

Clinical Trials: Rapporteur Session

AIDS Vaccine 2008

Cape Town

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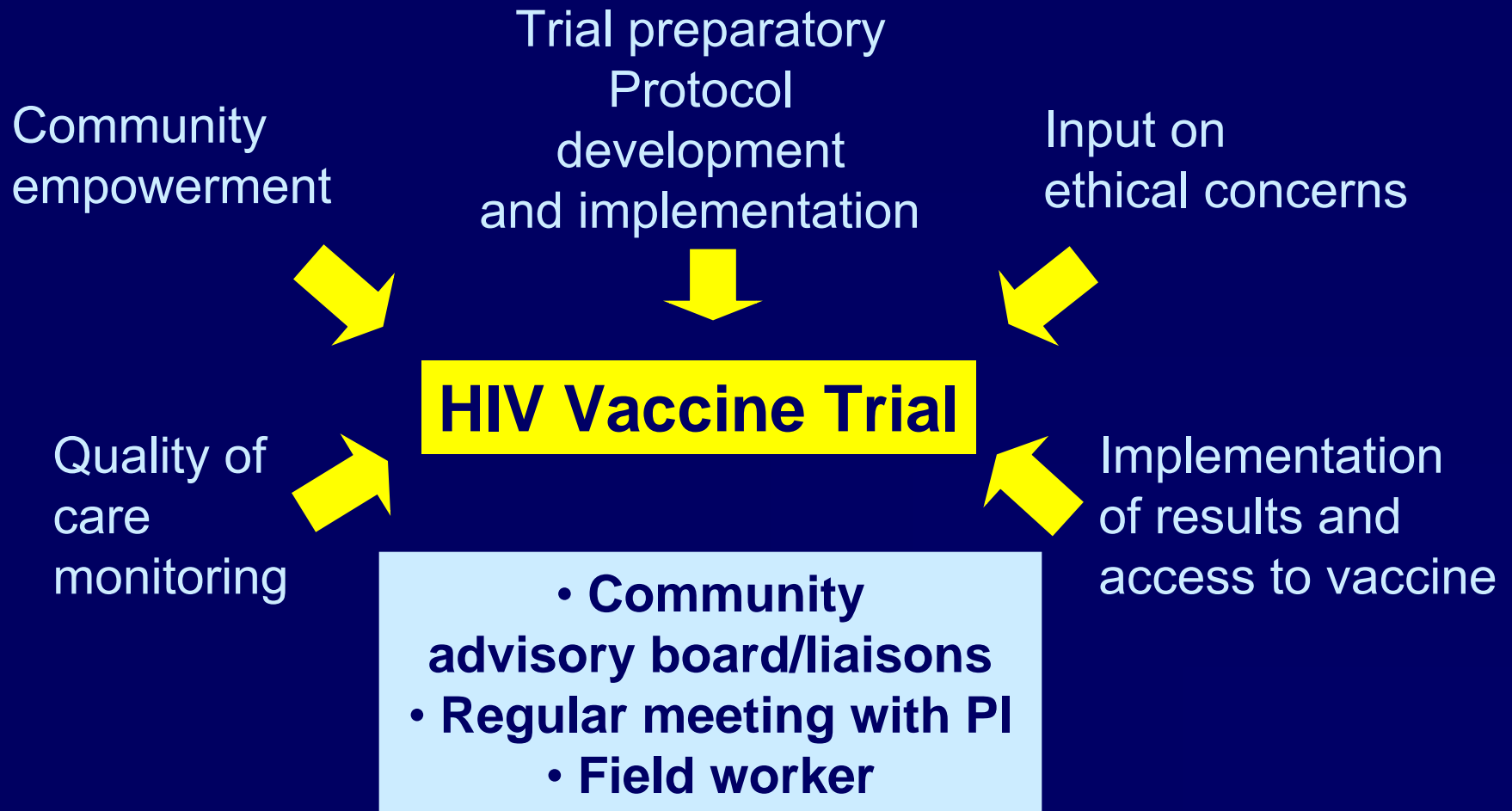
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Philip Renzullo, PhD, MPH (NIAID)

Outline

- Community involvement
- Preparing for HIV vaccine trials
- Lessons learned from the STEP trial
- Traditional/proposed trial development pathways
- The way forward

Community Involvement (Immediate, Larger, National, Global)



Preparing for HIV Vaccine Trials

- Community participation
- Knowing and identifying ways to improve acceptability to HIV vaccine intervention
 - Increase female participation in Western Kenya¹, Rwanda² and US (minority)³ by intensified recruiting strategy
- Involve adolescents in HIV vaccine trials^{4,5}

¹A. Adegga (P06-19, P06-18), ²K. Kayitenkore (OA08-05), ³P. Frew (OA08-02),
⁴H. Jansen (OA08-04), ⁵L. Bekker (RT01-05)

Preparing for HIV Vaccine Trials

- Using technology as a tool for enrollment and retention (free mobile phone minutes¹, radio², email³)
- Importance of regional reference ranges⁴

¹N. Chimbindi (P06-16), ²A. Sangowawa (P14-15), ³K. Louis (OA08-08), ⁴A. Kamali (P13-13)

Maintaining Vaccine Research Agenda in the Absence of Vaccine candidates

- 20 years of cohort and vaccine preparedness in Uganda but no vaccine is ready for efficacy trials
- Maintain existing cohorts, community interest and well-trained staff by
 - Long term research investment
 - Multidisciplinary approach to research and prevention
 - Integration of prevention and care
 - Human capacity and infrastructure development
- Diversification of research portfolio to non-HIV

Lessons Learned from the STEP Trial

■ Scientific issues¹

- Lower HIV viral load in Ad5 naive vaccinees with more IFN- γ -secreting T cells and those with more Gag CD8+ T cells
- Beneficial effect of protective HLA alleles observed in HIV+ cohorts particularly in vaccine recipients
- Further investigations
 - Role of Ad5 immunity in HIV acquisition
 - Potential confounders

■ Regulatory issues²

- Issues with use of live viral vectors
- Little guidance from FDA, EMEA, WHO and national regulatory authorities
- Clear stopping rules
- FDA advisory consultation

¹J McElrath (PL01-01), S Buchbinder (PL 02-03), ²H. Rees (SP01-05)

Lessons Learned from the STEP Trial

- Ethical issues
 - Trial-related harm
 - Obligation to provide monitoring and ARV without time limit
 - No obligation to provide monetary compensation unless stipulated in advance

 - Impact on future HIV vaccine trials
 - Inform volunteers on STEP trials
 - Factors that enhance HIV susceptibility
 - Similarities/differences of vaccine products/risk factors compared to STEP
 - Circumcision as required vs. encouraged

Phase III Antibody-based trials
Recombinant gp120 in US MSM
and in Thai IDUs



Phase III Antibody-
and T-cell based trials (TOC)
RV144 in Thailand
ALVAC/gp120 prime boost



Phase IIB T cell-based trials
(TOC)
Merck gag/pol/nef, Ad5
STEP and Phambili



Screening-Test-of-Concept Trial (STOC)

Number of volunteers
Large

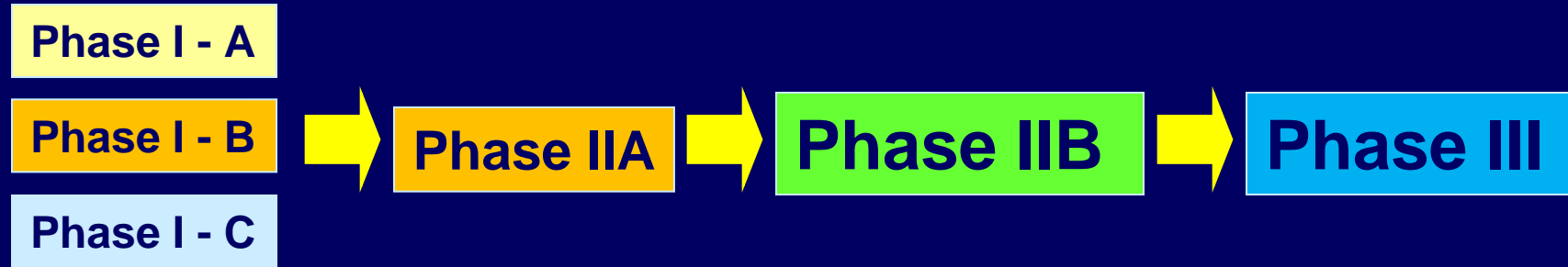
Population
Relatively heterogenous

Primary endpoints
Prevent HIV acquisition
Reduce HIV viral load

Screening-Test-of-Concept Trial (STOC)

- Screen vaccine candidates for evidence of impact on HIV viral load set point
 - Consider advancing candidate if $\geq 1.0 \log_{10}$ viral load reduction observed
 - Averaging at least 2 viral load measurements from a set window period (pre-ARV)
- Randomized 1:1 vaccine vs. placebo trial
 - 34 evaluable viral load endpoints required for 80% power against $1.0 \log_{10}$ viral load change
 - Total sample size of around 1000
 - Around 3 years in duration
 - Relatively homogenous population
- Not designed to directly assess HIV acquisition/enhancement and immune correlates

Traditional Trial Development Pathway



Proposed Trial Development Pathway



Discovery

Development

Phase I and/or II preventive clinical vaccine trials

- MVA - CRF01_AE¹
- DNA/MVA Multiclade²
- F4co/AS01- HIV subtype B p17/p24 gag, RT and Nef³
- ADVAX – Clade C/B⁴
- Tiantan Vaccinia – CRF07 B'/C⁵
- CD4 Multiepitope polypeptide (EP1043) alone or in combination with CTL multiepitope DNA⁶

HIV Vaccine as Part of Combination HIV Preventive Approach



Harm reduction

Circumcision

Condoms

STI treatment

ARV

Microbicides



UNAIDS/WHO
Ethical Guidance
2007

HIV prevention
trial participants
have access to
all state of the art
HIV risk
reduction
methods