Oncology as a Therapeutic Area in Clinical Trials

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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

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<th>Therapeutic Areas/Domains</th>
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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 causes cancer?
What is the link between genes and cancer?
How is cancer diagnosed?
Can cancer be prevented?
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
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
  - 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
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
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 (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)
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.ciplab.co.in)
Discussion and Q/A
Thank You

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