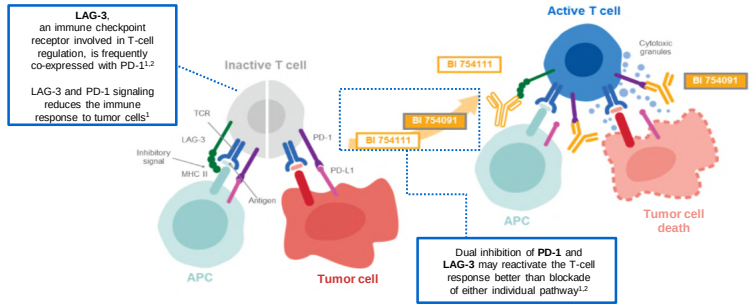
Safety of BI 754111, an anti-LAG-3 mAb, in combination with BI 754091, an anti-PD-1 mAb, in patients with advanced solid tumors

Poster #127

Melissa Johnson,[1,2]* Manish R. Patel,[1,3] Mohamad Cherry,[4] Yoon-Koo Kang,[5] Kensei Yamaguchi,[6] Do-Youn Oh,[7] Maen Hussein,[3] Shigehisa Kitano,[6,8] Shunsuke Kondo,[8] Aaron Hansen,[9] Ivor Percent,[3] Ben George,[10] Edward Arrowsmith,[2] Manabu Morimoto,[11] Christine Duffy,[12] Miaomiao Ge,[12] Maren Rohrbacher,[13] Mabrouk Elgadi,[14] Johanna Bendell[1,2]

[1]Sarah Cannon Research Institute, Nashville, TN, USA; [2]Tennessee Oncology, Nashville, TN, USA; [3]Florida Cancer Specialists, Sarasota, FL, USA; [4]University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; [5]Asan Medical Center, Seoul, South Korea; [6]Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; [7]Seoul National University Hospital, Seoul, South Korea; [8]National Cancer Center Hospital, Tokyo, Japan; [9]Princess Margaret Cancer Centre, Toronto, ON, Canada; [10]Department of Medicine, Division of Hematology and Oncology, Medical College of Wisconsin, Milwaukee, WI, USA; [11]Kanagawa Cancer Center, Yokohama, Kanagawa Prefecture, Japan; [12]Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, USA; [13]Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; [14]Boehringer Ingelheim (Canada) Ltd./Ltée., Burlington, ON, Canada

Introduction



APC, antigen-presenting cell; LAG-3, lymphocyte-activation gene 3; MHC II, major histocompatibility complex class II; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; TCR, T-cell receptor

Objectives

- To assess the safety and tolerability of BI 754111, an anti-LAG-3 monoclonal antibody (mAb), in combination with BI 754091, an anti-PD-1 mAb, in patients with advanced solid tumors

Methods

- Data from four trials were included; 333 patients who received the RD of BI 754111 600 mg in combination with BI 754091 240 mg q3w were included in this analysis
- Patients received treatment until disease progression or unacceptable toxicities
- *Additional information on individual trials is available via the QR code*

Study 1381.2 Phase I (N=118)

Dose escalation: advanced solid tumors
Dose expansion cohorts: anti-PD-1/L1 treatment-naïve MSS mCRC; anti-PD-1/L1 pre-treated TMB high/MSI-H/dMMR solid tumors; anti-PD-1/L1 pre-treated NSCLC (with secondary resistance to prior anti-PD-1/L1 treatment); first-line NSCLC

Study 1381.3 Phase I (N=6)

PET imaging biodistribution study in advanced NSCLC and HNSCC

Study 1381.4 Phase I (N=132)

Dose escalation: advanced solid tumors
Dose expansion cohorts: anti-PD-1 treatment-naïve gastric/GEJ cancer; anti-PD-1 treatment-naïve esophageal cancer; anti-PD-1 treatment-naïve HCC; anti-PD-1 pre-treated gastric/GEJ cancer, esophageal cancer and HCC

Study 1381.9 Phase II (N=77)

Platform trial in: anti-PD-1 pre-treated GEC; advanced solid tumors with primary and secondary resistance to anti-PD-1 treatment

dMMR, deficient mismatch repair; GEC, gastroesophaegeal cancer; GEJ, esophagogastric junction; HCC, hepatocellular carcinoma; HNSCC, head and neck squamous cell carcinoma; mCRC, metastatic colorectal cancer; MSI-H, microsatellite instable-high; MSS, microsatellite stable; PET, positron emission tomography; q3w, every 3 weeks; RD, recommended dose; TMB, tumor mutational burden

Key findings and conclusions

- In patients with advanced solid tumors, the combination of BI 754111, an anti-LAG-3 mAb, and BI 754091, an anti-PD-1 mAb, had a relatively well-tolerated safety profile, similar to other checkpoint inhibitors
- Further investigation will assess the efficacy of this combination in the treatment of patients with solid tumors

Tqr.bz/1mS

Scan the QR code for an electronic copy of the poster and supplementary content†, plus references

†Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from ASCO® and the authors of this poster

*Corresponding author email address: mjohnson@tnonc.com

Patients

1381.2 (N=118)	1381.3 (N=6)	1381.4 (N=132)	1381.9 (N=77)
Male, n (%): 65 (55.1)	Male, n (%): 5 (83.3)	Male, n (%): 104 (78.8)	Male, n (%): 40 (51.9)
Age range: 25–85 years	Age range: 53–77 years	Age range: 23–80 years	Age range: 38–88 years

Safety

AEs (≥10% incidence)

RD population, n (%)	All grades (N=333)	Grade ≥3 (N=333)
Any AE	304 (91.3)	107 (32.1)
Fatigue	82 (24.6)	4 (1.2)
Pyrexia	63 (18.9)	1 (0.3)
Decreased appetite	59 (17.7)	3 (0.9)
Nausea	59 (17.7)	3 (0.9)
Diarrhea	46 (13.8)	2 (0.6)
Vomiting	42 (12.6)	2 (0.6)
Constipation	40 (12.0)	0 (0.0)
Anemia	39 (11.7)	17 (5.1)
Cough	39 (11.7)	0 (0.0)
Dyspnea	38 (11.4)	5 (1.5)

- In total, 182 (54.7%) patients experienced AEs defined as drug related by investigators
  - Of these, 40 (12.0%) were Grade ≥3

Immune-related AEs (≥2.5% incidence)

RD population, n (%)	All grades (N=333)	Grade ≥3 (N=333)
Any immune-related AE	98 (29.4)	25 (7.5)
IRR	17 (5.1)	3 (0.9)
Hypothyroidism	15 (4.5)	0 (0.0)
Rash maculo-papular	13 (3.9)	2 (0.6)
Hyperthyroidism	11 (3.3)	1 (0.3)
ALT increase	9 (2.7)	2 (0.6)
Pruritus	9 (2.7)	0 (0.0)

- Overall, 32 (9.6%) patients discontinued the study drug due to AEs, 20 of which were Grade ≥3 (6.0%)
  - The most common reason for discontinuation was IRR (n=7), 3 of which were Grade ≥3 (<1%)

Drug-related SAEs (≥0.5% incidence)

RD population, n (%)	All grades (N=333)	Grade ≥3 (N=333)
Any drug-related SAE	24 (7.2)	18 (5.4)
IRR	3 (0.9)	2 (0.6)
AST increase	2 (0.6)	2 (0.6)
Diabetic ketoacidosis	2 (0.6)	2 (0.6)
Febrile neutropenia	2 (0.6)	2 (0.6)
Hyperthyroidism	2 (0.6)	1 (0.3)

- During the study, 4 (1.2%) patients experienced an AE that resulted in death, none of which were deemed drug related:
  - Disease progression
  - Acute kidney injury
  - Hypotension
  - Pneumonia

AEs, adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase; IRR, infusion-related reaction; SAEs, serious AEs

Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting, Virtual Format, May 29-31, 2020

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 assistance, supported financially by Boehringer Ingelheim, was provided by Nadia Fowler, of GeoMed, an Ashfield company, part of UDG Healthcare plc, during the development of this poster