Comprehensive Support Project

Phase II trial of combination treatment with paclitaxel, carboplatin and cetuximab (PCE) as first-line treatment in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (CSPOR-HN02)

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Background (1)

- The prognosis for patients with recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN) is poor.

- The goal of R/M SCCHN is to extend survival while ensuring good quality of life.

- According to EXTREME study [1], platinum-based chemotherapy in combined with cetuximab (PFE) is considered to be standard regimen as 1st-line treatment of R/M SCCHN.

1. Vermorken JB et al. N Engl J Med 2008; 359: 1116-1127.

Background (2)

- However, PFE requires hospitalization to ensure proper hydration and continuous infusion of 5-FU, and causes concerned toxicities including mucositis, anorexia and fatigue, leading to worsen patient's quality of life.

- In the previous study for R/M SCCHN patients, combination with paclitaxel, carboplatin and cetuximab (PCE) demonstrated promising clinical activity with response rate of 56% and median time to progression of 5 month [2].

2. Buentzel J, et.al. 2007 ASCO Annual Meeting. JCO, 2007; No. 18S (June 20 Suppl) abstr 6077.

Objectives

- To evaluate the efficacy and safety of PCE as 1st-line treatment in patients with R/M SCCHN.

Endpoints

- Primary endpoint: overall response rate (ORR)
- Secondary endpoints:
  - ✓Safety
  - ✓Treatment completion rate
  - ✓Progression-free survival (PFS)
  - ✓Overall survival (OS)
  - ✓Clinical benefit rate (CBR)

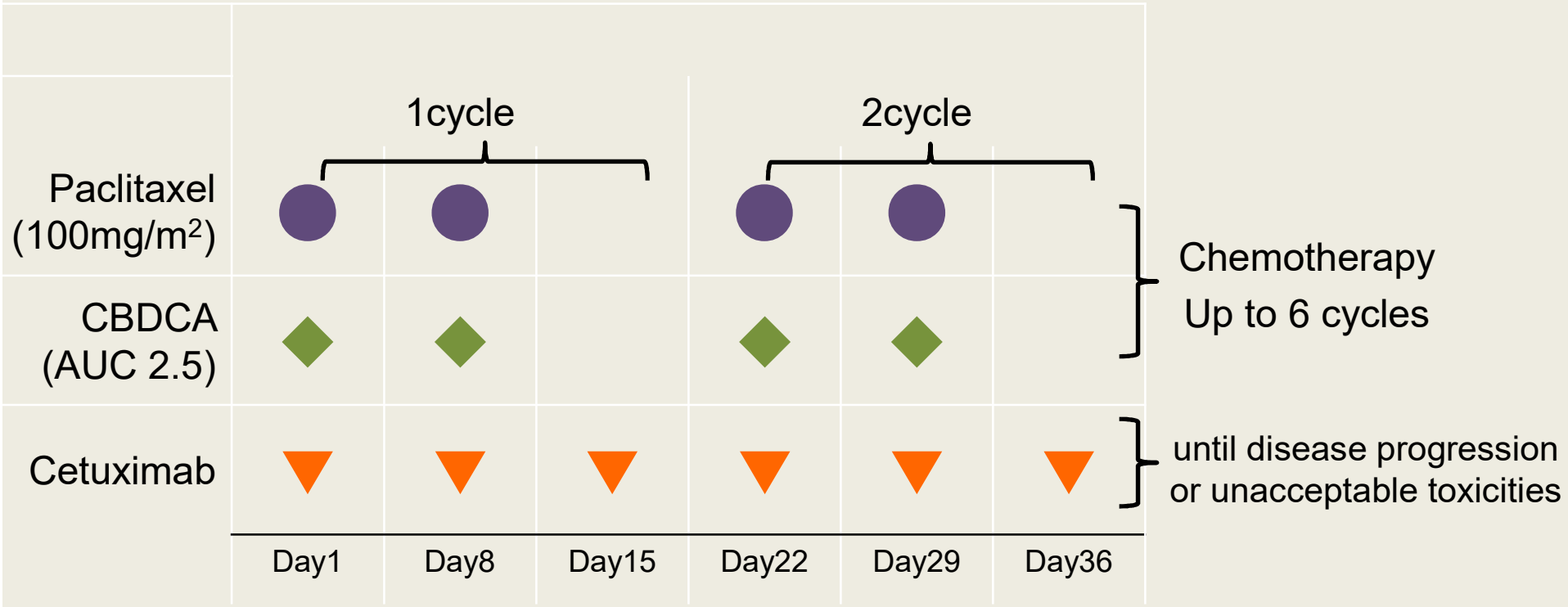
Key eligibility criteria

1) Histologically proven squamous cell carcinoma
2) Primary lesion located larynx, oropharynx, hypopharynx or oral cavity
3) No prior chemotherapy expect > 6 month previous chemotherapy as a curative therapy
4) No prior systemic chemotherapy for R/M disease

Study design

This is a single arm, open-label, multicenter, phase 2 study (UMIN000010507)

Treatment


1cycle
2cycle
Paclitaxel
(100mg/m2)
CBDCA
(AUC 2.5)
Cetuximab
Chemotherapy
Up to 6 cycles
until disease progression
or unacceptable toxicities
Day1
Day8
Day15
Day22
Day29
Day36

Statistical analysis

- The objective of primary analysis is to confirm whether response rate of PCE is non-inferior as compared with that of PFE
  - Assumed the response rate of PFE is 40%
  - Acceptable range of less than 5%
- Targeted accrual: 45 patients in total

Patient Characteristics (1)

n=45

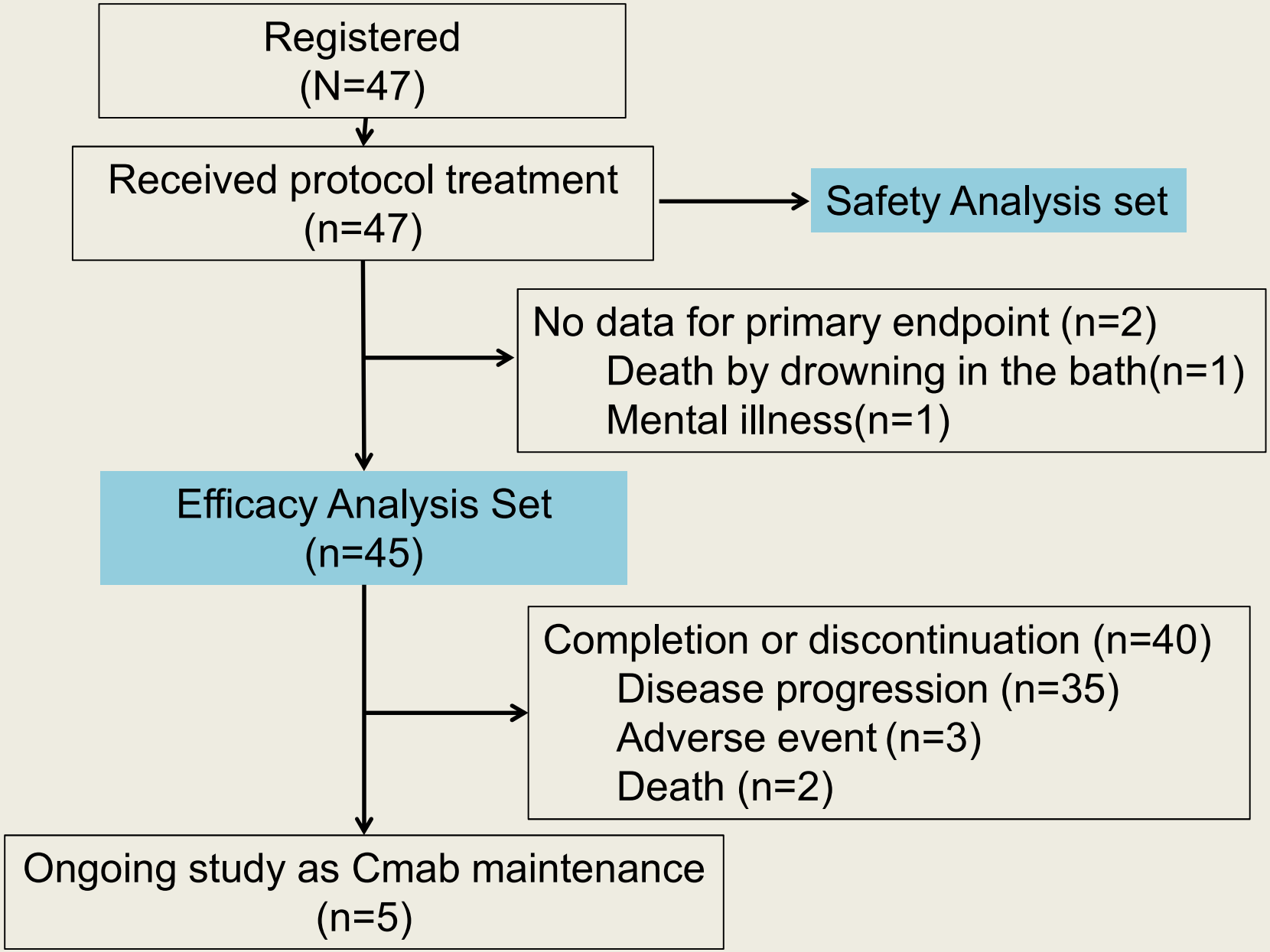
Variable		n
Age	Age (yr) - median, range	63 (41-76)
	＜65yr	25
	≧65yr	20
Sex	Female	5
	Male	40
PS	0	23
	1	22
Primary site	Hypopharynx	17
	Oropharynx	11
	Oral cavity	10
	Larynx	7

Patient Characteristics (2)

n=45

Variable		n
Extent of disease		
	Only locoregionally recurrent	8
	Metastatic with or without locoregional recurrence	37
Previous treatment		
	Radiation	28
	Chemotherapy	13
	Postoperative chemoradiotherapy	4
Smoking history		
	Smokers	36
	Non-smokers	9

Patient Flow Diagram



Compliance

Median cycle of PCE was 6.

	Median duration-week (range)	Relative dose intensity %
Paclitaxel	16.9 (1.9-28.0)	82.5
CBDCA	7.1 (1.9-28.0)	82.5
Cetuximab	22.0 (2.0-128.0)	90.6
Cetuximab monotherapy*	11.9 (1.0-116.0)	90.6

*during the maintenance period

	No. of patients (%)
Completion of 6 cycles of PCE	16 (35.6%)
Received cetuximab monotherapy*	29 (64.4%)

*during the maintenance period

Analysis of primary endpoint: Response (N=45) on central review

The primary end point was met with ORR of 40.0% (95% exact CI, 25.7-55.7).

Response	No. of patients (%)
Complete response	2 (4.4%)
Partial response	16 (35.6%)
Stable disease	9 (20.0%)
Progressive disease	16 (35.6%)
Not Evaluable	2 (4.4%)

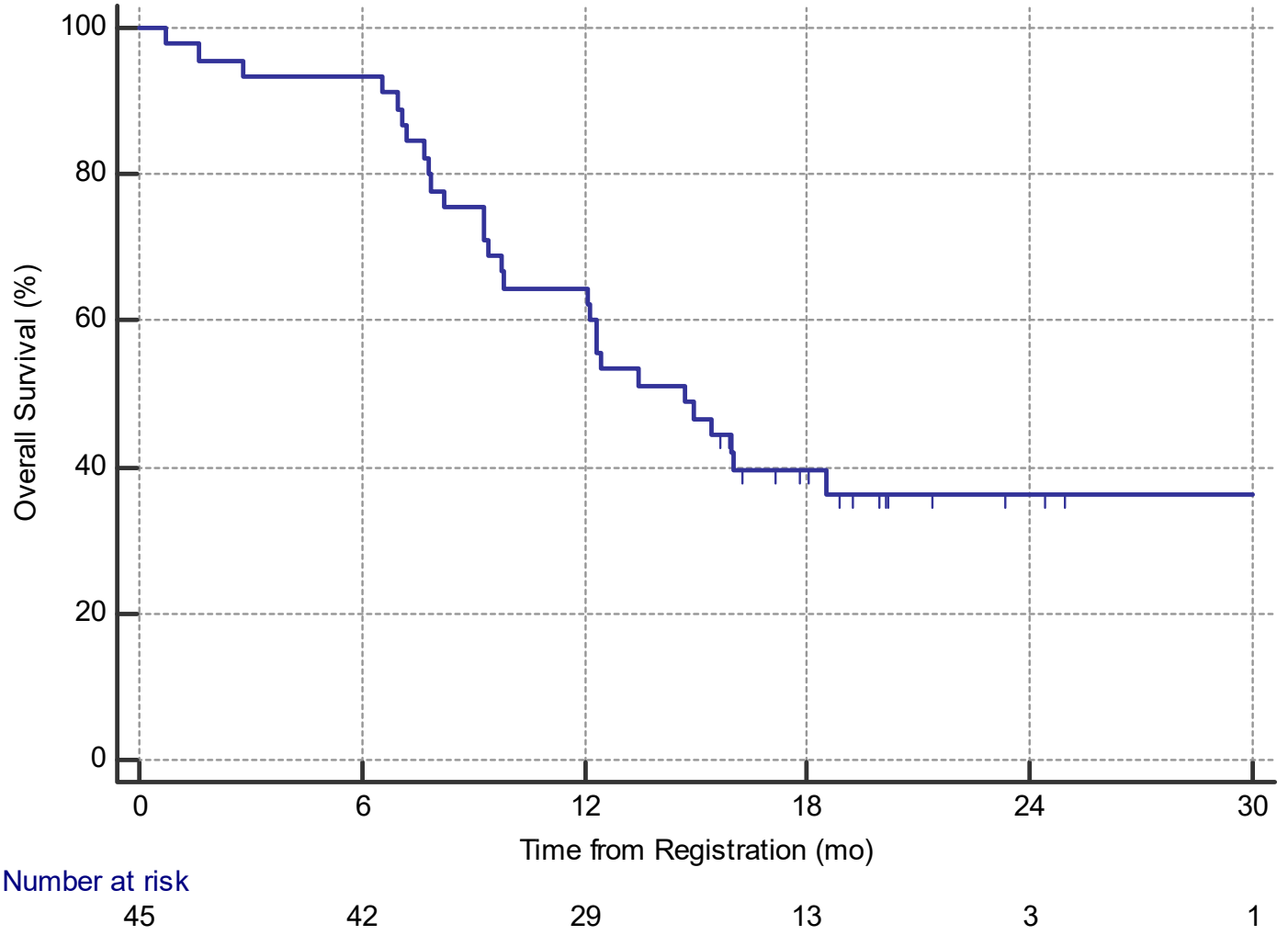
RECIST version1.1

OS

Median follow-up was 20.0 months.

MST; 14.7 months (95% CI, 9.8–Not Reached)

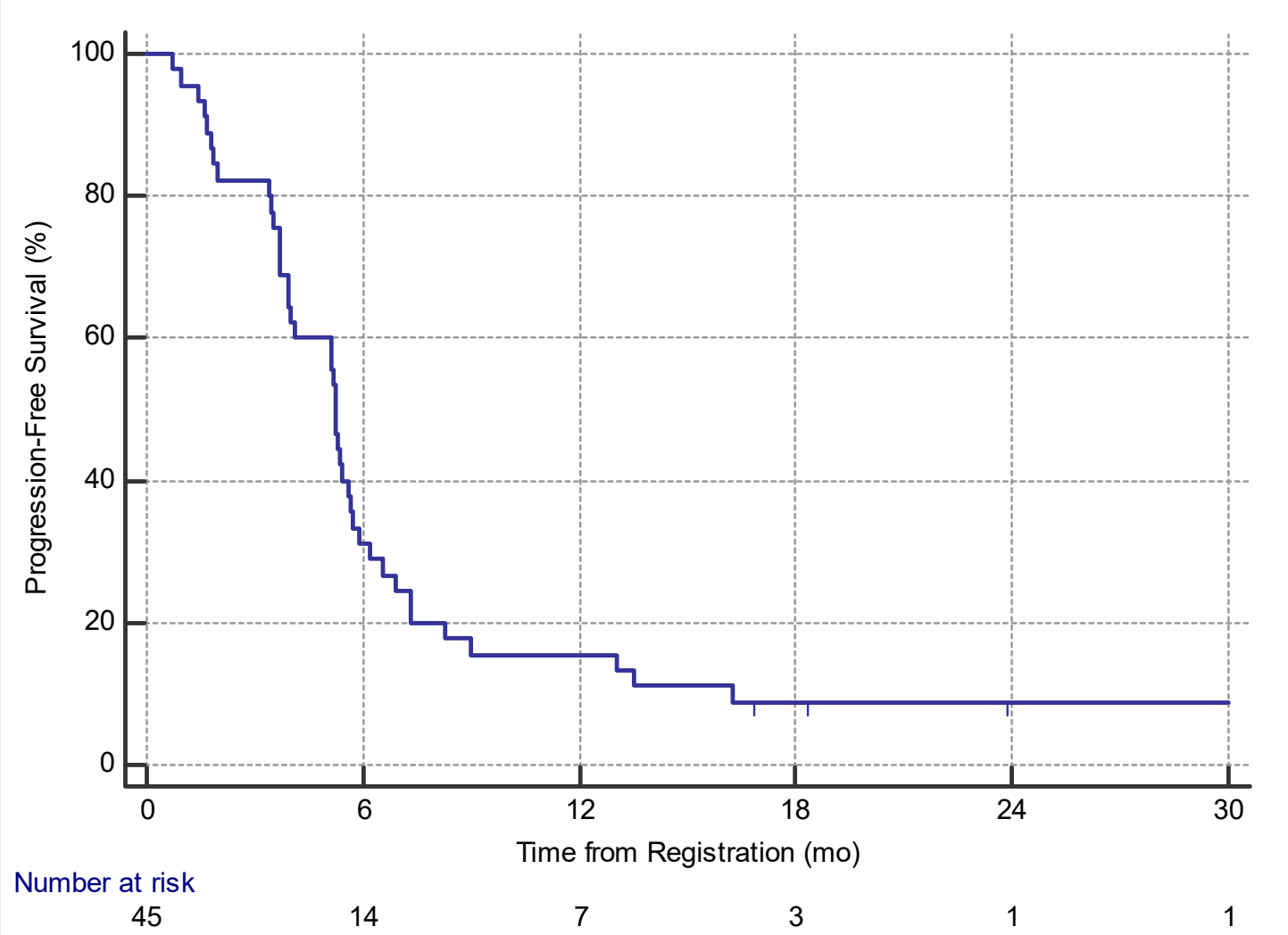
Number of observed death was 28 (62%).



PFS

Median PFS; 5.2 months (95% CI 3.9–5.6).

5 patients are still receiving cetuximab maintenance.



Adverse events during PCE (N=47)

CTCAE version 4.0

AE	Gr1 (n)	Gr2 (n)	Gr3 (n)	Gr4 (n)	Gr3-4 (%)
Neutropenia	2	9	19	13	68%
Rash acneiform	14	23	2	0	4%
Skin reaction	12	20	7	0	15%
Febrile neutropenia	-	-	4	0	9%
Anemia	21	22	3	0	6%
Anorexia	13	9	3	0	6%
Hyponatremia	16	0	2	0	4%
Hypomagnesemia	24	3	1	1	4%
Diarrhea	7	2	1	0	2%
Nausea	10	3	1	0	2%
Peripheral neuropathy	19	6	1	0	2%
Mucositis	10	8	1	0	2%
Hypoalbminemia	30	6	1	0	2%
Hypocalcemia	7	2	0	1	2%
Constipation	17	6	0	0	0%
Thrombocytopenia	28	1	0	0	0%

A potentially treatment-related death occurred in one patient with intestinal pneumonia.

Adverse events during Cmab maintenance (N=29)

CTCAE version 4.0

AE	Gr1 (n)	Gr2 (n)	Gr3 (n)	Gr4 (n)	Gr3-4 (%)
Rash acneiform	10	13	3	0	10
Skin reaction	11	14	3	0	10
Neutropenia	5	3	2	0	7
Thrombocytopenia	6	1	1	0	3
Anorexia	10	1	1	0	3
Peripheral neuropathy	14	4	0	0	0
Constipation	6	3	0	0	0
Dysgeusia	5	3	0	0	0
Anemia	21	5	0	0	0
Hypomagnesemia	13	4	0	0	0

Summary

- The primary end point was met with ORR of 40.0% (95% exact CI, 25.7-55.7) on central review.
- After a median follow-up of 20.0 months,
  - Median PFS: 5.2 months
  - Median OS: 14.7 months
- Grade 3 or 4 AE included neutropenia (68%), skin reaction (15%), and febrile neutropenia (9%). A potentially treatment-related death occurred in one patient with intestinal pneumonia.

Conclusion

- The PCE regimen shows promising activity with acceptable toxicity in 1st line treatment for patients with R/M SCCHN.
- Further studies are needed to compare PCE with PFE in this population.

Acknowledgments

- The authors would like to thank the study patients, study investigators, and the clinical research teams. This study was conducted by Comprehensive Support Project of the Public Health Research Foundation (CSPOR) in Japan. This study fund was provided to CSPOR with Support from Merck Serono.

Meeting Information

- Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 3–7, 2016; Chicago, Illinois, USA