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?