2023年10月24日

各　位

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《続報》ESMO年次総会におけるCBP501臨床第2相試験結果のポスター発表について

当社の抗がん剤候補化合物CBP501の臨床第2相試験データについて、2023年10月20日から24日までスペイン・マドリードで開催されている欧州臨床腫瘍学会（ESMO）年次総会でポスター発表が行われました。
発表されたポスターを別紙のとおり公表いたします。

表題：　“Multicenter, randomized, parallel group, phase 2 study to establish the efficacy and safety of CBP501, cisplatin, and nivolumab for ≥3rd line treatment of patients with exocrine pancreatic cancer and WBC <10,000/mm^3 at screening”
（参考訳）「白血球数10,000/mm^3未満でスクリーニングした3次治療以降の外分泌膵臓がん治療における CBP501・シスプラチン・ニボルマブ3剤併用の有効性安全性を確立するための多施設無作為化並行群臨床第2相試験」
プレゼンテーション番号：1625P
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同ポスターに関する解説は、追って当社ウェブサイト www.canbas.co.jp 等に掲載いたします。

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以上

MADRID 2023 ESMO congress

FPN# 1625P

Multicenter, randomized, parallel group, phase 2 study to establish the efficacy and safety of CBP501, cisplatin, and nivolumab for ≥3rd line treatment of patients with exocrine pancreatic cancer and WBC <10,000/mm^3

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INTRODUCTION

Metastatic pancreatic ductal adenocarcinoma (PDAC) is an aggressive disease without third line standard-of-care treatment option and a low survival rate[1]. CBP501 is a synthetic, cell-permeable dodecapeptide (12-amino acid) G2 checkpoint abrogator and calmodulin-modulating peptide that increases platinum influx into tumor cells inducing tumor immunogenic cell death, suppresses M2 macrophages, reduces cancer stem cell populations and tumor cell migration and enhances anti-tumor activity with anti-programmed cell death-1 (anti-PD-1).

OBJECTIVES

This multicenter, randomized, parallel group, phase 2 study was conducted to assess the efficacy and safety of CBP501, cisplatin, and nivolumab for ≥3rd line treatment in patients with exocrine pancreatic cancer and white blood cell count (WBC) <10,000/mm^3 (NCT: 04953962).

METHODS

Patients with metastatic PDAC, who received 2 or more lines of systemic therapy, with WBC <10,000/mm^3 were stratified by Eastern Cooperative Oncology Group (ECOG) status (0 vs 1) and liver metastasis (present vs absent) and randomized 1:1:1:1 to one of the following 4 arms:

1 - CBP501 25 mg/m^2 + cisplatin 60 mg/m^2 + nivolumab 240 mg
2 - CBP501 16 mg/m^2 + cisplatin 60 mg/m^2 + nivolumab 240 mg
3 - CBP501 25 mg/m^2 + cisplatin 60 mg/m^2
4 - cisplatin 60 mg/m^2 + nivolumab 240 mg

Therapy was administered every 3 weeks. Patients received up to 4 cycles of combination therapy, then, for patients without disease progression, up to 6 cycles of single-agent nivolumab every 21 days (nivolumab arms only). The primary endpoint was 3-month progression-free survival rate (3M PFSR) in the Intent-To-Treat (ITT) population. Secondary endpoints were safety, progression-free survival (PFS), confirmed and timepoint objective response rate (cORR/ORR) by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, duration of response (DOR), disease control rate (DCR) and overall survival (OS).

A Fleming 2-stage design was used. In stage one, if ≤1 patient was progression-free at 3 months, the treatment group was stopped for futility. If ≥4 patients were progression-free at 3 months, the treatment group was stopped, and the null hypothesis rejected. Otherwise, 14 additional patients were to be accrued to the study arm in the second stage.

RESULTS- PATIENT CHARACTERISTICS

Between 09 December 2021 and 03 August 2022, a total of 36 patients enrolled at 14 sites in the US; nine patients were randomized to each of the 4 treatment arms. Overall, the median age was 69.0 years (range 41-81 years); the majority were male (19 patients, 52.8%), white (32 patients, 88.9%) and had baseline ECOG status of 1 (23 patients, 63.9%). Most patients had liver metastases (24 patients, 66.7%) and received a median of 3 prior lines of systemic therapy. No significant differences in demographics and baseline characteristics were observed across treatment arms.

RESULTS- EFFICACY: PRIMARY ENDPOINT (3M PFSR)

Arms 1 and 2 met the primary efficacy objective, achieving the end-point threshold pre-defined for the study (35%). On 28 October 2022, the safety monitoring committee recommended not to proceed to the second stage for all treatment arms due to the favorable outcomes in the experimental arms.

Parameter	Arm 1 (N=9)	Arm 2 (N=9)	Arm 3 (N=9)	Arm 4 (N=9)	Overall (N=36)
3M PFSR, n (%)	**4 (44.4)**	**4 (44.4)**	**1 (11.1)**	**3 (33.3)**	**12 (33.3)**
(Lower 90% CI)	(21.04)	(21.04)	(1.16)	(12.95)	(22.85)

3M PFSR – 3-month progression-free survival rate, PFS time greater than 81 days after randomization, considering the planned tumor assessment schedule and visit window allowed; CI – confidence interval

RESULTS- EFFICACY: SECONDARY ENDPOINTS

Progression-Free Survival

Parameter	Arm 1 (N=9)	Arm 2 (N=9)	Arm 3 (N=9)	Arm 4 (N=9)	Overall (N=36)
Events, n (%)	7 (77.8)	9 (100)	6 (66.7)	8 (88.9)	30 (83.3)
Patients who had progressive disease	6 (66.7)	9 (100)	5 (55.6)	8 (88.9)	28 (77.8)
Patients who died	1 (11.1)	0	1 (11.1)	0	2 (5.6)
Censored observations, n (%)	2 (22.2)	0	3 (33.3)	1 (11.1)	6 (16.7)
Median PFS, months (95% CI)	**2.8** (1.35-5.86)	**2.1** (1.35-3.03)	**1.6** (1.38-NA)	**1.5** (1.18-4.47)	**1.7** (1.48-2.80)
6-Month PFS, % (95% CI)	**15.6** (0.79-49.09)	**11.1** (0.61-38.77)	**0** (NA-NA)	**12.5** (0.66-42.27)	**10.4** (2.67-24.38)

CI – confidence interval; NA – not available; PFS – progression-free survival,
Note: a patient was censored at date of randomization if death was observed without any post-baseline tumor assessments performed.

Objective Response Rate

Parameter	Arm 1 (N=9)	Arm 2 (N=9)	Arm 3 (N=9)	Arm 4 (N=9)	Overall (N=36)
Best Overall Response, n (%)					
n	9	9	9	9	36
Complete Response (CR)	0	0	0	0	0
Partial Response (PR)	**2 (22.2)**	**0**	**0**	**0**	**2 (5.6)**
Stable Disease	1 (11.1)	1 (11.1)	0	3 (33.3)	5 (13.9)
Progressive Disease	4 (44.4)	8 (88.9)	5 (55.6)	5 (55.6)	22 (61.1)
Not Evaluable	2 (22.2)	0	4 (44.4)	1 (11.1)	7 (19.4)
Confirmed ORR, n (%) (95% CI)	**2 (22.2)** (2.81-60.01)	**0 (0.0)** (0.00-33.63)	**0 (0.0)** (0.00-33.63)	**0 (0.0)** (0.00-33.63)	**2 (5.6)** (0.68-18.66)

CI – confidence interval; ORR – objective response rate, includes randomized patients without measurable disease at baseline and at least 1 post-baseline tumor assessment; best overall response was considered not evaluable if no post-baseline tumor assessment was performed.

Disease Control Rate

Parameter	Arm 1 (N=9)	Arm 2 (N=9)	Arm 3 (N=9)	Arm 4 (N=9)	Overall (N=36)
DCR, n (%) (95% CI)	**3 (33.3)** (7.49-70.07)	**1 (11.1)** (0.28-48.25)	**0 (0.0)** (0.00-33.63)	**3 (33.3)** (7.49-70.07)	**7 (19.4)** (8.19-36.02)

CI – confidence interval; DCR – disease control rate

Duration of Response

Parameter	Arm 1 (N=9)	Arm 2 (N=9)	Arm 3 (N=9)	Arm 4 (N=9)	Overall (N=36)
Median DOR*, days 95% CI	**124.5** (107.0-NA)	**NA** (NA-NA)	**NA** (NA-NA)	**NA** (NA-NA)	**124.5** (107.0-NA)

* Complete response and partial response only (n=2)
CI – confidence interval; DOR – duration of response; NA – not applicable

Overall Survival

Parameter	Arm 1 (N=9)	Arm 2 (N=9)	Arm 3 (N=9)	Arm 4 (N=9)	Overall (N=36)
OS					
Events, n (%)	6 (66.7)	8 (88.9)	9 (100)	7 (77.8)	30 (83.3)
Censored Observations, n (%)	3 (33.3)	1 (11.1)	0	2 (22.2)	6 (16.7)
Median OS, months (95%, CI)	**6.3** (0.79-NA)	**5.3** (2.89-10.36)	**3.7** (0.86-5.39)	**4.9** (1.09-NA)	**4.7** (2.96-5.66)

CI – confidence interval; NA – not available; OS – overall survival

RESULTS- SAFETY

Safety was evaluable in 33 patients. Most treatment-emergent adverse events (TEAEs) were grade 1-2 (20 patients, 60.6%). TEAEs leading to dose interruption were due to infusion-related reactions (IRR) related to CBP501 (17 patients, 51.5%). TEAEs that led to treatment discontinuation occurred in 1 patient (3.0%), with disease progression as the primary reason for treatment discontinuation.

Parameter, n (%)	Arm 1 (N=8)	Arm 2 (N=9)	Arm 3 (N=8)	Arm 4 (N=8)	Overall (N=33)
TEAE	7 (87.5)	9 (100)	8 (100)	8 (100)	32 (97.0)
Treatment-related	7 (87.5)	9 (100)	8 (100)	5 (62.5)	29 (87.9)
CBP501-related	7 (87.5)	8 (88.9)	7 (87.5)	-	22 (66.7)
TEAE Grade ≥3	5 (62.5)	4 (44.4)	3 (37.5)	0	12 (36.4)
Treatment-related	2 (25.0)	0	2 (25.0)	0	4 (12.1)
CBP501-related	1 (12.5)	0	2 (25.0)	-	3 (9.1)†
Serious TEAE	3 (37.5)	2 (22.2)	2 (25.0)	0	7 (21.2)
TEAE leading to dose reduction of any study drug	1 (12.5)	1 (11.1)	1 (12.5)	0	3 (9.1)
Treatment-related	1 (12.5)	1 (11.1)	1 (12.5)	0	3 (9.1)
CBP501-related	1 (12.5)	0	1 (12.5)	-	2 (6.1)Ŧ
TEAE leading to study discontinuation	0	0	1 (12.5)*	0	1 (3.0)
TEAE leading to death	0	0	1 (12.5) §	0	1 (3.0)

† anemia, acute kidney injury, hypertension Ŧ decreased creatinine clearance and anemia * CBP501-related Grade 2 IRR
§ pancreatic carcinoma (death was not related to treatment)

Most Common TEAEs (≥20% of Patients Overall), n (%)	Arm 1 (N=8)	Arm 2 (N=9)	Arm 3 (N=8)	Arm 4 (N=8)	Overall (N=33)
Infusion-related reaction	7 (87.5)	6 (66.7)	7 (87.5)	0	20 (60.6)
Fatigue	3 (37.5)	6 (66.7)	3 (37.5)	4 (50.0)	16 (48.5)
Constipation	1 (12.5)	4 (44.4)	4 (50.0)	2 (25.0)	11 (33.3)
Nausea	2 (25.0)	4 (44.4)	1 (12.5)	3 (37.5)	10 (30.3)
Decreased appetite	2 (25.0)	5 (55.6)	1 (12.5)	1 (12.5)	9 (27.3)
Abdominal pain	2 (25.0)	2 (22.2)	3 (37.5)	0	7 (21.2)
Weight decreased	2 (25.0)	1 (11.1)	2 (25.0)	2 (25.0)	7 (21.2)

The most common CBP501-related TEAE was IRR (19 patients, 57.6%) among those who received CBP501; no grade 3 IRRs occurred. Only 1 SAE (acute kidney injury) was probably related to CBP501 (definitely related to cisplatin [Arm 3]). One TEAE (pancreatic carcinoma) led to death but was not related to treatment.

CONCLUSIONS

CBP501 with cisplatin and nivolumab yielded durable responses and clinically meaningful improvement in 3M PFSR, PFS and OS, with tolerable safety as third-line treatment for metastatic PDAC. This chemoimmunotherapy treatment combination warrants further investigation.

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