Clinical Trial Details (PDF Generation Date :- Sun, 27 Nov 2022 10:30:33 GMT)

CTRI Number	CTRI/2018/02/011808 [Registered on: 09/02/2018] - **Trial Registered Retrospectively**
Last Modified On	05/02/2019
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Other (Specify) [Molecular analysis directed therapy selection and administration in relapsed refractory cancer cases]
Study Design	Single Arm Study
Public Title of Study	Personalized cancer therapy for Cancer
Scientific Title of Study	The assessment of potential benefits of molecular analysis and in vitro chemo response directed at opening treatment options for relapsed and refractory metastatic solid organ tumors.

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	Dr Raj V Nagarkar MS MRCS Edin DNB BSSUK MNAMS
Designation	Chairman and Surgical Oncologist
Affiliation	HCG Manavata Cancer Centre
Address	HCG Manavata Cancer Centre Near Mahamarg Bus Stand Mumbai Naka Nashik 422 004. Nashik MAHARASHTRA 422 004 India
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Details Contact Person (Scientific Query)

Details Contact Person (Scientific Query)	
Name	Dr Darshana Patil
Designation	Medical Director
Affiliation	Datar Cancer Genetics Limited
Address	F-8, D Road MIDC Ambad, Nashik, Maharashtra 422010 Nashik MAHARASHTRA 422010 India
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Name	Dr Darshana Patil
Designation	Medical Director
Affiliation	Datar Cancer Genetics Limited
Address	F-8, D Road MIDC Ambad, Nashik, Maharashtra 422010 Nashik MAHARASHTRA 422010 India
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Email	drdarshanap@datarpgx.org

Source of Monetary or Material Support

Source of Monetary or Material Support
> Datar Cancer Genetics Limited, F-8, D Road MIDC Ambad, Nashik, Maharashtra 422010.

Primary Sponsor

Primary Sponsor Details	
Name	Datar Cancer Genetics Limited
Address	F-8, D Road MIDC Ambad, Nashik, Maharashtra 422010
Type of Sponsor	Other [Private molecular laboratory]

Details of Secondary Sponsor

Name	Address
NIL	NIL

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Dr Dadasaheb Akolkar	Datar Cancer Genetics Limited	Department of Research and Innovation, F-8, D Road MIDC Ambad, Nashik, Maharashtra 422010 Nashik MAHARASHTRA	07387705888 dadasaheb.akolkar@datarpgx.com
Dr Raj V Nagarkar	HCG Manavata Cancer Centre	Near Mahamarg Bus Stand Mumbai Naka Nashik 422 004. Nashik MAHARASHTRA	9823061929 drraj@manavatacancercentre.com

Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Datar Cancer Genetics Limited Ethics Committee	Approved	12/12/2017	No
Manavata Clinical Research Institute Ethics Committee	Approved	14/12/2017	No

Regulatory Clearance Status from DCGI

Status	Date
Not Applicable	No Date Specified

Health Condition / Problems Studied

Health Type	Condition
Patients	Metastatic refractory, relapsed / recurrent metastatic solid organ cancer patients
Patients	Neoplasms

Intervention / Comparator Agent

Type	Name	Details
Comparator Agent	The drugs taken during most recent chemotherapy (just before enrollment on study project) as per standard of care will be the comparator agent	In this trial chemotherapy and non-chemotherapy drugs currently available in the market will be administered to the study participants.These drugs will be selected based on results of in-vitro and molecular analysis of tumor sample and patients blood sample. The results of response to such drugs selected based on comprehensive cancer

		molecular profiling will be compared with response obtained by last standard of care chemotherapy drugs.
Intervention	Available drugs will be individualized as per in vitro or molecular analysis reports or as applicable.	This trial is not for any new drug or molecule. In this trial chemotherapy and non-chemotherapy drugs currently available in the market will be administered to the study participants.These drugs will be selected based on results of in-vitro and molecular analysis of tumor sample and patients blood sample.

Inclusion Criteria

Inclusion Criteria	
Age From	18.00 Year(s)
Age To	70.00 Year(s)
Gender	Both
Details	1. Age – 18 to 70 years (male or female); 2. Cancer of any solid organ, Sarcomas, Melanomas 3. Should have ECOG score of maximum 2; 4. Patient should have progressed on at least 3 SOC lines, if any, of therapy and have no further SOC option/ option is beyond financial reach (such as immunotherapy/ targeted therapy etc.). Three SOC lines would include surgery / RT / Cytotoxic therapy / targeted therapy; 5. Patient should be willing and fit for fresh tissue biopsy for obtaining live tumor cells / tapping of ascetic fluid / pleural fluid/ CSF etc. as the case may be; 6. The last failed SOC therapy should have resulted in a Progression Free Survival of <90 days; 7. Patient should be able and willing to undertake treatment as may be advised after the analysis by DCGL with good compliance history in the past; 8. Patient should be willing and ready for baseline PET Scan and/or CT and/or USG and/or MRI and follow-up scans (usually the first follow-up scan is after 30 days followed by further scans at 75 days and 120 days); 9. Patient is willing and can tolerate cytotoxic and targeted therapy (labelled / off-label / repurposed / natural tumor inhibiting supplements); 10. Female patient is not pregnant / lactating; 11. Provision of signed and dated informed consent form 12. Stated willingness to comply with all study procedures 13. Patients must have measurable disease on radiological imaging post biopsy to monitor treatment response

Exclusion Criteria

Exclusion Criteria	
Details	1. Lymphomas, Leukemias, Myelomas. 2. Life threatening co-morbidities such as HIV, HPV, HBV, HCV, Tuberculosis, CHF, Impaired Hepatic or Renal Function or any psychological deficits etc. 3. Not fulfilling inclusion criteria

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

Primary Outcome

Outcome	Timepoints
Amongst others, the purpose of the study is to evaluate in study participants who are treated	The baseline evaluation will be conducted prior to beginning of therapy (preferably within prior

with therapy guidance obtained from integrative molecular and cytology analysis provided by the DCGL investigation platform (Exacta) – (a) Objective Response Rate (ORR); (b) Benefit of Progression Free Survival (PFS); (c) Quality of Life;	two weeks of therapy initiation). Follow up evaluations will be usually conducted after 30 days followed by further scans at 75 days and 120 days and so on. The evaluation also will be conducted based on clinical need and judgement of the clinician.

Secondary Outcome

Outcome	Timepoints
Any other incidental or significant observation or finding relevant for the science or clinical management of cancer;	Six months from completion of study

Target Sample Size	**Total Sample Size=**200 **Sample Size from India=**200 **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	Phase 2/ Phase 3
Date of First Enrollment (India)	16/12/2017
Date of First Enrollment (Global)	No Date Specified
Estimated Duration of Trial	**Years=**0 **Months=**6 **Days=**0
Recruitment Status of Trial (Global)	Not Applicable
Recruitment Status of Trial (India)	Closed to Recruitment of Participants
Publication Details	None yet
Brief Summary	Study Rationale: Responses to Cancer Therapy and outcomes are governed by various factors. These may either be genetic, epigenetic or environmental. Genetic alterations and differential regulations in metabolic pathways contribute to chemoresistance in tumor cells. Pharmacogenetics, lifestyle and health status contribute to safety, activity and metabolism of drugs, owing to various combinations of intrinsic and extrinsic factors. These factors may be emanating from the hosts or from the malignancies. Moreover, therapy safety and efficacy are not universally constant and differ from individual to individual. Owing to these reasons, selection of chemotherapeutics based on statistical / anecdotal or empirical basis are reported to be associated with risks of failure. Precision Oncology aims to achieve the goal of Personalized Therapy by customizing the therapy choice as well as the treatment plan based on two factors, viz, the unique molecular biomarker profile of the malignancy in each patient, as well as the in vitro sensitivity of the tumor cells to a panel of approved and off-label therapies. Analysis of tumor DNA reveals abnormalities such as point mutations, gene amplifications as well as translocations genome segments which are linked to altered functions – therapies targeted at these alterations are associated with higher rates of success and may hence be beneficial to the patients. Analysis of tumor RNA provides evidence on differential expression of key genes (e.g., cell cycle regulation, cell-surface receptors, signaling molecules), the polypeptide products of which may be potential druggable targets for therapies, thus contributing to higher rates of success. Characterization of molecular biomarkers thus not only helps oncologists better characterize the malignancy, but also presents relevant therapy choices, including off-label use of existing chemotherapeutic drugs. To exemplify, a minor population of NSCLCs carry a deletion in Exon 19 of Epidermal Growth Factor Receptor (EGFR), that renders the tumor chemosensitive to EGFR-Tyrosine Kinase Inhibitors (EGFR-TKI) such as Gefitinib. A proportion of EGFR-mutated NSCLC also exhibit amplification of the MET gene leading to Gefitinib resistance in these tumors. Similar information is vital in selection of relevant efficacious therapy.

Subsequently, the other arm of Precision Oncology, i.e., in vitro chemo-sensitivity testing, offers direct evidence of action of chemotherapeutics drugs against the patient's own cancer cells. Cancer cells isolated from tumor biopsy are maintained in vitro in culture medium, and treated with various drugs (single agents as well as combinations). Analysis of the proportion of apoptotic cancer cells, following treatment, is a direct measure of drug efficacy since cytotoxic chemotherapeutics induce cell killing by apoptosis.

This assay may be used for testing of approved drugs, off-label activities, as well as for evaluating repurposed drugs. Indeed, several repurposed drugs have been reported to potentiate the activity of chemotherapeutics, when used in combination. Repurposed drugs also offer advantages of minimal or no toxicity to the host. To cite an example – recent reports detail the potentiating effect of Chloroquine, an anti-malarial drug, when used in combination with Erlotinib, in NSCLC. The clinical efficacy of Erlotinib is limited to NSCLC patients with EGFR sensitizing mutation; Erlotinib resistance has been reported following prolonged exposure. Combination treatment with Erlotinib and Chloroquine not only increases the efficacy, but also prolongs the efficacy period.

Identification of genetic and metabolic signatures, via tumor DNA and RNA, and selection of potential therapy choices, followed by in vitro evaluation of therapy options on tumor derived cells is expected to contribute to a quantum leap in terms of safety, efficacy and probability of favorable prognosis. Several studies have reported the merits of both approaches, when used individually as well as in combination. These approaches may potentially benefit patients with advanced refractory tumors, in whom conventional treatment approaches have failed and no other approved or experimentally described approaches exist.

Inclusion Criteria:

1. Age – 18 to 70 years (male or female);

2. Cancer of any solid organ, Sarcomas, Melanomas

3. Should have ECOC score of maximum 2;

4. Patient should have progressed on 3 SOC lines of therapy and have no further SOC option/ option is beyond financial reach (such as immunotherapy etc.). Three SOC lines would include surgery / RT / Cytotoxic therapy / targeted therapy;

5. Patient should be willing and fit for fresh tissue biopsy for obtaining live tumor cells / tapping of ascetic fluid / pleural fluid/ CSF etc. as the case may be;

6. The last failed SOC therapy should have resulted in a Progression Free Survival of <90 days;

7. Patient should be financially able to undertake treatment as may be advised after the analysis by DCGL with good compliance history in the past;

8. Patient should be willing and ready for baseline PET Scan and/or CT and/or USG and/or MRI and follow-up scans (usually the first follow-up scan is after 30 days followed by further scans at 75 days and 120 days);

9. Patient is willing and can tolerate cytotoxic and targeted therapy (labelled / off-label / repurposed / natural tumor inhibiting supplements);

10. Female patient is not pregnant / lactating;

11. Provision of signed and dated informed consent form;

12. Stated willingness to comply with all study procedures;

13. Patients must have measurable disease on radiological imaging post biopsy to monitor treatment response

The malignancies to be covered in the study should be fairly representative of the statistical

landscape of cancer i.e. adequate representation for patients with breast, cervix, ovarian, endometrial, lung, liver, prostate, sarcomas, melanoma, gliomas etc.

Exclusion Criteria:

1. Cases of Lymphomas, Leukemias, Myelomas.
2. Life threatening co-morbidities such as HIV, HPV, HBV, HCV, Tuberculosis, CHF, Impaired Hepatic or Renal Function or any psychological deficits etc.
3. Patients not fulfilling inclusion criteria

Study Objective:

Amongst others, the purpose of the study is to evaluate in study participants (refractory + relapsed / recurrent metastatic cancer patients) who are treated with therapy guidance obtained from integrative molecular and cytology analysis provided by the DCGL investigation platform (Exacta) – (a) Objective Response Rate (ORR); (b) Benefit of Progression Free Survival (PFS); (c) Quality of Life; (d) Any other incidental or significant observation or finding relevant for the science or clinical management of cancer;

Number of patients to be recruited:

Pre-screening – About 250 to achieve target post screening sample size of 200

Timeline of study:

(i) Initiation – After approval of respective ethics committees - December 16,2018

(ii) Recruitment to be completed – After completion of target sample size

(iii) Patient-wise Primary end point:

(a) Patient opts out;

(b) Patient is non-compliant;

(c) Patient is clinically unfit to receive further treatment;

(d) Patient dies at any stage before end point;

(e) Patient achieves Progression Free Survival of 2.5 times the Progression Free Survival of the last failed therapy under SOC.

(f) Patient has progressive disease on the first and fall back option on the therapy within the Progression Free Survival duration equal to the last failed therapy;

(g) Patient becomes pregnant of otherwise becomes unfit for the study on the clinical evaluation of HCG-MCC / DCGL.

Drugs that will be recommended by DCGL for administration for treatment of cancer:

(i) Cytotoxic drugs/ targeted therapies approved by USFDA / EMA / IP for treatment of any neoplastic disorder;

(ii) Any drug approved by USFDA / EMA / IP for treatment of any condition other than cancer for human use;

(iii)Vitamins and supplements that do not require regulatory approval.