Advances in Chronic Hepatits C Management and Treatment

REPORTING ON EASL 2015

Comprehensive Expert Review and Discussion of Key Presentations

C-EDGE COINFECTION: PHASE 3 STUDY OF GRAZOPREVIR/ELBASVIR IN PATIENTS WITH HCV/HIV

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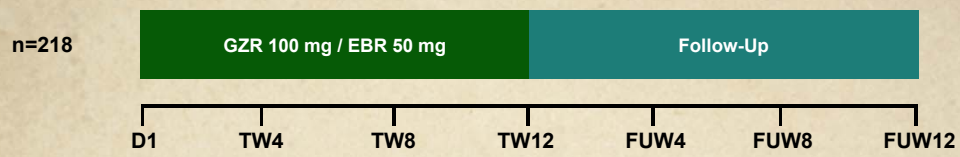
Abstract P0887

C-EDGE Co-infection: Study Design



- An open-label, single-arm, multicenter study across Europe, USA, and Australia
- Primary endpoint: SVR12 (HCV RNA <15 IU/mL*)
- Treatment-naive patients with HCV GT1, 4 or 6 infection with or without cirrhosis
- Co-infected with HIV-1:
  - Naive to ART with CD4+ >500 cells/mm^3 and HIV RNA <50,000 copies/mL
  - On stable on ART† for ≥8 weeks and CD4+ >200 cells/mm^3 and undetectable HIV RNA

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C-EDGE CO-INFECTION: Demographics

	All Patients N = 218
Age, years mean (SD)	48.7 (8.9)
Sex, n (%)	
Male,	183 (83.9)
Female	35 (16.1)
Race, n (%)	
White	167 (76.6)
Black or African-American	38 (17.4)
Asian	6 (2.8)
Other	7 (3.2)
Ethnicity, n (%)	
Hispanic / Latino	14 (6.4)
Not Hispanic / Latino	194 (89.0)
Not reported	10 (4.6)
HCV genotype, n (%)	
1a	144 (66.1)
1b/other	45 (20.7)
4	28 (12.8)
6	1 (0.5)
Baseline HCV RNA >800,000 IU/mL, n (%)	130 (59.6)
Cirrhotic*, n (%)	35 (16.1)
IL28B CC (%) , n (%)	77 (35.3)

*Of the 35 patients (16.1%) with cirrhosis, 27 were diagnosed by Fibroscan, 6 by biopsy, and 2 by Fibrotest and APRI.

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C-EDGE CO-INFECTION: Demographics

	All Patients N = 218
Antiretroviral therapy, n (%)	
Receiving ART with undetectable HIV RNA	211 (96.8)
Naive to ART	7 (3.2)
Baseline CD4 count (cells/μL)	
Mean (SD)	613 (0.57)
Median (1st quartile – 3rd quartile)	568 (424-766)
Antiretroviral therapy, backbone n (%)	
Abacavir-containing regimen	47 (21.6)
Tenofovir-containing regimen	164 (75.2)
Antiretroviral therapy, third agent n (%)	
Raltegravir	113 (51.8)
Dolutegravir	59 (27.1)
Rilpivirine	38 (17.4)

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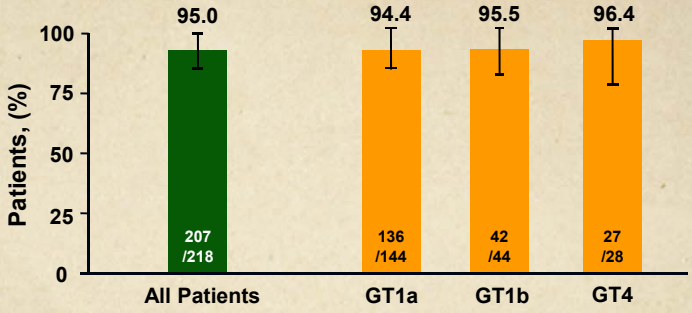
C-EDGE COINFECTION: Phase 3 Study Grazoprevir/Elabasvir in HCV/HIV



	All Patients	GT1a	GT1b	GT4
LTFU or discontinued unrelated to VF	4	3	1	0
Breakthrough	0	0	0	0
Relapse	6	4	1	1
Reinfection	1	1	0	0

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C-EDGE TN: Resistance-Associated Variants in Relapse

	HCV GT	ART Regimen	Resistance-Associated Variants			
			At Baseline		At Failure	
			NS3	NS5A	NS3	NS5A
56-year-old black/AA male	1a	Tenofovir emtricitabine, rilpivirine	V36M/L	L31M/L	Q80K, D168A	Q30K, L31M
63-year-old black/AA male	1a	None	Q80K	Y93S	Q80K, D168a	Q30R, Y93S
37-year-old white male	1a	Tenofovir, emtricitabine, raltegravir	WT	WT	WT	Q30R/Q
43-year-old white male	1a	Abacavir, lamivudine, raltegravir	WT	WT	WT	WT
35-year-old white male	1b	Abacavir, lamivudine, raltegravir	WT	WT	Y56F, V107I/V	WT
53-year-old white male	4	Tenofovir emtricitabine, rilpivirine	WT	WT	WT	L28S
43-year-old white male	1a	Lenofovir, emtricitabine, rilpivirine	V55A/V	WT	N/A (GT3)	N/A (GT3)

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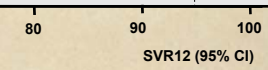
C-EDGE CO-INFECTION: SVR12
Subgroup Analysis (Full Analysis Set)

Variable		n/m	SVR12 % (95% CI)
ALL		207/218	95.0 (91.2, 97.5)
Gender			
	Male	172/183	94.0 (89.5, 97.0)
	Female	35/35	100.0 (90.0, 100.0)
Age			
	<65 years	201/212	94.8 (90.9, 97.4)
	≥65 years	6/6	100.0 (54.1, 100.0)
Race			
	White	158/167	94.6 (90.0, 97.5)
	African American	36/38	94.7 (82.3, 99.4)
	Asian	6/6	100 (54.1, 100.0)
IL28B genotype			
	CC	74/77	96.1 (89.0, 99.2)
	Non-CC	133/141	94.3 (89.1, 97.5)
Cirrhosis			
	No	172/183	94.0 (89.5, 97.0)
	Yes	35/35	100 (90.0, 100.0)
Baseline viral load			
	≤800,000 IU/mL	84/88	95.5 (88.8, 98.7)
	>800,000 IU/mL	123/130	94.6 (89.2, 97.8)



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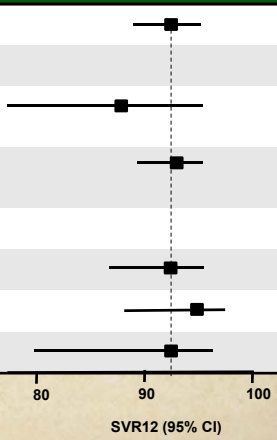
C-EDGE CO-INFECTION: SVR12
Subgroup Analysis (Full Analysis Set)

Variable		n/m	SVR12 % (95% CI)
ALL		207/218	95.0 (91.2, 97.5)
ART regimen			
	Abacavir-containing	43/47	91.5 (79.6, 97.6)
	Tenofovir-containing	158/164	96.3 (92.2, 98.6)
ART third agent			
	Raltegravir	107/113	94.7 (88.8, 98.0)
	Dolutegravir	58/59	98.3 (90.9, 100.0)
	Rilpivirine	36/38	94.7 (82.3, 99.4)



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C-EDGE CO-INFECTION: Adverse Events

Patients with:	All Patients N = 218
Serious AE, n (%)	6 (2.8)
Serious drug-related AE, n (%)	0 (0)
Discontinuation due to AE, n (%)	0 (0)
Deaths, n (%)	0 (0)
Any adverse event, n (%)	167 (76.6)
Fatigue	29 (13.3)
Headache	27 (12.4)
Nausea	20 (9.2)
Late ALT or AST >5.0 x ULN, n (%)	2 (0.9)
Lowest hemoglobin on treatment, n (%)	
≥8.5 to <10 g/dL	1 (0.5)
Elevation of total bilirubin, n (%)	
>2.5 – 5.0× baseline	8 (3.7)
>5.0× baseline	1 (0.5)
Creatinine >2.5x baseline, n (%)	0 (0)

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