# PREVALENCE OF NS5A RESISTANCE ASSOCIATED SUBSTITUTIONS AND HCV DAA TREATMENT OUTCOMES AMONG PEOPLE LIVING WITH HIV IN AUSTRALIA

**Authors:**
Bartlett SR[1], Martinello M[1], Applegate T[1], Finlayson R[2], Baker D[3], Bloch M[4], Doyle J[5,6], Shaw D[7], Hajkowicz K[8], Read P[9], Hellard M[5,6], Filep E[1], Yee J[1], Martinez M[1], Lamoury FMJ[1], Lin L[1], Dore GJ[1,10], Matthews GV[1,10]

[1]The Kirby Institute, UNSW Sydney, Sydney, NSW, Australia; [2]Taylor Square Private Clinic, Sydney, NSW, Australia; [3]East Sydney Doctors, Sydney, NSW, Australia; [4]Holdsworth House Medical Practice, Sydney, NSW, Australia; [5]Burnet Institute, Melbourne, VIC, Australia; [6]Alfred Hospital, Melbourne, Vic, Australia; [7]Royal Adelaide Hospital, Adelaide, SA, Australia; [8]Brisbane Sexual Health Clinic, Brisbane, Qld, Australia; [9]Kirketon Road Clinic, Sydney, NSW, Australia; [10]St Vincent's Hospital, Sydney, NSW, Australia.

**Introduction:**
Efforts to eliminate HCV infection among people living with HIV in Australia are underway. Rapid treatment scale up has begun, however prevalence and impact on treatment outcome of HCV resistance associated substitutions (RASs) among this population is unknown. This analysis aimed to assess prevalence and impact of NS5A RASs on DAA treatment outcome among HIV/HCV co-infected adults in the Control and Elimination of HCV from HIV-infected individuals within Australia (CEASE-D) study.

**Methods:**
Using the easyMAG™ (BioMérieux, France) system, RNA was extracted from dried blood spot (DBS) samples collected at enrollment between 2014-2016, In-house qPCR identified HCV RNA positive samples after reverse transcription with Superscript™ VILO (Invitrogen, USA), with positive samples amplified (HCV genotype [GT] 1a H77 position 6086-6722), and Sanger sequenced. Prevalence of NS5A RASs (Table 1) were investigated, using RECall and Geno2Pheno. Impact on treatment outcome was assessed using Pearson's chi-squared test.

**Results:**
Among HIV/HCV antibody-positive individuals with DBS samples, 72% (288/400) were HCV RNA positive, with 266 NS5A sequences generated. NS5A RASs were present among; 18% (31/171) of GT1, 23% (19/83) of GT3, and 25% (3/12) of GT 2/4 sequences. Among subjects with NS5A sequences, 198 received NS5A inhibitor-containing regimens (ledipasvir 51%, daclatasvir 38%, ombitasvir 9%, velpatasvir 1%, and pibrentasvir 1%), with 97% (177/183) achieving SVR. Among subjects achieving SVR, 81% (143/177) had no RAS detected, while 19% (34/177) had a RAS detected at baseline. Among subjects with virological failure, 33% (2/6) had an NS5A RAS present (both GT 3a, treated with daclatasvir; 30K and 30S+93H mutations detected). No difference in treatment outcome for NS5A inhibitor regimens was found between presence, or absence, of associated RASs at baseline.

**Conclusion:**

Prevalence of clinically relevant RASs in NS5A region in this population was consistent with previous studies. No association between treatment failure and presence of NS5A RASs was found.

**Table 1. NS5A RASs that were considered to confer resistance (shown to be associated with DAA resistance clinically and EC50>50).** For each RAS and NS5A-inhibitor, the HCV genotypes/subtypes that have been shown to have associated resistance are listed below.

| NS5A RAS | Ledipasvir | Ombitasvir | Daclatasvir | Elbasvir | Velpatasvir | Pibrentasvir |
|---|---|---|---|---|---|---|
| 28A | 1a | | | | | |
| 28M + 30H | | | 4a | | | |
| 28M + 31F | | 1b | | | | |
| 28M + 31M | 1b | | | | | |
| 28S + 31I | | | | | | 2a |
| 28T | 1a | 1a, 1b | 1a | 1a | | |
| 28V | | 4d | | | | |
| 28V + 31F | | 1b | | | | |
| 30D | | | 1a | | | 1a |
| 30E | 1a | 1a | 1a, 4a | | | |
| 30H | 4, 1a | | 1a, 4 | 1a | | |
| 30H + 31M | | | | | 1a | |
| 30H + 93H | | | | | 1a | |
| 30R + 31M | | | | | 1a | |
| 30R + 93H | | | | | 1a | 1a |
| 30K | 1a, 3 | | 1a, 3a | 3 | | 3 |
| 30R | 1a | 1a | 1a, 4a | 1a | | |
| 30S | 4 | | 4 | | | |
| 30V | | 1a | | | | |
| 31F | | | 3a | 1a, 1b, 3 | | |
| 31I | 1a | | | | | |
| 31M | 1a, 1b | | 1a, 3a | 1a, 1b | | |
| 31V | 1a | | 1a, 3a | 1a | | |
| 32 del | | | 1b | | | 1a |
| 32L | 1a | | 1b | | | |
| 58D | 1b | 1a | 1a | 1a | | |
| 58D + 93H | | | | | | 1a |
| 92K | 1b | | | | | |
| 93C | 1a | 1a | 1a | 1a | | |
| 93H | 1, 2, 3, 4, 5, 6 | 1, 2, 3, 4, 5, 6 | 1, 2, 3, 4, 5, 6 | 1, 2, 3, 4, 5, 6 | 1, 2, 3, 4, 5, 6 | |
| 93N | 1a | 1a | 1a, 1b | 1a | 1a | 1a |
| 93R | | | 4a | | 1a | |
| 93S | 1b | 1a | | | | |
| 93T | 1a | | | | | |
| 93W | 4 | | 4 | | 1a | |

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