Government of **Western Australia**
East Metropolitan Health Service

Royal Perth Hospital

Treating Patients with Hepatitis C Genotype 1 Using Viekira Pak™ in the "Real World" – An Australian Nursing Perspective

Nazareth S[1], Fragomeli V[2], Leembruggen N[1], Jones T[3], Mason S[4], How-Chow D[5], Colman A[6], Warner S[7], Tilley E[8], Altus R[8]

[1]Royal Perth Hospital, [2]Nepean Hospital, [3]John Hunter Hospital, [4]Royal Prince Alfred Hospital, [5]St Vincent's Hospital, [6]Royal Adelaide Hospital, [7]Monash Health, [8]Flinders Medical Centre

Background

Viekira Pak™ (paritaprevir/ritonavir/ombitasvir, dasabuvir) +/- ribavirin was the first interferon-free compassionate programme delivered in Australia for the treatment of hepatitis C. The Special Access Scheme (SAS) was made available to patients with genotype 1 who were either intolerant or ineligible for approved therapy or therapy through a clinical trial.

The combination consisted of a protease inhibitor (paritaprevir) with ritonavir, a NS5A inhibitor (ombitasvir) and a non-nucleoside polymerase inhibitor (dasabuvir) with or without ribavirin. Patients were treated and managed in liver clinics throughout Australia.

Rationale

Published data demonstrated good safety and efficacy of Viekira Pak™ in clinical trials. However, little was known about the implementation, safety and efficacy of interferon-free regimes in the "real world" clinical setting. "Real world" studies play an important role in understanding the true effectiveness of therapy in a population and situation similar to what is encountered in clinical practice.

Objectives

The aim of this study is to:

- Describe the implementation of Viekira Pak™ via SAS in a "real world" setting
- Determine sustained virological response (SVR12) rates
- Assess adverse events, laboratory abnormalities and drug-drug interactions
- Assess patient compliance and adherence

Method

This prospective data registry incorporates data routinely recorded in medical records. Data was collected from 140 patients across eight Australian Liver Clinics over 12 months from October 2014 to September 2015. Baseline characteristics, pathology results, adherence, compliance, treatment outcomes and adverse events were collated and analysed. All patients with hepatitis C genotype 1 who commenced therapy with Viekira Pak™ through the SAS at a participating hospital were included.

Results

The majority of patients were infected with genotype 1a and assessed to have compensated cirrhosis. Ten patients had a history of decompensation, including one patient with prior liver transplant (Table 1).

Table 1.

Baseline Characteristics n=140, n (%)

Age, mean (years)	56
Male	91 (65.0)
Weight, mean (kgs)	84.8
Caucasian	133 (95.0)
Genotype 1a	90 (64.3)
Treatment Naïve	71 (50.7)
Prior Null Response (Interferon)	26 (18.6)
Cirrhosis (F4)	109 (77.9)
History of Decompensation	10 (7.1)

95.0% (n=133) of patients enrolled in the study achieved an SVR12.

Seven patients (5.0%) did not achieve an SVR12.

- One patient (0.7%) experienced virological failure on treatment (table 2)
- One patient (0.7%) relapsed after completing treatment (table 3)
- One patient (0.7%) was lost to follow-up
- Four patients (2.9%) discontinued prematurely

Of the four patients who discontinued prematurely and did not achieve an SVR12, two (1.4%) ceased due to hyperbilirubinaemia at week 1 and week 6. The remaining two patients (1.4%) ceased due to unrelated pre-existing medical conditions at week 1 and week 3.

Two additional patients (1.4%) discontinued at week 3 and week 6 due to an infection and decompensation respectively, however they both achieved an SVR12.

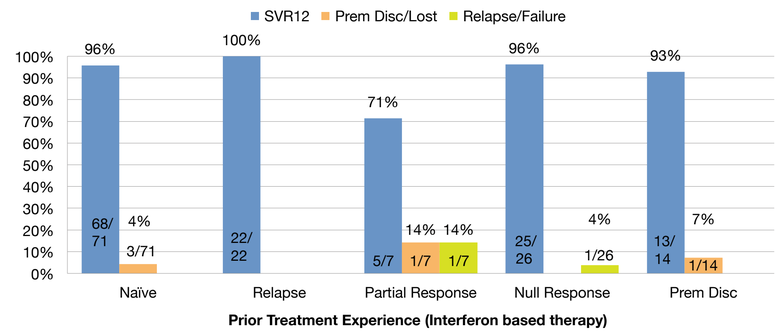
Table 2. Key characteristics of patient experiencing virological failure

Baseline Characteristics	Caucasian male, 56 years of age, BMI 26.2
Viral Characteristics	Genotype 1a, baseline viral load 4,190,000IU/mL
Fibrosis Stage	Cirrhosis, FibroScan 15.4kPa, no history of decompensation
Medical History	Diabetes mellitus, anxiety, depression
Prior Treatment	Partial response
Baseline Pathology Results	AFP 15kIU/L, ALT 71U/L, AST 31U/L, Albumin 38g/L, Bilirubin 41umol/L, Platelets 84x10^9/L, INR 1.2
Treatment Duration	Allocated 24 weeks, ceased at week 10 due to virological failure at week 8
Compliance and Adherence	100% self-reported dosing,100% appointment attendance

Table 3. Key characteristics of patient experiencing relapse post treatment

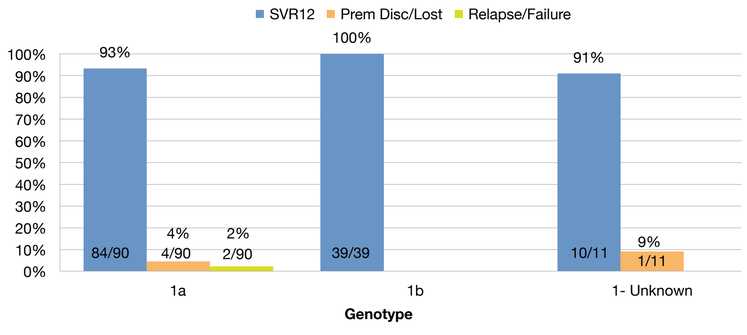
Baseline Characteristics	Aboriginal male, 44 years of age, BMI 33.0
Viral Characteristics	Genotype 1a, baseline viral load 820,000IU/mL
Fibrosis Stage	Cirrhosis, FibroScan 34.3kPa, no history of decompensation
Medical History	Diabetes mellitus, haemophilia, hypertension
Prior Treatment	Null response
Baseline Pathology Results	AFP 10kIU/L, ALT 197U/L, AST 123U/L, Albumin 39g/L, Bilirubin 37umol/L, Platelets 79x10^9/L, INR 1.2
Treatment Duration	Allocated 24 weeks, completed 23 weeks
Compliance and Adherence	100% self-reported dosing, 100% appointment attendance

Graph 1. Treatment outcomes by prior treatment experience n=140



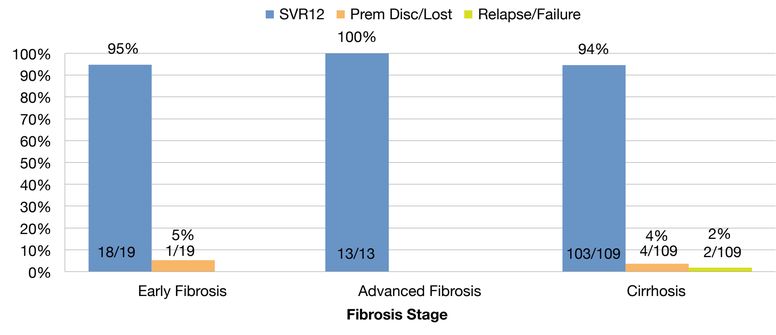
There was no significant difference in SVR12 rates between treatment naïve and experienced patients.

Graph 2. Treatment outcomes by genotype n=140



100% (39/39) patients with genotype 1b achieved an SVR12. SVR12 rates for genotype 1a and genotype 1 with sub-type unknown were 94% and 91% respectively (graph 2).

Graph 3. Treatment outcomes by fibrosis stage n=140



Patients with cirrhosis, assessed by a FibroScan ≥ 12.5kPa, a liver biopsy score of F4 or Hepascore of ≥ 0.85, had an SVR12 rate of 94%. The patients experiencing virological failure and relapse were both cirrhotic.

126 (90.0%) patients reported adverse events, mainly mild to moderate fatigue, nausea and headache. Bilirubin elevation was observed in 47.9% of patients; with grade 4 hyperbilirubinaemia in 3 patients (2.1%).

Serious adverse events were reported for 19 (13.6%) participants. The most common serious adverse event was hyperbilirubinaemia, followed by decompensation and anaemia. 18/19 (95.0%) serious adverse events resulted in hospitalisation, no deaths were reported. One potential drug-drug interaction was identified resulting in lithium toxicity.

Table 4. Serious adverse events reported, n (%)

	All patients n=140	No cirrhosis n=32	Compensated Cirrhosis n=99	History of decompensation n=10
Hyperbilirubinaemia	4(2.9)	0(0)	3(3.0)	1(10.0)
Decompensation	3(2.1)	0(0)	2(2.0)	1(10.0)
Anaemia and transfusion	2(1.4)	1(3.1)	1(1.0)	0(0)
Dehydration	1(0.7)	0(0)	1(1.0)	0(0)
Lithium Toxicity (possible drug-drug interaction)	1(0.7)	0(0)	1(1.0)	0(0)
Suicidal Ideation	1(0.7)	0(0)	1(1.0)	0(0)
Other	7(5.0)	2(6.3)	4(4.0)	1(10.0)
Total	**19(13.6)**	**3(9.4)**	**13(13.1)**	**3(30.0)**

Patients were predominantly reviewed by nurses with an average (mean) of 5.1 clinic visits from week 1 to week 12 post treatment. 85.0% of patients attended all scheduled visits. 85.0% of patients reported 100% adherence to medication.

Conclusion

This "real world" analysis of Viekira Pak™ demonstrated high SVR12 rates of 95% in this sample of complex patients who were ineligible or intolerant to other regimes. High SVR12 rates were maintained in patients with "difficult to treat" characteristics including with genotype 1a, cirrhosis and/or prior null response.

Reported serious adverse events in 13.6% of patients and potential drug-drug interactions highlight the need for adequate monitoring. Serious adverse events included hyperbilirubinaemia, decompensation and anaemia and 95% resulted in hospitalisation. No deaths were reported.

Good adherence and compliance was reported. Patients required an average of only 5.1 clinic visits and were predominantly reviewed and managed by nurses.