PEP Case 3
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Session 1:
HIV Treatment

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PEP Case 3

- 50 yo dermatologist at your hospital is doing a MOHS procedure on a patient with AIDS and squamous cell CA of back. She calls you immediately after a percutaneous exposure to ask what to do!!
  - Exposure is with a suture needle visibly contamined with blood during a bloody procedure;
  - dermatologist is wearing two sets of gloves;
  - there is visible blood on her finger;
  - washes her hands with soap and water and her associate completes the procedure
- Patient has AIDS, CD4 100, HIV RNA 20,000, recently was HBV ab positive, core antibody positive, surface antigen negative, HCV antibody negative

PEP Case 3: Source Patient

ARV History:

- AZT monotherapy 1990
- Subsequent regimens 1992 -1999:
  - AZT DDI
  - AZT 3TC IDV
  - D4T 3TC RTV SAQ
  - ABC EFV RTV SAQ
- Subsequent regimens 2000 – 2008
  - TDF DDI 3TC kaletra
  - TDF 3TC RTV Fosamprenavir
- Current Regimen: TDF 3TC RTV DRV Maraviroc
- Remains naive to T20, raltegravir, etravirine

Genotype on current regimen: RT

Resistance associated RT Mutations: M41L*, E44D, D67N, T69D, V108I, V118I*, M184V*, H208Y*, L210W*, T215Y*, K219R

Nucleoside and Nucleotide RT Inhibitors	Resistance Interpretation
zidovudine (AZT)	Resistance
didanosine (ddI)	Resistance
lamivudine (3TC)/emtricitabine (FTC)	Resistance
stavudine (d4T)	Resistance
abacavir (ABC)	Resistance
tenofovir (TDF)	Resistance

NonNucleoside RT Inhibitors	Resistance Interpretation
nevirapine (NVP)	No Evidence of Resistance
efavirenz (EFV)	No Evidence of Resistance

Genotype on current regimen: PR

Resistance associated PR Mutations: I13V, I15V, K20R, V32I, L33F, M36I/L, M46I, I47V, I54L/V, L63P, A71V, G73A/T, V82T, L90M

Protease Inhibitors	Resistance Interpretation
saquinavir + ritonavir (SQV/r)	**Resistance**
indinavir (IDV)	**Resistance**
IDV/r **	**Resistance**
nelfinavir (NFV)	**Resistance**
amprenavir (APV)/fosamprenavir (FPV)	**Resistance**
APV/r or FPV/r **	**Resistance**
lopinavir + ritonavir (LPV/r)	**Resistance**
atazanavir (ATV)	**Resistance**
atazanavir + ritonavir (ATV/r) **	**Resistance**
tipranavir + ritonavir (TPV/r)	*Possible Resistance*
darunavir + ritonavir (DRV/r)	*Possible Resistance*

** Protease Inhibitors administered with low-dose ritonavir for pharmacological boosting.

- Patient is also known to have D/M HIV by Tropism Assay

Summary: PEP Case 3

- High risk source patient
- Low-risk exposure

Genotype shows

- 5 TAMS in RT (7 TPV mutations, 3 DRV mutations)
- 14 PI Mutations
- Patient has dual-tropic HIV
- Patient has hx of EFV exposure but no current NNRTI mutations
- Patient has no prior exposure to T-20, raltegravir, or etravirine

- ARS Question

PEP Case 3: Follow-up

- Dermatologist successfully completes tenofovir, emtricitabine, etravirine plus raltegravir x 28 days
- Her HIV antibody test results at 6 weeks, 12 weeks, and 6 months after exposure are negative
- One year later, patient's CD4 is 250, VL is < 50 on tenofovir, emtricitabine, etravirine plus raltegravir

Etravirine Rash

	Etravirine (n=599)	Placebo (n=604)	
Rash	17%	9.4%	p<0.001
Grade 3/4 Rash	1.3%	0%	

- Early onset**:** median 12 days
- Limited duration**:** median 11 days
- Most mild to moderate; 1.3% grade 3, none grade 4
  - mostly maculopapular; no mucosal involvement
- 2.2% of patients discontinued treatment due to rash (0% with placebo)
- Higher incidence in women: 28% vs 16% in men
- No association with baseline CD4 cell count or prior NNRTI-related rash

Haubrich R, et al. IDSA 2007. Abst 1210.

ETV Rash Warning: Revised Package Insert

5 WARNINGS AND PRECAUTIONS

5.1 Severe Skin and Hypersensitivity Reactions

Severe, potentially life-threatening, and fatal skin reactions have been reported. These include cases of Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme. Hypersensitivity reactions have also been reported and were characterized by rash, constitutional findings, and sometimes organ dysfunction, including hepatic failure. In Phase 3 clinical trials, Grade 3 and 4 rashes were reported in 1.3% of subjects receiving INTELENCE™ compared to 0.2% of placebo subjects. A total of 2% of HIV-1-infected subjects receiving INTELENCE™ discontinued from Phase 3 trials due to rash [*see Adverse Reactions (6)*]. Rash occurred most commonly during the first 6 weeks of therapy.

Discontinue INTELENCE™ immediately if signs or symptoms of severe skin reactions or hypersensitivity reactions develop (including, but not limited to, severe rash or rash accompanied by fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, facial edema, hepatitis, eosinophilia). Clinical status including liver transaminases should be monitored and appropriate therapy initiated. Delay in stopping INTELENCE™ treatment after the onset of severe rash may result in a life-threatening reaction.

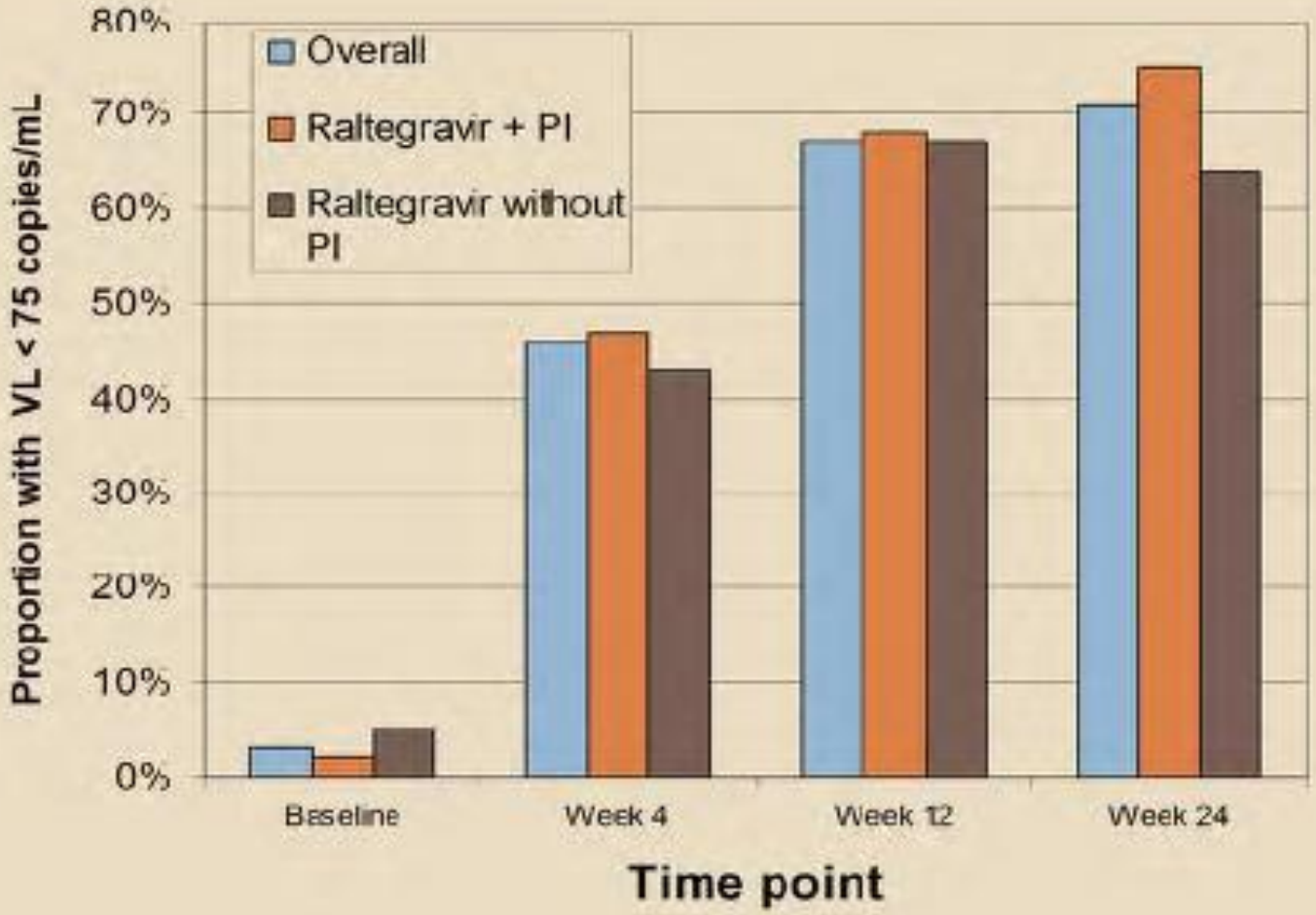
Etravirine package insert, August, 2009

BRAVO background and baseline characteristics

- 15 sites from raltegravir EAP program
- Retrospective analysis of patients starting on RAL based salvage with (n = 332) or without (n = 110) r/PI as part of optimized background
- Primary endpoint: proportion achieving VL < 400 at week 12
- Baseline characteristics: VL 5 log, GSS 1.7 – 1.8 in each arm
- PI cohort: 87% DRV use, 36% ETV use, 10% ENF
- No PI cohort: 66% ETV use, 17% ENF use, 13% MVC use

Skiest D et al, 5th IAS, CapeTown, South Africa, 2009; Abstract 1212, MOPEB072

Percent with VL < 75 copies/mL



Skiest D et al, 5th IAS, CapeTown, South Africa, 2009; Abstract 1212, MOPEB072