Patient Care in Clinical Pharmacology Oncology Trials: Principal Investigator Perspective

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Objectives

- Describe the current experience of cancer patients participating in phase I clinical trials
- Introduce new considerations in phase I clinical trials in an era of novel cancer therapies
- Discuss tissue collection issues
- Address ethical considerations when including healthy volunteers in phase I studies

Phase I Trials in Oncology: Current Model

- Generally does not include healthy volunteers due to ethical considerations and concern for toxicity
- Primary aim is safety
- Risks of biopsies – location, amount of tissue, bleeding, infection
- Completed in patients with incurable and/or refractory cancers
  - Experiencing loss of independence
  - Countless appointments
  - Highly symptomatic – fatigue, weight loss, anorexia, pain
  - Progression on multiple lines of treatment
  - Cachetic, weak
  - Multiple drug/drug interactions

Why Do Cancer Patients Participate in Phase I Trials?

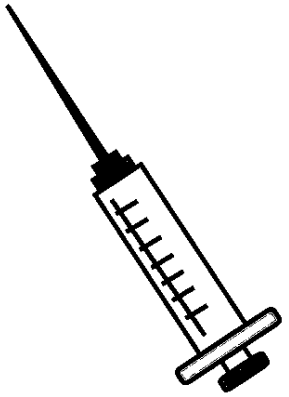
- Not ready to “give up”
- “Hope” defined by continued cancer treatment
- “Nothing to lose”
- Patients participate given “possible” therapeutic benefit (e.g., pembrolizumab)
- Legacy

Muro et al, Lancet Oncology 2016

Cancer Phase I Clinical Trials: New Considerations

- Non-cytotoxic anticancer therapies with lower toxicity
- Investigation of bioavailability/pharmacokinetics
- Data not confounded by disease, comorbidities, and other drugs
- Reduction in patient exposure to ineffective drugs and/or doses
- Potential faster accrual to study
- However, stricter regulatory requirements for preclinical data

Tissue Collection Challenges



- “Healthy” - Lack of tumor-derived tissue
- Degree of invasiveness and risk
- Samples
  - Blood draws
  - Saliva
  - Urine
  - Biopsies
- Imaging
- Financial considerations of future earnings (i.e., rights to DNA)

Would *you* participate in a cancer phase I study?

Healthy Volunteers: Setting A Higher Bar

- Motivation
- Decisional capacity
- Learning and communication assessment
- Informed consent
- Safety
- Coercion, incentives

Decisional Capacity in Ill Patients

- In my medical opinion, “John” has decision-making capacity as demonstrated by his ability to perform the following:
  1. To receive information
  2. To understand one's condition - ??
  3. To understand the treatment options, including consequences (benefits/risk) of the treatment as well as non-treatment
  4. To explain the reasoning behind the choice
  5. To express a choice consistently, over time

Huffman et al, J Clin Psychiatry 2003
Tunzi et al, Am Fam Physician 2001

Learning & Communicating

- “How do you best learn?”
- Move away from paper forms and legal jargon to preferred learning mediums of the participant
- Clear, everyday language
- Use of interpreters
- Having patient repeat and verbalize their own understanding

Ethical Considerations

- Informed consent
- Clear understanding of risks, benefits, alternatives – over time!
- Vulnerable patient populations
- Compensation – financial assessments
- Rights, resources if poor outcomes or side effects

Ideal Healthy Volunteer in a Cancer Phase I Study

- Financially secure
- Educated
- Middle-aged (beyond child bearing potential)
- Informed
- Motivated by personal experience or societal benefit
- Limited participation in trials
- Higher ethical bar – should these be a protected patient population?

Do these people exist?