MONITORING VISIT REPORT

VISIT INFORMATION

Protocol Title:	A Randomized, Open-Label, Multicenter, Phase 3 Trial Comparing Veliparib Plus Carboplatin and Paclitaxel Versus Investigator's Choice of Standard Chemotherapy in Subjects Receiving First Cytotoxic Chemotherapy for Metastatic or Advanced Non-Squamous Non-Small Cell Lung Cancer (NSCLC) and Who Are Current or Former Smokers
Protocol Name:	M14-359
Site Name / Site #:	CBCC Global Research Inc. / SITE-022
Site Address:	Bakersfield, USA
Site Activation Date:	2024-05-16
Monitoring Visit Date:	2024-08-12
Visit Type:	On-Site
CRA:	CRA-004

SUMMARY OF MONITORING VISIT

This Monitoring Visit Report documents the second monitoring visit (IMV) conducted at CBCC Global Research Inc. for Protocol M14-359 (Veliparib Phase 3 NSCLC). The primary objective of this visit was to perform 100% Source Document Verification (SDV) for the two (2) subjects currently enrolled and randomized, review the Investigator Site File (ISF) for essential document compliance, and verify Investigational Product (IP) accountability. The site has screened and randomized two subjects (SUBJ-001 and SUBJ-002) since activation on 2024-05-16. Both subjects have technically 'completed' the study participation phase as per the database status, which was verified during this visit as early discontinuation due to rapid disease progression (PD) confirmed by RECIST 1.1 criteria in both cases.

A comprehensive review of the Regulatory Binder/ISF was conducted. While the majority of essential documents are present and ALCOA+ principles are generally adhered to, a Critical Finding was identified regarding Investigational Product storage. A temperature excursion occurred in the ambient storage cabinet on June 04, 2024, which was not reported to the Sponsor within the required 24-hour window as per Protocol Section 5.2. Additionally, two minor findings were noted: a discrepancy in the Date of Visit (DOV) transcription for SUBJ-002's Cycle 1 Day 1 visit, and a missing updated CLIA certification for the local safety lab in the ISF. These issues were discussed in detail with the Study Coordinator and Principal Investigator during the visit.

Despite the findings, the site staff demonstrates a high level of engagement and clinical competence. The Principal Investigator, Dr. Patel, was available for the close-out discussion and acknowledged the breakdown in the IP excursion reporting process. A Corrective and Preventive Action (CAPA) plan was drafted on-site to address the communication gap regarding temperature monitoring. Data entry in the EDC is timely, with queries resolved within 48 hours on average. The focus for the next visit will be to ensure the CAPA for IP management is fully implemented and to monitor the recruitment strategy to meet the target enrollment of 24 subjects.

Overall Impression:

The site is performing adequately regarding clinical care and data entry, but immediate remediation is required regarding IP storage compliance and safety reporting workflows.

Exit Interview Comments:

Discussed the Critical Finding regarding the unreported temperature excursion. Dr. Patel acknowledged the oversight and instructed the SC to re-train all staff on the 'IP Management Plan' v2.0 immediately. The missing CLIA certificate was requested from the lab manager during the visit. The transcription error for SUBJ-002 was corrected in the EDC during the visit.

URGENT ISSUES

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Yes

A. CRITICAL: Unreported Temperature Excursion. On 04-JUN-2024, the ambient drug storage thermometer (S/N: T-992) recorded a maximum temperature of 28.5°C (Limit: 25.0°C) for a duration of 4 hours. This excursion was not reported to the Sponsor/IVRS system. IP is currently quarantined pending stability assessment.

PERSONS PRESENT

Name	Position/Title
Dr. Ravi Patel	Principal Investigator
Sarah Jenkins	Study Coordinator
Michael Chen	Pharmacist

ENROLLMENT STATUS

Screened:	2
Consented:	2
Pre Randomization Failure:	0
Randomized:	2
Completed:	2
Ongoing:	0
Withdrawn:	0

Recruitment Plan Notes:

The site has enrolled 2 subjects against a target of 24. Recruitment has stalled slightly in July. The PI noted that the specific inclusion criteria regarding 'current or former smokers' with non-squamous histology is limiting the pool, as many candidates have squamous histology. We reviewed the pre-screening log; 15 patients were reviewed, 13 failed pre-screen. The site remains committed to the target.

Recruitment Rate Adequate? Yes

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MONITORING CHECKLIST

Informed Consent

1	Is the current IRB/EC-approved ICF version being used?	Yes	Version 3.0 verified as current.
2	Was ICF signed prior to any study-specific procedures?	Yes	Verified via source notes and time-stamps for SUBJ-001 an
3	Is the correct version of the ICF signed and dated by the subject and person obt	Yes	Signatures are present and personally dated.
4	Is re-consent required for any subjects?	No	No new ICF amendments since activation.

Site Staff/Facilities

5	Is the Principal Investigator available for supervision?	Yes	Dr. Patel met with CRA at 14:00 for 30 minutes.
6	Are Sub-Investigators qualified and delegated appropriately?	Yes	CVs and medical licenses for Dr. Smith (Sub-I) are current i
7	Is the Study Coordinator trained on the protocol?	Yes	S. Jenkins training log verified. Completed EDC training 202
8	Are pharmacy facilities adequate?	No	Generate CAPA for temp monitoring.
9	Is the laboratory certified (CLIA/CAP)?	No	Obtain current CLIA.
10	Is equipment calibrated and maintained?	Yes	ECG and Centrifuge calibration records reviewed. Current.
11	Is the Delegation of Authority Log current?	Yes	Updated to include new phlebotomist on 2024-06-15.
12	Is the Training Log complete for all staff?	Yes	All staff signed off on Protocol v3.0 training.
13	Are CVs current and signed?	Yes	PI and Sub-I CVs signed within last 2 years.

ISF / Monitoring

14	Is the Investigator Site File (ISF) complete?	Yes	Binder is well organized. Tabs 1-15 reviewed.
15	Are essential documents current?	Yes	FDA 1572 matches current staff list.
16	Is the Site Visit Log signed?	Yes	Signed by CRA and SC upon arrival.
17	Are prior visit follow-up items complete?	N/A	First monitoring visit.

Research Ethics Board

18	Is IRB/EC approval current?	Yes	WIRB approval letter dated 2024-04-15 present.
19	Are protocol amendments approved?	Yes	Amendment 2 approved.
20	Are safety reports submitted to IRB?	Yes	IND Safety Reports submitted via portal. Receipts filed.
21	Is annual renewal current?	N/A	Study started <1 year ago.
22	Is site-specific consent approved?	Yes	Approved 2024-04-20.
23	Is SAE reporting compliant with IRB requirements?	Yes	No SAEs to date, but process is in place.

Safety

24	Is AE reporting timely?	Yes	Grade 1 Nausea (SUBJ-001) reported in source and EDC.
25	Are SAEs followed to resolution?	N/A	No SAEs reported.
26	Is pregnancy reporting compliant?	N/A	No pregnancies.
27	Are protocol deviations documented?	Yes	One minor deviation (missed vital sign timepoint) logged.
28	Is the safety database reconciled?	Yes	EDC matches source for AEs.
29	Are SUSAR notifications timely?	Yes	Filed in ISF.
30	Are DSMB recommendations implemented?	N/A	No DSMB letters yet.
31	Is risk-benefit assessment current?	Yes	IB v4.0 in place.

Compliance

32	Is protocol compliance acceptable?	Yes	Adherence to inclusion/exclusion criteria verified for 2 sub
33	Is GCP compliance maintained?	Yes	Source documentation meets ALCOA+ standards.
34	Is regulatory compliance current?	Yes	FDA 1572 and Financial Disclosures are current.

Study Investigational Product

35	Is IP storage adequate?	No	Quarantine affected IP.
36	Is IP accountability current?	Yes	Logs updated for all dispensed kits.
37	Is IP dispensing correct?	Yes	IWRS confirmation matches dispensing logs.
38	Are IP returns documented?	Yes	Used vials from SUBJ-001 returned and counted.
39	Is temperature monitoring compliant?	No	Report to Sponsor immediately.

Study Supplies/Vendors

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40	Are lab kits/supplies adequate?	Yes	Inventory checked. Sufficient kits for next 3 months.
SDV & Review			
41	Are source documents available?	Yes	EMR access granted to CRA.
42	Is SDV completed per plan?	Yes	100% SDV for SUBJ-001 and SUBJ-002.
43	Are data discrepancies identified?	Yes	Query issued.
44	Does CRF data match source?	Yes	Generally yes, aside from noted discrepancy.
45	Is query resolution timely?	Yes	No open queries > 1 week.
46	Are data corrections documented?	Yes	Audit trail in EDC confirms authorized corrections.

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SOURCE DOCUMENT VERIFICATION & CHART REVIEW

Subject	Visits Reviewed	Comments	Action Required
SUBJ-001	Screening, C1D1, C2D1, EO	Subject is a 64-year-old male, former sm	None
SUBJ-002	Screening, C1D1, EOT	Subject is a 58-year-old female, former	Site to correct C1D1 visit date.

CRA ASSESSMENT

Overall, CBCC Global Research Inc. is operating at a satisfactory level regarding patient safety and data integrity, with the notable exception of the Investigational Product temperature excursion management. The site staff are experienced and the documentation for the two enrolled subjects was thorough, logically organized, and compliant with ALCOA+ principles. The rapid progression of both subjects is unfortunate but appears consistent with the advanced disease state of the enrolled population (Stage IV NSCLC) and does not immediately suggest a site-specific quality issue, though I have flagged this for the Medical Monitor's awareness.

The critical finding regarding the unreported temperature excursion (28.5°C on 04-JUN) indicates a gap in the site's standard operating procedure for checking the 'Min/Max' memory on the digital thermometer. The site staff had been recording the 'Current' temperature daily but failing to check the memory for overnight excursions. The re-training initiated during this visit is expected to resolve this. I have confidence in the site's ability to rectify this issue given the PI's immediate involvement.

Recruitment is currently slow (2 subjects in 3 months vs target of 24), but the site has a robust pre-screening log. I reviewed the log and confirmed that the high screen failure rate is due to valid protocol exclusion criteria (specifically histology requirements) rather than lack of effort. I recommend continuing close monitoring of the IP logs and recruitment rate at the next visit, tentatively scheduled for October 2024.