**Objectives**

1. **Primary objectives**
   - Characterise safety of BI 764532 + ezabenlimab and determine MTD and/or RDE/PD
   - Determine the pharmacokinetic profile of BI 764532 + ezabenlimab
   - Conduct a preliminary assessment of the efficacy of BI 764532 + ezabenlimab by assessing objective response

2. **Secondary objectives**
   - Determine the pharmacokinetic profile of BI 764532 + ezabenlimab
   - Conduct a preliminary assessment of the efficacy of BI 764532 + ezabenlimab by assessing objective response

**Inclusion and exclusion criteria**

**Inclusion**

- Locally advanced, metastatic or relapsed cancer of following confirmed histologies:
  - SCLC
  - LCNEC of the lung
  - NEC of the NEC

**Exclusion**

- Persistent toxicity from previous treatments that has not resolved to CTCAE grade 5
- Patient with active autoimmune disease or a documented history of autoimmune disease, that requires systemic treatment

**Endpoints**

- **Primary endpoints**
  - Occurrence of DLTs during the on-treatment period
  - Objective response, defined as best overall response of CR or PR, according to RECIST 1.1

- **Secondary endpoints**
  - Occurrence of DLTs during the on-treatment period
  - Pharmacokinetic parameters: \( C_{max} \) and AUC

**References**

- [9] Yiyuan Ma
- [10] Lijiang Geng
- [11] Boehringer Ingelheim France S.A.S., Reims, France; Boehringer Ingelheim (China) Investment Co., Ltd., Shanghai, China; TU Dresden University of Technology, NCT/UCC Early Clinical Trial Unit, Dresden, Germany

**Trial design**

- **This is a Phase 1, non-randomised, open-label, multicentre dose escalation trial of BI 764532 (DLL3/CD3 IgG-like T-cell engager)**

**Mechanism of action of BI 764532, a novel DLL3-targeting T-cell engager**

**Introduction**

**Efficacy of BI 764532 in patients with SCLC or NECs treated in a Phase I study (NCT04429087)**

- A Phase I, dose escalation and expansion study with BI 764532 is ongoing in patients with SCLC, epNEC, or LCNEC (N=107)\(^2\)
- MTD has not been reached and dose escalation is ongoing\(^2\)

**Populations**

- **Dose Level 1:** Ezabenlimab
- **Dose Level 2:** BI 764532 + Ezabenlimab
- **Dose Level 3:** BI 764532 + ezabenlimab

**Dose escalation**

- BI 764532 will be administered IV with step-in doses followed by the target doses
- Dose escalations will be made at 200% increase from the previous dose level (in the absence of DLTs)\(^3\)
- Ezabenlimab will be administered IV every 3 weeks
- Dose escalation for BI 764532 will be guided by a Bayesian Logistic Regression Model with overdose control
- Dose escalation will continue until the MTD is reached, or upon decision of the Dose Escalation Committee

**Trial rationale**

- BI 764532 has been shown to upregulate the PD-L1 pathway in preclinical studies
- Therefore, combining BI 764532 with the PD-1 inhibitor, ezabenlimab, might enhance efficacy

**Trial design**

- **This is a Phase 1, non-randomised, open-label, multicentre dose escalation trial of BI 764532 + ezabenlimab in patients with DLL3-positive SCLC or epNECs who have failed or are not eligible for available standard therapies (NCT06799786)**

- **Secondary endpoints**
  - Determine the pharmacokinetic profile of BI 764532 + ezabenlimab
  - Conduct a preliminary assessment of the efficacy of BI 764532 + ezabenlimab by assessing objective response

**Inclusion and exclusion criteria**

**Inclusion**

- Locally advanced, metastatic or relapsed cancer of following confirmed histologies:
  - SCLC
  - LCNEC of the lung
  - NEC of the NEC
- Patients who failed conventional treatment and are not eligible for established treatment options
- At least one evaluable lesion outside of the CNS as defined per RECIST 1.1
- Tumour positive for DLL3 expression by IHC (central pathology review)\(^1\)
- Adequate liver, bone marrow and renal organ function

**Exclusion**

- Prior anti-cancer therapy: any other anti-cancer drug within 4 weeks or within 5 half-life periods or extensive field radiation 2 weeks prior to first administration of BI 764532

**Endpoints**

- **Primary endpoints**
  - Occurrence of DLTs during the on-treatment period
  - Objective response, defined as best overall response of CR or PR, according to RECIST 1.1

- **Secondary endpoints**
  - Occurrence of DLTs during the on-treatment period
  - Pharmacokinetic parameters: \( C_{max} \) and AUC

**References**

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