BACKGROUND

• Resistance-associated substitutions (RASs) to HCV direct-acting antivirals (DAAs) have been associated with virologic failure and may limit retreatment options.
• Approximately 10–15% of HCV genotype (GT) 1 infected patients without prior exposure to NS5A inhibitors will have detectable NS5A RASs prior to treatment.1
• People who inject drugs (PWID) are the main driver of the HCV epidemic and are at highest risk for HCV transmission and reinfection.
• In this study, we report on RASs at baseline (BL) and following virologic failure in treatment-naïve (TN) and treatment-experienced (TE) methadone-maintained PWID with HCV GT1a/b.

OBJECTIVE

• To determine prevalence of HCV RASs among a cohort of methadone-maintained PWID.

METHODS

• NS3/4A, NS5A and NS5B regions from 150 GT1a/b viruses from PWID in a trial examining 3 models of care for HCV treatment between 11/2013 and 5/2016 were sequenced.
• 139/150 (92.7%) participants were treatment naïve.
• DAA regimens included: TVR/RBV/IFN = 3, SMV/SOF N=11, SOF/RLV ± IFN N= 32, and SOF/LDV N=104.
• We report substitutions relative to genotype/subtype specific H77 (GT1a) and Con1 (GT1b) reference sequences.
• We performed phylogenetic analyses of NS3 sequences obtained at baseline and follow up visits using neighbor-joining methods (MEGA) for PWID with evidence of treatment failure.

RESULTS

Table: HCV RASs Among Treatment Naive PWID

<table>
<thead>
<tr>
<th>RAS</th>
<th>BL Frequency</th>
<th>Follow-up Frequency</th>
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<tbody>
<tr>
<td>NS3</td>
<td></td>
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<td>NS5A</td>
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<td>NS5B</td>
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Figure 1. HCV RASs Among Treatment Naive PWID

Figure 2. Specific RASs Among Treatment Naive PWID

Figure 3. Phylogenetic tree of GT1a NS3 sequences at BL and following treatment failure

CONCLUSIONS

• Of 139 TN PWID, 82/139 (59.0%) had BL RASs – 66/139 (47.5%) with NS3, 24/139 (17.3%) with NS5A, 8/139 (5.8%) with NS5B (Figure 1).
• The prevalence of specific RASs is shown in Figure 2.
• Of the 11 TE patients, 10 had BL NS3 RASs (V36L N=1, Q80K N=7, S122G N=1, I132V N=1), 4 had BL NS5a RASs (M28V N=3, H58P N=1). Two (1.3%) patients died while on treatment and 7 (4.7%) failed therapy – 4 SOF/RBV, 3 SOF/LDV.
• One SOF/LDV failure had a baseline H58P. Otherwise no class specific pre-treatment RASs were present.
• No RASs were detected following SOF/RBV failure.
• All three SOF/LDV failures had NS5A mutations (Q30H/R N=2, H58P, Y93H) post-BL.
• One patient treated with SMV/SOF had different viral substitutions and lost a BL Q80K at 24 weeks post-treatment suggestive of reinfection, which was confirmed using phylogenetic analysis (#5, Figure 3).

REFERENCES & ACKNOWLEGMENTS


We thank Elizabeth Anton for assistance with the phylogenetic analysis.