FREQUENCE OF HCV RESISTANCE ASSOCIATED SUBSTITUTIONS AT BASELINE AND RELAPSE.

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Introduction: Amino acid changes in the HCV NS3, NS5A and NS5B regions can confer resistance (known as resistance associated substitutions or RAS) to direct acting antivirals (DAAs). RAS likely pre-exist and are observed in patients who relapse after DAA therapy. There are few data describing the baseline prevalence of HCV RAS in Australia or their on-treatment emergence following failure of DAA therapy. Such information may be beneficial in the selection of initial DAA regimen and for the planning of salvage therapy.

Methods: Baseline samples and samples from patients experiencing relapse after DAA therapy were assessed for the presence of HCV NS5A RAS by PCR and population-based sequencing. A proportion of these samples were tested to identify known HCV RAS in the NS3, NS5A and NS5BB regions using the *Sentosa* NGS (Next Generation Sequencing) HCV genotyping assay (Vela Diagnostics, Singapore).

Results: More than 500 samples were available for assessment with the majority from patients infected with HCV genotype 1a (50%) or HCV 3a (35%). In samples from patients experiencing treatment failure, the prevalence of HCV NS5A RAS approached 90%. The predominant HCV NS5A RAS from HCV 3a relapsers was at position Y93 whereas for HCV 1a relapsers RAS where found at Q30, L31 and Y93. Overall baseline prevalence of HCV NS5A RAS was <10% and greater for HCV 3a (11.7%) than HCV1a (7%). RAS in the HCV NS3 and NS5B regions were uncommon.

Conclusion: Our preliminary data indicate that the prevalence of baseline HCV NS5A RAS is lower than that found in overseas studies. Most treatment failure could be attributed to the presence of HCV NS5A RAS. The low prevalence of baseline HCV RAS makes it difficult to justify the cost of pre-therapy screening but resistance testing may be a useful tool for identifying HCV RAS in those patients considering re-treatment.

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