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	CRC, Air Force Specialized Hospital (AFSH)
Address of inspected CT site	El-Nasr Street (N Teseen St), 5th Settlement, Cairo, Egypt
Inspection details	
Dates of inspection	30 July 2024
Type of inspection	Routine Inspection
Introduction	
General information about the sponsor and CT site	The inspected site is the CRC, Air Force Specialized Hospital (AFSH), conducting clinical studies for the sponsor (F. Hoffmann-La Roche Ltd) through CRO (IQVIA) Principal Investigator: Dr. Tarek Hesham. Inspection scope: Routine surveillance of GCP compliance focusing on review of trial master file and source documents.
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, Open-Label, Randomized Study of Atezolizumab with Lenvatinib or Sorafenib Versus Lenvatinib or Sorafenib Alone in Hepatocellular Carcinoma Previously Treated with Atezolizumab and Bevacizumab (ImBrave251) Protocol Number: MO42541 Trial ID: ImBrave251 Phase: III EudraCT Number: 2020-005231-78 EDA Approval: 31/1/2022
Type of IMP	Biological-Monoclonal Antibody (Atezolizumab – IV infusion) + Lenvatinib or Sorafenib (oral, administered at home)
Part 2	
1. Facilities and equipment system	

1.1. Facilities and Trial Conduct	-The trial site at CRC, Air Force Specialized Hospital was confirmed to have adequate facilities and equipment to support the conduct of the trial, including A designated examination room, consultation room, and procedure room were all available and rendered operational. -An emergency trolley in Procedure Room Fully stocked within expiry dates; regular checking records available. Defibrillator, intubation/resuscitation equipment, and oxygen supply confirmed satisfactory. -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; as per inspection team recommendation. -There was no evidence for calibration of the following equipment (CT scan, PET, and MRI). As this equipment had not a calibration label during inspection visit including its Serial Number and calibration dates. (Accordingly, serial number(s) found in the calibration certificates in TMF could not be verified against these equipment). As per CAPA implementation, the calibration labels with serial numbers and dates were affixed to the devices (CT, PET, and MRI devices) and certificates were filed at each device and in the TMF, per ICH-GCP E6(R2) -Disposal containers in the IMP administration room were unlabeled and non-compliant with international color-coding at inspection. Corrected: compliant labeled and color-coded containers were procured and installed, per WHO/FWC/WSH/17.05.
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	The site had a quality assurance system described in SOPs in place for Evacuation from the CRC in the event of a medical emergency, CRC Archiving, CRC internal audit, training the PI and CRC staff, Pharmacy SOP and Pharmacy key-holding policy, Informed consent management process guidance, Investigational product destruction The study was monitored according to the monitoring plan.
2.2. SOPs and Documentation	-The following key essential documents were verified at the site: Signed protocol; all EDA, IRB, and MOH approvals; contracts with all interested parties; laboratory accreditation certificates; trial initiation monitoring report; approved ICFs; Investigator's Brochure; eCRFs; eCRF completion guidelines; site signature and delegation log; site administrative approval; safety reporting forms; laboratory manuals; SUSAR line listings; MOH and EDA progress reports; pharmacy manual; and training log and materials. -No SAE reporting SOP was in place at the time of inspection which Corrected by

	developing a formal SAE reporting SOP that approved, implemented, and all relevant staff were trained on its content, per EDA GCP regulatory guideline and ICH GCP E6(R2) -Any form used in the trial was confirmed to have sponsor approval. Any document not approved for implementation was removed from the trial master file.
2.3. Deviation Management	Deviation management procedures were available. Deviations were handled per available SOPs.
2.4. CAPA System	- A CAPA system was in place. Comprehensive CAPA responses addressing all findings and recommendations were prepared and submitted within defined timeline - All corrective actions were implemented and supported with documentation as proof of correction in compliance with applicable GCP and regulatory standards.
3. Ethics and Participant Protection	
3.1. Informed Consent Process	- Principal Investigator and Co-Investigator confirmed and documented the process of participants' recruitment from Air Force Specialized Hospital. - The informed consent process was reviewed. The approved informed consent forms were used throughout the study and were confirmed to be the correct, IRB-approved versions (V3 dated 22\2\2023). - 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
3.2.Ethics Committee Approval	AFSH IRB Approvals: 26/5/2021 MOH Approvals: 22/11/2023. All approvals were confirmed to be available, current, and filed appropriately in the site master file.
3.3. Participant Safety	-Site SOPs and monitoring visit logs were reviewed and confirmed the sponsor's active oversight of participant safety through structured follow-up and timely emergency response. An SAE SOP was developed and implemented as a corrective action to address the finding of missing Safety SOP, reinforcing the site's preparedness to detect, escalate, and manage adverse events and training of site staff. -SAEs events were reported to the sponsor within the protocol-specified timeline, demonstrating that the sponsor maintained effective oversight of participant safety through robust follow-up mechanisms and readiness to respond to emergencies, and, per ICH GCP E6(R2) -SAE reported within protocol-specified and EDA timelines.
4. Personnel and Training	

4.1. Training and qualifications	- Curriculum Vitae of the PI, Co-I(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	
5.1.1IMP handling	- IMP was stored in an access and temperature-controlled pharmacy room. Atezolizumab was stored in the refrigerator and Lenvatinib in a fireproof wood cupboard, in accordance with the study protocol. - Transportation procedure was confirmed to be available. A data logger of temperature during transportation was available. - IMP labels confirmed to include batch number, expiry date, and "for clinical trial use only" statement. - Randomization was conducted via a randomization system by the PI/Co-I. - Recommendation (Implemented): Daily temperature log sheets for the IMP storage refrigerator were confirmed to be available in the storage room following the inspection.
6. Clinical Trial Conduct	
6.1. Protocol Compliance	- Approved Signed protocol (v. 4 dated 09/11/2022) was confirmed to be implemented at the site. - Based on the documents reviewed, facilities inspected, and considering the findings of the inspection, study MO42541 (ImBrave251) was conducted at an acceptable level of compliance with the protocol, GCP guidelines, and applicable regulatory requirements. - The inspectorate was satisfied that the Principal Investigator at the clinical trial site (Air Force Specialized Hospital) was in control to ensure that the clinical trial was conducted in compliance with GCP as prescribed in the ICH Guide to GCP.
6.2. Source Data and CRFs	- Participant records were confirmed to be available for verification and safely kept in fire and waterproof wood cupboards, secured against unauthorized access. - Source data were confirmed to be legible, well organized reviewed and confirmed to be maintained in compliance with GCP requirements.
6.3. Delegation of Duties	- Site signature and delegation of responsibilities 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. - Delegation updates were confirmed
7. Laboratory and Bioanalytical Activities (if applicable)	

- Local site lab and External Laboratories used for analysis.
- All laboratories were confirmed to be accredited with valid calibration records.
- The laboratory procedures were defined in the laboratory manual filed in the Investigator Site File, along with the reference ranges to be accessible to the study staff.
- Withdrawn samples were stored at protocol-specified temperatures per the laboratory manual. Daily temperature records were confirmed to be available for all laboratory equipment.

8. Safety Reporting (SAE)

- SAE was reported to the sponsor within the protocol-specified timeline. SAE reporting to Bio Inn-EDA was within the specified time.

-No SAE reporting SOP was in place at the time of inspection which Corrected by developing a formal SAE reporting SOP that approved, implemented, and all relevant staff were trained on its content, per EDA GCP regulatory guideline and ICH GCP E6(R2)

Part 3	Inspection outcome

Based on the reviewed documentation, inspected facilities, and observations identified during the inspection, the clinical trial site (CRC, Air Force Specialized Hospital) was confirmed to have been operating at an acceptable level of compliance with GCP guidelines and applicable regulatory requirements.

The inspectorate was satisfied that the Principal Investigator at the clinical trial site was in control to ensure that the clinical trial, protocol number MO42541 (ImBrave251), was conducted in compliance with GCP as prescribed in the ICH Guide to GCP as a comprehensive CAPA response addressing all findings and all recommendations was prepared and submitted within the specified timeline. All corrective and preventive actions were implemented and confirmed to be appropriate.

-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 ED
3. A 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
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