

Duke's Phase I Trials Go Electronic

a report by

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Electronic data capture (eDC) systems have revolutionised clinical trials, enabling more efficient and accurate data management and potentially saving costs along the way. While eDC has proved extremely useful for larger-scale phase II and III studies, implementation into smaller phase I trials has proved problematic due to inherent differences in the way in which they are run. However, eDC solutions specifically tailored to phase I are now gaining pace. Duke University Medical Center has just opened a new clinical research unit focused on phase I trials: the Duke Clinical Research Unit (DCRU). The new unit has just begun the shift from paper-based to eDC systems, and has been scouring the market for the best tools. After evaluating several vendors, Duke selected ALPHADAS® from Logos Technologies, a technology that will meet its current and future requirements.

The system has proved hugely successful at other institutions, and will hopefully help Duke maintain its competitive edge. Perhaps one of the most exciting features of the technology is its ability to interface with Duke's existing technologies. The DCRU is teaming up with Logos Technologies to build a first-of-a-kind system that will interface the ALPHADAS system with Duke's newly acquired Mortara digital electrocardiogram (EKG) wireless system. While there will be initial challenges in setting up the system, establishing ALPHADAS should be seen as a long-term investment that will provide clients with a better and more efficient product. This will potentially increase trial turnover, bringing drugs to market more quickly and making the DCRU a more attractive option for clients.

Duke University's Clinical Research Unit

Phase I clinical trials may be smaller and more short-lived than their later-phase counterparts, but they are no less important in the drug development pathway. Since phase I studies can act as a springboard for new drug development, it is highly important that trials are efficient, accurate and safe.

eDC technologies have been hugely beneficial for running phase II and III clinical trials across the board – for example, Duke has had huge

success with its Siebel enterprise system from Oracle – enabling more streamlined and efficient processes that reduce both errors and costs. However, phase I trials have been slow to catch on to the technology, as the standard platforms used for running phase II and III studies have proved incompatible with smaller and more rigorous phase I studies. Now, established technologies such as ALPHADAS 'cut to fit' phase I are poised to fill the gap.

The DCRU for phase I clinical trials is now working on incorporating new eDC technologies in order to step up its game among the competition. The DCRU is still in its preliminary phase, but it is growing: by June 2009 it will house 30 adult confinement beds, six paediatric confinement beds and 13 hospital beds. It will also run outpatient-based trials. The unit will have a total capacity of 30,000 square feet. The DCRU is already in its eighth month of trials and, once it is at full speed, will be running some 40–50 phase I studies per year. The DCRU is also one of the few institutions that runs phase I trials in paediatric patients.

Phase I – An Exercise in Safety

Phase I trials represent the first introduction of a new drug into humans; therefore, safety and precision are paramount. At this point investigators are looking at the safety, rather than the efficacy, of the drug. Subjects must be watched extremely closely to ensure the limitation of toxic and adverse events. In fact, the protocols could be likened to an emergency situation.

Because of the intense nature of phase I, trials tend to be very short-lived, lasting only one to three months on average. Typically, there is no long-term follow-up work, as seen in phase II or III. Compared with later phases, there are only a small number of subjects – perhaps 12–24 individuals in various cohorts – so that exposure to the drug will be limited. The team must then determine an appropriate dose and dosing interval by examining the pharmacokinetics of the drug.

The patient population in a phase I trial can include healthy volunteers (a 'first-in-human' trial) or patients within a specific disease state (a 'first-in-subject' trial). Recently, there has been a trend towards using first-in-subject populations, as agencies and pharma increasingly demand that the disease population is studied first. In this way, researchers can assess drug function in the disease at an earlier stage. In line with this, Duke is focusing its energies on selecting first-in-subject populations in the majority of cases; all of the unit's current studies, bar one, concentrate on disease populations.

Traditionally, phase I trials were run on paper, since the majority of eDC systems were not up to the task of running these rigorous studies.



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Clearly, with any paper-based system there is a huge risk of error, and ultimately any uncertainties make querying data extremely difficult. Furthermore, paper is not a time-sensitive data collection tool, and extra labour can be required when inputting information retrospectively into a data set. It is inevitable that the industry will make the shift to electronic data platforms that can capture information without question in realtime.

ALPHADAS gives the DCRU a standardised platform for phase I trials. Using this system will considerably reduce the margin for error as data can be captured in realtime. Because phase I is such a risky and experimental stage, where errors can determine the fate of a drug, ALPHADAS has been designed to take precise measurements at the bedside free from interference, and also allows the user to make rapid changes even after the trial has begun. Compared with phase III, for example, phase I allows less room for errors and less opportunity for 'look-backs' and making changes.

A Phase I Electronic Data Capture Solution

Duke has been combing the market for a phase-I-specific eDC solution that is cost-effective, user-friendly and 'decision-support'-friendly. Today, there are a variety of products available, but not many have matched Duke's requirements. In addition, some can be very cumbersome to use and can require a lot of support. One system Duke looked at requires some eight individuals just to manage the information technology (IT) platform. After a 12-month search and diligence on all vendors, the DCRU chose the ALPHADAS system developed by Logos Technologies. An analysis of the platform in other institutions showed improvements in trial efficiency and accuracy. In addition, the fact that it is a web-based product means that investigators and the pharmaceutical companies involved will have first-hand data at their fingertips, and yet the data will remain clean. Most remarkably, the system has the capability to build interfaces with other technology products – something that has helped Duke secure a market first.

The ability to interface ALPHADAS with existing technologies will allow huge leaps forward in the way in which phase I trials are run. Currently, DCRU is working on interfacing its new telemetry EKG platform Mortara with the ALPHADAS source document; no other organisations in the phase I arena have this capability at present. Talks on building this interface began a number of weeks ago between the manufacturer, Mortara Instruments, and Logos Technologies at Mortara's base in Bologna, Italy. The system still needs to be validated, but should be up and running in around six months' time. This will make Duke the first centre to use this tool, which is a unique and potentially valuable technology for the industry.

Adaptability

The system will also place Duke in a better position when it comes to offering expertise and guidance on trials outsourced to them by the pharmaceutical industry. Clients occasionally present with studies that are not optimally designed, and the DCRU then has the opportunity to help those companies re-design, re-tool and potentially make their projects more successful in the subject population studied. As well as partnering with Logos Technologies on ALPHADAS, the DCRU team hopes to be able to aid in the future development of the platform. The unit will become intricately involved in providing feedback to Logos



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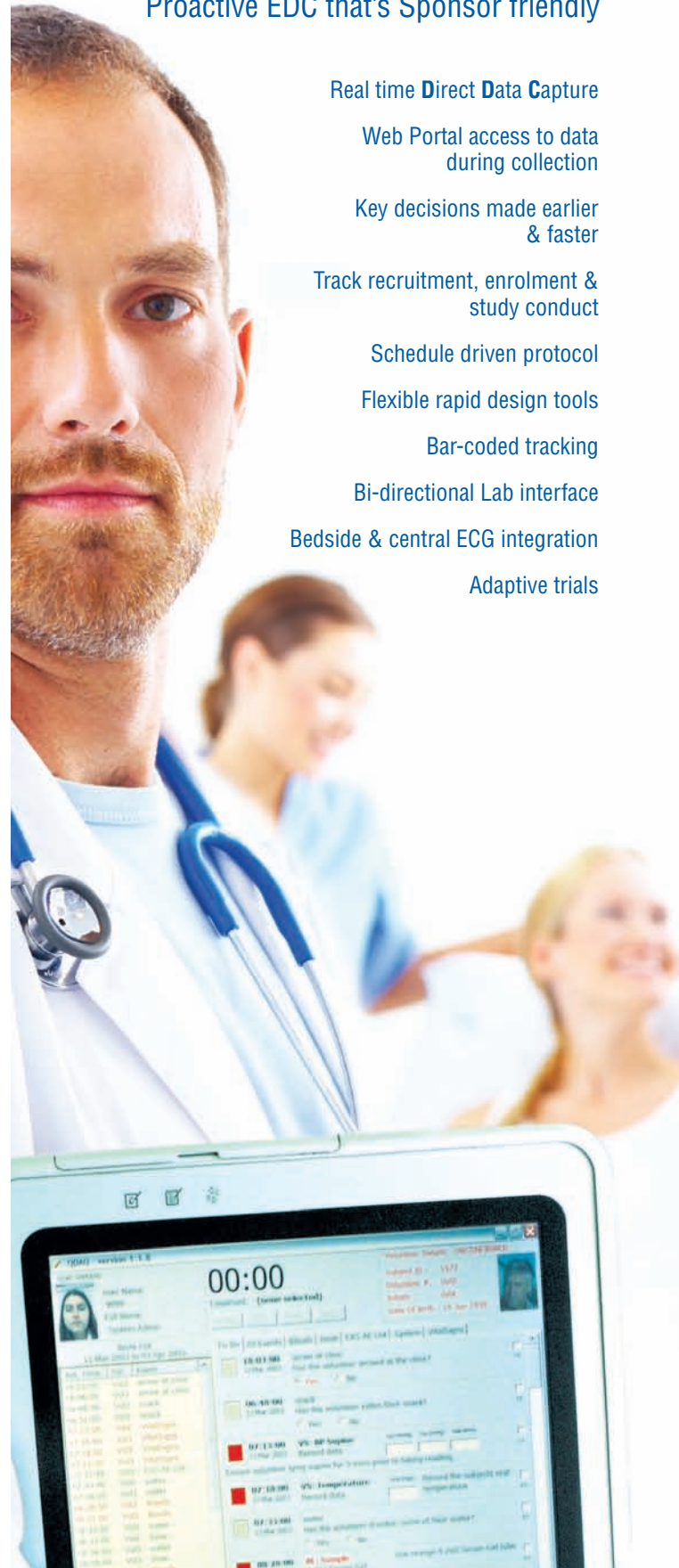
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Adaptive trials



Data Capture and Management

Technologies on the product in order to improve its performance not just for Duke, but also for other institutions. It also plans to become a beta tester for new releases and add-ons for the system.

As for the ALPHADAS hardware, it consists first of a secure central server that Duke already has in place. Only around eight people in

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total have access to this mainframe. In terms of portable hardware, investigators will be able to input data at the bedside on tablets, personal digital assistants (PDAs), notebooks and handheld bedside pieces. The DCRU will predominantly use mobile bedside carts to collect information.

Cutting Costs

While installing ALPHADAS obviously requires some start-up capital, in the long run DCRU expects it will reduce overall expenditure. ALPHADAS will reduce the need for administrative staff, and monotonous tasks such as inputting data, by automating these processes. This will free up researchers to perform other tasks that help progress the trial.

The amount of automation that the system allows will also help preserve finances in the long-term. In the day-to-day execution of a paper-based trial, for example, investigators would first need to enter subjects into the data set, and then fill out case report forms (CRFs). Then there would be the business of collecting data at the bedside. With ALPHADAS, all of these processes are carried out electronically and, to an extent, automatically. Also, there will be prompts to co-ordinators within the unit to proactively collect certain pieces of data at certain time-points, to avoid mistakes. This will also improve the tracking of vital signs, making it easier to spot any adverse events and anomalies.

There is also the issue of efficiency. Duke expects that as the system becomes an integral part of the infrastructure, trials will run more safely and efficiently and, therefore, more quickly. In the long run, this may open Duke to accepting more business within a given time-frame, allowing a higher turnover of trials. The end-point of this is that drugs can get to the market more quickly, and one can be more assured of their safety record. This could be hugely influential in attracting new clients to the DCRU.

A more specific way in which Duke hopes to cut expenditure is by utilising ALPHADAS' interface with Labcorp. DCRU will now use Labcorp as its vendor for all of its screening and speciality laboratories. ALPHADAS has a built-in HL7 interface with Labcorp, which allows Duke to co-ordinate activities with the lab vendor. Using this system, samples that are barcoded and entered into ALPHADAS are then sent

to the laboratory at Labcorp. Because the vendor uses the same software, its staff can then barcode the sample into its automated equipment, and so human hands need never touch the data again. In fact, because the system is seamlessly automated between the two organisations, Labcorp will no longer have to 'hand-enter' any data into data sets at their end and then port it to Duke. As well as improving accuracy, this change alone saves the DCRU around US\$2,000 per study. As for personnel, DCRU predicts that ALPHADAS will require only one and a half people to maintain the system: one member of staff is needed to manage the platform within Duke's own infrastructure from a server perspective, and the extra half a person will have the day-to-day responsibilities for maintaining the hardware on-site. In the meantime, the DCRU will be monitoring how this set-up progresses. It may not yet be the final solution, but it is a considerable improvement on a system that requires over eight staff for standard maintenance.

ALPHADAS also goes a long way towards bringing Duke's systems in compliance with the US Food and Drug Administration's (FDA's) 21 CFR Part 11 directive for maintaining electronic documentation and records. ALPHADAS also makes it easier to provide data sets for review by regulatory agencies, since it is collected in such a way that it is easier to extract for the final study report. Naturally, there are hurdles in the shift to electronic phase I trials, and Duke has by no means discounted these. To run ALPHADAS, institutions must find a candidate keenly interested in phase I clinical research who must also have the expertise to carry out all relevant tasks in both the healthcare and IT environments. There are not many such individuals being trained at the moment, and so it is a competitive environment. The DCRU is currently in the process of recruiting for this role.

The Future for Phase I

The shift to electronic in all areas of clinical trial management is an obvious trend and it was only a matter of time before phase I trials followed suit. Keeping up with these changes is key to staying afloat in the competitive landscape. There are now various phase-I-specific eDC platforms on the market, and it is important to choose one that suits the institution. The ALPHADAS system answers all of the DCRU's needs, offering a standardised platform that allows the running of safer and more efficient phase I trials. Furthermore, the ability to

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interface with Duke's own products – for example, coupling with the Mortara digital EKG wireless system – is something that will really put the DCRU ahead of the pack.

Moving into the future, Duke's new eDC-enabled phase I set-up will bring the DCRU in line with its phase II and III eDC systems. By using the ALPHADAS system, Duke hopes to boost its growing phase I capabilities, improve the clinical research environment and enhance subject safety. ■