Treatment of Hepatitis C with Sofosbovir & Ledipasvir During Pregnancy in Srinagar, India

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India accounts for a large bulk of the worldwide HCV burden

- India has 1/5th of world’s population: > 130 billion
- Prevalence of HCV: 1-1.5%
- ~13-19 million HCV infected individuals in India
- < 5% have been diagnosed &
- < 0.2% have received Rx
The hidden iceberg matters in reaching elimination goals.
History of HCV Treatment: The Bad, The Ugly, and The Good

- **IFN based therapies:** Poor efficacy, S/E (cytopenias, fever...), risk of decompensation
  - Interferon (1986)
  - Ribavirin (1998)
  - Pegylated interferon (2001)

- **Direct-acting antivirals (DAAs) improved efficacy:** Additional adverse effects & cost
  - Telaprevir (2011)
  - Boceprevir (2011)

- **New DAAs dramatically improve efficacy:** Few adverse effects at substantial cost
  - Sofosbuvir (2013)
  - Simeprevir & many others since then...
Same evolution is occurring in the management during pregnancy

HCV Treatment With LDV/SOF During Pregnancy

- Open-label, phase I study of ledipasvir/sofosbuvir (LDV/SOF) for 12 wks in pregnant women with HCV

- Pregnant women 18–39 yrs of age with chronic HCV genotypes 1, 4, 5, or 6 HCV and detectable VL at screening; HDV, HIV negative; 23-24 wks of gestation with singleton gestation and no detectable abnormalities (N = 9)

- Primary endpoint: PK of LDV/SOF 90/400 mg therapy in pregnancy
- Secondary endpoints: SVR12, maternal and neonatal safety, neonatal growth, MTCT rate

AASLD 2018
We too have started the journey
IMPACT OF HCV INFECTION ON PREGNANCY

1) Impact of HCV on Maternal outcome

2) Impact HCV on Foetal outcome

3) Chances of MTCT of HCV

4) Any preventive options of MTCT of HCV
IMPACT OF HCV ON PREGNANCY

MATERNAL
- Maternal gestational diabetes
- Cholestasis of pregnancy
- Caesarian section
- Preeclampsia
- Preterm delivery

FETAL
- Small for gestational age
- Low birth weight
- Need admission to the neonatal intensive care unit
- Require assisted ventilation

(Wijarnpreecha, 2017) (Puljic, 2016); (Tan, 2008).
DAA's IN PREGNANCY

- DAA therapy not approved yet

- Animal studies show no embroyotoxity with some of DAAs.

- Assessment of their use in pregnancy needs to be researched.

- Some studies and clinical trails are underway
STUDY DESIGN

- **Setting**: Single centre, prospective observational study from March 2016 to February 2019 at SKIMS, Srinagar

- **Inclusion criteria**
  - Age 18-40 years
  - Chronic HCV infection with detectable HCV RNA
  - Single foetus with no baseline malformation by ultrasound
  - Informed consent

- **Exclusion criteria**: HIV or HBV infection, contraindicated drug-drug interactions

- **Ethical clearance**: from our institutional ethics committee.

- **Evaluations**:
  - HCV RNA at 4 weeks (RVR) and 12 weeks after treatment (SVR)
  - U/S during treatment and at delivery for fetal malformation
  - Monitoring for side effects, fetal well being, and malformations with obstetrician and pediatrician
  - Infant anti-HCV at 6 and 18 months; HCV PCR for those with anti-HCV+

- **Intervention**: Ledipasvir/Sofosbuvir 90/400mg FDC x 12 weeks initiated in second or third trimester

- **Primary efficacy endpoint**: SVR at 12 weeks and MTCT
## BASELINE CHARACTERISTICS (n=26)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (YRS)</td>
<td>28 ± 3.5</td>
</tr>
<tr>
<td>BILIRUBIN (mg/dl)</td>
<td>0.9 ± 0.3</td>
</tr>
<tr>
<td>ALT (u/l)</td>
<td>69 ± 37</td>
</tr>
<tr>
<td>ALBUMIN</td>
<td>3.6 ± 0.4</td>
</tr>
<tr>
<td>CREATININE</td>
<td>0.6 ± 0.25</td>
</tr>
<tr>
<td>INR</td>
<td>1.07 ± 0.09</td>
</tr>
<tr>
<td>FIBROSCAN</td>
<td>5.2 ± 1.6</td>
</tr>
<tr>
<td>PLATELETS</td>
<td>187 ± 68x10^3</td>
</tr>
<tr>
<td>HCV RNA (COPIES/ML)</td>
<td>9.2x10^5</td>
</tr>
<tr>
<td>GENOTYPE</td>
<td>GT1- 5 (19%); GT3 – 19 (73%); GT4 – 2 (8%)</td>
</tr>
<tr>
<td>TRIMESTER OF TREATMENT INITIATION</td>
<td>2^{ND} – 15 (58%); 3^{RD} – 11 (42%)</td>
</tr>
</tbody>
</table>
## VIROLOGIC RESPONSE (n=26)

<table>
<thead>
<tr>
<th>Response Type</th>
<th>Success (n)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAPID VIROLOGICAL RESPONSE (RVR)</td>
<td>26/26</td>
<td>100%</td>
</tr>
<tr>
<td>END OF TREATMENT RESPONSE (ETR)</td>
<td>26/26</td>
<td>100%</td>
</tr>
<tr>
<td>SUSTAINED VIROLOGICAL RESPONSE (SVR12)</td>
<td>26/26</td>
<td>100%</td>
</tr>
</tbody>
</table>
# Pregnancy Outcome (n=26)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTRAUTERINE DEATH</td>
<td>0/26</td>
</tr>
<tr>
<td>NEONATAL DEATH</td>
<td>0/26</td>
</tr>
<tr>
<td>MINOR CONGENITAL ABNORMALITIES</td>
<td>0/26</td>
</tr>
<tr>
<td>MAJOR CONGENITAL ABNORMALITIES</td>
<td>0/26</td>
</tr>
</tbody>
</table>
# Adverse Drug Effects (n=26)

<table>
<thead>
<tr>
<th>Effect</th>
<th>Count</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>4</td>
<td>16%</td>
</tr>
<tr>
<td>Headache</td>
<td>7</td>
<td>27%</td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td>27%</td>
</tr>
<tr>
<td>None</td>
<td>8</td>
<td>30%</td>
</tr>
</tbody>
</table>
MTCT OF HCV

TOTAL NO. OF INFANTS = 26

Anti HCV + = 4/26

Anti HCV –VE = 22/26

HCV RNA Detected = 0/4
PHOTOGRAPHS of babies born to treated patients
CONCLUSIONS

- Ledipasvir / Sofosbuvir combination is well tolerated despite some minor ADRs.

- Virologic response is good during pregnancy (although small sample)

- No major or minor fetal malformations were observed in the study group.

- No infant was infected among studied cohort. (small sample)

- The combination seems to be safe, well tolerated and effective for treating chronic hepatitis C during pregnancy. However larger studies are needed.
THANKS