RISK/BENEFIT CONSIDERATIONS IN EARLY PHASE STUDIES

- Risks are **not** offset by potential benefit
- Assume prospect of direct benefit to study participants is extremely low
  - This is not fundamentally different from many other early phase trials, e.g. oncology
  - The enrollment of refractory cancer patients seems justifiable because if there was going to be a benefit, they would be the ones who most need it;
  - Need to distinguish between *hoping for benefit* and *reasonable probability of benefit*
- But in reality there is another implicit justification that it is more acceptable to expose these cancer patients to risk because they have exhausted all other options--
- In contrast, in HIV cure research with well controlled patients, study participants “have a lot to lose” in terms of having relatively good health
Some phase I oncology trials

- Patients are typically enrolled in early phase studies when their disease is refractory after exhausting options for standard treatment regimens.
- Patients and providers hope for direct benefit in the trials but usually recognize potential for benefit is remote.
- Risks can vary from minimal to significant.
- Patient motivations for enrollment vary but often consist of combination of altruism and hope for benefit.

Some early phase HIV cure trials

- Patients typically enrolled are those with chronic infection that is well-controlled on antiretroviral therapy.
- While these patients could benefit from an eventual cure, their health status is relatively good and their life expectancy near normal.
- Patients and providers recognize that potential for direct benefit is remote.
- Adverse reactions may be better tolerated because of the relative good health of the patients.
- Drug toxicity may be less if the duration of therapy is shorter than required in an oncology setting and when not used in conjunction with other toxic drugs.
A FEW ETHICAL CONSIDERATIONS

Selection of study participants: uncontroversial criteria

(1) Health status good enough that there are no serious confounders in the research; that is, poses no serious risks to the scientific validity of the study;

(2) Health status does not pose any additional risks to the patient, e.g., presence of co-morbidities that make the study intervention more risky;

(3) Able to comply with protocol

(4) Willing to join the study and provide informed consent; willingness may also depend on additional factors below;

Additional, not settled criteria:

5) Member of a group that may benefit in the future from a successful cure intervention;
   ➢ Is this a necessary criterion?

By analogy, is it necessary to conduct a pK study of a new TB drug in TB patients? Frequently healthy patients not affected by a disease or condition participate in early phase trials; risk level must be closely managed;

6) Patients who “do not have a lot to lose” in the sense of risking good health in the context of trial;

Enrolling patients with poor health status using this rationale would conflict with criteria (1) and (2)

In reality, (5) is not ethically required and (6) is not scientifically viable in many studies