



Client Success Study: **Asthmatx Inc.**

Electronic patient diaries are helping subjects and sites participate in a pivotal IDE study evaluating the safety and efficacy of **Bronchial Thermoplasty™**, the first non-drug treatment for asthma. The investigative procedure uses the **Alair® System** from **Asthmatx Inc.** and has the potential to revolutionize asthma care for millions.

Asthma and the AIR2 Trial

According to industry estimates, more than 20 million people in the United States suffer from asthma, many of whom regularly take multiple medications to treat their symptoms. More than 5,000 Americans die from asthma annually, and 2 million visit the ER. The Phase III Asthma Intervention Research 2 (AIR2) Trial, sponsored by Asthmatx, investigates a novel non-drug procedure intended to improve the quality of life for patients with moderate to severe asthma.

The AIR2 trial is a unique international, multicenter, randomized study being conducted at 40 sites globally, and uses innovative electronic patient reported outcome (ePRO) technology from **PHT Corporation** to collect reliable PRO data and manage it in real time. Asthmatx has deployed over 500 **LogPad® Systems**, electronic patient diaries implemented by PHT on proven Palm® handhelds and smartphones, as part of the trial. Subjects use the eDiaries (in 6 languages) to record and transmit daily asthma symptoms and medication use data during baseline and up to a 12-month period following treatment. eSource data quality controls and real-time access provide sites with complete confidence that the patient data they receive is timely and trustworthy.

Bronchial Thermoplasty

Asthma involves greater than normal responsiveness of airways in the lungs to a variety of stimuli. This increased responsiveness can take the form of thickening of the airway wall, excess mucus production that can clog the airways, and significant narrowing of the airways when tiny muscles in the airway wall – called airway smooth muscle – contract.

During bronchial thermoplasty, physicians use a flexible bronchoscope inserted through the nose or the mouth to position the Alair catheter, which delivers thermal energy to the airway walls. The controlled heat is designed to reduce the amount of smooth muscle in the airway wall, thereby reducing the ability of the airway walls to contract, narrow and spasm in response to normal asthma triggers.

In the AIR2 Trial, physicians perform bronchial thermoplasty to treat the entire lung in three treatment sessions with one-third of the lung being treated during each session. Each procedure is performed in a bronchoscopy suite and takes approximately one hour to complete. It is performed as an outpatient procedure under conscious sedation. Patients maintain their baseline asthma medications through the course of the study. Patients are assigned individual PHT LogPads, which are used daily in the morning and evening to record peak expiratory flow (PEF) rates, asthma symptoms, and rescue medication use. This data will help scientific researchers evaluate the success of bronchial thermoplasty as a new asthma treatment.

Success at a Glance



Sponsor: Asthmatx Inc.



Study: Asthma Intervention Research 2 (AIR2) Trial

Purpose: To demonstrate the safety and efficacy of the Alair System in a population of patients with moderate to severe asthma who are still symptomatic despite being managed on conventional therapy of high doses of inhaled corticosteroids and long-acting β_2 -agonists

Therapeutic Area: Asthma

Patients: Enrolling approx. 300

Sites: 40 sites globally (23 in the United States, five in the United Kingdom, four in Brazil, three in Canada, three in Australia, one in Denmark and one in the Netherlands)

eDiary Languages: English, French Canadian, Portuguese, Spanish, Danish and Dutch



Bronchial Thermoplasty delivers thermal energy to the airway walls

The Site Experience

Below, two investigative sites participating in the AIR2 Trial discuss the benefits of using PHT's LogPad System, including PHT StudyWorks™, an online portal for real-time data review and management.

Confidence in the Validity of Self-Reported Patient Assessments

As patient reported outcome (PRO) data continues to be increasingly leveraged for primary and secondary end points (particularly in therapeutic areas such as respiratory/asthma), and as the FDA issues further guidance on PRO, sponsors and sites alike realize they can no longer rely on outcome data collected using conventional paper diary methods. The LogPad's restricted time response windows, defined by protocol specifications, and timestamped data ensure patients actually complete reports when they claim to, thereby eliminating unplanned retrospective or prospective data entry, as well as batches of diary entries.

"I think it's a great tool to capture time-sensitive data," said Nadia N. Hansel, MD, MPH, Instructor, Division of Pulmonary and Critical Care Medicine at **Johns Hopkins University**. "In daily symptom diaries, I think recall bias is a real problem and that it's difficult to assess actual compliance rates. The LogPad has worked out great – the patients have been very happy with it, and from our perspective it improves the accuracy of the data."

Real-time Access to Patient Data

In addition to improving data quality and timeliness, PHT's LogPad System also provides real-time data access through StudyWorks, an online portal for sites, sponsors and monitors. Complete with standard and custom reports and data summaries, StudyWorks delivers tangible improvements in trial management efficiencies (e.g. compliance and enrollment management) and capabilities (e.g. symptom monitoring and email alerts).

"From my perspective, the LogPad System is a very innovative way to ensure that we're collecting valid, real-time data," said Pulmonologist Jeff B. Hales, MD, **Pulmonary and Medical Associates of Northern Virginia**. "It's not retrospective, it's not a patient's recollection; it's valid and real-time data that's downloaded and monitored on a daily basis."

Site personnel can use compliance reports to identify patients who haven't transmitted their diary entries for a period of time, and follow up with a telephone call (or even a text message sent to the patient's LogPad) as encouragement, as a reminder or to offer assistance if needed. Other reports show actual patient data, which can trigger alerts, and enable sites to respond quickly to worsening of a patient's symptoms.

"With StudyWorks, we can monitor on a daily basis what the (patients') symptoms are," said Dr. Hansel. "You can obviously see any change in their symptoms and be alerted to potential problems in a more timely fashion."

eSource Data

ePRO data collected by the LogPad is guaranteed to have a complete, logical and legible timestamp due to numerous quality controls including data entry rules, automatic screen sequence controls, and restricted and properly formatted response options. The result is that sites have to spend less time reviewing diaries with patients to ensure items were answered correctly. The eSource format of the data also eliminates data entry and most data queries.

"With paper, there is a much higher workload going through every daily diary entry with a patient and having to record that information," said Dr. Hansel. "With the LogPad, it's all automatic, and doesn't take away from the data management person's time."

"Because the data is eSource, and is collected and downloaded directly into the study database, it removes the opportunity for error in the transcription of data from paper to electronic formats," said Dr. Hales. "Therefore, there are no mistakes, such as accidentally keying in one decimal point wrong."

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Storage Space

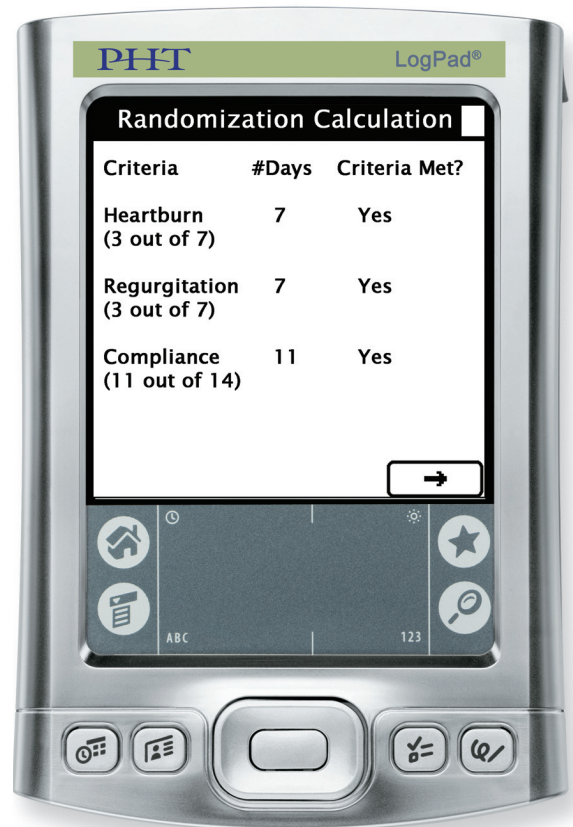
Physical storage space can be at a premium at any facility, but especially at smaller study sites. While the LogPads and accessories may occupy space prior to patients being enrolled, inventory is quickly depleted as LogPads are issued to patients. Once the trial is underway, the eSource data takes literally no space at the site – a striking contrast to the volumes of paper forms which can become overwhelming, in terms of space management to a conventional paper diary trial.

“One of the best parts of the LogPad,” Dr. Hales noted, “is it means no more piles of paper in the office.”

Eligibility Calculations

Most PHT clients take advantage of the LogPad’s ability to perform automatic calculations for eligibility criteria and display the results on-screen in order to aid sites with randomization decisions.

“Inclusion requirements in the AIR2 Trial necessitated that patients have symptoms for a certain number of days during the screening period in order to be eligible,” said Dr. Hansel. “They also have to show an ability to complete a certain percentage of diary reports for compliance. It helps to have that data on-hand and available electronically without having to do manual analysis. It is all automatic because of the LogPad.”



An example LogPad eligibility calculation screen

Excluding Inconsistent Patients

The LogPad’s eligibility reporting and minimum compliance requirement during the screening phase also provides insight into the type of patient being evaluated for inclusion in the study.

“Compared to other trials, our dropout rate in the present study is lower than expected. One of the few patients who was dropped at our site was for poor compliance with keeping the daily diary at baseline,” explained Dr. Hales. “It wasn’t so much that he couldn’t use the eDiary, but that he was distracted with different obligations and wasn’t fully vested in the study. To me, the low compliance on the LogPad proved that he wouldn’t have been a consistently dedicated patient throughout the trial. Because key endpoints in this study include quality of life and other patient reported outcome data, poor diary compliance by patients would compromise the study outcomes. Thus for a long-term clinical trial requiring patient data, it is good to know up-front if the patient is fully vested, and the LogPad helps us identify and exclude non-compliant patients from the study.”

Regulatory Compliance

At the completion of the trial, PHT will provide each site with a study archive of all data collected at the site, complete with audit trails, on special durable CD-ROM or DVD-ROM media. This further reduces the storage space required, but it also makes it easy to comply with FDA regulations for trial reconstruction through its use of XML source data and metadata. PHT’s unique use of XML in the study archive enables searches on the data and ensures it will always be human readable, even if current standards for electronic portability (i.e. PDF) should change. PHT’s expert internal Study Support Center, available in multiple languages 24/7, helps sites understand how to use the archive in advance of FDA or other regulatory audits. To date, no issue has been raised with any of PHT’s ePRO systems.

Advancing Research Facility Reputations

State-of-the-art sites are trained and able to use cutting-edge technology to attract new and innovative studies, such as the AIR2 Trial. Dr. Hales is leading a concerted effort to advance Virginia Hospital’s reputation in this department.

“Of course PHT’s LogPad System helps us in this endeavor,” said Dr. Hales. “Any technology that makes it easier to collect the data for clinical research and collect real-time, valid data furthers these goals.”

The Patient Perspective

Years of scientific research and experience demonstrate that patients of all ages, with varying conditions and living in diverse communities around the globe, are easily able to use eDiaries – and even enjoy using them. Patients using PHT's LogPad in clinical research report they feel more connected to their site because they use the eDiary to communicate indirectly with study coordinators every day. In the AIR2 Trial specifically, patients are easily able to record and transmit information about how they are feeling with clear and formatted eDiary items:

Morning Diary	Morning Diary	Evening Diary	Evening Diary
Check the box that best describes any WHEEZE during the night: ☐ None ☐ Slept well - slightly wheezy ☒ Sleep disturbed by wheeze ☐ Severe - awake most of the night	Number of times you woke up last night due to asthma symptoms. 3	Check the box that best describes how BREATHLESS you were during the day: ☐ Not breathless ☐ More breathless than normal on vigorous exertion ☐ Breathless on moderate exertion ☒ Breathless on mild exertion	Indicate reason: ☒ Didn't take any medications ☐ Took less than normal ☐ Took more than normal

Asthmatx makes it as convenient as possible for their patients to record and send information about how they're feeling. With eDiaries running on Palm Tungsten E2 handhelds or Treo 650 smartphones, patients easily enter symptoms into the pocket-sized device from virtually any location. Palm devices also have long battery life, which has helped with patients who don't have access to electric power all the time.

"We're very pleased with the system and things are going very well," said Dr. Hales. "I'm pleased with the way patients respond to this and they seem to enjoy it – it's not a hassle for them. It's as easy as possible for them to get the information to us."

"In general, it's worked out great," added Dr. Hansel. "The patients have been very happy with it, and from our perspective it makes the accuracy of the data because they filled it out in a timely manner."

Why PHT?

Asthmatx chose to use PHT's LogPad System to collect critical patient self-reported data in this pivotal trial. Given the rigorous regulatory procedures required for a medical device such as the Alair System, any questionable or inconclusive data can delay the submission of trial results and potentially prolong the approval process resulting in lost revenue.

"We selected PHT primarily because of their experience with respiratory trials and the ease-of-use of the LogPad System," said Narinder S. Shargill, Ph.D., Vice President of Clinical Affairs at Asthmatx. "Because this is a pivotal trial, it is imperative that we work with an ePRO provider with knowledge of respiratory clinical trials and standardized questionnaires for such studies. We also appreciated that PHT was able to demonstrate the flexibility, willingness and expertise needed to meet our dynamic trial requirements."

About Asthmatx

Asthmatx Inc. is a development stage medical device company located in Mountain View, California that is focused on helping patients breathe easier.



Asthmatx Inc. designs, develops and manufactures catheter based medical devices incorporating thermal energy for a variety of indications. Asthmatx has developed the Alair® System, which consists of a single-use device and a controller that delivers radiofrequency energy during an investigative outpatient bronchoscopic procedure known as Bronchial Thermoplasty. The Alair® System provides a different investigational treatment approach for severe asthma that uses radiofrequency energy to apply controlled heat to the airway wall to reduce the amount of airway smooth muscle and restrict its ability to narrow the airway. Bronchial Thermoplasty has been shown to reduce the narrowing of airway passages in response to bronchoconstrictors, and may potentially improve asthma symptoms in patients with this condition. Asthmatx is currently conducting a pivotal study investigation to evaluate the safety and efficacy of the Alair® System for the treatment of severe asthma.

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