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	National Hepatology Tropical and Medicine Research Institute "NHTMRI"
Address of inspected CT site	Kasr Al Ainy Street, Cairo, Egypt
Inspection details	
Dates of inspection	02 July 2025
Type of inspection	Routine Inspection
Introduction	
General information about the sponsor and CT site	The inspected site is the National Hepatology Tropical and Medicine Research Institute (NHTMRI), Kasr Al Ainy Street, Cairo, Egypt, conducting clinical studies for the sponsor (AstraZeneca) through CRO (IQVIA) in accordance with applicable regulatory requirements and ethical standards. Principal Investigator: Prof. Dr. Mohamed El Kassas. The inspection was a routine surveillance of GCP compliance focused on reviewing the trial master file and the source documents. 0
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, 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 Trial ID: EMERALD-3 EudraCT Number: 2021-003822-54 EDA Approval: 08 Feb 2024

	IRB Approval: 21 Jan 2024 MOH Approval: 04 March 2024 Supreme Council Approval: Renewal on 13 May 2025
Type of IMP	Durvalumab (Biological / Monoclonal Antibody) + Tremelimumab ± Lenvatinib – administered concurrently with Transarterial Chemoembolization (TACE)
Part 2	
1. Facilities and equipment system	
1.1.Facilities and Trial Conduct	The trial site at National Hepatology Tropical and Medicine Research Institute (NHTMRI) 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, and a procedure room. - The expiry dates of some emergency medicines differed from those recorded in the emergency medication sheet; however, no expired medicines were found. The emergency medication sheet was updated to accurately reflect the actual expiry dates, and a regular review and reconciliation procedure was implemented **in compliance with WHO Annex 7.** - No calibration certificate was available for the DC shock device, and discrepancies were found between calibration dates on equipment labels and certificates for the Colon endoscope. All equipment was confirmed to be within valid calibration dates. A valid calibration certificate for the DC shock device was obtained and filed, all calibration labels and certificates were reconciled and updated, and a process was implemented to ensure accurate maintenance of calibration documentation going forward, **in compliance with ICH E6(R3).**
1.2. 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	Site SOPs and monitoring visit log were verified during the inspection. The site had a quality assurance system described in SOPs in place. The study was monitored according to the monitoring plan. GCP training records for all responsible staff who took part in the conduct of the clinical trial were verified and confirmed. - No SOP for SAE reporting was available at the time of inspection. This finding was identified and fully addressed. A formal SAE reporting SOP was developed, approved, implemented, and made available at the site. All relevant staff were trained on its content **in compliance with ICH E6(R3).**
2.2.SOPs and Documentation	SOPs governing all clinical trial activities were maintained and confirmed to be implemented.

	The following key essential documents were verified at the site: Signed study protocol, Investigator Brochure, Informed Consent Forms, Case Report Forms/eCRFs, Valid Insurance Certificate, IRB approval, and EDA approval.
2.3. Deviation Management	Deviations were handled per available SOPs and documented appropriately. - ECG reports for study participants contained corrections to the recorded gender, age, date, and time, attributed to limited experience in operating the ECG machine. The incorrect entries were corrected by the Co-Investigator and appropriately documented with his signature and date. Adequate ECG machine training was provided to all relevant staff, and proper documentation and correction practices were reinforced **in compliance with ICH E6(R3).**
2.4. CAPA System	A CAPA system was in place. The response included a full account of corrective actions taken, preventive measures implemented to avoid recurrence, and supporting documentation as proof of correction for each identified observation. All corrective and preventive actions were evaluated to ensure their appropriateness and effectiveness.
3. Ethics and Subject Protection	
3.1.Informed Consent Process	Prof. Dr. Mohamed El Kassas (PI) confirmed and documented the process of participants' recruitment from the National Hepatology and Tropical Medicine and Research Institute (NHTMRI). The approved informed consent forms were used All informed consent forms were verified to have been signed before any study-related procedures were performed. The procedure for obtaining informed consent from participants was confirmed to be fully in line with the requirements of GCP guidelines.
3.2.Ethics Committee Approval	IRB Approvals: on 21 Jan 2024 MOH Approvals: on 04 March 2024 EDA Approvals: on 08 Feb 2024 Supreme Council Approval: Renewal on 13 May 2025. All approvals were confirmed to be available, current, and filed appropriately in the site master file.
3.3. Subject Safety	Site SOPs and monitoring visit logs were verified. An SAE SOP (Management and control of adverse event reporting) was developed and implemented as a corrective action to address Minor Finding 4. Two SAEs were reported for: 1. Bleeding per rectum (Rectal hemorrhage). Outcome: Recovered. Causality: The investigator did not consider there was a reasonable possibility of a causal relationship between the study therapy and the event. 2. Disturbed conscious level, hypoglycemia (Altered state of consciousness). Outcome: Death. Causality: The investigator did not consider there was a

	reasonable possibility of a causal relationship between the study therapy and the event. Both SAEs were reported to the sponsor within the protocol-specified timeline.
4. Personnel and Training	
4.1. Training and qualifications	GCP training records for all responsible staff who took part in the conduct of the clinical trial were verified and confirmed to be complete and current. - An ECG machine operation training gap was identified and corrected. Additional training was provided to the Co-Investigator and relevant study personnel, and training records were documented and filed. Shipping records, IMP dispensing responsibilities, delegation log, and signature log were all verified and confirmed to be complete, accurate, and reflective of the actual roles and responsibilities of each study team member.
5. Investigational Product (IMP) Management	
5.1.1IMP handling	Shipping records, IMP dispensing responsibilities, storage conditions, temperature monitoring, accountability records, dispensing records, and drug destruction procedures were all verified, confirmed to be complete, accurate, and compliant with protocol requirements. The pharmacy/investigational product storage room was confirmed to be adequately maintained. - Emergency medicine documentation discrepancies and equipment calibration documentation discrepancies were identified and fully corrected. The emergency medication sheet was updated to reflect actual expiry dates, and a regular review procedure was implemented. A valid calibration certificate for the DC shock device was obtained and filed, and all calibration labels and certificates for the Colon endoscope, CT scan, and ECG machine were reconciled, updated, and confirmed to be within valid calibration periods.
6. Clinical Trial Conduct	
6.1.Protocol Compliance	Approved study protocol was confirmed to be implemented at the site. Based on the documents reviewed, facilities inspected, and considering the findings of the inspection, study D910VC00001 (EMERALD-3) was conducted at an acceptable level of compliance with the protocol, GCP guidelines, and applicable regulatory requirements. The site demonstrated a generally acceptable level of compliance with GCP principles, the study protocol, and regulations. No findings were discovered that potentially affected the ethical conduct of the trial and/or participants' rights.
6.2. Source Data and CRFs	Source documents and CRFs were reviewed and confirmed to be legible, well organized, and maintained in compliance with GCP requirements. - ECG report corrections to recorded gender, age, date, and time were identified in both enrolled participants' records, attributed to limited ECG machine operating experience. The incorrect entries were corrected and appropriately documented

	with the Co-Investigator's signature and date. Additional ECG machine training was provided to all relevant study personnel, and proper correction documentation practices were confirmed **in compliance with ICH E6(R3).**
6.3. Delegation of Duties	The delegation log and signature log were confirmed to be available, accurately completed, signed by the PI, and reflective of the actual roles and responsibilities assigned to each study team member. IMP dispensing responsibilities were verified and confirmed to be clearly delegated.
7. Laboratory and Bioanalytical Activities (if applicable)	
-No site lab. To be inspected -External Central Laboratories used for analysis were verified and confirmed to be operational and equipped for study-related activities by valid CAP Accreditation Calibration certificates for laboratory equipment were reviewed.	
8. Safety Reporting (SAE)	
All SAEs were reported to the sponsor within the protocol-specified timeline and in compliance with GCP requirements. - No SOP for SAE reporting was available at the time of inspection. This finding was identified and fully addressed. A formal SAE reporting SOP was developed, approved, implemented, and made available at the site. All relevant staff were trained on its content **in compliance with ICH E6(R3).**	
Part 3	**Inspection outcome**
Based on the reviewed documentation, inspected facilities, and findings of the routine GCP inspection conducted at the National Hepatology Tropical and Medicine Research Institute (NHTMRI) on 02 July 2025: The GCP inspection was conducted with an overall accepted level of compliance. Study D910VC00001 (EMERALD-3) was conducted at an acceptable level of compliance with the protocol, GCP guidelines, and applicable regulatory requirements. No findings were discovered that potentially affected the ethical conduct of the trial and/or participants' rights. A comprehensive CAPA response addressing all four minor findings was prepared and submitted by the applicant within the defined timeline. All corrective and preventive actions were evaluated by EDA inspectors to ensure their appropriateness. 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
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	
AE:	Adverse Event
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
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