ARV Therapies and Therapeutic Strategies

REPORTING ON CROI 2015

Comprehensive Expert Review and Discussion of Key Presentations

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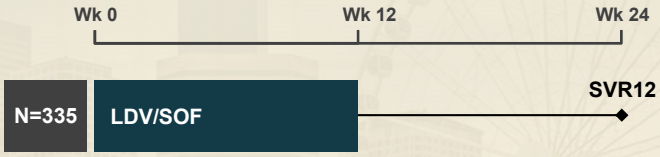
Ledipasvir/Sofosbuvir for 12 Weeks in Patients Coinfected With HCV and HIV-1 (ION-4)

Susanna Naggie; Curtis Cooper; Michael S. Saag; Jenny C. Yang; Luisa M. Stamm; Phillip S. Pang; John McHutchison; Douglas Dieterich; Mark Sulkowski

Abstract 152LB

ION-4 Trial in HIV-HCV: Study Design



- **Phase 3, multicenter, open-label study (NCT02073656)**
- **HCV GT 1 or 4 patients in US, Canada, and New Zealand**
- **Broad inclusion criteria**
  - HCV treatment-naïve or treatment-experienced
  - 20% with compensated cirrhosis
  - Platelets ≥50,000/mm^3; hemoglobin ≥10 mg/dL, CrCl ≥60 mL/min
  - HIV-1 positive, HIV RNA <50 copies/mL; CD4 cell count >100 cells/mm^3
- **ART regimens included emtricitabine and tenofovir disoproxil fumarate plus efavirenz, raltegravir, or rilpivirine**

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ION-4: Baseline Characteristics

	LDV/SOF 12 weeks N=335
Mean age, y (range)	52 (26-72)
Male, n (%)	276 (82)
Black, n (%)	115 (34)
Hispanic or Latino, n (%)	56 (17)
Mean BMI, kg/m^2 (range)	27 (18-66)
IL28B CC, n (%)	81 (24)
GT 1	327 (98)
HCV treatment experienced, n (%)	185 (55)
Cirrhosis, n (%)	67 (20)
Mean HCV RNA, $\log_{10}$ IU/mL ± SD	6.7 ± 0.6
Median CD4 cell count, cells/µL (range)	628 (106-2069)
HIV ARV Regimen	
Efavirenz + FTC + TDF	160 (48)
Raltegravir + FTC + TDF	146 (44)
Rilpivirine + FTC + TDF	29 (9)

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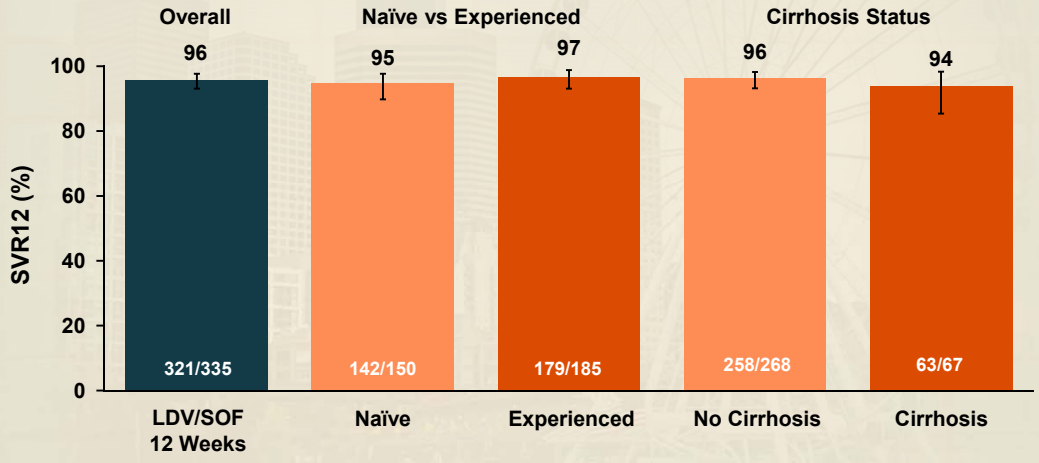
ION-4: SVR12 by Prior Treatment and Cirrhosis



Error bars represent 95% confidence intervals.

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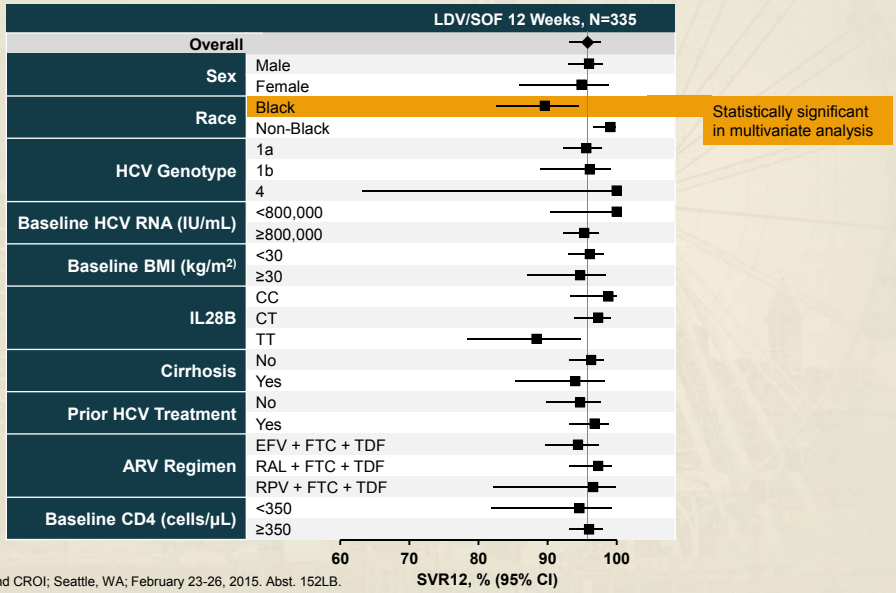
ION-4: SVR12 in Subgroups



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Results: Safety Summary HIV-HCV (ION-4)

	Patients, n (%)	LDV/SOF 12 Weeks N=335
Overall Safety	AEs	257 (77)
	Grade 3–4 AE	14 (4)
	Serious AE	8 (2)*
	Treatment D/C due to AE	0
	Death	1 (<1)†
	Grade 3–4 laboratory abnormality	36 (11)

- Stable CD4 counts through treatment and follow-up phase
- No patient had confirmed HIV virologic rebound

*Serious AEs in >1 patient were hepatocellular carcinoma (n=2) and portal vein thrombosis (n=2) in patients with cirrhosis.
†Confirmed IV drug user developed Staphylococcus aureus sepsis, endocarditis with associated embolic brain abscesses, and multi-organ system failure.

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High SVR Regardless of Time to Suppression with Ombitasvir/Paritaprevir/r & Dasabuvir + RBV

Studies Included in Post-hoc Analyses

Study	N	Genotypes	pegIFN/RBV Treatment-Experienced	Cirrhosis	HIV-1 Co-Infection
SAPPHIRE-I	473	1a, 1b	No	No	No
SAPPHIRE-II	297	1a, 1b	Yes	No	No
PEARL-II	186	1b	Yes	No	No
PEARL-III	419	1b	No	No	No
PEARL-IV	305	1a	No	No	No
TURQUOISE-II	380	1a, 1b	Yes & No	Yes	No
TURQUOISE-I	63	1a, 1b	Yes & No	Yes & No	Yes

Phase 3 studies
Phase 2 study

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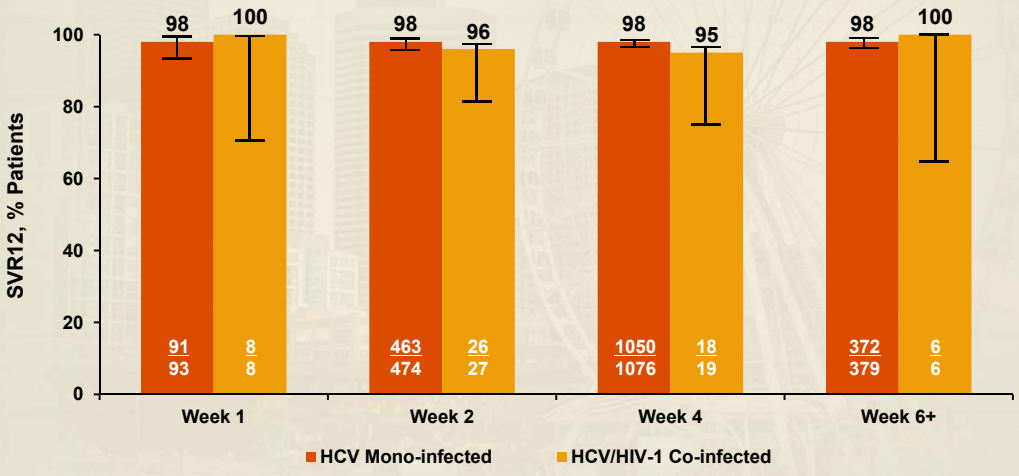
High SVR Regardless of Time to Suppression with Ombitasvir/Paritaprevir/R & Dasabuvir + RBV

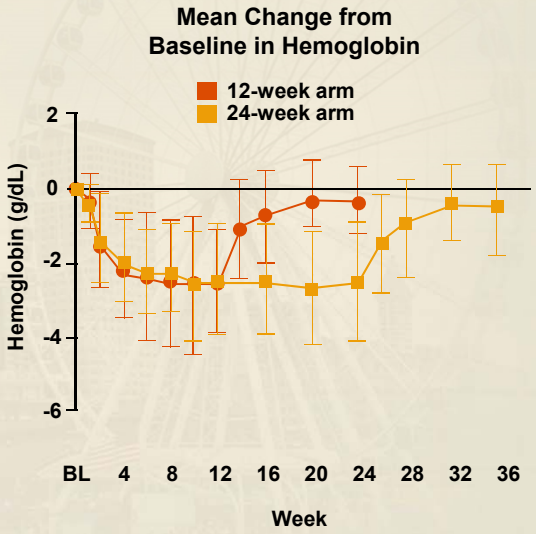
SVR12 by Time to HCV RNA Suppression <15 IU/mL



Wyles D , et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 147.

Hematologic Analysis of Paritaprevir (ABT-450) /R/Ombitasvir and Dasabuvir + RBV in TURQUOISE-I

- Hemoglobin declines to <10 g/dL were infrequent with 3D + RBV treatment
- All patients whose RBV dose was modified due to declines in hemoglobin achieved SVR12



Sulkowski M, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 691.