

Phase II study of combination therapy of DFP-14323 and low dose afatinib in patients for NSCLC with EGFR mutation.

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Disclosure

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Background -> DFP-14323

- ✓ DFP-14323 (INN:Ubenimex) is low molecular(MW.308.7) dipeptide and known as Immuno-potentiator for cancer patients.
- ✓ DFP-14323 is an inhibitor of aminopeptidase N (APN), also called CD13 on cancer stem cell.
- ✓ APN is well known as one of prognostic factors for several cancer patients, including non-small-cell lung cancer (NSCLC).
Zhang Q, Wang J, Zhang H, et al., J Cancer Res Ther. 2015
- ✓ The same active ingredient as Bestatin® with the indication of "extension of survival by combination with maintenance chemotherapy after induction of complete remission for adult acute non-lymphocytic leukemia".

Background -> DFP-14323+Low-dose Afatinib

- ✓ Afatinib is one of the standard treatments in NSCLC patients with EGFR mutation, but the toxicities often require dose reduction.
- ✓ Recently, it is suggested that reducing afatinib doses can decrease treatment-related adverse events without affecting efficacy.

Yokoyama T, et al. Lung Cancer 2019

- ✓ We aimed to examine efficacy of DFP-14323 with low-dose afatinib by conducting phase II study in patients with metastatic NSCLC harboring EGFR mutation.

Study Design

Key inclusion Criteria

- ◇ Non-small cell lung cancer
- ◇ Stage III/IV or Postoperative recurrence
- ◇ Common *EGFR* mutations (Del 19 or L858R)
- ◇ Performance Status of 0~2
- ◇ No prior systemic therapy or curative chest radiation therapy

DFP-14323 10mg/day

+

Afatinib* 20mg/day

Up to 72 weeks or PD

*The dose can be increased up to 30mg/day only if no \geq Grade 2 adverse events occur within 4 weeks after the start of administration.

Endpoints

Primary endpoint : Disease control rate (DCR)

Secondary endpoints : Efficacy

- (1) Overall response rate (ORR)
- (2) Progression-Free Survival (PFS)
- (3) Neutrophil/Lymphocyte ratio
- (4) Variation of Tumor Markers

Safety

- Types and Degrees of Adverse Events

Patients Characteristics

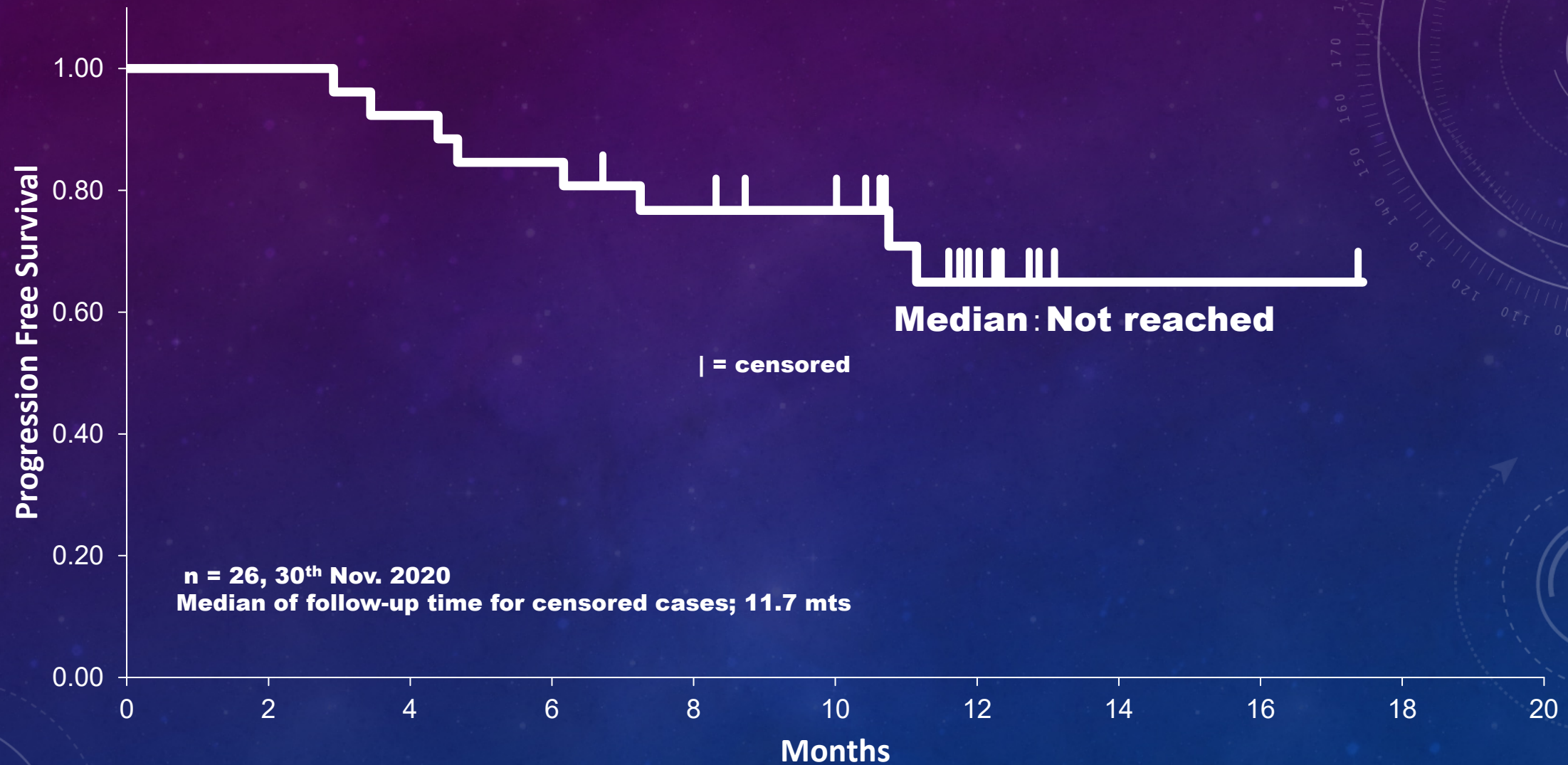
N=26

Age	mean (SD)	72.2 (7.1)
	median (IQR)	72.8 (66.9 – 77.3)
Gender	Male (%)	5 (19.2)
	Female (%)	21 (80.8)
Performance status	0 (%)	10 (38.5)
	1 (%)	16 (61.5)
Smoking history	Yes (%)	0 (0)
	No (%)	16 (61.5)
	Past (%)	10 (38.5)
Metastases	bone (%)	8 (30.8)
	brain (%)	11 (42.3)
	liver (%)	3 (11.5)
	lymph (%)	4 (15.4)
	other (%)	15 (57.7)
	no (%)	9 (34.6)
EGFR gene mutation	Del19 (%)	13 (50)
	L858R (%)	13 (50)
	Other (%)	0 (0)
Histological type	adenocarcinoma (%)	25 (96.2)
	non-small cell lung cancer (%)	1 (3.8)
Stage	III (%)	1 (3.8)
	IV (%)	17 (65.4)
	Postoperative recurrence (%)	8 (30.8)

Summary of Response

Summary of response	N	%	[95%CI*] * clopper-pearson
Patients with measurable lesions	26		
CR: Complete Response	1	3.8	[0.1 - 19.6]
PR: Partial Response	16	61.5	[40.6 - 79.8]
SD: Stable Disease	9	34.6	[17.2 - 55.7]
PD: Progressive Disease	0	0.0	[0.0 - 13.2]
NE: Not Evaluable	0	0.0	[0.0 - 13.2]
DCR: Disease Control Rate	26	100.0	[86.8 - 100.0]
ORR: Objective Response Rate	17	65.4	[44.3 - 82.8]

PFS (tentative)



Adverse Events

~ 30th Nov. 2020, >10% and important adverse events

	All events						Events caused by DFP-14323						Events caused by Afatinib							
			worst Grade						worst Grade						worst Grade					
	total	(%)	G1	G2	G3	total	(%)	G1	(%)	G2	(%)	G3	total	(%)	G1	(%)	G2	(%)	G3	(%)
any AEs	26	(100.0)	26	16	8	7	(26.9)	6	(23.1)	3	(11.5)		26	(100.0)	25	(96.2)	16	(61.5)	6	(23.1)
Haematologic																				
Anaemia	1	(3.8)		1									1	(3.8)			1	(3.8)		
Neutropenia	3	(11.5)	2	1		1	(3.8)	1	(3.8)				3	(11.5)	2	(7.7)	1	(3.8)		
Thrombocytopenia	1	(3.8)	1			1	(3.8)	1	(3.8)				1	(3.8)	1	(3.8)				
Lymphopenia	3	(11.5)		2	1								3	(11.5)			2	(7.7)	1	(3.8)
Gastrointestinal																				
Diarrhoea	23	(88.5)	17	5	1	3	(11.5)	2	(7.7)	1	(3.8)		22	(84.6)	17	(65.4)	4	(15.4)	1	(3.8)
Stomatitis/Chelitis	17	(65.4)	11	1	1	2	(7.7)	2	(7.7)				14	(53.8)	12	(46.2)	1	(3.8)	1	(3.8)
Weight decreased	6	(23.1)		5	1								3	(11.5)	1	(3.8)	2	(7.7)		
Abdominal discomfort	3	(11.5)	2	1		1	(3.8)	2	(7.7)	1	(3.8)		2	(7.7)	1	(3.8)	1	(3.8)		
Cheilitis	3	(11.5)	3			1	(3.8)	1	(3.8)				3	(11.5)	3	(11.5)				
Decreased appetite	3	(11.5)	3										3	(11.5)	3	(11.5)				
Hepatic																				
Hepatic disorder(included Lab.)	6	(23.1)	5	1		2	(7.7)	2	(7.7)				4	(15.4)	3	(11.5)	1	(3.8)		
Nervous																				
Dizziness	3	(11.5)	2	1		1	(3.8)	1	(3.8)				1	(3.8)	1	(3.8)				
Dysgeusia	3	(11.5)	2	1									3	(11.5)	2	(7.7)	1	(3.8)		
Thoracic																				
Epistaxis	3	(11.5)	3										3	(11.5)	3	(11.5)				
Oropharyngeal pain	3	(11.5)	3																	
Interstitial lung disease	1	(3.8)	1										1	(3.8)	1	(3.8)				
Skin and Nail																				
Paronychia	19	(73.1)	8	8	3								19	(73.1)	8	(30.8)	8	(30.8)	3	(11.5)
Rash	17	(65.4)	14	3		1	(3.8)			1	(3.8)		16	(61.5)	13	(50.0)	3	(11.5)		
Dry skin	12	(46.2)	11	1		1	(3.8)	1	(3.8)				12	(46.2)	11	(42.3)	1	(3.8)		
Dermatitis acneiform	4	(15.4)	2	1	1								4	(15.4)	2	(7.7)	1	(3.8)	1	(3.8)
Pruritus	3	(11.5)	2	1									3	(11.5)	2	(7.7)	1	(3.8)		

Conclusion

- ✓ Combination of DFP-14323 and low-dose afatinib showed promising efficacy and good tolerability.
- ✓ We are planning a phase III study to evaluate this combination therapy after evaluation of PFS.

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