Perspective of the ACIP dengue vaccines workgroup on the evaluation of assays for pre-vaccination screening

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Workgroup Perspective (1)

• CDC evaluation had a small sample size (n=107); generalizability is limited
  • Goal to address problematic areas for specificity and cross-reactivity
• Most tests that work well for acute diagnosis did not perform adequately for pre-vaccination screening
• One ELISA assay and two versions of a rapid test performed best
• CDC results may be conservative (i.e., represent minimum performance) as the samples were selected to highlight problematic areas for sensitivity and specificity
• The test sponsor is planning on conducting a large prospective evaluation of the rapid test in Puerto Rico and the mainland
Workgroup Perspective (2)

- Prioritized assessing that an acceptable test(s) are/will be available for implementation of pre-vaccination screening
- Evidence to Recommendation Framework, draft recommendations will be presented to ACIP in spring for vote in June
- Minimal and optimal performance characteristics (target product profile) will be included in MMWR with ACIP recommendations
- The jurisdiction will have a role in ensuring that recommended test characteristics are met for pre-vaccination screening
Example Target Product Profile for a Dengue Test for Pre-vaccination Screening (Annecy, France Jan 2020)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Minimal</th>
<th>Optimal</th>
<th>CDC Evaluation Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>≥85%</td>
<td>≥95%</td>
<td>68–82%</td>
</tr>
<tr>
<td>Specificity</td>
<td>≥95%</td>
<td>≥98%</td>
<td>97–98%</td>
</tr>
</tbody>
</table>
Workgroup Perspective (3)

- International target product profile can be adapted for U.S. territories context
  - High levels of flavivirus exposure (Zika virus)
- Specificity more important than sensitivity to “cause no harm”
- A sub-group is working on developing a target product profile for dengue vaccines workgroup review
Population-level impacts of the dengue vaccine in Puerto Rico

Total numbers of symptomatic and hospitalized cases across a 10-year timeframe for a cohort of 9-year-olds in Puerto Rico, as well as cases averted and additional hospitalizations among vaccinees. This represents a scenario with screening assay sensitivity = 0.80 and specificity = 0.98.

<table>
<thead>
<tr>
<th>Prior exposure in 9-yr-olds</th>
<th>Baseline</th>
<th></th>
<th>Averted</th>
<th></th>
<th>Additional</th>
<th></th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Symptomatic</td>
<td>Hospitalizations</td>
<td>Symptomatic</td>
<td>Hospitalizations</td>
<td>Hospitalizations</td>
<td>averted/additional</td>
<td></td>
</tr>
<tr>
<td>30%</td>
<td>224,853</td>
<td>51,561</td>
<td>1,708</td>
<td>1,655</td>
<td>123</td>
<td>13/1</td>
<td></td>
</tr>
<tr>
<td>50%</td>
<td>263,515</td>
<td>62,205</td>
<td>4,417</td>
<td>3,531</td>
<td>59</td>
<td>60/1</td>
<td></td>
</tr>
<tr>
<td>60%</td>
<td>275,738</td>
<td>64,635</td>
<td>6,093</td>
<td>4,734</td>
<td>35</td>
<td>135/1</td>
<td></td>
</tr>
</tbody>
</table>

Questions

• Does ACIP concur with including pre-vaccination screening dengue IgG test target product profile in MMWR that accompanies ACIP recommendations?

• Are there other considerations the workgroup should address?