New Treatment for HCV G4
Towards an End to HCV Epidemic in Egypt

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Hepatitis C Genotypes

- In Europe: <10%
  - In US >15%

- Middle East: >80%

- South-East-Asia: >30% in some areas

- India: >80%
- Thailand: >70%

- South Africa: (>50%)

- In Europe: 20%
- i.v. drugs
- India: >80%
- Thailand: >70%
Genotype 4

• HCV genotype 4 accounts for approximately 15% of all cases of chronic HCV worldwide.
• Genotype 4 predominates throughout the Middle East and parts of Africa, often in association with a high population prevalence as in Egypt.
• More than 90% of Egyptian HCV isolates belong to genotype 4.
• Phylogenetic analysis of the complete genomic sequence of genotype 4 revealed a closer relationship between genotype 4 and genotype 1 than with other genotypes.

Habib et al, Hepatology 2001; 33: 248-253
Angelico et al, J Hepatol 1997; 26: 236-43
# Epidemiology of G4

<table>
<thead>
<tr>
<th>HCV genotype 4 prevalence %</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>91 %</td>
<td>Egypt</td>
</tr>
<tr>
<td>76 %</td>
<td>Cameroon</td>
</tr>
<tr>
<td>71 %</td>
<td>Gabon</td>
</tr>
<tr>
<td>60 %</td>
<td>Nigeria</td>
</tr>
<tr>
<td>60 %</td>
<td>Saudi Arabia</td>
</tr>
<tr>
<td>30 %</td>
<td>Lebanon</td>
</tr>
<tr>
<td>30 %</td>
<td>Syria</td>
</tr>
<tr>
<td>14 %</td>
<td>Southern Spain</td>
</tr>
<tr>
<td>7.4 %</td>
<td>Southwestern France</td>
</tr>
<tr>
<td>6.2 %</td>
<td>Southern India</td>
</tr>
<tr>
<td>3.6 %</td>
<td>Germany</td>
</tr>
<tr>
<td>3.1 %</td>
<td>Northern Italy</td>
</tr>
<tr>
<td>1.4 %</td>
<td>Southern Italy</td>
</tr>
</tbody>
</table>

Wautuck et al., Aliment Pharmacol Ther 2014
Egyptian National Control Strategy for Viral Hepatitis

2008-2012

April 2008

Arab Republic of Egypt, Ministry of Health and Population
National Committee for the Control of Viral Hepatitis
HCV Egypt 2008

Overall Prevalence 14%

[Bar chart showing age-specific prevalence rates for HCV among men and women in Egypt 2008, with the overall prevalence labeled as 14%]
HCV Egypt 2008

- Rural Lower Egypt
- Lower Egypt
- Rural Upper Egypt
- Urban Lower Egypt
- Urban Upper Egypt
- Urban Governorates
- Frontier Governorates

Men:
- Rural Lower Egypt: 4.9
- Lower Egypt: 14.4
- Rural Upper Egypt: 11.2
- Urban Lower Egypt: 17.7
- Urban Upper Egypt: 19.4
- Urban Governorates: 20.2
- Frontier Governorates: 22.3

Women:
- Rural Lower Egypt: 7.6
- Lower Egypt: 10.1
- Rural Upper Egypt: 2.4
- Urban Lower Egypt: 11.5
- Urban Upper Egypt: 13.4
- Urban Governorates: 15
- Frontier Governorates: 16.5
HCV Prevalence National Surveys 1996 vs 2008 15-60 Ys

- **Men 1996**: 22.95%
- **Women 1996**: 14.18%
- **Men 2008**: 11.81%
- **Women 2008**: 16.61%
- **All 1996**: 20.06%
- **All 2008**: 25.76%

Legend:
- Men 1996
- Women 1996
- Men 2008
- Women 2008
- All 2008
- All 1996
HCV Prevalence National Surveys 1996 vs 2008
Women 15-60 Ys

Women 1966 Women 2008

Women 2008: 35
HCV Prevalence National Surveys 1996 vs 2008
Men 15-60 Ys

Men 1996  Men 2008

15-19: 5.5 vs 4.4
20-24: 4.4 vs 3.0
25-29: 8.0 vs 9.3
30-34: 13.1 vs 14.3
35-39: 42.3 vs 39.9
40-44: 42.3 vs 40.0
45-49: 49.3 vs 43.9
50-54: 49.3 vs 33.6
55-59: 43.5 vs 33.6

Men 1996 vs Men 2008
Geographic HCV prevalence

- **Alexandria**: 5.9% (95% CI: 4.2-7.7)
- **Middle Egypt**: 26.5% (95% CI: 23.7-29.4)
- **Upper Egypt**: 19.4% (95% CI: 17.2-21.6)
- **Lower Egypt**: 28.4% (95% CI: 27.1-29.2)
- **Cairo**: 8.2% (95% CI: 6.7-9.8)

*Frank et al., (2000)*
Age and gender distribution of anti-HCV prevalence, Egypt, 2008

Chris Estes, unpublished data
Annual mortality due to liver related and background cause, 2013-2030

Chris Estes, unpublished data
Expanded graph of viremic cases by disease stage for cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma, 1950-2030.

Chris Estes, unpublished data
Egyptian Strategy for HCV Control
PEG INF Cost Per Course (MSF)
Opening of 23 national treatment centres, 2007-2013

Egyptian National Control Strategy for Viral Hepatitis 2008-2012

Total number of patients treated with PEG-IFN (2007-2013): 350,000
Annual number of new patients treated: 45,000
Annual budget from the Ministry of Health: 90 million $
Response Rates of treated patients
National HCV treatment program: Positive outcomes

- Governmental appreciation of the magnitude of HCV problem in Egypt
- National guidelines for treatment of chronic HCV
- MOH and universities cooperation
- Treatment for more than 350,000 patients
- >90% governmental funding
- Data to answer a lot of questions
Number of Patients with Hepatitis C in Egypt
Current Incidence (2.5/1000)

- Current therapy 50% Efficacy, 50,000/yr
- Current therapy 50% Efficacy, 100,000/yr
- DAA, 90% Efficacy, 250,000/yr

Annual mortality assumed at: 50/100,000 Or 5/1000 for HCV positive patients
Number of Patients with Hepatitis C in Egypt
90% Reduction in Incidence (0.25/1000)

Annual mortality assumed at: 50/100,000 Or 5/1000 for HCV positive patients
Decrease incidence

• Blood safety.
• Avoid unneeded injection.
• Auto destructive syringes.
• Infection control.
• Media awareness.
• Case detection and treatment by Ideal drug
Quantifying Epidemic Severity in Egypt

R0 theory

• R0: the expected number of secondary cases that an infected individual causes in a fully susceptible population during their entire infectious period.

• R0 of the untreated HCV epidemic in the Egyptian community is 3.50 (95% CI 2.95-4.03).

• The treat early strategy would be more effective because it reduces transmission by timely treatment and decreases incidence..
High Injection Rate

• There is high heterogeneity in health care access in Egypt; 5% of the population takes more than 50% of all injections (2008 DHS).

• The epidemic is maintained by <5% of the population, consisting mostly of individuals with high injection rates.

• Prioritizing access to treatment early and by injection rate may be highly effective in reducing incidence.
Sofosbuvir for HCV Treatment in Egypt
Agreement with Gilead

• The course for 3 months will cost 900 $ instead of 84 000 $ in USA.

• Manufactured outside Egypt but with different color (FDA approved) and written on it (to be sold only in Egypt).

• Renewal of the agreement every year.
COST EFFECTIVENESS CHART

SVR %

P/R 48
120,000 L.E
12,000 L.E

P/R/SOF 12 WK
9600 L.E

R/SOF 24 WK
12,600 L.E

*R/SOF 12 WK
6600 L.E

*NAÏVE, NON CIRRHOTIC, LOW VIREMIA,
Treatment Protocols

• Patients who are **eligible** to receive Interferon (according to the currently used inclusion/exclusion criteria for combined IFN/RBV treatment) will be treated with daily Sofosbuvir (400 mg) and weight-based RBV (1000 mg [$<75$ kg] to 1200 mg [$>75$ kg]) plus weekly PEG for **12 weeks**.

• Recommended regimen for patients who are **not eligible** to receive IFN is daily Sofosbuvir (400 mg) plus weight-based RBV (1000 mg [$<75$ kg] to 1200 mg [$>75$ kg]) for **24 weeks**.
<table>
<thead>
<tr>
<th>Genotype</th>
<th>Recommended</th>
<th>Alternative</th>
<th>NOT Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>IFN eligible</strong>: SOF + PEG/RBV x 12 weeks</td>
<td><strong>SMV x 12 weeks + PEG/RBV x 24-48 weeks</strong></td>
<td><strong>PEG/RBV x 48 weeks</strong></td>
</tr>
<tr>
<td></td>
<td><strong>IFN ineligible</strong> [1]: SOF + RBV x 24 weeks</td>
<td></td>
<td><strong>Monotherapy with PEG, RBV, or a DAA</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Any regimen with TVR or BOC</strong></td>
</tr>
</tbody>
</table>
Priority

• Priority for treatment will be directed towards patients with F3 and F4.

• No differentiation in treatment priority will be established based on the previous treatment experience.
Non Invasive detection of Hepatic Fibrosis

• Serum markers (Laboratory investigations)
  
  Fib-4

• Imaging techniques
  
  Fibroscan
Fibrosis Assessment

Omit tissue assessment in the following situations:

- Cirrhosis by US + varices by endoscopy
- Cirrhosis by US + Child B 7 or 8 score
- Fib-4 > 3.25
- If Fib-4 < 1.45 F.U after 6 months.
- F3-4 stage will be considered if both Fibroscan result is more than 9.5 and FIB4 score is more than 1.45.
When to do Endoscopy?

- Upper GI endoscopy is mandatory in the following circumstances:
  - a. Histological evidence of cirrhosis by liver biopsy
  - b. Fibroscan > 19.2 K.Pa
  - c. Platelet count < 100,000
INF free (Dual Therapy)

• Inclusion criteria for treatment will be expanded to adapt for more advanced liver fibrosis patients (who will be treated with Interferon free regimen) as defined with the presence of one or more of the following:
  - Child score up to 8
  - Hemoglobin concentration ≥ 10 mg
  - T.bilirubin <5 mg  Platelet count>30.000

• Otherwise, waiting for new DAAs combination is advised.
Hepatic Contraindications

- Patients with more decompensated liver disease will be excluded from treatment until enough data will be available and this will be applied to:
  - Child C patients with scores ≥ 9
  - Presence of ascites
  - Patients with HCC except after successful radical curative intervention (4 months after resection or successful local ablation) evident by triphasic CT.
Special Groups

• Priority for treatment will be offered for post liver transplantation, post kidney transplantation patients and combined HCV/HBV infection $>\text{F1}$

• Patients with documented extra-hepatic manifestations will be prioritized for treatment regardless the fibrosis stage.
No of patients registered since 18 Sep 2014 till now in www.nccvh.org.eg

738,423

Year 2014: 337,920
Year 2015: 400,503
Presented patients at treatment centers till end of 2014

- 202521
- 135399

Only 60% showed up

33942 patients  25% eligible for treatment
Summary of flow till end of 2014
Number of patients with fill data in different treatment centers

- TMRI
- Kafr Elshekh
- Mansora
- Tanta
- Zagazeg
- Bany Swif
- Fatemiya
- Shark Elmadina (Alex)
- Elmenia
- Kabary (Alex)
- Sohag
- Asuit
- Shalal Elmenia
- Shark Elmadina (Alex)
- Fatemiya
- Bany Swif
- Zagazeg
- Tanta
- Mansora
- Kafr Elsheikh
- TMRI

0 1000 2000 3000 4000 5000 6000

- Damnhor: 106
- Kabary: 136
- Ismailiya: 305
- Domiat: 633
- Qena: 857
- Monofiya-1: 934
- Mahala: 996
- Banha: 1012
- Faiyom: 1042
- Kabary (Alex): 1161
- Sohag: 1345
- Asuit: 1521
- Elmenia: 1877
- Shark Elmadina (Alex): 1900
- Fatemiya: 1919
- Bany Swif: 2003
- Zagazeg: 2301
- Tanta: 2384
- Mansora: 2475
- Kafr Elsheikh: 4034
- TMRI: 4950

33942 patients
Gender distribution

Number of patients

- 24,128
- 9,814
Age groups

- From 18-30 yrs: 6.6%
- From 31-40 yrs: 12.85%
- From 41-50 yrs: 27.15%
- From 51-60 yrs: 37.11%
- Above 60 yrs: 16.2%
80% of treated Patients Achieved RVR

<table>
<thead>
<tr>
<th></th>
<th>RVR</th>
<th>Non RVR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Mean ± SD</td>
<td>54±8</td>
<td>54±8</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>M/F</td>
<td>342/140</td>
<td>77/29</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>Mean ± SD</td>
<td>29.1±4.4</td>
<td>29.5±3.4</td>
</tr>
<tr>
<td><strong>HCV RNA</strong></td>
<td>↓600/↑600</td>
<td>271/203</td>
<td>51/53</td>
</tr>
<tr>
<td><strong>Platelets</strong></td>
<td>Mean ± SD</td>
<td>132±66</td>
<td>118±47</td>
</tr>
<tr>
<td><strong>Albumin</strong></td>
<td>Mean ± SD</td>
<td>3.8±0.7</td>
<td>3.7±0.7</td>
</tr>
<tr>
<td><strong>Fib-4</strong></td>
<td>Median (IQR)</td>
<td>4.5 (4)</td>
<td>4.6 (4.3)</td>
</tr>
<tr>
<td><strong>Treatment protocol</strong></td>
<td>Dual/Triple</td>
<td>322/160</td>
<td>74/32</td>
</tr>
</tbody>
</table>
Modification of NCCVH Guidelines
Jan 2015

• Extension of treatment to F2 defined as:
  Previous LB with $\uparrow F1$ or
  Fib4 $\uparrow 2.5$ or
  Fibroscan $\uparrow 8$
Thank you!

Gamal Esmat