

Introduction

- In HIV patients co-infected with hepatitis C (HCV), chronic end stage liver disease is a leading cause of hospital admission and death in the developed world.
- Treatment with current standard of care, Pegylated Interferon and Ribavirin (PegInf/Rbv) has poorer outcomes in HCV genotype 1 patients and is associated with haematological and neuropsychiatric side effects excluding many patients from treatment.
- New HCV protease inhibitors (PI) (Telaprevir and Boceprevir) used in combination with PegInf/Rbv in genotype 1 patients significantly improve sustained virologic response. Initial Phase 2 trial data suggest similar improvement in HIV co-infection.
- Pharmacokinetic studies show these new HCV protease inhibitors should not be used with most Ritonavir boosted PI's. Telaprevir can be used with dose adjusted boosted Atazanavir.
- A significant proportion of the Western General Hospital co-infected cohort are on a Ritonavir boosted PI based HAART regimen. Several of these patients have psychiatric comorbidities or previous severe side effects that may prohibit the use of PegInf/Rbv.

Aim

To assess the eligibility of the Lothian HIV cohort co-infected with genotype 1 HCV for treatment with a new HCV protease inhibitor containing regimen.

Methods

- The HIV Western General Hospital database was searched for all patients co-infected with HCV genotype 1 and divided into HCV treatment naive and experienced.
- The inclusion and exclusion criteria for consideration of a HCV PI containing regimen was based on recent pharmacokinetic data on boosted PI's and criteria used for the Phase 2 trials for Telaprevir and Boceprevir.
- Inclusion criteria; co-infection with genotype 1 HCV only, CD4 count > 200/mm³, VL < 40 copies/ml, fibrosis of any grade, currently on or could be switched to a HAART regimen containing Tenofovir, Emtricitabine, plus boosted Atazanavir or Raltegravir.
- Exclusion criteria; current or previous significant untreated psychiatric disease, previous severe haematological or psychiatric side effects with side effects with PegInf/RBV, patients unable to switch to the HAART regimen above.

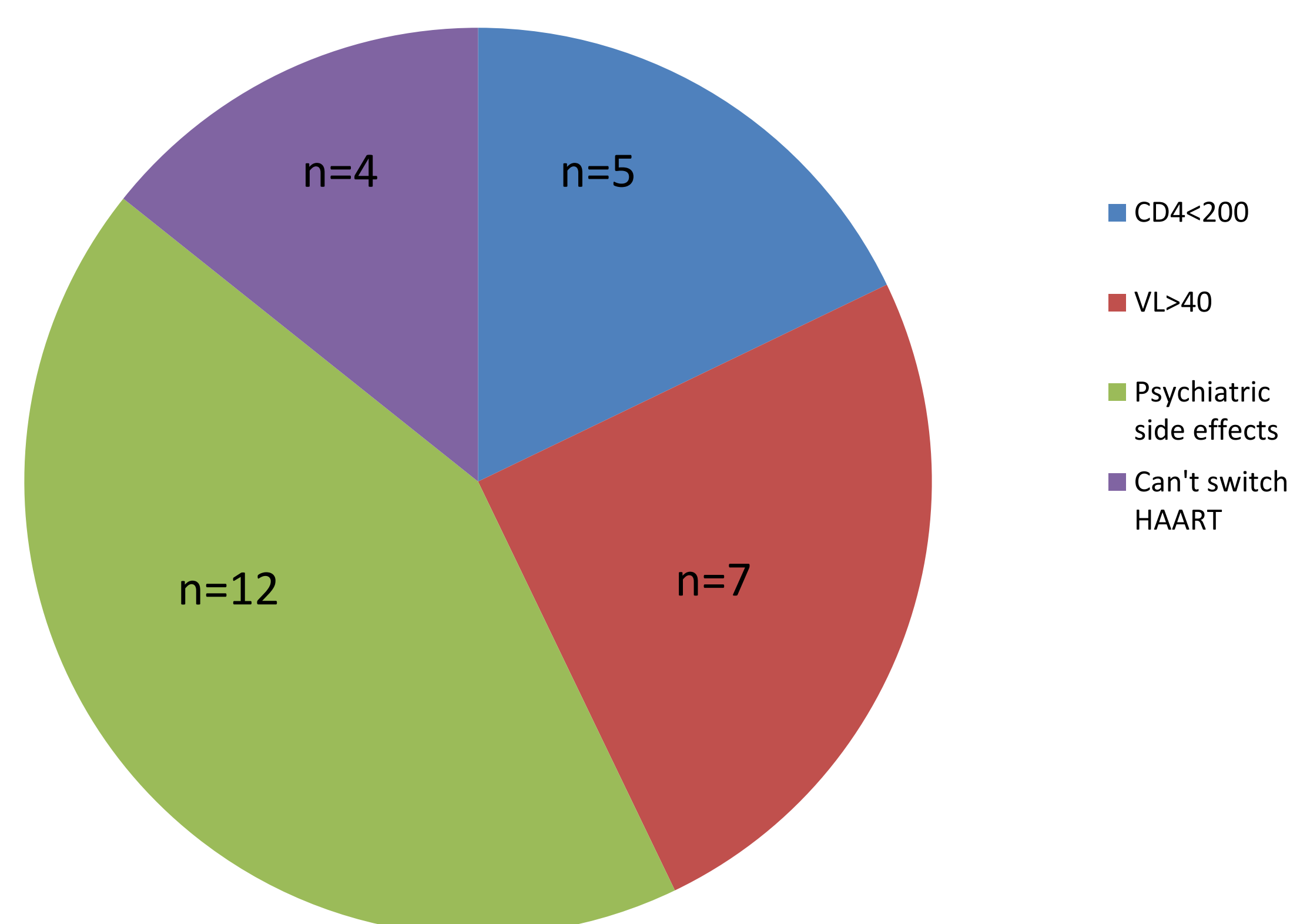
Results

Total cohort of HCV genotype 1 HIV co-infected patients **71**

Naive Patients

Number of HCV treatment naive patients **55**

Number of HCV treatment naive patients not eligible for treatment **23**



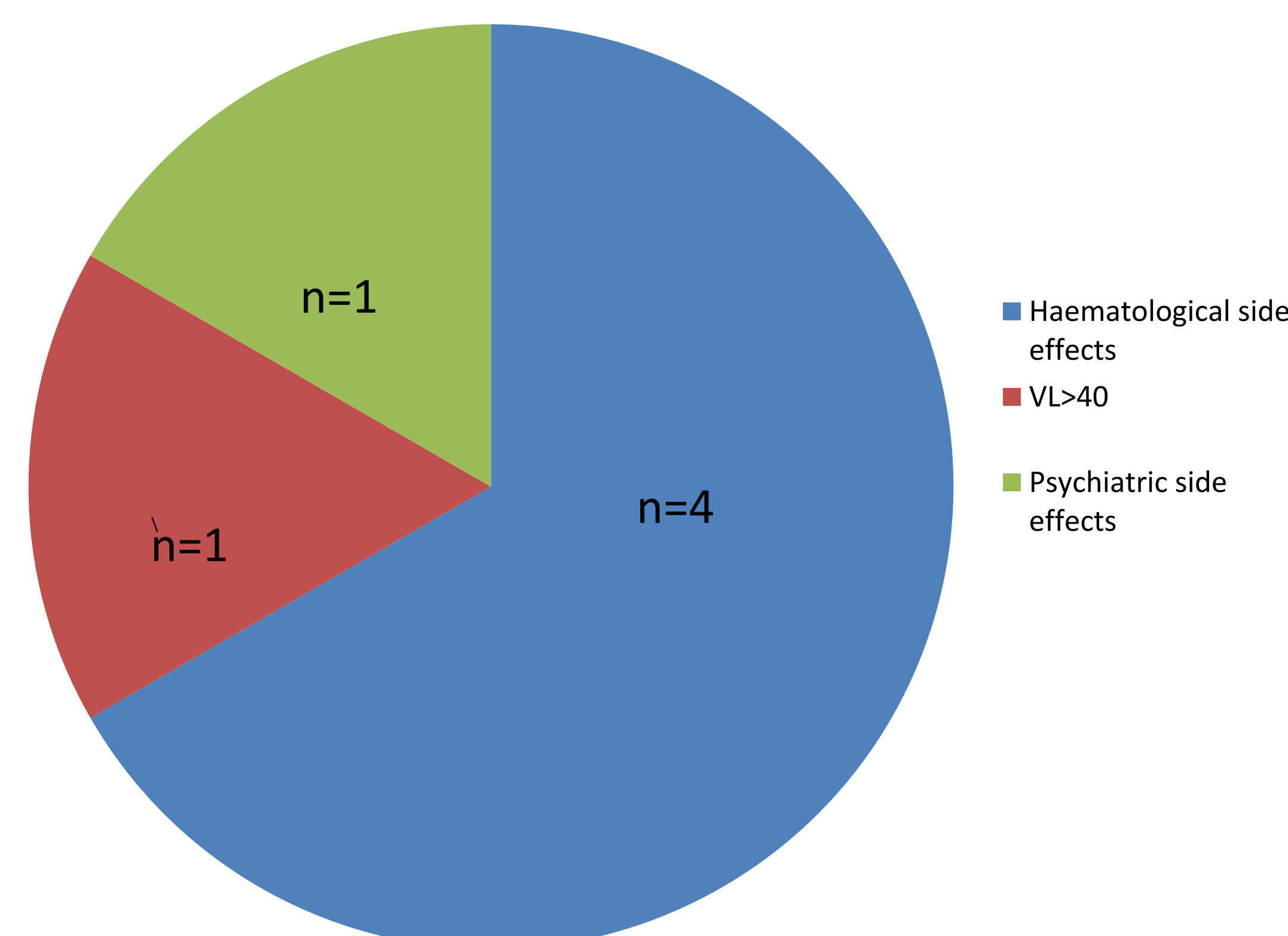
5 patients had more than one contraindication to treatment

Graph 1. Reasons why HCV treatment naive genotype 1 co-infected patients were not eligible for treatment

Experienced Patients

Number of HCV treatment experienced patients **16**

Number of HCV treatment experienced patients not eligible for treatment **6**



Graph 2. Reasons why HCV treatment experienced genotype 1 co-infected patients were not eligible for treatment

Conclusions

- Pre-existing psychiatric illness (12/23) was the most common cause of exclusion in the naive group.
- Haematological toxicity with Interferon and Ribavirin (4/6) excluded most in the experienced group.
- A PegInf sparing regimen is required to significantly increase the numbers of genotype 1 HCV co-infected patients who can be treated in Lothian.

Discussion

- Telaprevir and Boceprevir based triple therapy of treatment-naive and treatment-experienced HCV genotype 1 patients results in substantially increased SVR rates compared to PEG-INF- α and ribavirin alone
- This regimen does not negate the substantial issue of PegInf/Rbv side effects that make many patients unsuitable or decline treatment.
- The huge unmet need of a PegInf/Rbv sparing regimen may be addressed with a combination of direct acting antiviral agents (DDAs), which include PI's, currently in Phase 2 and Phase 3 trials. See Figure 1.

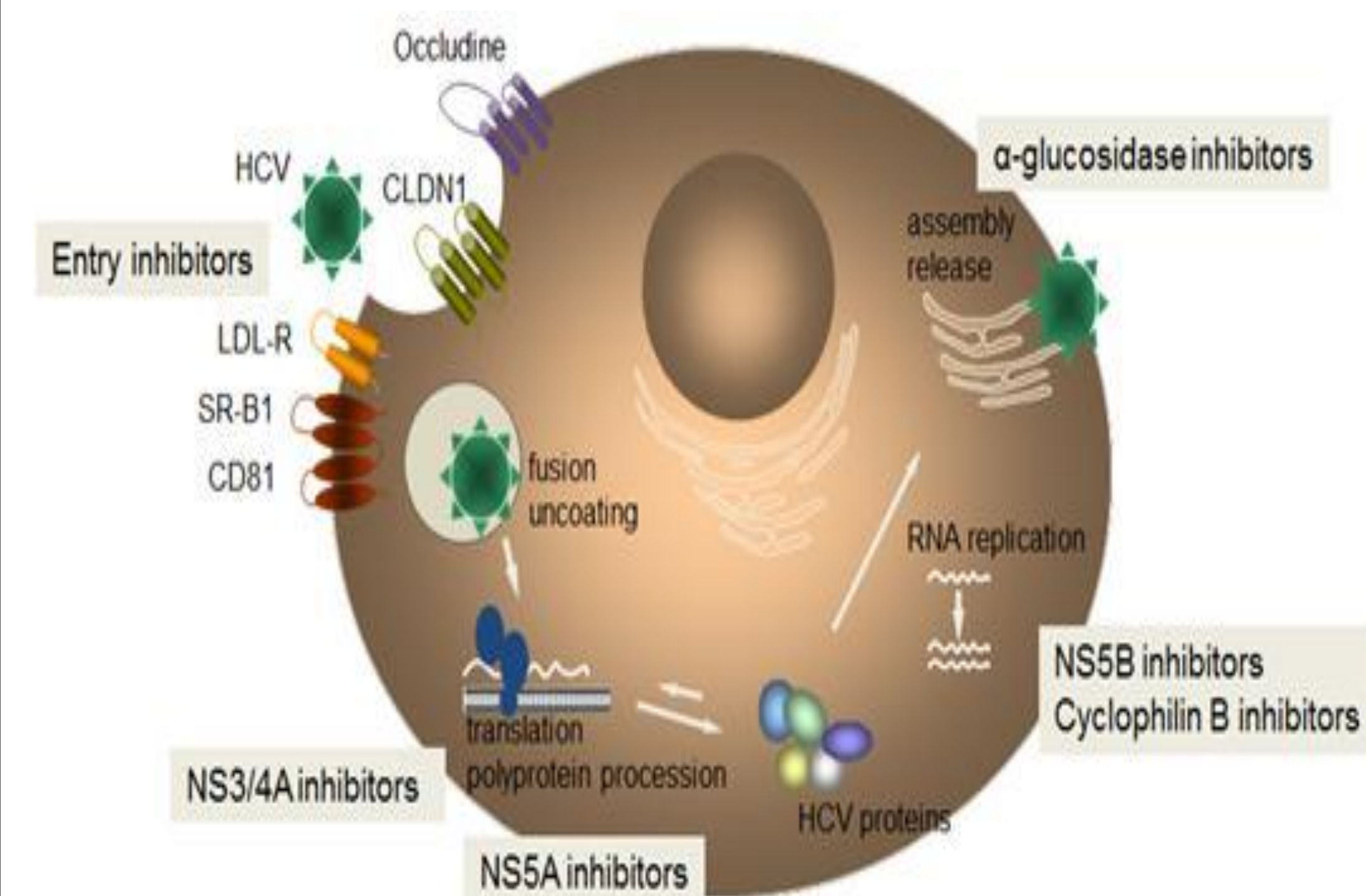


Figure 1. HCV Replication indicating Some of the current drug targets under Phase 2 and 3 trials.

Taken from Hepatology, a Clinical Textbook. 2012. Mauss et al

References

1. Buhler S, Bartenschlager. New targets for antiviral therapy of chronic hepatitis C. Liver International 2012; 32:9-16.
2. Gane E. Future hepatitis C virus treatment – interferon sparing combinations. Liver International. 2011; 31: 62-67