Overcoming oncology trial supply challenges with interactive response technology

Oncology trials present unique challenges when it comes to clinical trial supply – interactive response technology systems can help mitigate these to ensure a successful study

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There are many randomisation and trial supply management (RTSM) challenges unique to oncology trials. Here, we review some of them and outline how, if designed correctly, interactive response systems (IRT) can tackle those challenges to ensure the trial stays on track and patients continue treatment, even through unexpected (and some expected) changes.

Tracking different medication types

Multicentre oncology studies recruit across many countries and may require the management of many different medication types, as patients typically receive the standard-of-care (SoC) treatment for their diagnosis in addition to the investigational medical product (IMP). The sourcing of SoC treatments can differ based on each site's location and may vary from IMP that's sourced centrally. Sites in one country may need the IRT system to track and manage stocks of centrally sourced treatments, whereas sites in another country may be able to buy sufficient stocks locally.

In the scenario where medication is locally sourced, the labels on that medication do not include unique kit numbers that are identifiable by the IRT system. So, while the centrally sourced medication labels include specific kit numbers assigned to subjects, dispensing information and expiration dates that are maintained in the IRT system, the same is not true for locally sourced medications.

In some circumstances, medication sourced locally could be labelled and released into the IRT or, alternatively, the medication could be released into the IRT as a pure 'quantity' of non-uniquely labelled kits via dummy kit numbers. However, these options are not generally utilised, as they assume the medication is stored at a central depot. Shipments to the sites may not be required when the medication is truly sourced locally to the site.

This becomes challenging at the beginning of each medication assignment visit, when the IRT conducts a medication requirement check to ensure that suitable medication is available on-site for a successful patient visit. If medication is sourced locally and not tracked in the IRT, it will not be included in these checks and is assumed to always be available.

Inappropriate medication checks can be detrimental to the course of the trial, as they could result in a failed patient visit if the medication that the IRT does not track is not

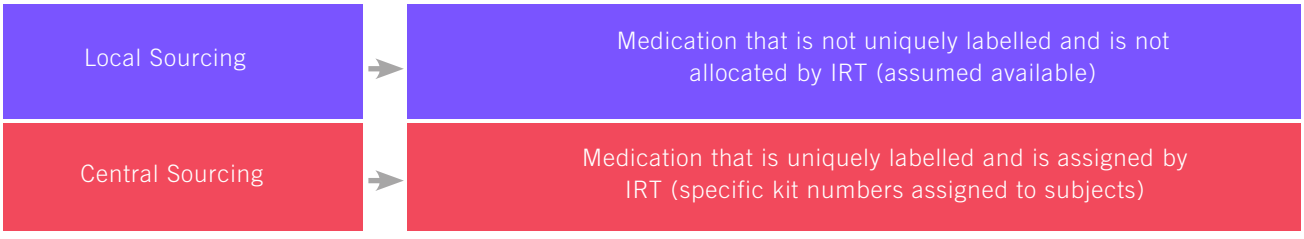

Figure 1: Local Sourcing vs Central Sourcing

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available. It could also result in a skipped randomisation record and forcing to the treatment that we assume is always available, in the case where forcing is allowed, and the medication tracked in the IRT system is depleted.

Trial length

Oncology trials are typically very long, with patients remaining in the protocol until disease progression. Monitoring patient progression will be a key focus and there could be an extension of the IRT visit schedule to accommodate survival beyond initial expectations. In addition, the longer the trial, the more likely that circumstances will arise dictating changes in how medication is sourced. This could occur if the availability of the locally sourced medication changes, for example; the need to centrally source is removed through greater local availability of the SoC treatment, or alternatively, the local source has become scarce or burdensome for the sites to source. The country could also need to change from local sourcing to central sourcing or vice versa for an individual medication type during the trial. Any change to medication sourcing will have an impact on medication checks, IRT dispensing schedules, visit reporting information and shipments to sites. If not managed well, the IRT could resupply sites with kits they do not require, which contributes to excessive drug wastage, or alternatively fail to supply the medication that is needed by patients at the site.

Disease progression

In oncology trials, patients continue to be treated until the disease progresses. This leads to unknowns in how many visits a patient will have, which can cause issues during the set-up of some IRT systems. This is another reason why flexibility in your IRT system is key.

An advanced IRT system should assume that the drug may outperform its mid-trial expectations and delay disease progression beyond initial estimates. This enables flexibility to be built in from the start, which caters to the need for additional visits and avoids reprogramming to ensure added patient dispensing visits are recorded accurately.

If further visits are needed, there will be a natural impact on the need for drug. The overage created for the protocol will be utilised in this scenario, but this can also result in the sponsor facing issues related to drug expiration. This is because the visits will be taking place for longer than initially planned.

Visit naming

Another unique RTSM challenge in oncology trials is the different naming conventions used to define patient visits. Typically, a patient visit is called a 'visit', while in oncology trials, the protocol most often reflects where the patient is in their treatment 'cycle,' which is what investigative sites understand as the patient visit schedule. It's very important that it's clear to the Investigator what visit they're registering, as well as what cycle and visit schedule the patient is in. So, it's critical that the naming of the visit schedule in the system matches the protocol.

This becomes even more important in instances when patient visit schedules are interrupted because rescue medication is required during or in between scheduled visits, meaning the patient may have to go off the study drug before they are able to return to their normal schedule. Or, in the incidence of an adverse event, which has further considerations for the IRT system in terms of safety pathways. Ensuring the IRT system has the flexibility for site personnel to confirm the visit and cycle number removes confusion, keeps the trial on track and supports patient safety throughout lengthy oncology trials.

Rescue medication – impact on study drug expiration

In addition to not knowing how many visits each patient will complete, oncology clinical trial sponsors face unknowns as to whether patients might need to discontinue treatment and begin using rescue medication – or for how long – raising concerns not only for patient safety but also for study budgets. As oncology treatments are typically very expensive, sponsors strive to minimise the amount of study drug wasted during clinical development. Any time a patient experiences an adverse event and must pause treatment to begin rescue medication, there is a risk of the study drug expiring before the patient can resume treatment.

To reduce the risk of excessive drug wastage but to ensure study drug availability when the patient can continue treatment, the IRT system must be designed with flexibility. Not only because when the patient resumes treatment they may be on a different visit/treatment schedule, but also because most often it's unknown how long the patient will be on rescue medication.

An effective IRT system should be designed assuming that rescue medication could be needed at any point – during or in between site visits – and that if needed, the patient will remain on it for the maximum amount of time allowed by the protocol. The IRT design can be configured to monitor the length of time in the rescue status for a patient. Understanding the real-world application of the rescue process is key to identifying the most efficient IRT design for the medication that will be dispensed.

The next scheduled visit could be impacted by the rescue medication allocation, with adjustments required to move the patient in the visit schedule. If site staff are suitably trained, they could select the next scheduled visit at the patient's restart point, however, the IRT can include rules to assist investigative site personnel in adhering to the correct point in the correct schedule.

How much medication is needed?

The IRT system can be designed with a fraction amount that automatically tweaks the amount of drug (rescue drug, in this case) needed at each site based on the number of patients for the fraction. This Fractional Prediction strategy allows for flexibility based on site recruitment and is helpful for minimising the amount of SoC and/or rescue drug needed at each site, based on the number of patients enrolled.

Consider this scenario. If one site has ten enrolled patients – and it's highly unlikely that all ten will need rescue medication at one time – the system can assign a fraction, say, 0.2, and only send 2 packs of rescue medication to accommodate that number of patients. But if a site has only one enrolled patient, then the 0.2 is rounded up to 1.0 and the system sends only one pack of rescue medication. The fraction that is predicted is an important variable: setting the fraction too high can increase drug wastage while setting it too low could result in dispensing failures. If the assumptions used to set the fraction are not borne out during the running of the trial, the figure can be amended.

Conclusion

The RTSM needs of clinical trials are complex. But, with advanced and flexible IRT technology, sponsors can tackle the complexities – often without knowing they exist – in even the most complicated study designs, those involving oncology treatments.

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