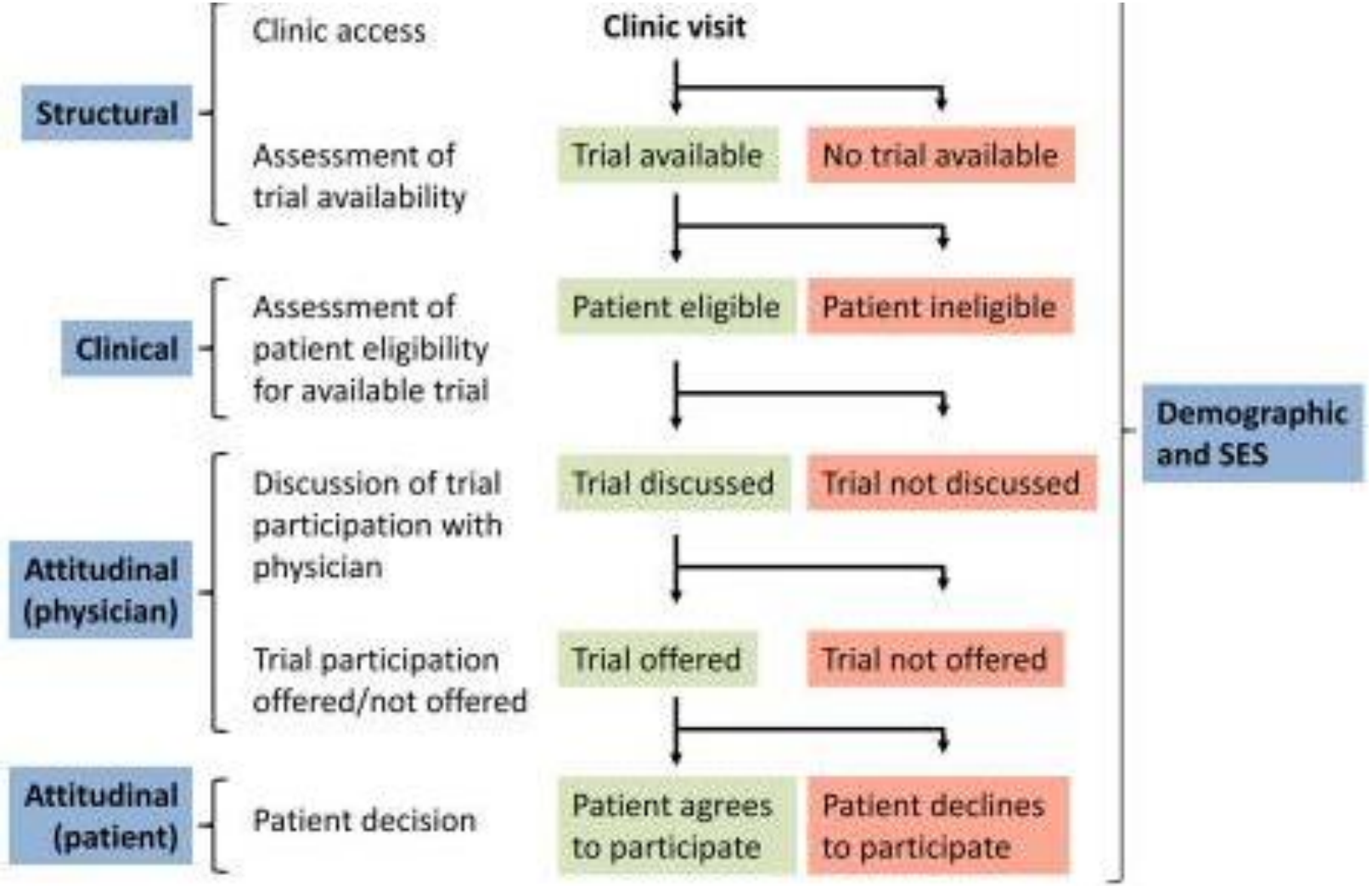
- Awareness by patients
  - Awareness changes attitudes toward clinical trials, enrollment and benefits of participation.
    - 85% of patients were either unaware/unsure that participation in a clinical trial was an option at time of diagnosis
    - 75% of these patients said they would have been willing to enroll had they known it was possible
    - (Harris Interactive Survey 2001)
  - Focus groups with the public and caregivers found that many lacked familiarity with clinical trials and were unaware of opportunities for participation by healthy volunteers.
    - They generally expressed negative attitudes about participation.
    - These attitudes significantly changed after learning more about clinical trials (NIH CRA Focus Groups 2011)

Challenges to Clinical Trials

- Physician Attitudes and Awareness:
  - Most agree clinical trials provide high quality care and benefit patients.
  - Many have strong inclination toward specific treatment.
  - Randomization.
  - Time prohibitive.
- Demographic /Socioeconomic

Challenges to Clinical Trials

- Patient Attitudes:
  - Ultimately decision rests with patient
  - Mistrust of medicine
  - Easy to read consents
  - Fear of experimentation/randomization “guinea pig”
  - More frequent monitoring (time, QOL)
  - Cost (second most frequent reason)

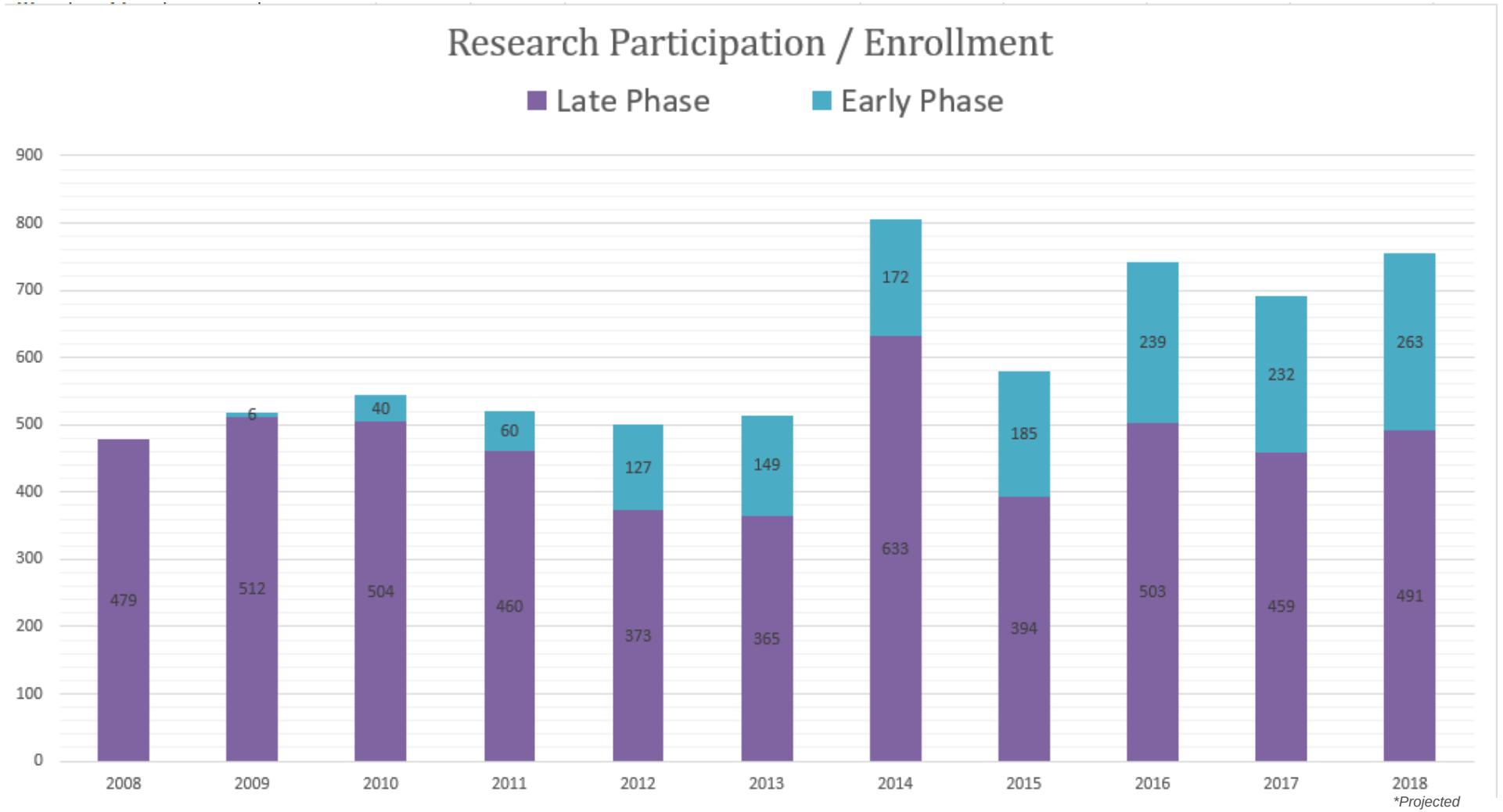

Clinic visit
Structural
Clinic access
Assessment of trial availability
Trial available
No trial available
Clinical
Assessment of patient eligibility for available trial
Patient eligible
Patient ineligible
Attitudinal (physician)
Discussion of trial participation with physician
Trial discussed
Trial not discussed
Trial participation offered/not offered
Trial offered
Trial not offered
Attitudinal (patient)
Patient decision
Patient agrees to participate
Patient declines to participate
Demographic and SES

Hope

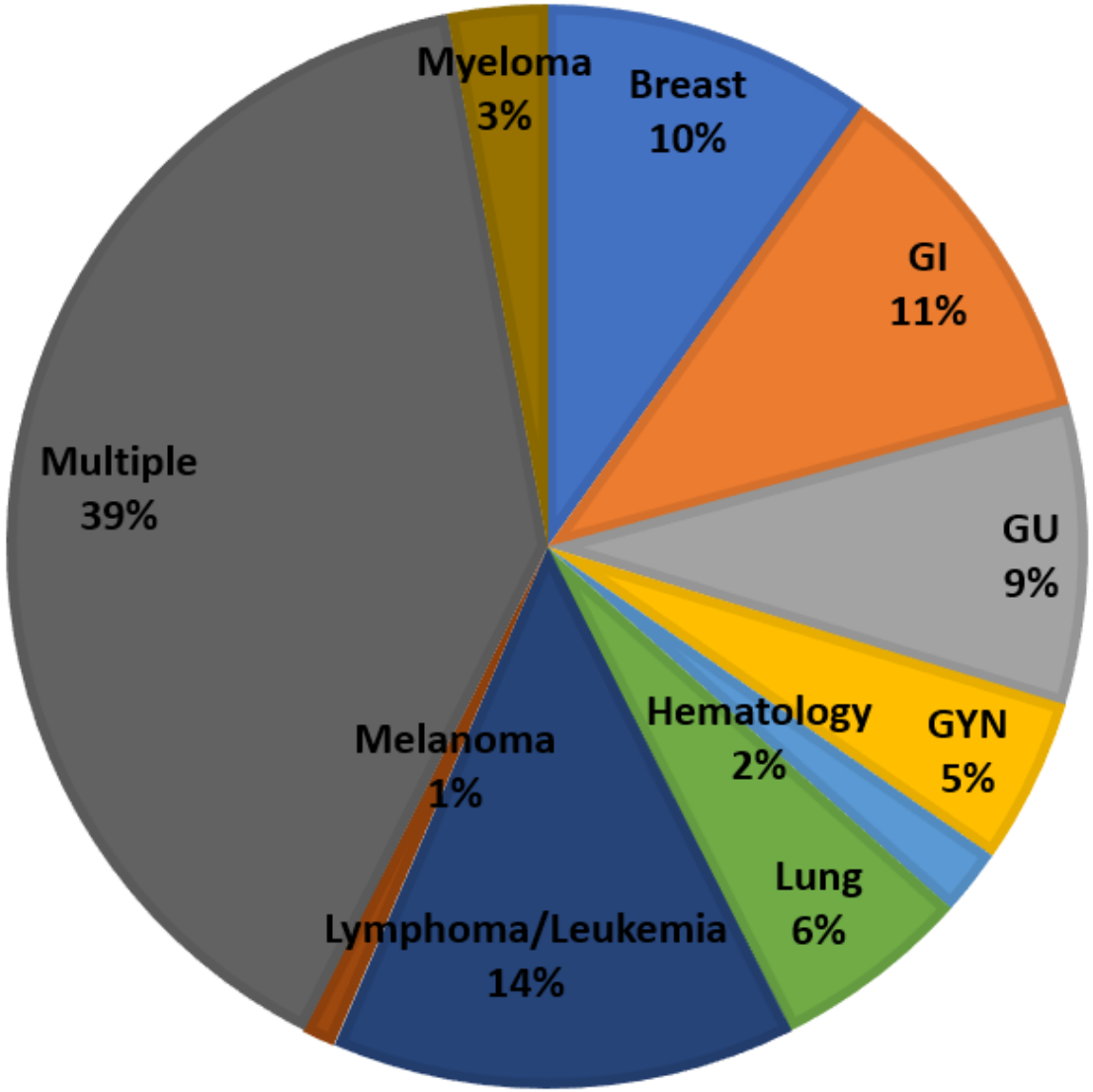
- We have work to do
- Increase availability of clinical trials
- Awareness of Trials available on web

Ongoing Clinical Trials

- Combination Immune Check Point Inhibitors with other treatments
  - Doublets and triplets
- Adjuvant CDK 4/6 inhibitors
  - For early HR+ Breast Cancer
- Trastuzumab deruxtecan, tucatinib, margetuximab
  - For advanced HER2+ breast cancer
- New approaches with CAR-T cells
  - For Leukemia, lymphoma, and myeloma
- Precision Medicine
  - Trials for specific genomic alterations and mutations
- Liquid biopsy
  - Early drug resistance, minimal residual disease, and precision medicine trials


Research Participation / Enrollment
Late Phase
Early Phase
900
800
700
600
500
400
300
200
100
0
479
512
6
504
40
460
60
373
127
365
149
633
172
394
185
503
239
459
232
491
263
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
*Projected

CLINICAL TRIAL MENU



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