AIDS Vaccine Research: An overview MAY 2015

Neutralizing Antibodies

OVERVIEW **DEVELOPMENT PROGRAMS** regions of epitopes for broadly-neutralizing antibodies gp41 membraneproximal external region (MPER) V3-qlycan CD4 ···: binding site V1/V2-glycan

HIV trimer target	Antibody	Research highlights*
CD4 binding site	3BNC117	Phase I dose escalation trial in HIV-positive individuals not on ART who received the safety in all groups and sustained viral load reductions highest dose; further treatment and prevention studies planned (Germany, US)
	VRC01	Preliminary Phase I dose escalation results have shown impact on viral load; HVTN 104 Phase I trial in HIV-negative adults ongoing with follow-on efficacy trial planned; Phase I infant safety trial being explored; planned treatment trials to look at VRC01 + ART in acute infection (US)
	VRC07-523	A variant of VRC01, which in animal testing has shown increased potency, indicating clinical relevance for preventing HIV infection at lower doses
V1/V2-glycan	CAP256-VRC26	Currently in preclinical testing for development for treatment and prevention (South Africa)
	PG9	Ongoing Phase I trial establishing safety and optimal doses of AAV vector gene-transfer approach (UK)
	PGDM1400	Identified in animal studies as exceptionally broad and potent with cross-clade neutralization coverage of 83% at low doses
V3-glycan	10-1074	Animal studies have shown potency in reducing viral load; moving to clinical testing in 2015 as possible treatment and/or component of a cure strategy (US)
	PGT121	Reduction in viral load has been shown in animal studies; in manufacturing process for future clinical studies as possible treatment and/or component of cure strategy (US)

ADDITIONAL VACCINE APPROACHES

STATE OF THE FIELD

- Neutralizing antibodies are potent immune cells that block HIV activity.
- Identification of broadly neutralizing antibodies (bNAbs) has defined discreet targets on HIV envelope glycoprotein, or trimer.
- Data from small-scale animal and human studies show bNAbs generally safe, tolerable and reduce viral load.
- Future directions include multiple bNAbs in combination, to target different sites on HIV trimer and may be able to block a wider breadth of HIV strains.

ADVOCATE'S CHECKLIST

NEUTRALIZING ANTIBODIES

✓ EXPLORE FEASIBILITY

bNAb research is generating excitement, but still mostly upstream and conceptual
 Explore feasibility of bNAbs as scalable, cost-effective options for prevention and treatment as research progresses.

✓ EDUCATE STAKEHOLDERS

Clinical trials will become increasingly complex
 Ensure communities who may be impacted by bNAb trials understand the science and can play a meaningful role.

✓ ENGAGE DECISION MAKERS

Research pathways of bNAb-inducing preventive vaccines are still unknown

Remain vigilant around promising antibodies and prioritization for vaccine development.

^{*} See Px Wire Volume 8 No 2 for additional pipeline information (www.avac.org/pxwire/vol8no2).