berlinger

Joint Case Study

From Temperature to Full Condition Monitoring - A Revolution in Safeguarding Advanced Targeted Drugs

A Collaborative Journey by Debiopharm and Berlinger

Contents

Introduction

The landscape of drug development is evolving rapidly, marked by the emergence of biologics, targeted therapies, personalized medicine, and the revolutionary strides in cell and gene therapy. As the pharmaceutical industry embraces innovation, the intricacies of managing Investigational Medicinal Products (IMPs) have intensified. Notably, the demand for temperature-sensitive solutions has surged, compelling the clinical supply chain to adopt increasingly sophisticated monitoring systems. It became even more crucial to ensure the seamless preservation of the cold chain during transportation and storage, safeguarding the efficacy of these advanced therapeutic modalities.

Addressing this need, Berlinger has introduced SmartSystem, a revolutionary solution for safeguarding advanced targeted drugs with full condition monitoring. SmartView, the cloud-based software solution, serves as the analytical powerhouse of SmartSystem, delivering mission-critical insights into the supply chain. Complemented by SmartMonitor hardware, which is redefining real-time monitoring for shipments and site management. Collectively, this integrated system ensures on-time product release, fulfilling strict quality standards, and ultimately reduces wastage and cost.

Berlinger had the privilege of implementing SmartSystem for shipment monitoring in a Debiopharm trial as a pilot project. This case study delves into the challenges faced, the innovative solutions deployed, and the tangible impact observed during the trial. The Debiopharm trial, characterized by its first-in-class approach, demanded an extra layer of precision and care in managing the investigational products.

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About Debiopharm

Debiopharm is a highly innovative mid-sized biotech company that specializes in oncology and infectious diseases. The company's pipeline includes small molecules, antibody-drug-conjugates, and peptides, the latter of which are highly temperature-sensitive when transporting radioisotopes.

About the Trial

Highly complex and sensitive to various factors is Debiopharm's new investigational drug**,** a first-in-class **theranostic pair**, combining a **diagnostic imaging agent (Debio 0328)** and a **therapeutic radiopeptide (Debio 0228)**. This novel theranostic approach targeting the Carbonic Anhydrase IX (CA IX) allows pre-identification and subsequent treatment of cancer patients expressing this well-studied target.

"Debio 0228/0328" in action

This investigational drug consists of a peptide, one end of which has a **binding domain (1)** for docking to CA IX molecules on the surface of the cancer cells, while at the other end a **"cage" of the peptide carries a radionuclide (2)**. This radionuclide will make the cancer light up in a PET scan (in the case of Gallium 68) and subsequently deliver damaging radioactivity to the tumor cells (in the case of Lutetium 177). To ensure the isotope stays in the cage, the drug has to be stored and transported at approximately - 80°C, which makes the trial extremely sensitive.

Up to this point, the drug shipments were accompanied by passive loggers whose temperature data was read upon arrival at the sites.

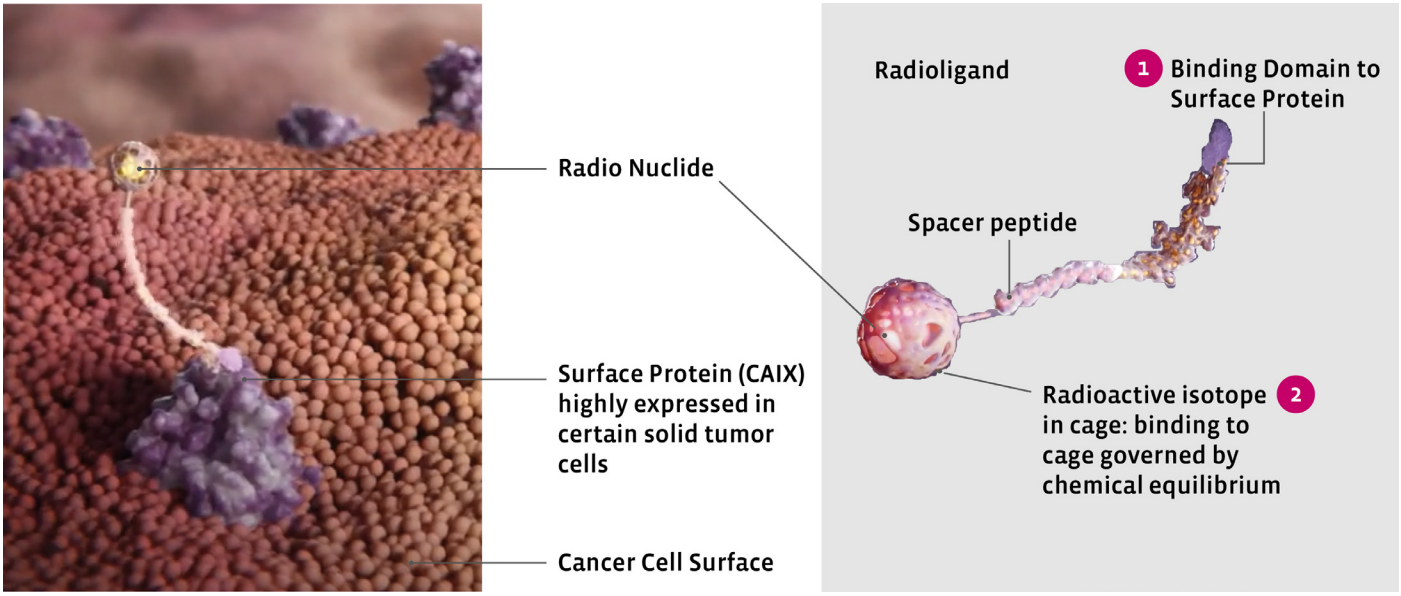

Figure 1: Debiopharm's new investigational drug Debio 0228/0328 demands for storage and transport at approx. - 80°C to ensure the isotope stays in the cage.

Trial key facts:

- **Clinical Trial:** Debio 0228-101
- **Study Phase:** Phase I/II
- **Number of IMPs:** 2
- **Number of constituents to be shipped:** 2: cold precursor kit, constituent
- **Temperature ranges:** IMP1: -80°C, IMP2: n/a, constituent 1: RT, constituent 2: -20°C
- **Number of sites:** up to 25
- **Number of patients:** up to 147
- **Number of shipments:** up to 316 / year
- **Duration of the trial (recruitment and treatment phases combined):** 36 months

Unlocking Success with SmartSystem

This new generation of highly advanced targeted drugs, exemplified by **Debio 0228/0328**, presents the clinical supply chain with a whole new series of challenges, which were effectively tackled in this trial through the utilization of SmartSystem.

Maintaining the targeted temperature range is paramount to prevent the radionuclide of this IMP from leaving its 'cage'. This could result in the radioactivity not being administered in a targeted, but rather in a systemic way, impacting efficacy and rendering the IMP "not fit for use". Therefore, the SmartSensor ULTRA LOW, capable of measuring temperatures as low as -100°C, was attached to the SmartMonitor device.

The radionuclide has a half-life of just under seven days. Consequently, any disruption or delay in the transport process may jeopardize the integrity of the IMP, potentially resulting in the IMP no longer being active enough to be administered to the patients. SmartSystem's innovative communication and sensor technologies enabling full condition monitoring play a crucial role in mitigating these risks.

Debiopharm leveraged the location tracking, facilitated by the GPS capability of the SmartMonitor SHIP L shipment logger. This integration ensures full visibility of the location of the drug kit in the SmartView software. In the event of a delay, which could lead to the drug exceeding its shelf life of only seven days, the initiation of a replacement shipment could be facilitated immediately.

Furthermore, the inclusion of a light sensor serves as an additional safeguard. Any delay detected, along with a corresponding light event visible in SmartView, serves as an indicator of potential tampering or customs intervention. This data proves invaluable when conducting CAPA (Corrective and Preventive Actions) and minimizing delays.

Figure 2: Transport at approx.-80°C was carried out using a dewar vessel with solid CO_2.

Some solutions for shipping materials at approximately -80°C require them to be maintained in an upright position to ensure the payload remains at the correct distance from the bottom of the vessel and within the desired temperature range.

While Envirotainer asserts that temperature levels within CryoSure® dewars (the cryogenic shipping container used in this trial) are unaffected by orientation, the package is intended to be transported in an upright position, per a requirement set by Debiopharm. Therefore, the SmartMonitor SHIP L's tilt sensor was activated and assessed in SmartView, allowing full monitoring of the package's handling during transport and having visiblity on occuring tilt alarms.

Insights & Results

Before the initiation of the study, SmartSystem underwent thorough validation by Debiopharm to align with Debiopharm's Standard Operating Procedures (SOPs), ensuring smooth operation and maximizing efficiency for the shipments during the study.

Four SmartMonitor SHIP L devices were dispatched from Berlinger's facilities to Seibersdorf Labor GmbH as participating CDMO. These were utilized for a pilot shipment (empty box) and a mock shipment (inactive drug) to a site in France and one in Australia, respectively. All mock and pilot shipments were used to establish and test the processes at all stakeholders and also served to assess the respective lanes. The mock shipments also served to establish that the sites could handle approx. -80°C materials as well as radioactive materials and were a part of site Identification.

Using the map tracking in SmartView, the pilot and mock shipments could be tracked in real-time.

Figure 3: The map in SmartView shows the locations over the course of the mock shipment, from the CDMO facility to the site.

Ahead of each shipment, the Berlinger team together with Debiopharm and the respective CDMO jointly checked and assured its proper setup in the system and analyzed it afterwards to conclude the lessons learned and improve the process if needed.

Packaging and preparation of the shipments were carried out at the CDMO facility. The graphic in the SmartView dashboard allows to precisely track the temperature and relevant events - here with **light and tilt (1)** - that the sensitive drug was exposed to during each step with alarms of the environmental factors.

After the acclimatization phase, the SmartSensor inside the packaging monitors the **target temperature of approximately -80°C (2)**, while the SmartMonitor device generates the **temperature curve outside the packaging (3)** during the shipping process.

With this thorough oversight of the shipment, the stakeholders involved in the trial have the ability to closely monitor its progress, take immediate action as necessary, and guarantee timely and transparent product release.

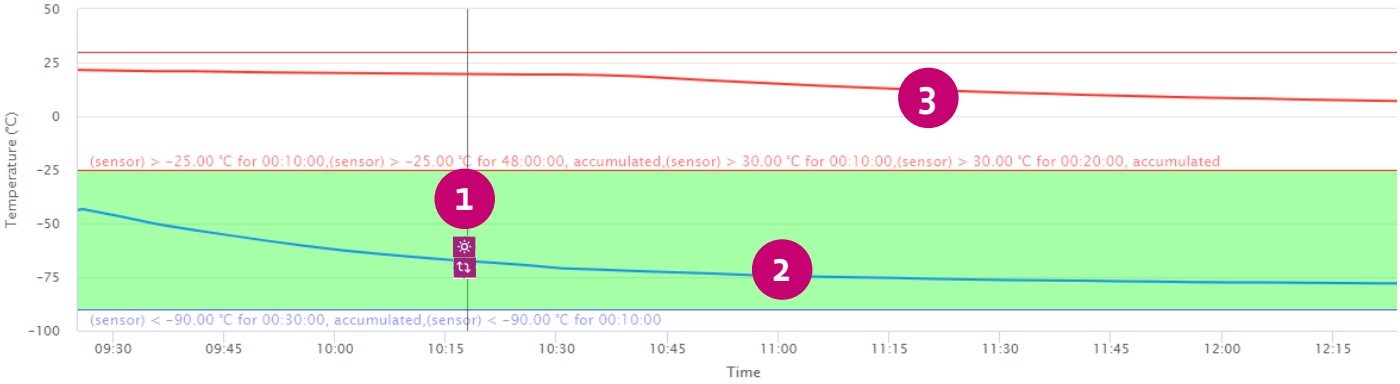

Figure 4: Temperature curves with registered events in SmartView during shipping preparation and setup at the CDMO facility.

SmartSystem, with its state-of-the-art technology, is setting new standards for transparency and control in the supply chain of clinical trials.

Learnings

SOPs for preventive actions
SmartSystem provides Debiopharm a high level of oversight and transparency in the clinical trial. This aids in risk mitigation throughout the supply chain. Preventive actions, such as the decision to initiate a replace shipment, can be made early in the shipping process, well before reaching the final destination.

Enhanced shipment planning and product availability
Alarms on light signals (or their absence) can confirm whether the parcel has been tampered with, while tilt and free fall signals (or their absence) provide insights into potential rough handling of the package. These data significantly enhance shipment planning for clinical sites, ultimately resulting in product availability at the patient, and lowering costs.

Workload reduction through automation
All data and information are uploaded to SmartView in a fully automated fashion, substantially reducing the workload for clinical supply chain management. Similarly, Debiopharm's supply chain managers found the operation of SmartView to be intuitive and logical, minimizing the time required for familiarization. Moreover, Debiopharm started using SmartView as an archive, consolidating all relevant information on site shipments in one place and further reducing administrative burdens.

Additionally, clinical sites benefited from the system post-pilot setup for validation purposes, a crucial step that yielded valuable insights.

Onboarding and Training for Stakeholders
To ensure that stakeholders were well-prepared for their roles, live training sessions were conducted ahead of the pilot and again after the first two shipments had been delivered. This comprehensive training covered the intricacies of each stakeholder's responsibilities within the shipment process and addressed any emerging challenges. This way, stakeholders were equipped with the knowledge and skills necessary to navigate in SmartView effectively and handle the SmartMonitor devices with ease. The collaborative environment facilitated proactive problem-solving, leading to continuous process improvement.

User Adoption Beyond Expectations by the Sites
A noteworthy revelation during the trial was the enthusiastic adoption of SmartSystem by the sites. Somewhat contrary to initial expectations, the first sites actively sought to establish an account in SmartView, driven by the desire to actively monitor the clinical supply chain.

This proactive engagement showcased the inherent value perceived by the sites, not just as a regulatory requirement but as an empowering tool that augmented their role in ensuring the success of the Debiopharm trial. By utilizing SmartView they had real-time access to data like where the shipment was currently located, if it was delayed and if it had been subjected to rough handling, which allowed them to be aware well in advance if a replacement shipment was needed or not.

CRO Collaboration
An equally positive surprise was the receptiveness of the CRO to become part of the SmartSystem ecosystem. The willingness of the CRO to utilize the monitoring system exemplifies the potential for enhanced collaboration between trial sponsors and CROs in adopting cutting-edge technologies for mutual benefit.

Outlook

Following the successful validation of SmartSystem in shipment monitoring, the focus now shifts to actively implementing and using SmartSystem in clinical trials conducted by Debiopharm and extending the system's validation to further Debiopharm studies. Specifically, the goal is to validate the system from the perspective of site monitoring. This expansion is essential to ensuring seamless continuity of data collection within the broader spectrum of Debiopharm's studies and ensuring end-to-end real-time monitoring with SmartSystem.

Elevating Clinical Supply Chain Integrity with End-to-End Real-Time Monitoring

Integrating Berlinger's SmartSystem for both shipment and site monitoring establishes an end-to-end real-time condition monitoring solution. The SmartMonitor modular device platform, coupled with Berlinger's cloud solution SmartView, delivers comprehensive control and flexibility throughout the clinical supply chain.

Engineered to align with the demands of both shipment and site monitoring, the system ensures compatibility and reliability through meticulous design and development. The SmartSystem affords complete oversight of product integrity, leveraging a state-of-the-art platform with real-time devices featuring intercommunication capabilities. This adaptability caters to diverse monitoring requirements across your product portfolio.

The device modularity facilitates seamless intercommunication among SmartMonitor devices via Bluetooth Low Energy technology, enhancing supply chain visibility and automating data read-out to SmartView. This connectivity spans all device types, optimizing costs and time efficiency while ensuring redundancy.

In essence, SmartSystem serves as a comprehensive solution supporting quality, operations, sustainability, and procurement objectives. Real-time records for product, shipment, and site monitoring are accessible remotely through Berlinger's SmartView cloud. This accessibility provides timely operational insights and immediate notifications in the event of humidity and/or temperature excursions.

SmartView further facilitates timely product release by offering comprehensive monitoring data and seamless integration into other systems via API (Application Programming Interface). The platform also establishes robust audit trials, streamlining efforts related to Corrective and Preventive Action and audit processes.

Berlinger's modular real-time system contributes to corporate sustainability strategies by minimizing waste. A comprehensive reuse and refurbishment concept further diminishes device waste, aligning with environmentally conscious practices.

About Berlinger & Co. AG

Berlinger & Co. AG develops, produces, and distributes temperature monitoring solutions for pharmaceutical, biotechnology and research organizations. With over 30 years' experience, Berlinger's innovative site and in-transit temperature recording devices, along with the data management software, improve efficiency for excursion management and increase patient safety.

Berlinger offers a fully integrated temperature monitoring solution based around the SmartView platform and temperature devices, allowing full integration with the customer's IRT system. Swiss innovation, a commitment to research and development (R&D) investment, and a dedication to quality form the core essence of Berlinger. The fundamental goal is to achieve customer success by consistently delivering the highest quality, distinguishing Berlinger through exceptional service, and forging enduring relationships, all characterized by the unmistakable Berlinger style.

Visit the Berlinger website to learn more: www.berlinger.com

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Learn how to implement End-to-End Real-Time Monitoring in your Clinical Supply Chain!

Contact the Berlinger team at:
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