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	Egyptian Liver Research Institute and Hospital "8704"
Address of inspected CT site	Sherbin, Mansoura, Damietta highway, Dakahlia
Inspection details	
Dates of inspection	17 August 2024
Type of inspection	Routine
Introduction	
General information about the sponsor and CT site	- The inspected site is a Clinical Trial Site (**Egyptian Liver Research Institute and Hospital**) that conducts clinical studies for the sponsor (**AstraZeneca**) in accordance with applicable regulatory requirements and ethical standards. - PI name: **Prof. Dr. Gamal Shiha** - Activities include participant recruitment, clinical conduct, sample collection, safety monitoring, and data documentation.
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 - Bioanalytical / laboratory facilities (if applicable) - Source documents and Case Report Forms (CRFs) - Archiving and documentation system - Quality management system
Out of scope	Not defined
Inspected Clinical medical research	The inspection focused on the following study(ies): - Protocol Title: A Phase III, Randomized, Open-Label, Sponsor-Blinded, Multicenter Study of Durvalumab in Combination with Tremelimumab ± Lenvatinib Given Concurrently with Transarterial Chemoembolization (TACE) Compared to TACE Alone in Patients with Locoregional Hepatocellular Carcinoma - Protocol Number: D910VC00001 (EMERALD-3) -Phase: III

	- EDA initial approval date: 08/02/2024
Type of IMP	Biological Monoclonal antibody (Durvalumab)
Part 2	
1. Facilities and equipment system	
1.1. Facilities and Trial Conduct	- The site facilities were generally adequate for trial conduct. - Equipment maintenance, calibration, and emergency preparedness were in place. -Dedicated consenting/examination and procedure rooms were available for study-related activities. The medical equipment used during the trial, including thermometers, sphygmomanometers, ECG, patient monitor, CT scanner, centrifuges, and ultra-low temperature freezers, had valid calibration records. -An emergency trolley and emergency equipment were available in the procedure room. However, Deficiencies were identified in the management and control of emergency equipment at the site **according to ICH E6(R2) guideline**, specifically the absence of calibration documentation for the DC shock device and inadequate access control of the emergency trolley, both of which indicated shortcomings in equipment maintenance practices. In response, the sponsor implemented a comprehensive corrective and preventive action plan that encompassed calibration of the DC shock device with full supporting documentation, repair of the emergency trolley lock to restore appropriate access control, verification of all corrective actions through a subsequent on-site monitoring visit to confirm sustained compliance, and retraining of relevant site personnel on equipment calibration procedures and emergency trolley maintenance protocols to prevent recurrence. The submitted CAPA was reviewed by EDA and considered acceptable. -A dedicated, access-controlled pharmacy was available for investigational medicinal product (IMP) storage and dispensing, with IMPs stored under the required storage conditions and monitored using calibrated temperature monitoring systems. -Participant records and essential study documents were maintained in secure, access-controlled archiving room.
1.2. Computerized system	Electronic data capture, as eCRF and randomization systems were in use.
2. Pharmaceutical Quality System	

2.1. Quality Management System	The site has established a Quality Management System supported by SOPs governing trial conduct, documentation, safety reporting, and IMP handling to ensure compliance with GCP principles, ethical standards, and regulatory requirements. The system aims to ensure participant safety, rights, and data integrity.
2.2. SOPs and Documentation	The site maintains SOPs governing clinical trial activities. Documents are controlled, periodically reviewed, and implemented. During the inspection, essential trial documents were reviewed and verified, including the approved protocol and amendments, regulatory and ethics committee approvals, investigator qualifications and training records, confidentiality agreements, insurance certificates, contractual agreements, laboratory accreditation certificates, monitoring reports, informed consent forms, Investigator's Brochure, delegation logs, pharmacy and laboratory manuals, investigational product management records, safety reports, progress reports, participant logs, and other study-specific essential documents.
2.3. Deviation Management	Deviations were handled according to SOPs. Documentation of deviations, investigations, and CAPA was generally adequate. Some deficiencies were noted
2.4. CAPA System	A CAPA system was established at the site. CAPA responses for findings identified during this inspection were submitted by the site and evaluated by EDA inspectors. The identified findings were appropriately addressed by the site through corrective and preventive actions
3. Ethics and participant Protection	
3.1. Informed Consent Process	The informed consent process was reviewed and found to be compliant with GCP requirements. The correct IRB-approved versions of the informed consent forms were used throughout the study, and all participants signed the informed consent forms prior to the performance of any study-related procedures.
3.2. Ethics Committee Approva	Approvals from IRB/IEC were available: • **IRB approval** on: 27/01/2024 • **MOH approval(s)** on: 04/03/2024
3.3. Participant Safety	Safety monitoring procedures were in place. However, no SAE reporting till the inspection date. And all line listing AE was reported in quarterly submitted progress reports to EDA which verified during inspection.
4. Personnel and Training	
4.1. Training and qualifications	- Roles and responsibilities of study personnel were clearly defined. - GCP training records were available and reviewed.

	- The training system was generally adequate. -Current curriculum vitae (CVs) of the Principal Investigator and Sub-Investigators were available and appropriately maintained. -Study-specific training records, including trial initiation and investigator meeting documentation, were reviewed during the inspection, demonstrating that study personnel had received the required training to perform their assigned trial-related responsibilities.
5. Investigational Product (IMP) Management	
5.1. 1IMP handling	- IMP storage conditions, temperature monitoring, and accountability records were reviewed. - Shipping, receipt, and dispensing procedures were implemented. - Labeling and traceability were generally adequate.
6. Clinical Trial Conduct	
6.1. Protocol Compliance	- The study was generally conducted according to the approved protocol. -Protocol-required procedures, including participant recruitment, informed consent, investigational medicinal product (IMP) management, safety reporting, and study documentation, were reviewed during the inspection. Based on the documents reviewed, facilities inspected, and the inspection findings, the study was conducted at an acceptable level of compliance with the approved protocol, Good Clinical Practice (GCP) guidelines, and applicable regulatory requirements.
6.2. Source Data and CRFs	- Source documents and CRFs were reviewed. - Data were generally consistent. -Participant records were maintained in a secure and organized manner, with confidentiality preserved throughout the study. -Source data were found to be legible and well organized, and no discrepancies between the source documents and CRFs were identified with compliance with ALCOA principles during the inspection.
6.3. Delegation of Duties	Delegation logs were available, duly signed by the Principal Investigator, and clearly reflected the roles and responsibilities assigned to each member of the study team; however, a deficiency was identified **according to CT law 214/2020 , its executive regulation 927/2022 , and Guideline for Good regulatory oversight of clinical trials by Egyptian Drug Authority** whereby two Sub-Investigators had been delegated study-related duties without prior notification to the Egyptian Drug Authority (EDA), constituting non-compliance with the applicable regulatory requirements governing documentation of changes to study personnel. To address this finding, the sponsor formally notified EDA of

	the delegated Sub-Investigators through the follow-up progress report submitted to the Authority. Furthermore, as a preventive measure, the Clinical Research Associate (CRA) and Regulatory Specialist underwent retraining on EDA requirements pertaining to the timely notification of study personnel changes, with the completed training documented in the study-specific training log. The submitted CAPA was considered acceptable by EDA.

7. Laboratory and Bioanalytical Activities (if applicable

- External international laboratory used for analysis of bio samples and External national radiology center for nuclear medicine services.
- Laboratory procedures were generally defined.
- Sample handling and analysis were reviewed.

-The laboratories were accredited. Laboratory procedures were defined in the laboratory manuals maintained in the Investigator Site File (ISF), with protocol-required manuals available for the central laboratory.

-Laboratory equipment used for sample processing and storage was considered appropriately calibrated through laboratory accreditation.

8. Safety Reporting (SAE)

- SOPs for SAE reporting were available.

Part 3	**Inspection outcome**

Based on the reviewed documentation, inspected facilities, and observations identified during the inspection: The clinical trial site was considered to be operating at an acceptable level of compliance with GCP guidelines and applicable regulatory requirements as All identified deficiencies were communicated to the site. Corrective and preventive actions (CAPA) were implemented to address the observations.

This EDA-GCP-PIR remains 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 EDA Chairman Decree No.111 for 2022.
3. Guideline for Good Regulatory Oversight of Clinical Trials by Egyptian Drug Authority "EDREX.GL.Bioinn.006".
4. Guideline for Good Clinical Practice ICH E6r2.
5. Declaration of Helsinki
6. WHO Handbook for Good Clinical Research Practice (GCP) -Guidance for Implementation

Abbreviation	
AE	Adverse Event
ALCOA	Attributable, Legible, Contemporaneous, Original, Accurate
CAPA	Corrective and Preventive Action
CHMP	Committee for Medicinal Products for Human Use
CRA	Clinical research associate
CRF	Case Report Form
CRC	Clinical Research Center
CT	Clinical Trial
CV	Curriculum Vitae
EDA	Egyptian Drug Authority
EMA	European medicines agency
GCP	Good Clinical Practice
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Conference of Harmonization
IMP	Investigational Medicinal Product
IRB/IEC	Institutional Review Board / Ethics Committee
ISF	Investigational site file
MOH	Ministry of Health
PI	Principal Investigator
PIR	Public Inspection Report
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
WHO	World Health Organization

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