Novinky z ASCO GI 2019 u nádorů horního GIT

Radka Obermannová

PRAGUE ONCO 23.1.2019

Obsah

- Karcinom jícnu II. linie- KEYNOTE- 181
- Karcinom žaludku I.linie- GAMMA
- HER 2 pozitivní karcinom žaludku- I.linie
- TAS 102 u pacientů s- a bez gastrektomie
- Oligometastatické onemocnění
- ChemoRadioterapie versus esofagektomie u stadia I karcinomu jícnu

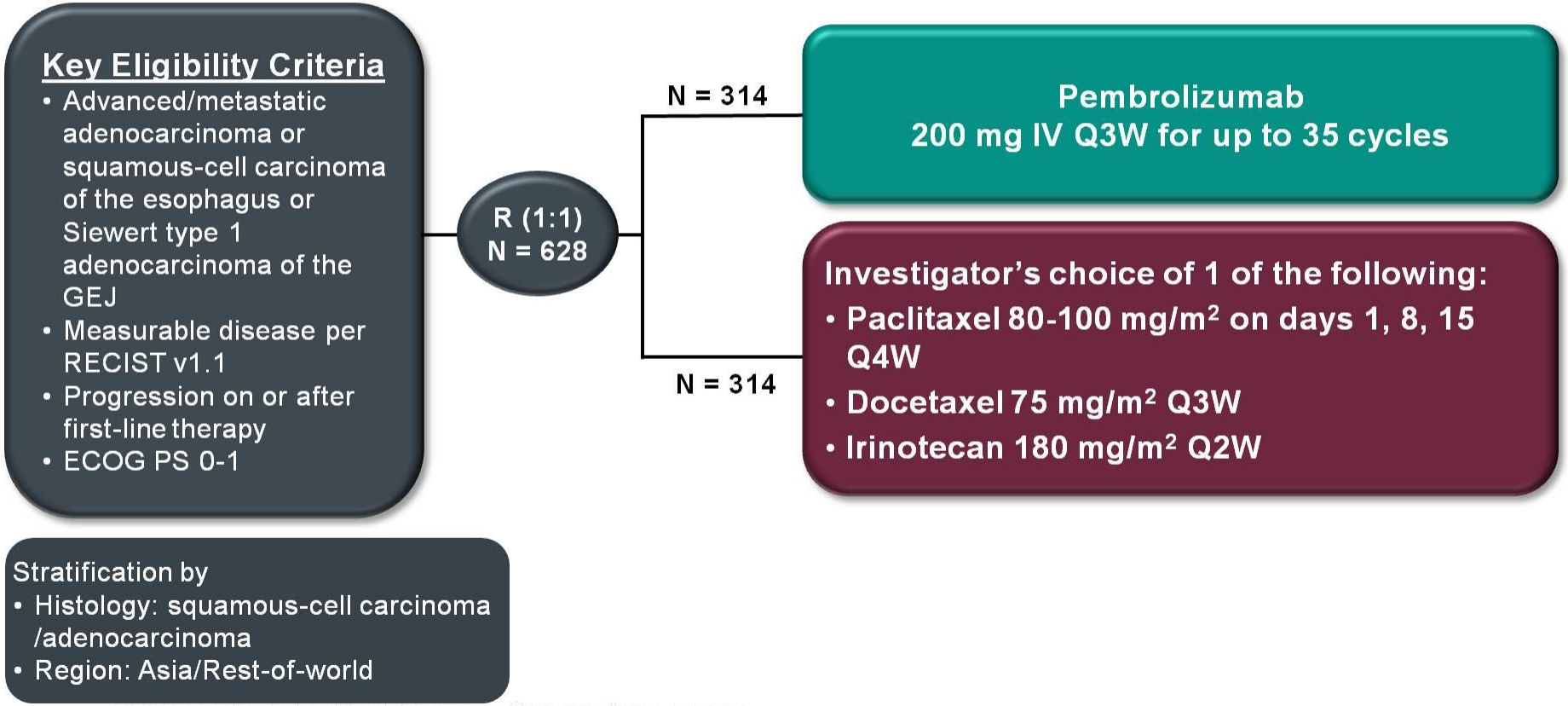
Pembrolizumab Versus Chemotherapy as Second-line Therapy for Advanced Esophageal Cancer: The Phase 3 KEYNOTE-181 Study

Takashi Kojima,[1] Kei Muro,[2] Eric Francois,[3] Chih-Hung Hsu,[4] Toshikazu Moriwaki,[5] Sung-Bae Kim,[6] Se-Hoon Lee,[7] Jaafar Bennouna,[8] Ken Kato,[9] Lin Shen,[10] Shu-Qui Qin,[11] Paula Ferreira,[12] Toshihiko Doi,[13] Antoine Adenis,[14] Peter Enzinger,[15] Manish Shah,[16] Ruixue Wang,[17] Pooja Bhagia,[17] S. Peter Kang,[17] Jean-Philippe Metges[18]

[1]National Cancer Center Hospital East, Kashiwa, Japan; [2]Aichi Cancer Center Hospital, Nagoya, Japan; [3]CLCC Antoine Lacassagne, Nice, France; [4]National Taiwan University Hospital, Taipei, Taiwan; [5]University of Tsukuba Hospital, Tsukuba, Japan; [6]Asan Medical Center, Seoul, South Korea; [7]Samsung Medical Center, Seoul, South Korea; [8]Institut de Cancerologie de L'Ouest, Nantes, France; [9]National Cancer Center Hospital, Tokyo, Japan; [10]Beijing Cancer Hospital, Beijing, China; [11]PLA Cancer Centre of Nanjing Bayi Hospital, Nanjing, China; [12]Instituto Portugues de Oncologia Do Porto Francisco Gentil E.P.E., Porto, Portugal; [13]National Cancer Center Hospital East, Chiba, Japan; [14]Institut du Cancer de Montpellier, Montpellier, France; [15]Dana Farber Cancer Institute and Harvard Medical School, Boston, MA, USA; [16]Weill Cornell Medical College, New York, NY; [17]Merck & Co., Inc., Kenilworth, NJ, USA; [18]CHU Brest - Institut de Cancerologie et d'Hematologie, Arpego Network Brest, France

PRESENTED AT: 2019 Gastrointestinal Cancers Symposium | #GI19

Phase 3 KEYNOTE-181 Study (NCT02564263)



Analysis Populations and Endpoints

- Analysis populations
  - Efficacy: assessed in patients with PD-L1 CPS ≥10, SCC, and ITT
  - Safety: assessed in all patients who received ≥1 dose of study drug
- 3 primary endpoints
  - Overall survival in
    1. Patients with PD-L1 CPS ≥10
    2. Patients with SCC
    3. All patients (ITT)
- Secondary endpoints
  - Progression-free survival
  - Objective response
  - Safety

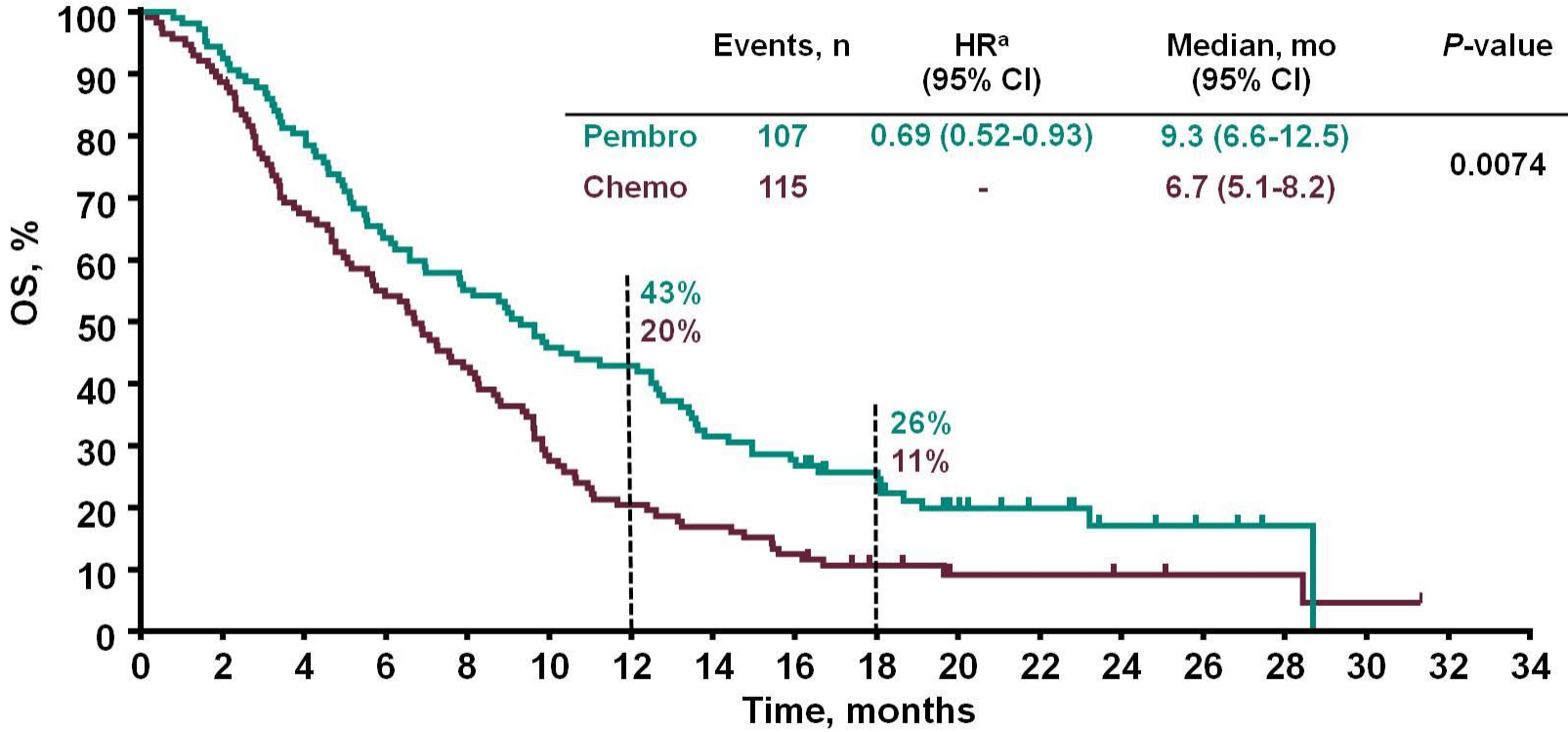
SCC, squamous cell carcinoma; ITT, intent-to-treat; PD-L1 CPS: defined as number of PD-L1 positive cells (tumor cells, macrophages, lymphocytes)/total number of tumor cells x 100.

Baseline Characteristics (ITT)

Characteristic, n	Pembrolizumab N = 314	Chemotherapy N = 314
Median age, years (range)	63 (23-84)	62 (24-84)
≥65 years	139 (44.3)	133 (42.4)
Male	273 (86.9)	271 (86.3)
Asia	121 (38.5)	122 (38.9)
Rest of World	193 (61.5)	192 (61.1)
ECOG PS 1	187 (59.6)	197 (62.7)
Squamous-cell carcinoma	198 (63.1)	203 (64.6)
Adenocarcinoma	116 (36.9)	111 (35.4)
PD-L1 CPS ≥10[a]	107 (34.1)	115 (36.6)
Metastatic disease	290 (92.4)	286 (91.1)
0-1[b] prior therapies	305 (97.1)	310 (98.7)
≥2 prior therapies	9 (2.9)	4 (1.3)

[a]6 patients in pembrolizumab and 3 in chemotherapy group were not evaluable; [b]2 patients in pembrolizumab group had 0 prior therapies; Data cutoff: October 15, 2018.

Overall Survival (PD-L1 CPS ≥10)

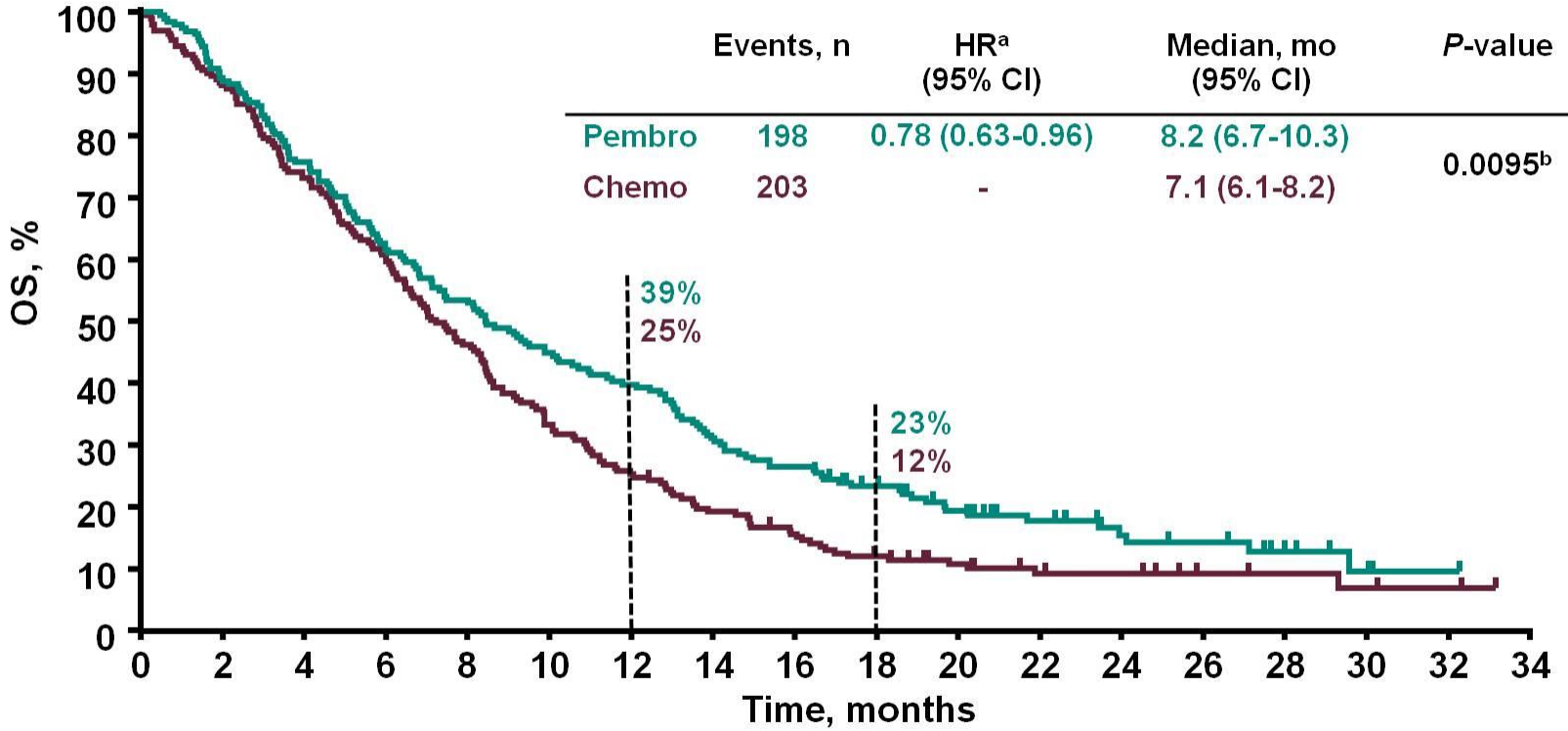


	Events, n	HR[a] (95% CI)	Median, mo (95% CI)	*P*-value
Pembro	107	0.69 (0.52-0.93)	9.3 (6.6-12.5)	0.0074
Chemo	115	-	6.7 (5.1-8.2)	

No. at risk																		
Pembrolizumab	107	100	86	68	59	49	45	33	29	23	13	9	5	3	1	0	0	0
Chemotherapy	115	102	76	61	48	31	23	19	14	8	4	4	3	2	2	1	0	0

[a]Based on Cox regression model with treatment as a covariate stratified by region and histology.
Data cutoff: October 15, 2018.

Overall Survival (SCC)

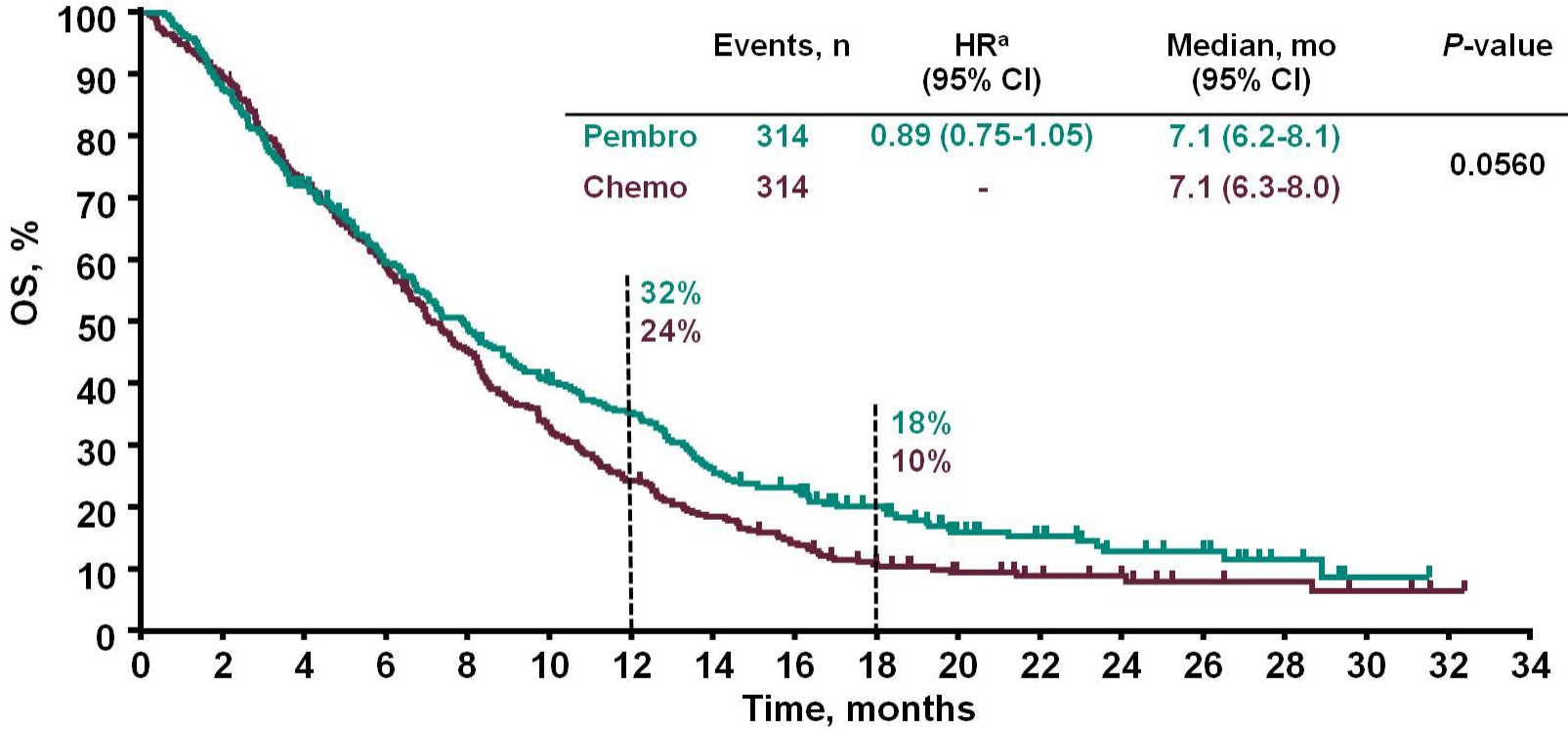


	Events, n	HR[a] (95% CI)	Median, mo (95% CI)	*P*-value
Pembro	198	0.78 (0.63-0.96)	8.2 (6.7-10.3)	0.0095[b]
Chemo	203	-	7.1 (6.1-8.2)	

No. at risk																		
Pembrolizumab	198	177	150	121	103	86	77	57	52	38	24	17	12	10	5	1	0	0
Chemotherapy	203	179	147	118	91	64	50	38	27	20	13	10	8	5	4	2	1	0

[a]Based on Cox regression model with treatment as a covariate stratified by region and histology; [b]Not significant based on pre-specified statistical boundaries of $P \leq 0.0077$ for superiority of OS in SCC; Data cutoff: October 15, 2018.

Overall Survival (ITT)

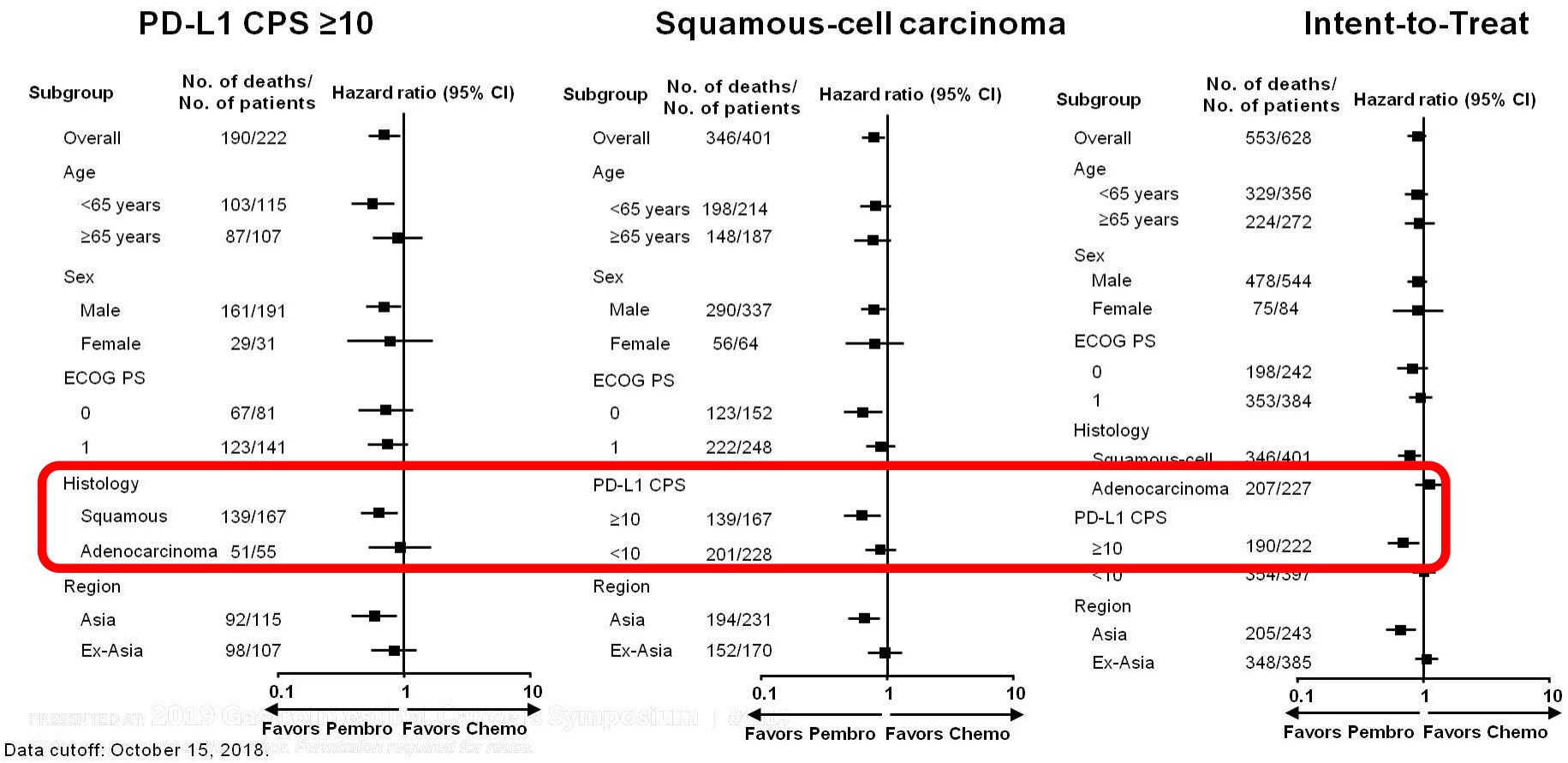


	Events, n	HR[a] (95% CI)	Median, mo (95% CI)	*P*-value
Pembro	314	0.89 (0.75-1.05)	7.1 (6.2-8.1)	0.0560
Chemo	314	-	7.1 (6.3-8.0)	

No. at risk																		
Pembrolizumab	314	275	224	176	143	116	100	73	63	46	28	20	14	10	5	1	0	0
Chemotherapy	314	280	226	181	139	98	75	56	41	26	18	13	9	6	5	3	1	0

[a]Based on Cox regression model with treatment as a covariate stratified by region and histology.
Data cutoff: October 15, 2018.

OS in Key Subgroups



Data cutoff: October 15, 2018.

Závěry

- Pembrolizumab v II. linii metastatického esofageálního karcinomu signifikantně prodlužuje OS u pacientů s:

✓PD-L1 CPS≥10 (HR 0,69)

✓ spinocelulární histologií (HR 0,78)

- Bezpečnostní profil lepší než chemoterapie (AE grade 3-5 18,2 versus 40,9%)
- Pembrolizumab= alternativou v 2.linii?- pro selektovanou skupinu pacientů

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Andecaliximab Combined With mFOLFOX6 as First-Line Treatment in Patients With Advanced Gastric or Gastroesophageal Junction Adenocarcinoma (GAMMA-1)

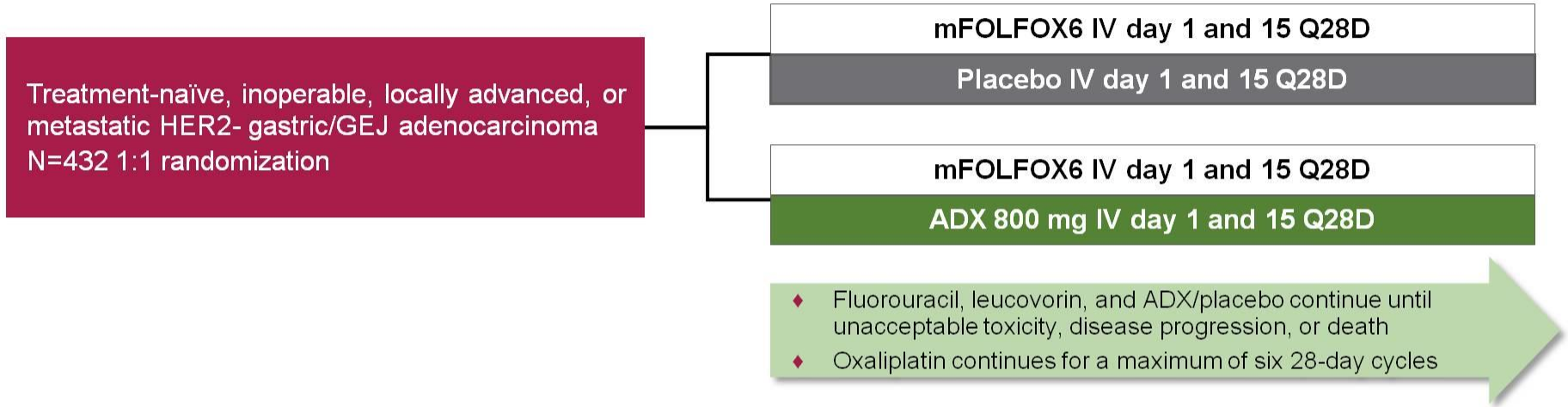
Manish A. Shah[1], Eduardo Yañez Ruiz[2], Gyorgy Bodoky[3], Alex Starodub[4], David Cunningham[5], Desmond Yip[6], Zev A. Wainberg[7], Johanna Bendell[8], Dung Thai[9], Pankaj Bhargava[9], Jaffer Ajani[10]

[1]Weill Cornell Medicine, NewYork-Presbyterian Hospital, New York, NY, United States; [2]Universidad de la Frontera, Temuco, Chile; [3]Szent László Hospital, Budapest, Hungary; [4]Parkview Comprehensive Cancer Institute/Parkview Health, Fort Wayne, IN, United States; [5]The Royal Marsden NHS Foundation Trust, Sutton and London Hospital, Sutton, United Kingdom; [6]ANU Medical School, Australian National University, Canberra, Australia; [7]David Geffen School of Medicine at UCLA, Los Angeles, CA, United States; [8]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, United States; [9]Gilead Sciences, Inc., Foster City, CA, United States; [10]The University of Texas MD Anderson Cancer Center, Houston, TX, United States

Introduction

- Andecaliximab (ADX) is a monoclonal antibody that inhibits matrix metalloproteinase 9 (MMP9), an extracellular enzyme involved in matrix remodeling, tumor growth, and metastasis
- A phase 1/1b study of mFOLFOX6 + ADX revealed encouraging anti-tumor activity in patients with gastric or gastroesophageal junction (GEJ) adenocarcinoma
  - Median first-line, progression-free survival (PFS) of 9.9 months and an objective response rate (ORR) of 50%

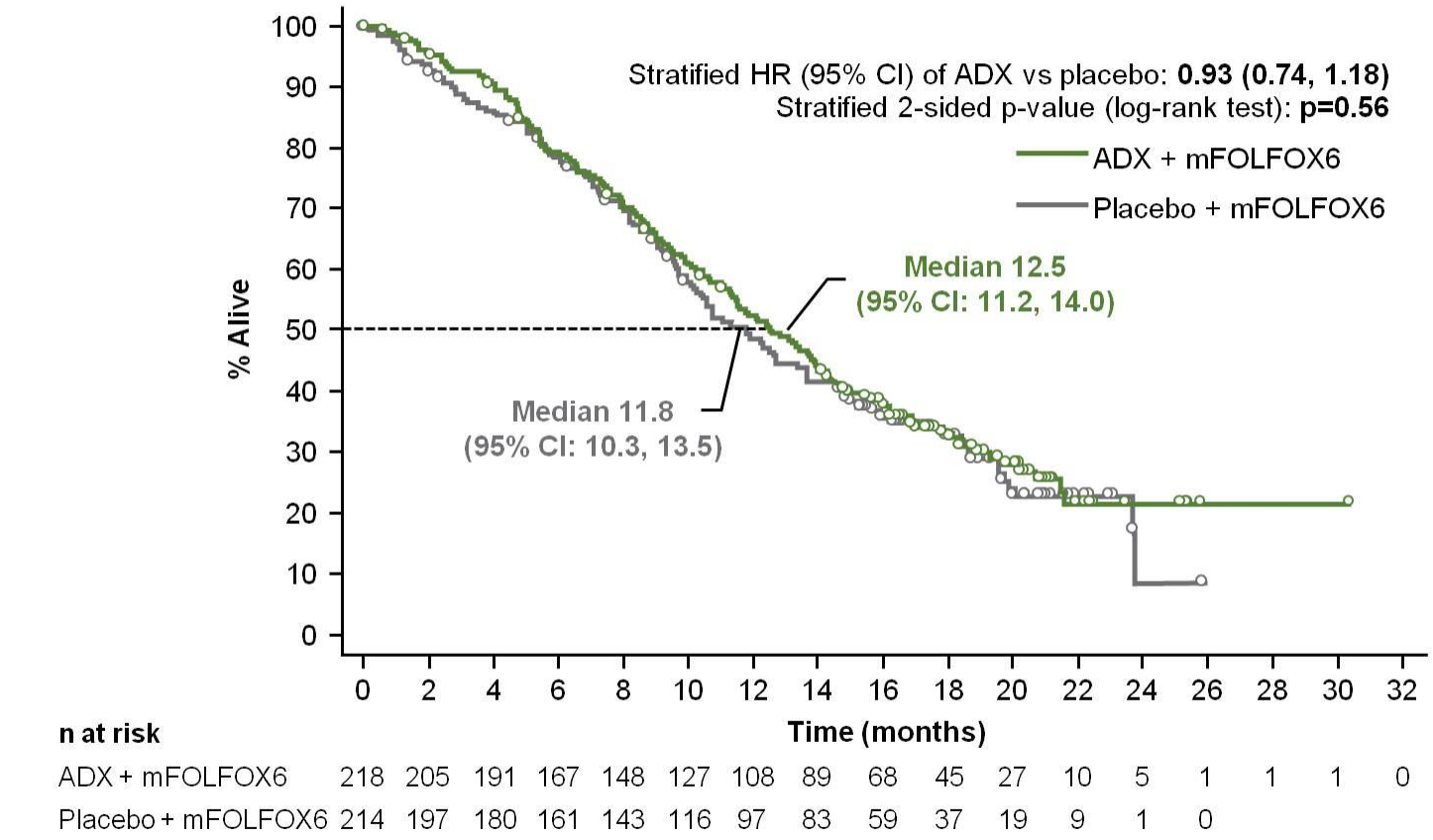
GAMMA-1 Phase 3 Study Design



Disease assessments	Imaging Q8W, after treatment discontinuation survival follow-up every 3 months x 5 years
Stratification factors	ECOG PS, region (Latin America vs Rest of World), primary tumor site (gastric vs GEJ)
Primary endpoint	OS
Secondary endpoints	PFS, ORR, safety

Q28D, every 28 days; Q8W, every 8 weeks; ECOG PS, Eastern Cooperative Oncology Group performance status; OS, overall survival.

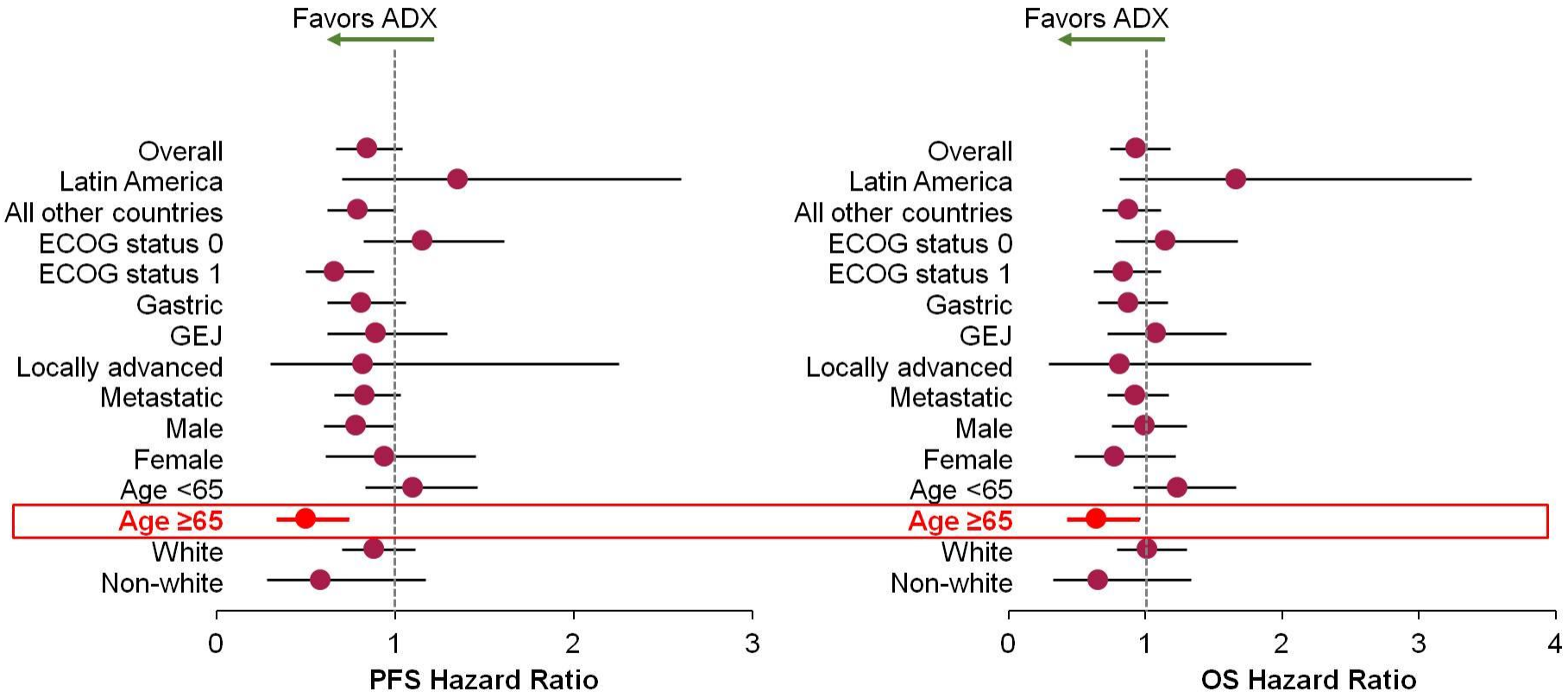
OS KM Curve



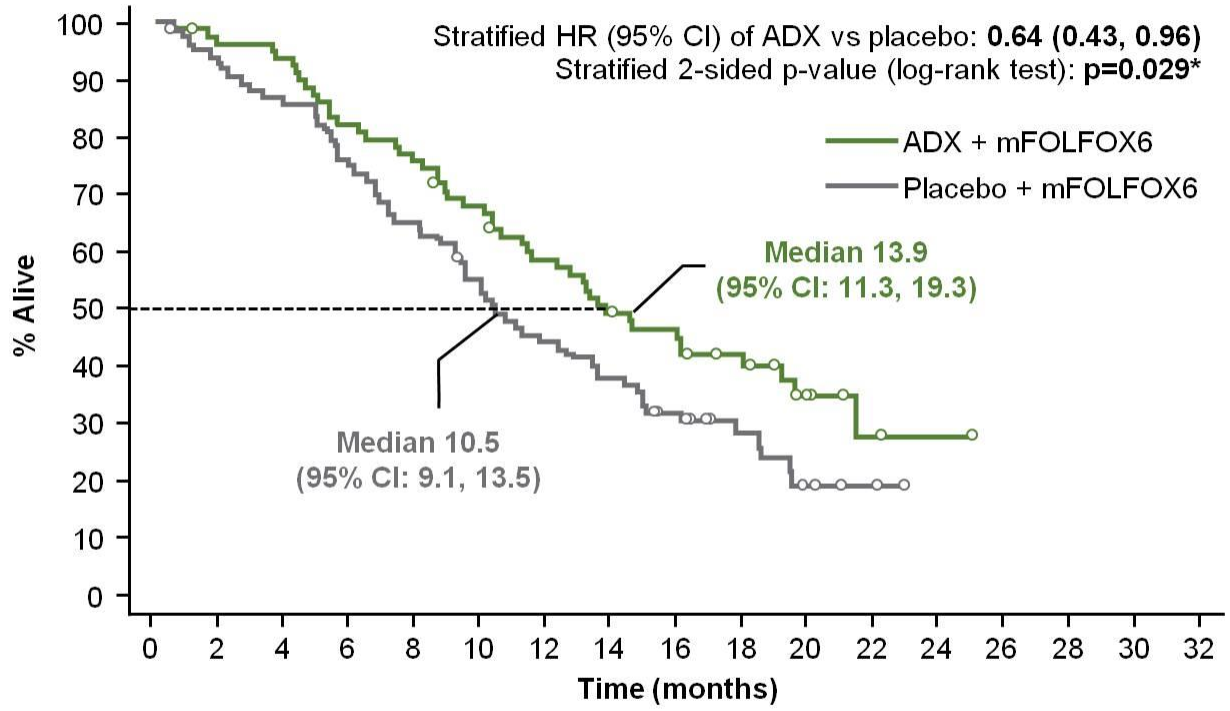
n at risk																	
ADX + mFOLFOX6	218	205	191	167	148	127	108	89	68	45	27	10	5	1	1	1	0
Placebo + mFOLFOX6	214	197	180	161	143	116	97	83	59	37	19	9	1	0			

Presented By Manish Shah at 2019 Gastrointestinal Cancer Symposium

PFS and OS HR by Subgroups



OS KM Curve, Age ≥65



n at risk														
ADX + mFOLFOX6	81	76	74	64	59	52	44	37	32	22	12	3	1	0
Placebo + mFOLFOX6	86	79	72	62	54	44	36	31	23	13	7	4	0	

* The analysis is exploratory and for hypothesis generation. The result is not statistically significant after adjusting for multiplicity due to subgroup analyses.

Závěry

- Andecaliximab v kombinaci s FOLFOX neprodlužuje přežití u pacientů s HER 2- metastatickým karcinomem žaludku a GEJ léčených první linií
- Lepší výsledky andecaliximabu u pacientů ≥ 65 let musí být validovány
- Nejsou známky neočekávatelné toxicity

First-line pembrolizumab, trastuzumab, capecitabine and oxaliplatin in HER2-positive metastatic esophagogastric adenocarcinoma
Abstract #62

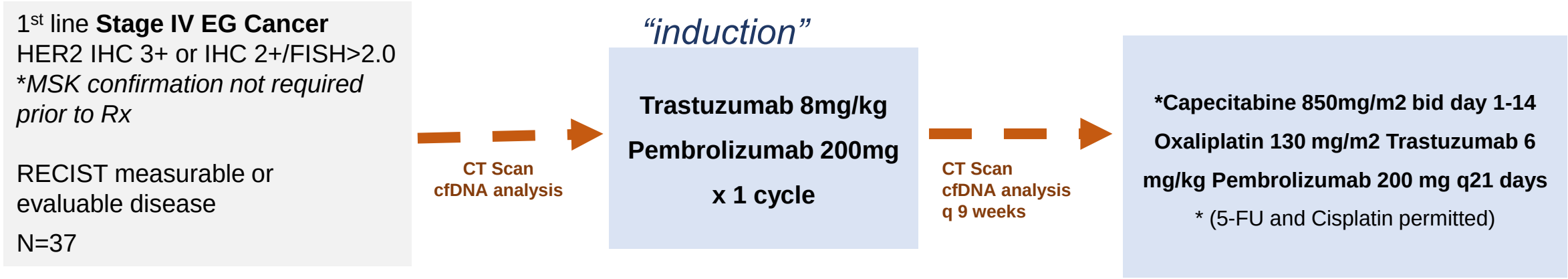
Yelena Y. Janjigian, Joanne F. Chou, Marc Simmons, Parisa Momtaz, Francisco Sanchez-Vega, Marina Shcherba, Geoffrey Y. Ku, Elizabeth Won, Curtis R. Chong, Hans Gerdes, David P. Kelsen,

David H. Ilson, David B. Solit, Nikolaus Schultz, Pari M. Shah, Marinela Capanu, Jaclyn F. Hechtman

ASCO #GI19 @yjanjigianMD
January 17, 2019

Pembrolizumab/Trastuzumab/Chemotherapy

Phase II study schema



Primary endpoint: 6-months PFS, 26 or more patients progression free at 6 months

Secondary endpoints:

- *OS*
- *ORR & DCR by RECIST 1.1*

Biomarker analysis:

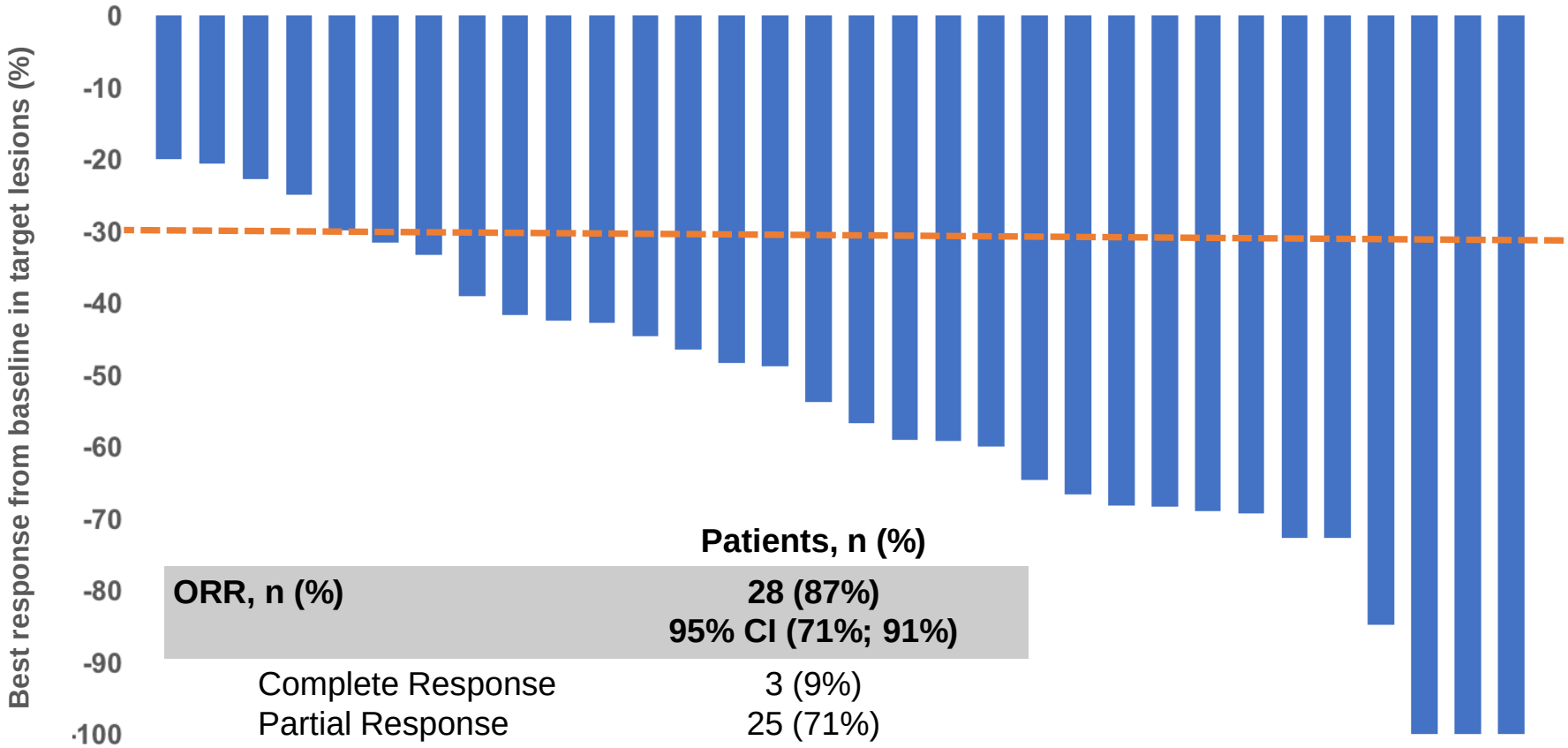
- *MSK HER2 IHC/FISH*
- *PDL-1 IHC (Clone E1L3N, Cell Signaling Technology)*
- *CPS score = PDL-1-pos (tumor cells+lymphocytes +macrophages /# of tumor cells x 100)*
- *NGS by IMPACT at baseline & POD*
- cfDNA analysis

Baseline Characteristics (n=35)

Pembrolizumab/Trastuzumab/Chemo	Patients, n (%)
Age, median (range), years	61 (20-83)
Male	27 (77)
Race	
White	29 (82)
Asian	2 (6)
Black	1 (3)
Hispanic/Other	3 (9)
Primary site	
Esophageal	14 (40)
GEJ	12 (34)
Gastric	9 (26)
HER2 MSK confirmation	
Positive	28 (80)
Negative	6 (17)
Not available	1 (3)
Pretreatment PD-L1 status	
CPS <1 (negative)	12 (34)
CPS >=1	14 (40)
Not available	9 (26)

Best Response (n=32)

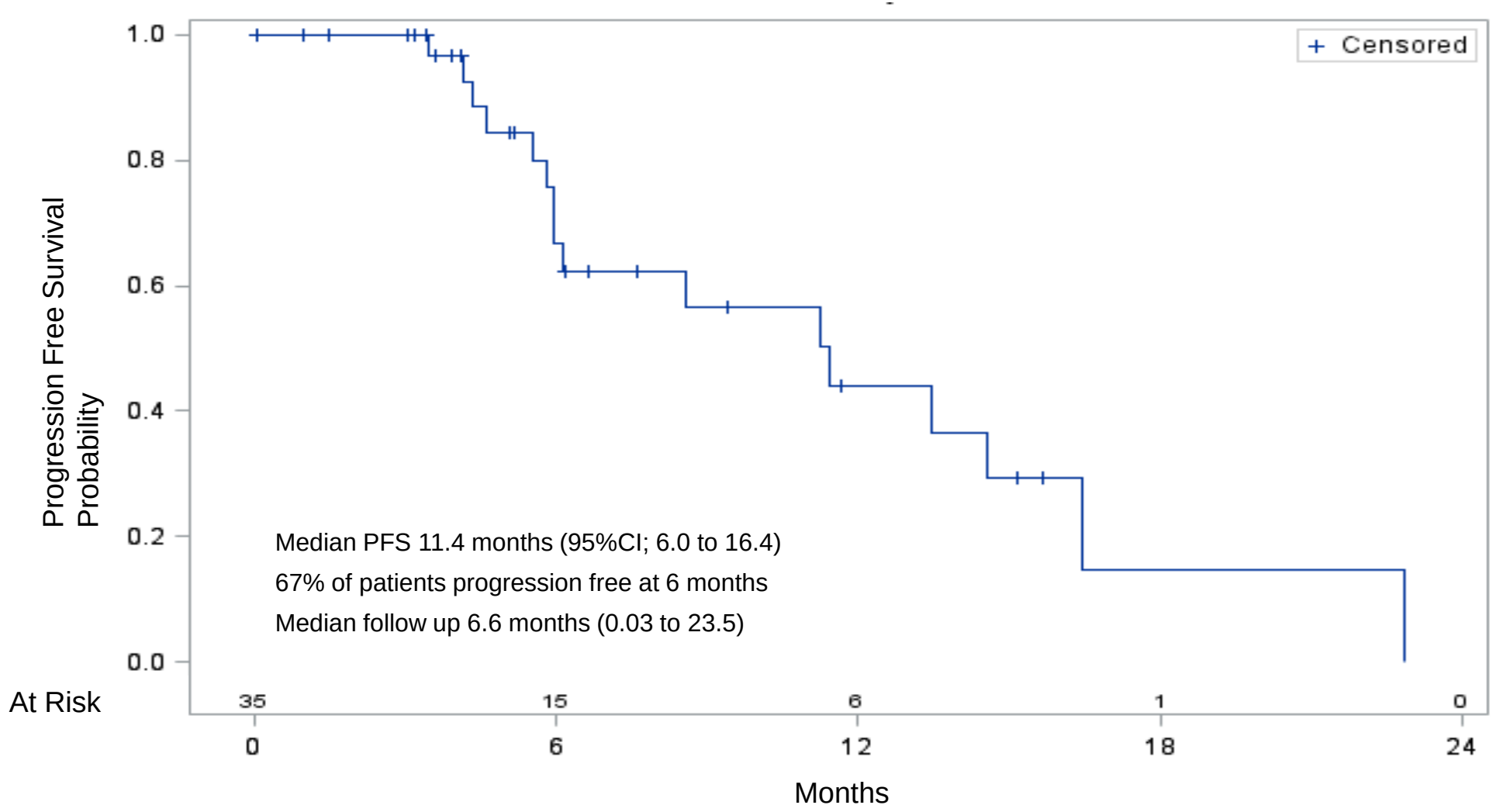
Pembrolizumab/Trastuzumab/Chemotherapy



	Patients, n (%)
ORR, n (%)	**28 (87%)** **95% CI (71%; 91%)**
Complete Response	3 (9%)
Partial Response	25 (71%)
Stable Disease	4 (11%)
Progressive Disease	0
Not Evaluable	3 (9%)
Disease Control Rate	**100%**

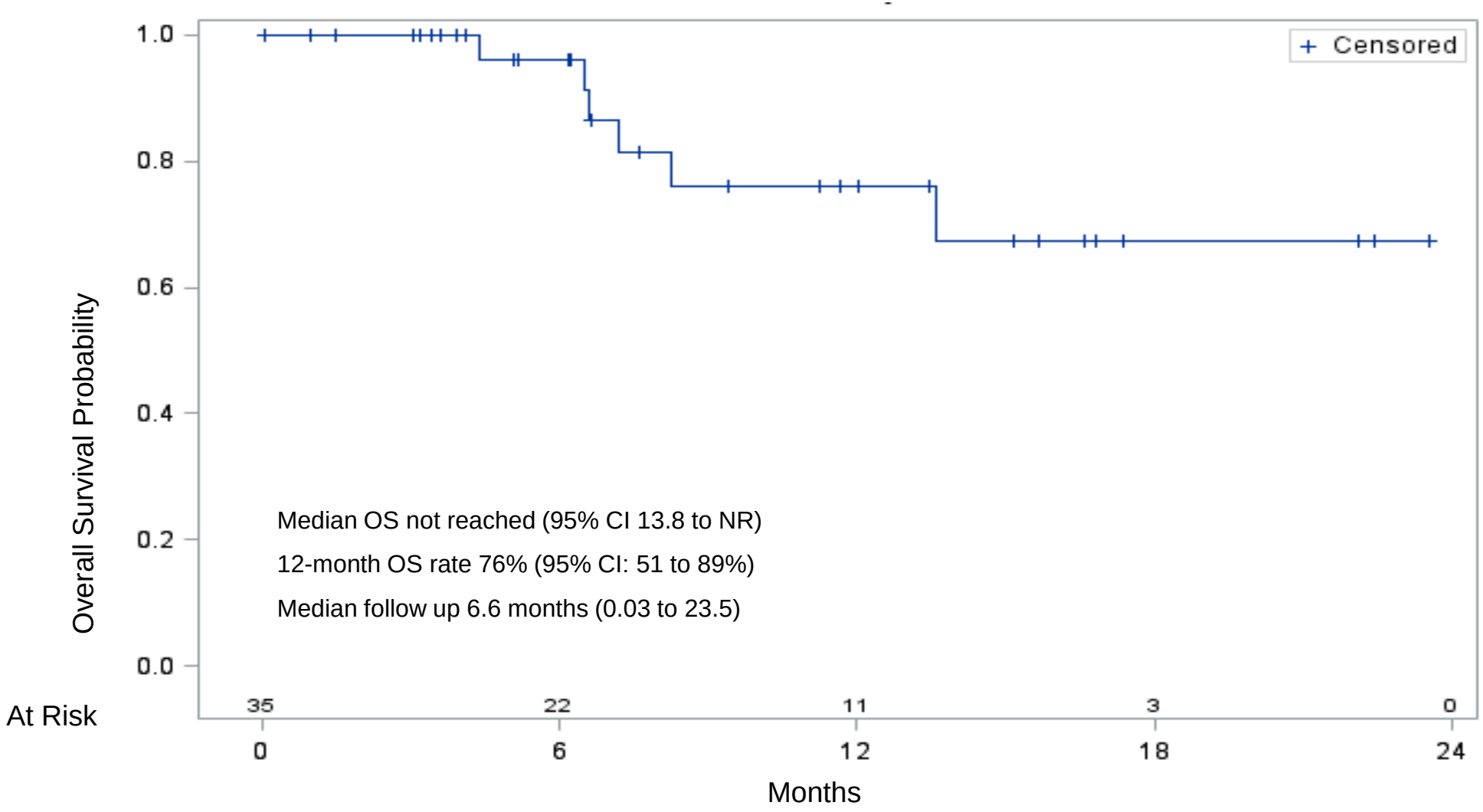
Progression-Free Survival (n=35)

Pembrolizumab/Trastuzumab/Chemotherapy

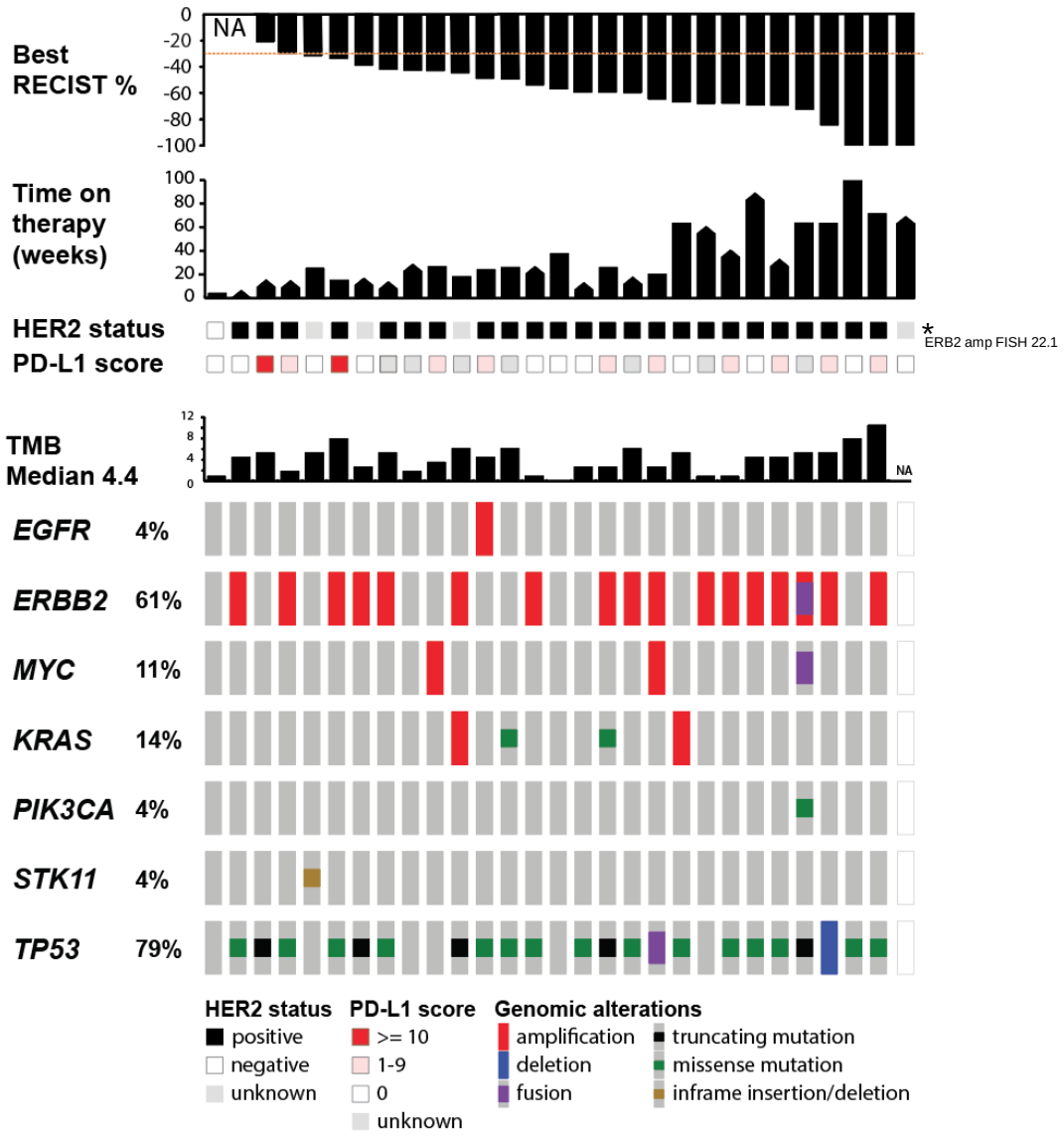


Overall Survival (n=35)

Pembrolizumab/Trastuzumab/Chemotherapy



Biomarker Analysis (n=29)



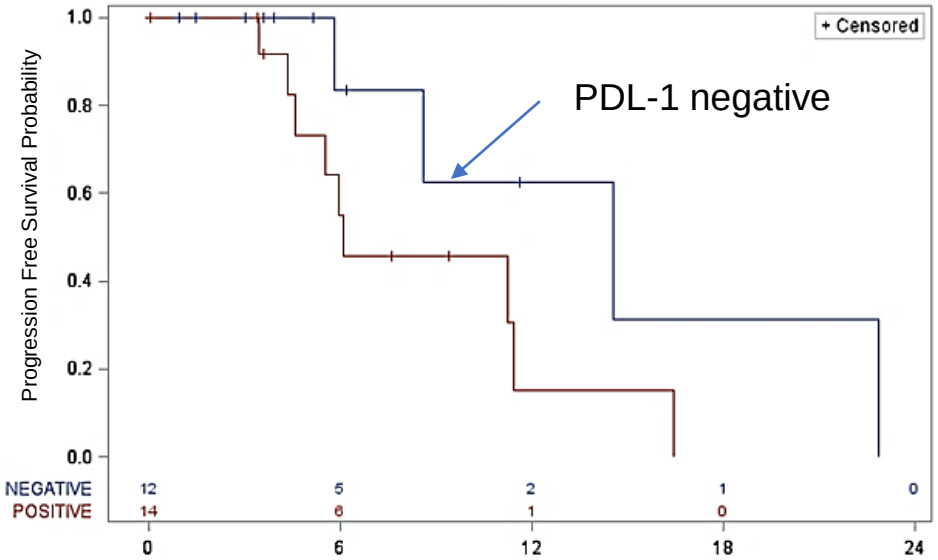
- No MSI tumors in HER2+ mEGA

  -- Median TMB 4.4 mut/MB (range 0 to 10.6)

- PDL-1 status is not a predictor

  -- PFS (log-rank p=0.10) or OS (log-rank p=0.60) between PDL-1 + vs PDL-1-

PFS by PDL-1



- *ERBB2 non-amp by NGS* is associated with short duration of response

  -- 33% of patients with co- occurring RTK/RAS/PIK3CA alterations

KEYNOTE-811

Global Randomized Double-Blind Phase III Trial Pembrolizumab/Trastuzumab/Chemotherapy vs. Placebo/Trastuzumab/Chemotherapy

NCT03615326

1st line **Stage IV Gastric/GEJ Cancer**

HER2 IHC 3+ or IHC 2+/FISH>2.0

**Central confirmation required prior to Rx*

RECIST measurable disease

N=692

Pembrolizumab
Trastuzumab/Chemotherapy
N=346

Placebo
Trastuzumab/Chemotherapy
N=346

Stratification: PD-L1 status, Region (Asia vs. US vs. ROW), and chemotherapy regimen
Cisplatin + 5-FU or CapeOx or SOX

Primary enpoint: Dual endpoint PFS and OS
Secondary enpoint: ORR, Biomarker analysis

PI Janjigian

Závěry

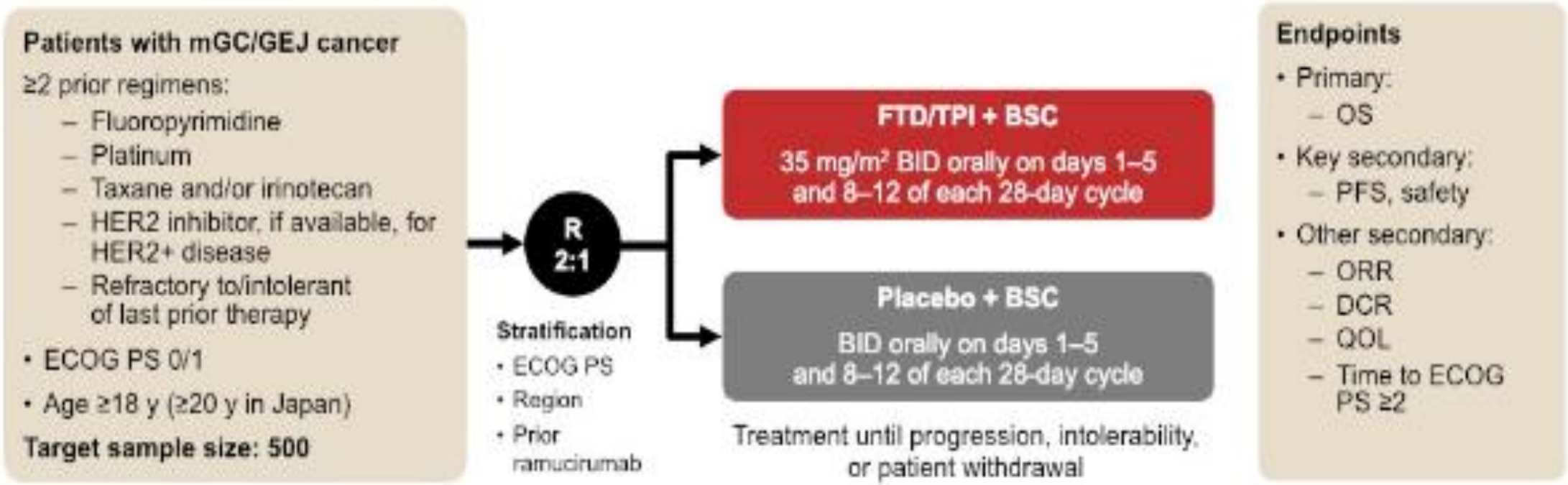
- Pembrolizumab/Trastuzumab/CAPEOX byl dobře tolerován
- Nadějné ORR 87% (ve srovnání s historickou kontrolou 47%)
- Probíhá fáze III Keynote 811 (NCT03615326)
- Biomarkery- probíhá analýza korelace průběhu s TCR clonality, MDSC I a cfDNA
- HER2 status zůstává důležitým prediktivním faktorem, PDL-1 status NENÍ prediktorem PFS

Efficacy and safety of trifluridine/tipiracil in patients with metastatic gastric cancer with gastrectomy: Results from a phase 3 study (TAGS)

David H. Ilson,[1] Aliaksandr Prokharau,[2] Tobias Arkenau,[3] Michele Ghidini,[4] Kazumasa Fujitani,[5] Eric Van Cutsem,[6] Peter Thuss-Patience,[7] Giordano D. Beretta,[8] Wasat Mansoor,[9] Edvard Zhavrid,[10] Maria Alsina,[11] Ben George,[12] Daniel Catenacci,[13] Robert E. Winkler,[14] Lukas Makris,[15] Toshihiko Doi,[16] Kohei Shitara[16]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Minsk City Clinical Oncology Dispensary, Minsk, Belarus; [3]Sarah Cannon Research Institute, Cancer Institute, University College London, London, UK; [4]Azienda Ospedaliera di Cremona, Cremona, Italy; [5]Osaka General Medical Center, Osaka, Japan; [6]University Hospitals and KU Leuven, Leuven, Belgium; [7]Charité – Universitätsmedizin Berlin, Berlin, Germany; [8]Humanitas Gavazzeni, Bergamo, Italy; [9]The Christie NHS Foundation Trust, Manchester, UK; [10]Alexandrov National Cancer Centre of Belarus, Minsk, Belarus; [11]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [12]Medical College of Wisconsin, Milwaukee, WI, USA; [13]University of Chicago, Chicago, IL, USA; [14]Taiho Oncology, Inc., Princeton, NJ, USA; [15]Stathmi, Inc., New Hope, PA, USA; [16]National Cancer Center Hospital East, Chiba, Japan

TAGS – Multicenter, Randomized, Double-blind, Phase 3 Study[a]

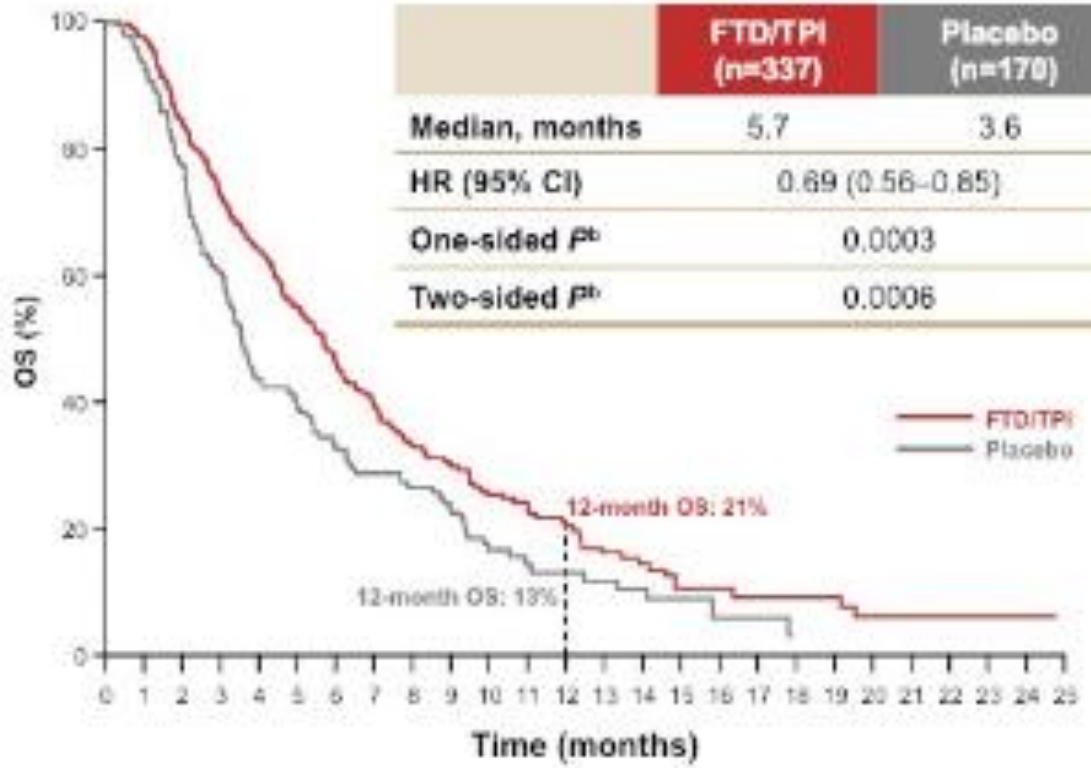


- Planned analyses of subgroups, including patients with gastrectomy, although not powered for statistical significance
- Patients with prior gastrectomy
  - FTD/TPI: n=147
  - Placebo: n=74

OS and PFS in the Overall Study Population[a]

OS

	FTD/TPI (n=337)	Placebo (n=170)
Median, months	5.7	3.6
HR (95% CI)	0.69 (0.56–0.85)	
One-sided *P*[b]	0.0003	
Two-sided *P*[b]	0.0006	

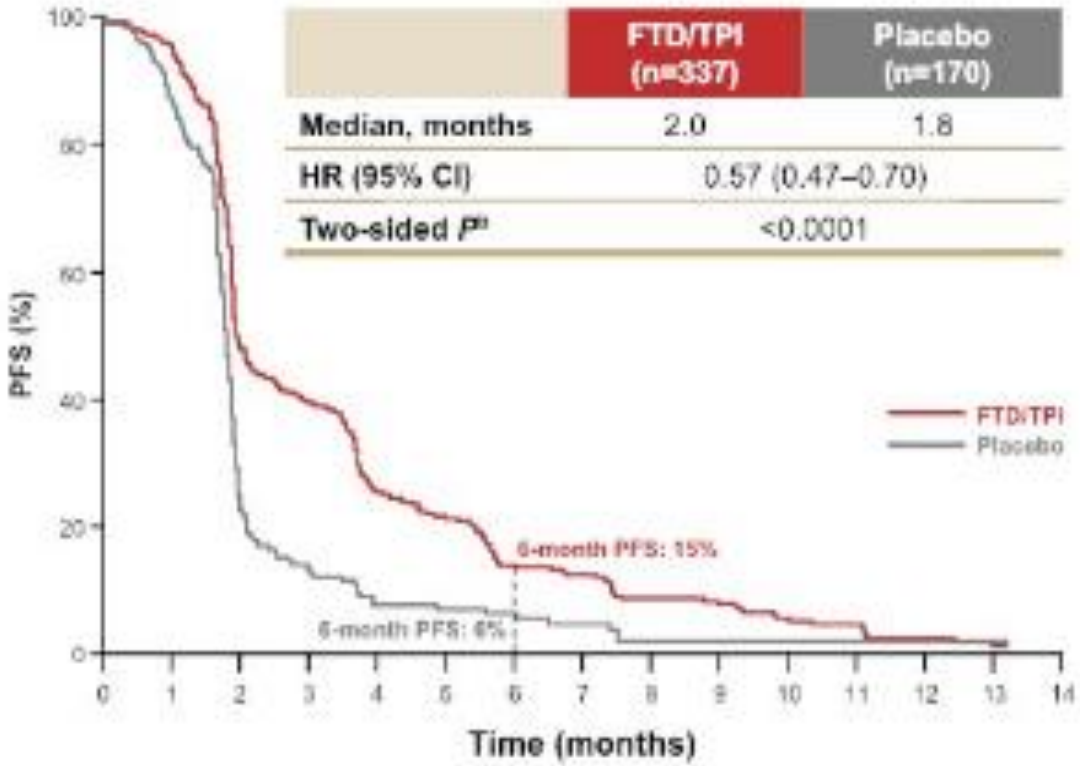


No. at risk

FTD/TPI	337	328	282	246	201	161	134	102	80	69	51	42	31	22	16	11	9	7	7	7	6	4	4	3	1	1
Placebo	170	156	131	101	71	60	47	40	34	29	17	12	10	8	7	6	2	2	2	2	0	0	0	0	0	0

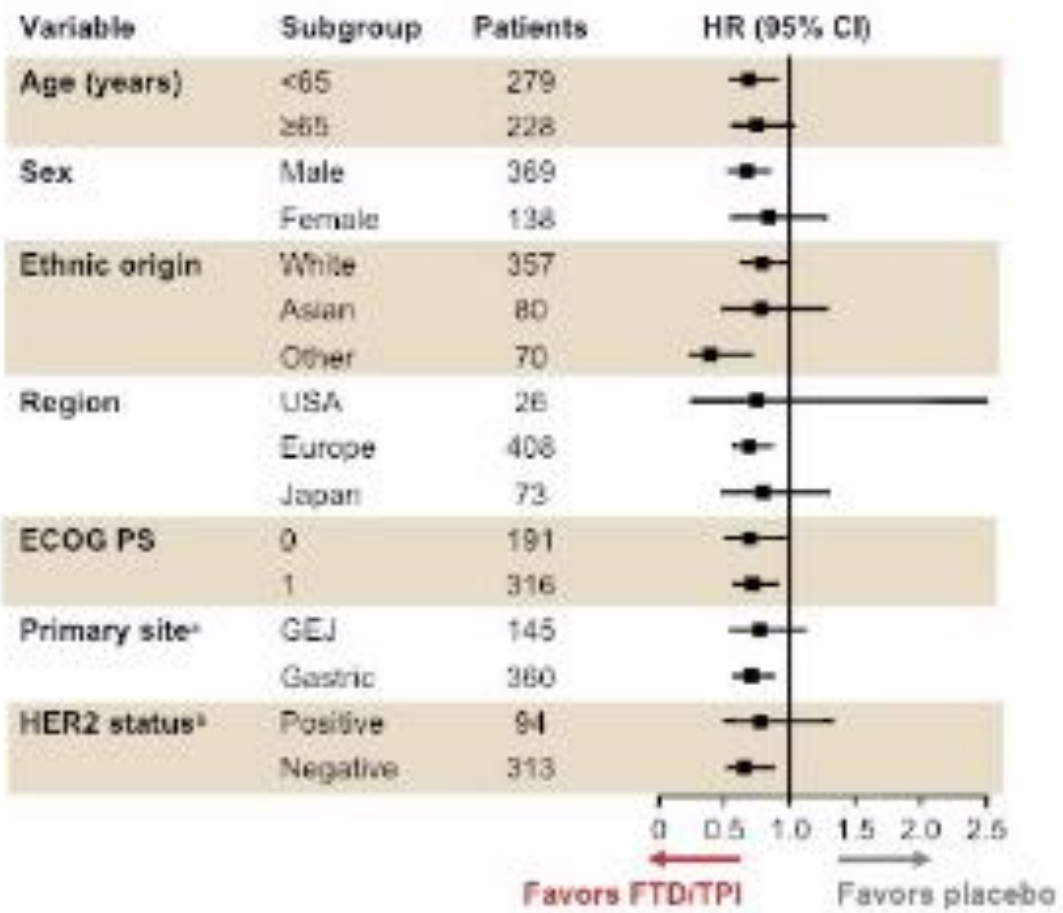
PFS

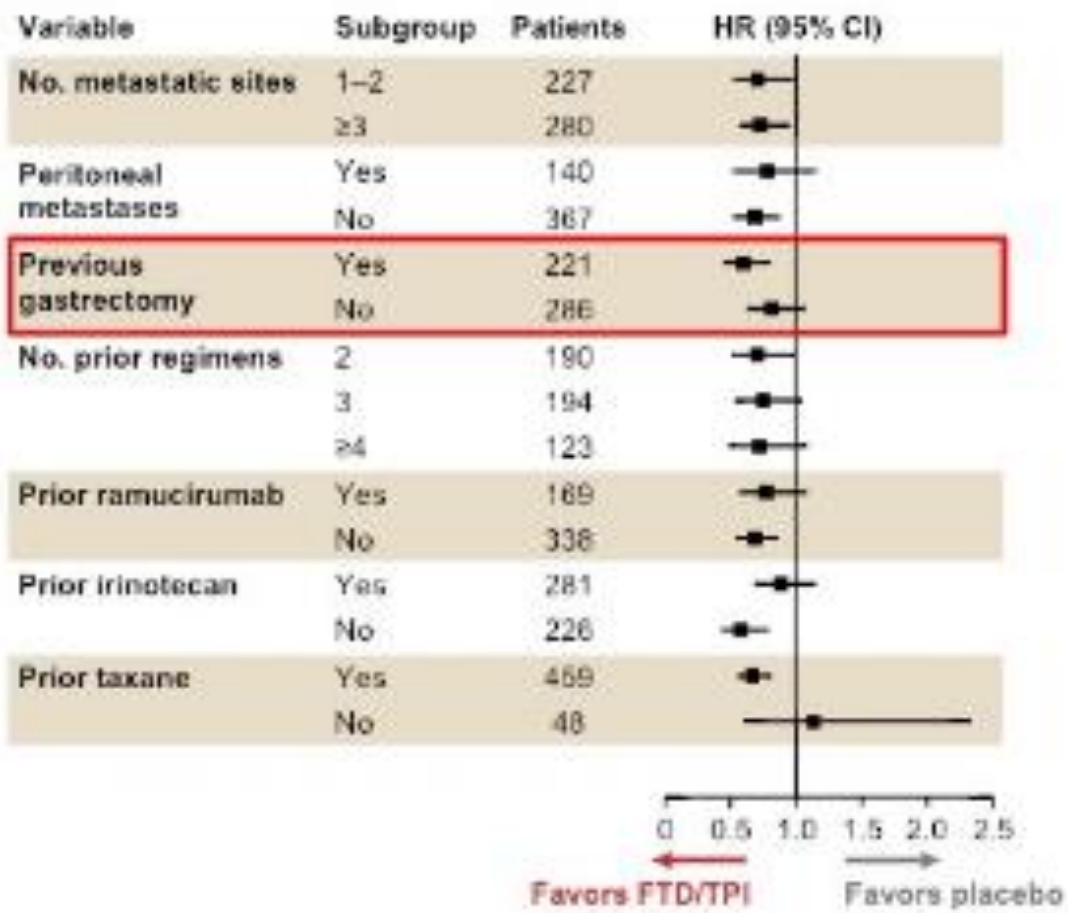
	FTD/TPI (n=337)	Placebo (n=170)
Median, months	2.0	1.8
HR (95% CI)	0.57 (0.47–0.70)	
Two-sided *P*[b]	<0.0001	



337	314	154	122	72	60	37	32	20	18	12	8	4	2	1
170	145	41	21	12	11	8	5	2	2	1	1	1	1	1

OS Subgroup Analysis

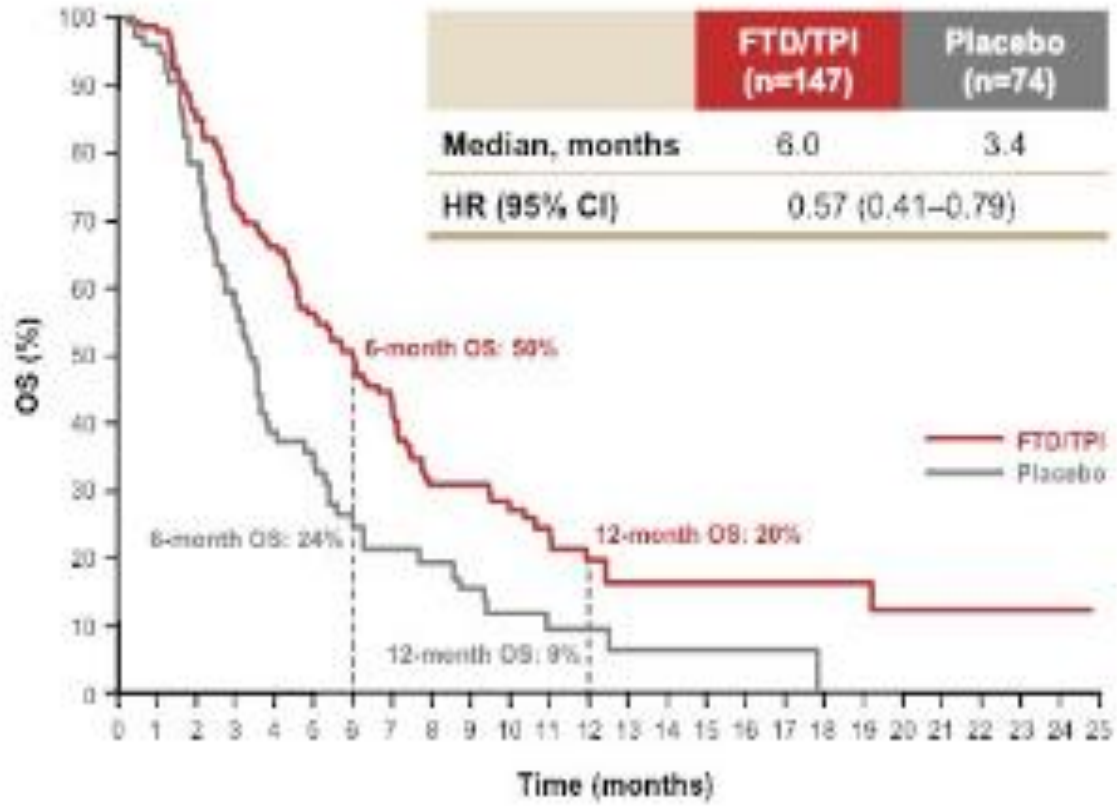




OS and PFS in Patients With Gastrectomy[a]

OS

	FTD/TPI (n=147)	Placebo (n=74)
Median, months	6.0	3.4
HR (95% CI)	0.57 (0.41–0.79)	

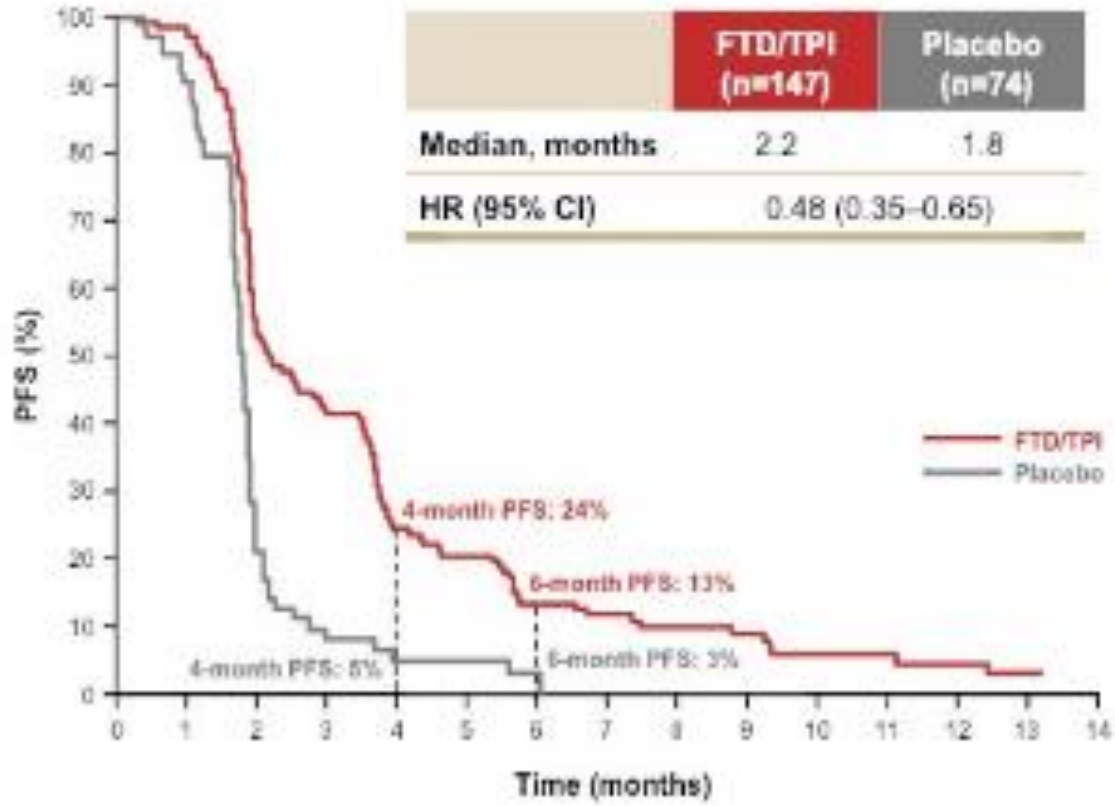


No. at risk

FTD/TPI	147	144	128	102	93	70	59	45	32	27	22	16	12	9	6	5	4	3	3	3	3	3	3	3	1	0	
Placebo	74	71	58	42	27	22	14	12	10	6	6	4	3	2	2	2	1	1	0	0	0	0	0	0	0	0	

PFS

	FTD/TPI (n=147)	Placebo (n=74)
Median, months	2.2	1.8
HR (95% CI)	0.48 (0.35–0.65)	



	147	135	75	54	37	26	17	10	10	9	6	6	3	2	0												
	74	62	15	5	3	3	1	0	0	0	0	0	0	0	0												

Závěry

- TAS 102 prodlužuje OS u pacientů s metastatickým karcinomem žaludku a GEJ- předléčených ≥2 liniemi chemoterapie
  - bez ohledu na provedenou gastrektomii

Abstract #7 Parallel-group controlled trial of esophagectomy versus chemoradiotherapy in patients with clinical stage I esophageal carcinoma (JCOG0502)

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Background

- ✓ Esophagectomy is the standard of care for stage I esophageal squamous cell carcinoma (ESCC).
- ✓ From the result of JCOG9708, definitive chemoradiotherapy (CRT) showed 87.5% of complete response rate and 75.5% of 5-year survival rate for the patients with stage I ESCC.
- ✓ A parallel-group controlled trial including randomized arms to confirm the non-inferiority of CRT to Esophagectomy for stage IA ESCC was conducted.

Objectives

✓To confirm non-inferiority of CRT in the mortality compared to esophagectomy as the current standard therapy for stage IAthoracic ESCC in a randomized controlled trial.

✓In addition, the second objective is to conduct a comparison in a non-randomized trial, if obtaining informed consent for the randomization is difficult.

Key eligibility criteria

1. Histologically proven squamous cell carcinoma, adenosquamous carcinoma, or basaloid carcinoma of esophagus
2. All lesions located in the thoracic esophagus
3. Clinical stage IA (T1bN0M0), according to UICC-TNM seventh edition
4. Aged 20 to 75 years old
5. ECOG Performance status 0 or 1
6. No prior therapy for esophageal cancer except complete resection by endoscopic mucosal resection or submucosal dissection with pT1a
7. No prior chemotherapy, radiotherapy, or endocrine therapy for any malignancy
8. Adequate organ functions
9. Written informed consent

Endpoints & Statistical considerations

Primary endpoint:

- Overall survival (OS) of arm A and B

Secondary endpoints:

- Overall survival (OS) of arm C and D
- Complete response (CR) rate of arm B and D
- Adverse events
- Late adverse events
- Progression free survival (PFS)

Statistical consideration:

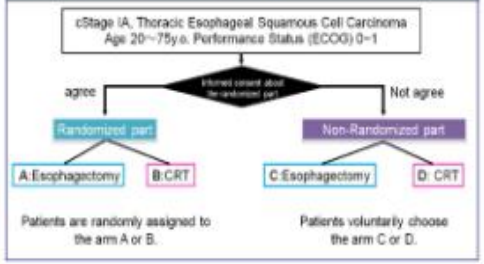
Planned Number of Subjects:

Randomized part (A group + B group) 114

Non-randomized part (C group) 156* (D group) 156*

dCRT arm is not inferior to esophagectomy arm in terms of OS, with one-sided α of 0.1, power of 70% for randomized part, and one-sided α of 0.025, power of 85% for non-randomized part, and a non-inferiority margin of **15% at 5-year** OS.
Non-inferiority will be concluded if the upper limit of the confidence interval of the hazard ratio does not exceed the limit of 1.78, the non-inferiority margin.
Comparison of non-randomized part is adjusted by weighting propensity score.

Study schema of JCOG0502



Study treatment

Esophagectomy (arm A and C)

Esophagectomy with a D2 or greater lymphadenectomy
[As long as a D2 or greater lymphadenectomy is applicable, there is no restriction on surgical modality (open thoracic or minimal invasive surgery), or the extent of lymph node dissection (two fields or three fields)]

Definitive chemoradiotherapy (arm B and D)

5-FU: 700 mg/m²/day, Day 1-4, Day 29-32
CDDP: 70 mg/m²/day, Day 1, Day 29
RT: 60 Gy/30 fr/6 w (5 days/week) × 6 weeks
PTV will be determined as an area of CTVs added appropriate margins (ca. 0.5-1 cm laterally and ca. 1-2 cm craniocaudally)

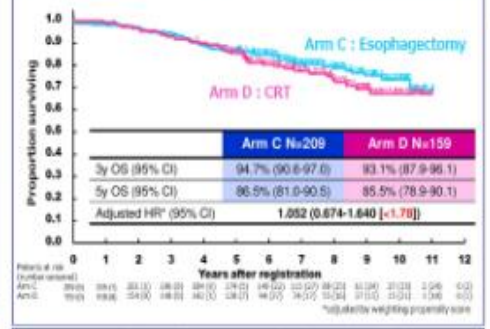
CONSORT diagram

- Randomized part was terminated due to slow accrual
- Comparison of arm C and arm D of non randomized part was performed.

Patient characteristics (N=368)

	Arm C N=209	Arm D N=159
Median Age (range)	62 (41-75)	65 (42-75)
Sex Male / Female	173/36	140/19
PS 0 / 1	208 / 1	156 / 3
Tumor location Upper / Middle / Lower	27 / 131 / 51	13 / 98 / 48
Histology Squamous / others	208 / 1	159 / 0
Long diameter of tumor ≦4cm / >4cm	146 / 63	99 / 60
Multiple lesions Absent / Present	189 / 20	135 / 24

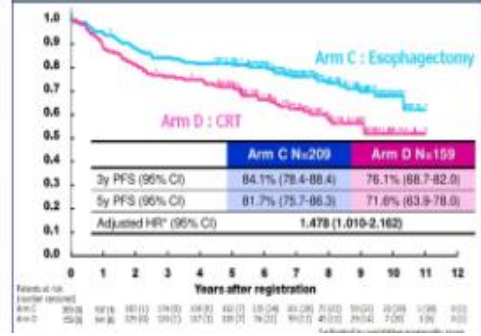
Overall survival (N=368)



	Arm C N=209	Arm D N=159
3y OS (95% CI)	94.7% (90.6-97.0)	93.1% (87.9-96.1)
5y OS (95% CI)	86.5% (81.0-90.5)	85.5% (78.9-90.1)
Adjusted HR* (95% CI)	1.052 (0.674-1.640 [<1.78])	

*adjusted by weighting propensity score

Progression-free survival (N=368)



	Arm C N=209	Arm D N=159
3y PFS (95% CI)	84.1% (78.4-88.4)	76.1% (68.7-82.0)
5y PFS (95% CI)	81.7% (75.7-86.3)	71.6% (63.9-78.0)
Adjusted HR* (95% CI)	1.478 (1.010-2.162)	

*adjusted by weighting propensity score

Complete response ~ Arm D (N=158)

138/158 = **87.3%** (95%CI, 81.1-92.1)

CR*: CR confirmation based on central review

Postoperative morbidity after surgery (N=207*)

CTCAE ver.3.0	Gr.1	Gr.2	Gr.3	Gr.4	%Gr.3-4
Anastomotic leak	5	9	**11**	**2**	6.3
Atelectasis	12	31	**2**	**2**	1.9
Pneumonia	–	10	**11**	**5**	7.7
Recurrent nerve paralysis	10	24	**3**	**3**	2.9
Fistula	0	0	**3**	**1**	1.9
Any obstruction	0	0	**4**	**0**	1.9
AST	110	67	**16**	**2**	8.7
ALT	76	71	**41**	**2**	20.8
Hb	68	69	**16**	**0**	7.7
T-Bil	52	40	**18**	**0**	8.7

* Two patients who didn't undergo surgery and withdraw consent was excluded

Acute adverse events of CRT (N=158*)

CTCAE ver.3.0	Gr.1	Gr.2	Gr.3	Gr.4	%Gr.3-4
Leukocytes	40	92	**17**	**1**	11.4
Neutrophils	46	67	**15**	**3**	11.4
Platelets	23	12	**2**	**0**	1.3
Esophagitis	61	58	**16**	**0**	10.1
Anorexia	53	45	**16**	**0**	10.1
Nausea	60	30	**8**	**0**	5.1
Vomiting	20	6	**0**	**0**	0
Diarrhea	15	0	**1**	**0**	0.6
Stomatitis	32	6	**0**	**0**	0
Febrile neutropenia	-	-	**3**	**0**	1.9
Hyponatremia	100	-	**17**	**0**	10.8
ALT	57	8	**2**	**0**	1.3
Creatinine	61	8	**0**	**0**	0

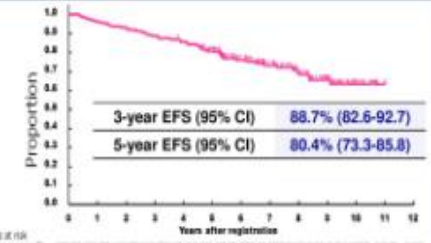
* One patient who didn't receive CRT was excluded

Late adverse events of CRT (N=158*)

CTCAE ver.3.0	Gr.1	Gr.2	Gr.3	Gr.4	%Gr.3-4
Esophagitis	24	12	**1**	**0**	0.6
Fistula, GI-Esophagus	0	0	**0**	**0**	0
Dyspnea	3	2	**3**	**1**	2.5
Pneumonitis	44	4	**3**	**0**	1.9
Pleural effusion (non-malignant)	17	0	**4**	**0**	2.5
Cardiac ischemia	0	0	**2**	**3**	3.2
Pericardial effusion (non-malignant)	28	–	**0**	**0**	0

* One patient who didn't receive CRT was excluded

Esophagectomy-free survival ~ Arm D (n=159)



Subsequent therapy (n=367*)

	Arm C n=208*	Arm D n=159
Absent	152	102
Present	56 (26.9%)	57 (35.8%)
Endoscopic Resection	0	**16**
Chemotherapy	48	24
Radiation	6	7
Surgery	10	**21**

* One patient who didn't undergo surgery and withdraw consent was excluded in Arm C

Conclusions

- ✓ Esophagectomy and CRT both showed long term activity and acceptable safety for the patients with stage I ESCC.
- ✓ CRT showed non-inferiority compared to esophagectomy on overall survival in non-randomized part.
- ✓ CRT seemed to be one of the standard treatment options for stage I ESCC.

Acknowledgement

All the patients and families who participated in this study.

Participating Institutions (36 institutions)

- Hokkaido University Hospital
- Iwate Medical University
- Tohoku University Hospital
- Yamagata Prefectural Central Hospital
- Tochigi Cancer Center Hospital
- National Cancer Center Hospital East
- Chiba University Hospital
- Chiba Cancer Center
- Tokyo Dental University Ichikawa Hospital
- National Cancer Center Hospital
- Tokyo Women's Medical University Hospital
- National Hospital Organization Tokyo Medical Center
- Keio University Hospital
- Tokyo Medical and Dental University Hospital
- Cancer Institute Hospital
- Toshiomachi Hospital
- Tokai University Hospital
- Kanagawa Cancer Center
- Niigata University Medical and Dental Hospital
- Niigata Cancer Center
- Shizuoka Cancer Center
- Shizuoka General Hospital
- Aichi Cancer Center Hospital
- Kyoto University Hospital
- Osaka University Graduate School of Medicine
- Osaka International Cancer Institute
- National Hospital Organization Osaka Medical Center
- Osaka City General Hospital
- Osaka Medical College
- Kobe University Graduate School of Medicine
- Hyogo Cancer Center
- Hiroshima University Hospital
- Hiroshima City Asa Hospital
- National Hospital Organization Shikoku Cancer Center
- Kochi Health Sciences Center
- National Hospital Organization Kyushu Cancer Center
- Kyushu University Hospital
- Kurume University Hospital

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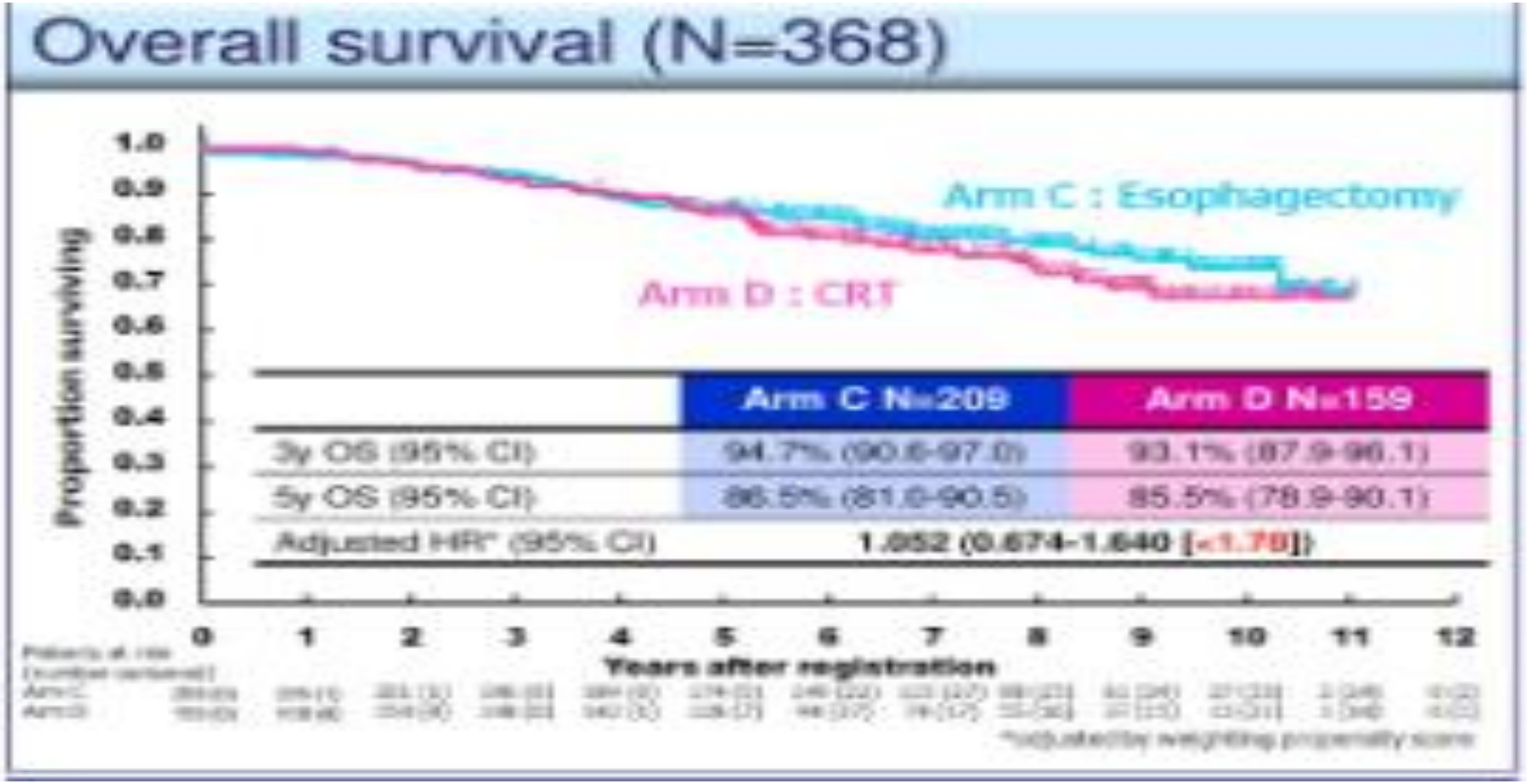
CHT/RT versus esofagektomie=non- inferiorní OS u klinického stádia I



Gastric cancer liver metastasis: optimal management for oligometastatic disease

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BACKGROUND

The role of surgery for gastric cancer liver metastasis (GCLM) remains controversial.

The aim of this study was to review the outcome for our patients with GCLM who underwent liver resection, and to define the optimal selection criteria for resection.

METHODS

- *Patient*:
  - The patients with GCLM who underwent partial liver resection with curative intent from 1993 through 2018 in our center
- *Criteria for resection:*
  - Absence of extrahepatic disease
  - Limited number of liver metastases (often 3 or less)
- *Evaluated outcomes:*
  - Long-term outcomes including recurrance-free survival (RFS) and overall survival (OS)

RESULTS

Patient demographics

	Total (N=101)
Age (median, range)	66 years (32-86)
Male gender, n (%)	77 (76)
Metachronous disease, n (%)	54 (54)
Disease free interval* (DFI), median (range)	4 months (0-49)
Chemotherapy prior to liver resection	52 (52)

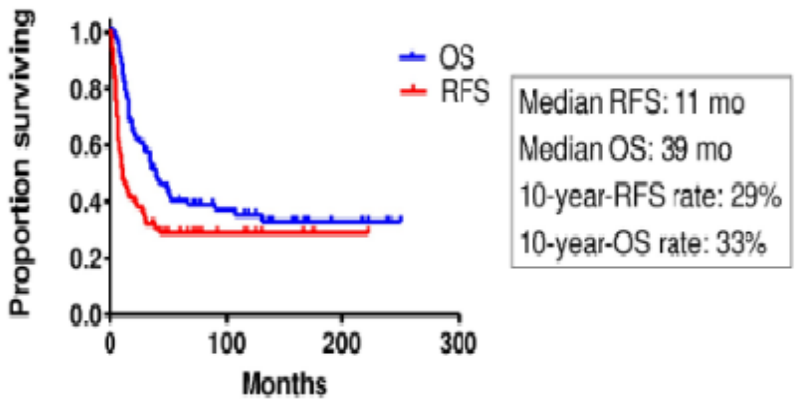
Tumor characteristics

Variables for liver metastases		
Number of metastasis, n (%)		
	1	62 (61)
	2	18 (18)
	2+	21 (21)
Size of the largest tumor		
	Median in cm (range)	
	>= 5cm, n (%)	17 (17)
CEA prior to liver resection, median (range)		5.0 (0.4-1212)
Variables for primary disease, n (%)		
pT		
	1	8 (8)
	2	14 (14)
	3	54 (54)
	4	25 (25)
pN*		
	0	24 (24)
	1	27 (27)
	2	32 (31)
	3	17 (17)
High grade tumor (por/sig), n (%)		25 (25)

Operative characteristics

Liver resection, n (%)	
Major (=>3 segments)	20 (20)
Minor (<3 segments, wedge resections)	81 (80)
Gastrectomy, n (%)	
Total	42 (42)
Partial	58 (57)

RFS and OS for patients with GCLM following liver resection



Analysis for the impact of clinicopathological variables for RFS and OS following liver resection for patients with GCLM

	RFS			OS		
	UV	MV		UV	MV	
Variables	p	HR (95%CI)	p	p	HR (95%CI)	p
Primary pT4	0.078			0.013	2.9 (1.6-5.3)	0.001
Primary pN+	0.021	1.8 (0.9-3.7)	0.087	0.085		
Simultaneous resection	0.36			0.88		
Major liver resection*	0.41			0.31		
Multiple liver tumors	0.12			0.26		
Liver tumor size >=5 cm	0.88			0.05	2.1 (1.1-4.0)	0.02
CEA** >=50 ng/ml	0.001	2.3 (1.3-4.2)	0.005	0.004	3.0 (1.6-5.7)	0.001
NAC for liver metastasis	0.29			0.43		
Adjuvant chemotherapy after liver resection	0.20			0.53		

*resection of 3 segments or more, ** at the time of liver resection, NAC neoadjuvant chemotherapy

Závěry

- CHT/RT prokázala noninferiorní efekt ve srovnání s radikální esofagektomií je alternativou k radikální esofagektomii u klinického stádia I

- Metastazektomie přináší benefit v PFS a OS u pacientů s oligometastatickým onemocněním(počet MTS ≤3) a může být individuálně zvažována v léčeném algoritmu metastatického onemocnění

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Welcome

Praha 8.-11.5.2019

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