AASLD 2015 San Francisco

Benefits of SVR

Current SOC treatment (Real world experience and factors impacting SVR)

Unique populations (decompensated cirrhosis, acute hepatitis, renal disease, PWID)

Just around the corner (Grazoprevir/elbasvir, Sofosbuvir/Velpatasvir)

New drugs: new doubles and triples.

Fibrosis reversal possible and transient elastography may be reasonable way to follow patients after SVR

SVR significantly reduced liver complications in compensated and decompensated cirrhosis.

Treatment of wait-listed patients results in delisting of minority (16% over 1 year)

Potential for predicting likelihood of achieving clinical and biochemical benefits in presence of decompensation cirrhosis = child-pugh score.

Treating genotype 1:

SVR results mirror those in clinical trials = high rate of success.

8-wk treatment among treatment naive, non-cirrhotic, genotype 1 patients with VL <6 million IU/ml is underutilised.

Cirrhosis/advanced disease associated with lower SVR rates.

Non-use of PPI is associated with lower SVR rate (potentially modifiable factor to maximise SVR rates)

African –American may have lower response rates (reason unclear)

Genotype 3 and cirrhosis:

SVR rates DCV + SOF +/- RBV can achieve SVR rates 85-90% in patients with cirrhosis. (if decompensated cirrhosis, SVR rates 80%)

If treating cirrhosis, add RBV and treat for 12-24 weeks (if unable to add RBV, treat for 24 weeks with SOF + DCV)

If decompensated cirrhosis, add RBV and treat for 24 weeks

Still room to improve on SVR rates.

Unique population: renal failure, acute hepatitis C, injection drug users, decompensated cirrhosis

Baseline testing not recommended by guidelines but there may be role for select testing

Cirrhotic patients receiving LDV-SOF (consider adding RBV and /or extending treatment)

DAA combinations that target multiple targets and includes sofosbuvir may be a strategy to treat patients with DAA resistance (NS3/NS5A)

Just around the corner (Grazoprevir/elbasvir, Sofosbuvir/Velpatasvir)

EBR/GZR +/- RBV

High efficacy cross a broad spectrum of patients

Subgroups in which longer therapy +/- may be considered.

Treatment experience (non-responders):

- 16/18 weeks + RBV if cirrhosis
- 16/18 weeks + RBV if baseline EBR RAVs

Safe with rare elevation of ALT (without bilirubin increase)

SOF/VEL:

SOF/VEL for 12 weeks yield high SVR rates in patients with HCV GT 1-6.

SOF/VEL is superior to SOF/RBV for 12 wks in GT2

SOF/VEL is superior to SOF/RBV for 24 wks in GT3

Presence of baseline NS5A RAVs do not appear to impact SVR12

SOF/VEL for 12 weeks was well tolerated, with a safety profile similar to that of placebo treatment.

New therapies: more doubles, triples and injections

Striving for the penultimate therapy:

- Pangenotypic
- No need for Ribavirin
- One pill a day
- High barrier to resistance
- Short duration (8 weeks or less=lower cost, improved adherence, reduce emergence of resistance, simplicity

Conclusion:

Currently approved drugs achieved SVR rates in clinical practice similar to that of clinical trials (large life cohorts are identifying the factors associated with treatment failure)

Availability and success of therapies in traditional and new “special population” ESRD, decompensated cirrhosis, PWID

More intense scrutiny of the impact of baseline and treatment- emerging RAVs on SVR rates (small but important studies on treatment strategies).

Exiting drug pipeline that is focused on attaining DAA combinations that are pangenotypic, safe, high efficacy AND short duration.

Novel solutions to address enhance awareness, diagnosis and linkage to care – first steps on cascade of care.

Diagnostics:

There were two items of interest during conference.

1. Importance of viral load measurement at baseline and during first 48 hours of therapy as indication for success in treatment (response guided therapy/RGT)/ Dr Lau poster.

Conclusion: All non-cirrhotic GT1b CHC IL28 CC Chinese with RVR at day two treated with triple DAAs regimens achieved SVR12.

2. New HCV Ag EIA with capture Abs for core, NS3, NS4 and NS5. Ultra-sensitive HCV Ag test.