Trial Description

Title

Phase II, Open-label, Study in Patients with anaplastic (ATC) or poorly differentiated thyroid carcinomas (PDTC) to investigate the Clinical Efficacy and Safety of the Combination Therapy of Lenvatinib and Pembrolizumab

Trial Acronym

ATLEP

URL of the trial

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Brief Summary in Lay Language

The aim of the study is to evaluate the efficacy and safety of a combination therapy of lenvatinib and pembrolizumab in ATC/PDTC patients and to establish the combination therapy as a new therapy standard after standard therapies/chemotherapy. In addition, the study will provide us with first indications of which biomarkers are predictive for response to therapy.

Brief Summary in Scientific Language

The primary objective of the trial is to obtain first information on the efficacy of combination therapy of lenvatinib and pembrolizumab in patients with ATC or PDTC, measured as Objective Response Rate (ORR) obtained 12 weeks after start of the study treatment. Secondary objective is to assess Overall Survival (OS), Progression Free Survival (PFS), Clinical Benefit Rate (CBR), response duration and safety of combination therapy.

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

No

Description IPD sharing plan

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Organizational Data

- DRKS-ID: **DRKS00013336**
- Date of Registration in DRKS: **2019/05/16**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**

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Date of Registration in DRKS: **2019/05/16**
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Investigator Sponsored/Initiated Trial (IST/IIT): **yes**

- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **283/18 (Mono) , Ethik-Kommission der Albert-Ludwigs-Universität Freiburg**

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2017-004570-34**

Health condition or Problem studied

- ICD10: **C73 - Malignant neoplasm of thyroid gland**

Interventions/Observational Groups

- Arm 1: **In this study, patients receive continuous oral Lenvatinib therapy with a starting dose of 20 mg/day. This is combined with an i.v. immunocheckpoint inhibitor therapy with Pembrolizumab 200 mg absolute (every 3 weeks), starting 3 weeks after the start of Lenvatinib therapy. If side effects occur, the Lenvatinib dose can be gradually reduced to 10 mg/day.**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

ORR obtained 12 weeks after start of treatment

Secondary Outcome

OS, PFS, CBR, duration of response (DOR), Quality of Life (QOL)

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Med. Klinik 1, Freiburg im Breisgau**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2019/05/28**
- Target Sample Size: **36**
- 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

1.Male or female patients aged >18 years without upper age limit
2.Patient with histologically confirmed anaplastic or poorly differentiated thyroid carcinoma
3.At least one measurable target lesion according to irRECIST meeting the following criteria:
•Lymph node (LN) lesion that measures at least 1 dimension as ≥1.5 cm in the short axis
•Non-nodal lesion that measures ≥1.0 cm in the longest diameter
•The lesion is suitable for repeat measurement using computerized tomography/magnetic resonance imaging (CT/MRI). Lesions that have had external beam radiotherapy (EBRT) or locoregional therapy must show radiographic evidence of disease progression based on irRECIST to be deemed a target lesion

4.ECOG performance status of 0-1
5.Adequately controlled blood pressure (BP) with or without antihypertensive medications, defined as BP ≤160/90 mmHg at screening and no change in antihypertensive medications within 1 week before registration.
6.Adequate renal function defined as creatinine ≤1.5xULN or calculated creatinine clearance ≥30 mL/min per the Cockcroft and Gault formula if creatinine level is >1.5xULN
7.Adequate bone marrow function defined by:
•Absolute neutrophil count (ANC) ≥1,000/µL
•Platelets ≥70,000/µL
•Hemoglobin ≥8 g/dL
8.Adequate blood coagulation function defined by International Normalized ratio (INR) ≤1.5
9.Adequate liver function defined by:
•Total bilirubin ≤1.5xULN except for unconjugated hyperbilirubinemia of Gilbert's syndrome
•Alkaline phosphatase (AP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) ≤3 xULN (in the case of liver metastases ≤5xULN), unless there are bone metastases, in which case liver specific alkaline phosphatase must be separated from the total and used to assess the liver function instead of the total alkaline phosphatase. In case alkaline phosphatase is >3 xULN (in absence of liver metastases) or >5 xULN (in presence of liver metastases) AND subject also is known to have bone metastases, the liver specific alkaline phosphatase must be separated from the total and used to assess the liver function instead of the total alkaline phosphatase
10.Written informed consent obtained according to international guidelines and local laws

Exclusion criteria

1. Patients who have previously received lenvatinib for more than 4 weeks or pembrolizumab or any other immune checkpoint inhibitor therapy (other kinase inhibitor therapies like sorafenib are permitted)
2. Patients with central nervous system (CNS) metastases, unless they have completed local therapy and have discontinued the use of corticosteroids for this indication for at least 1 week before starting treatment in this study; any signs (e.g., radiologic) or symptoms of brain metastases must be stable for at least 2 week before registration.
3. Active other malignancy within the last two years life expectancy <1 year (except for ATC/PDTC) besides adequately treated local cancer (skin cancer, prostate cancer, breast cancer without metastasis). Antihormonal treatments besides aromatase inhibitors are allowed.
4. Known intolerance to study drug (or any of the excipients)
5. Radiation therapy within 14 days prior to start of study treatment with the exception of palliative radiotherapy to bone lesions, which is allowed if completed one day prior to the first intake of lenvatinib.

Addresses

■ **Primary Sponsor**

Universitätsklinikum Freiburg

Primary Sponsor

Universitätsklinikum Freiburg
Hugstetter Strasse 49
79095 Freiburg
Germany

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Fax: **[---]***
E-mail: **[---]***
URL: **www.uniklinik-freiburg.de**

■ **Contact for Scientific Queries**

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■ **Contact for Public Queries**

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URL: **[---]***

Sources of Monetary or Material Support

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

Universitätsklinikum Freiburg
Hugstetter Strasse 49
79095 Freiburg
Germany

Telephone: **[---]***
Fax: **[---]***

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

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79095 Freiburg
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Fax: **[---]***
E-mail: **[---]***
URL: **www.uniklinik-freiburg.de**

- **Commercial (pharmaceutical industry, medical engineering industry, etc.)**

Eisai GmbH
Lyoner Str. 36
60528 Frankfurt/Main
Germany

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

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

Trial Publications, Results and other documents

- Approval of ethics comm. (mandatory for transfer to Studybox) **initiales EK Votum**
- trial protocol (mandatory for transfer to Studybox) **ATLEP_CTP_V3_26.05.2020**

** 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.*