eAdjudication in clinical trials could save Sponsor's time and effort while improving the quality and compliance of endpoints assessment in clinical studies having subjective endpoints

eAdjudication® for Actelion's SERAPHIN

ACTELION

"Using an online eAdjudication portal for our SERAPHIN study endpoints assessment improved the efficiency of the data collection and the quality of our processes, allowing a timely completion of the study.

On-line management of Adjudication allowed rapid assessments of the study endpoints and greatly facilitated the work of the external clinical experts. The tool provided them an integrated quality controlled environment and all the information and forms required to assess the submitted endpoints."

Loïc Perchenet, PhD
Director, Global Post-Approval Studies
Global Medical Affairs Actelion Pharmaceuticals Ltd.

Actelion Ltd

Actelion Ltd. is a leading biopharmaceutical company focused on the discovery, development and commercialization of innovative drugs for diseases with significant unmet medical needs.

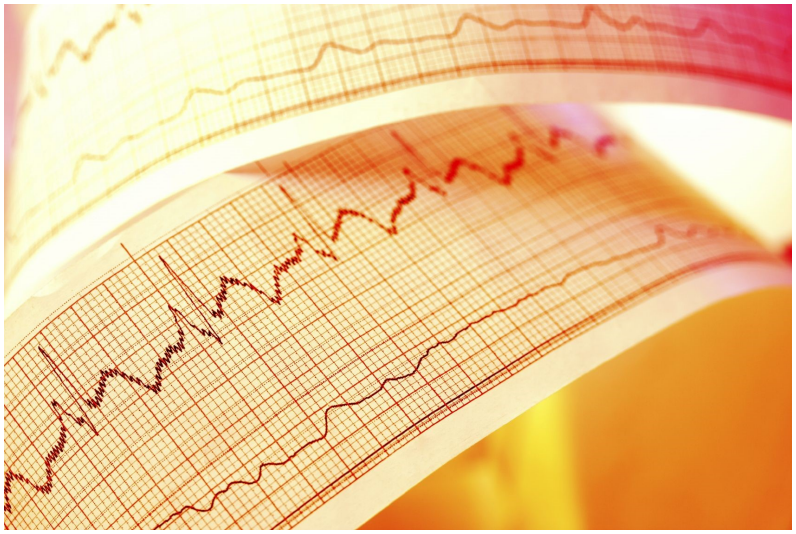
Actelion is a leader in the field of pulmonary arterial hypertension (PAH). Our portfolio of PAH treatments covers the spectrum of disease, from WHO Functional Class (FC) II through to FC IV, with oral, inhaled and intravenous medications. Although not available in all countries, Actelion has treatments approved by health authorities for a number of specialist diseases including Type 1 Gaucher disease, Niemann-Pick type C disease, Digital Ulcers in patients suffering from systemic sclerosis, and mycosis fungoides in patients with cutaneous T-cell lymphoma.

Founded in late 1997, with now close to 2,400 dedicated professionals covering all key markets around the world including the US, Japan, China, Russia and Mexico, Actelion has its corporate headquarters in Allschwil / Basel, Switzerland.

Actelion shares are traded on the SIX Swiss Exchange (ticker symbol: ATLN) as part of the Swiss blue-chip index SMI (Swiss Market Index SMI®). All trademarks are legally protected.

Ethical GmbH

Ethical is a software / service company based in Basel (CH) offering eClinical software applications design, data management services and consulting to pharma and biotech companies.



SERAPHIN

SERAPHIN (Study with an Endothelium Receptor Antagonist in Pulmonary arterial Hypertension to Improve clinical outcome) was the largest and longest randomized, controlled study in PAH patients to include a clearly defined morbidity/mortality primary endpoint.

The pivotal Phase III study was designed to evaluate the efficacy and safety of Macitentan (Opsumit®) - a novel dual endothelin receptor antagonist that resulted from a tailored drug discovery process - through the primary endpoint of time to first morbidity and all-cause mortality event in patients with symptomatic PAH.

Global enrollment was completed in December 2009 with a total of 742 patients. Patients were randomized 1:1:1 to receive two different doses of macitentan (3 mg and 10 mg once daily) or placebo.

This event-driven study was conducted in 151 centers from almost 40 countries in North America, Latin America, Europe, Asia-Pacific and Africa and was completed in the first half of 2012, with 287 patients having an adjudicated event.

The first approval globally of the new drug application for Opsumit (macitentan) was issued by the US Food and Drug Administration (FDA) on 18 October 2013 for the treatment of pulmonary arterial hypertension.

Opsumit (macitentan) is also approved for PAH in the EU, Australia, Canada, and Switzerland. Regulatory reviews in other countries are ongoing.

Clinical Endpoint Adjudication

Clinical Endpoint Adjudication improves the quality of clinical trials where endpoints are complex to assess, include subjective components and/or cannot be blinded.

The central assessment of efficacy or safety events, made by a panel of independent experts following a blinded standardized procedure, increases accuracy, independency and homogeneity of judgments.

Using an online eAdjudication® portal to manage the Adjudication process provides even more advantages in terms of:

Data Quality
easing the building and delivery of the events' information package to the experts through standard automated procedures.

Process Quality
exploiting role-based workflows to enforce the compliance of the whole process with Sponsor SOPs.

Time & Cost savings
for the Sponsor reducing cycle times to assess an event as a study endpoint; for the independent Experts supporting their decisions with an easy to use system and its tools to deal with data visualization, versioning and assessment.

Ethical eAdjudication®

Ethical eAdjudication® is a cloud online portal designed to support clinical endpoints assessment and adjudication by expert clinicians.

The system is focused in providing the adjudication committee members with accurate, clean and complete data, coming from different data sources (CRF or e-CRF, site documents, images, external providers), and to manage members roles in order to implement a well predefined, fully transparent and documented operating procedure for assessment, thus leading to reliable results.

Main system functions are about:

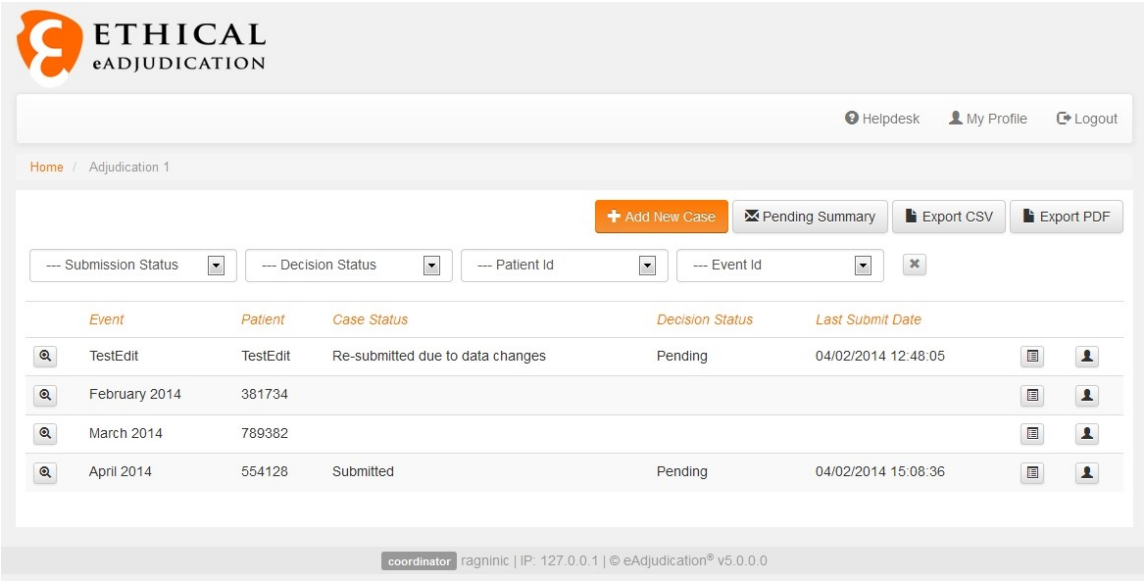
• real time events & materials submission and notification;

• centralized repository and tools to visualize, compare and track event information (data, documents, images);

• experts' judgement acquisition through online forms specially designed to guide the experts during the assessment;

• users' profiles strict management and process workflow enforcement;

• audit trail and validation to ease system regulation compliance.



SPONSOR AT A GLANCE

- **Company**: Actelion Pharmaceuticals Ltd
- **Headquarter**: Allschwil, Switzerland
- **Industry sector:** Biopharmaceuticals

SUPPLIER AT A GLANCE

- **Company**: Ethical GmbH
- **Headquarter**: Basel, Switzerland
- **Industry sector:** eClinical software & services

CHALLENGE

Actelion Ltd. is a leading biopharmaceutical company focused on the discovery, development and commercialization of innovative drugs for diseases with significant unmet medical needs.

Clinical endpoints assessment and Adjudication is crucial for reducing patients' risks and bias related with multi center studies with subjective endpoints.

External very expert clinicians should receive clinical data and documents and make their assessment in a blinded trackable way.

All the process and tools should be designed to reduce the burden for the experts and the average endpoint cycle times.

SOLUTION

Actelion decided to adopt for their adjudication committee members management an eAdjudication portal based on the web.

The Ethical eAdjudication® system incuded a centralized repository to visualize, compare and tracking event information and the adjudication forms allowing the experts to make their assessment in a quality workflow enforced environment

The experts were alerted when a new event/information was available in the system.

They connected to the portal to review and assess the potential events using very simple to use tools and online forms.

RESULTS

Actelion time and costs for events' package delivery and assessment tracking were significantly reduced.

Experts time and training effort were minimized through simple online forms and role based pre-defined operations

Process compliance to the Adjudication Charter, SOP and Regulations were enforced and controlled by running the system in a validated environment.

The SERAPHIN Study was a great success for Actelion and for patients suffering the Pulmonary arterial hypertension (PAH) chronic disorder.

For more information on Ethical eAdjudication®
visit the website http://**www.ethical.ch**

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