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MEETING SUMMARY
ASCO GI 2018, San Francisco, USA

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CANCERS OF THE UPPER GI TRACT

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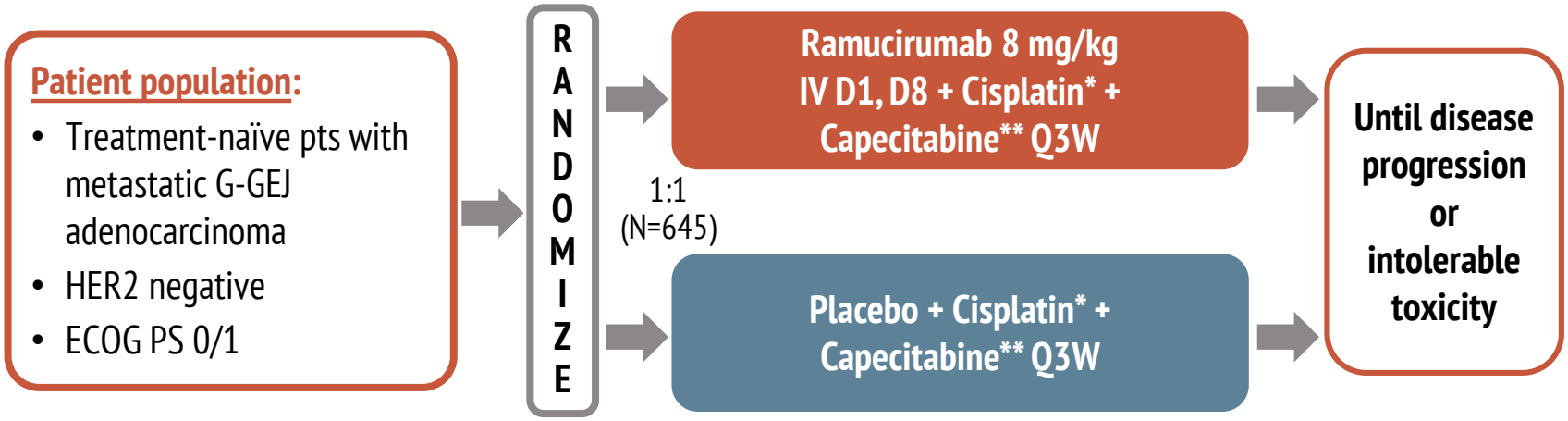
RAINFALL: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 STUDY OF CISPLATIN (CIS) PLUS CAPECITABINE (CAPE) OR 5FU WITH OR WITHOUT RAMUCIRUMAB (RAM) AS FIRST-LINE THERAPY IN PATIENTS WITH METASTATIC GASTRIC OR GASTROESOPHAGEAL JUNCTION (G-GEJ) ADENOCARCINOMA

Charles S. Fuchs et al. J Clin Oncol. 36, 2018 (Suppl 4S; Abstr 5)

RAINFALL TRIAL DESIGN



Stratification Factors:

- ECOG PS 0 vs 1
- Primary tumor location (gastric vs gastroesophageal junction)
- Disease measurability
- Geographic region (Japan vs other countries)

Drug Doses:

* Cisplatin 80 mg/m^2 IV D1, max of 6 cycles

** Capecitabine 1000 mg/m^2 oral bid D1-D14

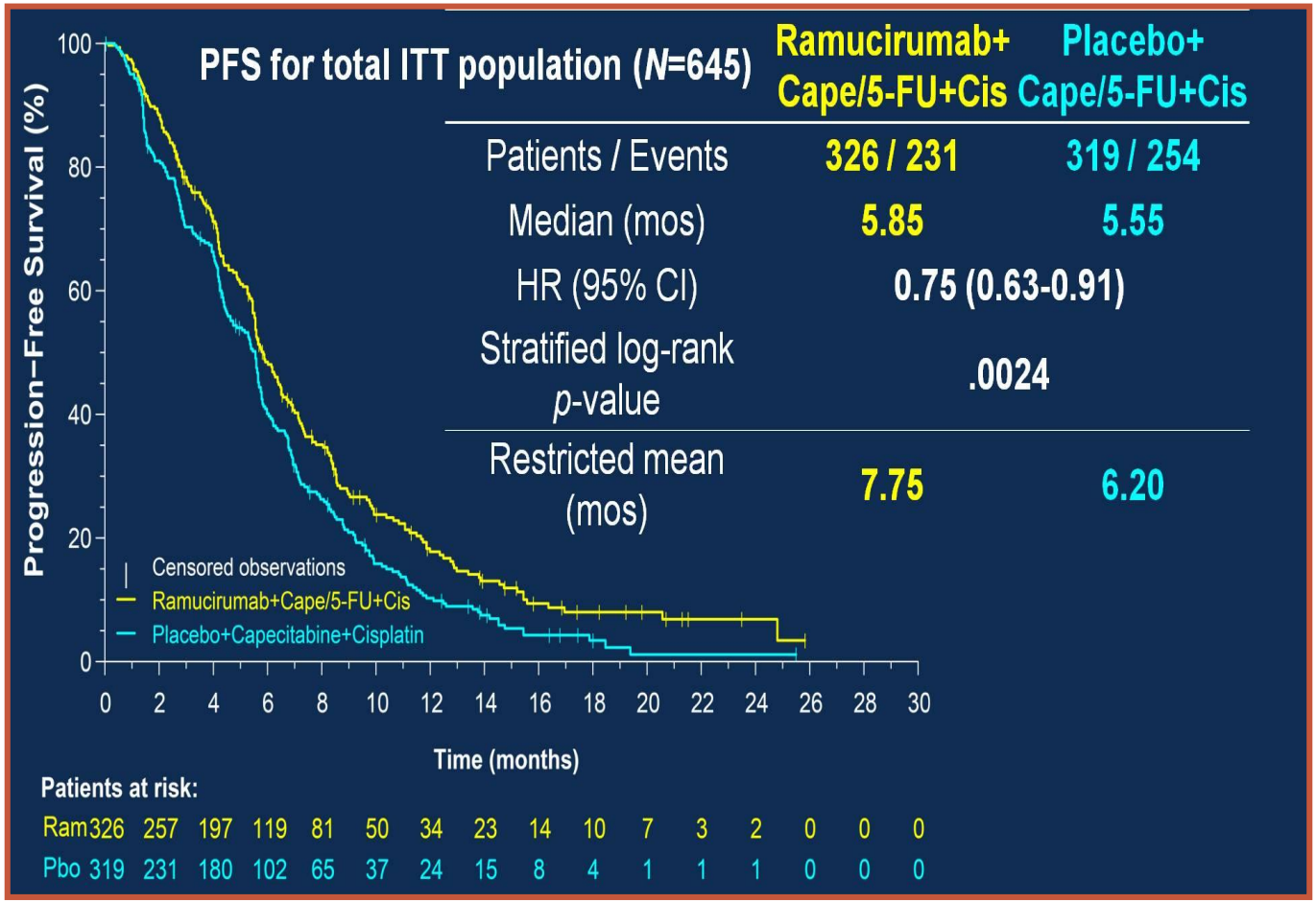
** 5-FU (800 mg/m^2/day IV D1-D5) was allowed for patients not able to swallow capecitabine

ClinicalTrials.gov # NCT02314117

Presented By Charles Fuchs at 2018 Gastrointestinal Cancers Symposium

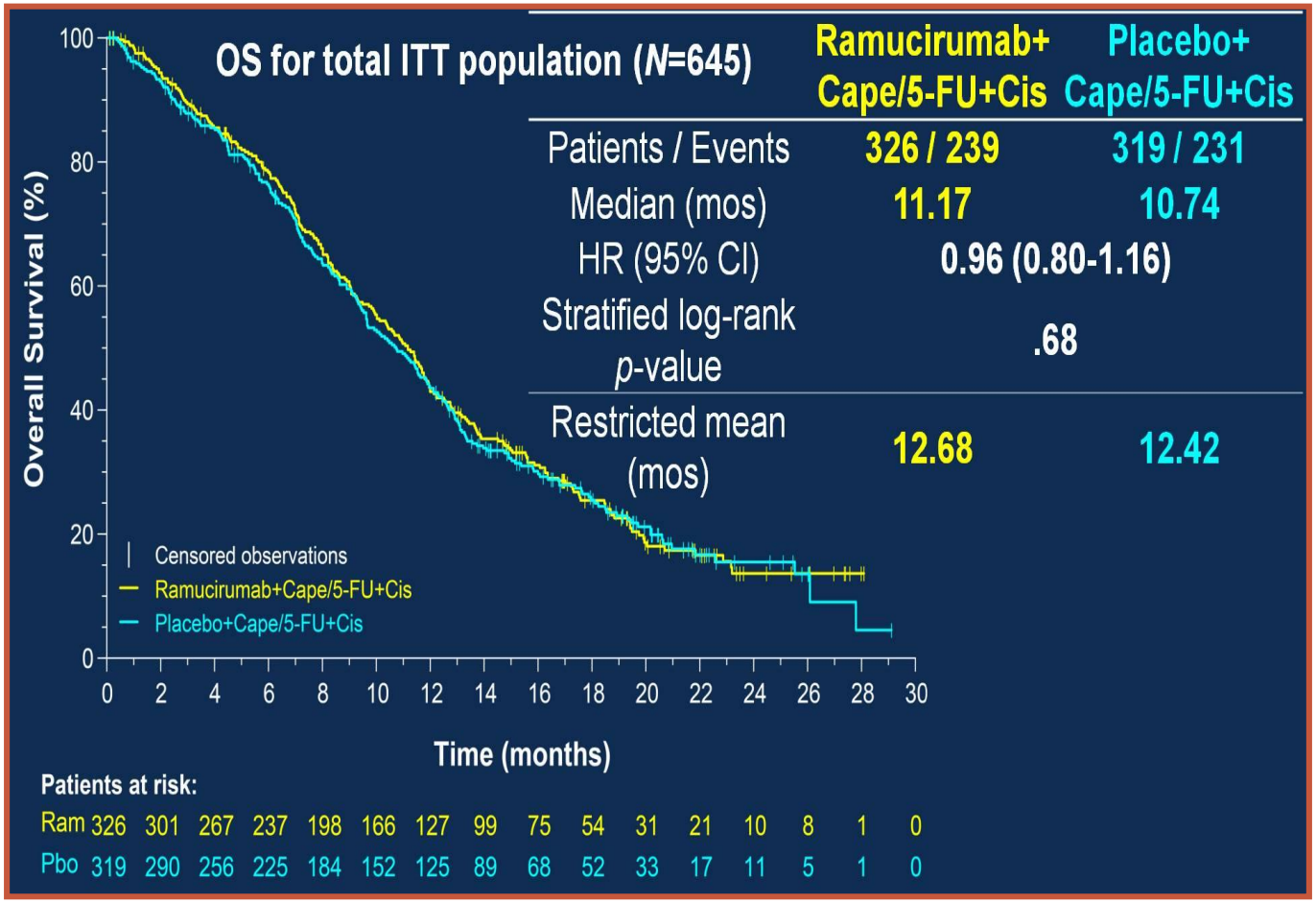
ECOG PS, Eastern Co-operative Oncology Group Performance Status; HER2, human epidermal growth factor receptor; 5-FU, fluorouracil

RESULTS: PROGRESSION-FREE SURVIVAL (PFS)



Presented By Charles Fuchs at 2018 Gastrointestinal Cancers Symposium
ITT, intention to treat; HR, hazard ratio; CI, confidence interval

RESULTS: OVERALL SURVIVAL (OS)



	Ramucirumab+ Cape/5-FU+Cis	Placebo+ Cape/5-FU+Cis
Patients / Events	326 / 239	319 / 231
Median (mos)	11.17	10.74
HR (95% CI)	0.96 (0.80-1.16)	
Stratified log-rank *p*-value	.68	
Restricted mean (mos)	12.68	12.42

CONCLUSION

- Similiar to anti-VEGF plus chemo (AVAGAST trial) the concept of anti-VEGFR-2 plus chemo (RAINFALL) in first line failed to improve prognosis of metastatic gastric / gastroesophageal junction cancer patients
- Progression free survival was slightly, but significantly improved (HR 0.75, $p < 0.01$; ΔmPFS = 0.3 month)
- No new or unexpected safety findings emerged

J Clin Oncol. 36, 2018 (suppl 4S; abstr 723)
VEGF, vascular endothelial growth factor

KEYNOTE-059 COHORT 1: PEMBROLIZUMAB MONOTHERAPY IN PREVIOUSLY TREATED ADVANCED GASTRIC OR GASTROESOPHAGEAL JUNCTION (G/GEJ) CANCER IN PATIENTS WITH PD-L1 + TUMORS: ASIAN SUBGROUP ANALYSIS

Muro et al. J Clin Oncol. 36, 2018 (Suppl 4S; Abstr 723)

KEYNOTE-059

- Pembrolizumab has been shown to be beneficial for treating patients with
  1. Recurrent locally advanced or metastatic G/GEJ adenocarcinoma, whose disease has progressed on or after ⩾2 prior therapies and whose tumors express PD-L1
  2. Unresectable or metastatic, microsatellite instability-high (MSI-H) solid tumors that have progressed after prior therapy and who have no fitting options
- An Asian subgroup analysis from cohort 1 of KEYNOTE-059 (NCT02335411), a global, phase 2 study in advanced G/GEJ cancer was presented

J Clin Oncol. 36, 2018 (suppl 4S; abstr 723)
PD-L1, programmed death-ligand 1

METHODS

- Eligible patients had measurable recurrent or metastatic G/GEJ adenocarcinoma whose disease had progressed on ⩾2 prior chemotherapy regimens. Patients received pembrolizumab 200 mg Q3W up to 2 years
- PD-L1+ tumors had a CPS ⩾1
- Primary endpoints were ORR (RECIST 1.1, by central review) and safety

ORR, objective response rate; RECIST, Response Evaluation Criteria In Solid Tumors

RESULTS

- 259 patients; 57% had PD-L1+ tumors. MSI status was evaluable in 174 tumor samples; of these, 7 were MSI-H
- Overall ORR was 12% (95% CI, 8-17) and median (range) DOR was 14 mo (2-19+)
- In patients with PD-L1+ tumors, ORR was 16% (95% CI, 11-23) and median (range) DOR was 14 mo (3+-19+)
- In patients with MSI-H tumors, ORR was 57% (95% CI, 18-90) and median (range) DOR was not reached (5-14+ mo)
- 41 patients were Asian and 218 patients were non-Asian. Safety and efficacy were similar in Asian and non-Asian patients

DOR, duration of response

CONCLUSION

Pembrolizumab showed durable clinical benefit in previously treated patients with advanced G/GEJ cancer, especially those with PD-L1+ or MSI-H tumors

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