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BHIVA 'Best of CROI' Feedback Meetings

London | Birmingham
Haydock | Wakefield | Newcastle
Edinburgh | Cardiff

CROI 2013 – hepatitis/TB and opportunistic infections and malignancies - summary

- Some continuing interest in HBV and specific issues
  - Protective effect of TDF based regimens (HBV PrEP)
  - Intensification with PegIFN?
  - HBV in the resource-poor setting
- HCV is the new HIV!
  - 2 oral abstract driven sessions
  - 1 symposium
  - 1 young investigator session
  - Numerous poster sessions
- TB and other opportunistic infections
  - Timing of ART in cryptococcal meningitis
  - Use of urine-LAM for TB diagnosis
  - New anti-TB drugs and more on drug-drug interactions

OA 33: Heuft et al, Protective effect of anti-HIV therapy against HBV

Methods - 1

- **setting:** OLVG cohort (1983 – 2012; N=2942)
- **selection:**
  - all HBV susceptible patients at entry
    - anti-HBc & anti-HBs negative (<10 IU/L)
  - 2nd sample available in time for follow-up HBV serology
    - if possible: before start or switch treatment
- **analysis:**
  - incident infection *(anti-HBc conversion)*
    - relation with exposure to HBV active cART (3TC, FTC, TDF)
    - Kaplan Meier (HBV-free survival) & log-rank test
  - vaccination success *(anti-HBs conversion)*

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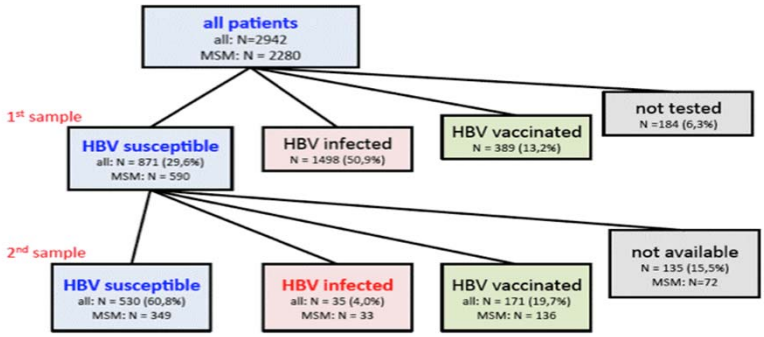
results – 1
flow chart



results – 2
Kaplan Meier: HBV free survival (MSM)

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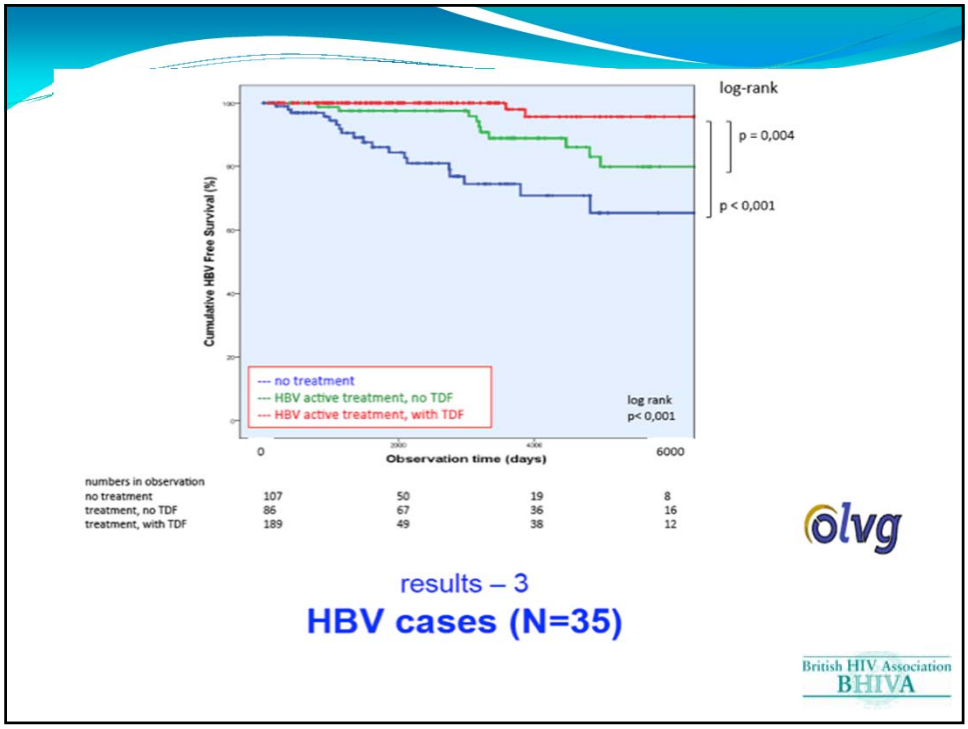
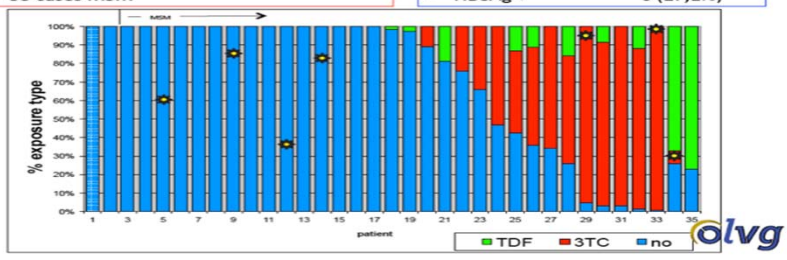


results – 3

HBV cases (N=35)

- 1 case: woman (HBsAg negative)
- 1 case: heterosexual man (HBsAg negative)
- 33 cases MSM

hepatitis (ALT 2x)	7 (20,0%)
HBsAg +	6 (17,1%)
HBeAg +	6 (17,1%)



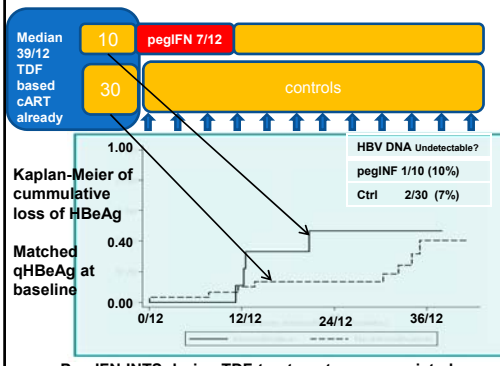
results – 4

observations

- incident HBV infection indeed rare (N=35)
  - *NB since 2002: >200 cases acute HCV (in MSM)*
- most TDF users also used 3TC a/o FTC
- case-record analysis for hepatitis:
  - most converters: asymptomatic
  - 3 cases on 3TC-regimen (ALAT > 2x ULN)
    - 1 case on ABC/3TC: no YMDD mutation in HBV-DNA
  - no cases on TDF-regimen

Can pegIFN intensification help clear HBeAg in TDF treated HBV/HIV co-infection?

- PA 668 Anders Boyd et al.
- Case control from larger French HIV/HBV prospective cohort



- **Peg-IFN-INTS during TDF-treatment was associated with accelerated HBeAg-loss**
- **But no effect on qHBeAg/qHBsAg decline or long-term serological outcomes.**
- **Adding peg-IFN to a TDF-containing regimen may not be a beneficial option in co-infection**

- PA669 Patrick Miailhes et al.
- The ANRS HB01 EMVIPEG Study
- N=51, no control group

	on pegIFN	24/52 post pegIFN
HBeAg loss	12/51 (24%)	8/51 (16%)
HBeAb seroconversion	6 (12%)	4 (8%)
HBsAg loss	2 (4%)	2 (4%)

- **addition of pegIFN did not allow to increase the rate of HBe seroconversion in HBeAg⁺ HIV co-infected patients**

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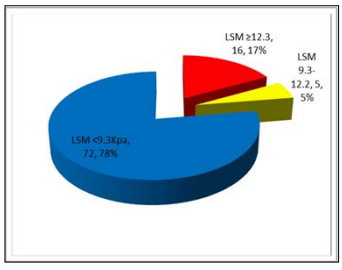
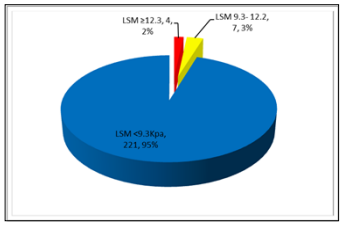
PA 654: Agbaji et al, HBV in the resource-poor setting; how useful is FibroScan?

HBV/HIV co-infected



HIV mono-infected



	Univariate		Multivariate	
	OR, 95% CI	p value	OR, 95% CI	p value
Age ≥30 yrs	0.83 (0.26,3.03)	0.74	0.50 (0.14,1.87)	0.30
Male gender	1.52 (0.50,4.51)	0.40	1.18 (0.35,3.92)	0.79
HBV DNA ≥3.3 log IU/mL 1,2	6.5 (1.99, 22.97)	0.0003	6.09 (1.96,18.91)	**0.002**
HBeAg reactive	2.50 (0.69, 8.41)	0.10	-	-
Married	1.1 (0.37, 3.46)	0.86	-	-
Current alcohol use	2.62 (0.81, 8.19)	0.06	2.38 (0.74,7.60)	0.15
ALT ≥303	0.80 (0.27, 2.46)	0.66	-	-
BMI ≥25	0.44 (0.10-1.57)	0.17	0.52 (0.14,1.82)	0.29
CD4 <200	1.72 (0.53,5.30)	0.30	1.26 (0.37,4.29)	0.71
HIV VL ≥400,000	1.16 (0.18, 5.35)	0.83	-	-
Platelets <150	2.18 (0.45, 9.76)	0.24	-	-

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HCV CROI 2013

Pertinent issues:

- new drugs and data in co-infected patients
- More on drug-drug interactions
- IFN-free studies – results from mono-infected patients
- Who can wait for new treatments and how do we monitor them?

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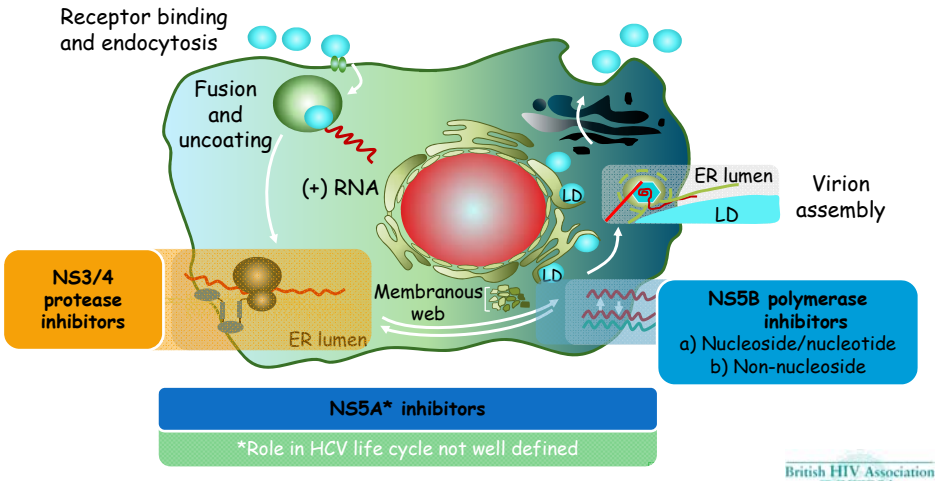
Essential knowledge: HCV Life Cycle and DAA Targets



Adapted from Manns MP, et al. Nat Rev Drug Discov. 2007;6:991-1000.

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NS3/4 Protease inhibitors + PegIFN + R

- TVR and BOC in 'real life'
  - Patients failing previous IFN-based therapies
  - Patients with advanced stages of fibrosis
- Newer NS3/4 PIs
  - BI201335 – Faldaprevir
  - TMC435 - Simeprevir
- TVR for acute HCV

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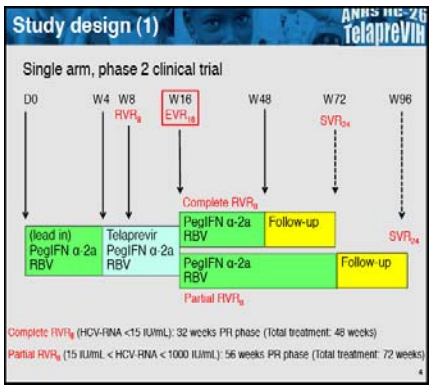
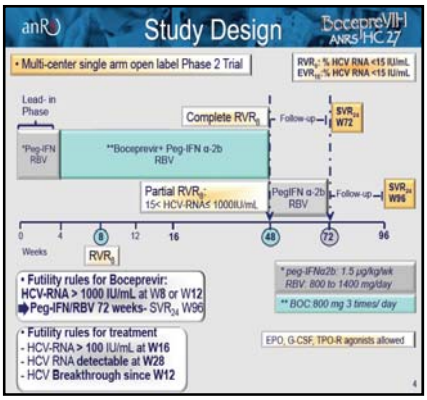
OA 36/37: ANRS TVR and BOC for previously treated co-infected patients





Patients with de-compensated cirrhosis excluded

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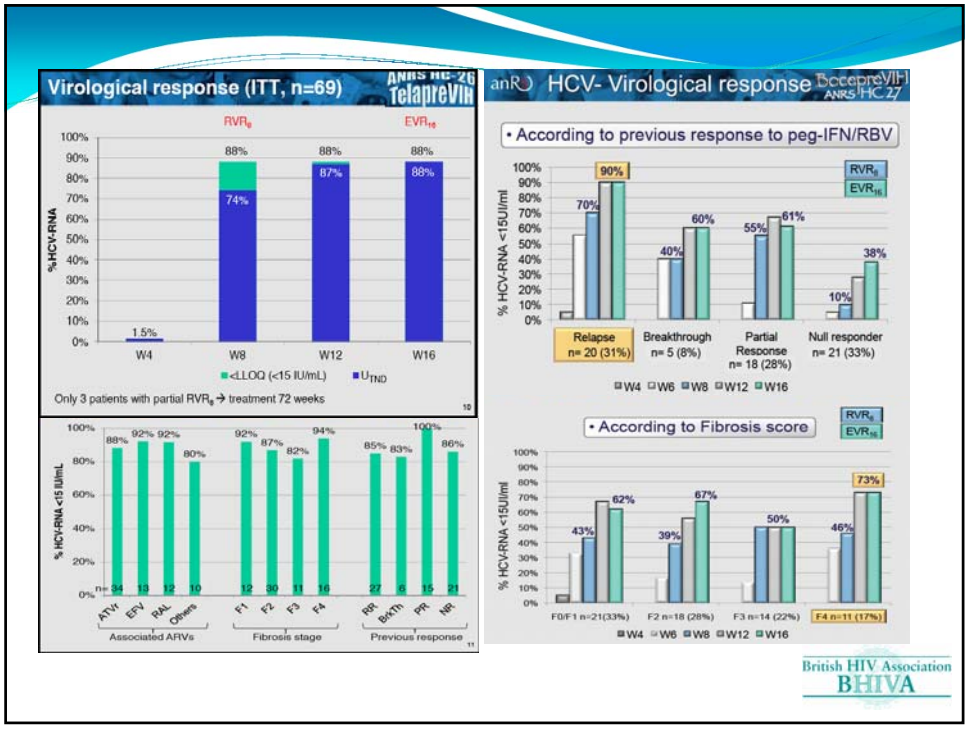
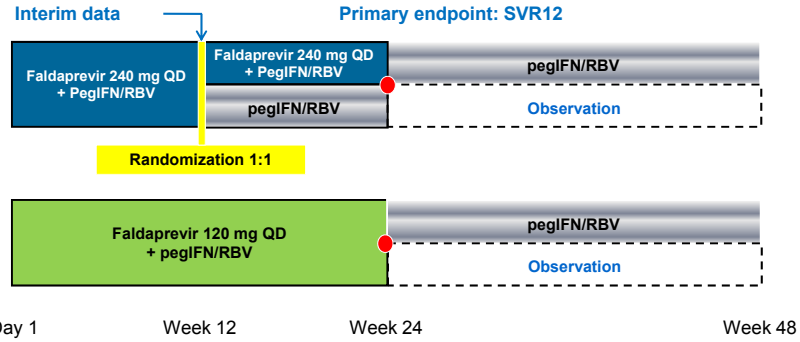


OA40LB: Faldaprevir STARTVerso 4 Early Virological Responses: Study design

Phase III open-label, sponsor-blinded study in treatment-naïve and relapser patients with chronic HCV GT-1 and HIV infection



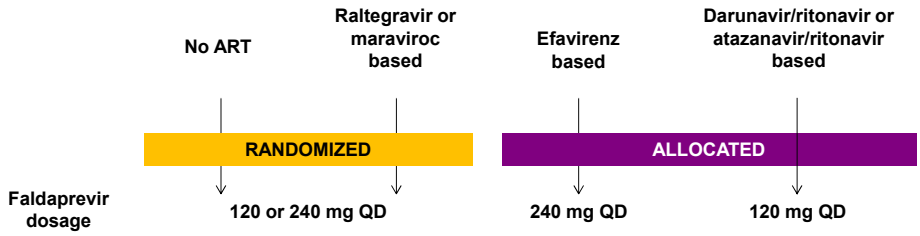
● **Patients who achieved ETS were re-randomized 1:1. Patients who did not achieve ETS continued PegIFN/RBV**

ETS: Week 4 = HCV RNA below lower limit of quantification (LLoQ, 25 IU/mL, target detected) and Week 8 = HCV RNA 'target not detected' at Week 8

All patients were observed for 24 weeks following cessation of therapy

ETS, early treatment success; LLoQ, lower limit of quantification <25 IU/mL, target detected; PegIFN: pegylated interferon alfa-2a 180 µg once weekly; QD, once daily; SVR, sustained virologic response at 12 weeks after end of treatment.
RBV: ribavirin 1000 or 1200 mg daily dose for body weight <75 kg or ≥75 kg, respectively

- **Chronic HCV GT-1 infection, compensated cirrhosis**
  - **HCV treatment-naive or relapsed following prior treatment with pegIFN/RBV**
- **Chronic HIV infection**
  - **Patients were either ART-naïve or on stable ART**



Permitted antretrovirals:
Abacavir, 600 mg QD or 300 mg BID; atazanavir/ritonavir, 300 mg/100 mg QD; darunavir/ritonavir, 800 mg/100 mg QD; efavirenz, 600 mg QD; emtricitabine 200 mg QD; lamivudine, 300 mg QD or 150 mg BID; raltegravir, 400 mg BID; maraviroc, 300 mg BID

ART, antiretroviral therapy; BID, twice daily; HAART, highly active antiretroviral therapy; NRTI, nucleoside reverse transcriptase inhibitor

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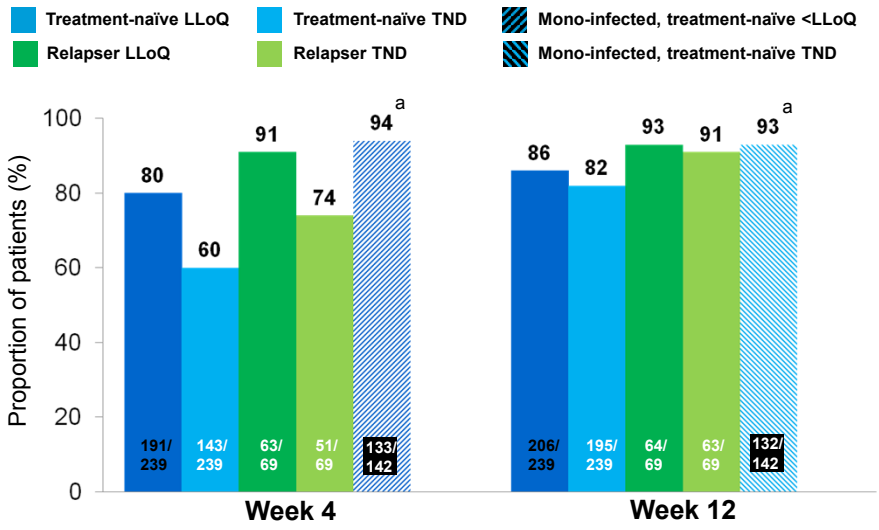
Early virologic response in HIV/HCV co-infected patients:
HIV/HCV co-infected patients vs HCV mono-infected patients



[a]SILEN-C1 study arm of 240mg QD FDV plus pegIFN/RBV in HCV GT1 treatment-naïve monoinfected patients without cirrhosis; data on file

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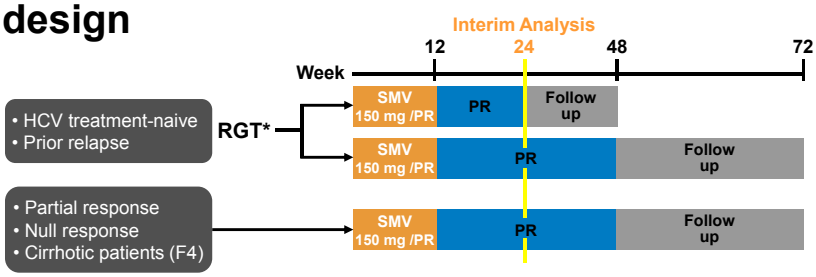
OA 154LB: Simeprevir (TMC435) C212 study design



- Primary endpoint: SVR12, safety and tolerability
- Secondary endpoints: virologic response at other time points, on-treatment failure and relapse rates
- Interim analysis:
  - all patients included in the analysis had completed 24 weeks of treatment or had discontinued prior to that point
  - patients numbers:

    Week 24: 100
    Week 28: 71
    Week 36: 27

*RGT criteria: HCV RNA <25 IU/mL (detectable or undetectable) at Week 4 and undetectable at Week 12; SMV, simeprevir; PR, peginterferon-α2a + ribavirin

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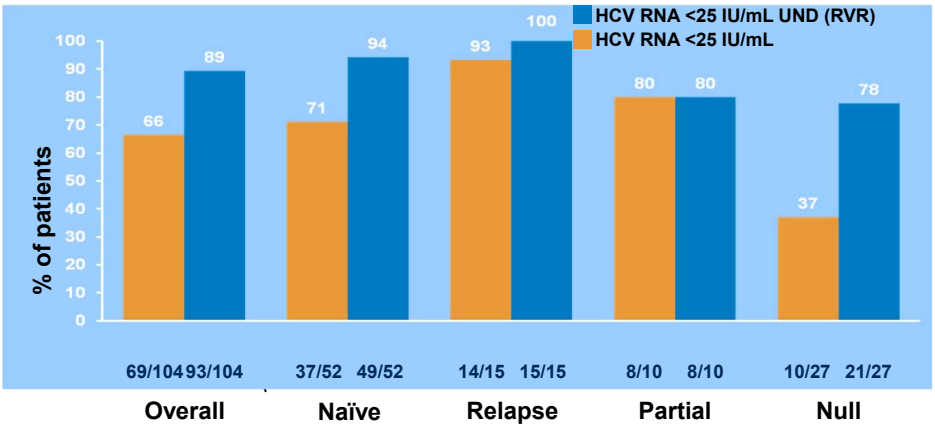
C212: Virologic response of patients treated with SMV/PR at Week 4 (RVR)



RVR, rapid virologic response; SMV, simeprevir; PR, peginterferon; UND, undetectable

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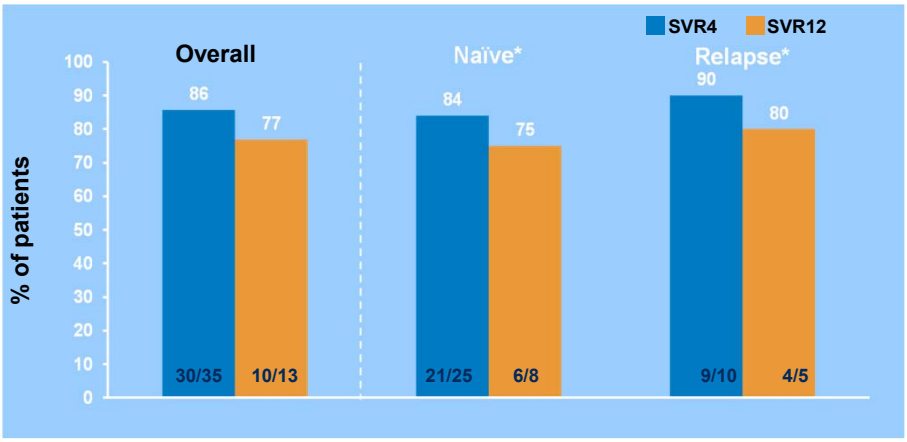
C212: Preliminary SVR4 and SVR12 rates in patients treated with SMV/PR



- Data presented for patients with SVR data available at the time of the interim analysis
- Treatment-naïve patients were RGT-eligible and prior relapsers were non-cirrhotic

*Including only non-cirrhotic patients. SMV, simeprevir; PR, peginterferon + ribavirin

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Faldaprevir & Simeprevir - summary

- Once daily NS3/4 PIs
- Well-tolerated
  - No major treatment limiting SEs (over & beyond IFN+R)
  - Hyperbilirubinaemia – probable class effect (+R effect)
- Excellent EVRs
- RGT (shortened total duration to 24 weeks) may be possible
- Early indication is that >80% EVR16 this will translate into SVR12
  - Will previous null responders have a similar response?

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OA 516LB: Shortened duration of therapy with TVR + pegIFN + R for acute G1 HCV?

- Single-arm, open label, single centre study of TVR+PegIFN+R in HIV+ patients with acute HCV
- STD definitions of acute HCV
- 40 assessed
- 18 went on to therapy
- Response Guided Therapy – stop at week 12 if RVR, otherwise 12 further weeks of PegIFN and R
- 15(83%) achieved SVR4
  - All had achieved an RVR
  - 2 requested further 12 weeks of PegIFN + R
  - 3 treated for <5 weeks
- 2 never achieved VL <100, I rebounded at week 12
- Issues
  - ?enough time for spontaneous clearance
  - ~75% of the Rx population IL28B CC
- Will shortened duration of therapy be possible for geno 1 acute HCV Infections?

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Drug-drug interactions, anti-HCV therapy

- TVR and RBV
- BOC and RPV (NB: BOC not compatible with EFV, boosted-PIs, except possibly ATV/r)
- FDV and EFV, DRV/r

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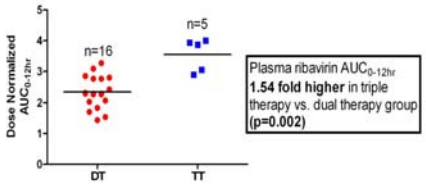
Telaprevir-Ribavirin: Study NCT01097395 (PA 34, Hammond *et al*)

- Incidence of anaemia doubles with triple therapy (TT) RBV, PEG-IFN, TLV vs dual therapy (DT) RBV-PEG-IFN
- Increased RBV exposure in presence of HCV PI may explain increased incidence of anaemia
- Comparison of RBV plasma and phosphorylated intracellular concentrations in patients receiving TT vs DT

Ribavirin Plasma AUC

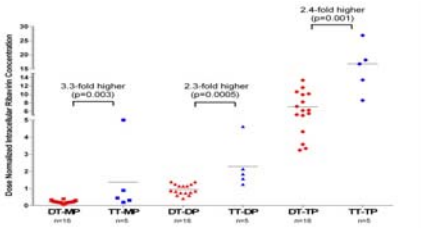


Possible Mechanisms

•Telaprevir effect on transporters?

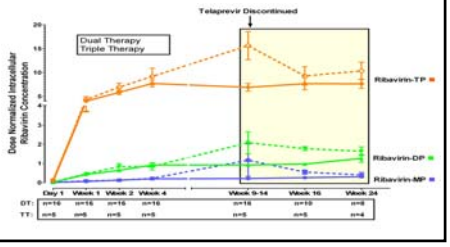
•Food effect?
- RBV AUC and C_{max} ↑42% and 66% respectively, when taken with a high fat meal. Telaprevir taken with food

Ribavirin RBC concentrations



- Similar results observed for ribavirin PBMC concentrations

Ribavirin RBC concentrations over course of treatment



Boceprevir-Rilpivirine (Abstract 537, Rhee *et al*)

Boceprevir
-time-dependent inhibitor of CYP3A4
-Metabolised via aldo-ketoreductase and CYP3A4, substrate of P-gp transporter

Rilpivirine
-Primarily metabolised by CYP3A4
-Potentially a P-gp substrate and inhibitor

Period 1: BOC 800mg TDS (6 days)
Period 2: RPV 25mg OD (11 days)
Period 3: RPV 25mg OD + BOC 800mg TDS (11 days)

Pharmacokinetics of RPV following multiple doses of RPV alone and in combination with BOC

	RPV alone	RPV+BOC	GMR (95% CI)
PK parameters	**GM (95% CI)**	**GM (95% CI)**	
$AUC_{0\text{-last}}$ (ng.h/ml)	2636 (2198-3162)	3659 (2994-4473)	1.39 (1.27-1.52)
C_{24hr} (ng/ml)	96.3 (80-116)	145.4 (118.6-178.1)	1.51 (1.36-1.68)
C_{max} (ng/ml)	177 (144-219)	205 (165-254)	1.15 (1.04-1.28)
T_{max} (hr)	4 (3-5)	4 (4-12)	

•RPV had no significant effect on BOC pharmacokinetics

•Co-administration of RPV and BOC increased exposure to RPV
- No serious clinically/laboratory adverse events
- No change in ECG parameters
- Increase in RPV exposure less than observed with telaprevir, HIV protease inhibitors, ketoconazole

→ **No dose adjustment of RPV recommended when co-administered with BOC**

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Faldaprevir (BI201335) PK Interactions with EFV, TDF, DRV/r (Abstract 35, Sabo *et al*)

- Faldaprevir (FDV) is a substrate and moderate inhibitor of CYP3A4, mild inhibitor of CYP2C9, inhibitor of UGT1A1

Treatment	n	GMR (90% CI)		
		Cmax	AUC	Cmin
DRV/r+FDV	14	1.28 (1.16-1.43)	1.15 (1.01-1.31)	0.88 (0.69-1.13)
TDF+FDV	16	0.95 (0.85-1.05)	1.22 (1.12-1.33)	1.47 (1.35-1.61)

Effect of FDV on DRV and TFV exposure

Unlikely to be clinically relevant

- DRV/r 800/100mg OD-FDV 240mg OD
- TDF 300mg OD-FDV 240mg BD

Treatment	n	GMR (90% CI)	
		Cmax	AUC
MDZ+FDV	15	1.11 (0.85-1.44)	2.24 (1.87-2.69)
MDZ+FDV -EFV	14	0.41 (0.27-0.62)	0.39 (0.30-0.51)

Effect of FDV and FDV-EFV on midazolam exposure

Net induction of CYP3A4 when FDV administered with EFV

- EFV 600mg-FDV 240mg BD-MDZ 7.5mg single dose

Treatment	Cmax (ng/ml)	AUC (ng.h/ml)	Cmin (ng/ml)
FDV+DRV/r*	↑64%	↑129%	↑283%
FDV+EFV-MDZ	↓28%	↓35%	↓46%
FDV+TDF	↓18%	↓22%	↓25%

Effect on FDV exposure

- CYP3A4 inhibition by DRV/r
- CYP3A4 induction by EFV

*Based on cross trial comparisons

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IFN-free therapies: 'teasers' with data from HCV mono-infection

- Sofosbuvir (Gilead Nuc NS5b inhibitor) + ribavirin for G1 difficult to Rx
- Final results Electron study - Sofosbuvir + Ledipasvir (Gilead NS5a inhibitor) + R for G1
- Analysis of risk of relapse/ideal Rx duration from the Abbott IFN-free study (Aviator)
  - ABT450/r (PI) - od
  - ABT 267 (NS5a inhibitor) - od
  - ABT333 (Non-nuc polymerase inhibitor) - bd
  - +/- Ribavirin
- Combination of Sofosbuvir + Simeprevir +/- R for G1 Null responders

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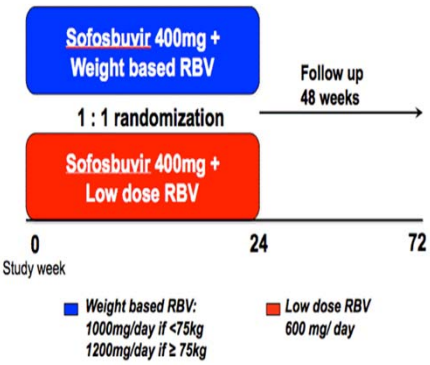
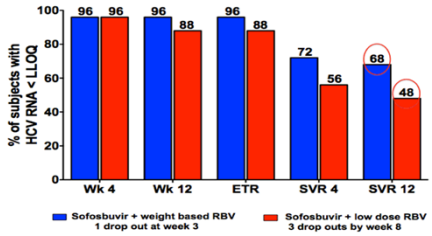
OA 157LB: Sofosbuvir plus high/low dose ribavirin for 'difficult to treat' G1 HCV infection (SPARE study)

Study Design (Part 2)

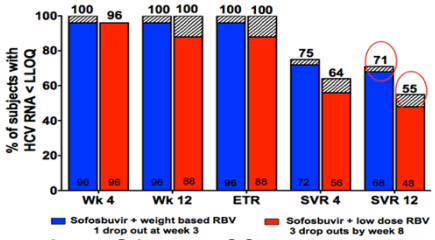
- 50 subjects with all stages of liver disease (including compensated cirrhosis)



Treatment Response (ITT)



Treatment Response (MITT)



Difficult to Rx = Rx naïve, >75% African-American, G1a, non-CC F3/4 – 25%

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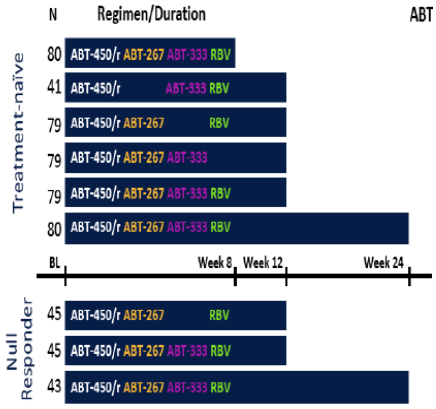
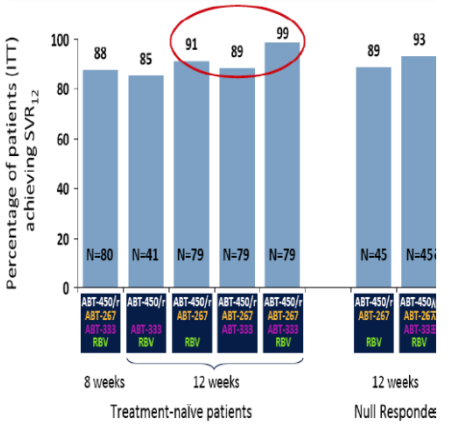
OA38: Aviator study - predictors of relapse

Background: AVIATOR Study Design



Updated SVR_{12} Rates (ITT) in the AVIATOR Study



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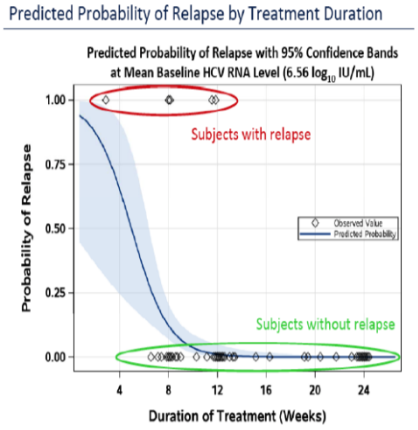
OA38: Aviator study predictors of relapse – quadruple Rx arms only (8, 12 or 24 weeks Rx)



- Probability of relapse after 8 weeks of Rx – 12.2%
- Probability of relapse after 12 weeks – 1.0%
- Marginal association of relapse with genotype 1a and high viral load
- No association with IL28B SNPs (CC vs non-CC)

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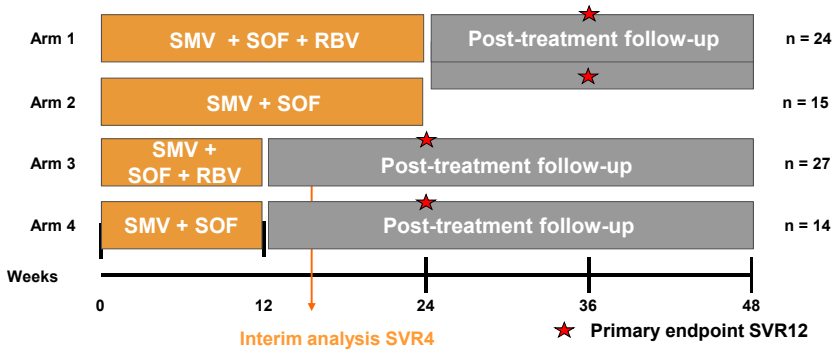
OA 155LB: SVR4 results of a once-daily regimen of simeprevir (TMC435) plus sofosbuvir (GS-7977) with or without ribavirin in HCV genotype 1 null responders (COSMOS study)*



- Cohort 1: n=80 patients randomized 2:1:2:1
- Cohort 2: n=87 patients randomized 2:1:2:1
- SMV 150 mg QD + SOF 400 mg QD with/without RBV (Copegus®) 1000 or 1200 mg/day (BID)
- Interim analysis of Cohort 1 conducted when all patients in 12 week treatment arms (arms 3 and 4) reached SVR4 time point or discontinued early

COSMOS: efficacy results

Patients	24 weeks		12 weeks	
	SMV + SOF + RBV	SMV + SOF	SMV + SOF + RBV	SMV + SOF
RVR[1], n/N (%)	18/22 (81.8)	10/15 (66.7)	23/27 (85.2)	8/14 (57.1)
Undetectable end of treatment, n/N (%)	10/12 (83.3)	8/9 (88.9)	27/27 (100.0)	14/14 (100.0)
Relapse, n	0	0	1	1
SVR4, n/N (%)	4/6 (66.7)	5/5 (100.0)	26/27 (96.3)	13/14 (92.9)
SVR8, n/N (%)	4/6 (66.7)	5/5 (100.0)	26/27 (96.3)	13/14 (92.9)

Of the patients in the 12 week arms who achieved SVR8
- 24/24 who reached post-treatment Week 12 had undetectable HCV RNA (SVR12)
- 8/8 who reached post-treatment Week 24 had undetectable HCV RNA (SVR24)

[1]RVR is based on patients with available data at Week 4 (2 patients discontinued before Week 4)
EOT, end of treatment; RVR, rapid virologic response; SMV, simeprevir;
SOF, sofosbuvir; SVR, sustained virologic response

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Thoughts about IFN-free therapies

- IFN-free therapies are going to be a reality in the next few years
  - Gilead Photon 2 study (phase 3) Sofosbuvir + Rib for HIV/HCV G1, 2, 3 and 4 patients just about too kick-off in Europe
- Nuc + ribavirin for G1 (and other difficult to treat patients) will probably need 24 weeks of therapy
- Combinations of DAAs may allow duration of therapy to shorten to 12 weeks even for difficult to treat patients
- At least at the moment, Ribavirin appears to be an important component

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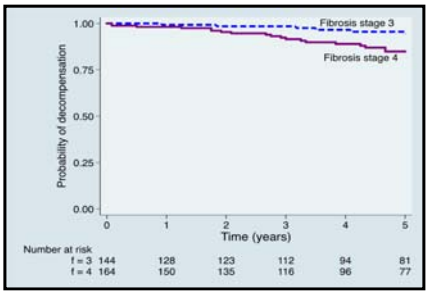
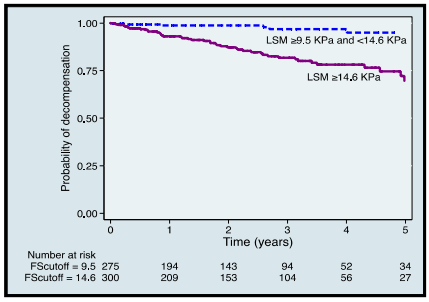
PA 727: Risk of Decompensation events Among HIV/HCV-co-infected Individuals with Advanced Fibrosis: Implications for the Timing of Therapy Against HCV

Juan Macías et al.

To assess the risk of decompensation events among HIV-infected individuals with chronic hepatitis C and advanced liver fibrosis

- Retrospective multi-centre cohort study~575patients
- HCV/HIV with F3/F4 fibrosis
  - 317 biopsy assessed
- 45% previous anti-HCV treatment
- 12 year follow-up





Risk of decompensation:

a) Fibrosis stage
   F4 on biopsy or LSM >14.6

b) Platelet count
   <105

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CROI 2013: HCV – implications for clinical practice

- TVR and BOC work for 'difficult to treat' co-infected G1 patients
  - Probably need 48 weeks
  - Numerous side-effects
- Beware drug-drug interactions
- New generation once daily NS3/4 PIswith PegIFN and Ribavirin (faldaprevir and simeprevir) around the corner
  - Better tolerated, excellent EVRs
- Shortened duration triple therapy (12 weeks) may be possible for acute G1 HCV/HIV
  - Enrol on to clinical trials wherever possible
- IFN-free therapies may be a reality in the next 2-3 years
- If waiting for new or IFN-free be aware of risk of hepatic de-compensation events
  - F4 on biopsy, Liver stiffness >14.5 or platelet counts <100

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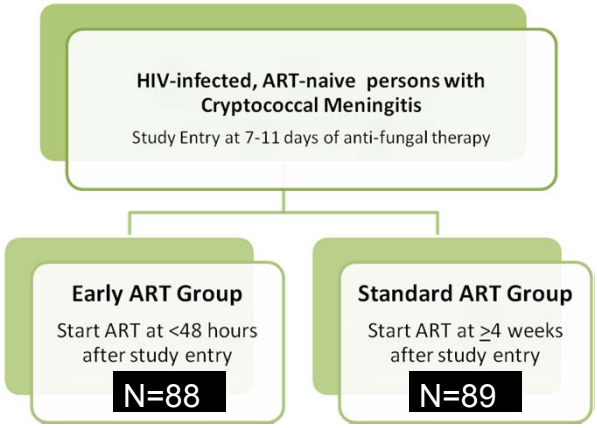
OA144: Randomized Strategy Trial
Cryptococcal Optimal ART Timing (COAT) Trial



Clinicaltrials.gov NCT01075152

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Treatment for Cryptococcal Meningitis

Medication and Dose	2 weeks	~ 3 weeks	8 weeks	46 weeks
Amphotericin (0.7-1.0 mg/kg/day)				
Fluconazole 800mg daily	Continue until CSF is sterile[1]			
Fluconazole 400mg daily				
Fluconazole 200mg daily				Continue for ≥12 months AND until CD4 > 200 cells/mL for ≥ 6 months
Treatment Phase	**Induction**		**Consolidation**	**Secondary Prophylaxis**

[1] Longer duration of consolidation therapy if CSF culture positive at 2-weeks.

Therapeutic LPs at Diagnosis, Day 7, Day 14, and additional LPs as needed for pressure control

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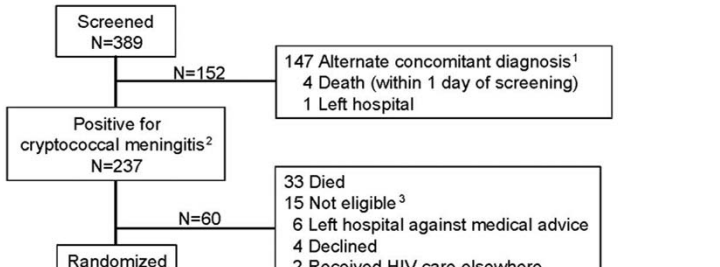
Patient disposition



	GCS[4] <15	GCS =15	Randomized Group: Early ART	Randomized Group: Deferred ART
Kampala N=115	13		6	7
		102	51	51
Mbarara N=35	9		5	4
		26	12	14
Cape Town N=27	2		1	1
		25	13	12
Overall	24	153	88	89

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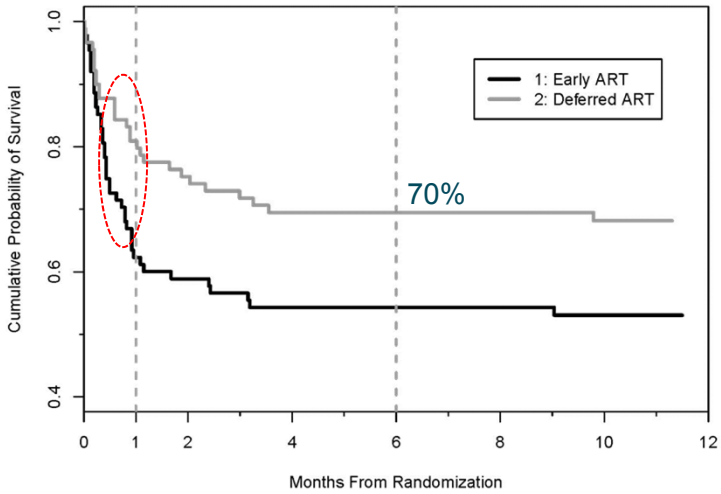
Overall Survival



Number at Risk:

1:	88	54	51	47	47	45	44
2:	89	71	65	60	60	58	57

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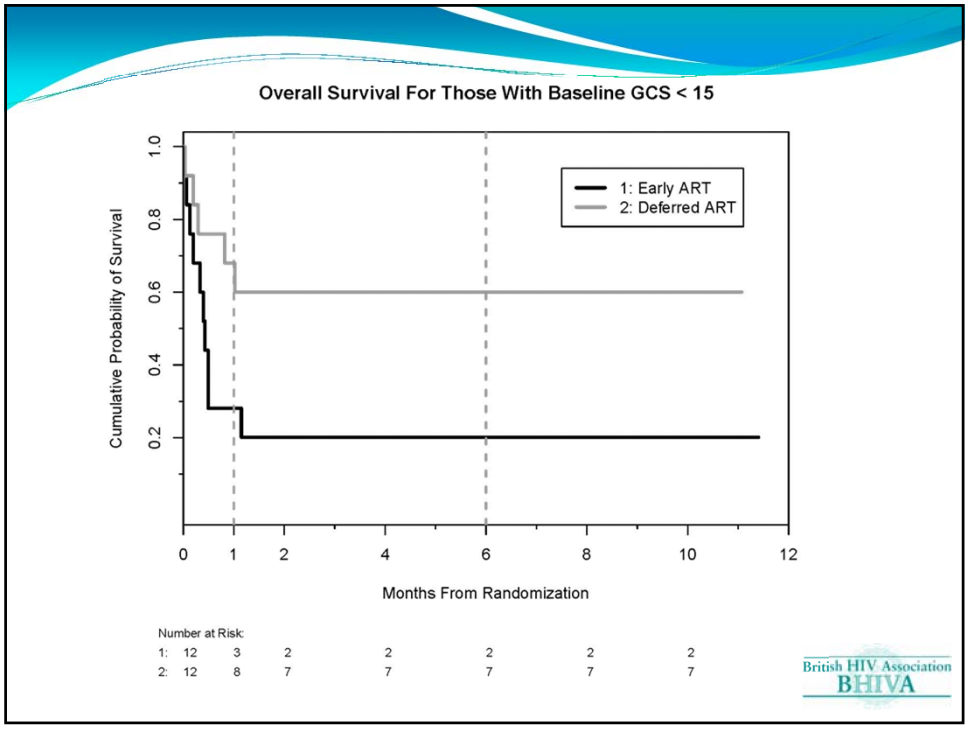
Overall Survival For Those With Baseline GCS < 15
Cumulative Probability of Survival
1.0
0.8
0.6
0.4
0.2
1: Early ART
2: Deferred ART
0
1
2
4
6
8
10
12
Months From Randomization
Number at Risk:
1: 12 3 2 2 2 2 2
2: 12 8 7 7 7 7 7
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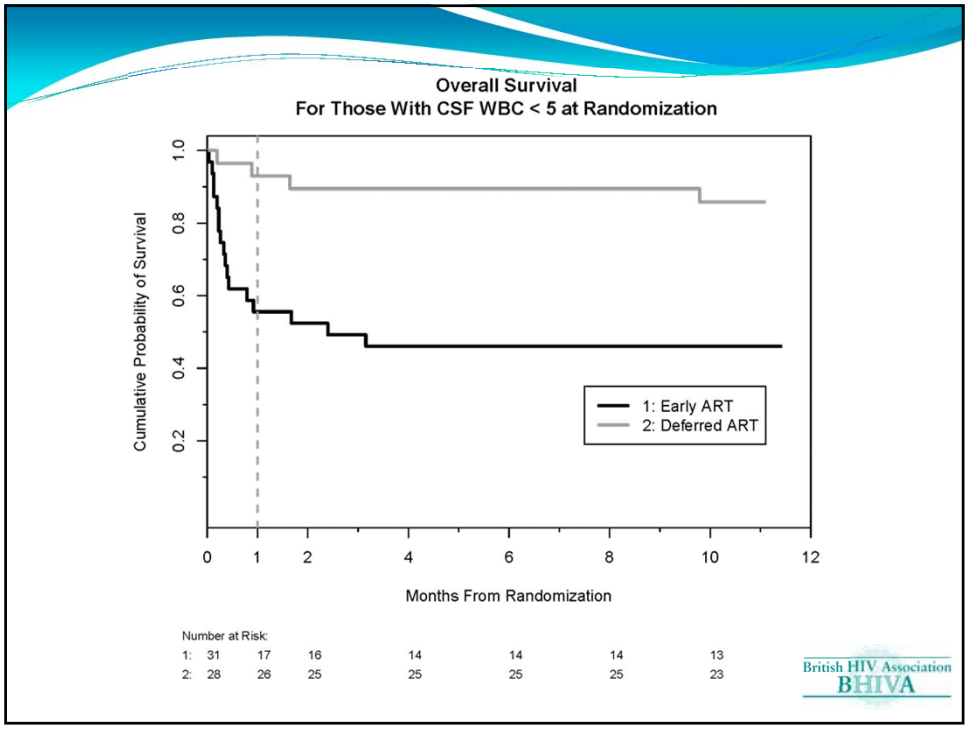
Overall Survival
For Those With CSF WBC < 5 at Randomization
Cumulative Probability of Survival
1.0
0.8
0.6
0.4
0.2
1: Early ART
2: Deferred ART
0
1
2
4
6
8
10
12
Months From Randomization
Number at Risk:
1: 31 17 16 14 14 14 13
2: 28 26 25 25 25 25 23
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IRIS Incidence

Subjects with IRIS Events - By Treatment Group (Adjudicated)			
	Early ART	Deferred ART	P-value [1]
Subjects with at least one event			
Definite/Probable CM-IRIS	5 (5.7%)	5 (5.6%)	0.999
Possible CM-IRIS	9 (10.2%)	2 (2.2%)	
No CM-IRIS	74 (81.8%)	62 (69.6%)	
Died before ART	2 (2.3%)	20 (22.4%)	
Overall	88 (100.0%)	89 (100.0%)	
Definite/Probable/Possible CM-IRIS of those receiving ART	14 (16.2%)	7 (10.1%)	0.347

[1] Fisher's exact p-value

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Causes of Death

- Early vs. Deferred
- cryptococcosis (21 vs. 10)
- septicemia (8 vs. 5)
- TB (2 vs. 2)
- IRIS-related (1 vs. 2)

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Prevalence of Fluconazole resistant *Cryptococcus neoformans* in HIV patients in Kampala

- Prospective cohort of HIV patients with Cryptococcal meningitis, as a nested study within the COAT trial.

Fluconazole MICs at CM diagnosis (n=80):

Fluconazole MIC	Interpretive category	Number of isolates
≤ 8 mcg/mL	Sensitive (S)	17 (21.3%)
16-32 mcg/mL	Dose dependant susceptible(S-DD)	55 (68.8%)
≥ 64mcg/mL	Resistant (R)	8 (10%)

4 of 8 patients with resistant fluconazole MICs died.

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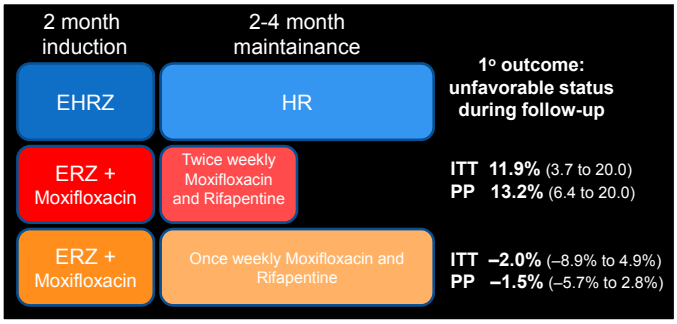
OA147LB
High-dose Rifapentine with a Quinolone for Treatment of Pulmonary TB: The RIFAQUIN Trial

- TB Rx takes 6-8months
- Problems = cost, adherence, logistics
- Can using oxifloxacin and Rifapentine simplify / shorten the regimen?
- In mice : droping INH ↑ sterilisation ability

Rifapentine + Moxi + Z completely sterilises mouse TB

- N= 827 Smear +ve PTB
- 28% HIV, median CD4 312 and not on cART
- Single Blind RCT in RSA, Botswana, Zimbabwe + Zambia



Conclusion

- 4 months regime was inferior, mainly due to increased relapse
- 6 month regimen was non inferior to standard Rx
- Few grade 3 or 4 AE in all arms

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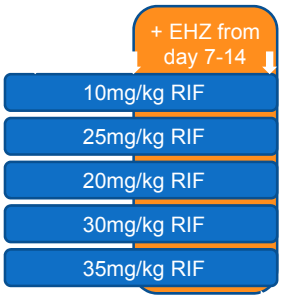
OA148LB
What Is the "Right" Dose of Rifampin?

- Current Rifampicin (RIF) dose of 10mg/kg is arbitrary – no maximum tolerated dose (MTD) study
- Murine and Human data suggest increased RIF dose might enable shorter treatment
- 1º aim: assess MTD of RIF in Sm+ve PTB



Results

- Adverse effects

= no difference

- Fall in CFU over days 1,7,14

= highest in 35 mg/kg RIF

- Time to positivity of liquid medium days 1,7,14

= dose related and highest in 35mg/kg RIF

Conclusion

- RIF up to 35 mg/kg was safe and well tolerated with the highest activity seen with 35 mg/kg indicating that the current accepted treatment dose of RIF may be too low

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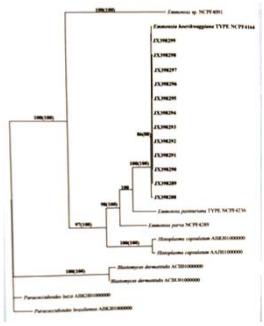
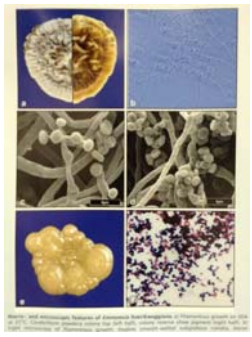
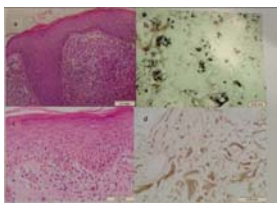
Paper #874
Southern African, HIV and Disseminated Histoplasma? Think again – the emergence of *Emmonsia hoerikwaggiana* sp. nov.

- 2008-2011, University of Cape Town, South Africa
- 13/24 cases initially diagnosed disseminated H capsulatum
- PCR identified new species
- 3 died, 10 responded to ART and variety of antifungals

Night sweats	4 (31)
Fever >38	**12 (92)**
Loss of Weight	**10 (77)**
Lymphadenopathy	**13 (100)**
Skin lesions	1 (8)
Anaemia Hb<12g/dL	13 (100)
Abnormal CXR	**11 (85)**
CD4 T cell <100 cells/μL	12 (92)
Elevated GGT and or ALP	8 (89)







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- **Dr D Asboe,** *Chelsea and Westminster Hospital, London*
- **Dr S Bhagani,** *Royal Free Hospital, London*
- **Dr D Chadwick,** *James Cook University Hospital, Middlesbrough*
- **Dr D Churchill,** *Royal Sussex County Hospital, Brighton*
- **Dr P Collini,** *University of Sheffield*
- **Dr S Das,** *Coventry and Warwickshire Hospital*
- **Dr D Dockrell,** *Royal Hallamshire Hospital, Sheffield*
- **Dr T Doyle** *Royal Free Hospital, London*
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