Clinical trials report high SVR rates with LDV/SOF. These results have been reproduced in the real world.

Liver fibrosis was assessed. Cirrhosis was defined by Diabetes (DM) was determined using the American Diabetes Association guidelines of a hemoglobin A1C ≥7%.

Factors associated with virological relapse have been identified in previous studies: IDO-1 (nonadherence), IDO-4 (Black race, TT allele), and Chronic Kidney Disease (CKD).

Adherence rates were 79% (n=23). Patients enrolled in POLARIS Target were randomized to either LDV/SOF + RBV or LDV/SOF alone.

Relapse was determined by any detectable virus after completion of therapy. Data were collected across most patient subgroups.

No re-infection was observed. All patients who had repeat GT testing after failure (n=23) relapsed for the same GT.

73% of the patients that had resistance testing had Y93 RA identified; 53% had multiple RAs.

Factors associated with LDV/SOF treatment failures in the reported literature include:

- Male sex and Black race favored relapse.
- Cirrhosis and platelets <100,000 per mm³ favors relapse.
- The outcome of LDV/SOF treatment failures is emerging.

Summary and Conclusions

- Clinical trials report high SVR rates with LDV/SOF. These results have been reproduced in the real world.
- Several risk factors for LDV/SOF failure have been reported in the literature: male sex, Black race, T allele, cirrhosis, platelets <100,000 per mm³, RAs, and resistance testing.
- No re-infection was observed. All patients who had repeat GT testing after failure (n=23) relapsed for the same GT.
- 73% of the patients that had resistance testing had Y93 RA identified; 53% had multiple RAs.

### Baseline Patient Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N=29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range) years</td>
<td>59 (32-70)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>28 (86.7%)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>White 4 (13.8%); Black-American 17 (58.6); Hispanic 8 (27.6%)</td>
</tr>
</tbody>
</table>

### Comorbidities, n (%)

- Diabetes (DM): 11 (37.9%)
- Hypertension: 12 (41.4%)
- Glomerular filtration rate (GFR) <60 mL/min/1.73m²: 7 (24.1%)

### Adverse Events

- Virologic failure: 3 (19.0%)
- Adherence rates: 79% (n=23)
- 24 patients (82.8%) relapsed by their first PTW visit, and all patients relapsed by PTW 24 visit.

### Timeline of Post Treatment Follow Up Visits and Relapse Detection

- PTW 4 visit: SVR4 n=3 (19%)
- PTW 24 visit: SVR24 n=4 (0%) Relapsed n=13 (100%)

### Retreatment of Patients Who Failed LDV/SOF

- 23 patients had repeat GT testing after relapse. All relapsed for the same GT.
- No re-infection was observed. All patients who had repeat GT testing after failure (n=23) relapsed for the same GT.

### Summary and Conclusions

- Clinical trials report high SVR rates with LDV/SOF. These results have been reproduced in the real world.
- Several risk factors for LDV/SOF failure have been reported in the literature: male sex, Black race, T allele, cirrhosis, platelets <100,000 per mm³, RAs, and resistance testing.
- No re-infection was observed. All patients who had repeat GT testing after failure (n=23) relapsed for the same GT.
- 73% of the patients that had resistance testing had Y93 RA identified; 53% had multiple RAs.
- Information about patients who fail treatment may identify groups of patients who would benefit from a longer duration of therapy or a triple-dose regimen.

### References

- Altmann RR. Virologic failure with All Oral DAA Regimens: Real World Experience from the TriOS Network Academic and community treatment of real-world heterogeneous population. AASLD 2016.

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### Background

- Ledipasvir/Sofosbuvir (LDV/SOF) fixed dose combination is approved for treatment of hepatitis C virus (HCV) genotypes (GT) 1, 4, 5, and 6. In clinical trials LDV/SOF resulted in sustained virologic response (SVR) rates of 94 to 98% across most patient subgroups.
- Recent studies of real world outcomes report similar SVR rates of 94 to 97%.
- As more patients are treated with this regimen, a population of LTD/SOF treatment failures is emerging.

### Methods

- This case series includes all adult patients treated at one of seven Mount Sinai Medical Center outpatient clinic locations for chronic hepatitis C, who failed LDV/SOF therapy between November 2014 and January 2016 (n=29).
- This study was Institutional Review Board approved, informed consent was waived.
- Demographic, virological and clinical data were collected through review of electronic medical records, including patient’s adherence to therapy. Nonadherence was determined if a patient missed at least one week of therapy.
- Relapse was determined by any detectable virus after completion of therapy. Data were collected through Post Treatment Week 24 visit.
- Diabetes (DM) was determined using the American Diabetes Association guidelines of a hemoglobin A1C ≥7%.
- Chronic Kidney Disease (CKD) was defined as a glomerular filtration rate (GFR) <60 mL/min/1.73m².
- Liver fibrosis was assessed. Cirrhosis was defined by FibroScan with symptoms.
- Where applicable, resistance testing was conducted using LabCorp HCV Genuscore N5A4A and NISSA Drug Resistance Assay to identify resistance associated variants (RAVs).
- A convenience sample of patients (n=10) who failed LT/SOF with Gilead were differed to compare the Case patients to identify factors associated with treatment failure. Statistical analysis of factors previously associated with LDV/SOF failure (male sex, Black race, cirrhosis, platelets <100,000 per mm³) was conducted using a chi-squared test. HCV positive patients were excluded from this analysis.

### Results

### Timeline of Post Treatment Follow Up Visits and Relapse Detection

- PTW 4 visit: SVR4 n=3 (19%)
- PTW 24 visit: SVR24 n=4 (0%) Relapsed n=13 (100%)

- Weeks of Treatment 8 (n=13.8%), 12 (n=24, 82.8%), 24 (n=1, 3.4%)