

HIV Vaccine Development

Issues related to Goals:

Prevention vs. Treatment

Neutralizing antibodies vs. cell-based (CD4/CD8)

Mucosal vs. Intravenous immunity

Issues related to Means:

Protein(s) - which one(s) and how presented

Whole virus - attenuated* / killed

***trials appear to have led to HIV infection**

Vectors - viral, DNA

Prime and Boost



Vaccines in Clinical Trials

Treatment Trials

REMUNE: gp120-depleted killed whole HIV-1 virus

**Phase III in US - was disappointing,
Focused on HAART patients with
low/undetectable HIV-1 RNA**

**Increased CD4+ counts, some decreased
HIV-1 RNA, but not as promising as hoped**

**Sponsor company Immune Response underwent
Restructuring, now plans on testing a
reformulated vaccine for prevention**



Vaccines in Clinical Trials

AIDSVAX - gp120-based vaccine for prevention

originally co-sponsored by NIH, since pulled support due to lack cell-based response.

Phase III clinical trial showed no effect in patient population as a whole; however, certain minority groups showed a modest effect - not statistically/biologically relevant

Sponsor Company VaxGen is being sued by investors for not being up-front with preliminary clinical trial data



Vaccines in Clinical Trials

Aventis: ALVAC

**canarypox vector expressing
HIV-1 env-gag-pol**

Merck: Ad5

adenovirus vector expressing gag

Phase I trial scheduled for:

Ad5 “prime” then ALVAC “Boost”



Vaccines in Clinical Trials

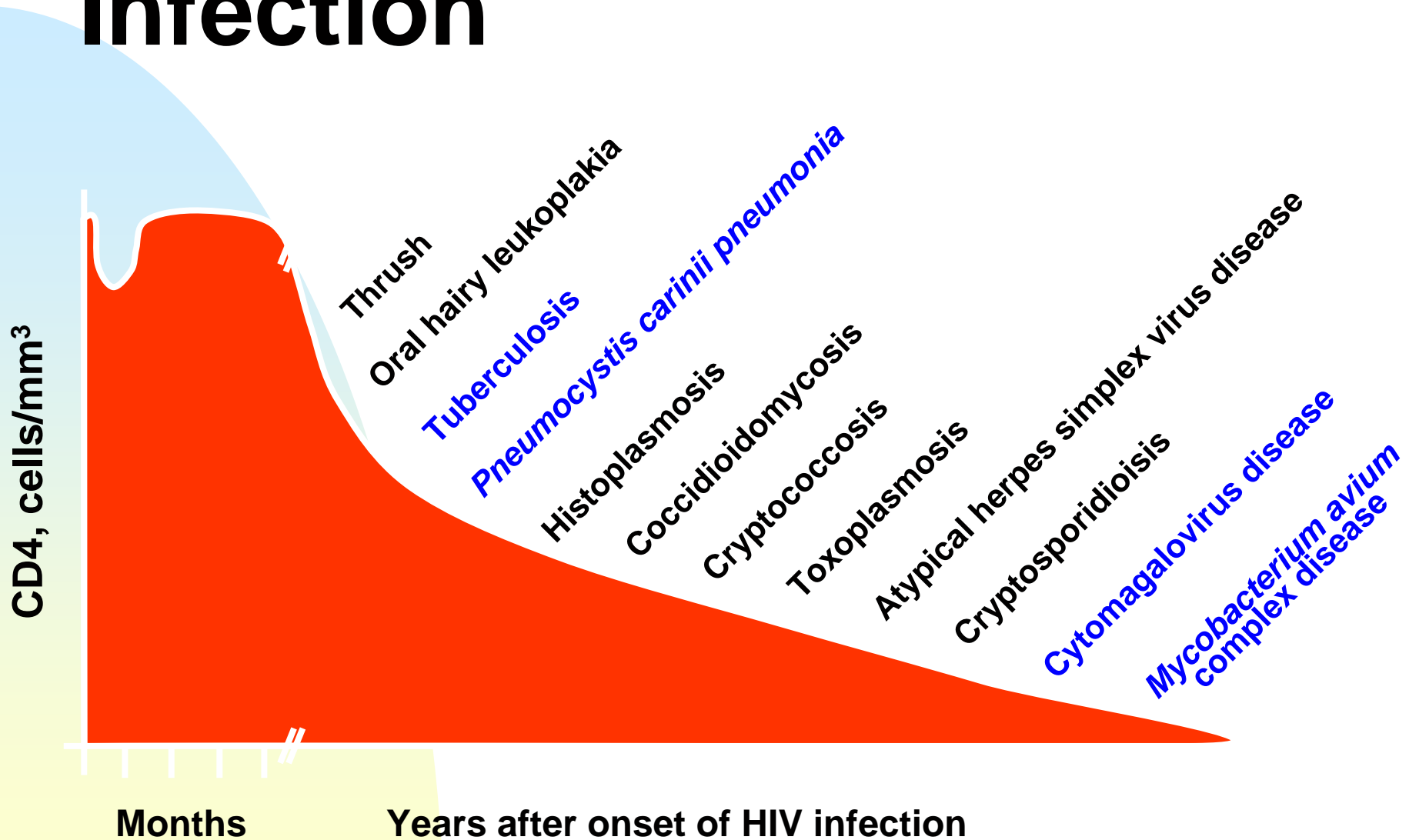
Epimmune: EP HIV-1090

**DNA-based vaccine includes 21 key elements
HIV-1 epitopes plus a Universal
Helper T-cell epitope (to enhance
magnitude and duration of response)**

**Phase I trials just began with Nat'l Inst. Of
Health (NIH)**



Natural History of HIV-1 Infection



Pneumocystis carinii (PCP)

- Considered protozoa by some and fungus by others
- Most common life-threatening infection in HIV infected patients
 - ◆ 75-80% of HIV pts will develop without prophylaxis
- Risk increases as CD4 count decreases
 - ◆ 80-95% of cases seen with CD4 count <200
- 5-20% mortality with first episode of PCP



Opportunistic Infections

Pneumocystis carinii pneumonia (PCP)

Recently Approved:

- Bactrim
- Septra
- NebuPant (pentamidine)
- Pentam (pentamidine)
- Neutrexin (trimetrexate)
- Mepron (atovaquinone)

In Trials:

- dapsone



Cytomegalovirus (CMV)

- Commonly infects HIV patients when the CD4+ count falls < 50
- Retinitis is most commonly recognized infection
 - ◆ Can lead to blindness without therapy
 - ◆ Diagnosis by ophthalmic exam
- Other organs infected
 - ◆ Brain (meningitis)
 - ◆ Lungs (pneumonitis)
 - ◆ GI tract (colitis, esophagitis)



Opportunistic Viral Infections

Cytomegalovirus (CMV)

Recently Approved:

- Vistide (cidofovir)
- **Vitravene (fomivirsen)**
- Foscavir (foscarnet)
- Cytovene (ganciclovir)

Herpes Simplex Virus (HSV)

Recently Approved:

- Valacyclovir (Valtrex)



Mycobacterium Avium Complex (MAC)

- Most common mycobacterial infection in HIV pts
 - ◆ 5-10% of all mycobacterial infection in US are atypical
- Diagnosis
 - ◆ abdominal pain
 - ◆ signs and symptoms of infection
- Can infect lungs, GI tract, or bone marrow
 - ◆ Disseminated infection in up to 50% of HIV pts
 - ◆ Increased morbidity and mortality with disseminated



Opportunistic Mycobacterial Infections

Tuberculosis

Recently Approved:

-Rifapentine

**Mycobacterium avium complex /
Mycobacterium avium intracellulare (MAC/MAI)**

Recently Approved:

- Zithromax (azithromycin)
- Mycobutin (rifabutin)
- Biaxin (clarithromycin)

