HIV VACCINE AWARENESS DAY

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Experimental Medicine Vaccine Trials (EMVTs)

Opportunities and Challenges

HIV vaccine trials to date have answered some scientific questions, but raised many others that must be answered if the world is ever to develop an effective HIV vaccine. The lack of efficacy in the Uhambo, Imbokodo, AMP, and Mosaico trials, all large, late-phase efficacy trials, have prompted researchers to look for trial designs that can quickly ask and answer key questions, inform decisions about which vaccine candidates to advance into larger trials and, hopefully, increase the probability of demonstrating efficacy. Researchers, funders and vaccine developers are now focusing on experimental medicine vaccine trials (EMVTs) to build on current knowledge and help to advance the field.

What are Experimental Vaccine Trials (EMVTs)?

EMVTs are clinical investigations undertaken to test or generate a scientific hypothesis that advances vaccine discovery and development. They do not provide direct prevention or treatment benefits to the participant, rather, they are designed to answer a scientific question. They are also sometimes referred to as Discovery Medicine trials.

Why Might EMVTs Be Important?

EMVTs may speed the investigative process, resulting in more rapid iterations, testing hypotheses and generating faster findings to inform the next round of trials.

EMVTs differ from product development trials where vaccine candidates progress through Phase 1 to 3 trials with an ultimate objective of product licensure. Designed as small Phase 1 trials, but setting aside the necessity for a licensable product, EMVTs aim to quickly and safely answer if an experimental agent induces a potentially protective response, and may offer researchers a more viable way to sift through the many variables that may contribute to successful HIV vaccine design. The focus of EMVTs is **to accelerate vaccine science rather than progress individual products**. They are iterative by nature and offer a path to quickly investigate the potential of vaccine candidates. Faster findings then inform the next round of trials.

The EMVT approach would address questions that cannot be resolved in animal testing, providing a method for an early validation that innovative vaccine strategies show promise in humans. EMVTs do not compromise safety protocols or standards, nor do they increase the risk to participants. EMVTs may involve more intense biological sampling such as biopsies or blood draws to collect as much information as possible.

EMVTs could bring savings and efficiency in a number of ways: small teams could test candidates on shorter timelines, using standardized manufacture, toxicology and regulatory procedures; and multiple candidates could be tested in parallel.

Why This Approach?

EMVTs have been discussed as a promising strategy for a number of years in the HIV vaccine field. Interest in EMVTs is growing as the field recognizes the need to accelerate the pace of research, on the heels of disappointing results from recent efficacy trials.

	Traditional Phase I	Experimental Medicine Phase I
Purpose of the trial	Product development	Scientific information
Next step	Hopefully Phase II	Improve vaccine design / Phase I
Number of Volunteers	~20-100	Defined by scientific question
Use of Controls / Placebo	Yes	Potentially No
Duration (months)	~12-18 months	Usually <12 months
Laboratory monitoring of volunteer	Safety / mostly regular immunogenicity	Safety / mostly special assays
Preclinical (animal) evaluation	Extensive (up to protection)	Limited / generic for platform (safety)
Vaccine Manufacturing	Scalable product (reproducibility)	Pilot / small scale lot
Product characterization	Suitable for Ph3 trials; long term stability	Description of product (qualified assays); purity, potency, stability
Regulatory	IND / IMPD	IND / IMPD
Ethics	IRB approval; involves large communities	IRB approval; involves individuals
Industrial partner	Highly desirable	Desirable, but not essential

Challenges for EMVTs

To move forward at scale, some challenges must be confronted.

- Some regulatory bodies provide greater flexibility for EMVTs, but there is much complexity around communicating highly adaptable trial designs to regulatory and ethics bodies. A global standard is needed.
- Currently, there is no commercial incentive for the private sector to manufacture small batch vaccine candidates.
- It will be ethically imperative and complex to communicate the lack of a direct benefit to participants. This, coupled with more intensive biological sampling, may justify increased incentives for volunteers, within strictly observed ethical boundaries.
- While the US FDA has provisions to reduce the risk of investment in drug development and late-stage failure, no specific provision exists to mitigate the risk of investment in vaccine development.

ADDITIONAL RESOURCES

- Experimental Medicine Vaccines for Advocates—Recording of a session with Imperial College London's, Robin Shattock: https://www.youtube.com/watch?v=0Hj93ApieE0
- *Experimental Medicine for HIV Vaccine Research and Development*, by Holly Prudden, Roger Tatoud, Cathy Slack, Robin Shattock, Pervin Anklesaria, Linda-Gail Bekker and Susan Buchbinder, Vaccines, May 2023, https://www.mdpi.com/2076-393X/11/5/970.