Considerations for clinical endpoints in CHIKV vaccine trials

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Clinical outcome considerations

• Need for clinical case definition with which to determine if there is a need for testing (ie – who do we need blood from)

• Disease versus infection
  • Infection: proportion of infected with asymptomatic illness -- >80% symptomatic
  • Disease: acute versus chronic

• Clinical
  • Fever
  • Arthralgia
  • Fever/Arthralgia
  • Rash?

• How evaluate?
Clinical evidence from the Americas

- USVI – 72% with lab confirmed infections reported symptoms

- Nicaragua – 51% symptomatic (but lineage dependent) in first epidemic with higher symptomatic rate in subsequent outbreak

- Puerto Rico – 63% cases were symptomatic

Conclusion → symptomatic rate still high

Acute versus Chronic?

• Meta-analysis $\rightarrow$ 52% develop chronic symptoms

• Wide variation based on study, population

• Relation to vaccine efficacy?
  • Post licensure info – lower percentage of arthralgia among vaccinees over time?
  • Not realistic for clinical trials (II/III)
  • Chronic associated with acute symptoms
Which symptoms to use?

• Most common: Fever and arthralgia
Which symptoms to use?

- Most common:

<table>
<thead>
<tr>
<th>Symptom or sign</th>
<th>Frequency range (% of symptomatic patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>76–100</td>
</tr>
<tr>
<td>Polyarthralgias</td>
<td>71–100</td>
</tr>
<tr>
<td>Headache</td>
<td>17–74</td>
</tr>
<tr>
<td>Myalgias</td>
<td>46–72</td>
</tr>
<tr>
<td>Back pain</td>
<td>34–50</td>
</tr>
<tr>
<td>Nausea</td>
<td>50–89</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4–59</td>
</tr>
<tr>
<td>Rash</td>
<td>26–77</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>12–32</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>3–56</td>
</tr>
</tbody>
</table>

*Table compiled from a number of different studies."
Which symptoms to use and how to evaluate?

• Most common: Fever and arthralgia

• For vaccine trials
  • Any AFI → collect sample within 1 week, RT-PCR for CHIKV
  • Inclusion of arthralgia without fever?
    • Mayotte – 98% polyarthralgia, 85% fever
Discussion and questions

For more information, contact CDC
1-800-CDC-INFO (232-4636)

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