

CROI 2006, Update

Stephen E. Follansbee
Medical Director, HIV Services
Kaiser SFO
February 22, 2006

Ritonavir and Fluticasone

- Poster 772: Hull et al., Canadian HIV Trials Network
- Advair®, Flonase®, Flovent®
- Ritonavir Package Insert Data, RTN
100mg BID:
 - FP C_{max} increases 26.7 fold
 - FP AUC increases 368 fold

Ritonavir and fluticasone

- 50 patients tested sequentially
- 7 patients had fasting cortisol <28 nmol/L and 43 had normal (controls)
- 7/7 on RTN/FP and 1/43 on RTN/FP
- Median time on ART 8 mo and 6/7 on FP >10 months
- 5/7 on RTN >100 mg/D; 2/7 females

Ritonavir and Fluticasone

- 3 asymptomatic
- 4 symptomatic
 - 2 Cushingoid features
 - 1 Easy bruising
 - 1 Loss of diabetes control

ROLL for routine fasting cortisol and/or cotrosyn stimulation tests if no alternative to co-administration exists

Prevention of CMV disease

- OP 150, ACTG 5030
- Randomized, placebo-controlled trial of Valganciclovir to prevent CMV end-organ disease in subjects with detectable plasma CMV DNA PCR.
- Entry criteria:
 - CD4 <100 and HIV RNA >400 copies/ml

Prevention of CMV disease

- CMV DNA PCR q 8 weeks (Step 1)
- Randomized to VGCV induction/maintenance or placebo if CMV PCR detectable, i.e. >400 copies/mL (Step 2)
- 338 subjects, 88% ART
- Median CD4 30 and HIV RNA 4.98 log₁₀
- 68 CMV PCR +; 47 randomized

Prevention of CMV disease

- Randomization: 24 VGCV / 23 P
- Median CD4 12; 65 weeks median F/U
- 9 with confirmed or probable CMV (4 VGCV / 5 P)
- 15 died (7 VGCV / 8 P)
- Additional 10 developed CMV and 52 died prior to randomization (Step 1)

Prevention of CMV disease

Conclusions

- Historic: much lower rate of CMV disease in ART era (>50% with CD4 <50 pre-ART)
- Pre-emptive anti-CMV therapy does not significantly reduce the risk of CMV end-organ disease or of death in subjects receiving ART
- Role for routine CMV PCR screening?

HSV-2 Shedding Rates in HIV/HSV-2 co-infected

- Spak et al., Poster 787, Seattle
- 45 persons (38 men; 7 women)
- Daily genital swabs for HSV-PCR (penile, vulvar, cervical, perianal) for 60 days q YR x 3
- 105 sampling sessions
 - Men: 1023/5520 (18.5%) days + (813 asym)
 - Women: 204/892 (22.9%) days + (162 asym)

HSV-2 Shedding Rates in HIV/HSV-2 co-infected

- <200 CD4+

- W/I 90d ART 33%
- Est ART 31%, p=.26
- No ART 24%, p=.05

- >200 CD4+

- W/I 90d ART 26%
- Est ART 14%, p<.001
- No ART 7%, p<.001

MRSA bacteremia

- Burkey, et al., Poster 789, Baltimore
- 2000-2003
- Case-control, 1:4
- 3554 patients; 8280 person-years, 158 episodes of *S. aureus* bacteremia (19.1 events/1000 person-years)
- Overall, 60 cases MRSA bacteremia, 38.0%, 7.2 events/1000 person-years

MRSA bacteremia

- Proportion MRSA increased from 23.8% 2000 to 46.7% 2003
- Adjusted multi-variant analysis OR
 - Inj. Drug use 6.50 (95% CI 2.76, 15.3)
 - ESRD 18.0 (4.47, 71.8)
 - HIV-1 RNA >400 copies 2.69 (1.03, 7.04)
 - CD4 <200 cells 4.88 (2.22, 10.7)

HIV Prevention: non-occ. PEP

- 5 Presentations
- Session 14 (web-cast)
- Rabaud, et al. Poster 905, French
- Tolerability of 4 PEP regimens
- SOC: 2nRTI + PI
- CBV/NLF vs CBV/LPV/RTN vs CBV/TDF vs TDF/3TC/ATZ-RTN
- No HIV sero-conversion in any group

Rabaud, et al. PEP (1)

	zl + n	zl + l/r	Zl + t	L+t+a/r
N	401	169	171	152
%Sexual exp.	30.0	56.7	28.6	17.0
%msm	25.5	33	31	24
%msw	74.5	67	69	76
Lost f/u	100 (25%)	30 (18%)	23 (13.5%)	26 (17%)

Rabaud, et al. PEP (2)

* P < .05 to each regimen

	ZI + n	ZI + l/r	ZI + t	L+t+a/r
%Discontinuation	Y: 34.5* N: 65.5	Y: 22.5 N: 77.5	Y: 18.5 N: 81.5	Y: 21 N: 79
%clinical AE-all	Y: 79* N: 21	Y: 59 N: 41	Y: 55 N: 45	Y: 55 N: 45
%clinical AE-28d	Y: 68.5* N: 31.5	Y: 47 N: 43	Y: 45.5 N: 54.5	Y: 43.5 N: 56.5

Risk reduction counseling

- Michelle Roland et al., P902, San Francisco
- 457 subjects randomized to standard STND (2) vs enhanced ENH (5) sessions
- 12 month follow-up
- Overall reduction in # unprotected sex acts/6 months: -1.8 STND and -2.3 ENH
- Δ ENH-STND: +1.6 acts if <4 vs -6.2 if >4

Risk reduction counseling

	STND <4 acts	ENH <4 acts	STND >4 acts	ENH > 4 acts
% cum. Incidenc. Re-PEP	21.1	17.2	31.5	17.1
% cum. Incidenc. HIV acquisit.	.67	2.7	12.3	2.4

Drug-drug interactions

Tipranavir

- DeRequena et al., P 579, Italy. C_{trough} TPV and RTN raised 40% with T-20; no change in AUC or C_{max}
- Scholler et al., P 583, Germany. HIV-ve TMC125-AUC, C_{max} , C_{min} reduced 76%, 71%, 82% with TPV/RTN 500/200; no change in TPV or RTN

Drug-drug interactions

Tipranavir

- Harris et al, P 575b, Canada. 15 HIV+ adults (13 men; 2 women) on stable LPV/RTN/SQV + >2 nRTI, to which TMC125 800 BID added.
 - Varying doses 400-533/100-200/800-1000 BID, respectively.
 - C_{max} , C_{min} , AUC of PI's were >80% of baseline (significant only for LPV C_{max} and AUC).
 - Figure 5 suggests TMC125 pK not different from single PI historic controls (15-20 fold variability in TMC125 AUC)

Drug-drug interactions

Tipranavir

- Harris et al, P 584, Canada. HIV+ men. To LPV/RTN 400/100 BID, added TPV/RTN 500/200 BID. LPV- C_{trough} <4.0 ug/ml in up to 50% participants. Need TDM.
- Peytavin et al, P 591, France. HIV+ TPV/RTN 500/200 BID. TDM led to increase in FAPV/RTN to 1400/200 and LPV/RTN to 533/233 BID to achieve therapeutic TPV/FAPV/LPV levels.

ATZ and LPV/RTN

Pharmacokinetic Interaction

- Pham et al, P585, Baltimore
- 15 HIV- adults, 14/15 males, 12/15 black
- Periods:
 - 1: ATZ/RTN 300/100 QD d1-10
 - 2: ATZ 300 QD + LPV/RTN 400/100 BID d11-24
 - 3: 1 + LPV/RTN 400/100 BID d25-34

ATZ and LPV/RTN

Pharmacokinetic Interaction

	P-1	P-2	P-3	2 vs 1 GMR	3 vs 1 GMR	3 vs 2 GMR
ATV Cmax	4.23	3.49	3.60	.83 P=.057	.85 P=.087	1.03 P=.60
ATV Cmin	.51	.75	.84	1.45 P=.006	1.64 P=.0002	1.13 P=.34
ATV AUC	39.62	36.40	39.59	.92 P=.28	1.00 P=.99	1.09 P=.14
LPV Cmax	9.8 (historic)	9.99	9.67	1.05 P=.27		.97 P=.56
LPV Cmin	5.5 (historic)	3.99	5.12	.80 p=.11		1.28 P=.001
AUC	92.6 (historic)	85.77	89.70	.96 p- .44		1.05 p=.34