Study of Efficacy and Safety of LXH254 Combinations in Patients With Previously Treated Unresectable or Metastatic Melanoma

NCT-Nummer:
NCT04417621

Studienbeginn:
Oktober 2020

Letztes Update:
28.04.2021

Wirkstoff:
LXH254, LTT462, Trametinib, Ribociclib
Indikation (Clinical Trials):
Melanoma

Geschlecht:
Alle

Altersgruppe:
Alle

Phase:
Phase 2

Sponsor:
Novartis Pharmaceuticals

Collaborator:
-

Studien-Informationen

Brief Summary:

The primary purpose of this study is to evaluate the efficacy of LXH254 combinations in previously treated unresectable or metastatic melanoma

Ein-/Ausschlusskriterien

Inclusion Criteria:

Male or female must be ≥ 12 years For adolescents only (12-17 years): body weight > 40kg

Histologically confirmed unresectable or metastatic cutaneous melanoma

Previously treated for unresectable or metastatic melanoma:

- Participants with NRAS mutation:

- Participants must have received prior systemic therapy for unresectable or metastatic melanoma with an anti-PD-1/PD-L1 checkpoint inhibitor as a single agent or in combination with anti-CTLA-4. No additional systemic treatment is allowed for unresectable or metastatic melanoma

- A maximum of two prior lines of systemic immunotherapy for unresectable or metastatic melanoma are allowed

- The last dose of prior therapy (anti-PD-1, anti-PD-L1 or anti-CTLA-4) must have been received more than four weeks before randomization

- Participants must have documented confirmed progressive disease as per RECIST v1.1 while on/after treatment with checkpoint inhibitor therapy. The last progression must have occurred within 12 weeks prior to randomization in the study

- Participants with BRAFV600 mutant disease:

- Participants must have received prior systemic therapy for unresectable or metastatic melanoma with anti-PD-1/PD-L1 as a single agent or in combination with anti-CTLA-4. Additionally, participants must have received targeted therapy with a RAFi as a single agent or in combination with a MEKi as the last prior therapy. No additional systemic treatment is allowed for advanced or metastatic melanoma

- A maximum of three prior lines of systemic therapy for unresectable or metastatic melanoma are allowed

- The last dose of targeted therapy (last prior therapy) must have been received more

than 2 weeks prior to randomization

- Participants must have documented progressive disease as per RECIST v1.1 while on/after treatment with targeted therapy. The last progression must have occurred within 12 weeks prior to randomization in the study Other protocol-defined inclusion criteria may apply.

Exclusion Criteria:

Treatment with any of the following anti-cancer therapies prior to the first dose of study treatment within the stated timeframes:

- ≤ 4 weeks for radiation therapy or ≤ 2 weeks for limited field radiation for palliation prior to the first dose of study treatment.
- ≤ 4 weeks or ≤ 5 half-life (whichever is shorter) for small molecule therapeutics.
- ≤ 4 weeks for any immunotherapy treatment including immune checkpoint inhibitors.

Participants participating in additional parallel investigational drug or medical device studies.

All primary central nervous system (CNS) tumors or symptomatic CNS metastases that are neurologically unstable History or current evidence of retinal vein occlusion (RVO) or current risk factors for RVO (e.g. uncontrolled glaucoma or ocular hypertension, history of hyperviscosity or hypercoagulability syndromes).

Any medical condition that would, in the investigator's judgment, prevent the patient's participation in the clinical study due to safety concerns or compliance with clinical study procedures.

Other protocol-defined exclusion criteria may apply

Studien-Rationale

Primary outcome:

1. Overall Response Rate (Time Frame - 35 months):
Confirmed ORR using RECIST v1.1, per local assessment

Secondary outcome:

1. Duration of Reposnse (DOR) (Time Frame - 4 years):
Local and central assessment

2. Progression Free Survival (PFS) (Time Frame - 4 years)

3. Disease Control Rate (DCR) (Time Frame - 3 years):
Using RECIST v1.1, per local and central assessment

4. Overall Survival (OS) (Time Frame - 4 years)

5. Derived PK parameter (Cmax) for LXH254 & LTT462 (Time Frame - Up to 5 months)

6. Derived PK parameter (Cmax) for LXH254 & trametinib (Time Frame - Up to 5 months)

7. Derived PK parameter (Cmax) for LXH254 & ribociclib (Time Frame - Up to 5 months)

8. Derived PK parameter (AUC) for LXH254 & LTT462 (Time Frame - Up to 5 months)

9. Derived PK parameter (AUC) for LXH254 & trametinib (Time Frame - Up to 5 months)

10. Derived PK parameter (AUC) for LXH254 & ribociclib (Time Frame - Up to 5 months)

11. Incidence of adverse events (AEs) and serious adverse events (SAEs) (Time Frame - 35 months):
Number of participants with Adverse Events (AEs) and SAEs as a measure of safety and tolerability

12. Dose Interruptions (Time Frame - 35 months):
Tolerability measured by the number of subjects who have interruptions of study treatment and reason for interruptions

13. Dose reductions (Time Frame - 35 months):
Tolerability measured by the number of subjects who have reductions of study treatment and reason for reductions

Studien-Arme

- Experimental: LXH254 + LTT462
- Experimental: LXH254 + trametinib
- Experimental: LXH254 + ribociclib

Geprüfte Regime

- LXH254:
  LXH254 will be supplied as tablet for oral use.
- LTT462:
  LTT462 will be supplied as hard gelatin capsule for oral use.

- Trametinib:
  Trametinib will be supplied as film-coated tablet for oral use
- Ribociclib:
  Ribociclib will be supplied in tablets and hard gelatin capsules.

Kontakt

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University of Miami

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Quelle: ClinicalTrials.gov