PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Noninvasive tumor detection by sensitive profiling of circulating tumor DNA in saliva

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

Background and objectives: An important subject of current cancer research is the accurate characterization of cancers at the DNA level. Changes at the DNA level (mutations) can have prognostic and therapeutic relevance. Certain cancertypes have known characteristic mutations that can be detected in routine pathological studies of tumor tissue. When cancer cells die, portions of the DNA are released which - circulating with blood flow - can be detected in various body fluids (including blood plasma, liquor, urine, saliva). The detection of tumor DNA from the blood or bone marrow is already part of standard diagnostics for some cancer entities and is also frequently used as a biomarker for disease monitoring. There are indications that tumor DNA detection is also possible from other body fluids, especially saliva. Due to various advantages (e.g., easier availability, overcoming spatial heterogeneity, e.g., in the presence of metastases), the detection of specific tumor mutations in different liquid biomaterials (also called liquid biopsy) is rapidly developing. Bone marrow punctures and blood sampling, however, are invasive or minimally invasive procedures and can lead to complications such as bleeding or infection. The aim of the present project is to examine whether these mutations, which are characteristic of a tumor, can also be measured in saliva samples from tumor patients, since the collection of saliva by means of a buccal swab or a mouth rinse is a completely non-invasive method.
Procedure and subjects: To assess the suitability of saliva for liquid biopsy diagnostics, saliva and blood samples from patients with various active tumor diseases and known tumorspecific mutations are assayed by a digital droplet PCR, a sensitive biochemical method to find smallest DNA molecules. In addition, two different carrier materials for saliva (cotton swabs and saline solution) will be compared in this context. Patient samples from the Freiburg Biobank are used. The specificity of the method will be tested by comparison with healthy controls.

Brief Summary in Scientific Language

Background: Tumor cells of hematological and solid entities are detectable in different body fluids. In particular, when tumor cells die, DNA fragments are released which - circulating with blood flow - can be detected in various body fluids (including blood plasma, cerebrospinal fluid, urine, saliva) and are therefore

referred to as circulating tumor DNA (ctDNA). Together with the DNA fragments released from healthy cells, they form the entirety of cell-free DNA (cfDNA). Various advantages (e.g., easier availability, overcoming spatial heterogeneity in the presence of metastases) have increasingly placed the detection of specific liquid biopsy tumor mutations ("liquid biopsy") in the focus of current translational research. The detection of tumor-specific DNA sequences from the blood or bone marrow is already part of standard diagnostics for some tumor entities and can be used as a biomarker for disease monitoring. Bone marrow punctures and blood sampling, however, are invasive or minimally invasive procedures and can lead to complications such as bleeding or infection.

Aims and implementation: In this pilot study, we would like to establish the detection of ctDNA from saliva using highly sensitive methods. For this purpose, saliva samples are to be examined for the presence of ctDNA in patients with various tumor diseases and specific tumor mutations (known from previous tumor or blood samples). The rate of ctDNA detection from saliva (ctDNA-S) will be determined as well as the rate of ctDNA detection from blood plasma (ctDNA-P) as positive control.
Saliva samples are obtained by two different techniques: once with a buccal swab and once with a NaCl mouthrinse. The performance of both techniques will be compared. The required biomaterials (blood and saliva samples) come from the CCCF Biobank in Freiburg, for which they were collected and stored frozen for later analysis. cfDNA is isolated from both saliva (cfDNA-S) and blood plasma (cfDNA-P) from the same patient. The ctDNA detection is carried out by means of a droplet digital PCR (ddPCR). To further characterize the mutation pattern, it is planned to use a Next Generation Sequencing method in addition. Primary endpoint is the detection rate of ctDNA in the saliva of tumor patients compared to the detection rate in the blood. To determine specificity, we intend to perform the same analyzes in a collective of healthy controls. The purpose of this pilot study is to assess the suitability of saliva as a non-invasively collectable biomaterial for liquid biopsy studies.

Do you plan to share individual participant data with other researchers?

[---]*

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00019849**
- Date of Registration in DRKS: **2020/03/25**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **44/19 , Ethik-Kommission der Albert-Ludwigs-Universität Freiburg**

Secondary IDs

Health condition or Problem studied

- ICD10: **C00-C97 - Malignant neoplasms**

Interventions/Observational Groups

- Arm 1: **Examination of saliva with two different carrier media (in comparison to plasma) for patient-specific tumor mutations at initial diagnosis or relapse. Saliva (on two different carrier media) and blood from patients with known tumor mutations and active disease is collected for later processing. The biomaterials are compared with regard to the detection of tumor mutations.**

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Other**
- Allocation: **Other**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Other**
- Purpose: **Basic research/physiological study**
- Assignment: **Other**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

1. Detection rate of ctDNA from saliva
2. Correlation of ctDNA levels between saliva and blood plasma

Secondary Outcome

1. Detection rate of ctDNA from saliva collected with a buccals swab or with NaCl solution

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Freiburg im Breisgau**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2019/11/01**
- Target Sample Size: **40**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Patients:
- tumor activity
- known tumor mutation
- presence of blood plasma and saliva in the Freiburg Biobank

healthy subjects:
- minimum 18 years old
- ready to donate two saliva samples and to have peripheral blood drawn (36ml)

Exclusion criteria

Healthy subjects:
- pre-existing chronic disease, especially cancer or rheumatological diseases
- pregnancy

Addresses

- **Primary Sponsor**

  Universitätsklinikum Freiburg
  Hugstetter Strasse 49
  79106 Freiburg
  Germany

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■ **Contact for Scientific Queries**

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Sources of Monetary or Material Support

■ **Institutional budget, no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*