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Evaluation of in vitro functional response profiling for precision medicine approaches in lymphomas and chronic lymphoproliferative syndromes

Submission date
21/03/2019

Recruitment status
No longer recruiting

Registration date
27/03/2019

Overall study status
Completed

Last Edited
02/11/2020

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Matching the right drug with the right patient at the right time is a challenging task in cancer treatment. In cancer, most if not all precision medicine strategies investigated so far are based on molecular profiling or genomics. However, patient stratification and patient-drug matching based on these approaches has been found to be highly limited due to the still incomplete understanding of the relationship between cancer genotype and phenotype. Functional diagnostic tests measure how living tumor cells extracted from patients react after being exposed to drugs in-vitro and can support the identification of effective and personalized treatments. Unfortunately there are no standardized in-vitro diagnostic platforms to execute these tests and whose clinical utility has been demonstrated. The aim of this study is to test the performance of the Sponsor's in-vitro diagnostic test to predict a patient's response to anticancer drugs, where the test is executed by an automated and standardized analytical system that measures the response of live tumor cells of the patient exposed in-vitro to the drugs.

Who can participate?
Patients aged 18 and over with a confirmed diagnosis of Chronic Lymphocytic Leukemia (CLL), Hodgkin Lymphoma (HL) or Non Hodgkin Lymphoma (NHL) requiring drug-based treatment or, in case of CLL in "watch and wait" status.

What does the study involve?
Patients follow the prescribed therapeutic indications according to regular clinical practice and do not undergo any procedure different from the standard clinical practice. Lymph node biopsies (tissue samples) from lymphoma patients are analyzed before treatment start. Fresh and frozen blood or bone marrow samples from lymphoma and Chronic Lymphocytic Leukemia (CLL) patients are nalyzed both before treatment start and during treatment. Patients do not undergo any procedures different from the standard clinical practice. Samples collected are processed to test the response of the tumor cells to treatments selected by the clinician. The

treatments tested on the cells extracted from the patient samples can include the standard treatment selected by the clinician, other treatments approved for CLL or Lymphomas as well as treatments approved for other diseases. Test results are compared with the response of the patients to the treatment.

What are the possible benefits and risks of participating?
There are no benefits or risks to the patient from participating in this study because there are no invasive tests/practices and the clinical course of the patients isn't affected. If the test works, a larger study will be performed to confirm these findings and help improving therapy personalization.

Where is the study run from?
1. AOU di Bologna, Bologna (Italy)
2. Ospedale San Raffaele, Milano (Italy)
3. Istituto Nazionale Tumori, Milano (Italy)
4. Ospedale Niguarda, Milano (Italy)

When is the study starting and how long is it expected to run for?
April 2019 to April 2025

Who is funding the study?
Cellply S.r.l., Bologna (Italy)

Who is the main contact?
Dr Pier Luigi Zinzani
pierluigi.zinzani@unibo.it

Contact information

Type(s)
Public

Contact name
Miss Laura Rocchi

Contact details
Via Massarenti, 61
Bologna
Italy
40138
+39 (0)510397670
laura.rocchi@cellply.com

Type(s)
Scientific

Contact name
Prof Pier Luigi Zinzani

Contact details

Institute of Hematology “L. e A. Seràgnoli”, AOU Policlinico S.Orsola-Malpighi
Via Massarenti, 9
Bologna
Italy
40138
+39 (0)512144042
pierluigi.zinzani@unibo.it

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CP-CS-002

Study information

Scientific Title
Evaluation of in vitro functional response profiling for precision medicine approaches: an experimental investigation of diagnostic accuracy in lymphomas and chronic lymphoproliferative syndromes

Acronym
MYLYMPH

Study objectives
The identification of effective treatments through precision medicine approaches based on genomics is hampered by intra-tumoral heterogeneity and by the limited understanding of the relationship between genotype and phenotype. Functional profiling based on the analysis of the in-vitro drug response of live tumor cells sampled from patients can support the identification of effective and personalized treatments. There are no standardized in-vitro diagnostic platforms to execute these tests and whose clinical utility has been demonstrated. The present study aims to evaluate the clinical impact of a standardized and automated in-vitro diagnostic platform for the execution of functional profiling tests.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/02/2019, Comitato Etico di Area Vasta Emilia Centro della regione Emilia-Romagna (CE-AVEC), Azienda Ospedaliero-Universitaria di Bologna, Policlinico s.Orsola-Malpighi via Albertoni 15-40138 Bologna, Italy, Email: cometico@aosp.bo.it, ref: 729/2018/Sper/AOUBo

Study design
Prospective multicenter experimental investigation of diagnostic accuracy with biological sample collection study

Primary study design
Observational

Secondary study design
Experimental investigation of diagnostic accuracy

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Lymphomas and chronic lymphoproliferative syndromes

Interventions
The study is focused on in-vitro studies of drug response determined by evaluating the functional response of living cells extracted from patient samples, exposed in-vitro to multiple drug-based treatments. Selected samples are characterized through molecular analysis, to correlate these results with the functional and pharmacological profile. Samples from patients in “watch and wait” status will be collected for the optimization of test parameters.

Patients will follow the prescribed therapeutic indications according to regular clinical practice and will not be subject to any procedure different from the standard clinical practice. Lymph node biopsies from lymphoma patients will be analyzed before treatment start. Fresh and frozen blood or bone marrow samples from lymphoma and Chronic Lymphocytic Leukemia patients will be analyzed both before treatment start and during treatment. Patients will not be subjected to any procedure different from the standard clinical practice. Samples collected will be processed to define the in-vitro response of each patient’s tumor cells to both the treatment selected by the clinician within the standard clinical practice (including single drug treatments or combinations) and other treatments approved for the indications considered in this study or for other indications. Test results will be correlated with results from clinical tests and clinical data used to classify the disease and the response to the therapy.

Intervention Type
Other

Primary outcome measure
1. Sensitivity determined as the proportion of the responders to the treatment that are correctly identified as such by Sponsor’s test
2. Specificity determined as the proportion of the non-responders to the treatment that are correctly identified as such by Sponsor’s test
3. Positive predictive value (PPV) determined as the proportion of the responders to the

treatment among all the patients defined as responders by the Sponsor's test
4. Negative predictive value (NPV) determined as the proportion of the non-responders to the treatment among all the patients defined as non-responders by the Sponsor's test
5. Accuracy determined as the proportion of patients (both responders and non-responders) whose outcomes correctly predicted by the test among all the patients tested
[Timepoint: each restaging event]

Secondary outcome measures
1. Objective Response Rate (ORR) in patient populations identified by the test defined as the proportion of patients with complete remission or partial remission according to the Revised Response Criteria for Malignant Lymphoma (Cheson et al., 2007; Hallek et al., 2008). [Timepoints: each restaging event]
2. Progression-Free Survival (PFS) in patient populations identified by the test defined as the time from start of study treatment to first documentation of objective tumor progression or to death due to any cause, whichever comes first [Timepoint: 1 year]
3. Duration of response in patient populations identified by the test defined as the time from start of the first documentation of objective tumor response (complete response, CR or partial response, PR) to the first documentation of objective tumor progression or to death due to CLL /lymphoma, whichever comes first. [Timepoint: every 3 months for the first 2 years post treatment]
4. Clinical response, a classification of patients according to the Revised Response Criteria for Malignant Lymphoma (Cheson et al., 2007; Hallek et al., 2008) [Timepoints: each restaging event]

Overall study start date
01/04/2019

Completion date
08/04/2025

Eligibility

Key inclusion criteria
Inclusion criteria for Arm A (chronic lymphocytic leukemia):
1. Confirmed diagnosis of CLL
2. Age greater than or equal to 18 years
3. Patient treatment-naïve or relapsed/refractory after previous therapy(ies)
4. Patient in "watch and wait" status or patient requiring drug-based treatment for CLL
5. Availability of clinical data (demographic data, medical history)
6. Patients must provide written informed consent

Inclusion criteria for Arm B (lymphomas):
1. Histologically-confirmed diagnosis of Hodgkin Lymphoma (HL) or Non Hodgkin Lymphoma (NHL)
2. Age greater than or equal to 18 years
3. Patient requiring drug-based therapy for the treatment of HL or NHL
4. Patient requiring a nodal or extranodal biopsy before treatment (only patients with availability biopsy performed during normal clinical practice before treatment will be enrolled)
5. Availability of clinical data (demographic data, medical history)
6. Patients must provide written informed consent

Participant type(s)

Patient

Age group
Mixed

Lower age limit
18 Years

Sex
Both

Target number of participants
500

Key exclusion criteria
Exclusion criteria for Arm A and Arm B:
1. Current therapy with anti-neoplastic or investigational agents
2. Known human immunodeficiency virus (HIV) positivity
3. Known hepatitis B surface antigen-positivity or known or suspected active hepatitis C infection
4. Patients with dementia or an altered mental state that would preclude the understanding and rendering of informed consent

Date of first enrolment
08/04/2019

Date of final enrolment
08/10/2022

Locations

Countries of recruitment
Italy

Study participating centre
AOU di Bologna, Policlinico S.Orsola-Malpighi, UO di Ematologia
via Massarenti 9
Bologna
Italy
40138

Study participating centre
Ospedale San Raffaele, Unità linfomi, Dipartimento di Onco-Ematologia
Via Olgettina, 58
Milano
Italy
20132

Study participating centre
Istituto Nazionale Tumori, Dipartimento di Ematologia e Onco-ematologia pediatrica
via Venezian 1
Milano
Italy
20133

Study participating centre
Ospedale Niguarda, Dipartimento di Ematologia e Oncologia
Piazza Ospedale Maggiore 3
Milano
Italy
20162

Sponsor information

Organisation
CellPly.S.r.l.

Sponsor details
Via Massarenti, 61
Bologna
Italy
40138
+39 (0)510397670
info@cellply.com

Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Cellply S.r.l.

Results and Publications

Publication and dissemination plan
The results of the study will be presented and national and international conferences. Moreover, publication of results in a high-impact peer-reviewed scientific journal is planned within one year from the completion of the study

Intention to publish date
08/04/2026

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date