MP14-01 Predictive impact of an early change in serum C-reactive protein levels in nivolumab therapy for metastatic renal cell carcinoma

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Conclusions

➢ The CRP change during the early phase of nivolumab monotherapy was significantly associated with mRCC patient survival.

➢ The early CRP change may be used for outcome prediction of nivolumab.

Introduction

✓ Serum CRP level is one of the most intensively studied inflammatory factors, and its level acts as a predictor of mRCC.
[Saito, Eur Urol, 2009; Beuselinck, BJU Int, 2014]

✓ Several studies found no significant association between the pretreatment CRP levels and PFS in nivolumab therapy.
[Ishihara, Targeted Oncol, 2019; Shirotake, Anticancer Res, 2019; Suzuki, Int J Clin Oncol, 2019]

✓ The CRP change was reported to reflect the outcomes of targeted therapy for mRCC.
[Teishima, BJU Int, 2016; Yasuda, Int J Clin Oncol, 2017]

Objective

◆ We evaluated the predictive impact of the CRP change during the early phase of nivolumab monotherapy.

◆ We focused on the early CRP change, which could be assessed during the initial phase and evaluated its use as a predictor in nivolumab.

Patient and Methods

Patients

✓ A total of 70 patients who received nivolumab monotherapy after the failure of at least 1 targeted therapies for mRCC between 6/2013 and 7/2019.

Early CRP Change

✓ CRP change within the initial 3 months after nivolumab initiation

Group	pretreatment	Within the initial 3 months
Normal	<1 mg/dL	-
Normalized	≥ 1 mg/dL	<1 mg/dL
Non-normalized	≥ 1 mg/dL	≥ 1 mg/dL

Endpoints

✓ PFS & OS after nivolumab therapy initiation

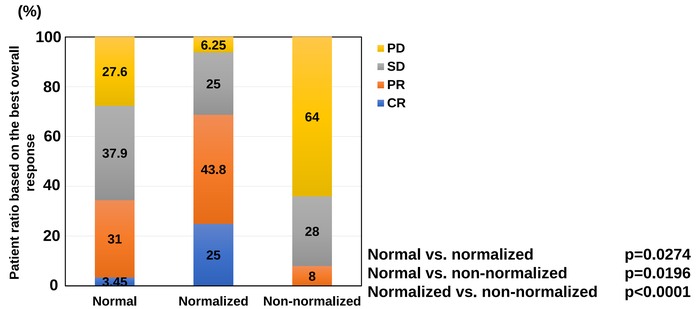
【Statistical analysis】
Kaplan-Meier method and log-rank test
Cox proportional hazard regression model
RECIST ver. 1.1.

Results

Patient Background according to CRP Change

Variable	Normal (n=29)	Normalized (n=16)	Non-normalized (n=25)	p
Age, years ≥65 (ref. <65)	19 (65.5%)	9 (56.3%)	16 (64.0%)	0.818
Sex Male (ref. female)	23 (79.3%)	12 (75.0%)	16 (64.0%)	0.441
Histopathology Clear-cell (ref. non-clear cell)	24 (82.8%)	12 (75.0%)	21 (84.0%)	0.748
IMDC risk				0.0005
Favorable	4 (13.8%)	0	0	
Intermediate	20 (69.0%)	12 (75.0%)	8 (32.0%)	
Poor	5 (17.2%)	4 (25.0%)	17 (68.0%)	
No. of targeted therapies 1 (ref. ≥2)	20 (69.0%)	9 (56.3%)	14 (56.0%)	0.552
No. of metastatic organ sites Multiple (ref. single)	19 (65.5%)	8 (50.0%)	15 (60.0%)	0.596
Liver metastasis status Presence (ref. absence)	3 (10.3%)	2 (12.5%)	8 (32.0%)	0.0969

Objective Response Rate according to CRP Change



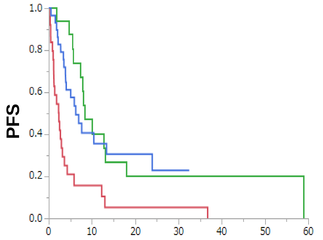
Normal vs. normalized p=0.0274
Normal vs. non-normalized p=0.0196
Normalized vs. non-normalized p<0.0001

ORR 34.5% 68.8% 8.00%

➢ ORR was significantly higher in the normalized group.

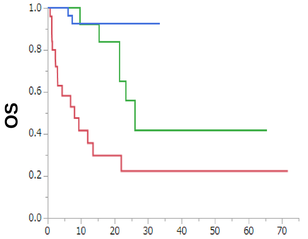
Survival according to CRP Change

Normal vs. normalized p=0.610
Normal vs. non-normalized p=0.0009
Normalized vs. non-normalized p=0.006



Median (95% CI), months
Normal 6.28 (3.85-13.4)
Normalized 8.38 (5.69-13.1)
Non-normalized 2.33 (1.12-3.16)

Normal vs. normalized p=0.0454
Normal vs. non-normalized p<0.0001
Normalized vs. non-normalized p=0.0047



Median (95% CI), months
Normal N.R. (N.R.-N.R.)
Normalized 26.0 (15.4-N.R.)
Non-normalized 8.02 (2.93-22.0)

➢ The CRP change was significantly associated with PFS & OS.

Multivariate Analysis for PFS & OS

Variable	PFS HR (95% CI)	PFS p	OS HR (95% CI)	OS p
Age, years ≥65	0.67 (0.35-1.31)	0.236		
Histopathology Clear-cell	0.56 (0.28-1.18)	0.123		
IMDC risk Poor	2.01 (1.01-3.99)	0.0479	2.27 (0.90-5.97)	0.0808
Liver metastasis status Presence			3.40 (1.30-8.41)	0.0138
CRP change		0.0025		0.0009
Normalized (ref. normal)	0.67 (0.30-1.40)	0.287	3.91 (0.89-26.9)	0.0727
Non-normalized (ref. normal)	2.33 (1.18-4.61)	0.0153	11.0 (2.84-63.0)	0.0002

➢ CRP change was an independent factor for PFS & OS.

COI

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