Interleukin 28-B testing

Recent genome-wide association studies have shown that a set of single nucleotide polymorphisms in the region of the interleukin-28B (IL-28B) gene on chromosome 19 are associated with treatment response to current combination therapy in people infected with HCV genotype 1. The same IL-28B polymorphisms have also been shown to be associated with spontaneous clearance in untreated people. These polymorphisms appear to be of less benefit for people infected with HCV genotype 2 or 3. No TGA-approved assay is yet available for IL-28B testing; however, it is likely that the identification of a person's IL-28B genotype will be used in clinical management and aid in the individualisation of therapy. The identification of a non-favourable IL-28B genotype should not be sufficient to defer therapy in people most in need of treatment but should inform a discussion on treatment options. When a test for IL-28B is approved by the TGA, the test **should** be recommended to all people with genotype-1 people pre-treatment to inform their treatment decisions until newer agents become available.

HCV resistance testing

The addition of direct-acting antiviral (DAA) agents to pegylated interferon (PEG-IFN) and ribavirin (RBV) enhances treatment efficacy for peoples with chronic HCV genotype 1 infection. Despite enhanced efficacy, development of HCV resistance-associated variants (RAVs) during triple therapy with PEG-IFN/RBV and either of the initial two licensed DAA agents (protease inhibitors, telaprevir and boceprevir) is well described. However, there is no current clinical utility for HCV resistance testing pre or on-treatment due to the low pre-treatment prevalence of RAVs on standard population sequencing, the strong relationship between virological failure and RAV development, and the lack of current options for re-treatment of HCV with RAVs.

The protease inhibitors telaprevir and boceprevir when added to pegylated interferon and ribavirin increase sustained viral response rates in genotype-1 infected people from less than 50% to 70%. The antiviral efficacy of the first-generation DAAs against other HCV genotypes remains to be elucidated. These new therapies will require new paradigms of treatment dose and duration as well as assessment of response to be established. The recommendations in this Policy provide for these variations.