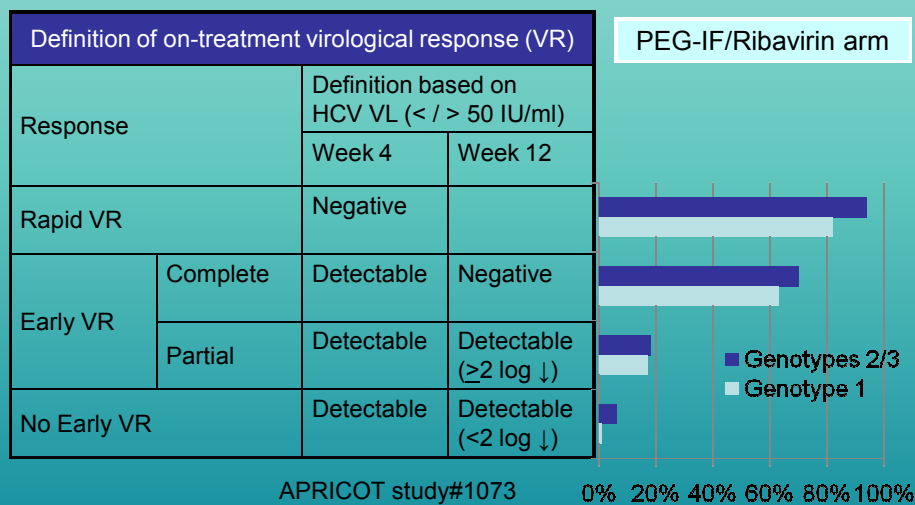


Hepatitis and Other Co-Infections

On treatment responses at 4w and 12w predict sustained virological response (SVR)



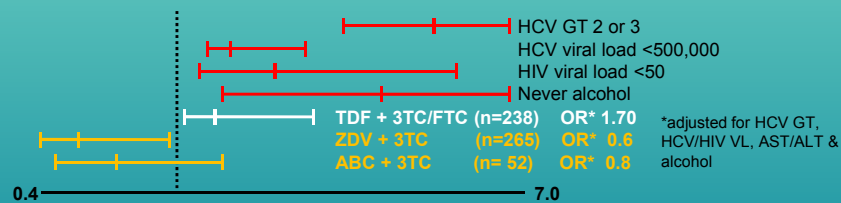
TDF plus 3TC/FTC associated with improved response to PEG IF/RIB in HCV/HIV

DESIGN

- Retrospective multicentre cohort
- HIV/HCV co-infected patients
- on PEG IF-RBV & HAART
- Exclusions: other nRTI, HBSAg+

TDF + 3TC/FTC	N=238
ZDV/D4T/ABC + 3TC	N=481

MULTIVARIATE ANALYSIS:



GESIDA #1076

TDF plus 3TC/FTC associated with improved response to PEG IF/RIB in HCV/HIV

DESIGN

- Retrospective multicentre cohort
- All HIV/HCV co-infected patients
- All on PEG IF-RBV & HAART
- Comparison of 2NRTIs

TDF + 3TC/FTC	N=186
ABC + 3TC	N=70

RESULTS

- Response to PEG-IF/RBV > in those receiving HAART containing TDF + 3TC/FTC
- Multivariate analysis significant OR:
 - HCV viral load Log decrease
 - HIV undetectable viral load
 - Genotype 2-3
 - TDF + 3TC/FTC

1.85
3.5
8.9
2.6

Mira et al #1074

Successful treatment for HIV/HCV co-infection reduces liver related morbidity

DESIGN

- Observational cohort
- HIV/HCV co-infected
- PEG-IF/RIB start Jan '00-'06
- 6m follow-up: clinical, lab, liver biopsy, USS, AFP
- SVR = -ve HCV VL 24w post-treatment

Clinical outcome rate/100 person yrs	SVR	No SVR	P
All-cause death	0.46	3.12	.003
Liver-related death	0.23	1.65	.028
Decompensated liver disease	0.23	4.33	<.001
HCC	0	0.83	.099
Liver transplantation	0	1.02	.034
New AIDS event	0.23	0.93	.144

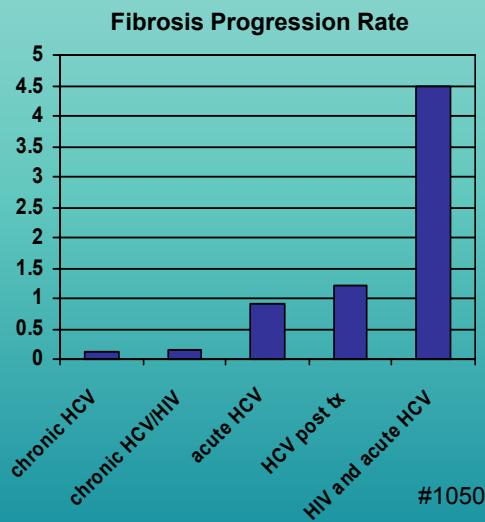
GESIDA 3603 - #60

Rapid fibrosis after acute HCV infection in MSM

DESIGN

- Prospective cohort study of HIV +ve MSM with acute HCV
- Liver histology and risk factors
- Acute HCV infection was diagnosed using a combination of 3 criteria:
 - HCV antibody seroconversion
 - ALT >10-fold ULN
 - Wide fluctuation in HCV viral load

- Fibrosis progression rate (FPR) = $\frac{\text{Fibrosis stage}}{\text{interval between date of biopsy and peak ALT}}$



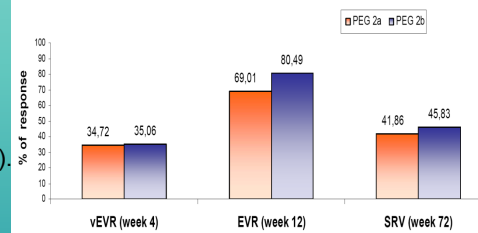
Pegylated IF α 2a vs. α 2b in HIV/HCV no significant differences

DESIGN

- Randomised, MC, open label
- Inclusion criteria: detectable HCV RNA, ALT >1.5-fold ULN, abnormal liver histology, CD4 >250 cells/mL, HIV RNA <50000 c/mL.
- Treatments:
 - PEG α 2b (80 to 150 μ g/week adjusted to body weight)
 - PEG α 2a (180 μ g/week)
 - Both plus RBV (weight adjusted).
- Duration of treatment 48w.
- Primary endpoint SVR = HCV RNA negative at week 72

RESULTS

- Global vEVR, EVR and SVR:



- No difference across genotypes
- Similar adverse effects

#1081b

Kwa Zulu Natal, South Africa

Tugela Ferry

Continuing Cases with High Mortality

Jan 2005 to Sept 2007

- **Total Cases MDR / XDR TB = 471**
 - MDR TB = 205 (43%)
 - XDR TB = 266 (57%)
- **Mortality**
 - XDR TB Deaths = 223 (84%)
 - MDR TB Deaths = 135 (66%)

Gerald Friedland, #112

XDR TB outbreak is due to cross-infection

Genotyping of isolates from XDR TB outbreak in Tugela Ferry (South Africa)

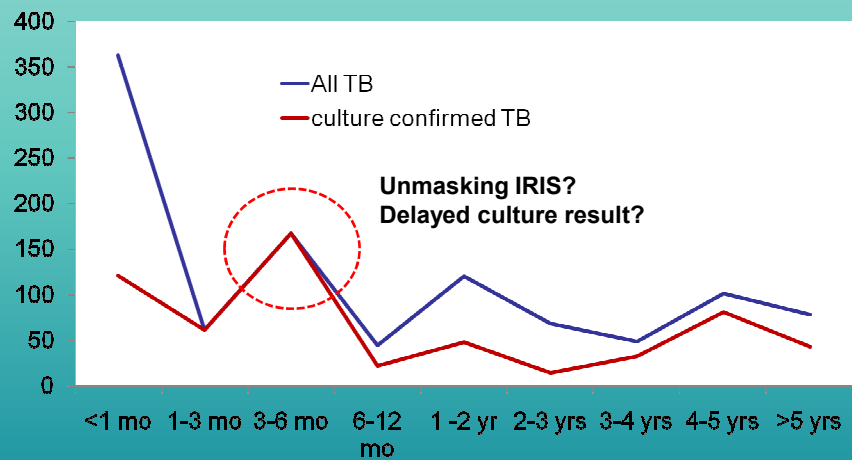
6/2005-6/2006

- 7 (41%) susceptible > MDR
- 8 (47%) susceptible > XDR
- 1 (6%) MDR > XDR
- 1 (6%) susceptible > MDR > XDR
- All follow-up isolates had different spoligotypes compared with initial isolates
- → exogenous re-infection

Andrews et al #143 (USA/South Africa)

TB after HAART in US & Canada

9937 HIV+ patients in US & Canada (IeDEA cohort) 1995-2006
Incidence of new TB after HAART initiation



Sterling et al #1001

TB – IRIS: No evidence for increased Interferon response to TB antigens

50 Thai patients initiating ART with TB treatment
 12/50 developed IRIS
 Quantiferon Gold assay for IFN release
 Contrary to Bourgarit et al. AIDS 2006; 20(2):F1-7. «IRIS = Cytokine Burst»
 Subgroup IRIS treated with steroids: lower f/u IFN-y

Figure 2: IFN-γ Response to MTB Antigens

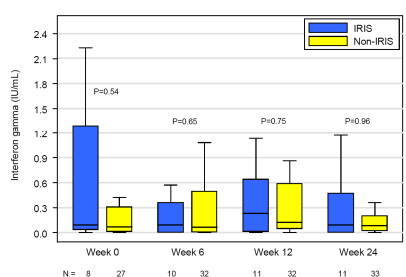
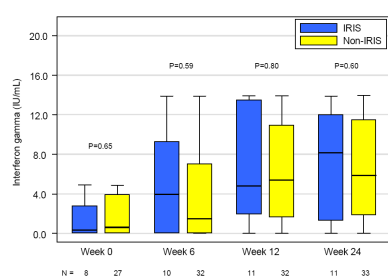


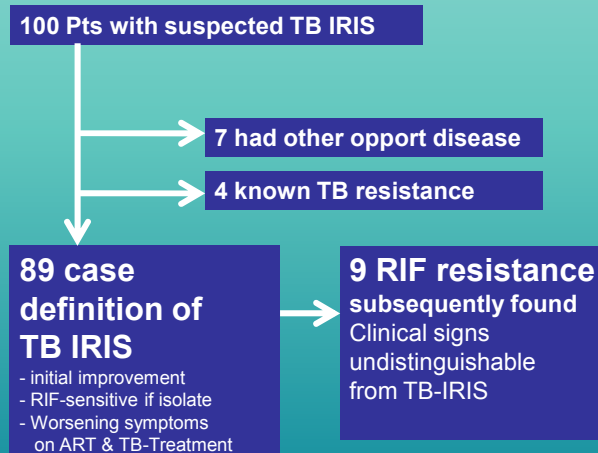
Figure 3: IFN-γ Response to PPD



Van Thieu #1008

High rate of MDR TB in patients with suspected TB-IRIS

Large HIV / TB centre in Cape Town



Rebe et al, #1009

Early ART in Cryptococcal Meningitis reduced mortality

- 92 patients with first episode CM in Botswana
- 26 on ART for 93 days [47 – 310]
- Comparing untreated versus ART-treated
- Inpatient mortality:
 - 2/26 (8%) versus 14/66 (21%)
 - adjusted OR 0.19 [0.04 – 1.00]

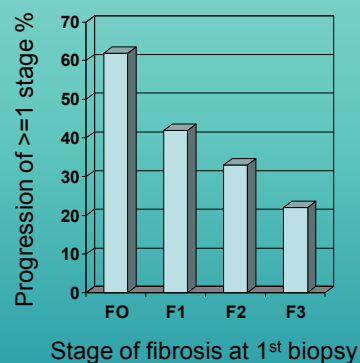
Bisson et al #1010

Rapid progression of fibrosis in HCV/HIV co-infected despite HAART

DESIGN

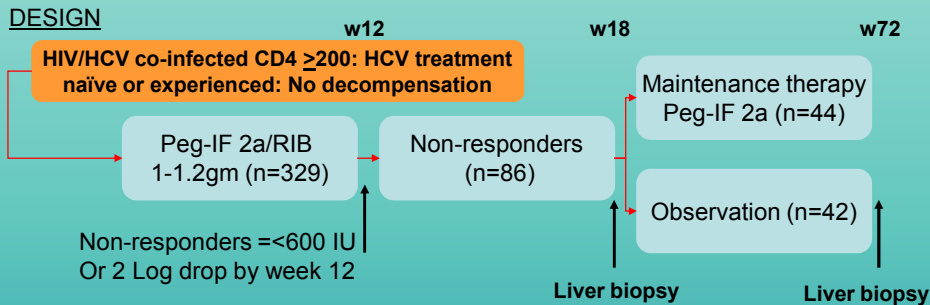
- Retrospective cohort study
- Inclusion:
 - HCV/HIV
 - 2 liver biopsies >1 yr apart
 - No cirrhosis on 1st biopsy
 - No alternative cause for liver disease
 - Regardless of HCV/HIV treatment
- Scheuer histology index used (fibrosis 1-4 score)
- Median time between biopsies 40m: 81% on HAART
- Outcome:
 - change in fibrosis score

Progression of at least 1 stage between liver biopsies



#1055

No benefit to PEG IF 2a monotherapy in HIV/HCV non-responders to PEG IF/RIB



RESULTS

- Interim analysis of those who have completed 72w with paired liver biopsies
- No change in observation arm > study stopped
- Trend towards worsening fibrosis in therapy arm
- Limitations – short term follow-up, small numbers so far.

Sherman et al (ACTG A5178) #59

Immediate vs Deferred ART in acute opportunistic infection

- Randomised trial in 282 pts with OI other than TB
- 63% PCP, 13% Cryptococcal Meningitis, 10% Pneumonia

	Immediate ART	Deferred ART
Median time to ARV start	12 days	45 days
Death or further AIDS defining OI	14% *	24%
No progression, VL detectable	38%	31%
No progression, VL <50	48%	45%
Time to CD4 > 50	8.1 weeks	3.9 weeks
IRIS	6%	9%

Zolopa et al (ACTG A5164) #142

Gene Markers for IRIS

- Longitudinal observation of HIV+ patients starting ART
- 38 controls without opportunistic infection -
- 28 after recent cryptococcal meningitis [CM] (35 +/- 12 days after dx)
- 22 patients developed IRIS (with/without CM)
- Gene array from RNA from whole blood
- Baseline gene expression for T-cell activation, cell death, and chemokine/cytokine signalling predicted IRIS
- Needs confirmation in second sample
- Translation into available tests?

Boulware et al #1007 (Minneapolis / Kampala / Denver)