Endpoints in Clinical Trials: Advantages and Limitations

Leonardo Roever*
Department of Clinical Research, Federal University of Uberlândia, Uberlândia, Brazil

*Corresponding author: Roever L, Department of Clinical Research, Av Pará, 1720-Bairro Umuarama, Uberlândia-MG-CEP 38400-902, Brazil, Tel: +553488039878; E-mail: leonardoroever@hotmail.com

Rec Date: 11 December, 2015; Acc Date: 18 December, 2015; Pub Date: 25 December, 2015

Copyright: © 2016 Roever L. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Introduction

Primary endpoints in clinical trials must meet 3 criteria:

A) Clinically relevant

B) Sensitive to treatment effect

C) Measurable and interpretable. Secondary endpoints could provide a more global view of the benefit of the treatment being tested and by clarifying its risk-to-benefit ratio; may be of 2 types: A) Those that, like primary endpoints, are clinically relevant and may be taken into consideration for drug indications; and B) "Feel-good" endpoints, which are not likely to lead to a new indication or a change in labelling but might provide reassurance about the primary endpoint along with new information about the disease. Some secondary endpoints might be exploratory analyses, although they might demonstrate biologically plausible effects, they remain hypothesis-generating and will need to be confirmed by additional studies. Table 1 and 2 shows the terms and definitions used in the outcomes of clinical trials [1-4].

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomarker (biological marker)</td>
<td>A characteristic that is measured and evaluated objectively as an indicator of normal biologic processes, pathogenetic processes, or pharmacologic responses to a therapeutic intervention.</td>
<td>Universally accepted measure of direct benefit Easily and precisely measured</td>
<td>May require a larger trial population and longer follow-up to show statistical difference between groups Includes deaths unrelated to disease</td>
</tr>
<tr>
<td>Clinical endpoint</td>
<td>A characteristic or variable that reflects how a patient feels or functions or how long a patient survives.</td>
<td></td>
<td>Validation as a surrogate for survival can be difficult in some treatment settings Not precisely measured (i.e., measurement may be subject to bias)</td>
</tr>
<tr>
<td>Surrogate endpoint</td>
<td>A biomarker that is intended to substitute for a clinical end point, i.e., a biomarker that is expected to predict clinical benefit, harm, or lack of benefit or harm.</td>
<td></td>
<td>Requires frequent radiologic or other assessments Requires balanced timing of assessment among treatment arms</td>
</tr>
<tr>
<td>Intermediate endpoint</td>
<td>A characteristic that is intermediate in the causal pathway between an intervention and the clinical end point.</td>
<td></td>
<td>Does not adequately distinguish efficacy from other variables, such as toxicity</td>
</tr>
</tbody>
</table>

Table 1: Shows the outcomes in major clinical trials.
Overall response rate (ORR) | Proportion of patients with reduction in disease burden of a predefined amount | Can be assessed in single-arm trials | Requires a smaller population and can be assessed earlier compared with survival trials | Effect is attributable directly to the drug, not the natural history of the disease | Not a comprehensive measure of drug activity

Duration of Response (DoR) | Time from documentation of disease response to disease progression | Patient perspective of direct clinical benefit. | Reporting sometimes incomplete | Small symptoms and signs of difficult to assess Few validated instruments Sometimes patients do not report accurately the effects adverse

(Quality Of Life - QOL) Symptoms Reported by Patients | Outcome self-reported by patients using wellness scales, presence of adverse effects and toxicity therapeutic | Definition of the benefit/risk balance of therapy | Sometimes patients do not report accurately the effects adverse

Toxicity | Rate of adverse effects

| Other CommonEndpoints |

Response rate (RR) | Response rate measures disease size, usually using a scan or X-ray. |

Complete response (CR) | Disappearance of all clinical evidence of disease. |

Partial response (PR) | At least 30% reduction in size of all measurable disease |

Stable disease (SD) or No change (NC) | Between a 30% reduction or <25% increase in the size of all detectable disease |

Progressive disease (PD) | Patients or proportion of patients with a ≥ 25% increase in size of disease since previous measurement |

Objective response rate (ORR) Percentage of patients whose disease decreased (Partial response – PR) and/or disappears (Complete response – CR) after treatment |

Disease control rate (DCR) or clinical benefit rate (CBR) Percentage of patients whose disease shrinks or remains stable over a certain time period. DCR is the sum of the complete, partial and stable disease rates. |

Duration of response (DR) Time from confirmation of a partial response (PR), complete response (CR) or stable disease (SD), until the disease has been shown to progress following treatment (progressive disease or PD). |

Performance status (PS) Measure of how well a patient with a disease diagnosis can perform ordinary tasks in daily life before, during or after treatment. Specific numeric PS scales indicate levels of disability due to disease, and/or severity of symptoms. Two main scales are. |

Table 2: Outcomes in major clinical trials. *Not all trials are randomized. In nonrandomized trials, time from study enrolment is commonly used.

References