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ACTG 5221: BACKGROUND

- TB is the most important co-infection of HIV in Africa, Asia, Latin America
- High rates of mortality are reported in HIV infecte patients with TB (15-30%)
- Optimal timing of ARV initiation in TB patients no known. This topic was identified as highest priority research question among international investigators

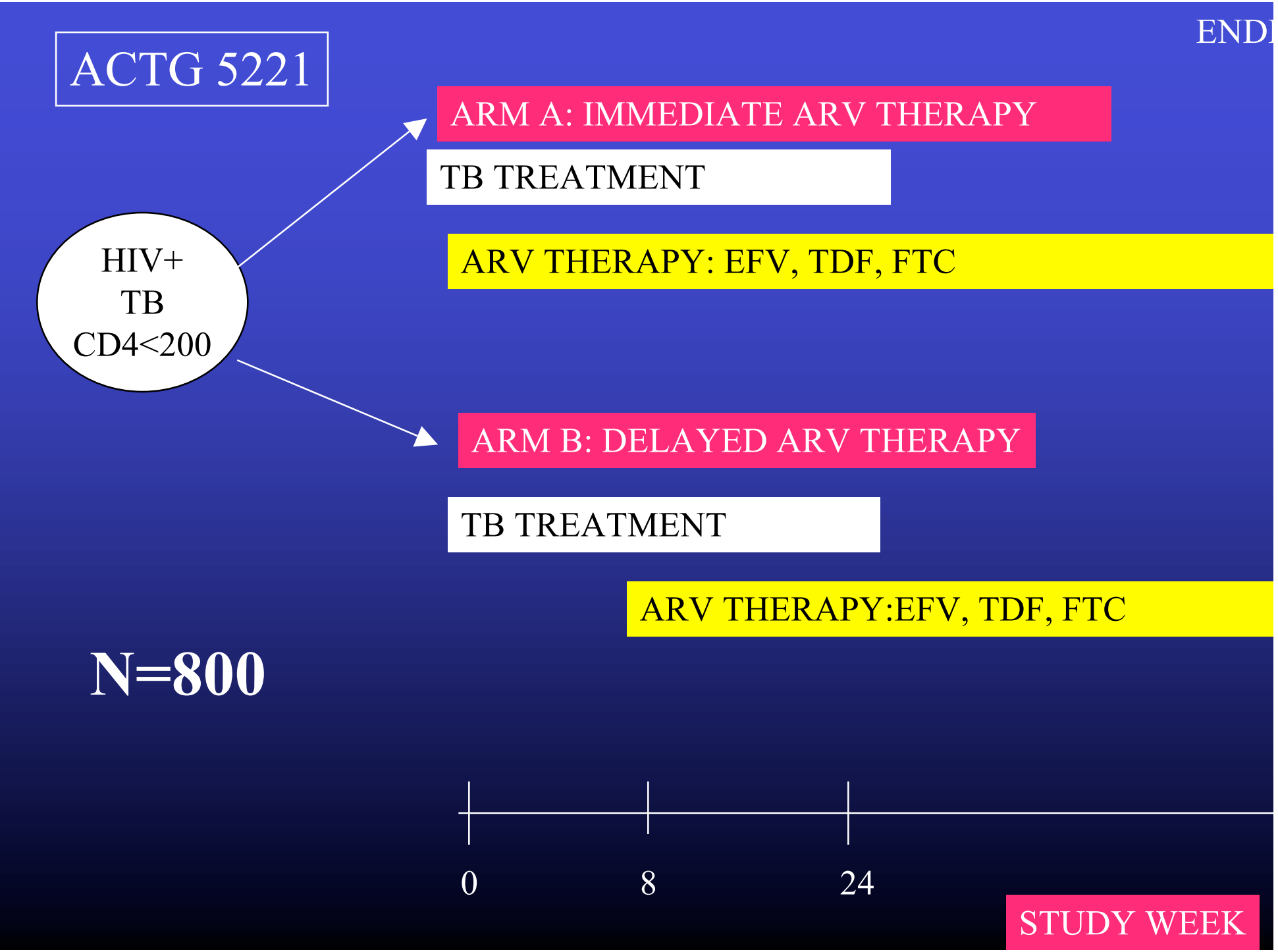
BENEFITS AND RISKS OF STARTING AR THERAPY IMMEDIATELY IN PATIENTS STARTING TB TREATMENT

BENEFITS

- Reduced morbidity
- Reduced mortality
- Improved TB outcome

RISKS

- Increased toxicity to TB and ARV therapy
- Drug interactions betwe HIV and TB medications
- Pill burden
- Immune Reconstitution Inflammatory Syndrome (IRIS)


ACTG 5221
END
ARM A: IMMEDIATE ARV THERAPY
TB TREATMENT
ARV THERAPY: EFV, TDF, FTC
HIV+
TB
CD4<200
ARM B: DELAYED ARV THERAPY
TB TREATMENT
ARV THERAPY:EFV, TDF, FTC
N=800
0
8
24
STUDY WEEK

Study Medications for Clinical Trials

- Investigator develops concept proposal
- Concept developed and approved by ACTG Scientific and Steering Committee
- Industry colleagues approached for drug donatic
- Industry colleagues review protocol
- Industry participates in protocol development
- Contracts to supply drug facilitated through DAIDS

Study Timeline: ACTG 5221

- March 2004: Protocol Development begins
- August 2004: Approach collaborators for study drug : Gilead, Bristol, Merck, Gates Foundation
- September 2004: Gilead agrees to participate
- March 2005: Clinical Trials Agreement with Gilead Completed, source of TDF/FTC secured
- March 2005: Final DAIDS approved protocol
- September 2005: IRB approved or submitted at sites

Study cannot begin without source of efavirenz identifi

STUDY DRUG PURCHASE:
MERCK ACCESS PRICES FOR STOCRIN

J'burg	$29,145
Durban	$29,145
Port-au-Prince	$64,320
Chaing Mai	$29,145
Pune	$64,320
Channia	$64,320
Harare	$29,145
Blantyre	$29,145
Lilongwe	$29,145
Rio de Janeiro	$64,320
Porto Alegre	$64,320
	→ $525,615

800 participants, stocrin/EFV 600 mg, 30 tabs/bottle, 12 bottles/person/yea, 25% o

AUROBINDO PRICING FOR GENERIC EFAVIRENZ

Total annual cost: $468,000

Investigator Perspective: What are the consequences?

- High priority scientific questions may not be addressed.
- Valuable time is expended.
- Collaborations and credibility are threatened.
- Productivity is diminished.
- Participants in this process including our trainee are discouraged.

Summary

- ACTG 5221 exemplifies a clinical study addresses criti
  global issue on optimal use of antiretroviral therapy;
  results will guide policy.
- The study has NIH support; 2/3 study drug cost covere
  through Gilead collaboration; continued ARV access
  through US and in country programs.
- Access to efavirenz is the limiting factor for study star
- Complicating factors: large study, multiple sites, multip
  industry collaborators, dependence on efavirenz
- Industry, private foundation, NIH, investigators unable
  come up with a solution to date.