Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

SUPPLEMENTARY APPENDIX

Table of Contents

Other Therapeutic Pipelines ................................................................. Page 2

Table ........................................................................................................... Page 4

References .................................................................................................. Page 4
Other Therapeutic Pipelines

Because interferon-α has been an essential component of HCV treatment regimens for many years, research has focused on developing alternative or improved forms of interferon. The pegylated form of interferon-α (either α2a or α2b) with improved efficacy, has replaced regular interferon-α in practice. Other forms of interferons, such as consensus interferon, albuferon, and control-release interferon-α have been or are being tested in the clinics.¹ None of them have made it to the mainstream for various reasons. Recently, a different form of interferon, interferon-λ, has been developed because of the strong association of genetic variations in one of the IFN-λ genes (λ3 or IL28B) with interferon-based treatment response.² In addition, IFN-λ may have a better side-effect profile because of the more restricted expression of its receptors throughout the body.² Early clinical studies suggest that it may indeed have fewer side effects but similar efficacy as compared to peginterferon-α.³ Interferon inducers, such as agonists of toll-like receptors (TLR3, 7, 8, and 9), are currently being evaluated in clinical trials, but their advantage over interferon remains to be demonstrated.⁴ The major question is whether interferon will still be necessary in the future should, as is expected, interferon-free regimens achieve an efficacy rate of 90-100% in all HCV-treated patients.

Other therapeutic strategies targeting the host are being explored. Therapeutic vaccines, aiming to boost the host anti-HCV immune responses, are in early clinical trials, and in general, appear not very potent.⁵ As discussed earlier, host targets that are important in HCV propagation may expand the therapeutic armamentarium and
improve response. The advantage of host-targeting antivirals is a relative lack of drug resistance. On the other hand, it may be associated with more toxicity. Since HCV propagation is closely linked to lipid metabolism, lipid-altering agents, like statins and PPAR-γ agonists, have been studied in clinical trials but have shown minimal benefits. Novel host targets identified by recent functional genomic approaches may provide promising alternatives to HCV therapeutic development. For example, PI4KCA, a membrane-associated signaling molecule, was identified as a crucial host factor in HCV replication and pharmacologic inhibition of its activity potently blocks HCV replication.
### Table: Ishak Scoring System for Fibrosis Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No fibrosis</td>
</tr>
<tr>
<td>1</td>
<td>Fibrous expansion of some portal areas with or without short fibrous septa</td>
</tr>
<tr>
<td>2</td>
<td>Fibrous expansion of most portal areas with or without short fibrous septa</td>
</tr>
<tr>
<td>3</td>
<td>Fibrous expansion of most portal areas with occasional portal to portal bridging</td>
</tr>
<tr>
<td>4</td>
<td>Fibrous expansion of most portal areas with marked bridging (portal to portal and portal to central)</td>
</tr>
<tr>
<td>5</td>
<td>Marked bridging (portal to portal and portal to central) with occasional nodules (incomplete cirrhosis)</td>
</tr>
<tr>
<td>6</td>
<td>Cirrhosis</td>
</tr>
</tbody>
</table>

### References