Topical Imiquimod Before Intradermal Hepatitis B Vaccination Overcome Hyporesponsiveness in Chronic Renal Failure Patients on Dialysis, a Double Blind Randomised Controlled Trial

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Disclosure

• Member of advisory board for Pfizer and Gilead
• Received travel grant from Pfizer, Gilead and MSD
• No other conflict of interests
Introduction

- Chronic HBV: 2 billions people worldwide
- High prevalence in Hong Kong >8%
- HBV remains an important virus infection on RRT patients
- Suboptimal response towards IM HBV vaccination
- Seroconversion rate: 40-50%
- Similar HD and CAPD
- Strategies: multiple doses, adjuvants, GM-CSF, ID vaccine, Pre-S2 antigens

http://www.info.gov.hk/hepatitis
Gilbert CL et al Vaccine 2014;32:6521-6
Fabrizi F et al. Aliment Pharmacol Ther 2006;24
Introduction

• Our team has demonstrated topical imiquimod (TLR-7 agonist) pretreatment expedite and improve influenza vaccine immunogenicity

• Young population and elderly with comorbidity

• Heterologous protection against not vaccine strains

• Prospective double-blind RCT to evaluate effect and safety of topical imiquimod before ID HBVv in RRT patients

Material/ Methods

- Adult patients on RRT
- CAPD or HD
- Prospective double blind RCT
- Nov 2015 – Feb 2017
- Inclusion:
  - HBsAg-ve
  - Anti-HBs -ve; anti-HBc -ve
- Vaccine
  - Sci-B-Vac™; 3 antigens
  - 10μg/ 1mL
- Needle
  - MicronJet600™ needle (Nanopass)

https://www.vbivaccines.com/sci-b-vac/
Levin Y et al. Hum Vaccin Immunother 2015;11:991-7
Methods

- Randomized into 3 groups by research nurse
- 3 doses Sci-B-Vac™ regime at 0, 1 and 6 months

- Group IQ: 10μg ID HBVv (0.5mL at two separate sites, same arm) + topical imiquimod pretreatment to deltoid 5 mins before vaccination

- Group ID: 10μg ID HBVv (0.5mL at two separate sites, same arm) + topical placebo aqueous cream pretreatment before vaccination

- Group IM: 10μg IM HBVv + topical placebo aqueous cream pretreatment

- All enrolled patients and investigators blinded to the topical treatment they received

- Anti-HBs titre measured at baseline, 1, 3, 6 and 12 months

- Primary outcome: Seroprotection rate at 1 month = % with anti-HBs ≥10 mIU/mL

- Secondary outcome: Seroprotection rate (3,6,12); median anti-HBs titre; safety
Results

• Interim analysis
• Nov 2015 to Feb 2017
• 69 patients recruited with anti-HBs level up to 6 months
• 24, 22 and 23 patients randomized to group IQ, ID and IM

• 41 male
• 51 CAPD and 18 HD
• Median 65.5 years
Results: Seroprotection Rate

P > 0.05
Results: Anti-HBs titre

mIU/mL

<table>
<thead>
<tr>
<th>Time</th>
<th>Value 1</th>
<th>Value 2</th>
<th>Value 3</th>
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</thead>
<tbody>
<tr>
<td>1 Month</td>
<td>51 vs 6</td>
<td>0</td>
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</tr>
<tr>
<td>3 Months</td>
<td>202 vs 147</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>6 Months</td>
<td>544 vs 480</td>
<td>13</td>
<td></td>
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<tr>
<td>12 Months</td>
<td>566 vs 170</td>
<td>21</td>
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P-values:
- 1 Month: P=0.07
- 3 Months: P=0.006
- 6 Months: P=0.003
- 12 Months: P=0.004
Adverse Events

Pain  Itchiness  Swelling  Induration  Fever  Lethargy

IQ  ID  IM

P>0.05
Limitations

• Interim analysis

• Need longer follow-up

• Dose sparing for ID vaccination + imiquimod pretreatment
Conclusions

• Procedure is safe

• Topical imiquimod before ID HBVv was highly effective

• Significantly overcome hyporesponsiveness in patients on RRT

• Consider in immunocompromised patients
Thank you!