P011

Real World Effectiveness of Ledipasvir/Sofosbuvir (LDV/SOF) for 8 Weeks in Patients Coinfected With HCV GT 1 and HIV-1

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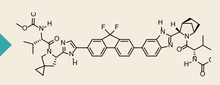
Introduction

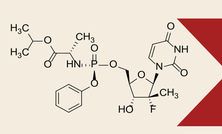
Ledipasvir/Sofosbuvir: A Single Tablet Regimen (STR)

- **Ledipasvir (LDV)**
  - Picomolar potency against multiple HCV genotypes
  - Effective against NS5B RAS S282T
  - Once-daily, oral, 90 mg

LDV NS5A inhibitor



- **Sofosbuvir (SOF)**
  - Potent antiviral activity against HCV GT 1–6
  - Effective against NS5A RASs
  - High barrier to resistance
  - Once-daily, oral, 400-mg tablet



SOF - NS5B nucleotide polymerase inhibitor

- **Ledipasvir/Sofosbuvir STR**
  - Once-daily, oral fixed-dose (90/400 mg) combination tablet, RBV-free
  - Limited DDIs, no food effect

LDV NS5A inhibitor + SOF - NS5B nucleotide polymerase inhibitor

Background

- With the introduction of Direct Acting Antivirals (DAAs), the EASL and AASLD/IDSA/IAS-USA Guidance state “HIV/HCV coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications”.
- LDV/SOF was approved by the FDA and EMA for HIV/HCV coinfection with the same dosage recommendations as in HCV monoinfection.
- Real world cohorts (RWC) have demonstrated excellent efficacy of LDV/SOF for 8 weeks in HCV monoinfected patients.
- The aim of this analysis was to describe the effectiveness of LDV/SOF for 8 weeks in HCV genotype 1 patients with HIV/HCV coinfection in RWC and clinical trials using a pooled analysis.

Objectives

- Descriptive analysis to evaluate the effectiveness of LDV/SOF 8 week treatment regimens in HIV/HCV coinfected patients in the real world.
- Describe SVR12 rates in real-world and clinical trial cohorts.
- Describe SVR12 rates in HIV/HCV coinfection versus monoinfection.

Methods

- Two prospective clinical trials and four real world cohorts were reviewed and pooled.
- Cohorts with fewer than 15 patients were excluded.

Studies Included

Study/ Cohort Name (N=294)	Russian/ Estonia Cohort N=59	Ruane Medical and Liver Health Institute N=20	DHC-R N=76	Madrid-CoRe N=93	Department of Veterans Affairs N=31	Saint Michaels Medical Center N=15
	Isakov et al.	Ain et al.*	Deutsches Hepatitis C-Register	Madrid Coinfection Registry	Backus et al.	Slim et al.
	Gilead Sponsored or Investigator Sponsored Trials (n=79)		Real World Cohorts (n=211)			

* Supported by Gilead Sciences

Results

Baseline Demographics

Characteristic	Russian/Estonia Cohort N=59	Ruane Medical N=20	DHC-R N=76	Madrid-CoRe N=93	VA N=31	Saint Michaels N=15
Mean age, years (range)	34 (23-58)	52 (35-66)	43 (24-67)	49 (45-53)	61 (49-73)	61 (41-77)
Male, n (%)	34 (58)	18 (90)	67 (88)	70 (75)	31 (100)	12 (80)
Race, n (%)						
White	59 (100)	11 (55)	73 (96)	93 (100)	9 (2)	1 (7)
Non-White	0	9 (45)	3 (4)	0	22 (71)	14 (93)
Tx Experienced, n (%)	0	0	58 (76)	0	0	0
Cirrhosis, n (%)	0	0	3 (4)	0	7 (23)	0
Mean HCV RNA $\log_{10}$ IU/mL	6.1	6.0	5.6*	5.9	6.1	1.4
Median CD4 count (range)	531 (417-1006)	514 (106-1038)	400 (200-400)**	N/A	553 (186-1131)	578 (226-1318)
On HIV ARVs, n (%)	49 (83)	19 (95)	69 (91)	89 (95)	30 (97)	14 (93)
TDF-containing regimen, n (%)	21 (36)	15 (75)	49 (64)	N/A	22 (71)	3 (20)
GT 1a, n (%)	15 (25)	17 (85)	64 (84)	67 (72)	21 (68)	9 (60)
GT 1b, n (%)	44 (75)	3 (15)	7 (9)	20 (22)	8 (26)	6 (40)
Unspecified GT 1/ Other, n (%)	0	0	3 (4) / 2 (3)	6 (6)	2 (6)	0

* Data available for 75 patients; ** Data available for 60 patients

Results (Cont’d)

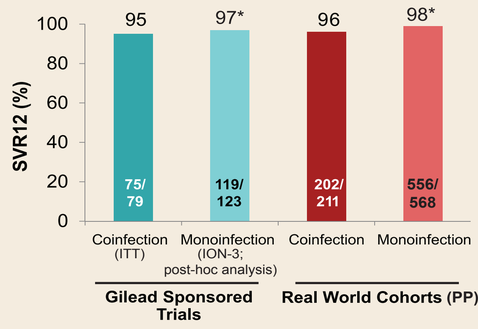
Summary of Results with LDV/SOF for 8 weeks in Patients with HIV/HCV GT 1 Coinfection

Study	Study Design	Treated (N)	SVR** (N%)	Relapse (N%)	LTFU (N%)	Death
Russian/ Estonia Cohort	Prospective	59	57 (97)	2 (3)	0	0
Ruane Medical*	Prospective	20	18 (90)	1 (5)	0	0
DHC-R	Retrospective	76	73 (96)	3 (4)	0	0
Madrid-CoRe	Prospective	93	85 (91)	6 (6)	2 (2)	0
VA	Retrospective	31	30 (97)	0	1 (3)	0
Saint Michaels	Retrospective	15	14 (93)	0	1 (7)	0

* One patient viral non-responder; ** Intention to Treat

- Results from both clinical trials and RWC showed low relapse rates and no deaths.

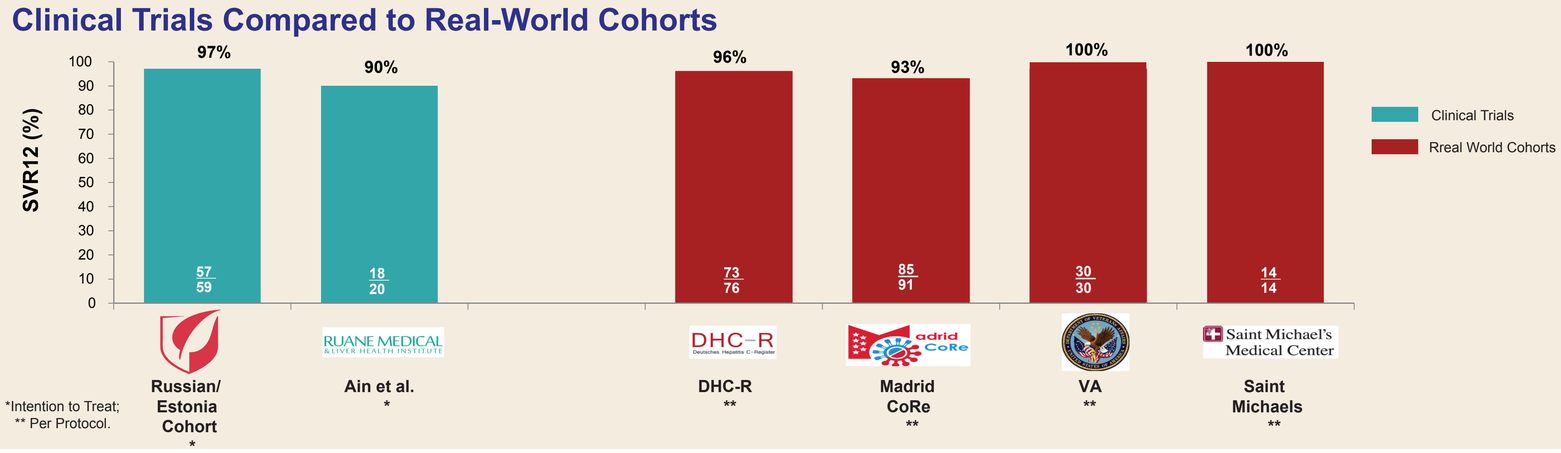
Overall SVR12 in HCV GT 1 Clinical Trials and RWC Treated with LDV/SOF for 8 Weeks



- Similar response rates observed in HIV/HCV coinfected patients compared to HCV monoinfected patients

* TN, non-cirrhotic patients with HCV RNA<6 million IU/mL

SVR12 in HIV/HCV GT 1 Coinfected Patients Treated with LDV/SOF for 8 weeks: Clinical Trials Compared to Real-World Cohorts



*Intention to Treat; ** Per Protocol.

Clinical Trial Cohorts

Russia and Estonia Phase 3b Study

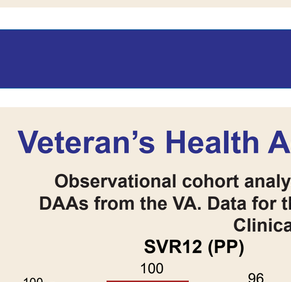
Phase 3b, nonrandomized, open label, multicenter, prospective study evaluated 8 weeks LDV/SOF in TN, NC HIV/HCV GT1 in Russia and Estonia*

- Two patients experienced virologic relapse:
  - 33 year old, GT 1a, White male with HCV VL 6,400,000 IU/mL concomitantly on efavirenz (EFV) + lamivudine (3TC) + atazanavir (ATV); no NS5B or LDV RASs at baseline or relapse
  - 34 year old, GT 1a, White male with HCV VL 3,530,000 IU/mL concomitantly on EFV+3TC+ATV; no NS5B or LDV RASs at baseline or relapse
- Overall treatment was well tolerated with no D/C due to AEs and no SAEs

* Study enrolled 7 patients with HCV RNA > 6 million IU/mL

Ruane Medical and Liver Health Institute

Phase 2, single-center, open-label pilot study with LDV/SOF for 8 Weeks in TN, non-cirrhotic, HIV/HCV GT 1 coinfected patients with HCV VL <6 million IU/mL

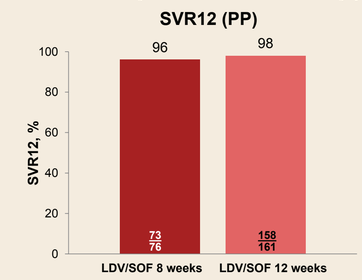


- One patient with virologic non-response: 49 year old, GT 1a, White male with HCV VL 7,850,000 IU/mL (COBAS AmpliPrep/COBAS TaqMan; RealTime PCR 4,570,882 IU/mL) concomitantly on fosamprenavir/ritonavir (FVP/r) + emtricitabine/tenofovir (FTC/TDF). 100% LDV/SOF adherence by pill count
- One patient with virologic relapse: 54 year old, GT 1a, White male with HCV VL 561,000 IU/mL (COBAS AmpliPrep/COBAS TaqMan) concomitantly on dolutegravir (DTG) + FTC/TDF
- In both patients with virologic failure, no NS5A RASs or NS5B S282T were observed at baseline or at time of failure
- LDV/SOF was safe, well tolerated, with no treatment discontinuations due to adverse events

Real-world Cohorts

German Hepatitis C-Registry (DHC-R)

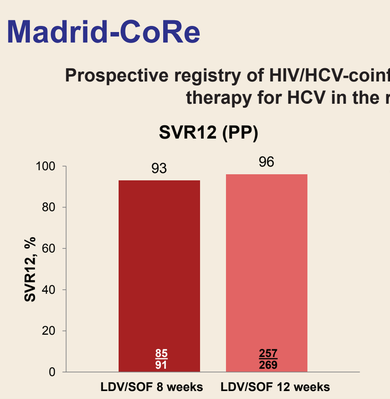
The German Hepatitis C registry is a national multicenter cohort. Treatment regimens were at the discretion of the physician. Data was collected by a web-based data system and confirmed by plausibility checks and on site monitoring



- LDV/SOF for 8 weeks achieves comparable SVR rates to 12 week treatment in HIV/HCV GT 1 patients

Madrid-CoRe

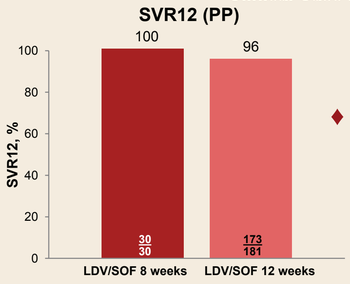
Prospective registry of HIV/HCV-coinfected adults undergoing DAA therapy for HCV in the region of Madrid



- No significant differences were found in effectiveness and safety with LDV/SOF for 8 or 12 weeks for GT 1 in treatment-naïve, noncirrhotic coinfected patients.

Veteran’s Health Administration

Observational cohort analysis of HCV-infected veterans receiving HCV DAAs from the VA. Data for this study were obtained from the VA’s national Clinical Case Registry for HCV

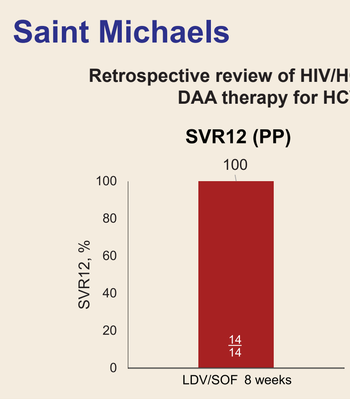


- LDV/SOF for 8 weeks achieves comparable SVR rates to 12 week treatment in HIV/HCV GT 1co-infected patients.

73% (22/30) of patients were Black; all achieved SVR

Saint Michaels

Retrospective review of HIV/HCV GT 1 coinfected adults undergoing DAA therapy for HCV in the region of Newark, NJ



- 8 weeks of LDV/SOF was highly efficacious in predominantly Black (n=13), coinfected patient population.

Conclusions

- This descriptive analysis demonstrates that SVR rates from RWC are comparable to clinical trials.
- High SVR results in this pooled analysis support the use of LDV/SOF for 8 weeks in HIV/HCV GT 1 coinfected patients.
- In the RWC, SVR rates were high across diverse populations, including Black patients (100%, 35/35) from the EU and US.
- The results support the EASL guidelines which recommends the same treatment regimens for
- HIV/HCV coinfected and HCV monoinfected persons (A1 GRADE).
- Early LDV/SOF initiation in coinfected patients before the onset of advanced fibrosis leads to high SVR12 and may reduce morbidity & mortality.

References & Disclosures

Peter Buggisch: Janssen, Abbvie, BMS: Advisory Committees or Review Panels; Falk, MSD, Gilead, Merz Pharma: Speaking and Teaching. **Ana Moreno:** No conflict of interest. **Vasily Isakov:** Abbvie, Gilead, Merck, Janssen, R-pharm: Advisory Committees or Review Panels, Speaking and Teaching; BMS: Speaking and Teaching. **Lisa Backus:** No conflict of interest. **Dani Ain:** No conflict of interest. **Peter Ruane:** Gilead: Advisory Committees or Review Panel, Consulting, Grant/Research Support, and Stock Shareholder; Merck: Speaking and Teaching; Boehringer: Advisory Committees or Review Panel, Speaking and Teaching, Grant/Research Support; Janssen and Abbott: Consulting, Advisory Committees or Review Panel, Speaking and Teaching, Grant/Research Support; Idenix: Grant/Research Support; ViiV: Advisory Committees or Review Panel, Speaking and Teaching; BMS: Consulting, Grant/Research Support, and Speaking and Teaching. **Juan Gonzalez-Garcia:** Gilead, MSD, Abbvie, Janssen, Ciliag, and BMS: Board Membership, Speaking and Teaching. **Sarjita Naik, Swarup Mehta, Jina Lee, Michael Mertens, Joe Llewellyn, Macky Natha, Kathryn Kersey, and Anu Osinusi:** Gilead Sciences, Inc.: Employment. **Jihad Slim:** Gilead, Abbvie, Merck, ViiV: Consulting, Non-CME/CE services, Contracted Research; Janssen: Consulting and Non-CME/CE services; BMS: Non-CME/CE services. **Konstantin Zhdanov:** MSD, Novartis, Roche, Biocad: Speaking and Teaching; BMS: Consulting; Abbvie, Gilead, R-pharm: Grant/Research Support; Janssen: Advisory Committees or Review Panels. **Juan Berenguer:** No conflict of interest. **Stefan Zeuzem:** Abbvie, BMS, Gilead, Merck, and Janssen: Consulting. **J Mendez-Navarro:** Gilead Sciences PHMA Mexico

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