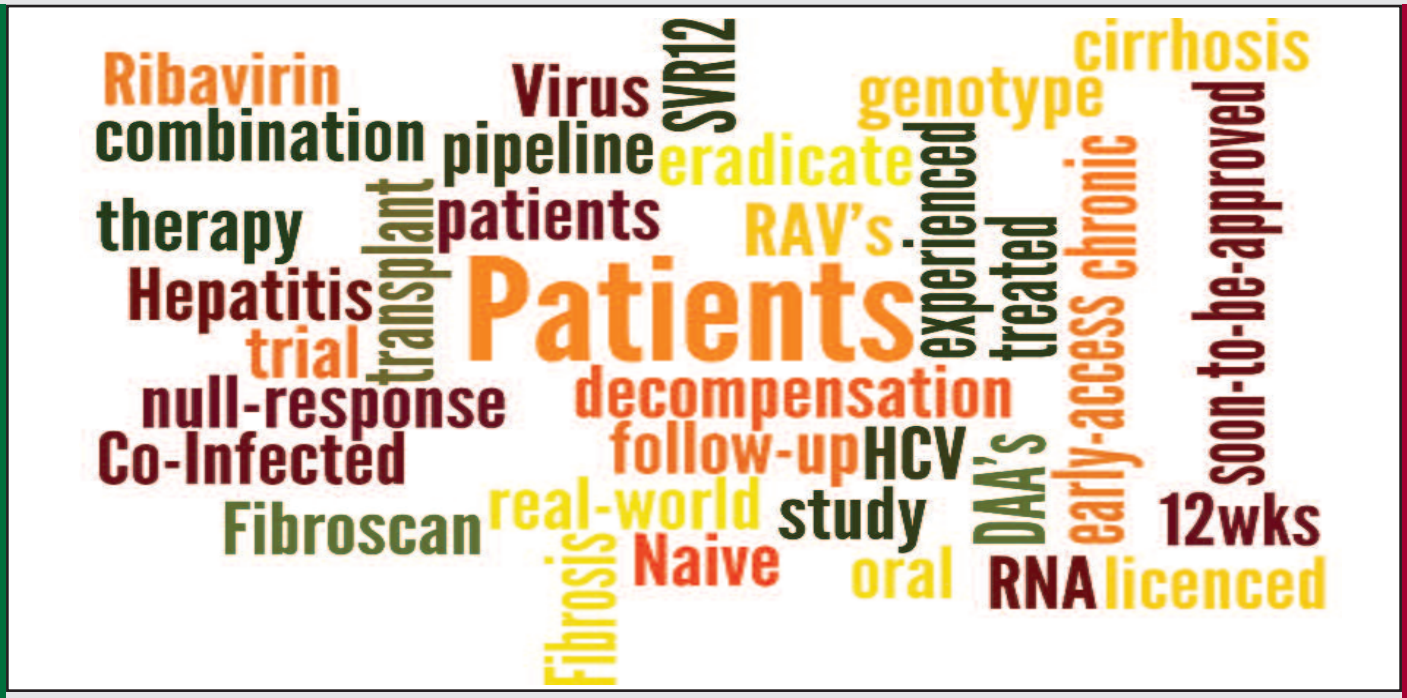
Positive News

Information Magazine for people with Hepatitis C and HIV

The Irish Haemophilia Society

Representing people in Ireland with haemophilia and related bleeding disorders



Welcome to the December 2014 edition of **'Positive News'**, an information magazine for people with hepatitis C and HIV, produced by the Irish Haemophilia Society. In this edition you will find some very interesting articles on the new generation of direct acting antiviral therapies for the treatment of hepatitis C that will be used in 2015, an update on treatment regimes and soon to be approved regimes, and on ageing and HIV.

The hepatitis C treatment landscape is changing rapidly. New generations of direct acting antivirals (DAA) are now licenced and several will be licenced and available in 2015.The therapies used up to this point in time will continue to be available. It is worth noting that the success rate with the current triple therapies in people with haemophilia was 80% with 16 of the 20 people treated achieving a sustained virological response (SVR) or effectively a cure. This SVR rate is significantly greater than the SVR rate of 51% in the overall Irish group of people treated with these therapies. This is a staggering difference in outcome. It is due primarily, in our view, to the very significant difference in compliance with the treatment regime. In the overall group of 136 Irish patients, discontinuation due to viral failure was 14% and was 15% in the haemophilia group. Discontinuation due to non-compliance or adverse events including the debilitating side effects associated with these therapies was 29% in the overall group and in the haemophilia group not a single individual stopped treatment because of the inability to tolerate side effects. The excellent compliance with what was a very difficult course of treatment was due to the education of our members on hepatitis C and treatments, the preparation they had taken for treatment, the support from the Hepatology and infectious disease teams and the very strong co-ordinated and continuing support from the Society and peer support among those on treatment. This support will continue to all those members who will be treated in the future until hepatitis C infection is eradicated from people with haemophilia in Ireland. Prior to the general availability of these new therapies, an early access programme for those in the greatest clinical need was approved by the Minister for Health in November and started in early December. This followed many representations by the Society and ICORN, the clinicians group. There is no doubt that this early access programme will save lives.

Edition: December 2014

EARLY ACCESS PROGRAMME

In 2014, four new drugs have been licensed for the treatment of hepatitis C as follows:

- Sofosbuvir (Sovaldi ®)
- Simeprevir (Olysio ®)
- Daclatasvir (Daklinza ®)
- Sofosbuvir/Ledipasvir (Harvoni ®)

Once licensed these drugs are submitted to the National Centre for Pharmacoeconmics (NCPE) for evaluation before a decision on reimbursement is made. Apart from Harvoni which is only used with or without Ribavirin, the other drugs can be combined with each other or with Peginterferon. The use of Ribavirin varies between different combinations.

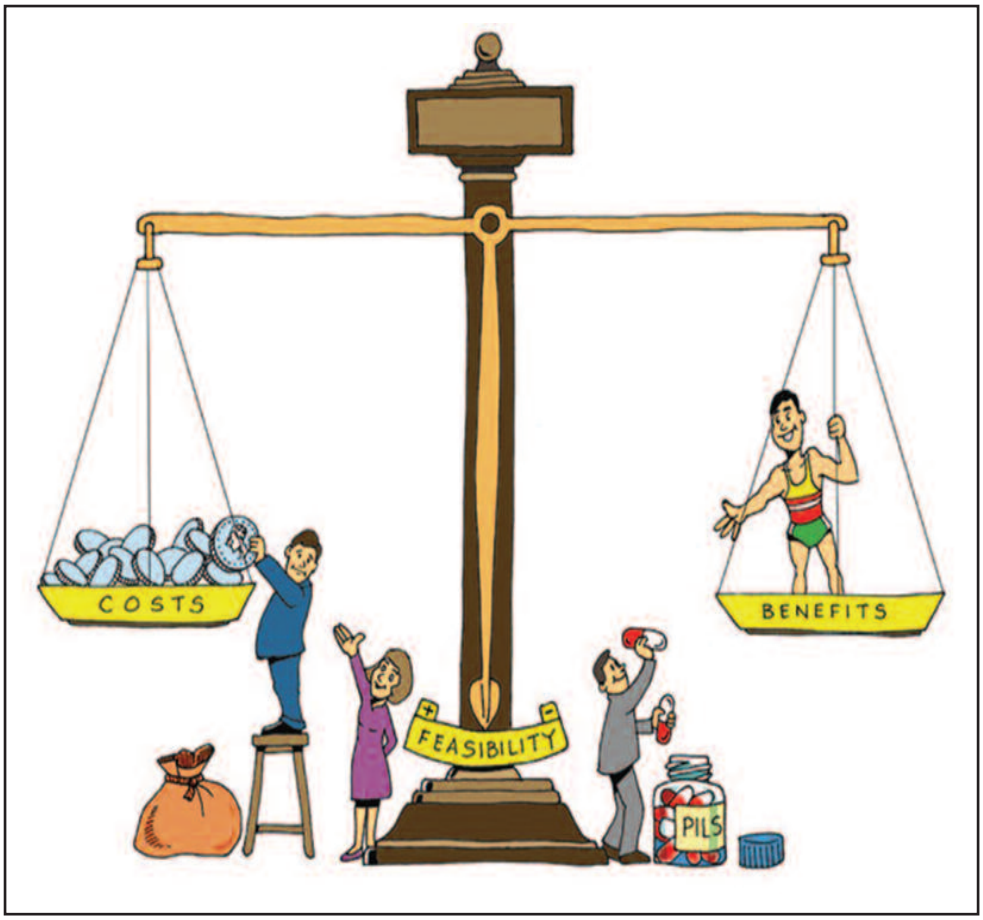
Finally, the different drugs and different combinations are effective against different Genotypes which makes assessment of these new treatments difficult with so many variations. So far, Sovaldi has been submitted and the recommendation is that it is cost-effective with PegInterferon with or without Ribavirin for certain sub-groups of people with hepatitis C.

Olysio, was recommended for reimbursement as a triple therapy regimen (co-administered with PegInterferon + Ribavirin) to treat Genotypes 1 and 4 who are treatment naïve or have previously been treated.

The combination of Olysio and Sovaldi is currently being reviewed, as well as all combinations with Daklinza. Harvoni has not yet been submitted as it only received a license shortly before this article was written.

As there are so many variations between drug combinations, stage of disease, previous treatments, as well as the potential budget impact the evaluation is difficult and most go for full evaluation which takes a total of 180 days. The problem is that it is not 180 consecutive days but a clock on – clock off situation.

If the NCPE require more information the clock is stopped and then restarted once the information is obtained. So in real time this can take longer than 6 months before combinations are recommended for reimbursement and then made available to patients. The majority of these evaluations will be finished in 2015.



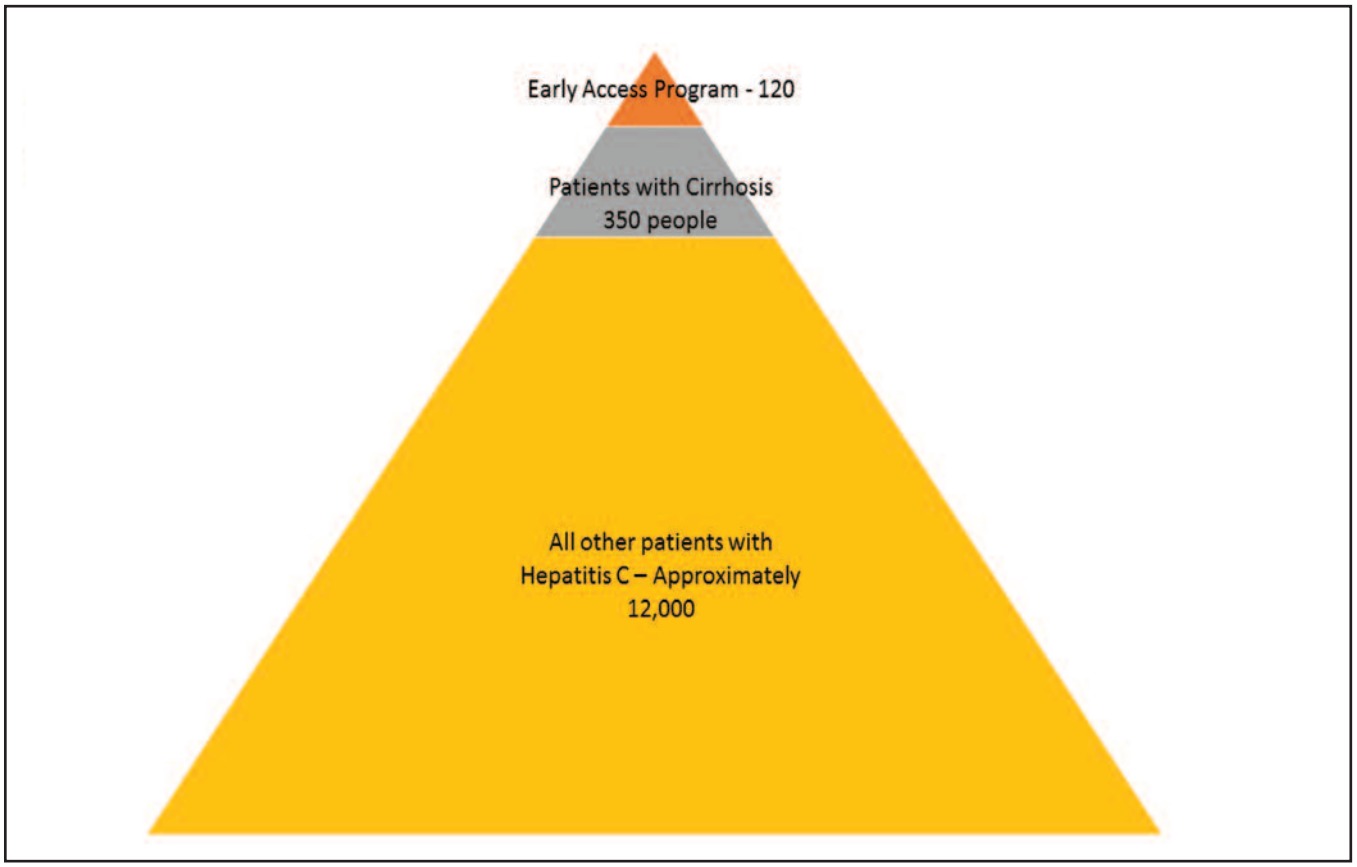
" The early access programme commenced at the start of December".

Whilst this is a hurdle for general reimbursement for all patients, it should not be a hurdle for those who are in most need. These drugs are producing very high cure rates, in both clinical trials and real world scenarios. They are also significantly less toxic on the liver. This means that even those patients who are in decompensation or post-liver transplant and other cohorts who were previously deemed too risky to try therapy using Interferon can take these treatments with a reduced likelihood of further liver damage. In the USA and Europe, with some of these being used in real world scenarios, patients have cleared hepatitis C and have been delisted from the liver transplant list due to improvements in the functioning of their livers. In these situations, these medications are very cost effective.

The Irish Haemophilia Society, clinicians and other organisations made repeated requests to the Department of Health and the HSE for access to the new treatments that are interferon free for hepatitis C patients who are in most need. In September, the Department of Health set up an advisory group to consider a multi-annual approach to the clinical and public health management of hepatitis C. Its aim was to make recommendations about extending access to these new drugs to a further group of patients. At this meeting again, it was strongly and repeatedly stated the importance of access in 2014 for those most in need.

On the 13th of November, the Minister for Health announced an early access programme for approximately 120 patients who are in the most urgent need of treatment. The patients were chosen by two main criteria which effectively narrowed patients to those who were at significant risk of death or irreversible liver damage within the next 6 - 12 months. Patients chosen had a one year mortality rate without treatment of 30%. Some of these patients are on the liver transplant list or may not be eligible for the list due to other circumstances, e.g infection, liver cancer, and heart or lung disease, etc.

The early access programme commenced at the start of December. The Minister, the Department of Health and the Health Service Executive (HSE) should be commended for realising the significant urgency around these patient's needs, as well as the rapid evolution of these new therapies and hence allowing access to these medications in advance of an evaluation report. Many of these patients will be here next year that wouldn't be if it was not for this intervention so, thank you!



In November this year, the American Association for the Study of Liver Disease (AASLD) held their annual conference called "The Liver Meeting". This is one of two state of the art conferences that take place annually. This was a frantic four days, with 379 posters and 44 oral presentations dedicated entirely to hepatitis C.

The following is a summary of the key areas since our last edition of 'Positive News':

- **HCV epidemiology**
- **Currently approved hepatitis C regimens**
  - Real world experience
  - Cirrhosis
- **Soon to be approved regimens**
- **Specific populations**
  - HIV
  - Transplants
- **Regimens in the pipeline**

HCV Epidemiology

There was a presentation from the Chronic Hepatitis Cohort Study (CHeCS) on the mortality and progression to decompensated cirrhosis in patients with HCV with varying degrees of liver damage. The study showed that the risk of the liver decompensating over a 4 year period at F2 (fibrosis) was 3.6%, rising to 10.1% in F3 (bridging fibrosis) and 27.7% in F4 (cirrhosis). The rate of decompensation was associated with fibrosis stage, low levels of platelets, albumin and other co-morbidities. However, the receipt of any therapy was a protective factor preventing the liver progressing to decompensation.

There was also an increase of liver cancer as the level of fibrosis increased from 1% in F2, to 2.7% in F3 and 8.3% in F4. This was matched by death rate of 4.9% in F2, 10.4% in F3 and 23.7% in F4. This group also looked at the treatment prioritisation of patients within the guidelines set up by AASLD.

The guidelines stated that the "Highest Priority" were patients with a fibrosis stage of F3 or higher or any patient who was below F3 who had chronic kidney disease. This resulted in 32.9% of the 8,504 patients in the cohort. The next group who were deemed "High Priority" were those patients with F2 fibrosis or patients with less than F2 fibrosis with a co-morbidities such as HIV, hepatitis B, severe fatty liver disease or diabetes. This was 28.9% of the cohort. These are the patients that are being assessed second in the group for treatment.

For those who have cleared the virus there was also a very interesting study looking at 129 studies on over 23,000 patients. They looked at the risk of liver cancer and liver transplant in those who achieved an SVR (cured) compared to those that did not (No SVR) after 5 years. The risk of liver cancer in general was 2.9% in patients who achieved an SVR compared to 9.3% in those that did not achieve an SVR. When this was broken down, in patients who had cirrhosis at the time of clearing the virus, 5.3% developed liver cancer compared to 13.9% in those who did not get an SVR. The risk of those co-infected with HIV patients of developing liver cancer was 0.9% after an SVR compared to 10% in those who did not achieve an SVR (Although there were only a few studies dealing with this). Trends we are seeing relating to liver transplant is a 36 fold reduction in the likelihood of needing a transplant in the patients who had cirrhosis when they achieved an SVR and 4 fold reduction in patients who were co-infected with HIV compared to those who did not achieve an SVR.

Finally, the reduction in risk of death after achieving an SVR was between 62-71%. Looking at the patients who had cirrhosis it was between 73-84% and in co-infected patients it was between 73-75%.

IMPLICATION
• EVIDENCE CONTINUES TO SHOW THAT HCV IS PROGRESSIVE AND OBTAINING AN SVR HAS MANY BENEFITS.

Currently Approved Hepatitis C regimens

This was the first conference where it was possible to report real world data from some of the Interferon free regimens. In the US there are 2 main options available for the non-interferon based treatments that combine DAA's:

1. Sovaldi (Sofosbuvir) and Olysio (Simeprevir) with and without Ribavirin.
2. Havroni (Sofosbuvir + Ledipasvir) with and without Ribavirin.

Whilst in Europe, there was also the addition of Daklinza (Daclatasvir) to Sovaldi. The real-world European data on this combination will be presented at the European meeting next April. (There is some information in the 'Soon to be approved' section of this article for the USA.)

Sovaldi (Sofosbuvir) and Olysio (Simeprevir) with and without Ribavirin

There were two different groups reporting their results with Sovaldi and Olysio combinations. The first was the TRIO network. In this cohort there were 876 patients who all completed 12 weeks of treatment. 30% had cirrhosis and 43% had received treatment previously. In the patients who had treatment previously, 35% were previous null responders, 62% were partial responders or relapsers.

Of these 320 patients with Genotype 1, received the combination of Olysio and Sovaldi with and without Ribavirin (although the majority of the patients were treated without Ribavirin, as some clinicians in the US stopped using Ribavirin after the results from the meeting in April 2014, in London).

Overall, SVR rates in patients who had never tried treatment before (Naïve) were 83% with or without Ribavirin. In those who had tried treatment before (Experienced), the SVR rate was 85% in the combination with Ribavirin and 80% without Ribavirin. Cirrhosis had an impact on the effect of the treatment, with 71% and 75% with and without Ribavirin respectively, in Naïve patients, and 86% and 72% with and without Ribavirin respectively in experienced patients. In those who had no cirrhosis, naïve patients achieved an SVR of 100% and 88% with and without Ribavirin, and 85% and 88% with and without Ribavirin in experienced patients.

The remainder of the patients in this cohort were treated with a combination of Sovaldi with Interferon and Ribavirin or Sovaldi with Ribavirin. In the Sovaldi with Interferon and Ribavirin group, which treated mostly Genotype 1 the SVR rates were 85%. In the Sovaldi with Ribavirin group it was mostly Genotype 2 patients and the SVR rates were 90%.

The other real-world study that is looking at the combinations is the HCV-TARGET study. There are 2,063 patients treated so far in the group. 52% were treatment experienced, 48% had cirrhosis, 10% had liver cancer, 11% had a transplant and 2% were co-infected. These were again split into to the same groups as TRIO: Sovaldi with Interferon and Ribavirin, Sovaldi with Ribavirin and Sovaldi and Olysio with and without Ribavirin. All of these results are preliminary results at 4 weeks after treatment.

In the Sovaldi with Interferon and Ribavirin group, which just looked at Genotype 1, 85% achieved an SVR. This group had the lowest number of patients who were treatment experienced, who had cirrhosis, liver transplant, liver cancer and the highest number of HIV co-infected patients. In the Sovaldi and Ribavirin group which was for Genotype 2, 90% of patients achieved an SVR.

The patients that were given Sovaldi and Olysio with or without Ribavirin were all Genotype 1 with much greater numbers of treatment experienced patients, cirrhotic patients, and liver cancer and liver transplant.

In the Naïve cohort with Sovaldi and Olysio with and without Ribavirin the overall SVR rate was 89%.

For those with no cirrhosis it was 92%, with cirrhosis it was 87% and in those who had prior decompensation it was 75%. In the experienced cohort of the same group the overall SVR rate was 81%. This was 85% in those without cirrhosis and 79% with cirrhosis.

When the results were adjusted to examine the use of Ribavirin with different characteristics such as: cirrhosis (85% without Ribavirin, 83% without Ribavirin), no cirrhosis (89% without Ribavirin, 90% without Ribavirin), Genotype 1a (84% without Ribavirin, 82% without Ribavirin), Naïve (89% without Ribavirin, 87% without Ribavirin) and experienced (85% without Ribavirin, 86% without Ribavirin), there was no clear difference in effect. Although in other studies presented at the conference, there was a trend towards increased SVR rates by a couple of percent but nothing statistically significant at this point.

Overall only 2.3% discontinued treatment due to side effects. One of the issues with this apart from the early results is the information around the duration of treatment. The report was based on the standard of care across 51 sites, all with slightly varying treatment regimens and it is unclear how many patients were on 12 week regimens and how many were on 24 week regimens.

Sovaldi and Olysio are both currently licenced in Europe. Harvoni (Sofosbuvir and Ledipasvir) received a licence in the US in October and in Europe in November. As the meeting was also in November there was no real-world data on this treatment. However, there were a few updates from clinical trials. In a prospective multicentre study patients, the combination of Sofosbuvir / Ledipasvir with Ribavirin for 12 or 24 weeks was assessed in 108 decompensated patients with Genotype 1 and 4. These were patients who were Childs-Pugh B and Childs-Pugh C. The Childs-Pugh score is based on 5 criteria (3 blood tests, the presence of ascites and the presence of encephalopathy). Each criteria has a maximum of 3 points allocated. The higher the score, the more damaged the liver is. A score from 7-9 is Childs-Pugh B and a score of 10-15 is Childs-Pugh C.

The overall SVR rate was 87% for 12 weeks and 89% for 24 weeks. When this was split, Childs-Pugh B patients had an SVR of 87% with 12 weeks of treatment and 89% on 24 weeks of treatment. In Childs-Pugh C, the SVR rates were 86% and 90%. 47 patients were rescored, 4 weeks after the end of treatment at the time of the presentation and 33 of them had a reduction in there Childs-Pugh Score, 10 were un-changed and 4 had worsened. There were only 3 patients who stopped treatment early. There were 6 deaths and one patient stopped early for a liver transplant on the trial. However, it is important to remember that these were patients had significant liver damage before commencing.

In another trial, in 155 cirrhotic patients who had previously failed triple therapy, Sofosbuvir and Ledipasvir with Ribavirin was given for 12 or 24 weeks of treatment. Only 1 patient stopped treatment early. The SVR rate in the 12 week group was 96% and 97% in the 24 week group.

In addition, another trial looked at patients who failed prior treatment with Sofosbuvir containing regimens. At the time of presentation only the results from the group who were receiving 12 weeks of Sofosbuvir and Ledipasvir with Ribavirin was available This was currently only 51 patients and 98% of these achieved an SVR.

Overall Sofosbuvir and Ledipasvir treatments were associated with a significant improvement in patient reported outcomes. The biggest predictor of issues relating to treatment are associated with the use of Ribavirin. Also in patients who achieved an SVR their reported outcomes significantly improved by up to 8.3%.

IMPLICATIONS

•PATIENTS WITH COMPENSATED OR DECOMPENSATED CIRRHOSIS CAN SAFELY ACHIEVE HIGH SVR RATES WITH ALL ORAL REGIMENS BUT MORE ADVANCED DISEASE CAN IMPACT THE RESPONSE RATES.

•INFORMATION IS STARTING TO DEVELOP THAT SVR IN CIRRHOSIS IS ASSOCIATED WITH IMPROVEMENT IN LIVER FUNCTION. HOWEVER, IT IS STILL UNCLEAR AS TO HOW THIS WILL HAVE AN IMPACT ON THE TRANSPLANT RATES.

•PATIENTS, INCLUDING THOSE WITH CIRRHOSIS, WHO PREVIOUSLY FAILED TRIPLE THERAPY OR SOFOSBUVIR BASED THERAPY CAN ACHIEVE AN SVR WITH ALL ORAL REGIMENS.

•PATIENT REPORTED OUTCOMES IMPROVE SIGNIFICANTLY AFTER AN SVR IS ACHIEVED.

Soon to be approved regimens

Next to the market is the 3D combination of Paritaprevir/Ombitasvir/Ritonavir (Viekirax) and Dasabuvir (Exviera). Licensing is expected in late January for Europe. For the purposes of this magazine it will continue to be called the 3D regimen. At the conference, a pooled data set of the four Phase 3 clinical trials was presented for Genotype 1a and 1b.

In the Genotype 1a group, patients who did not have cirrhosis were on 12 weeks of treatment with and without Ribavirin. Overall these patients achieved an SVR of 96% in both patients who were treatment naïve and treatment experienced. All patients who were treatment experienced received Ribavirin. In the naïve patients on the 3D regimen with Ribavirin the rates of SVR increased by 6% compared to those just on the 3D regimen. Also in this group, Ribavirin reduction was used but only in a small number of patients (6.7%), side effects were mild and generally more common in the patients taking Ribavirin.

In the cirrhotic patients the 3D regimen with Ribavirin was used in all patients. There was two durations of treatment, 12 weeks and 24 weeks. In this group overall, patients had SVR's of 88.7% on the 12 week treatment and 95% in the 24 week treatment. This was a little higher in treatment Naïve patients with cirrhosis (92.4% in 12 week and 94.6% in 24 week). In general the 3D regimen with or without Ribavirin had similar rates of SVR. However, the advantage of the 24 week treatment could be among the cirrhotic patients who did not respond to previous treatments (80% in 12 weeks and 93% in 24 weeks).

In Genotype 1b, all patients without cirrhosis were treated with 12 weeks of the 3D regimen or 3D regimen with Ribavirin. There was no impact of the Ribavirin for the patients without cirrhosis with all groups achieving between 98-100% whether they had prior treatment or not. All patients with cirrhosis were treated using 3D regimen with Ribavirin for 12 weeks or 24 weeks. There was no impact of extending the duration of treatment with patients overall achieving and SVR of 98-100%.

" Overall only 2.3% discontinued treatment due to side effects."

In the pooled analysis of six trials they examined if the effect of achieving an SVR was based on the time it takes for the virus to become undetectable. SVR rates were high for patients with or without cirrhosis regardless of the time it took to achieve an undetectable amount of virus (Week 1: 98-100%, Week 2: 94-98%, Week 4: 97-98%, Week 6:95-99%). What was found to take more time to clear the virus was the amount of the virus (more virus, longer to clear), Genotype 1a (more difficult genotype), older age (maybe poor circulation) and cirrhosis.

In Genotype 4, the PEARL-I study, Paritaprevir/Ombitasvir/Ritonavir (Viekirax) was used. This is sometimes known as the 2D regimen and which will be used in this magazine. The other drug (Dasabuvir) is not used as it is not effective on Genotype 4. This was tested in 135 patients without cirrhosis and it was tested with and without Ribavirin for 12 weeks. With the treatment naïve patients on the 2D regimen 95% was achieved. In the patients who were on the 2D regimen with Ribavirin, whether they had treatment before or not, the SVR rate was 100%. However, the numbers are small at this stage.

The Bristol Myers-Squibb combination of Daclatasvir /Asunaprevir /BMS-791325 is being tested in Genotype 1 Phase 3 trial called UNITY-1 in 415 patients. This is a 12 week regimen, no patients had cirrhosis and no Ribavirin was included. The overall SVR rate was 91%. In treatment naïve patients 92% of Genotype 1 patients achieved an SVR, with slightly better responses in Genotype 1b patients (98%), and in the treatment experienced patients with genotype 1 the SVR rate was 89%, again with Genotype 1b the rates were higher (100%). In the UNITY-2 trial of 202 patients, the combination is being assessed in cirrhotic patients with and without Ribavirin for 12 weeks of treatment. In treatment naïve patients on the combination without Ribavirin the SVR rate was 93% and 98% with Ribavirin. In patients who were treatment experienced the SVR rates were 87% without Ribavirin and 93% with Ribavirin. Side effects are mild in the Ribavirin groups. There was only one discontinuation. In relation to patients that relapse after treatment this occurred less often in Ribavirin containing arms.

Daclatasvir is also being tested in combination with Sofosbuvir for 12 weeks of treatment in Genotype 3 patients in the ALLY-3 trial. In total there is 151 patients, 21% of which had cirrhosis. In the treatment naïve patients the SVR rates are 90% and in the patients with previous treatments the SVR rates are 86%. Looking specifically at the patients with cirrhosis the SVR rates were 63%. 11% of patients relapsed after treatment and the majority of these were patients with cirrhosis.

IMPLICATIONS

• REGIMENS COMING IN THE NEXT 2 MONTHS TO A YEAR ARE SHOWING VERY HIGH SVR RATES ACROSS MOST OF THE PATIENT COHORTS.

•COMBINING MULTIPLE DRUGS FROM DIFFERENT CLASSES MINIMISES THE RISK OF THE VIRUS REAPPEARING DURING TREATMENT AND IN THE FEW FAILURES THAT ARE SEEN, THESE ARE DUE TO RELAPSE AFTER TREATMENT HAS FINISHED.

•THE ROLE OF RIBAVIRIN VARIES BY GENOTYPE AND TREATMENT REGIMEN AND IT DOES NOT LOOK LIKE IT IS GOING AWAY JUST YET.

•DURATION OF TREATMENT GREATER THAN 12 WEEKS MAY HELP IMPROVE SVR FOR CERTAIN POPULATIONS SUCH AS:

- ***PATIENTS WITH CIRRHOSIS WHO HAVE NOT RESPONDED BEFORE.***
- ***PATIENTS WITH GENOTYPE 3 AND CIRRHOSIS.***

Specific Populations

HIV

In the NIAID ERADICATE trial for patients with HIV, 12 weeks of treatment with Sofosbuvir/Ledipasvir was given. All patients were Genotype 1 and the majority had mild fibrosis.

There were two groups studied, 13 patients who had never had anti-retrovirals (ARV's) and 37 patients stable on ARV's. 100% of patients who never had ARV's achieved an SVR and 97% of those who were stable on ARV's achieved an SVR. There were no changes in the CD4 count or HIV viral load and there were no serious side effects and no discontinuations as a result of side effects.

In the Turquiose–I study, the 3D regimen, Paritaprevir/Ombitasvir/Ritonavir (Viekirax) and Dasabuvir (Exviera) was used 63 patients with HIV co-infection again showing high SVR rates. 20% of patients had cirrhosis and only 35% had received treatment previously and all patients were on ARV's.

Again all patients received the 3D regimen with Ribavirin. In patients who received 12 weeks of treatment the SVR rate was 94% and for those on 24 weeks of treatment 91% achieved an SVR.

Transplants

Another very interesting set of results for patients post liver transplant was presented at the conference. In real world data Sovaldi and Olysio was used in 109 Genotype 1 patients post-transplant using 12 weeks of treatment. 82% of patients were treatment experienced and 29% had cirrhosis. At the time of the presentation only 66 patients had reached 12 weeks post treatment to test for SVR. The overall success rate was 91%. There was a minimal difference between the groups on the use Ribavirin (89% with vs. 91% without). Genotype 1a patients had an 88% SVR rate compared to 96% in Genotype 1b. The biggest difference was seen in the fibrosis level of the liver. If the liver had no to moderate fibrosis the SVR rate was 96%. If there was bridging fibrosis or cirrhosis the SVR rates were 76%. The study has so far showed that the virus being clear at week 4 after starting treatment is not an indicator as to whether or not SVR is achieved.

In one multi-center study of 223 patients with Genotype 1 and 4, Sofosbuvir/Ledipasvir was used with Ribavirin for 12 or 24 weeks. There was a broad group of patients included from those without cirrhosis to those with decompensated cirrhosis. Ribavirin was given to all patients however, patients without cirrhosis and with cirrhosis with a Childs-Pugh A score were all put on weight based Ribavirin. Those with cirrhosis and Childs-Pugh B or C were put on low doses of Ribavirin and then increased to a tolerable level. The majority of patients were previously treated. The groups were split in 4 groups: No cirrhosis, Childs-Pugh A, Childs-Pugh B and Childs-Pugh C. In the group without cirrhosis the SVR rates were 96% for 12 weeks of treatment and 98% for 24 weeks of treatment. In the Childs-Pugh A, SVR rates were 96% for both 12 and 24 weeks. The patients who were Childs-Pugh B achieved an SVR of 85% on 12 weeks and 83% on 24 weeks of treatment. In the Childs-Pugh C group the response was significantly reduced to a 60% SVR rate after 12 weeks and 67% after 24 weeks. For patients who achieved an SVR there were significant improvements in their blood results, particularly, bilirubin and albumin.

Using the 3D regimen, Paritaprevir/Ombitasvir/Ritonavir (Viekirax) and Dasabuvir (Exviera), which was 24 weeks of treatment and included Ribavirin for all 34 Genotype 1 patients. There were no patients with cirrhosis. The SVR rate of 97.1%. Only one patient discontinued and 5 patients required EPO. A number of patients required dose reduction of Ribavirin and all who did still achieved an SVR.

IMPLICATIONS

• PEOPLE WITH LIVER TRANSPLANTS AND THOSE CO-INFECTED WITH HIV CAN BE SAFELY TREATED WITH THE NEW THERAPIES.

• EXTENDING THE LENGTH OF TREATMENT AND/OR INCLUDING RIBAVIRIN CAN OPTIMISE THE SVR RESPONSE IN POST-TRANSPLANT PATIENTS.

- AN SVR IN THESE PATIENTS DECREASES THE DISEASE SEVERITY.

Regimens in the Pipeline

In the C-Worthy trial a number of cohorts were examined. This is with a combination of Grazoprevir and Elbasvir for 12 or 18 weeks, with and without Ribavirin for Genotype 1 patients. In the cirrhotic group, with 12 weeks of treatment the SVR rates were 90% (with Ribavirin) and 97% (without Ribavirin). In the 18 week group the SVR rates were 97% (with Ribavirin) and 94% (without Ribavirin). In the patients who had no response to treatment before, with 12 weeks of treatment the SVR rates were 94% (with Ribavirin) and 91% (without Ribavirin). In the 18 week group the SVR rates were 100% (with Ribavirin) and 97% (without Ribavirin). The study also looked at treatment naïve patients with hepatitis C only as well as a group co-infected with HIV for 12 weeks of treatment. In the hepatitis C only group the SVR rates were 93% with Ribavirin and 98% without Ribavirin. In the co-infected group the SVR rates were 97% with Ribavirin and 87% without Ribavirin. Finally, they also looked at 8 weeks of treatment in the hepatitis C only group and with Ribavirin. The SVR rates were 80%.

In another trial, Sofosbuvir and GS-5816 was assessed for 8 and 12 weeks of treatment in all Genotypes for treatment naïve patients without cirrhosis. For 12 weeks of treatment without Ribavirin, Genotype 1 and 2 SVR rates were 100% and Genotype 3 SVR rates were 93%. In the group on 8 weeks of treatment for Genotype 1, the results were 90% with Ribavirin and 81% without Ribavirin. There were higher relapse rates in patients who received 8 weeks of treatment compared to 12 weeks and the use of Ribavirin did not seem to affect this result.

Getting into the shorter durations of treatment there is a test combination of Sofosbuvir with ACH-3102, which is looking at 6 and 8 weeks of treatment. Only the treatment rates of naïve patients without cirrhosis were available and these were 100% in 12 patients.

C-Swift is a combination of Sofosbuvir/Grazoprevir/Elbasvir looking at 4-6 weeks of treatment in patients without cirrhosis and 6-8 weeks in patients with cirrhosis. In the patients without cirrhosis the 4 week treatment has SVR rates of 39% and 87% in the 6 weeks of treatment. In the patients with cirrhosis on 6 weeks of treatment the SVR rate is 80% and in the 8 weeks of treatment group is 95%. Results are interesting but a little disappointing at the moment. All patients who failed to clear the virus were relapsers after the end of treatment, suggesting that a shorter time period may be a little further away than hoped.

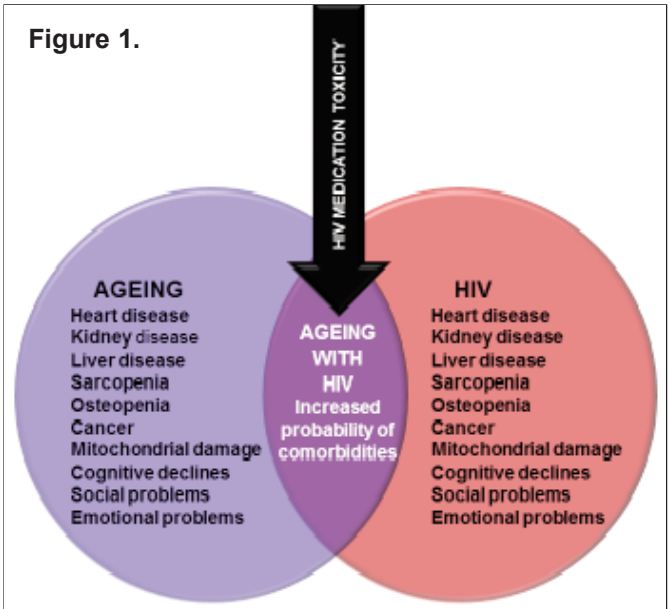
IMPLICATIONS

• THERE IS STILL A ROBUST PIPELINE OF NEW TREATMENTS THAT IS VERY PROMISING FOR CURING ALMOST EVERYONE WITH HEPATITIS C.

The greying group of people with HIV shows how well today's HIV treatments can work. However, HIV makes ageing itself more complicated. We fully expect that someone with HIV will live a long, healthy life, but that means they have to plan ahead and adopt healthy habits to stay that way, just like anyone without HIV.

There is little dispute that many of the diseases associated with ageing occur at much higher rates in people with HIV and at much younger ages than in people not living with the virus. In figure 1 below you will find some of those conditions.

Figure 1.



There are a number of factors that contribute to these problems, such as:

• Some medications, including ARV's, can contribute to bone loss, kidney damage, fat redistribution and elevated cholesterol and triglycerides.
• Being co-infected with hepatitis C increases the risk of liver cancer, liver failure, kidney disease and diabetes.
• Smoking which is one of the leading causes of heart attacks, strokes, lung cancer and emphysema.
• HIV can directly infect key tissues in the bone, brain, circulatory system and elsewhere, and it can cause inflammation-related damage to the heart, nervous system, liver and kidneys.

These factors are likely to play major roles in the increased rates of ageing related diseases and conditions seen in people with HIV. What experts haven't yet agreed upon is how much HIV infection itself might exacerbate underlying risk factors known to contribute to ageing related problems.

Although we're a long way from discovering a fountain of youth, there are a number of factors that are consistently associated with reducing the risk for developing age related conditions. Many are old standbys that we've been hearing about for decades, but there's a good reason that they've stuck around so long: They work!

Don't Smoke

Smoking is one of the most harmful things that people can do to their bodies—and to their chances of living a long (and healthy) life. Most people know it can cause lung cancer and other lung diseases. Some even know that it can increase the risk for heart attacks and strokes. What many don't know is that it is also associated with numerous other age-related ailments including bone mineral loss, muscle wasting, problems with memory and concentration and age related cancers, such as anal, breast, cervical and prostate cancer.

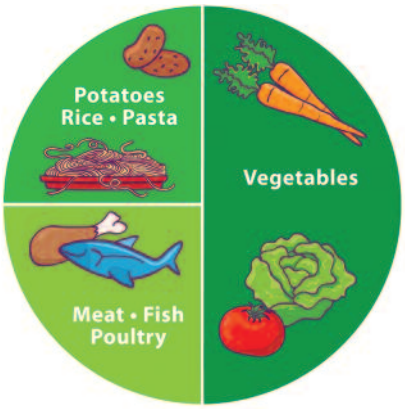
Exercise

People who exercise regularly, on average, are far healthier in numerous respects than people who don't exercise. As bad as smoking is on just about every part of the body, exercise is good for it. Benefits of regular exercise include reductions in the risk of:
• cardiovascular disease, diabetes and metabolic syndrome.
• age-related cognitive decline.
• bone-mineral and muscle loss.

Exercise also reduces inflammation throughout the body, improves symptoms of depression and anxiety, and hastens recovery when illness strikes. Not everyone is equally able to exercise, and a doctor should sign off on any exercise plan, but there are a number of ways to get moving. Start slow and build from there.

Eat Well

Aside from exercise, diet also helps determine who will live longest and healthiest. Experts are divided on the ideal diet. Some argue against the consumption of almost any fat. Others say that fats (at least healthy fats from nuts and fish) aren't the problem, but that sugar is. Some argue for a vegetarian way of life, while others say meats are just fine. Fad diets that come and go just confuse matters further. All of this can make it quite difficult to decide on the best diet.

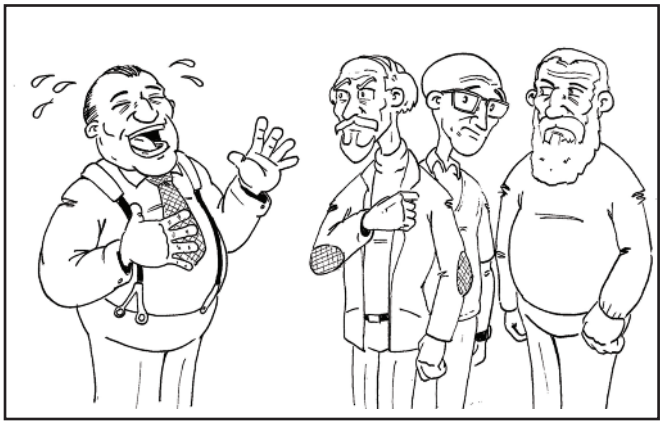


What most reputable diets have in common is watching caloric intake, along with an emphasis on including lots of fruits, vegetables, whole grains and beans, and then enjoying everything else in moderation. Most also stress the importance of eating the healthiest types of fish and limiting meat consumption to the leanest meats, such as from chicken and turkey, whenever possible. When it comes to fats, there is growing consensus that "healthy" fats for example, from olive oil, nuts and avocados are actually good for you.

What the most reputable diets also agree on is that too much sugar and too many processed and fried foods are a primary driver of diabetes, cardiovascular disease and a host of other health problems.

Stay Socially and Mentally Connected

Numerous studies have found that people who maintain social connections with their family, friends and colleagues and who engage in activities that they feel add meaning to their lives not only live longer, but also remain healthier than people who are socially isolated and who do not engage in meaningful activities. There are a variety of ways to get connected socially if you aren't close to family or do not have a big social circle. Volunteering with a charity that works on causes you believe in, or with a political campaign, can also help you connect socially. Finding local groups of people to exercise with would accomplish two goals: social connection and fitness. Websites are ways you can meet others who share your interests and hobbies.



If you are unable to get out of your house easily, or if you live in a rural area without many opportunities similar people, it is possible to connect with others online in forums.

Some final thoughts about HIV and Ageing

Potent combination ARV therapy is not perfect. All of the available treatments can cause some side effects; the drugs must currently be taken with almost perfect regularity and for the rest of one's life; and all can stop working. That said, many experts now agree that a person who starts ARV's soon enough should live a nearly normal life span. The big question for many, then, is "Will people with HIV be able to remain healthy over the course of their old age"?

Current research is seeking to answer that question. Though rates of age related diseases are much higher in people with HIV, this doesn't mean that everyone who is HIV positive will have multiple illnesses by the time they reach their 50's. In fact, the actual rates of some age-related diseases remain well under 10 percent in people with HIV. What isn't yet clear is who will be most at risk of which diseases, how vigilant we need to be in screening for various diseases and whether treatment for any diseases will need to be different in people with HIV. Researchers are actively working on these issues. In the meantime, the best available methods for preventing age-related physical and mental decline are the old standbys: dieting, exercising, maintaining social connections and abstaining from harmful behaviours.

AGEING & HIV - A PERSONAL VIEW

As a fortunate survivor (thus far) of HIV infection, I sometimes reflect, on how life has been since diagnosed in 1985. At that time life expectancy with HIV was up to two years. While too many of our relations and friends tragically died because of this virus, for a number of people infections did not occur, and as medical knowledge and treatment improved, long term survival became a fact of life for a lot of those infected. However, as we learned from our doctors, this is not the end of the matter.

At conferences over the past few years, with ageing and haemophilia being on the agenda, ageing, haemophilia and HIV (assuming you've cleared HCV!) is now the main issue. For a number of years I naively thought I was safely out of the woods only to be reminded (gently of course) by my consultant, that I am getting older. Being argumentative by nature I challenged my doctor's notion of old age. Since he is younger than me I needed to be sure he wasn't taking my children's view that I went to school in a cave, travelling there by ass and cart, or that I had to walk miles, barefoot, in the snow in order to change TV channels. However, being more intelligent than I (easily achieved) and highly qualified (not so easy) he produced evidence to show that non progressive HIV patients from 50 years old (middle aged surely?) fared better on retroviral treatment as they aged, as ageing conditions such as cardiovascular, prostate etc. can be exacerbated by being HIV positive.

The treatment he forced me to take (ok, I agreed to take it) is a triple therapy tablet. I was advised about side effects, with the main one being reported as 'vivid dreams'. Hmmm, what kind of vivid dreams? Vivid all right but not particularly entertaining. I have frequently seen a connection between daily events and dreams so one night I had a very realistic conversation with Jose Mourhino, having watched a Chelsea match the night before! Another night I dreamt I could fly (no I didn't wake up on the floor, don't be silly!) However, I have also dreamt I met and talked to deceased family members, which was weird but somewhat pleasant.

Hopefully this medication will help me avoid serious illness from HIV into the future. Unfortunately, it won't prevent old(er) age and the consequences thereof; such as having to return to the house every time because I've forgotten something, wondering why the Sunday paper isn't in the shops, on Saturdays! Needing a pick-up stick to avoid dizzy spells and having tablets delivered by dumper truck. The future is bright, thanks doc. (I wonder how old he is?)

Hepatitis C Conference

Date: Saturday 7th February, 2015

Venue: Castleknock Hotel, Castleknock, Dublin 15.

This one day conference, (organised by the Irish Haemophilia Society) will be an opportunity for people with hepatitis C who are contemplating treatment now or in the future to receive updates on hepatitis C treatment options and lifestyle. Speakers will include leading Irish Hepatologists, infectious disease consultants and people with hepatitis C who have experienced treatment. There is no charge to attend this conference but registration is required. Places are limited and will be given on a first come first served basis.

PROGRAMME

08.00 – 09.00hrs	Registration
09.00 – 09.15hrs	Welcome
09.15 - 09.30hrs	Official Opening by Minister of Health
09.30 - 10.00hrs	Hepatitis C – Clinical Progression, Why you should treat? • *Progression - Self clear, fibrosis, cirrhosis* • *Importance of treatment* • *How an SVR makes a difference*
10.00 – 10.45hrs	Treatment Options • *Introduction (Past Treatments)* • *Current treatments* • *Future treatments*
10.45 – 11.15hrs	Discussion
11.45 – 12.30hrs	Protocols, Access and Compliance • *Treatments protocols* • *Access* • *Compliance and engagement with the service*
13.00 – 14.00hrs	Lunch
14.00 – 15.00hrs	Managing your treatment • *Introduction* • *Panel discussion*
15.00 – 16.15hrs	Lifestyle - Waiting for treatment
16.15 – 17.15hrs	Organisational support
17.15 – 17.30hrs	Conclusion and Wrap-up

To register to attend this conference please:

- **Email your name, address and mobile number to: hepcconference2015@gmail.com**

OR

- **Call / text 087 916 8405 giving details of your name, address and mobile number.**

LOOKING FORWARD TO SEEING YOU AT REGISTRATION BETWEEN 8AM & 9AM ON 07/02/2015