DATE: October 26, 2023

FROM: Char-Dell Edwards, MT (ASCP), Consumer Safety Officer
Bioresearch Monitoring Branch (BMB)
Division of Inspections and Surveillance (DIS)
Office of Compliance and Biologics Quality (OCBQ)

THROUGH: Dennis T. Cato, Branch Chief, BMB

THROUGH: Carrie M. Mampilly, MPH, Director, DIS

TO: Catherine Tran, MS, RPM
Karin Knudson, PhD, Chair
Lianne Hu, PhD, MD, MPH, MS, Clinical Reviewer

SUBJECT: Bioresearch Monitoring Final Discipline Review
SPONSOR: Iovance Biotherapeutics, Inc.
PRODUCT: Lifileucel (AMTAGVI)
BLA: STN 125773/0

FINAL SUMMARY STATEMENT:
Bioresearch Monitoring (BIMO) inspection assignments were issued for the sponsor and three clinical investigators (CI) who participated in the conduct of study protocol C-144-01. The inspections did not reveal substantiative issues that impact the data submitted in this original Biologics License Application (BLA).

BACKGROUND:
The sponsor and three US CI study sites for protocol C-144-01 were identified for BIMO inspections. The BLA review committee concurred with the proposed sites. The sites were selected based upon sponsor-reported deaths, complaint of non-compliance, adverse events, protocol deviations, number of subjects enrolled, financial disclosure, and previous BIMO inspection histories.

The inspections were conducted in accordance with FDA's Compliance Programs (CP) 7348.811, Inspection Program for CI and CP 7348.810, Sponsors, Contract Research Organizations and Monitors. Information submitted in the BLA was compared to source documents at each inspected site. The inspection assignment also included specific questions concerning the clinical studies.

PROTOCOL:
C-144-01: A Phase 2, Multicenter Study to Assess the Efficacy and Safety of Autologous Tumor Infiltrating Lymphocytes (LN-144) for Treatment of Subjects with Metastatic Melanoma

The sponsor reported that a total of 50 sites screened subjects for participation in this study: United States (23), France (3), Germany (9), Hungary (1), Spain (8), Switzerland (2), and the United Kingdom (4). Of these, 42 sites enrolled subjects: United States (21), France (2), Germany (8), Hungary (1), Spain (5), Switzerland (1), and United Kingdom (4). As of the data cutoff date (September 15, 2021), the number of subjects planned/infused with Lifileucel (LN-144) were an approximate total of 171/179 (Cohort 1,2, and 4) and 10/11 (Cohort 3 re-treatment).

BIMO INSPECTIONS SUMMARY:

A Form 483 was issued to site 019 (see Clinical Investigator Issues). No significant BIMO inspectional findings were noted for sites 003, 004, and the sponsor. The table below summarizes site information and outcomes from BIMO inspections:

Site ID	Firm Name	Location	FDA Form 483 Issued	Final Classification
003	Amod Sarnaik, MD	Tampa, Florida	No	No Action Indicated (NAI)
004	Harriet Kluger, MD	New Haven, Connecticut	No	NAI
019	Karl Lewis, MD *	Aurora, Colorado	Yes	Voluntary Action Indicated (VAI)
Sponsor	Iovance Biotherapeutics, Inc.	San Carlos, California	No	NAI

* Dr. Theresa M. Medina, MD replaced Dr. Karl Lewis on 11/21/2022.

CLINICAL INVESTIGATOR ISSUES:

A Form FDA 483 was issued to Dr. Theresa M. Medina at site 019 for three inspectional observations.

1. An investigation was not conducted in accordance with the signed statement of investigator and investigational plan.
2. Failure to prepare or maintain adequate and accurate case histories with respect to observations and data pertinent to the investigation.
3. A copy of the written consent form which had been approved by the IRB and signed and dated by the subject or the subject's legally authorized representative, was not provided to the subject or the subject's legally authorized representative at the time of consent.

All observations were satisfactorily addressed through a written response from the CI.

SPONSOR ISSUES:

No significant sponsor issues were observed during the inspection.

FINANCIAL DISCLOSURE:

The CI CP directs the FDA investigator to ask the CI if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouse(s), and dependent children, as well as if and when the information was last updated. The information submitted to the BLA was verified for each of the inspected clinical study sites.

ADMINISTRATIVE FOLLOW-UP:
Post inspection correspondence was issued to the inspected parties. Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please email Char-Dell.Edwards@fda.hhs.gov or call (240) 402-2859.

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Char-Dell K. Edwards, BS, MT(ASCP)
Consumer Safety Officer

DISTRIBUTION

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