Upcoming ATI Trials and Lessons Learned

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HIV VACCINE TRIALS NETWORK

ACTG 5416/HVTN 806/HPTN 108

Protocol still in development

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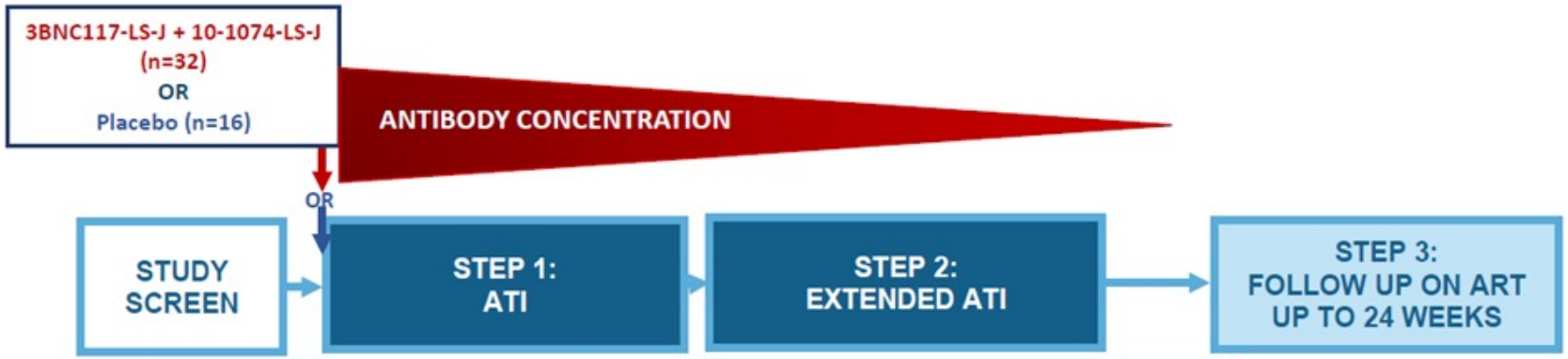
Collaborative bnAb combo + ATI study



	SCREENING	STEP 1 ATI		STEP 2 EXTENDED ATI			STEP 3 ART RE-INITIATION
	SCREEN	MONITORING WEEKS 0-8	MONITORING WEEKS 9-24	MONITORING WEEKS 25-52	MONITORING WEEKS 53-72	PRE-RESTART	MONITORING X 24 WEEKS
Plasma HIV RNA	✓	WEEKLY	Q2 WEEKS[1]	Q2 WEEKS[1]	Q4 WEEKS[1]	✓	WEEKS 4, 12 & 24
CD4+ T cell counts	✓	Q2 WEEKS	Q4 WEEKS[1]	Q4 WEEKS[1]	Q4 WEEKS[1]	✓	WEEKS 12 & 24
Hematology & Chemistries	✓	Q4 WEEKS		Q8 WEEKS		-	WEEKS 4, 12 & 24

[1]OR WEEKLY IF VL > LLQ

Figure Schema: Study design

Study objectives in plain language

“We are doing this study to answer several questions.

1. **Is it safe to give the study antibodies to people living with HIV, and do they cause any side effects?**
2. **Are people who get the study antibodies more likely to control HIV (undetectable viral loads) for a longer period of time without taking HIV treatment than people who get the placebo?**
3. **Do the study antibodies affect the level of HIV in your blood when you are not taking HIV treatment for an extended period of time?”**

Restarting ART

“ART Restart: Moving to Step 3

We don’t know if the study antibodies might help people to control HIV, or how long control could last. Some people will get the placebo, which does not control HIV. For this reason, people could skip Step 2 entirely, or could be in Step 1 or Step 2 for a shorter or longer amount of time. You will restart taking your HIV treatment and move to Step 3 if one of these things happen while you are in Step 1 or Step 2:

- your viral load increases to 1,000 copies/mL or higher, and stays at that level or higher for 4 weeks in a row
- if your CD4+ count drops to less than 350 cells/μL
- if you become pregnant
- if you develop “flu-like” symptoms that look like acute retroviral syndrome, similar to what you might have had when you were first diagnosed with HIV
- if you are not willing to use condoms for all sexual activity while you are in study Steps 1 or 2
- if you want to restart HIV treatment
- if your primary HIV healthcare provider thinks you should restart HIV treatment”

HVTN 807

Protocol still in development

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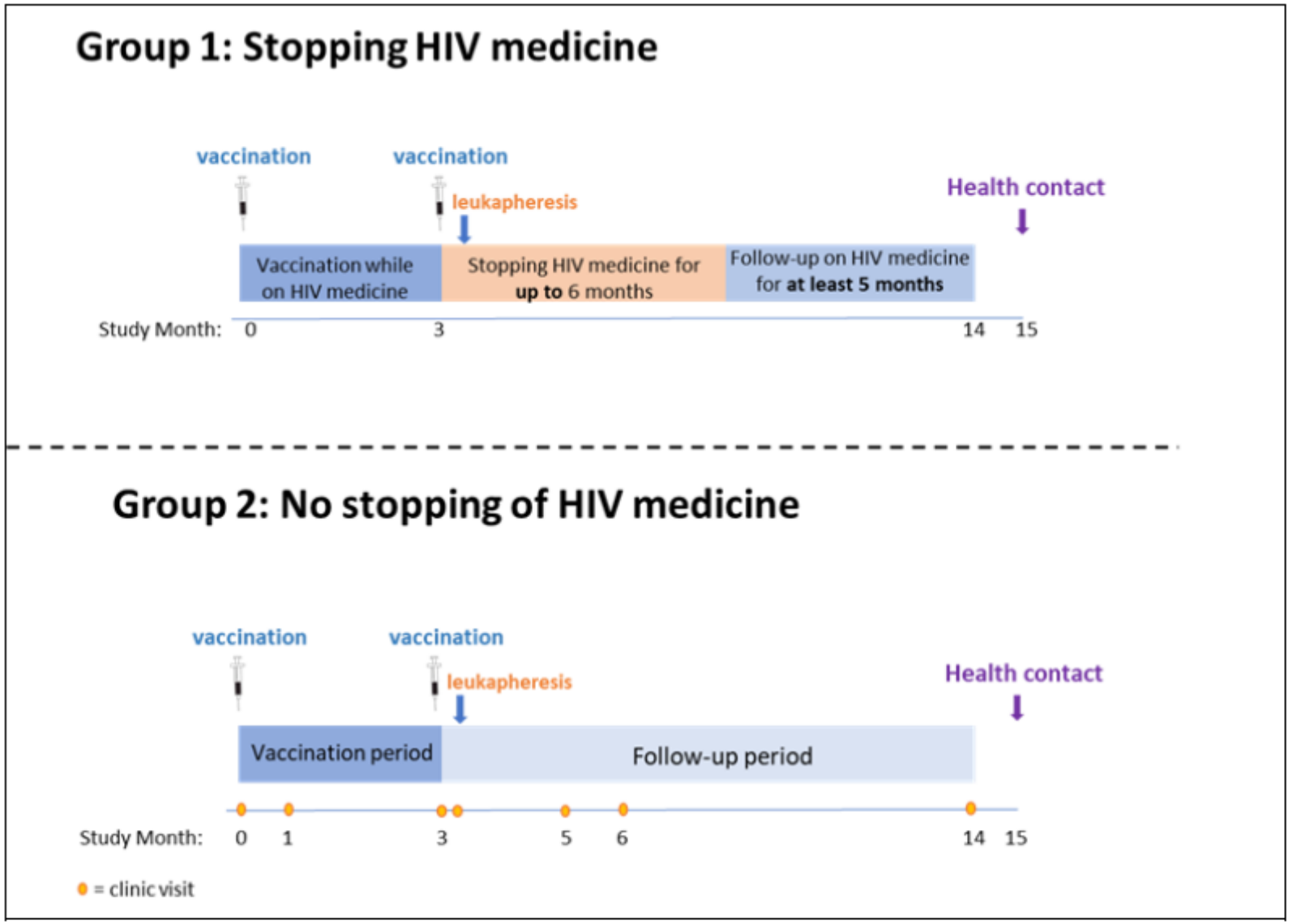
Vaccine with or without ATI study



Study objectives in plain language

“This study is divided into 2 groups with about 20 people in each group. We are doing this study to answer several main questions.

1. **Are the study products safe to give to people living with HIV who are taking HIV medicine?**
2. **Are people able to take the study products without becoming too uncomfortable?**
3. **How do people’s immune systems respond to the study products? (Your immune system protects you from infections and disease.)**
4. **How does an ATI affect this immune response to the study products? Do participants’ immune systems make the special kind of immune cell responses that researchers think are important for developing an effective HIV vaccine?”**

Restarting ART

"If any of the following things happen, you will restart your HIV medicine as soon as possible and move to the "Follow-up on HIV medicine" phase of the study.

- Your viral load gets too high and stays high for too long,
- You have any symptoms related to HIV rebound other than mild fatigue, such as unintentional weight loss, an unexplained fever that doesn't go away, night sweats or diarrhea that don't go away, oral candidiasis (a yeast infection in your mouth), and swollen lymph nodes in several places on your body;
- Your CD4 T-cell count drops too low and stays there or you develop an AIDS-defining condition or opportunistic infection;
- You report having condomless anal or vaginal sex with a partner who does not have HIV, or whose HIV status is unknown, who is not using PrEP to prevent HIV;
- You become pregnant;
- You would like to restart taking your HIV medicine;
- Your primary HIV healthcare provider or the doctor at the study clinic decides that you should restart your HIV medicines."

Lessons Learned from the AMP ATI trials

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Community input to AMP ATI trial design

2 key points heard from community members of the AMP ATI protocol teams at the time the trials were being designed:

1. Importance of protecting the sexual partners of participants
2. Importance of assessing mental health as a screening eligibility consideration: are people mentally in a good place to consider the risks of an ATI, and whether joining the study is a good choice?
   - Continued mental health assessments at several points throughout the study
   - Recognition that PLWH often struggle with mental health issues, and don't always have access to good support or necessary care
   - Recognition that a return to being viremic after at least one year of being undetectable could be very stressful and people might need support

Trial design addressed both issues - 1

- Condom use required for all sexual activity
- Contraception use required for ppts and their partners who could become pregnant
- Transmission Reduction Counseling available to partners if the enrolled ppt wanted to bring them into the clinic (respecting confidentiality)
- PrEP was made available to partners who wanted to use it
  - Gilead provided Truvada at no charge (continuation of what was offered to ppts in the AMP Studies)
  - sites identified local providers to prescribe and follow-up (since not all sites have “primary care” capacity)

Trial design addressed both issues - 2

- Sites were required to have a Mental Health Referral Plan in place, with providers and other resources identified prior to being approved to start enrolling
- Decisional Aid was used during the consent process (at Screening) like an Assessment of Understanding, confirming that people understood the informed consent
- Decision Making Assessment was adapted from cancer trials, helping the participant to consider study participation from all angles and ensure that it aligned with their personal values.
  - Done at start of study, again when ART was stopped, when ART was restarted and then at 3 mos, 6 mos and 1 year after restart (during monitoring period when person was seen to ensure a return to undetectable viral load)
- Psychosocial Assessment was used to assess overall mental health status
  - Done at start of study, again when ART was stopped, again at 3 months if still not using ART, when ART was restarted and then at 3 mos, 6 mos and 1 year after restart (during monitoring period when person was seen to ensure a return to undetectable viral load)

Acknowledgements

- Protocol team for ACTG 5416/HVTN806/HPTN 108, led by the ACTG

- Protocol team for HVTN 807

- Protocol teams for the two AMP ATI studies, HVTN 804/HPTN 095 (Americas) and HVTN 805/HPTN 093 (Africa)

THANK YOU

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