Clinical Trial Details (PDF Generation Date :- Mon, 03 Oct 2022 13:30:30 GMT)

CTRI Number	CTRI/2019/01/017219 [Registered on: 23/01/2019] - **Trial Registered Prospectively**
Last Modified On	01/01/2021
Post Graduate Thesis	No
Type of Trial	Observational
Type of Study	Cohort Study
Study Design	Other
Public Title of Study	Liquid biopsy for early detection of cancer
Scientific Title of Study	Realtime Enrichment Screen for Outright detection of Latent Undiagnosed malignant Tumors in asymptomatic individuals Efficiently

Secondary IDs if Any

Secondary ID	Identifier
NIL	NIL

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
Name	Mr Rajan Datar
Designation	Managing Director
Affiliation	Datar Cancer Genetics Limited
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Details Contact Person (Scientific Query)

Details Contact Person (Scientific Query)	
Name	Dr Dadasaheb Akolkar
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Details Contact Person (Public Query)

Details Contact Person (Public Query)	
Name	Dr Darshana Patil
Designation	Medical Director
Affiliation	Datar Cancer Genetics Limited
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Source of Monetary or Material Support

Source of Monetary or Material Support
> Datar Cancer Genetics Limited Canconnect Foundation

Primary Sponsor

Primary Sponsor Details	
Name	Datar Cancer Genetics Limited
Address	F-8, D Road, MIDC, Ambad, Nasik, Maharashtra 422 010
Type of Sponsor	Other [Molecular Laboratory and Research Centre]

Details of Secondary Sponsor

Name	Address
Canconnect Foundation	Flat No.12, Ameya Sankul,B Wing, Sharanpur Road, Nasik, Maharashtra 422 005

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Dr Darshana Patil	Datar Cancer Genetics Limited	Datar Cancer Genetics Limited, F-8, D Road, MIDC, Ambad, Nasik, Maharashtra 422 010. Phone No.: 0253 660 4828 Nashik MAHARASHTRA	9168726260 drdarshanap@datarpgx.org

Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Datar Cancer Genetics Limited Ethics Committee	Approved	01/01/2019	Yes
Datar Cancer Genetics Limited Ethics Committee	Approved	31/12/2020	No

Regulatory Clearance Status from DCGI

Status	Date
Not Applicable	No Date Specified

Health Condition / Problems Studied

Health Type	Condition
Patients	Neoplasms
Healthy Human Volunteers	Participants with no known diagnosis or past history of cancer

Intervention / Comparator Agent

Type	Name	Details

Inclusion Criteria

Inclusion Criteria	
Age From	40.00 Year(s)
Age To	75.00 Year(s)
Gender	Both
Details	Non-cancer arm- For Inclusion, an individual must meet all of the following criteria: 1.Age – 49 to 75 years for males and 40 to 75 years for females 2.Participants with no known diagnosis or past history of cancer 3.Willingness to provide blood sample as per study protocol 4.Patient should be willing for screening investigations proposed in study protocol. 5.Female patient is not pregnant / lactating (self-report) 6.Provision of signed informed consent form and expresses understanding of the protocol

	and its requirements, risks, and discomforts. 7.Stated willingness to comply with all study procedures Cancer arm- For Inclusion, an individual must meet all of the following criteria: 1.Age – 49 to 75 years for males and 40 to 75 years for females 2.Able to provide a written informed consent 3.Have either of the following: a.Confirmed cancer diagnosis (any stage I-IV) within 90 days prior to study blood draw, based upon assessment of a pathological specimen and are therapy naïve at the time of blood collection OR b.A high suspicion for a cancer diagnosis by clinical and/or radiological assessment, with planned biopsy or surgical resection to establish a definitive diagnosis within 6 weeks (42 days) after study blood draw and are therapy naïve at the time of blood collection 4.Willingness to provide blood sample as per study protocol 5.Female patient is not pregnant / lactating (self-report) 6.Provision of signed informed consent form and expresses understanding of the protocol and its requirements, risks, and discomforts. 7.Stated willingness to comply with all study procedures Benign lesions arm- For Inclusion, an individual must meet all of the following criteria: 1.Age – 49 to 75 years for males and 40 to 75 years for females 2.Able to provide a written informed consent 3.Have either of the following: a.Confirmed diagnosis of a benign lump within 90 days prior to study blood draw, based upon assessment of a pathological specimen and are therapy naïve at the time of blood collection OR b.A high suspicion for a benign lump by clinical and/or radiological assessment, with planned biopsy or surgical resection to establish a definitive diagnosis within 6 weeks (42 days) after study blood draw and are therapy naïve at the time of blood collection 4.Willingness to provide blood sample as per study protocol 5.Female patient is not pregnant / lactating (self-report) 6.Provision of signed informed consent form and expresses understanding of the protocol and its requirements, risks, and discomforts. 7.Stated willingness to comply with all study procedures

Exclusion Criteria

Exclusion Criteria	
Details	Non-cancer arm- For Exclusion, an individual may meet any of the following criteria: 1.Known current or prior diagnosis of cancer 2.Unable to provide informed consent 3.Unable to comply with all project screening procedures 4.Current treatment with any investigational drug or intervention 5.Pregnant or lactating women (by self-report) 6.Age less than 49 or more than 75 years for males and less than 40 or more than 75 years for females 7.Unable/unwilling to provide blood sample as per study requirement. 8.Oral or IV corticosteroid use in past 14 days prior to blood draw 9.Current febrile illness 10.Acute exacerbation or flare of an inflammatory condition requiring escalation in medical therapy within 14 days prior to blood draw. 11.History of blood transfusion/ PET-CT scan/CT-scan in last 30 days Cancer arm- For Exclusion, an individual may meet any of the following criteria: 1.Known prior history of cancer or history of prior or current cancer treatment 2.Unable to provide informed consent 3.Unable to comply with all project screening procedures 4.Current treatment with any investigational drug or intervention 5.Pregnant or lactating women (by self-report)

	6.Age less than 49 or more than 75 years for males and less than 40 or more than 75 years for females 7.Unable/unwilling to provide blood sample as per study requirement. 8.Oral or IV corticosteroid use in past 14 days prior to blood draw 9.Current febrile illness 10.Acute exacerbation or flare of an inflammatory condition requiring escalation in medical therapy within 14 days prior to blood draw. 11.History of blood transfusion/ PET-CT scan/CT-scan in last 30 days Benign lesions arm- For Exclusion, an individual may meet any of the following criteria: 1.Known prior history of cancer or history of prior or current cancer treatment or a high suspicion for a cancer diagnosis 2.Unable to provide informed consent 3.Unable to comply with all project screening procedures 4.Current treatment with any investigational drug or intervention 5.Pregnant or lactating women (by self-report) 6.Age less than 49 or more than 75 years for males and less than 40 or more than 75 years for females 7.Unable/unwilling to provide blood sample as per study requirement. 8.Oral or IV corticosteroid use in past 14 days prior to blood draw 9.Current febrile illness 10.Acute exacerbation or flare of an inflammatory condition requiring escalation in medical therapy within 14 days prior to blood draw. 11.History of blood transfusion/ PET-CT scan/CT-scan in last 30 days

Method of Generating Random Sequence	Not Applicable
Method of Concealment	Not Applicable
Blinding/Masking	Open Label

Primary Outcome

Outcome	Timepoints
Specificity	12 months

Secondary Outcome

Outcome	Timepoints
Sensitivity	12 months

Target Sample Size	**Total Sample Size=**61200 **Sample Size from India=**61200 **Final Enrollment numbers achieved (Total)=**Applicable only for Completed/Terminated trials **Final Enrollment numbers achieved (India)=**Applicable only for Completed/Terminated trials
Phase of Trial	N/A
Date of First Enrollment (India)	25/01/2019
Date of First Enrollment (Global)	No Date Specified
Estimated Duration of Trial	**Years=**2 **Months=**0 **Days=**0
Recruitment Status of Trial (Global)	Not Applicable
Recruitment Status of Trial (India)	Open to Recruitment
Publication Details	Akolkar D, Patil D, Crook T, et al. Circulating ensembles of tumor-associated cells: A redoubtable new systemic hallmark of cancer. International Journal of Cancer. 2020 Jun;146(12):3485-3494.

DOI: 10.1002/ijc.32815. Hallmark Circulating Tumor-Associated Cell Clusters Signify 230 Times Higher One-Year Cancer Risk Anantbhushan Ranade, Amit Bhatt, Raymond Page, Sewanti Limaye, Timothy Crook, Dadasaheb Akolkar and Darshana Patil Cancer Prev Res December 21 2020 DOI: 10.1158/1940-6207.CAPR-20-0322

Brief Summary

Background and Introduction:

Cancer is one of the leading causes of deaths in India and over 630,000 people die of cancer each year. According to the most recent predictions by the International Agency for Research on Cancer GLOBOCAN project, India's cancer burden will nearly double in the next 20 years, from a million new cases in 2012 to more than 1·7 million by 2035.[1,2]

The age-standardized prevalence of cancer is estimated to be 97 per 100,000 persons with greater prevalence in urban areas. The evidence suggests that cancer prevalence is highest among the elderly and also among females in the reproductive age groups.[3]

Cancer is the second leading cause of deaths worldwide and accounts for a share of 13 percent in total global deaths (or 8.7 million deaths).[4,5]

According to WHO, India has a cancer mortality rate of 79 per 100,000 deaths and accounts for over 6 percent of total deaths.[6]

In general, there is a consensus that about 60 percent of cancer deaths can be prevented with improved preventive (removing the causes of disease so theta exposure to risk is minimal) and screening (test or procedure used to detect disease) facilities.[7,8]

A key factor responsible for high cancer mortality (at 68% of the annual incidence) and lower survival in cancer patients is the late stage of

diagnosis. Late detection is not necessarily because of any negligence of the patient but is usually attributable to the fact that the insidious growth often produces no symptoms at all till a very late stage.

The top five cancers in men and women account for 47.2% of all cancers; these cancers can be screened for and/or detected early and treated at an early stage.[9] This could significantly reduce the death rate from these cancers.

Hence early detection is key to improve disease outcomes with increased disease free and overall survival. Currently there are no high sensitivity and specificity screening tools available which can detect all cancers at early stage with minimal harm to the patient and can be used as a mass screening tool even for the patients without access to advanced healthcare facilities.

Study Rationale:

The major cause of high fatality of cancer is late stage at diagnosis. It is thought that progression of cancer from early to late stage disease is a prolonged process, which becomes highly fatal after reaching late stage. To improve outcomes of cancer, it is imperative to detect them early. Even when metastasis has initiated but is not yet evident radiologically, cancers can be cured in up to 50% of cases with systemic therapies. Once large, metastatic tumors are formed, however, current therapies are rarely effective.

Current screening modalities are mostly non-blood based (except PSA) and thus are invasive. This leads to decreased compliance to screening

procedures and also are associated with sensitivity-specificity limitations. The approved tests for cancer detection include colonoscopy, mammography, LDCT and cervical cytology.

Efforts are being focused on evaluating blood based non-invasive screening tests. New blood tests for cancer must have very high specificity; otherwise, too many healthy individuals will receive positive test results, leading to unnecessary follow-up procedures and anxiety.

Current blood based screening tests under development mainly focus on cfDNA based approaches which detect somatic alterations in blood. However multiple studies have highlighted limitations of liquid biopsy sensitivity in early stages of cancers. Also emerging evidence of somatic alterations arising from clonal hematopoiesis of white blood cells, question the specificity of this approach. In addition, no studies have examined many healthy control individuals, which is essential for evaluation of the specificity of such tests. Liquid biopsies are also unable to identify underlying tissue of origin in majority of cases due to the fact that most somatic alterations are not cancer type specific.

Circulating tumor cells are the tumor cells which have detached from primary tumor site and have gained access to peripheral circulation. These may potentially lodge in distant organs giving rise to metastasis. Thus, CTC is a pre-requisite for disease spread and thus are detectable before late stage/metastatic disease develops. Also, CTCs have additional advantage of expressing tissue-of-origin specific markers in their cytoplasm/nucleus/membrane giving rise to feasibility of identification of primary tumor site. In certain cases, morphological classification into

probable cancer type e.g. squamous vs adenocarcinoma may be feasible, giving better access to patient management in addition to the diagnosis.

Study Conduct

a. STEP 0 (Recruitment and Consent):

Patients fulfilling eligibility criteria are recruited after providing detailed information about study protocol, its utility and limitations. Participant enters study only after providing written informed consent.

b. STEPS 1: (Screening procedure Non-cancer arm):

After consent, participants undergo screening procedures as proposed below-

Sr. No.	Investigation	Male	Female
1.	Mammography	-	Yes
2.	PAP Smear with HPV	-	Yes*

3.	LDCT	Yes	Yes
4.	PSA	Yes	-
5.	CA 19.9	Yes	Yes
6.	CA 125	-	Yes
7.	AFP	Yes	Yes
8.	CEA	Yes	Yes
9.	Clinical Examination	Yes	Yes
10.	CBC with peripheral smear examination	Yes	Yes
11.	15 ml blood sample collection for study protocol	Yes	Yes

* upto 65 years

c. STEP 3 (Data Evaluation):

The data from study analytes CTCs is compared with standard screening

procedures, clinical examination and clinical history details to determine sensitivity and specificity of CTCs as a cancer screening tool.

For benign lesion arm and cancer arm, the data from study analytes CTCs is compared with histopathology examination report.

Adverse Events

As it is an observational trial involving only blood sample collection and standard approved cancer screening procedures, no adverse events are anticipated.

Ethical Considerations

Discussion on the ethics of the study:

The participation in the study is entirely voluntary and after providing appropriate consent.

There is no active ongoing intervention involved in current study as it involves only single point peripheral blood draw and approved standard cancer screening procedures. Thus, this study will only offer advantage to its participants by offering approved cancer screening procedures. There will be no financial implications for the study participant.

Approvals:

The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC)/ Institutional review board (IRB) of host institution(s) for written approval. The PI will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

Participant Confidentiality:

The study staff will ensure that the participants' anonymity is maintained. The participants will be identified only by a participant identification number on all study documents and any electronic database. All documents will be stored securely and only accessible by study staff and authorized personnel. The study will comply with the Data Protection Act, which requires data to be anonymised as soon as it is practical to do so.

Informed Consent Process:

Prior to the beginning of the trial, the investigator should have the IRB's written approval for the protocol and the written informed consent form(s) and any other written information to be provided to the participants. Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study. Consent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. The investigator will explain the study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as

research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

Financial Implications:

Study participant will be under no financial burden for the study sponsored cancer screening procedures.

General ethics for the conduct of the study:

The study will be conducted in compliance with the ICMR Statement on Human Experimentation, the Declaration of Helsinki and the International Committee of Harmonisation (ICH) Harmonised Tripartite Guidelines for Good Clinical Practice (GCP)

The Investigator or a person designated by him/her will collect informed consent from all participants, prior to which the Investigator or co-investigator must inform each participant of the objectives, benefits, risks and requirements of the study. He/she will also provide the participant with an information sheet in clear, simple language. The study participant will be allowed ample time to inquire about details of the study and to decide whether or not to participate in the study. The study will not commence until approval has been obtained from the DCGL Ethics Committee and CTRI registration is completed.