File No. CT/23/22-DCG(I)

GOVERNMENT OF INDIA
CENTRAL DRUGS STANDARD CONTROL ORGANISATION (Headquarter)
(Directorate General of Health Services)
Ministry of Health & Family Welfare
FDA Bhavan
ITO, Kotla Road
New Delhi - 110002 (Delhi)
Phone No.: 91-11-23216367
Fax No.: 91-11-23236973
E-Mail : dci@nic.in

सत्यमेव जयते

File No. CT/22/000023

To,

M/s. AstraZeneca Pharma India Limited,
Block NO 1, 12th Floor Manyata Embassy,
Business Park, Rachenahalli Outer Ring Road,
Bangalore, Karnataka (India) – 560045.

Sir,

With reference to your application No. GCT/CT04/FF/2022/30859 (GCT/23/22) dated 28-02-2022, please find enclosed herewith the permission in Form CT-06 for conduct of clinical trial titled, **"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 (EMERALD-3)" Protocol Number: D910VC00001 Version 1.0 dated 05/11/2021** under the provisions of New Drugs and Clinical Trial Rules, 2019

The permission granted by the Central Licensing Authority to conduct clinical trial shall be subject to following conditions, namely:-

(i) Considering the high prevalence of the disease in the country, the number of subjects increased to 34, from the proposed 24 subjects;

(ii) Clinical trial at each site shall be initiated after approval of the clinical trial protocol and other related documents by the Ethics Committee of that site, registered with the Central Licencing Authority under rule 8;

(iii) where a clinical trial site does not have its own Ethics Committee, clinical trial at that site may be initiated after obtaining approval of the protocol from the Ethics Committee of another trial site; or an independent Ethics Committee for clinical trial constituted in accordance with the provisions of rule 7:

Provided that the approving Ethics Committee for clinical trial shall in such case be responsible for the study at the trial site or the centre, as the case may be:

Provided further that the approving Ethics Committee and the clinical trial site or the bioavailability and bioequivalence centre, as the case may be, shall be located within the same city or within a radius of 50 kms of the clinical trial site;

(iv) in case an ethics committee of a clinical trial site rejects the approval of the protocol, the details of the same shall be submitted to the Central Licensing Authority prior to seeking approval of another Ethics Committee for the protocol for conduct of the clinical trial at the same site;

(v) the Central Licencing Authority shall be informed about the approval granted by the Ethics Committee within a period of fifteen working days of the grant of such approval;

(vi) clinical trial shall be registered with the Clinical Trial Registry of India maintained by the Indian Council of Medical Research before enrolling the first subject for the trial;

(vii) clinical trial shall be conducted in accordance with the approved clinical trial protocol and other related documents and as per requirements of Good Clinical Practices Guidelines and the provisions of these rules;

(viii) status of enrolment of the trial subjects shall be submitted to the Central Licencing Authority on quarterly basis or as appropriate as per the duration of treatment in accordance with the approved clinical trial protocol, whichever is earlier;

(ix) six monthly status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted to the Central Licencing Authority electronically in the SUGAM portal;

(x) in case of termination of any clinical trial the detailed reasons for such termination shall be communicated to the Central Licencing Authority within thirty working days of such termination;

(xi) any report of serious adverse event occurring during clinical trial to a subject of clinical trial, shall, after due analysis, be forwarded to the Central Licencing Authority, the chairperson of the Ethics Committee and the institute where the trial has been conducted within fourteen days of its occurrence as per Table 5 of the Third Schedule and in compliance with the procedures as specified in Chapter VI;

(xii) in case of injury during clinical trial to the subject of such trial, complete medical management and compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of the receipt of order issued by Central Licencing Authority in accordance with the provisions of the said Chapter;

(xiii) in case of clinical trial related death or permanent disability of any subject of such trial during the trial, compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of receipt of the order issued by the Central Licencing Authority in accordance with the provisions of the said Chapter;

(xiv) the premises of the sponsor including his representatives and clinical trial sites, shall be open for inspection by officers of the Central Licencing Authority who may be accompanied by officers of the State Licencing Authority or outside experts as authorised by the Central Licencing Authority, to verify compliance of the requirements of these rules and Good Clinical Practices Guidelines, to inspect, search and seize any record, result, document, investigational product, related to clinical trial and furnish reply to query raised by the said officer in relation to clinical trial;

(xv) where the new drug or investigational new drug is found to be useful in clinical development, the sponsor shall submit an application to the Central Licencing Authority for permission to import or manufacture for sale or for distribution of new drug in India, in accordance with Chapter X of these rules, unless otherwise justified;

(xvi) the laboratory owned by any person or a company or any other legal entity and utilised by that person to whom permission for clinical trial has been granted used for research and development, shall be deemed to be registered with the Central Licensing Authority and may be used for test or analysis of any drug for and on behalf of Central Licensing Authority;

(xvii) the Central Licencing Authority may, if considered necessary, impose any other condition in writing with justification, in respect of specific clinical trials, regarding the objective, design, subject population, subject eligibility, assessment, conduct and treatment of such specific clinical trial;

(xviii) the sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.

(xix) Merely granting permission to conduct the clinical trial with the Investigational Drug Product does not convey or imply that, based on the clinical trial study data generated with the investigational drug, permission to market this drug in the country will automatically be granted to you;

(xx) The permission to initiate clinical trial granted under rule 22 in form CT-06 or automatic approval under rule 23 in Form CT 4A shall remain valid for a period of **two years** from the date of its issue, unless extended by the Central Licencing Authority.

Yours faithfully,

VENUGOPAL G SOMANI

(Dr. V. G. Somani)
Drugs Controller General (India)
Central Licencing Authority
Stamp

Digitally signed by VENUGOPAL G SOMANI
DN: c=IN, o=CENTRAL DRUGS STANDARD CONTROL ORGANIZATION, ou=DRUGS CONTROLLER GENERAL (INDIA), pseudonym=112046a34e24727bacb255748732c456d249073e55e953d9cb5b5874 8ee3113c, postalCode=110002, st=DELHI, serialNumber=e97f241aa0c0bba4152252 5ffca0705074b4997e6b2f4b5c8d81cf282 adeaf5d, cn=VENUGOPAL G SOMANI
Date: 2022.06.02 14:30:33 +05'30'

File No. CT/23/22-DCG(I)

FORM CT-06

(See rules 22,25,26,29 and 30)

PERMISSION TO CONDUCT CLINICAL TRIAL OF NEW DRUG OR INVESTIGATIONAL NEW DRUG

1. The Central Licensing Authority hereby permits **M/s. AstraZeneca Pharma India Limited, Block NO 1, 12th Floor, Manyata Embassy Business Park, Rachenahalli, Outer Ring Bangalore (India) - 560045** to conduct clinical trial of the new drug or investigational new drug as per **Protocol Number: D910VC00001 Version 1.0 dated 05/11/2021** in the below mentioned clinical trial sites [As per Annexure].-

2. Details of new drug or investigational new drug and clinical trial site [As per Annexure].

3. This permission is subject to the conditions prescribed in part A of Chapter V of the New Drugs and Clinical Trials Rules, 2019 under the Drugs and Cosmetics Act, 1940.

Place: New Delhi
Date _____

VENUGOPAL G SOMANI

Digitally signed by VENUGOPAL G SOMANI
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Date: 2022.06.02 14:30:50 +05'30'

(Dr. V. G. Somani)
Drugs Controller General (India)
Central Licencing Authority
Stamp

Note: The permission to initiate clinical trial granted under rule 22 in form CT-06 shall remain valid for a period of **two years** from the date of its issue, unless extended by the Central Licencing Authority.

Annexure:

Details of new drug or investigational new drug:

Names of the new drug or investigational new drug	1. Durvalumab(MEDI4736)+ 2. Tremelimumab
Therapeutic class:	Monoclonal Antibody mAb
Dosage form:	Concentrate solution for infusion
Composition:	Durvalumab MEDI4736 = 500.0000 milligram (mg) In House Specification Active Water for Injection= 1.0000q.s.U.S.P.,J.P.,Ph.Eur Inactive Polysorbate 80 = 2.0000 milligram (mg) J.P., Ph. Eur Inactive ,-Trehalose dehydrate = 1040.0000 milligram (mg) U.S.P., J.P., Ph. Eur Inactive

	Histidine hydrochloride monohydrate = 27.2000 milligram (mg) J.P., Ph. Eur Inactive Histidine = 20.2000 milligram (mg) U.S.P., J.P., Ph. Eur Inactive Tremelimumab = 25.0000 milligram (mg) In House Specification Active Water for Injection = 1.2000 gram (g) U.S.P., J.P., Ph. Eur Inactive Disodium edentate dehydrate = 0.1000 milligram (mg) U.S.P., J.P., Ph. Eur Inactive Polysorbate 80 = 0.3000 milligram(mg)U.S.P., J.P., Ph. Eur Inactive ,-Trehalose dihydrate = 105.0000 milligram (mg) U.S.P., J.P., Ph .Eur Inactive L-Histidine hydrochloride monohydrate = 4.1000 milligram(mg) J .P., Ph. Eur Inactive L-Histidine = 0.9000 milligram (mg) U.S.P., J.P., Ph. Eur Inactive
Indications:	Patients with Locoregional Hepatocellular Carcinoma not amenable to curative therapy

Annexure:

Details of clinical trial site:

Names and address of clinical trial site	**Ethics committee details**	**Name of investigator**
HCG Cancer, Centre, Sola Science city road, Near Sola Bridge Ahmedabad- S. G, highway-380060	HCG Multi-Speciality Ethics Committee, HCG Hospitals, Mithakali Ellisbridge Ahmedabad, Gujarat- 380006 India. ECR/92/Inst/GJ/2013/RR-19	Dr Viraj Lavingia
Aster CMI Hospital # 43/2 New Airport Road, NH-7, Outer Ring Road, Sahakar Nagar, Bengaluru-560092, Karnataka	Institutional Ethics Committee, Basement, Opposite to IP Pharmacy Room, # 43/2 New Airport Road, NH-7, Outer Ring Road, Sahakar Nagar, Bengaluru, Karnataka-560092 ECR/1084/Inst/KA/2018	Dr Vijay Agarwal
Health Care Global Enterprises Ltd., HCG Towers, #8, P. Kalinga Rao Road, Sampangi Ram Nagar, Bangalore, 560027	HCG-Central Ethics Committee, HCG Towers, #8, P. Kalinga Rao Road, Sampangi Ram Nagar, Bangalore, 560027 .ECR/386/Inst/KA/2013/RR-19	Dr Satheesh C T
Zydus Cancer Centre, C/O Zydus Hospitals & Healthcare Research Pvt Ltd, Zydus Hospital Road, Near Sola Bridge, Thaltej, Ahmedabad-380054, Gujarat, India	Zydus Hospital Ethics Committee, Zydus Hospitals & Healthcare Research Pvt Ltd, Zydus Hospital Road, Near Sola Bridge, Thaltej, Ahmedabad-380054, Gujarat, India ECR/855/Inst/GJ/2016/RR-19	Dr. Mithun Satish Shah

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Rajiv Gandhi Cancer Institute and Research Centre, Sector 5, Rohini, Delh-110085, India	Institutional Review Board, Rajiv Gandhi Cancer Institute and Research Centre, Sector 5, Rohini, Delhi110085, India ECR/10/Inst/DC/2013/RR-19	Dr Varun Goyal
Dr. B.L Kapur Memorial Hospital, Pusa Road, New Delhi-110005	Dr B.L Kapur Memorial Hospital Ethics Committee, Dr. B.L Kapur Memorial Hospital ECR/3/BLK/Inst/DL/2013/RR-19	Dr. Sajjan Rajpurohit
Sterling Hospital, 'A Unit of Addlife India Pvt. Ltd'., 2nd Floor Clinical Research Department, Sterling Hospital Road, Memnagar-380052, Ahmedabad, Gujarat, India	Sterling Hospital Ethics Committee, Basement, Sterling Hospital, Sterling Hospital Road, Memnagar-380052, Ahmedabad, Gujarat, India. ECR/340/Inst/Guj/2013/RR-20	Dr. Jay Dadhania
Sri Ram Cancer & Super speciality Centre, Mahatma Gandhi Medical College and Hospital, RIICO Institutional Area, Sitapura, Jaipur-302022	Institutional Ethics Committee, Mahatma Gandhi Medical College and Hospital, RIICO Institutional Area, Sitapura, Jaipur-302022 ECR/125/Inst/RJ/2013/RR-19	Dr. Hemant Malhotra
Medanta -The Medicity, CH Bakhtawar Chowk, Sector-38, Gurugram, Haryana-122001	Medanta Institutional Ethics Committee (MIEC), Medanta-The Medicity, CH Bakhtawar Chowk, Sector-38, Gurugram, Haryana-122001, India. ECR/282/Inst/HR/2013/RR-20	Dr Ashok Kumar Vaid
NH-Rabindranath Tagore International Institute of Cardiac Sciences, Premises No -1489, (124), Mukundapur, E.M. Bypass, Kolkata -700099, West Bengal, India	NHRTIICS Ethics Committee , 124, Mukundapur, E.M. Bypass, Kolkata –700099 ECR/316/Inst/WB/2013/RR-19	Dr Vivek Agarwala
Fortis Memorial Research Institute, Sector -44, Opp Huda City Centre, Gurugram, India-122002	FMRI Institutional Ethics Committee, Lower Ground Floor, Fortis Memorial Research Institute, Gurugram, India-122002 ECR/223/Inst/HR/2013/RR-19	Dr. Mukesh Patekar