

Japanese cross-sectional and cohort study of 1st line chemotherapy (CT) for metastatic colorectal cancer (mCRC) (EMERaLD study)



Evaluation of first-line treatment for Metastatic colorectal cancer, Especially Resection of liver metastasis and Long survival, in Japanese Database

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Background

An observational cohort study plays a crucial role to understand the current status of clinical practice and can be utilized as database for multi-purpose outcome research. Such database is available in Europe and the United States based on several cohort studies especially in mCRC, while there is no database available including treatments for mCRC patients in Japan. Therefore, we planned and conducted a large cohort study to establish database available including treatments for mCRC in Japan. We performed a preplanned interim analysis of 6-month efficacy and safety.

EMERaLD study design

UMIN-CTR UMIN000006392
mCRC, previously untreated, database
n=1,005
registration period: Oct, 2010~ Sep, 2011

- #### Key data inclusion criteria
- With first line CT including oxaliplatin and bevacizumab for mCRC
 - Treatment-initiated after January, 2010
 - Radiologically assessed during first line CT
 - Monitored by laboratory test and symptom check during first line CT
 - Able to provide observation data to this study

6 months follow-up data cut-off: Mar, 2012

- pts characteristics
- chemo (6 months follow-up)
- liver resection
- response to chemo
- 6-month PFS

2 years follow-up data cut-off: Sep, 2013

- PFS
- RFS after liver resection
- post-progression treatment
- 2-year OS

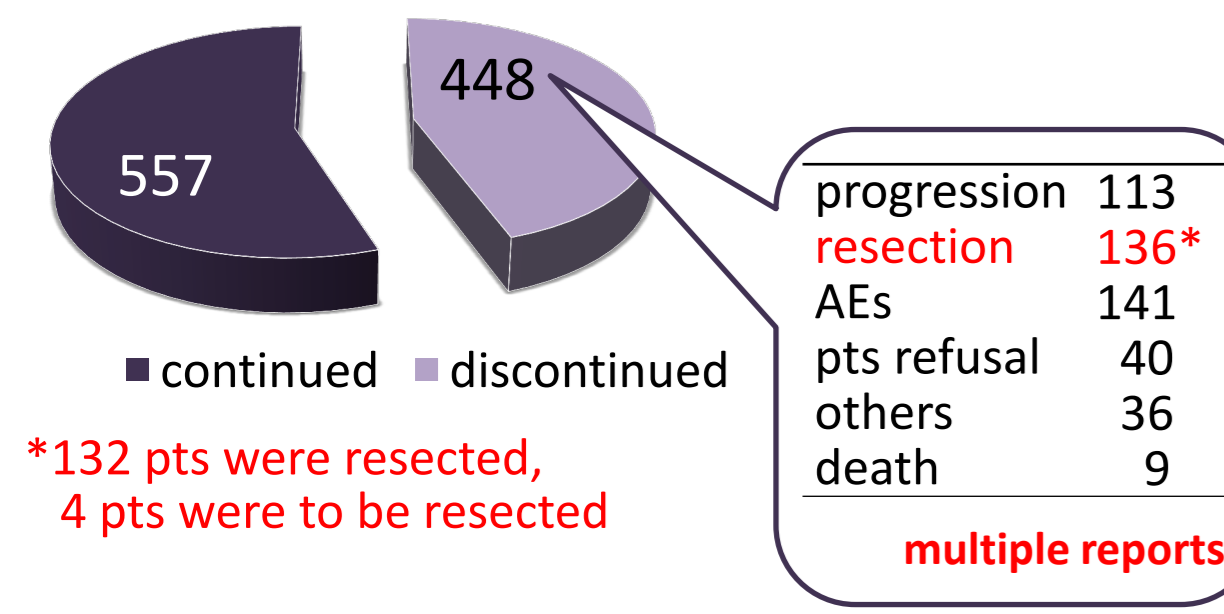
Primary endpoints

Overall survival, Liver resection rate, R0 liver resection rate

Secondary endpoints

Response rate, Progression-free survival, Safety, Sub-group analysis by regimens, KRAS status, etc

6-month treatment (n=1,005)

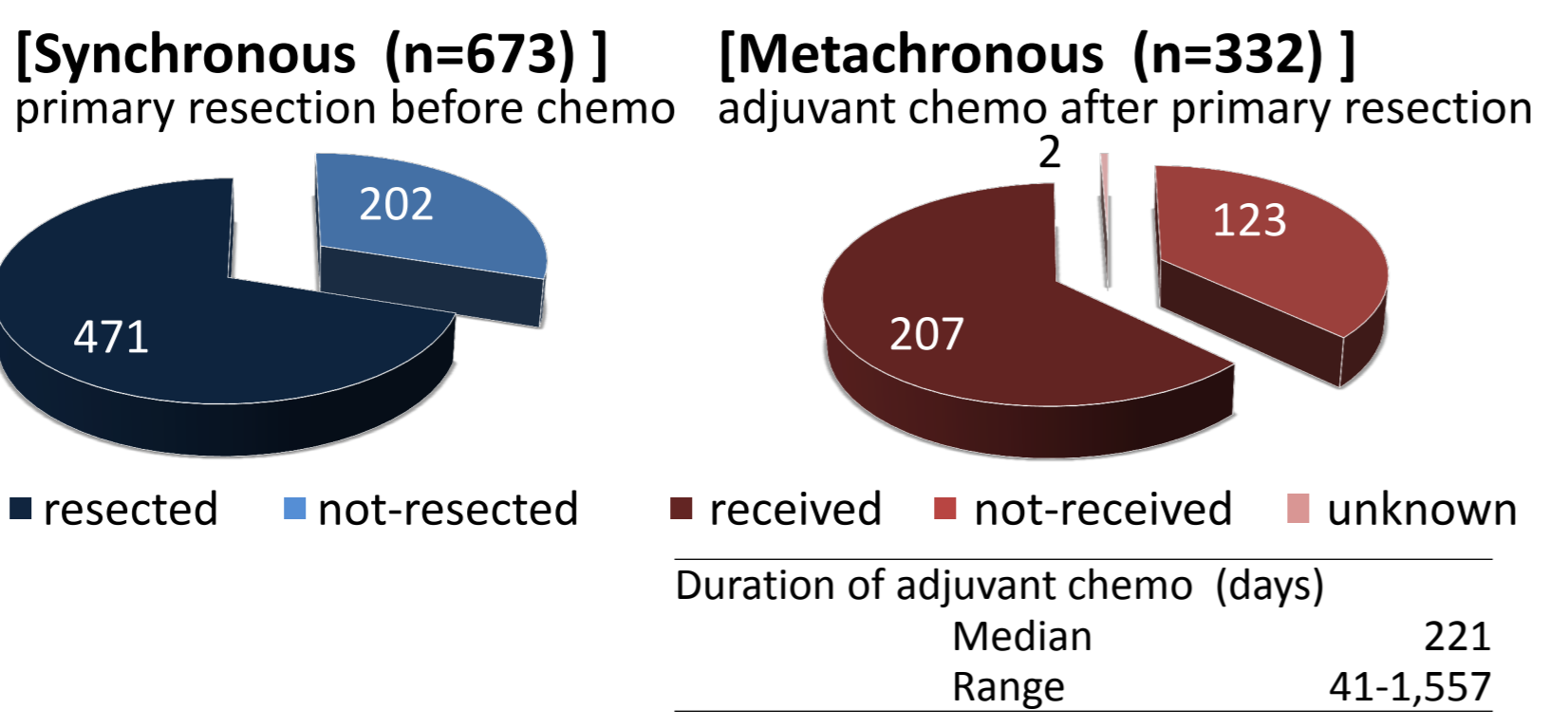


Pts characteristics (n=1,005)

Gender	Male	614 (61.1%)
	Female	391 (38.9%)
Age (yrs)	Median	65
	Range	27-89
	< 75 yrs	843 (83.9%)
	≥ 75 yrs	162 (16.1%)
ECOG PS	0	854 (85.0%)
	1	139 (13.8%)
	2	10 (1.0%)
	≥ 3	2 (0.2%)
CEA (ng/mL)	Median	15
	Range	0-90,055
Comorbidity	Without	628 (62.5%)
	With	358 (35.6%)
	Hypertension	220
	Diabetes	90
	Hyperlipemia	42
	COPD	9
	Chronic cardiac failure	2
	Chronic renal failure	5
	Chronic hepatitis	13
	Cerebrovascular dis.	10
	Others	85
	Unknown	19 (1.9%)
Chemo regimens	FOLFOX+BV	437 (43.5%)
	XELOX+BV	540 (53.7%)
	Other oxali. +BV	28 (2.8%)
KRAS mutation	Wild type	323 (32.1%)
	Mutant	241 (24.0%)
	Unknown	441 (43.9%)

Primary disease

Primary site	Colon	549 (54.6%)
	Rectum	451 (44.9%)
	Colon and rectum	5 (0.5%)
Synchronous/	Synchronous	673 (67.0%)
Metachronous	Metachronous	332 (33.0%)



Metastatic disease

[Liver mets (n=627)]	No.	Median	5
		1-4	296 (47.2%)
		5 ≤	321 (51.2%)
		unknown	10 (1.6%)
Max. diameter (cm)	Median	3.5	
	Range	0.25-23	
Vascular invasion	No	504 (80.4%)	
	Yes	102 (16.3%)	
	Unknown	21 (3.3%)	
[Lung mets (n=308)]	No.	Median	4
		1-1	1
Max. diameter (cm)	Median	1.1	
	Range	0.1-7.4	
Location	Unilobar	78 (25.3%)	
	Bilobar	18 (5.8%)	
	Bilateral	210 (68.2%)	
	Unknown	2 (0.6%)	

Results

Metastasectomy (n=1,005)

Metastasectomy	132 (13.1%)
Liver resection	106 (10.5%)
R0 liver resection	90 (9.0%)
R1 liver resection	9
R2 liver resection	4
RX	3
Lung resection	13 (1.3%)
LN resection	11 (1.1%)
Primary resection	29 (2.9%)
Local recurrence resection	5 (0.5%)
Others	10 (1.0%)

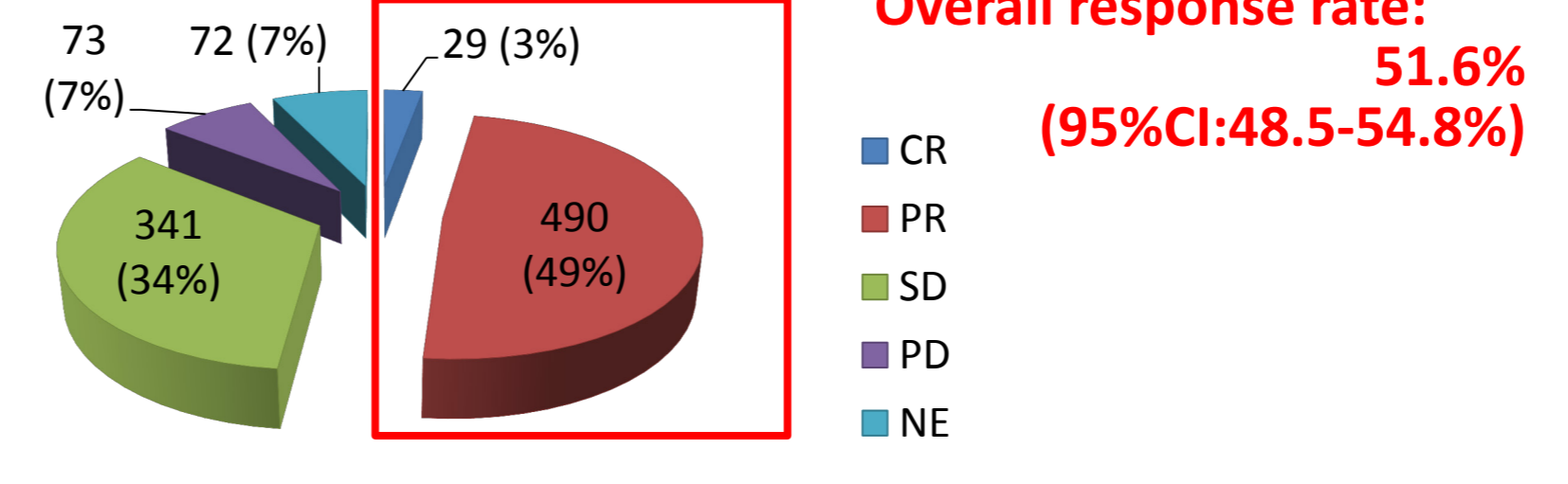
Subgroup analysis by chemo

Liver resection	106
FOLFOX+BV (n=437)	45 (10.3%)
XELOX+BV (n=540)	59 (10.9%)
Others (n=28)	2 (7.1%)
R0 liver resection	90
FOLFOX+BV (n=437)	39 (8.9%)
XELOX+BV (n=540)	50 (9.2%)
Others (n=28)	1 (3.6%)

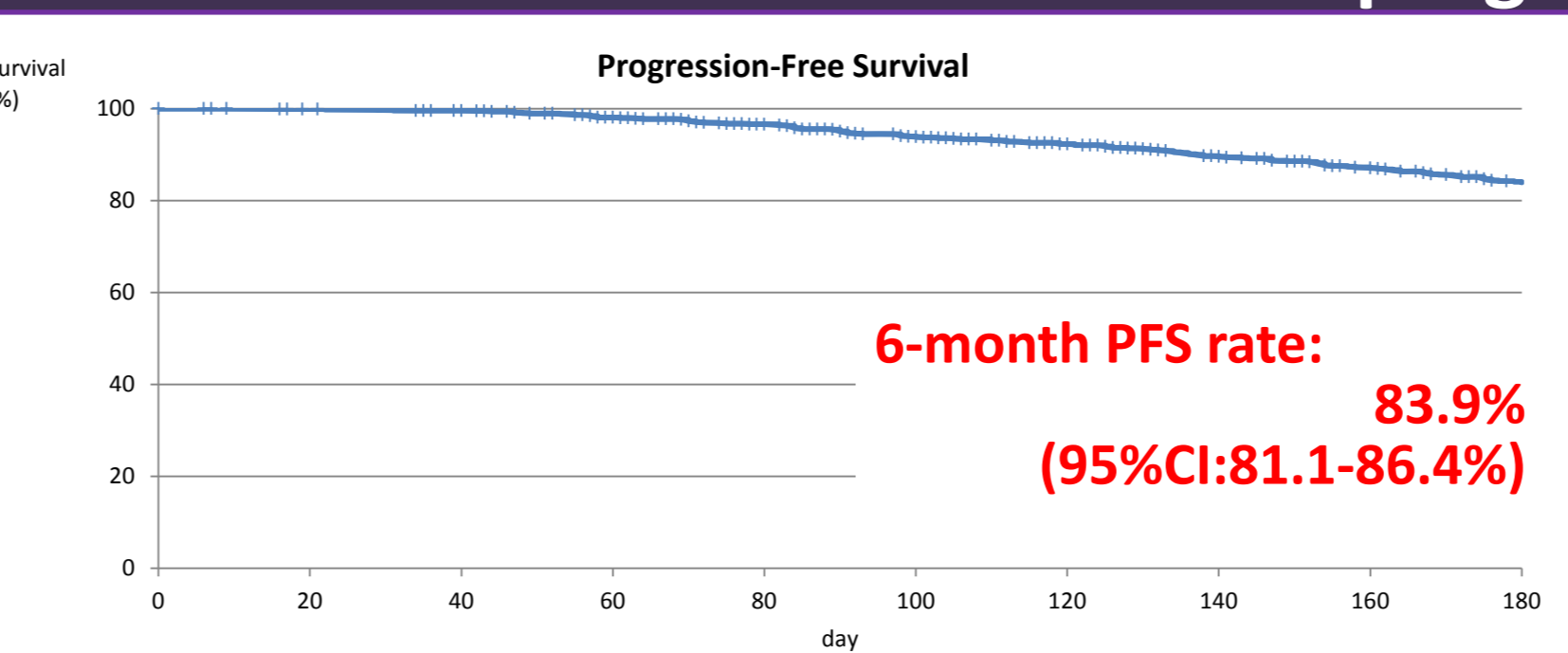
Subgroup analysis by KRAS

Liver resection	106
KRAS wild (n=323)	25 (7.7%)
KRAS mutant (n=241)	23 (9.5%)
KRAS unknown (n=441)	58 (13.2%)
R0 liver resection	90
KRAS wild (n=323)	20 (6.2%)
KRAS mutant (n=241)	21 (8.7%)
KRAS unknown (n=441)	49 (11.1%)

6-month response to chemo (n=1,005)



6-month progression-free survival rate (n=1,005)



Adverse Events (n=1,005)

✓ 141 pts discontinued chemo due to AEs as below at 6 months,

AEs (according to NCICTCAE ver3.0)	events	Grade 1	Grade 2	Grade 3	Grade 4
Platelets	8	1	3	2	2
Neutrophils	5	4	1		
Neuropathy-sensory	53	2	17	34	
Allergic reaction	17	2	3	10	2
Anorexia	10	3	7		
GI perforation	9		4	5	
Fatigue	9		4	5	
Vomiting	7	1	2	4	
Diarrhea	7		1	5	1
Mucositis	6	1	2	3	
Thrombosis/embolism	5		1	5	
HFS (Blum criteria)	5		1	4	
Ileus	3			3	

Metastasectomy (n=1,005)

Subgroup analysis by chemo

Liver resection	106
FOLFOX+BV (n=437)	45 (10.3%)
XELOX+BV (n=540)	59 (10.9%)
Others (n=28)	2 (7.1%)
R0 liver resection	90
FOLFOX+BV (n=437)	39 (8.9%)
XELOX+BV (n=540)	50 (9.2%)
Others (n=28)	1 (3.6%)

Subgroup analysis by KRAS

Liver resection	106
KRAS wild (n=323)	25 (7.7%)
KRAS mutant (n=241)	23 (9.5%)
KRAS unknown (n=441)	58 (13.2%)
R0 liver resection	90
KRAS wild (n=323)	20 (6.2%)
KRAS mutant (n=241)	21 (8.7%)
KRAS unknown (n=441)	49 (11.1%)

Subgroup analysis by primary

Liver resection	106
Colon (n=549)	59 (10.7%)
Rectum (n=451)	47 (10.4%)
Others (n=5)	0 (0%)
R0 liver resection	90
Colon (n=549)	50 (9.1%)
Rectum (n=451)	40 (8.9%)
Others (n=5)	0 (0%)

Subgroup analysis by synch./metach.

Liver resection	106
Synch.not-res* (n=202)	18 (9.0%)
Synch.res** (n=471)	64 (13.6%)
Metachronous (n=332)	24 (7.2%)
R0 liver resection	90
Synch.not-res* (n=202)	13 (6.4%)
Synch.res** (n=471)	54 (11.5%)
Metachronous (n=332)	23 (7.0%)

6-month response to chemo (n=1,005)

Subgroup analysis by chemo

Best overall response	519
FOLFOX+BV (n=437)	218 (49.9%)
XELOX+BV (n=540)	287 (53.2%)
Others (n=28)	14 (50.0%)

Subgroup analysis by KRAS

Best overall response	519
KRAS wild (n=323)	171 (52.9%)
KRAS mutant (n=241)	117 (48.6%)
KRAS unknown (n=441)	231 (52.4%)

6-month progression-free survival rate (n=1,005)

Subgroup analysis by chemo

6-month PFS rate	83.9%
FOLFOX+BV (n=437)	84.2%
XELOX+BV (n=540)	83.6%
Others (n=28)	88.9%

Subgroup analysis by primary

6-month PFS rate	84.0%
Colon (n=549)	84.0%
Rectum (n=451)	82.6%
Others (n=5)	NA

Subgroup analysis by synch./metach.

6-month PFS rate	87.1%
Synch.not-res* (n=202)	79.6%
Synch.res** (n=471)	83.6%
Metachronous (n=332)	87.1%

Summary

- ✓ 627 pts had liver metastases among 1,005 pts.
- ✓ 540 pts (53.7%) received XELOX + BV, whereas 437 pts (43.4%) received FOLFOX + BV.
- ✓ KRAS mutation was measured at 56.1% before 1st line chemo was started (between 2010 and 2011).
- ✓ 448 pts discontinued 1st line chemo at 6 months. Among 448 pts, 141 pts discontinued chemo due to AEs, mostly neuropathy and allergy.
- ✓ Regimens and KRAS mutational status don't make much difference on liver resection rate, response rate and 6-month PFS rate in Japanese clinical practice.

Conclusion

- ✓ We performed a preplanned interim analysis on 1,005 pts and this could be a large database to investigate 1st line chemo in clinical practice of mCRC pts in Japan.
- ✓ We performed subgroup analyses by regimens, KRAS mutation, primary site, and synchronous or metachronous on this database.
- ✓ We will further investigate and analyze the 2-year data including survival on all pts.
- ✓ This study is sponsored by the Public Health Research Center Foundation CSPOR in Japan.

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