Real-world utilization of the new fixed-dose combination elbasvir/grazoprevir in adult patients with chronic hepatitis C in Canada: Z-PROFILE study

Edward Tam[1], Chris Fraser[2], Julie Tremblay[3], Brian Conway[4], Benoit Trottier[5], Alnoor Ramji[6], Sergio Borgia[7], Kris Stewart[8], Janie B. Trepanier[9], Youb Chalabi[9]

[1]LAIR Centre, BC, Canada; [2]The Cool Aid Community Health Centre, BC, Canada; [3]Centre Sida Amitié, QC, Canada; [4]Vancouver Infectious Diseases Centre, BC, Canada; [5]Clinique Médicale du Quartier Latin, QC, Canada; [6]GI Research Institute (GIRI), Gastroenterology Division, BC, Canada; [7]William Osler Health System, ON, Canada; [8]Saskatchewan Infectious Disease Care Network, SK, Canada; [9]Merck Canada Inc., QC, Canada.

Background

- DAAs represent the standard of care for chronic HCV .
- Canada was the first country worldwide to approve EBR/GZR +/- RBV for GT1 and 4, and for GT3 with SOF.
- While initial access to EBR/GZR was predominantly compassionate or through private payers, public reimbursement is now beginning to be available in most provinces.
- MSD Care Hepatitis C Patient Support Program provides financial assistance including compassionate product for eligible patients who have no coverage, until coverage becomes available.

Objectives

PRIMARY

- Describe the patient profile and real-world effectiveness (SVR12) of EBR/GZR in patients with chronic hepatitis C followed in Canadian routine clinical care.

SECONDARY

- Describe the profile of patients treated with EBR/GZR based on the type of insurance coverage.
- Evaluate the treatment discontinuation rate per prescribed treatment duration.
- Exploratory: Assess factors associated with SVR12.

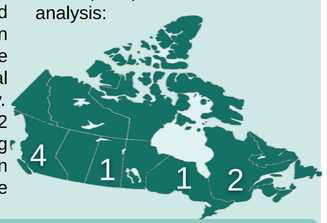
Methods

STUDY DESIGN

- Multicentre retrospective chart review study.
- Data from eligible patients' medical charts were extracted after treatment initiation with EBR/GZR, including historical data on prior HCV treatments.

STUDY POPULATION

- Adult patients with a confirmed diagnosis of cHCV that initiated treatment with EBR/GZR in Canadian routine clinical care were identified from medical charts and included in the study.
- In this interim analysis, 102 patients from 8 sites initiating EBR/GZR treatment between January 2016-March 2017 were analyzed.
- Sites per province for interim analysis:



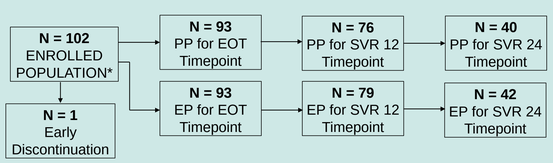
INCLUSION CRITERIA

- Male or female ≥18 years of age at time of EBR/GZR treatment initiation.
- Confirmed diagnosis of chronic hepatitis C.
- Patient was initiated on EBR/GZR treatment for their cHCV infection.

EXCLUSION CRITERIA

- Not applicable

STUDY FLOW CHART



* Includes patients initiating EBR/GZR therapy prior to November 15, 2017.

- Per Protocol (PP) Population (primary analysis): includes patients with outcomes (i.e. SVR12 timepoint) and virologic failures.
- Evaluable Population (EP) (secondary analysis): includes patients with outcomes, virologic and non-virologic failures (discontinuations, lost to follow-ups, reinfections).

STATISTICAL METHODS

- Descriptive statistics, including the mean and standard deviation (SD) for continuous variables and frequency distributions for categorical variables were produced.

Results

BASELINE DEMOGRAPHICS

Table 1: Baseline Characteristics

Characteristics	N=102
Age (years), mean (range)	52.6 (29.3-80.6)
Male, n (%)	62 (60.8%)
Ethnicity, n (%)	
Caucasian	80 (78.4%)
Aboriginal	6 (5.9%)
Other	16 (15.7%)
BMI, median (range) (n = 40)	25.6 (15.8-38.6)

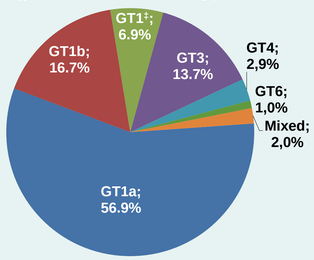
Table 2: Comorbidities

Comorbidities	N=102
HIV co-infected, n (%)	11 (10.8%)
HBV co-infected, n (%)	1 (1.0%)
Chronic Kidney Disease, n (%)	
Yes	30 (29.4%)
- Stage 3 (GFR 30-59 mL/min)	21 (20.6%)
- Stage 4-5 (GFR < 30 mL/min)	5 (4.9%)
- Missing	4 (3.9%)
No	72 (70.6%)
Diabetes, n (%)	
Type 1	5 (4.9%)
Type 2	7 (6.9%)
Kidney Transplant, n (%)	1 (1.0%)
HCC, n (%)	0 (0.0%)
Access to EBR/GZR, n (%)	
Compassionate	94 (92.2%)
Private	7 (6.9%)
Not Available	1 (1.0%)
Use of Acid-Reducing Agents, n (%)	
Any	19 (18.6%)
- Proton pump inhibitors (PPIs)	14 (13.7%)
- H2 Blockers	3 (2.9%)
- Antacids	4 (3.9%)

Table 3: Drug Use Reported

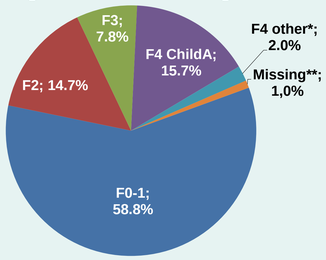
Drug Use	N=102
Currently on Opioid Agonist Therapy (OAT), n (%)	
Methadone	13 (12.7%)
Buprenorphine	5 (4.9%)
Unknown/Other	2 (2.0%)
Illicit drugs within 12 months prior to treatment initiation, n (%)	
Yes	28 (27.5%)
No	72 (70.6%)
Unknown	2 (2.0%)

Figure 1: HCV Genotypes



‡GT1: other or unspecified.
Mixed genotypes: 1 patient was infected with GT1A&GT1B; 1 with GT2&GT3.

Figure 2: Fibrosis Stage



*F4 Child-Pugh Score was missing.
**The fibrosis score assessment was not done for 1 patient.

- The majority of patients were infected by genotype 1a (57.8%) (Fig. 1).
- The patient infected by GT2 was prescribed EBR/GZR+SOF+RBV for 12 weeks. The patient was treatment naïve, had a mixed infection with GT3 and an HIV co-infection (not shown).
- The majority of patients had a fibrosis stage of F0-1 (58.8%) and 17.7% had cirrhosis (Fig. 2).

TREATMENT INFORMATION AT EBR/GZR INITIATION

RAS Testing

- Baseline resistance-associated substitutions (RAS) testing was performed for 13 (12.7%) patients.
  - The genotypes of the 13 patients tested for RAS testing were: GT1a (n=11), GT1b (n=1), GT1 (n=1).
  - 1 patient had NS5A RAS: H58wt/Y. This patient was treatment-naïve, infected by GT1a and prescribed 16 weeks + RBV.

EBR/GZR Treatment Duration & Concomitant Treatments

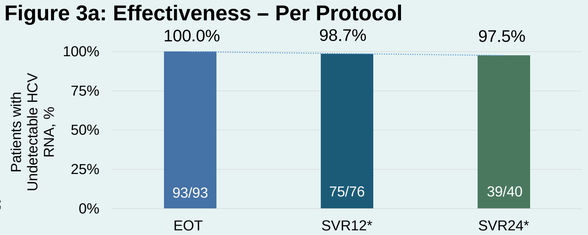
- The majority of patients (87.3%) were prescribed 12 weeks of EBR/GZR.
- 13 patients received 16 weeks EBR/GZR+RBV:
  - GT1a: 10, GT3: 1, GT4: 2 patients.1 had mixed GT1a&1b.
  - The majority were treatment-experienced (n=11) and failed
    - DAA (n=2)
    - 1st gen PI-boceprevir (n=3)
    - PegIFN+RBV OTF (n=3), IFN+RBV OTF (n=1)
    - PegIFN+RBV relapse (n=1)
    - SOF-PegIFN+ RBV (n=1)
  - 2 were treatment-naïve patients with GT1a and RAS (NS3 or NS5A).
- All 15 patients infected by GT3 were prescribed EBR/GZR in combination with sofosbuvir.

Table 4: Treatment History

Previous HCV Treatment	N=102
Treatment Naïve, n (%)	80 (78.4%)
Treatment Experienced, n (%)	22 (21.6%)
Last treatment:	
PegIFN+RBV Relapse	2 (2.0%)
PegIFN+RBV OTF	5 (4.9%)
PegIFN+RBV Reinfection	1 (1.0%)
IFN+RBV OTF	2 (2.0%)
IFN+RBV Reinfection	1 (1.0%)
PegIFN+RBV+1st generation PI*	5 (4.9%)
SOF+ PegIFN+RBV	2 (2.0%)
All-oral DAA**	4 (3.9%)

*1st generation PI include boceprevir and simeprevir;
**All-oral DAAs include 2 patients treated with SOF/RBV, 1 patient with SOF and simeprevir and 1 patient with SOF/DCV/RBV. Regarding genotype, 3 patients had GT3 and 1 patient had GT1a.
DAA: direct-acting antiviral; DCV: daclatasvir; IFN: interferon; OTF: on treatment failure includes partial, null or breakthrough response; PegIFN: peginterferon; PI: protease inhibitor; RBV: ribavirin; SOF: sofosbuvir.
This data represents the last treatment received. Some patients may have been treated more than once.

Figure 3a: Effectiveness – Per Protocol



Virological Failures			
Relapse	N/A	1[a]	1[a]
Breakthrough	0	0	0
Early discontinuation	1[b]	1[b]	1[b]
Reinfection†	N/A	1[c]	1[c]
Unknown**	N/A	1[c]	0

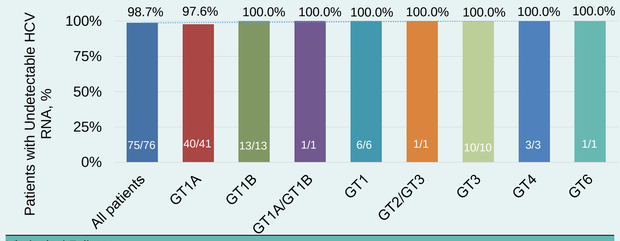
*Per Protocol Population: includes patients with outcomes (i.e. SVR12 timepoint) and virologic failures.
†Confirmed by genetic testing.
**HCV RNA became detectable post-EOT, unknown relapse /reinfection status.
[a] Patient previously treated with Peg-IFN+RBV (OTF), had GT1A and was prescribed 16 weeks EBR/GZR+RBV.
[b] Patient had missing data on EOT response. Despite early discontinuation SVR12 and SVR24 were achieved.
[c] Patient was treatment naïve, had GT1a and was prescribed 12 weeks EBR/GZR.
N/A=not applicable

Effectiveness

- Overall, at the end of treatment (EOT), all (100.0%) patients with available data had undetectable levels of HCV RNA.
- Sustained virologic response (SVR) at weeks 12 and 24 was achieved by 98.7% and 97.5% of patients with available data, respectively. (Fig. 3a)
- SVR12 for Evaluable Population = 76/79 (96.2%). (data not shown)
- SVR24 for Evaluable Population = 40/42 (95.2%). (data not shown)

- SVR12 was achieved by more than 97% of patients for all HCV genotypes. No remarkable differences were observed between genotypes. (Fig. 3b)
- SVR12 was achieved by all treatment naïve and experienced patients with the exception of 1 patient previously treated with PegIFN+RBV. (Fig. 3c)

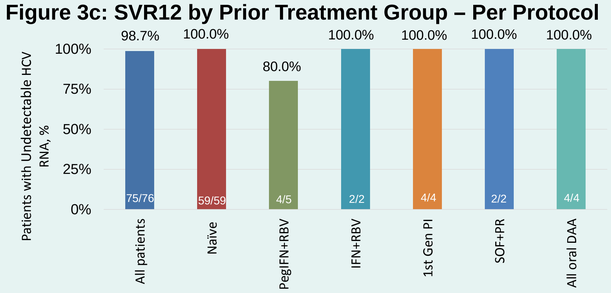
Figure 3b: SVR12 by HCV Genotype – Per Protocol



Virological Failures									
Relapse	1	1[a]	0	0	0	0	0	0	0
Breakthrough	0	0	0	0	0	0	0	0	0
Reinfection†	1	1	0	0	0	0	0	0	0
Unknown**	1	1	0	0	0	0	0	0	0

†Confirmed by genetic testing
**HCV RNA became detectable post-EOT, unknown relapse /reinfection status
[a] Patient previously treated with Peg-IFN+RBV (OTF), had GT1A and was prescribed 16 weeks EBR/GZR+RBV

Figure 3c: SVR12 by Prior Treatment Group – Per Protocol



Virological Failures							
Relapse	1	0	1[a]	0	0	0	0
Breakthrough	0	0	0	0	0	0	0
Reinfection†	1	1	0	0	0	0	0
Unknown**	1	1	0	0	0	0	0

†Confirmed by genetic testing
**HCV RNA became detectable post-EOT, unknown relapse /reinfection status
[a] Patient previously treated with Peg-IFN+RBV (OTF), had GT1A and was prescribed 16 weeks EBR/GZR+RBV

Conclusion

This study reports data on the real-world utilization and effectiveness of EBR/GZR in 102 patients across Canada.

Important findings from this study population include:

- In this Canadian cohort, the majority of individuals treated had early stage fibrosis and were infected by GT1a.
- 28% had documented illicit drug use within the last 12 months.
- 25% had Chronic Kidney Disease stage 3-5.
- SVR12 was achieved in 75/76 (98.7%) of patients with virologic data available at that timepoint.
- All patients with GT3 were treated with EBR/GZR+SOF±RBV and obtained an SVR12.
- SVR12 rates were comparable among HCV genotypes and among treatment-naïve and treatment-experienced patients.
- High SVR rates were achieved in GT1a infected patients, even in the absence of NS5A RAS screening for most patients.

More sites and more patients will be included in the near future.

Acknowledgments
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Conflict of Interest Disclosure
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*Contact: Dr. Edward Tam etam@laircentre.com