**Platform trial of ezabenlimab (BI 754091), an anti-PD-1 antibody, in patients with previously treated advanced solid tumors: combination with BI 836880, a VEGF/Ang2-blocking nanobody**

Maen Hussein,1,2* Johanna Bendell,3,3 Hendrik Tobias Arkenau,4,5 Quincy Chu,4 Aaron Hansen,7 Damijan Erzen,6 Sheng Qiu,8 Anthony Lucarelli,9 Ivor Percent10

1Florida Cancer Specialists, Lady Lake, FL, USA; 2Sarah Cannon Cancer Research Institute, Nashville, TN, USA; 3Tennessee Oncology, Nashville, TN, USA; 4Sarah Cannon Research Institute, London, UK; 5University College London Cancer Institute, London, UK; 6Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada; 7Princess Margaret Cancer Centre, Toronto, ON, Canada; 8Boehringer Ingelheim GmbH, Ingerheim, Germany; 9Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; 10Florida Cancer Specialists, Port Charlotte, FL, USA

**Introduction**

- VEGF and Ang2 play key roles in tumor angiogenesis and have an immunosuppressive effect in the tumor microenvironment.
- Combining anti-VEGF/Ang2 with anti-PD-1 therapy promotes an immunopermissive state supportive of T-cell-mediated tumor cell death (Figure 1).1,2 An ongoing Phase Ib trial utilizing this therapeutic approach observed preliminary safety and efficacy.3,4
- NCT03697304 is a Phase IIb platform trial assessing ezabenlimab (BI 754091), an anti-PD-1 antibody, in combination with other agents. Here we describe Module C, in which ezabenlimab will be combined with BI 836880, a humanized bispecific nanobody that targets VEGF and Ang2.

**Study Design**

- Patients are being enrolled in 5 cohorts, and will receive iv infusions of ezabenlimab (240 mg) and BI 836880 (720 mg) Q3W.
- Treatment will continue until progressive disease, unacceptable toxicity, withdrawal of patient consent or for a maximum of 1 year (treatment may be extended in case of clinical benefit).

**Cohort 1**: locally advanced, unsectable or metastatic gastric adenocarcinoma or GEC (N=30)

- ≥1 prior systemic treatment
- No prior anti-PD-(L)-1-based therapy

**Cohort 2**: any advanced/metastatic solid tumor, except non-squamous NSCLC or melanoma (N=30)

- Patients achieving benefit from prior anti-PD-(L)-1 treatment1,2 (i.e. at least stable disease for 4+ months and treatment duration of >2 months on prior anti-PD-(L)-1-based therapy)

**Cohort 3**: select advanced/metastatic solid tumors (N=30)

- Patients achieving no benefit from prior anti-PD-(L)-1 treatment1 (i.e. progressive disease within 4 months of beginning prior anti-PD-(L)-1-based therapy)

**Cohort 4**: locally advanced, unsectable or metastatic colorectal cancer (N=30)

- Microsatellite stable disease
- ≥1 prior systemic treatment; no prior anti-PD-(L)-1-based therapy

**Cohort 5**: advanced endometrial cancer (N=30)

- Mismatch repair proficient, microsatellite stable disease
- Progressed after 1 line of chemotherapy; no prior anti-PD-(L)-1-based therapy

**Key points**

- **Eligibility criteria**
  - Adult patients (≥18 years of age)
  - ECOG PS 0–1
  - Advanced or metastatic solid tumor
  - At least one measurable lesion according to RECIST v1.1
  - Patient must agree to pre- and on-treatment tumor biopsies

- **Endpoints**
  - **Primary endpoint**
    - Objective response per RECIST v1.1, as assessed by the Investigator
  - **Secondary endpoints**
    - Duration of response
    - Disease control
    - Progression-free survival

- **Further endpoints**
  - Anti-tumor activity by iRECIST
  - Safety and tolerability of ezabenlimab and BI 836880
  - Pharmacokinetics and pharmacodynamics
  - Overall survival

**Study status**

- The trial is planned to recruit at 18 sites in the UK and North America
- 9 sites are currently active
- As of December 04 2020:
  - 42 patients screened
  - 16 patients treated

**Study design**

- **Key inclusion criteria**
  - Adult patients (≥18 years of age)
  - ECOG PS 0–1
- **Key exclusion criteria**
  - Severe hemorrhagic or thromboembolic event in the past 12 months
  - Prior anti-angiogenic therapy (except colorectal cancer cohort)
  - Inherited predisposition to bleeding or to thrombosis
  - Significant cardiovascular or cerebrovascular disease
  - Symptomatic CNS metastases

**Presented at the ASCO GI Cancers Symposium, Virtual Format, January 15–17 2021**

This study was funded by Boehringer Ingelheim. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development and have approved the final version.

Medical writing support, financially supported by Boehringer Ingelheim, was provided by Jim Sinclair, of GeoMed, an Ashfield company, part of UDG Healthcare plc, during the development of this poster

**References**

8. As of December 04 2020
9. TPS152
10. *Corresponding author email address: mhussein@facs.com"