OUTCOMES STUDIED IN LEUKAEMIA CLINICAL TRIALS: A NEED FOR HARMONISATION?

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INTRODUCTION

Heterogeneity in outcomes measured in clinical trials (CTs) and clinical studies for antineoplastic therapies presents as a major barrier to evidence synthesis, increasing the complexity of regulatory, policy and healthcare decision-making. Highlighting the magnitude of inconsistency, sources report that over 25,000 of outcomes in cancer trials have only been used once or twice.1

AIMS

• To identify unique efficacy parameters investigated in leukaemia CTs
• To determine the degree of variability of efficacy outcomes studied in trials for the following four main leukaemia subtypes: Acute Lymphoblastic Leukaemia (ALL), Acute Myeloid Leukaemia (AML), Chronic Lymphocytic Leukaemia (CLL) and Chronic Myeloid Leukaemia (CML)

METHOD

Identification of Clinical Trials

European Union (EU) Clinical Trials Register search for the following CTs:
• Phase II – Phase IV
• Interventional
• Registered over the period January 2007 – December 2017

Application of Inclusion Criteria

Results screened according to inclusion criteria where eligible CTs: • Were described in the English language • Reported efficacy data • Investigated medicinal products of chemical, biological and biotechnological origin for the four main leukaemia subtypes

Extraction of Efficacy Data

• Unique primary and secondary efficacy endpoints extracted from trial protocols • Endpoints categorised according to type of measurement

Comparative Analysis

• Descriptive statistics for each main leukaemia subtype reported as:
  i. Percentage frequencies of CTs studying 1-3, 4-10 and >10 outcomes
  ii. Mean number of outcomes investigated per trial

RESULTS

• The register search generated 666 CTs with 378 satisfying inclusion criteria, representing around 103,000 trial subjects.
• Thirty-six unique efficacy measures were identified and grouped into the endpoint categories of survival (n=5), response rates and biomarkers (n=16), time-to-event (n=6) and other (n=9).
• Percentage frequencies and mean number of efficacy outcomes reported per CT for each of the four main leukaemia variants are presented in Figure 1.
• Efficacy studies conducted in CLL trials demonstrated the greatest variability with a mean number of outcomes reported per CT of 4.9.

CONCLUSION

Inconsistencies were observed in both the number and type of outcomes reported within trials for the main leukaemia subtypes, particularly in CLL. Systematic reviews and meta-analyses, as the most robust methods of collating evidence2, would be challenging to perform if contrasting elements are reported as primary and supporting evidentiary data between trials investigating the same leukaemia subtype. A clear demand is identified for cross-collaborative initiatives among multiple stakeholders to define trial outcomes that are collectively agreed upon in attempt of harmonising clinical outputs.

REFERENCES


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