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

Trial Description

Title

COMBI-r – A non-interventional, multi-centric, prospective trial of combined Dabrafenib and Trametinib treatment of advanced melanoma in the real-world setting

Trial Acronym

Combi-r

URL of the trial

[---]*

Brief Summary in Lay Language

COMBI-r is a non-interventional, prospective study to monitor the treatment in daily practice with Dabrafenib and Trametinib in combination (D + T) according to prescription of the attending physician, i. Patients must receive the treatment according to the application area in the respective specialist information of Tafinlar® and Mekinist®. Approx. 720 patients with non-resectable or metastatic melanoma with BRAF V600 mutation from approximately 60 centers in Germany are to be introduced and documented. The documentation of the treatment of patients in this non-interventional study starts with the treatment start with dabrafenib and trametinib in Combination according to prescription by the doctor. If a patient who has already started treatment with Dabrafenib and Trametinib (in a maximum 12-week period) prior to consent to participate in the study, the documentation can and should be retrospective for the time since the onset of treatment Inclusion continues to be prospective. Documentation ends when the patient withdraws or revokes his consent, or when the sponsor closes and ends the entire study, eg Because the required number of patients with the minimum observation period was reached or for other, unforeseeable reasons.

Brief Summary in Scientific Language

With the number of licensed treatments for advanced melanoma growing in the past years, physicians now have a broader choice of therapeutic options to tailor treatment to the patient. However, it is yet not know which sequence of the indicated treatments is the optimal therapeutic strategy. In addition, most of the studies have not covered the entire patient population, as it would be the case in the clinical routine. For example, patients with a more unfavorable performance status, cardiac, hematologic, renal or hepatic impairments, pre-treatments, certain tumor locations or symptomatic brain metastases are mostly excluded from the pivotal trials.
With the marketing authorization of Tafinlar ® and Mekinist ® for Europe to treat patients with unresectable or metastatic melanoma in combination therapy, it is now feasible to complement the data from pivotal COMBI-d and COMBI-v clinical trials with real-world data from a non-interventional study (NIS) in a large

European market.
COMBI-r is designed to include patients which have not been studied in the pivotal trials and report efficiency separately for these, while it will also report real-life safety and tolerability for the entire population the combination is indicated for.

Organizational Data

- DRKS-ID: **DRKS00011387**
- Date of Registration in DRKS: **2016/12/07**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **2905-2015 , Ethikkommission der Medizinischen Hochschule Hannover**

Secondary IDs

Health condition or Problem studied

- ICD10: **C43 - Malignant melanoma of skin**

Interventions/Observational Groups

- Arm 1: **The COMBI-r study aims to provide prospective data on the efficacy, safety and tolerability of the therapy in daily practice in a large population of patients with melanoma who receive the combination of Dabrafenib (Tafinlar®) and Trametinib (Mekinist®) according to the approvals of the summary of product characteristics.**

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Observational study**
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Supportive care**
- Assignment: **Single (group)**

Study Type: **Non-interventional**

Study Type Non-Interventional: **Observational study**

Allocation: **Single arm study**

Blinding: **[---]***

Who is blinded: **[---]***

Control: **Uncontrolled/Single arm**

Purpose: **Supportive care**

Assignment: **Single (group)**

- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **No**

Primary Outcome

PFS (progression-free survival), defined as the time from the start of treatment with Dabrafenib + Trametinib until the date of the first documented progression of the disease or death (any reason).
PFS rates after 6, 12, 18 months follow-up.
DCR (disease control rate), calculated as the proportion of treated patients who received a best clinical response from complete remission (CR) or partial remission (PR, partial remission), or a stabilization of the disease (SD, stable disease) (eg 12, 24 months after initiation of therapy)
OS (overall survival), defined as the time from the start of treatment with D + T to death (of any reason).
OS rates, e.g. 12, 24 months after initiation of therapy.
Multivariate analysis of clinical and biological markers for the identification of predictive factors for long-term use, defined as control of the disease (CR, PR or SD) 12, 24 or, as the case may be, 36 months after initiation of therapy
DOT (duration of therapy, therapy duration), calculated from the start of treatment with D + T up to and including the last day of the last dose
Percentage of patients who received other systemic therapies in the advanced, non-resectable or metastatic stage before initiation of therapy with D + T as well as the percentage of patients with other pre-treatment regimens (e.g., radiation, local therapies)
Frequency (by type) and number of pretreatments.
Frequency (by type) of treatment after therapy with D + T
Percentage of treated patients with one or more dose reduction (s).
Median duration of dose reductions, calculated as from the date of the modified dose until the date of return to the originally prescribed standard dose.
Reasons for dose reduction.
Calculated average dose (according to prescription).
Changes in the course of the therapy with D + T of the scores on the quality of life, measured by the instruments: EQ5D, Facit-F
Frequency and severity of adverse events.
Percentage of patients with discontinuation due to an undesirable event (by severity).
Percentage of different methods for mutation analysis
Frequency of post-test with a second method in case of negative initial testing
Panel of biomarkers studied

Secondary Outcome

It is not specified for primary and secondary endpoints

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Dermatologie, Freiburg im Breisgau**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2015/11/15**
- Target Sample Size: **720**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

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

Additional Inclusion Criteria

1. Age of 18 years
2. Diagnosis of non-resectable or metastatic melanoma with BRAF V600 mutation
3. Consent to participate in the present study after clarification by the physician
4. Treatment of melanoma with combination therapy from Dabrafenib (Tafinlar®) and Trametinib (Mekinist®) according to prescription by the treating physician, initiated no longer than 12 weeks before admission into this study or immediately after inclusion in this study Should be initiated

Exclusion criteria

1. Previous treatment by an MEK inhibitor in monotherapy (including trametinib) or by any other BRAF / MEK inhibitor combinations than dabrafenib / trametinib
2. Dabrafenib / Trametinib combination treatment more than 12 weeks before consent to the study and start of the documentation
3. Current or upcoming participation in a clinical trial (including melanoma)

4. Ongoing or pending treatment of a tumor disease other than that of melanoma with the exception of keratoacanthoma, squamous cell carcinoma or basal cell carcinoma of the skin

Addresses

- **Primary Sponsor**

  Novartis Pharma GmbH
  Roonstr. 25
  90429 Nürnberg
  Germany

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

- **Contact for Scientific Queries**

  Hauttumorzentrum Hannover, Medizinische Hochschule Hannover
  Mr. Prof. Dr. med Ralf Gutzmer
  Carl-Neuberg-Str. 1
  30625 Hannover
  Germany

  Telephone: **0511 / 532-0**
  Fax: **0511 532-18854**
  E-mail: **gutzmer.ralf at mh-hannover.de**
  URL: **www.mh-hannover.de**

- **Contact for Public Queries**

  Hauttumorzentrum Hannover, Medizinische Hochschule Hannover
  Mr. Prof. Dr. med Ralf Gutzmer
  Carl-Neuberg-Str. 1
  30625 Hannover
  Germany

  Telephone: **0511 532-0**
  Fax: **0511 532-18854**
  E-mail: **gutzmer.ralf at mh-hannover.de**
  URL: **www.mh-hannover.de**

Sources of Monetary or Material Support

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

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

Novartis Pharma GmbH
Roonstr. 25
90429 Nürnberg
Germany

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

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.*