

Oncology as a Therapeutic Area in Clinical Trials

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Dr. Digant Gupta

Experience and Accomplishments

- Over **15 years** of experience in Evidence-Based Clinical and Outcomes Research
- Designed, implemented and monitored clinical epidemiologic studies and trials
- Extensive experience with advanced statistical analysis
- Published **75** international papers and over **200** abstracts in peer-reviewed medical and scientific literature
- Member of the editorial board for **9** high-impact biomedical journals
- Invited scientific reviewer for **35+** high-impact biomedical journals

Education

- *Master of Public Health (MPH)* in Epidemiology and Biostatistics from the University of Illinois at **Chicago, USA**
- *Bachelors in Medicine and Surgery (MBBS)* from B.J. Medical College, **Pune, India**

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Agenda

- ❑ Importance of domain knowledge
- ❑ Introduction to cancer
- ❑ Cancer diagnosis and staging
- ❑ Basics of cancer treatment
- ❑ Clinical endpoints in cancer
- ❑ RECIST guidelines
- ❑ Discussion and Q/A

Importance of Domain Knowledge

Understanding of Domain

- ❑ Work in Clinical Trial Services **not just about effective usage** of analytical tools such as SAS
- ❑ Rather, it is much more about **applying the knowledge of the domain/therapeutic area** to determine the right procedure, approach and the tools to be used for the analysis
- ❑ A crisp orientation course on different therapeutic areas becomes crucial in order to ensure **a high level of performance** from professionals working on a project in a specific area
- ❑ SAS professionals/statisticians need to be able to **communicate with the domain team** in their language to be effective
- ❑ Domain concepts **different from** the basic clinical trial concepts that are common to all therapeutic areas

Therapeutic Areas/Domains

Allergy

Cardiovascular/Metabolic

CNS

Dermatology

Endocrinology

Gastroenterology

Haematology

Anti-infectives

Infectious Diseases

Musculoskeletal, Rheumatology & Osteology

Nephrology, Renal, & Urology

Neurosciences

Nutrition

Obstetrics/Gynaecology

Oncology

Ophthalmology

Pain Management

Rare Diseases

Respiratory and Immuno-Inflammatory

Transplantation

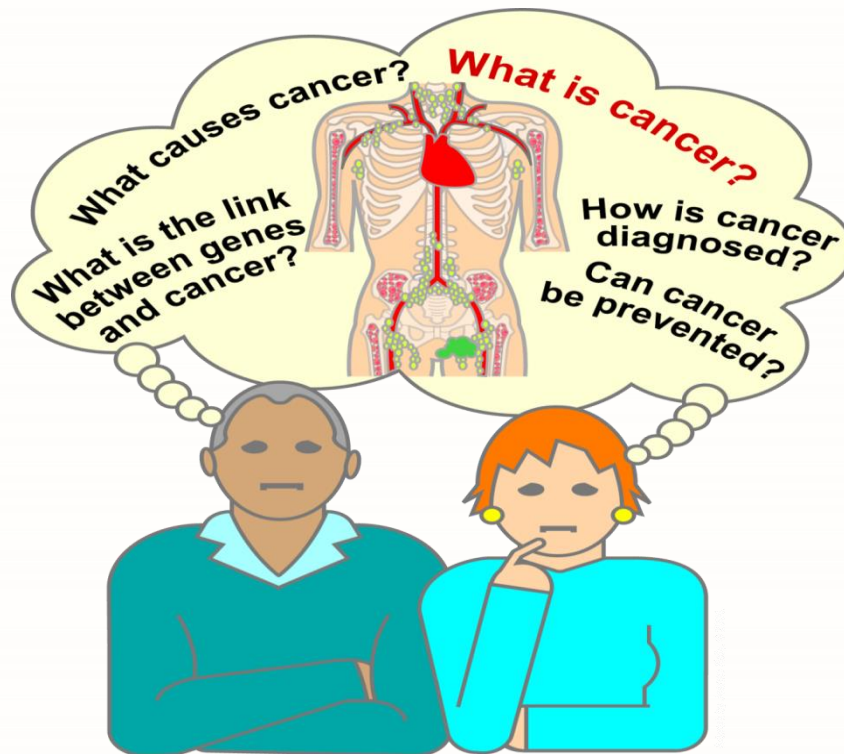
Vaccine & Virology

Why study Oncology?

- ❑ Medical specialty focusing on the **study, diagnosis and treatment of cancer**
- ❑ **Largest** and most **extensively studied** therapeutic areas in clinical research
- ❑ A tremendous amount of **research** conducted on all aspects of oncology has dramatically changed our understanding of the disease
- ❑ Oncology literature **very vast**, therefore, a basic understanding of the key concepts and terminology critical to a successful career in clinical research
- ❑ Clinical Trials in oncology somewhat more complicated than other therapeutic areas, with **Clinical Endpoint** and **Adverse Event Reporting** being some of the major differentiators

Introduction to Cancer

What is Cancer?



What is Cancer?

The term “*cancer*” refers to more than 100 different diseases that begin in the cells, the body’s basic unit of life.

Tumor Growth

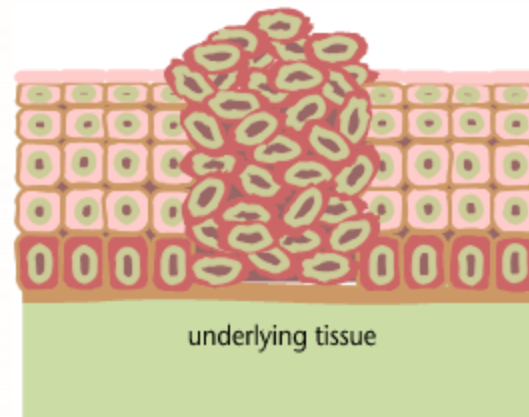
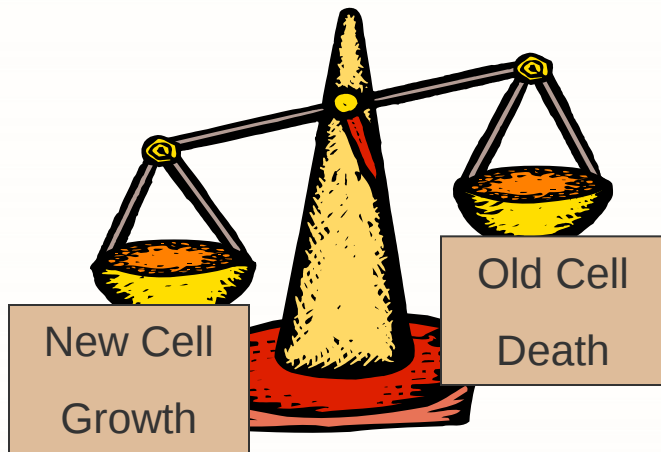


Image Source: National Cancer Institute

Benign Tumors

- ☐ Are not cancer
- ☐ Do not spread to other parts of the body
- ☐ Are usually not a threat to life

Malignant Tumors

- ☐ Are cancer
- ☐ Have cells that can grow without control and invade or damage other parts of the body
- ☐ When cancer (malignant tumor) spreads from the original site to another part of the body it is called metastasis

Types of Cancer

- ❑ There are over 100 different types of cancer
- ❑ Treatment decisions are based on knowing the type of cancer involved

Types of Cancer (contd)

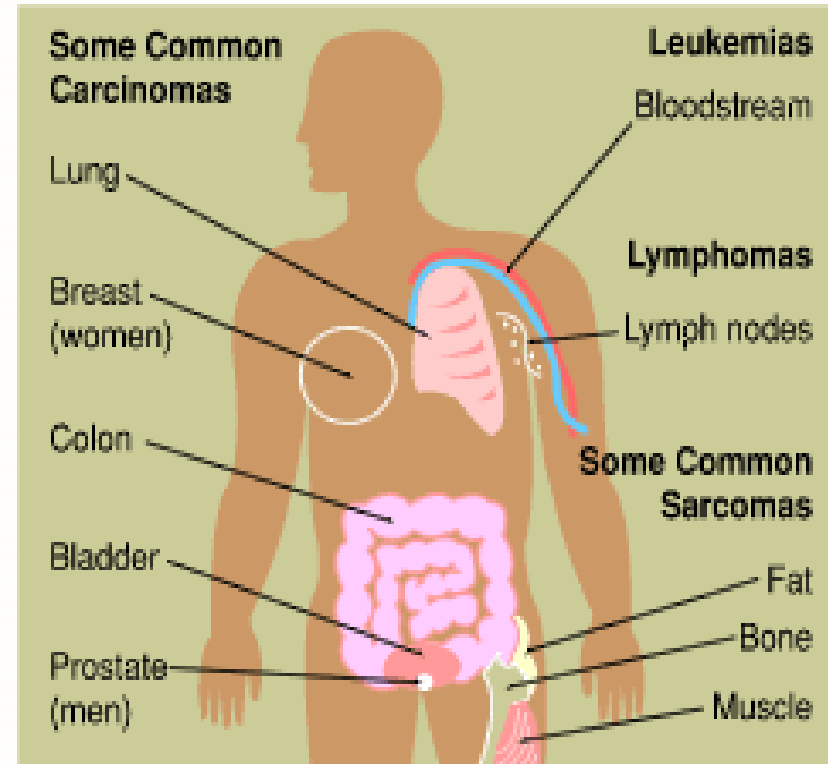
❑ Solid Tumors

- Carcinomas
- Sarcomas

❑ Cancers of the Blood & Bone Marrow

Marrow

- Leukemia
- Lymphoma
- Myeloma



Genetics

- ❑ Refers to the study of genes
- ❑ Plays a role in health and disease

Genes playing role in cancer development

- ☐ Oncogenes
- ☐ Tumor suppressor genes
- ☐ DNA repair genes

Cancer Diagnostics and Staging

Diagnosing Cancer

To diagnose the presence of cancer, a doctor must
remove a piece of affected tissue (biopsy) to look
at it under a microscope.

Biopsy

A biopsy is the surgical removal of a small piece of tissue for microscopic examination.



Photo credit: John Crawford | Source: NCI

Cell Differentiation

- ❑ Differentiation refers to how cancer cells look and function compared to normal cells.
- ❑ If the cells of the tumor and the organization of the tumor's tissue are close to those of normal cells and tissue, the tumor is called "well-differentiated".
- ❑ Poorly differentiated, or undifferentiated, cancer cells look abnormal and disorganized. The cells are often very different sizes and some may be larger than normal while others are smaller.

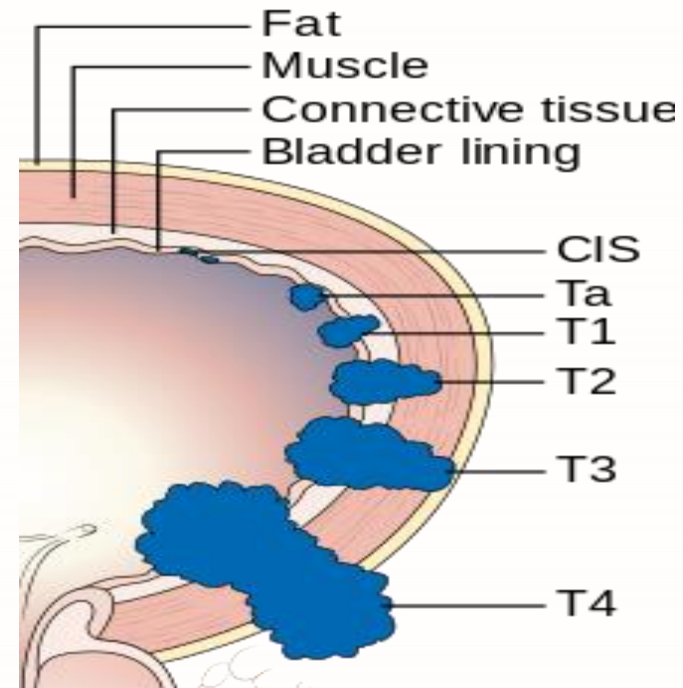
Grading (Histology)

- ❑ Degree of differentiation exhibited by cells
- ❑ How closely cells resemble normal tissue structure
 - Grade I – well-differentiated
 - Grade II – moderately differentiated
 - Grade III – poorly differentiated

Stages

The common stages of cancer are:

- In situ
- Localized
- Regional
- Distant
- Recurrent
- Unknown



Basics of Cancer Treatment

Cancer Treatment

The treatment team

- Patient
- Surgeons
- Medical oncologists
- Radiation oncologists
- Nurses
- Others

The treatment plan

- Surgery
- Chemotherapy
- Radiation therapy
- Hormone therapy
- Biological therapy
- Stem cell transplant
- Clinical trial

Local or systemic treatment?

Local treatment affects cancer cells in the tumor and the area near it

- Surgery
- Radiation therapy

Systemic treatment travels through the bloodstream reaching cancer cells all over the body

- Chemotherapy
- Hormone therapy
- Biological therapy
- Targeted therapy

Chemotherapy

Chemotherapy (also referred to as cancer chemotherapy) is the treatment of cancer with an antineoplastic drug or with a combination of such drugs into a standardized treatment regimen

Clinical Endpoints In Cancer

Overall Survival (OS)

□ Definition

- Defined as the time from randomization to death from any cause

□ Advantages

- Unambiguous endpoint that is not subject to investigator interpretation
- Universally accepted (gold-standard)

Overall Survival (OS)

❑ Drawbacks

- Requires large sample size and long follow-up
- Includes deaths unrelated to cancer

Time to Progression (TTP)

□ Definition

- Time from randomization until objective tumor progression; does not include deaths

□ Advantages

- Could use a smaller sample size and shorter follow-up than trials that require a survival endpoint
- Based on objective assessment

Time to Progression (TTP)

❑ Drawbacks

- Validation as a surrogate for survival can be difficult in some treatment settings
- Not precisely measured (i.e., measurement may be subject to bias)
- Definition may vary among trials
- Requires frequent radiologic or other assessments
- Requires balanced timing of assessment among treatment arms

RECIST Guidelines

What is RECIST?

- ❑ Response Evaluation Criteria In Solid Tumors (RECIST) is a set of published rules that define when cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progression") during treatments
- ❑ By an international collaboration including:
 - European Organisation for Research and Treatment of Cancer (EORTC)
 - National Cancer Institute of the United States
 - National Cancer Institute of Canada Clinical Trials Group
 - (3 years of regular meetings and exchange of ideas)

Eligibility

❑ What is **measurable disease**?

- *Measurable lesions* - lesions that can be accurately measured in at least one dimension with longest diameter ≥ 20 mm using conventional techniques or ≥ 10 mm with spiral CT scan.

Methods & Measurement

- ☐ CT and MRI best currently available methods to measure target lesions for response assessment
- ☐ Chest X-Ray lesions acceptable as measurable lesions when clearly defined and surrounded by aerated lung. However, CT is preferable
- ☐ No Ultrasound (US) to be used to measure tumor lesions
- ☐ Tumor markers alone never used to assess response

Suggested Online Courses

☐ Oncology Certificate Program

from University of Southern Indiana

☐ Understanding Oncology

from University of California, San Diego

☐ Monitoring Oncology Trials

from University of California, San Diego

☐ Oncology in Clinical Trials

from CliPLab (lms.cliplab.co.in)

Discussion and Q/A

Thank You

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