

PATIENT REPORTED OUTCOMES

ALK-Abelló used electronic collection methods of subject data for a dust mite allergy tablet-development clinical trial.

ePRO in Action: A Case Study

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ALK is currently developing a house dust mite (HDM) immunotherapy tablet. In the latest HDM clinical trial, ALK used an ePRO system from PHT to enable subjects to record their experiences in the trial. ePRO is the electronic capture of patient reported outcomes (PRO) data from study subjects. This was the seventh trial in which ALK used ePRO solutions from PHT.

The trial

The randomized, double-blind, placebo-controlled HDM trial began in August 2006. It encompassed 604 subjects at 81 sites in eight European countries. Participating subjects were randomly assigned to one of three doses of active treatment or a placebo treatment. In addition to taking the study drug, subjects were allowed to use predefined rescue medication to treat acute symptoms.

In the morning and evening, subjects recorded their allergy and asthma symptoms, use of rescue medication, and answered other PRO questions on PHT's eDiary, the LogPad. Questions included the number and severity of asthma symptoms, use of rescue medications, peak flow lung function measurements, and whether they took the study medication as directed. Each week, subjects entered their responses to a standardized questionnaire, the Asthma Control Questionnaire.

The questionnaires ALK used for the trial included information about medication dosage, severity of symptoms, and mood. ALK wanted to provide immediate feedback to subjects and study personnel, which is not possible with paper diaries. When the subject completed the diary, the LogPad reported medication compliance. Subject data was sent daily to sites so they could quickly identify those subjects who needed observation or follow up right away instead of waiting until the subjects' next visit. The LogPad reminded subjects of their next visit, decreasing the number of missed appointments.

Three different doses of HDM were compared with placebo to determine the safest effective dose. The drug's effectiveness was evaluated based on subjects' use of rescue medication, reported changes in quality of life measurements, and physiological measurements such as lung-function tests.

The main conclusion of the trial was very

positive. Subjects treated with the HDM immunotherapy tablet in the highest dose achieved a 50 percent reduction (median value) in their use of inhaled corticosteroids (rescue medication) compared to the amount used before treatment began.

Data collection

ALK used ePRO for this trial instead of paper, based on its eDiary experience and the trial design. The study team had previously used ePRO and was impressed with the ability to get real time observation of results, which could not have been obtained on paper diaries. The enhanced access to data made ePRO particularly suited for the HDM trial design.

The study included investigational sites both with and without experience using eDiaries. Investigators and study coordinators at the sites acted as subject support, helping subjects learn how to use the intuitive software and complete the questionnaire. Study physicians reviewed the subject responses in an online portal that provides real time access to data collected. After reviewing the data, physicians called each subject based on their responses.

ALK noted that the data quality captured from ePRO is superior to paper. While it took longer to set up eDiaries than to distribute paper ones, overall eDiaries required fewer resources. The exact time a subject entered the data could be tracked, providing a higher quality of data. A higher compliance was realized—the LogPad sent alerts to remind subjects to enter information on a routine basis.

Stig Christensen, International Planning and CRO Manager at ALK, said that the ePRO system was excellent and proactive, yielding high data quality. "The ePRO system resulted in higher subject compliance than ALK expected and subjects seemed positive about using the eDiaries, including the LogPad alerts which reminded them to complete their questionnaires on time."

ALK selected ePRO because it met ALCOA (attributable, legible, contemporaneous, original, and accurate) standards, recommended guidelines by international regulatory bodies. An ePRO system offered both ALK and its sites permission-based real-time access to the eDiary data through a

hosted central server. Sites could easily notice trends in subjects' response rates for the questions—site personnel could applaud subjects that were very compliant and encourage or troubleshoot with subjects that were not completing diaries.

Review

ALK sees PHT as a partner who provides ongoing consultation about merging science and technology efficiently, a commitment to quality and improvement, and in-house help desk for eDiary support. At the conclusion of the trial, PHT provided sites and sponsors with a fully-reconstructible archive—the archive is easy for regulatory bodies to re-create the trial and is simple for sites to use.

The complexity of the randomized, parallel-group, double-blind, placebo-controlled, multi-center, multi-country HDM trial reinforced the need for building institutional

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memory regarding ePRO, for future studies. This led to the innovative idea of starting an internal user group meetings forum. The group met regularly to exchange knowledge among the many employees who had worked on ePRO trials, develop best practices, and communicate efficiently with PHT. Discussions included study status, communication needs, and logistical issues.

For ALK, the user group meetings defined areas of improving processes both within ALK and PHT's study teams. One important result was setting up standard reports.

One year after the evaluation of the HDM trial, the user group met regularly with PHT for seamless knowledge transfer from one HDM trial to the next. The company developed an innovative communications approach that enabled new team members to quickly learn about the trial, provided executive insight into ALK's ePRO initiatives, and established a forum for developing new solutions and support strategies.

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