An open-label, Phase I trial of BI 754091 alone and in combination with BI 754111 in Asian patients with advanced solid tumors

Poster #118

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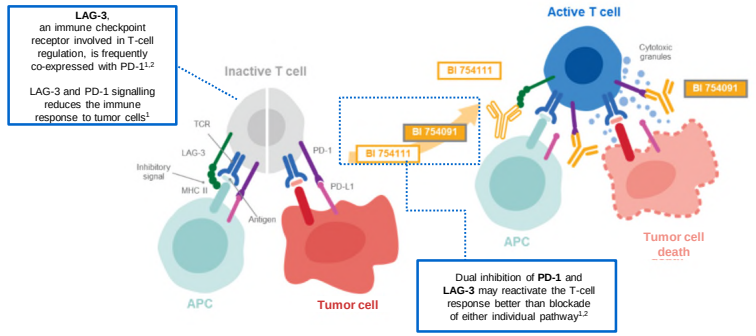
Introduction



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

- A Phase I trial to investigate BI 754091, an anti-PD-1 antibody, as monotherapy and in combination with BI 754111, an anti-LAG-3 antibody, in Asian patients with advanced solid tumors

Methods

- *Additional content can be accessed via the QR code*

Part 1 BI 754091, 240 mg via IV infusion; q3w

RP2D

Part 2 BI 754091 + BI 754111
Starting dose BI 754091: RD (Part 1) q3w
Starting dose BI 754111: 400 mg via IV infusion q3w

Patients with advanced unresectable, and/or metastatic solid tumors of any type

Primary endpoint: MTD based on DLTs in Cycle 1

RP2D

Part 3 BI 754091 + BI 754111 (at RP2D)

Cohort A	Gastric/esophagogastric junction cancer	No previous anti-PD-1/PD-L1 mAb therapy ≥1 line of systemic therapy
Cohort B	Esophageal cancer	
Cohort C	Hepatocellular cancer	
Cohort D	Gastric/esophagogastric junction, esophageal, or hepatocellular cancer	Previous anti-PD-1/PD-L1 mAb therapy

Primary endpoint: OR (CR or PR per RECIST 1.1)

CR, complete response; DLT, dose-limiting toxicity; IV, intravenous; mAb, monoclonal antibody; MTD, maximum tolerated dose; OR, objective response; PD-1, programmed cell death protein 1; PD-L1, programmed cell death-ligand 1; PR, partial response; q3w, once every three weeks; RD, recommended dose; RECIST, response evaluation criteria in solid tumors; RP2D, recommended Phase II dose

Key findings and conclusions

- MTD was not reached for BI 754091 monotherapy or for BI 754091 in combination with BI 754111
- The recommended dose for the combination was confirmed to be BI 754091 240 mg plus BI 754111 600 mg q3w
- Treatment was well tolerated and consistent with that observed in the global trial[3]
- Preliminary antitumor activity was observed

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Results

DLTs (Parts 1 and 2)

- In Part 1, 6 patients received BI 754091 240 mg; in Part 2, 9 patients received BI 754091 + BI 754111 (400/600/800 mg; n=3 per cohort). No DLTs were reported in Parts 1 or 2

Patient disposition (Part 3)

N (%)	Cohort A (N=36)	Cohort B (N=37)	Cohort C (N=20)	Cohort D (N=36)	Total (N=129)
Currently on treatment	**5 (13.9)**	**6 (16.2)**	**3 (15.0)**	**4 (11.1)**	**18 (14.0)**
Treatment discontinued	**31 (86.1)**	**31 (83.8)**	**17 (85.0)**	**32 (88.9)**	**111 (86.0)**
PD	28 (77.8)	27 (73.0)	14 (70.0)	29 (80.6)	98 (76.0)
AE	1 (2.8)	4 (10.8)	2 (10.0)	2 (5.6)	9 (7.0)
Patient decision	2 (5.6)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.6)
Completed	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.8)	1 (0.8)
Other	0 (0.0)	0 (0.0)	1 (5.0)	0 (0.0)	1 (0.8)

Best overall confirmed response according to RECIST 1.1 (Part 3)

N (%)	Cohort A (N=36)	Cohort B (N=37)	Cohort C (N=20)	Cohort D (N=36)	Total (N=129)
CR	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
PR	4 (11.1)	8 (21.6)	0 (0.0)	0 (0.0)	12 (9.3)
SD	10 (27.8)	8 (21.6)	9 (45.0)	6 (16.7)	33 (25.6)
PD	17 (47.2)	17 (45.9)	11 (55.0)	23 (63.9)	68 (52.7)
NE	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.8)	1 (0.8)

Safety (Parts 2 and 3)

N (%)	All Grade (N=138)	Grade ≥3
Total with AEs (in ≥10% of patients)	117 (84.8)	45 (32.6)
Pyrexia	33 (23.9)	0 (0.0)
Decreased appetite	23 (16.7)	3 (2.2)
Anemia	18 (13.0)	10 (7.2)
AST increased	14 (10.1)	5 (3.6)
Nausea	14 (10.1)	0 (0.0)
Total with immune-related AEs (in ≥5% of patients)	46 (33.3)	8 (5.8)
Hypothyroidism	11 (8.0)	0 (0.0)
Hyperthyroidism	7 (5.1)	1 (0.7)
Rash	7 (5.1)	0 (0.0)
Rash maculo-papular	7 (5.1)	0 (0.0)
Total with drug-related SAEs (in ≥2 patients)	9 (6.5)	6 (4.3)
Febrile neutropenia	2 (1.4)	2 (1.4)
Hyperthyroidism	2 (1.4)	1 (0.7)
Infusion-related reaction	2 (1.4)	1 (0.7)
ALT increased	2 (1.4)	2 (1.4)
AST increased	2 (1.4)	2 (1.4)

Two patients had AEs leading to death (not drug-related) → • Pneumonia • Acute kidney injury

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; NE, not evaluable; PD, progressive disease; SAEs, serious adverse events; SD, stable disease

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