Acute HCV

Treatment of acute HCV infection with interferon-based therapy is highly effective. The first landmark trial by Jaekel and colleagues reported a 98% rate of sustained virological response (SVR) with just 24 weeks of interferon monotherapy[1]. Subsequent studies have also shown high rates of response ranging from 71-94% with as little as 12 weeks of peginterferon monotherapy[2]. SVR rates decline significantly once HCV progresses to chronicity and therefore it is desirable to consider treatment in the acute phase. However, treatment is difficult and many patients, particularly actively using injection drug users, may not be ready or willing to start therapy. Ideally, patients who will spontaneously clear infection should not be treated, however identification of such individuals is very difficult.

Female sex, younger age and symptomatic infection are all predictors of spontaneous clearance[3]. Some studies have found that clearance is less common with genotype 1 HCV, however this has not been a universal finding[4]. More recently, the IL28B genotype has been recognized as an important predictor of spontaneous clearance[5]. Patients with the treatment-favorable CC genotype have a 53-64% chance of spontaneous clearance compared to 24-34% in heterozygotes and 6-23% in TT homozygotes[5,6]. Symptoms seem to be most relevant in patients with non-CC genotypes with a 43% clearance rate in symptomatic non-CC patients compared to 14% in those with no symptoms. Patients with a CC genotype have a high clearance rate with (56%) or without (61%) symptoms[6]. More recently, IP10 has also been shown to be a useful predictor of spontaneous clearance. In a study of 3 acute HCV cohorts, patients with high baseline serum IP10 levels are unlikely to spontaneously clear infection, with no patients with acute HCV and an IP10 above 380 pg/mL going on to spontaneous clearance[7]. Consequently, patients with a high IP10 should be prioritized for antiviral therapy, particularly given that although high IP10 levels are associated with poorer treatment outcomes in chronic HCV, IP10 levels were not predictive of SVR in treatment of acute infection. Interestingly, the IL28B genotype also does not appear to affect treatment outcome in acute HCV, however data are limited.

An issue that is frequently raised is how long to wait before instituting treatment. It is important to determine the date of infection, not the date of diagnosis, which may be difficult if either no clear exposure or multiple exposures exist. Most studies suggest that treatment success rates start to decline when treatment is started beyond 12 weeks after infection[8]. A variety of strategies may be considered. In patients with a favorable IL28B genotype (CC), it may be reasonable to delay treatment given the higher probability of spontaneous clearance and the high response rate even if treatment is required. In contrast, for non-CC patients, starting therapy early on to maximize the chance of treatment success may be prudent, particularly for patients with a high serum IP10[9]. Alternatively, Deuffic-Burban and colleagues proposed instituting treatment based on the timing of diagnosis irrespective of IL28B[10]. They argued that since treatment success is greatest when started within 8 weeks of infection, all patients
diagnosed within this window should have treatment instituted immediately. In contrast, for those in whom infection is identified beyond 8 weeks, they proposed delaying treatment until week 20 to maximize the chance of spontaneous clearance. Both approaches require close monitoring and should be discussed with patients.

Once therapy is considered, there is a question of what to use and for how long. Peginterferon or even standard interferon monotherapy are highly effective for HCV mono-infected individuals and can be given for as little as 12 weeks in those with undetectable viral levels by week 4[2,8]. For those with a slower response, treatment should probably be extended to 24 weeks however there are few prospective data to guide this decision[2,8]. It has been hard to show a clear benefit to the addition of ribavirin and its use remains controversial. Higher treatment failure rates among HIV/HCV co-infected patients have led most investigators to propose using dual therapy in this population, however there are no controlled data supporting this approach. A recent non-randomized study of acute or early chronic HCV showed improved early viral kinetics with the addition of ribavirin[11]. The large trials that would be required to clarify the role of ribavirin are unlikely to be performed. To date, direct acting antivirals (DAA) have not been used in acute HCV, however it is likely that they will be highly effective. The question will be whether the costs and potential toxicities are necessary given the high success rates with current treatment. Interferon-free DAA combinations will likely be successful in acute HCV and will be much more acceptable to patients and prescribers, however costs and accessibility will remain important considerations. With the rapid improvement of DAA therapy for chronic HCV, one could even make the case to withhold therapy for patients with acute infection with the hope that spontaneous clearance occurs and if not that highly effective therapy will be available before sequela of the disease develop. Although this approach may be reasonable, it is important to consider reports of rapidly progressive fibrosis in HIV-infected patients with acute HCV as well as issues such as the risk of extra-hepatic disease and loss to follow-up.

The data on treatment of acute HCV with considerations of how this area will evolve in the near future will be discussed.

References

