Covance recently formed a strategic alliance with Global Specimen Solutions giving clients access to a comprehensive and integrated solution that includes GlobalCODE®, snapTRACK® and wraparound services.

PRESERVING BILLIONS IN POTENTIAL REVENUE:

Actionable Insights from GlobalCODE® Analytics Rescue a Phase III Adaptive Oncology Trial

In a late stage oncology trial for a drug intended to be marketed in Asia, the Data Safety and Monitoring Board (DSMB) noted an apparent decrease in some patients' white blood cell counts in the new drug treatment arm. This was particularly apparent in the Asian subpopulation study. The client sought to understand whether the drug was responsible for this effect and, if so, what actions could be taken to improve the drug's safety. The company had partnered with Global Specimen Solutions, Inc. (GSS) to manage sample tracking, result analytics and informed consent.

Understanding the Challenge

- An observed low white blood cell count, or leukopenia, could indicate an increased risk of infection – with a higher incidence in the Asian subpopulation enrolled on the study, possibly representing an ethnic sensitivity reaction that would cause concern for dosing administration.
- Leukopenia was not represented in high percentages for other ethnic populations. However, as compared to other clinical trials in oncology, the Asian population was overrepresented due to the frequency of gastric malignancies in this population.
- The trial was nearing completion and a marketing exclusion for the Asian market could have a negative revenue impact of as much as $30B over the life of the drug.

Initial Findings Raise Concern

The initial finding of potential leukopenia was based on a trial design with safety testing that included a complete blood count (CBC) – at baseline and at day 30. Based on the CBC results, the client was concerned that the regulatory agencies would require an exclusion label preventing the sale of the drug to persons of Asian heritage. No interim time points were measured which might give reviewers more refined information about the potential effect of the drug.

The study safety testing did not include differentials, which would provide a high resolution understanding of the white blood cell population in each patient. Knowledge of the ratio of white blood cell types could provide insight into the patients' reaction to the drug and might provide a definitive answer to the question about any selective effects based on ethnicity. This determination would be a critical factor in this drug's eventual commercialization, if approved.

In-life Trial Design Change Initiated

The client was using GlobalCODE® from GSS, a proprietary data management tool that gives clients access to live specimen, assay result, and informed consent data and provides easy access to drug safety and performance insights. With GlobalCODE®, the client had the ability to quickly and easily see the trial data in a single view and make the determination that additional data may be required in order to verify the drug candidate's safety and efficacy. The client

could compare the data from the study under investigation with other clinical trials using the compound, and determine design differences that might impact result interpretation. GlobalCODE® was able to provide population and assay result comparisons using analytic tools unique in the market that enabled data review during the clinical study.

After reviewing the data with extensive analytic tools in GlobalCODE®, it was uncertain that the drug was causing a problem. Furthermore, it became clear that more differentials and an additional data point would be needed.

To fully understand the extent to which the drug was affecting the incidence of leukopenia, the client made the decision to institute an additional CBC at day 15 and include a differential to all CBC time points. When the additional tests were incorporated, the results showed that all populations displayed the same, transitory susceptibility to leukopenia, with a rapid rebound, and no difference in populations with diverse ethnicities. Moreover, there was no increased incidence of infection with the investigational product. What the client ultimately found was that the original Day 30 CBC data point was capturing blood count recovery. The initial interpretation that this was possibly a negative adverse event was in fact understood at the end of the trial to be reflective of compound potency because the therapy was more efficacious than other treatments.

The actionable insights provided by GlobalCODE® enabled the client to understand and properly interpret the potentially negative adverse event they were seeing in this trial. By providing additional metadata from the compound's development in other malignancies with multiple ethic group representations, the client was able to determine what trial design deficiencies could be corrected to enhance understanding of response. Because this data was incorporated with clinical data from definitive data sources rather than surrogate lab data sources, the client could rely on the data and use it to alter trial design and bring the compound safely to market for all patients.

The Right Data at the Right Time

The analytical tools in GlobalCODE® gave early, actionable insights that prompted a change to the trial testing schedule. This enabled the client to continue the trial with the Asian subpopulation included and, ultimately, to proceed to a new drug application without a safety exclusion. Unrestricted commercial capability, particularly in Asia, could be worth as much $30B USD over the drug's lifetime.

Learn more about our
drug development solutions at
www.covance.com

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The Americas + 1.888.COVANCE
(+1.888.268.2623) + 1.609.452.4440
Europe / Africa + 00.800.2682.2682 +44.1423.500888
Asia Pacific + 800.6568.3000 +65.6.5686588

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