EDA-GCP Public Inspection Report (PIR) of Clinical Trial Site

Part 1	**General information**
Clinical medical research site details	
CT site information	
Name of CT site	Assiut University, Faculty of Medicine, Clinical Oncology Department
Address of inspected CT site	Clinical Oncology Department, Assiut University Hospital, Al Walideyah St, Assiut, 71511, Egypt
Inspection details	
Dates of inspection	7 March 2024
Type of inspection	Routine Inspection
Introduction	
General information about the sponsor and CT site	The inspected site is the Clinical Oncology Department, Assiut University Faculty of Medicine, conducting clinical studies for the sponsor (AstraZeneca) through CRO (IQVIA) Principal Investigator: Professor Dr. Samir Shehata. Inspection scope: Routine surveillance of GCP compliance, including verification of compliance with the protocol, GCP procedures, and applicable regulatory requirements.
Brief report on inspection activities undertaken	
Scope and limitations	
Areas inspected	· Clinical operations (screening, dosing, follow-up) · Informed Consent Process · Investigational Medicinal Product (IMP) management · Pharmacy / IMP storage area · Source documents and Case Report Forms (CRFs) · Archiving and documentation system · Quality management system
Out of scope	None specified.
Inspected Clinical medical research	A Phase III, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study of Durvalumab Monotherapy or in Combination with Bevacizumab as Adjuvant Therapy in Patients with Hepatocellular Carcinoma Who Are at High Risk of Recurrence After Curative Hepatic Resection or Ablation (EMERALD-2) Protocol Number: D910 DC00001 Trial ID: EMERALD-2 Phase: III EudraCT Number: 2018-004105-85 EDA Approval: 19/5/2022

Type of IMP	Biological-Monoclonal Antibody (Durvalumab) ± Bevacizumab (Biological / Monoclonal Antibody) vs. Placebo – Adjuvant therapy administered intravenously
Part 2	
1. Facilities and equipment system	
1.1.Facilities and Trial Conduct	The trial site at the Clinical Oncology Department, Assiut University Hospital was confirmed to have adequate facilities and equipment to support the conduct of the trial, including a reception and waiting area, an examination room, a consultation room, a counseling room, a procedure room, a consenting/examination room, a procedure room, an archiving room, and a pharmacy/investigational product storage room. - A designated examination room, consultation room, and procedure room were all available and rendered operational. - Procedure Room: An emergency trolley equipped with emergency medications was placed and made readily available at the procedure area. - The study records were safely kept in a fire & waterproof (metal) cupboard and were secured against unauthorized access. - A dedicated Pharmacy/Investigational product storage room was established at the site; however, it was not inspected since there was no IMP at the site during the inspection time. - Multiple calibration documentation discrepancies were identified for the protocol specified equipment (Sphygmomanometer, ECG, Weight scale, CT device, Endoscopy device, Refrigerator and Thermometer). As per CAPA implementation for each device, valid calibration certificates were obtained, calibration labels were affixed, and all certificates and labels were reconciled and filed in the site master file. All equipment was confirmed to be within valid calibration periods, and procedures were reinforced to ensure consistent maintenance of calibration documentation in compliance with ICH-GCP.
1.1. Computerized system	Electronic data capture via eCRF and randomization systems were in use and confirmed to be functioning correctly.
2. Pharmaceutical Quality System	
2.1.Quality Management System	-The site had a quality assurance system described in SOPs, including Standard Operating Procedure for Site Initiation, Activation, Conduct, and Close-out, Delegation of Authorities, Reviewing and Obtaining Informed Consent Form, Managing Investigational Product, Safety Reporting, and Source Documentation. -The study has been monitored according to the monitoring plan. -IMP Handling instructions were verified and confirmed to be available. -Shipping of IMPs to investigation site and handling passive system shipper SOPs were verified and confirmed to be in place.

2.2.SOPs and Documentation	-The following key essential documents were verified at the site: Signed study protocol, Investigator Brochure, Informed Consent Forms, Case Report Forms of eCRFs, Valid Insurance Certificate, IRB approval, and EDA approval. -No SOP for SAE reporting was available at the time of inspection; the site had been following approved Protocol and local regulation for SAE reporting. As per CAPA implementation, A dedicated SAE reporting SOP was developed, approved, implemented, filed in the site master file, and all relevant staff were trained on its content in compliance with ICH-GCP E6.
2.3. Deviation Management	-Protocol deviations were handled per available SOPs and documented in the protocol deviation log. -The protocol deviations were identified and captured in the protocol deviation list -This protocol deviation was acknowledged, documented, and reported to the sponsor.
2.4. CAPA System	A CAPA system was in place. The site was required to address all observations and submit CAPA and supportive documentation as proof of correction, in the proposed time schedule for corrections. The identified findings were appropriately addressed by the site through corrective& preventive actions.
3. Ethics and Participant Protection	
3.1. Informed Consent Process	-The process of participants' recruitment and consenting was explained by the PI. The consenting process was verified to be in line with GCP principles. -The informed consent process was reviewed. The approved informed consent forms were used throughout the study and were confirmed that it was IRB-approved versions. All informed consents were signed by participants prior to the performance of any study-related procedures, in full compliance with GCP guidelines. The procedure for obtaining informed consent from participants was confirmed to be fully in line with the requirements of GCP guidelines -Some of the study questionnaire did not complete due to illiteracy of participant, in compliance with the ICF. As a corrective action, the ICF was modified to exempt illiterate patients from completing IPRO questionnaires.
3.2.Ethics Committee Approval	IRB Approvals: on 15/12/2021. All approvals were confirmed to be available, current, and filed appropriately in the site master file.
3.3. Participant Safety	-Safety monitoring procedures were in place, and the sponsor demonstrated appropriate oversight of participant safety throughout the trial. -One SAE was reported and the initial report was sent to the sponsor within reported timeline. The event resolved upon discontinuation of the study drug. The investigator assessed a reasonable possibility of a causal relationship between the study therapy (Bevacizumab/Placebo) and the event. -The SAE was reported to the sponsor within the protocol-specified timeline.

	-The emergency trolley was available at the site and was checked for completeness, expiry of contents, and functionality in accordance with site procedures, supporting the site's readiness to manage medical emergencies during participant visits.
4. Personnel and Training	
4.1. Training and qualifications	-Curriculum Vitae of the Principal Investigator, Co-Investigator(s), and Site Coordinator were confirmed to be available at the site, up to date, and filed appropriately in the Investigator Site File in compliance with GCP requirements. -GCP training records and workloads for all staff who took part in the conduct of the clinical trial were verified and filed at the site. Protocol-specific training records were reviewed and retained in the Investigator Site File.
5. Investigational Product (IMP) Management	
5.1. IMP handling	-Storage of the investigational product during the conduct of the trial was confirmed to be compliant with protocol requirements. -Shipping records of the IP detailing quantity and batch numbers were verified during the inspection and confirmed to be complete and accurate. -Transportation procedure was verified and confirmed to be in place. -Dispensing of IP by a registered pharmacist and administration by a registered physician were confirmed during the inspection. -IMP Handling instructions were all verified and confirmed to be available and implemented.
6. Clinical Trial Conduct	
6.1. Protocol Compliance	-Approved study protocol (V.3 dated: 19/02/2022) was confirmed to be implemented at the site. -Based on the documents reviewed, facilities inspected, and considering the findings of the inspection, study D910 DC00001 (EMERALD-2) was conducted in compliance with GCP as prescribed in the ICH Guide to GCP. -The inspectorate was satisfied that the principal investigator at the clinical trial site (Clinical Oncology Department, Assiut University) was in control to ensure that the clinical trial was conducted in compliance with GCP requirements.
6.2. Source Data and CRFs	-Participant records were available for verification and were maintained in an organized and accessible manner throughout the inspection period. -Source data were confirmed to be legible, well organized, and maintained throughout the study. -For missing documentation for pre-medications and concomitant medications across treatment cycles was identified and corrected. As Concomitant medication records were reviewed, updated, and completed for all relevant cycles in compliance with ICH-GCP.

	-multiple source document corrections that could potentially affect data integrity were identified and fully addressed. All affected source documents were reviewed and corrected in compliance with GCP standards, ensuring each correction was made with a single line, initialed, dated, and explained where necessary to maintain traceability and legibility in compliance with ICH-GCP -Site staff was trained on GDP
6.3. Delegation of Duties	The delegation log was confirmed to be available, accurately completed, signed by the PI, and reflective of the actual roles and responsibilities assigned to each study team member.

7. Laboratory and Bioanalytical Activities (if applicable)

- Site Laboratory: Not applicable, as all laboratory tests were performed at an external laboratory
- The laboratories involved in the study were appropriately accredited, and laboratory facilities were available to support protocol-required testing.
- Laboratory procedures were generally defined in the laboratory manuals maintained in the Investigator Site File (ISF), together with the applicable laboratory reference ranges to ensure accessibility by the study personnel during trial conduct.
- Sample handling and analysis were reviewed.
- Laboratory activities were generally conducted in accordance with the study protocol, Good Clinical Practice (GCP), and applicable regulatory requirements, and no deficiencies related to laboratory or bioanalytical activities were identified.

8. Safety Reporting (SAE)

-A dedicated SAE SOP was developed, approved, implemented, and all relevant staff were trained on its content in compliance with ICH-GCP.
-SAE was reported to the sponsor within the protocol-specified timeline. SAE reporting to Bio Inn-EDA was within the specified time.

Part 3	**Inspection outcome**
Based on the reviewed documentation, inspected facilities, and findings of the routine GCP inspection conducted at the Clinical Oncology Department, Assiut University Hospital on 7 March 2024: The inspectorate was satisfied that the principal investigator at the clinical trial site (Clinical Oncology Department, Assiut University) was in control to ensure that the clinical trial, protocol number D910 DC00001 (EMERALD-2), was conducted in compliance with GCP as prescribed in the ICH Guide to GCP. As a comprehensive CAPA response addressing all findings and recommendations was prepared and submitted by the applicant within the defined timeline, with supportive documentation as proof of correction for each identified observation. This EDA-GCP-PIR remained valid until the next inspection, provided no critical findings, safety concerns, or regulatory actions arise.	
Part 4	**List of national Laws and GCP Guidelines referenced in the inspection report**

1. Law of Regulating Clinical Medical Research no.214/2020.
2. Prime Minister's Decree No. 927 of 2022 On Promulgating the Executive Regulation of Law on Regulating Clinical Medical Research Promulgated by Law No. 214 of 2020
3. EDA Chairman Decree No.111 for 2022.
4. Guideline for Good Regulatory Oversight of Clinical Trials by Egyptian Drug Authority "EDREX.GL.Bioinn.006".
5. Guideline for Good Clinical Practice ICH E6R3.
6. Declaration of Helsinki
7. WHO Handbook for Good Clinical Research Practice (GCP) -Guidance for Implementation

Abbreviation	
ALCOA	Attributable, Legible, Contemporaneous, Original, Accurate
CAPA	Corrective and Preventive Action
CRF	Case Report Form
CRC	Clinical research Center
CT	Clinical Trial
EDA	Egyptian Drug Authority
GCP	Good Clinical Practice
GDP	Good Documentation Practice
ICF	Informed Consent Form
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International conference of Harmonization
IMP	Investigational Medicinal Product
IRB/IEC	Institutional Review Board / Ethics Committee
MOH	Ministry of Health
PI:	Principal Investigator
PIR	Public Inspection Report
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
WHO	World Health Organization
ALCOA	Attributable, Legible, Contemporaneous, Original, Accurate
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