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 #:	California Cancer Associates for Research and Excellence / SITE-033
Site Address:	Encinitas, USA
Site Activation Date:	2024-05-11
Monitoring Visit Date:	2025-06-20
Visit Type:	On-Site
CRA:	CRA-007

SUMMARY OF MONITORING VISIT

This Remote Monitoring Visit (Visit 6) was conducted for protocol M14-359 at California Cancer Associates for Research and Excellence (Site 033) on 20-Jun-2025. The primary objectives were to review subject safety, verify data accuracy against source documentation, and assess overall site compliance with the protocol and ICH-GCP. As the newly assigned Clinical Research Associate (CRA-007) for this site, this visit also served as an introductory assessment of site operations and filing systems. New CRA notes this is first visit to the site; familiarity with site operations still developing. While the site has met enrollment targets (21 randomized), the focus of this visit shifted significantly toward data quality remediation due to a backlog of monitoring activities.

During the review, it became evident that a significant volume of data entry and source generation occurred without adequate oversight in the preceding period. Although a visit was recorded in May, the depth of review appears to have been insufficient to address the accumulating data load. Consequently, this visit is effectively the first comprehensive review after a 3+ month monitoring gap. A backlog of overdue queries was discovered -- 12 queries aged >30 days identified during SDV review. Furthermore, the Electronic Data Capture (EDC) audit trail revealed numerous data corrections made without monitor oversight during the gap period, often lacking documented justification in the source notes. This raises concerns regarding GCP compliance and data integrity, specifically regarding the 'ALCOA+' principles of attributability and contemporaneousness.

Source Data Verification (SDV) identified significant discrepancies accumulated during the monitoring gap -- 8 subjects with CRF data not matching source documents. These discrepancies primarily involve concomitant medication start/stop dates and grading of adverse events. Additionally, the Investigator Site File (ISF) was found to be incomplete; several documents (specifically lab reports and safety correspondence) generated during the gap period were not filed. Urgent issues were identified regarding the accumulated data quality debt, which requires an immediate remediation plan. The site staff has been cooperative but appears overwhelmed by the administrative burden of the closed/completed subjects. A follow-up call is scheduled for next week to track the resolution of the 8+ Action Required items generated from this visit.

Overall Impression:

The site is struggling with a significant administrative backlog and data quality issues resulting from a period of reduced oversight; immediate remediation is required to bring the database and ISF to audit-ready status.

Exit Interview Comments:

Discussed the backlog with the SC and PI. The PI acknowledged the delay in query resolution, citing staffing changes at the site level. The SC committed to dedicating two full days next week to address the 12 overdue queries and file the loose regulatory documents. The remediation plan for the data discrepancies was agreed upon.

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URGENT ISSUES

Yes

A. Accumulated data quality debt requires immediate remediation plan.

B. 12 overdue queries, including 5 aged >45 days, requiring immediate PI attention.

PERSONS PRESENT

Name	Position/Title
Dr. Sarah Miller	Principal Investigator
Jessica Thorne	Study Coordinator

ENROLLMENT STATUS

Screened:	33
Consented:	25
Pre Randomization Failure:	8
Randomized:	21
Completed:	18
Ongoing:	3
Withdrawn:	0

Recruitment Plan Notes:

Enrollment target of 21 subjects has been met. Recruitment is closed. Focus is now on subject retention and data cleaning for the 3 ongoing subjects and 18 completed subjects.

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 is currently in use.
2	Was ICF signed prior to any study-specific procedures?	Yes	Verified for ongoing subjects SUBJ-019, SUBJ-020, and SU
3	Is the correct version of the ICF filed in the subject binder?	Yes	All reviewed subjects have the correct original signed docur
4	Is re-consent required for any protocol amendments?	N/A	No new amendments requiring re-consent since last visit.

Site Staff/Facilities

5	Is the Principal Investigator available for supervision?	Yes	PI participated in the exit interview.
6	Are Sub-Investigators qualified and delegated appropriately?	Yes	Delegation log reviewed; Sub-Is are current.
7	Is the Study Coordinator trained on the current protocol?	Yes	Training logs are up to date.
8	Are pharmacy facilities adequate for IP storage?	Yes	Access is restricted and temperature controlled.
9	Is the laboratory certified (CLIA/CAP) and current?	Yes	Current certifications filed in ISF.
10	Is site equipment calibrated and maintained?	Yes	Calibration logs for centrifuge and freezer reviewed.
11	Is the Site Delegation Log current and signed?	Yes	Log is current.
12	Is the Site Training Log complete for all staff?	Yes	All active staff have documented training.
13	Are CVs current and signed for all key staff?	Yes	CVs are within the 2-year validity period.

Investigator Site File / Monitoring Activities

14	Is the Investigator Site File (ISF) complete and up to date?	No	SC to file loose documents in the ISF by 30-Jun-2025.
15	Are essential documents current (FDA 1572, Financial Disclosure)?	Yes	Documents are current.
16	Is the Site Visit Log signed by the monitor?	Yes	Signed electronically for this remote visit.
17	Are follow-up actions from prior visits complete?	No	SC to resolve 3 legacy actions regarding SUBJ-004 con-me

Research Ethics Board

18	Is IRB/EC approval current for protocol and ICF?	Yes	Approval is valid through 2026.
19	Have all protocol amendments been approved?	Yes	Amendment 4 approval is on file.
20	Have safety reports been submitted to the IRB/EC?	Yes	IND safety reports submitted per local requirements.
21	Is the annual renewal/continuing review current?	Yes	Last renewal approved Jan 2025.
22	Is the site-specific consent form approved?	Yes	Approved and in use.
23	Is SAE reporting compliant with IRB requirements?	Yes	No late reports noted.

Safety

24	Are Adverse Events (AEs) reported in a timely manner?	No	SC to enter missing AEs for SUBJ-015 and SUBJ-018.
25	Are SAEs followed to resolution?	Yes	All reported SAEs are closed or stabilizing.
26	Is pregnancy reporting compliant?	N/A	No pregnancies reported.
27	Are protocol deviations documented?	Yes	Deviations log is present, though some data entry errors sh
28	Is the safety database reconciled with the EDC?	No	Reconcile AE dates for SUBJ-012.
29	Are SUSAR notifications acknowledged and filed?	Yes	Filed in ISF.
30	Have DSMB recommendations been implemented?	Yes	No new recommendations.
31	Is the risk-benefit assessment current?	Yes	PI confirms assessment remains favorable.

Compliance

32	Is protocol compliance acceptable?	Yes	General adherence is good, despite data entry lags.
33	Is regulatory compliance current?	Yes	No regulatory expirations noted.
34	Is GCP compliance maintained?	No	PI to provide signed note to file explaining data correction

Study Investigational Product

35	Is IP storage adequate and secure?	Yes	Stored in locked pharmacy, ambient temperature.
36	Is IP accountability current?	Yes	Logs match physical inventory.
37	Is IP dispensing correct per protocol?	Yes	Dispensing verified for ongoing subjects.
38	Are IP returns documented?	Yes	Returns from completed subjects are logged.
39	Is temperature monitoring compliant?	Yes	Excursion logs reviewed; no excursions.

Study Supplies/Vendors

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40	Are lab kits and supplies adequate?	Yes	Inventory sufficient for remaining visits.
Source Document Verification & Review			
41	Are source documents available for all subjects?	Yes	EMR access provided.
42	Was SDV completed per the monitoring plan?	Yes	100% SDV performed for active subjects; targeted review fo
43	Are data discrepancies identified?	Yes	Numerous discrepancies found due to lack of oversight.
44	Does CRF data match source documents?	No	See Item 45.
45	Are significant SDV discrepancies noted?	No	SC to correct data for listed 8 subjects.
46	Is query resolution timely?	No	SC/PI to answer all 12 overdue queries by 27-Jun-2025.

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SOURCE DOCUMENT VERIFICATION & CHART REVIEW

Subject	Visits Reviewed	Comments	Action Required
SUBJ-009	Visit 12	Data correction made to AE Grade without	Query issued.
SUBJ-011	Visit 10-12	Hematology values in EDC do not match th	Query issued.
SUBJ-015	Unscheduled Visit	Grade 1 Nausea noted in nursing notes bu	SC to enter AE.
SUBJ-020	Visit 4	Weight recorded as 72kg in source, enter	Query issued.

FOLLOW-UP FROM PRIOR VISIT

Action: Provide stop dates for SUBJ-004 concomitant medications | Status: Open | Action remains unresolved >3 months.
Action: Upload missing CV for Sub-I Dr. Evans | Status: Resolved | CV uploaded to portal.
Action: Clarify AE start time for SUBJ-004 | Status: Open | Query remains unanswered.

CRA ASSESSMENT

This visit highlighted a significant degradation in data quality and regulatory filing hygiene, likely attributable to the monitoring gap and lack of recent oversight. While the site is enrolling well and patient safety does not appear compromised, the 'data debt' is substantial. The presence of 12 overdue queries and 8 subjects with significant SDV discrepancies indicates that the site staff have fallen behind on administrative duties. The new CRA notes this is first visit to the site; familiarity with site operations still developing, but it is clear that the Study Coordinator requires more frequent check-ins to clear this backlog. I have established a weekly call schedule for the next month to ensure the remediation plan is executed. The site is rated as 'Requires Improvement' due to the volume of overdue actions and data corrections lacking justification.