Challenges of non-CRF data in oncology studies

Case Study

Cmed
Clinical Services
www.cmedresearch.com

Case Study:
Challenges of non-CRF data in oncology studies

Introduction

Cancer is second only to cardiovascular disease as the most common cause of death in the developed world. In fact, one in three people in the world will be diagnosed with cancer at some stage in their life, a statistic that puts the disease into perspective. As a result, every year billions of dollars are invested into oncology clinical studies across the world trying to tackle this growing global problem.

The last 5 years have seen a significant shift from the traditional endpoint oncology study designs which saw patients either discontinue due to disease progression and/or in many cases death, to studies that evaluate secondary endpoints and introduce much more complex designs. Cmed have conducted over 70 oncology studies to date, and as a result, have become regarded as specialists in this challenging therapeutic area by their clients.

This case study presents a phase III randomized open-label study of dose level 1 versus dose level 2 of [Study drug] in newly diagnosed, untreated patients with chronic myeloid leukaemia in chronic phase (CML-CP) using molecular endpoints as the key benchmark to evaluate efficacy in CML.

Background of the study

In chronic phase CML, cytogenetic response is usually considered as a critical goal. Historical trials have shown this to be a meaningful endpoint for long term survival and critically progression-free survival. Despite very encouraging cytogenetic responses being achieved with some of the leading compounds currently being researched, the majority of patients still have minimal residual disease (MRD) detectable. In this context, "molecular response" is emerging as a very important benchmark for evaluating efficacy in CML.

Cmed were approached by the sponsor to perform the clinical data management of the study based on previous successful experiences working on a similar study in the development of the compound. The study presented some very clear challenges from the outset:

- The study would be truly global and incorporate 96 sites over 21 countries
- Each site would be performing local laboratory examinations using site specific normal ranges
- The study included numerous external data sources that would be processed by third party vendors that were even more critical to the success of the study than the data collected on the CRF

Cmed would use their own proprietary data management system (Timaeus) to manage all of the clinical data from this study, including all third party data

Implementation

A key decision that Cmed had to make was resourcing the study in order to take advantage of existing therapeutic experience in-house. Cmed identified study leads with previous exposure to the studies indication and provided the whole DM team with specific disease training by external experts. This ensured the team had existing experience to refer to, but also a basic knowledge of the disease from the outset.

Cmed worked in conjunction with third party vendors to produce data specifications for all 9 different types of external data required in the study. Cmed created the database within 6 weeks of final protocol available and started receiving paper CRFs and external electronic data immediately.

The Challenges of non-CRF data

Processing external data is a challenge to any organization, especially performing reconciliation between data sources in different locations. Often listings are created and manual reconciliation takes place between visits, dates and times across CRF data and the data stored in third party datasets. There are many dangers that exist in this process, not only is it more difficult to spot erroneous and missing data across datasets, identifying duplicate records can be very difficult and if left undetected, will have serious consequences on the safety outputs. When oncology studies rely so heavily on this biomarker data, mistakes in the non-CRF data can be disastrous to the study, not to mention putting patient safety at risk.

The addition of numerous biochemistry and hematology ranges that need to be managed and updated throughout the lifetime of the study can be another challenge. If not managed smartly, normal ranges can be associated with the wrong results and for a CML study, erroneous ranges associated with hematology results can be the difference between a protocol violation and safety concern of the drug and an acceptable result.

Non-CRF data the Cmed way

Due to Cmed's intelligent Data Acquisition and Management system Timaeus, the DM team were able to benefit from managing all of the clinical data in a single data repository, offering total data visibility across all datasets. Timaeus incorporates electronic data loaders which not only ensure that the right data is loaded into the database and presents it exactly where the assessment took place in relation to the CRF, but also performs automated reconciliations between the current CRF data and the electronic data, producing reports of reconciliation errors without loading erroneous data into the clinical database. This represented not only a much safer technique to perform the reconciliation, but also showed huge time and cost savings in relation to FTE requirements for reconciliation within the DM team.

Timaeus uses reference points that allowed the DM team to enter the blood chemistry and hematology normal ranges within the database and compare the results with the normal ranges at point of entry. The reference points are fully customizable according to date, time, sex and even weight so processing and updating normal ranges was a painless exercise. Timaeus recognizes which reference to apply to each individual laboratory results page automatically and provides users instant feedback on data quality by comparing the result to the normal range, thus reducing the potential for data entry error at point of entry.

Cmed also provides as standard, access to the clinical database in read-only format to the client study team so not only could the data management team view all of the clinical data, the clinical team could view, run status reports and monitor metrics across the study inclusive of every single data aspect of the study, a term Cmed call "total clinical data visibility".

Summary

The Cmed DM team profited from a robust user friendly single system to manage all of the clinical data in a single repository which, through the efficiencies and smart operating methods Timaeus incorporates during the data management process, resulted in a clean and well organised process of dealing with the non-CRF data in the study.

The automated reconciliation checks ensured that the potential for duplication was eradicated and provided both the DM team and the client immediate feedback on the quality of data being loaded. Because the electronic data was presented within the corresponding CRF visit, cross checking between the electronic file and the CRF, including validation checking was a simple and painless process.

All of the efficiencies that Timaeus provided, coupled with the experience and professional approach of the Cmed data management team, ensured the clinical database locked on schedule and avoided any of the potential obstacles that are often presented when working with non-CRF data.

Cmed Clinical Services

About Cmed Clinical Services

Cmed Clinical Services is a long-established, flexible CRO with offices in the UK, US and Romania offering project management, clinical monitoring, data management, biostatistics, medical affairs, regulatory, consulting, and medical writing services. While Cmed's area of specialization is the design and delivery of both innovative and traditional phase I to IIb clinical trials, Cmed increasingly uses its experience and capabilities for existing clients phase III programs and for functional service provision of biometrics. Cmed Clinical Services is a privately held subsidiary of Cmed Group Ltd. To learn more, please visit **www.cmedresearch.com.**

Main Office:
Cmed (Clinical Research Services) Ltd
Holmwood, Broadlands Business Campus
Langhurstwood Road
Horsham RH12 4QP United Kingdom
Tel: +44(0)1403 755 050
Fax: +44(0)1403 755 051
Email: info@cmedresearch.com

United States:
Cmed Inc
430 Mountain Avenue, 4th Floor
Murray Hill, NJ 07974 United States
Tel: +1 908 795 2020
Fax: +1 908 665 9030
Email: info@cmedresearch.com

4620 Creekstone Drive
Suite 160
Durham, NC 27703 United States
Tel: +1 919 595 6900
Fax: +1 919 595 6901
Email: info@cmedresearch.com

Romania:
Cmed SRL
Str. Coriolan Brediceanu, Nr. 10
Timisoara, 300011 România
Tel: +40 356 43 39 02
Fax: +40 356 00 43 64
Email: info@cmedresearch.com