Timing for Definitive Cure in Clinical Trials for Visceral Leishmaniasis

Background: Visceral Leishmaniasis (VL) is a parasitic neglected tropical disease, endemic in developing countries. Treatment outcomes in VL clinical trials are measured at two time points: a) initial cure at end of treatment (EOT) and b) definitive cure after an extended follow-up of 6 months (M6). The probability of moving from state 1 to state 2 is written as \( P(1 \rightarrow 2) \) given the present state of the system, \( X \), the future of the system is independent of the past. If the Markov property holds and the transition probabilities do not depend on or can be derived from the process (a time-homogeneous Markov Chain).

Materials and Methods:

Data and outcomes from the following trials:
- LEAP 0104 (8) and LEAP 0106 (5,10).

Definition for follow-up:
The day of follow-up assessments has been calculated from EOT.
- A visit is considered to be at EOT (and of treatment) if it occurs on Day 38 (±30 days).
- A visit is considered to be at M3 (Day 120) if it occurs on Day 120 (±30 days).

For the purpose of this analysis, anything following the review visit was classified as missing and has been excluded from the final analysis. The extraction of information from the above criteria has been produced to help in understanding gaps arising from such trials.

Results:

**Treatment Outcomes: LEAP 0104 Multi-State Model**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Outcome</th>
<th>Overall</th>
<th>Treatment success</th>
<th>Treatment failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment 1</td>
<td>93 (83.3)</td>
<td>11 (10.9)</td>
<td>1 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Treatment 2</td>
<td>93 (83.3)</td>
<td>11 (10.9)</td>
<td>1 (1.0)</td>
<td></td>
</tr>
</tbody>
</table>

**Treatment Outcomes: LEAP 0106 Multi-State Model**

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EOT and M3: 127 person visits of data in which the treatment outcome was known. Among the 60 patients who had cure at EOT, 22 were lost to follow-up during M3 follow-up.

At each visit, some 98.8% of treatment success in the data remained unaltered and 94.4% of treatment failure. Conditional on a patient ever having a success, 98.9% of their observations had a success, similarly, conditional on ever having a failure, 92% of a patient's observation had a failure.

**DISCUSSION:**
The percentage of patients who are not being assessed within the expected follow-up time frame is high. This is because parasitology was only being done at the time when clinically indicated.

**ACKNOWLEDGEMENT:**
We would like to thank all the trial teams across the different trial sites within the LEAP countries (Sudan, Ethiopia, Kenya & Uganda).