Why We Do Research: Clinical Trials

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Objectives:

▪ Assess need for Research
▪ Define Clinical Trials
▪ Discuss Types of Clinical Trial
▪ Review History of Cancer Progress
▪ Explore recent and ongoing clinical trials
Have you ever ordered, educated about, infused, assessed, or treated any side effects for cancer treatment?

Yes
No
Definition of Clinical Trials

World Health Organization Definition: A **clinical trial** is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioral treatments, process-of-care changes, preventive care, etc.

Types of Research
WATChING YOUR STEP – THE DIFFERENT STAGES OF CLINICAL DEVELOPMENT AND WHAT THEY EXAMINE

PHASE I
Checking for safety
Sample: 10-20 healthy volunteers
Unexpected side effects may occur

PHASE II
Checking for efficacy
Sample: about 200 patients
Most research projects fail in Phase II due to product not being as effective as anticipated

PHASE III
Confirm findings in large patient population
Sample: more than 1,000 people
Likelihood to detect rare side effects increases with number of people involved

PHASE IV
Testing long-term safety in diverse patient population
Sample: "real life patients" – testing being carried out outside of clinical environment (post-marketing studies)
Previously untested groups may show adverse reactions

Source: AGCS
Cancer Progress 1990’s:

1991 – Ondansetron approved by FDA to prevent chemotherapy/radiation induced nausea and vomiting

1993 – Melanoma is linked to sun exposure

1997 – Rituximab becomes first ever targeted cancer drug approved by FDA

1999 – First targeted anti-breast cancer drug, Trastuzumab is approved

https://www.asco.org/research-progress/cancer-progress-timeline
Bladder Cancer: aboutcancer.com

Five Year Survival Rates for Bladder Cancer Cases Diagnosed in 1995 and 1996
All States / Data Reported from 1,688 Hospitals
Hospitals of Type: All

Survival at: diag, after 1 yr, after 2 yr, after 3 yr, after 4 yr, after 5 yr

Survival when diagnosed on stage: O, I, II, III, IV, Overall
Cancer Progress Early 2000’s:

2001 - Imatinib approved for CML, made CML a manageable, chronic disease

2003 – Scientists decode the human genome, targeted treatments for EGFR (Gefitinib and Erlotinib) are approved

2004 – Bevacizumab approved, adjuvant chemotherapy for lung cancer proven to dramatically improve NSCLC

2006 – Human Papillomavirus 0-Valent Vaccine approved for women ages 9-26 to help prevent cervical cancer

2010 – Ipilimumab approved for Advanced Melanoma, CT scanning found to reduce lung cancer deaths among heavy smokers

https://www.asco.org/research-progress/cancer-progress-timeline
Cancer Progress 2011 and Beyond:

2011 – Aromatase inhibitors found to decrease breast cancer risk in post-menopausal women.

2013 – CAR-T therapy trial let to complete remission of acute lymphoblastic leukemia (ALL) that had not responded to previous aggressive treatment in 2 children.

2014 – Four new drugs transform CLL: Obinutuzumab, Ofatumumab, Idealalisib and Brutinib; FDA approved Pembrolizumab and Nivolumab for Advanced Melanoma.

2015 – Cyclin-dependent kinase (CDK) inhibitors were developed and granted accelerated approval by FDA; FDA also approved 3 new immunotherapies for NSCLC: Nivolumab, Atezolizumab, and Pembrolizumab.

2016 – Studies showed childhood cancer survivors are living longer and healthier; The rate of death from any cause within 15 years of childhood cancer diagnosis declines by half (12% to 6%) among survivors treated in the 1990s vs. 1970s. Contributed to lower doses of radiation and anthracycline chemotherapy. First new treatment for bladder cancer in 3 decades was approved: Atezolizumab.

2017 – First gene therapy is approved by FDA: Chimeric Antigen Receptor-Modified T cell (CAR-T) Therapy Tisagenlecleucel causes complete remission in a majority of young patients with B-cell ALL that progressed despite previous treatment with standard therapies.

https://www.asco.org/research-progress/cancer-progress-timeline
Breast Cancer

% of Patients Surviving Five Years

Year of Diagnosis
Childhood ALL

[Graph showing survival rates over years since diagnosis for different time periods, with labels for each period and their respective sample sizes.]
CAR-T Cell for ALL

- 2 kids with relapsed and refractory B-Cell ALL received infusions of T cells transduced with anti-CD19 antibody and a T-cell signaling molecule
- In both patient’s CTL019 T cells expanded to a level that was more than 1000 times as high as the initial engraftment.
- Cells were identified in the bone marrow and CSF
- Can cause Cytokine release syndrome, etanercept and tocilizumab helped to reverse symptoms and did not prevent expansion of the CAR-T cells or antileukemic efficacy
- CR was observed in both pts. And 1 is ongoing 11 months post tx. The 2nd had a relapse 2 months after treatment but with blast cells that no longer expressed CD19

SWOG 0337: Gemcitabine vs. Saline

The study looked at Gemcitabine vs. Saline in the prevention of bladder cancer recurrence in non-muscle invasive bladder cancer (NIMIBC), published by Dr. Messing in JAMA.

Demonstrated a significant decrease both in the intention to treat a population of patients suspected of having low-risk NIMIBC and an even greater benefit among the per protocol analysis of patients with pathologically proven low risk disease.
POLO Trial

Phase III Trial

Found that maintenance therapy with Olaparib significantly delayed the progression of metastatic pancreatic cancer in patients with BRCA gene mutations compared with placebo (median PFS was 7.4 months vs. 3.8 months respectively)

Given to patients who had not progressed after completion of initial platinum based chemotherapy and after 2 years 22.1% of people receiving Olaparib has no PD vs 9.6% for those treated with placebo

Pending mature survival data
KeyNote-001

Showed Pembrolizumab was safe and effective

Substantially increased overall survival for advances NSCLC

23.2% of people who had not previously been treated with chemotherapy and 15.5% of previously treated patients were alive after 5 years with the greatest benefit observed in patients with higher PD-L1 expression

Marked improvement over 5 year survival rates from pre immunotherapy which averaged 5.5% for NSCLC
Access to Therapies

August 8, 2019

CMS released a national coverage determination (NCD) on CAR-T cell Therapy that provides increased access to Medicare beneficiaries.

Opened door to receive CAR-T cell therapy in an outpatient setting which will reduce the cost.

Removes ambiguity around what CMS will cover.

Still does not cover full cost.

https://www.ascopost.com/News/60327
Rules to Research by:

- Federal Code of Regulations 21 Part 11 compliant
- International Conference on Harmonization (ICH 6) and Good Clinical Practice
- Institutional Review Board
Randomization / Open Label

- What does it mean
- Why is it done
- Terms: Control Arm vs. Study Arm
Recruiting Tips

• Present Research Early

• Use EMR’s Effectively
  • Run Reports
  • View the reason for visit tab

• Prescreen Patients – targeting New Patients, Surgical referrals, Patient’s post imaging,

• Keep list of potential patients – if on 1st line now and you have a 2nd line study start the conversation

• Perfecting your Approach
EAP/Compassionate Use

Access to medication prior to FDA approval

- Sponsor needs to have a program for the compound
- Treating MD needs to write a letter of need
- Sponsor Approval/FDA Approval
- Must pass IRB approval
Resources:

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 315,240 research studies in all 50 states and in 209 countries.
ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

Before participating in a study, talk to your healthcare providers and learn about the risks and potential benefits.

Find a study (all fields required)

- Status:
  - Option 1: Recruiting and not yet recruiting studies
  - Option 2: All studies

- Condition or disease (For example: breast cancer)

- Other terms (For example: NCT number, drug name, investigator name)

- Country

Search Advanced Search
Resources:

Common Terminology Criteria for Adverse Events (CTCAE)
Version 4.0
Published: May 28, 2009 (v4.03: June 14, 2010)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Cancer Institute
• Everyone with XYZ cancer will qualify for this study

• Everything is free for patient’s on study

• Once you are on study you cannot get out

• Protocols are easy to write
• Everyone with XYZ cancer will qualify for this study
  • False— all studies have very specific inclusion/exclusion criteria for subjects to participate

• Everything is free for patient’s on study
  • False— majority of the exams on study will align with standard of care and go through the patient’s insurance, the sponsor is required to cover anything that is not approved or above the standard

• Once you are on study you cannot get out
  • False – subjects always have the option to stop the study, the treating physician can also take them off study if they feel there is a better option available

• Protocols are easy to write
  • True – most sites have a template and a team to help with this 😊
Questions