GASTRIC

CYRAMZA® (ramucirumab)

TAKE ACTION

ESTABLISHING A NEW STANDARD OF CARE

THE RAINBOW TRIAL: CYRAMZA + PACLITAXEL

The treatment landscape for patients with gastric cancer is rapidly evolving. Evidence from the RAINBOW trial has established CYRAMZA + paclitaxel as a standard-of-care regimen for patients with mGC or GEJ adenocarcinoma.

EFFICACY

STATISTICALLY SIGNIFICANT INCREASE IN OVERALL SURVIVAL[1]

9.6 MONTHS MEDIAN OS
CYRAMZA + paclitaxel
(95% CI: 8.5, 10.8)

VS

7.4 MONTHS MEDIAN OS
placebo + paclitaxel
(95% CI: 6.3, 8.4)

30% INCREASE IN MEDIAN OS

HR (95% CI)= 0.807 (0.678, 0.962); *P*=0.0169

CYRAMZA in combination with paclitaxel is indicated for the treatment of adult patients with advanced gastric cancer or gastro-oesophageal junction adenocarcinoma with disease progression after prior platinum and fluoropyrimidine chemotherapy.

In the RAINBOW trial[2]: Adverse drug reactions occurring with CYRAMZA at incidence rate ≥5%: leucopenia, neutropenia, thrombocytopenia, diarrhoea, gastrointestinal haemorrhage events,* stomatitis, fatigue, peripheral oedema, hypoalbuminaemia, proteinuria, epistaxis, hypertension†

Find out more about the **RAINBOW** trial at **[insert URL for regional website]**

mGC=metastatic gastric cancer; GEJ=gastro-oesophageal junction; OS=overall survival.
*Includes anal haemorrhage, diarrhoea haemorrhage, gastric haemorrhage, gastrointestinal haemorrhage, haematemesis, haematochezia, haemorrhoidal haemorrhage, Mallory-Weiss syndrome, melaena, oesophageal haemorrhage, rectal haemorrhage and upper GI haemorrhage.
†Includes hypertensive cardiomyopathy.

References: 1. CYRAMZA Summary of Product Characteristics. Eli Lilly Nederland B.V. December 2015. **2.** Data on file. Eli Lilly and Company. 2015. CDS10FEB2015.

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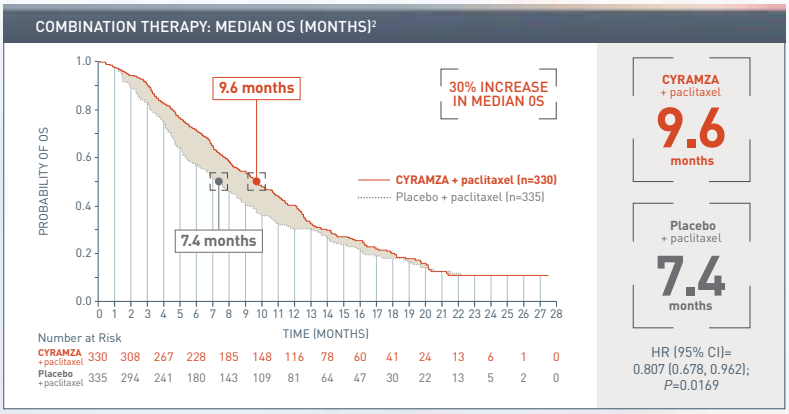
ADVANCED GASTRIC CANCER presents a significant challenge, despite your dedication to providing the best care possible.[1] With CYRAMZA, you have a new treatment that gives you the confidence to match your commitment.

TRAINED TO MAKE A DIFFERENCE ABLE TO MAKE AN IMPACT

Only CYRAMZA has data from 2 large phase III trials, offering a new standard of evidence-based care for advanced gastric cancer[2,3]



- CYRAMZA extends overall survival (OS) when combined with paclitaxel vs paclitaxel alone[2]
- CYRAMZA extends OS as a monotherapy vs best supportive care[3]

CYRAMZA monotherapy and in combination with paclitaxel was well tolerated in patients with advanced gastric cancer.[4]

CYRAMZA™ (ramucirumab) as a single agent is indicated for the treatment of patients with advanced gastric cancer or oesophago-gastric junction adenocarcinoma after prior chemotherapy.

CYRAMZA in combination with paclitaxel is indicated for the treatment of patients with advanced gastric cancer or oesophago-gastric junction adenocarcinoma after prior chemotherapy.

In a monotherapy study of CYRAMZA vs placebo[4]:

- Adverse drug reactions occurring with CYRAMZA at incidence rate ≥5%: abdominal pain,* diarrhoea, hypokalaemia, hyponatremia, headache, hypertension

In a combination therapy study of CYRAMZA with paclitaxel vs placebo with paclitaxel[4]:

- Adverse drug reactions occurring with CYRAMZA at incidence rate ≥5%: leucopenia, neutropenia, thrombocytopenia, diarrhoea, gastrointestinal haemorrhage events,† stomatitis, fatigue, peripheral oedema, hypoalbuminaemia, proteinuria, epistaxis, hypertension‡

*Includes hepatic pain.
†Includes anal haemorrhage, diarrhoea haemorrhage, gastric haemorrhage, gastrointestinal haemorrhage, haematemesis, haematochezia, haemorrhoidal haemorrhage, Mallory-Weiss syndrome, melaena, oesophageal haemorrhage, rectal haemorrhage and upper GI haemorrhage.
‡Includes hypertensive cardiomyopathy.

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VISIT WWW.XXXXX.COM TO LEARN MORE.

References: 1. National Cancer Institute. Surveillance, Epidemiology, and End Results Web site. http://seer.cancer.gov. Accessed April 8, 2014. **2.** Wilke H, Muro K, Van Cutsem E, et al; RAINBOW Study Group. *Lancet Oncol*. 2014;15(11):1224-1235. **3.** Fuchs CS, Tomasek J, Yong CJ, et al; REGARD Trial Investigators. *Lancet*. 2014;383(9911):31-39. **4.** Data on file. Eli Lilly and Company. 2015. CDS10FEB2015.

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Learn more about the RAINBOW study

Healthlink@professionalemail.hibbertgroup.com

To: John Doe <jdoe@emessagesubscriber.com>

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ESTABLISHING A NEW STANDARD OF CARE

THE RAINBOW TRIAL: CYRAMZA + PACLITAXEL

Gastric cancer is the 5th most common malignancy, and the 3rd-leading cause of cancer worldwide.[1] RAINBOW, a phase III clinical trial, was conducted to study the effects of CYRAMZA plus paclitaxel vs placebo plus paclitaxel in patients with mGC or GEJ adenocarcinoma. The combination of CYRAMZA plus paclitaxel proved to significantly increase overall survival (OS).[2]

EFFICACY: STATISTICALLY SIGNIFICANT INCREASE IN OS[2]

CYRAMZA in combination with paclitaxel achieved a statistically significant increase in OS across a broad patient base (9.6 months vs 7.4 months with placebo + paclitaxel; HR [95% CI]=0.807 [0.678, 0.962], *P*=0.017)

9.6 MONTHS MEDIAN OS
CYRAMZA + paclitaxel
[95% CI: 8.5, 10.8]

VS

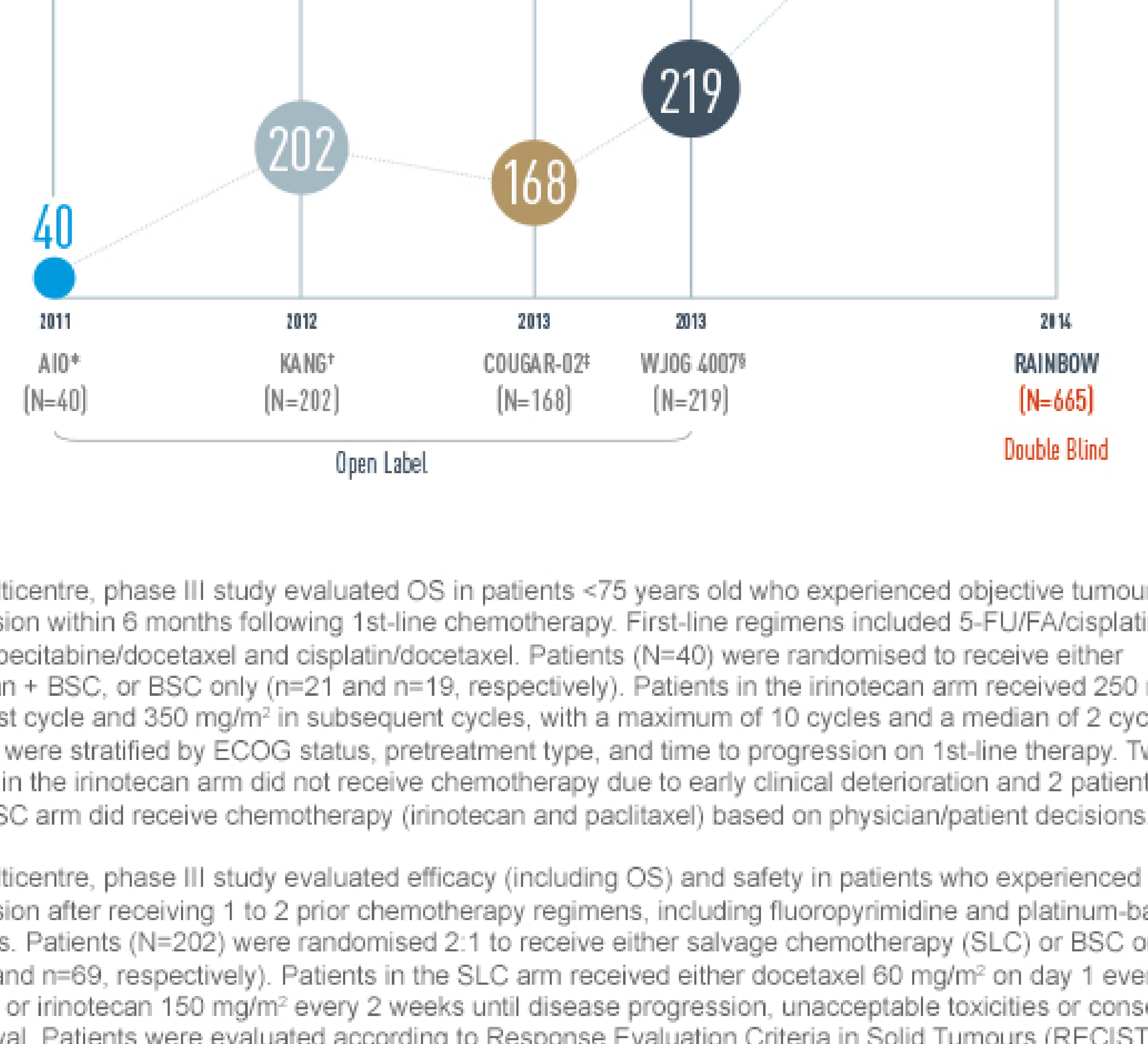
7.4 MONTHS MEDIAN OS
placebo + paclitaxel
[95% CI: 6.3, 8.4]

30% INCREASE IN MEDIAN OS

HR (95% CI)= 0.807 (0.678, 0.962); *P*=0.017

PRIOR TRIALS: BUILDING ON 2ND-LINE TRIALS IN mGC[1,3-6]

The RAINBOW trial builds on 4 previously conducted open-label trials in 2nd-line mGC



*This multicentre, phase III study evaluated OS in patients <75 years old who experienced objective tumour progression within 6 months following 1st-line chemotherapy. First-line regimens included 5-FU/FA/cisplatin, ECF, capecitabine/docetaxel and cisplatin/docetaxel. Patients (N=40) were randomised to receive either irinotecan + BSC, or BSC only (n=21 and n=19, respectively). Patients in the irinotecan arm received 250 mg/m^2 in the first cycle and 350 mg/m^2 in subsequent cycles, with a maximum of 10 cycles and a median of 2 cycles. Patients were stratified by ECOG status, pretreatment type, and time to progression on 1st-line therapy. Two patients in the irinotecan arm did not receive chemotherapy due to early clinical deterioration and 2 patients in the BSC arm did receive chemotherapy (irinotecan and paclitaxel) based on physician/patient decisions.

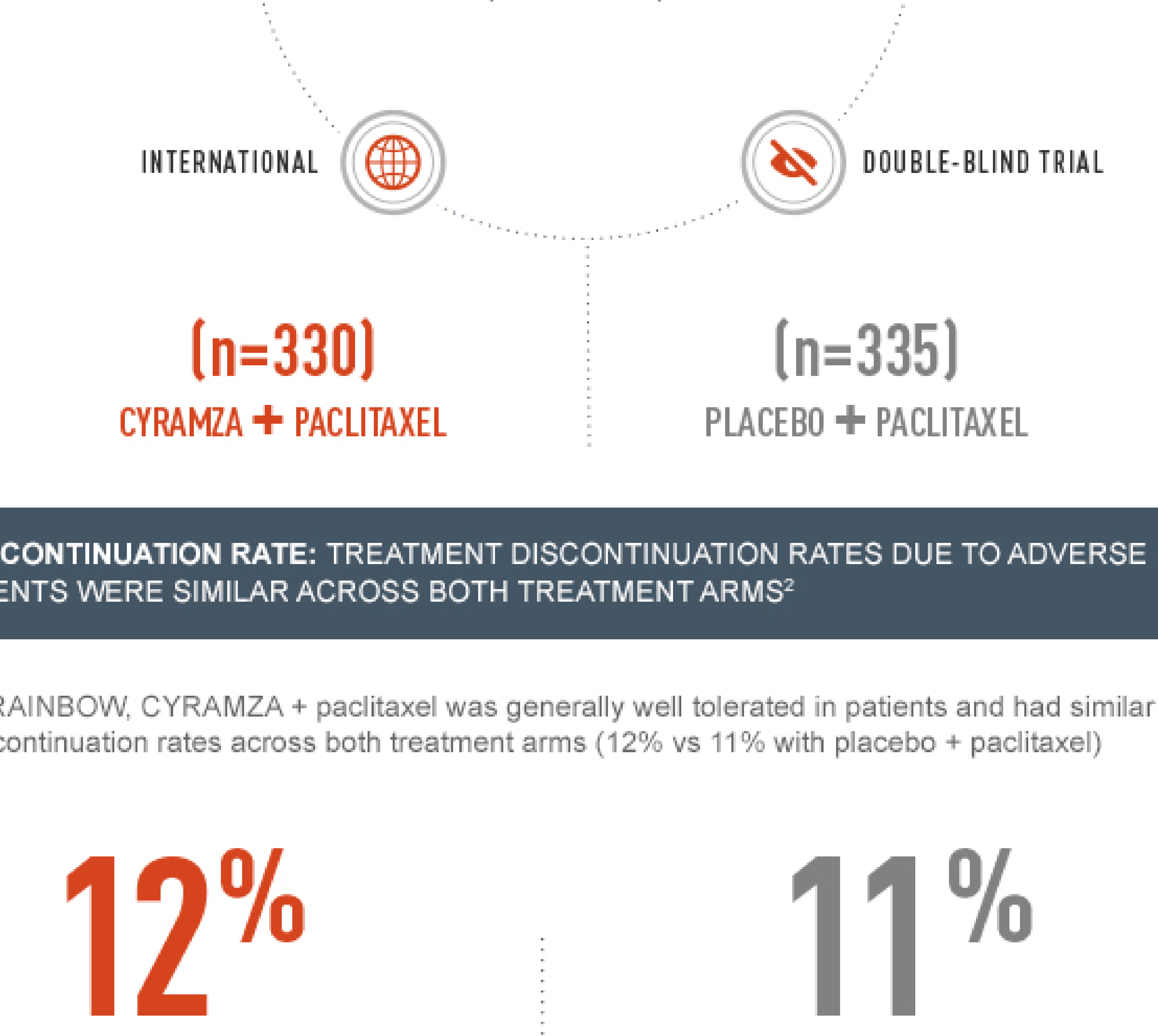
†This multicentre, phase III study evaluated efficacy (including OS) and safety in patients who experienced progression after receiving 1 to 2 prior chemotherapy regimens, including fluoropyrimidine and platinum-based regimens. Patients (N=202) were randomised 2:1 to receive either salvage chemotherapy (SLC) or BSC only (n=113 and n=69, respectively). Patients in the SLC arm received either docetaxel 60 mg/m^2 on day 1 every 3 weeks or irinotecan 150 mg/m^2 every 2 weeks until disease progression, unacceptable toxicities or consent withdrawal. Patients were evaluated according to Response Evaluation Criteria in Solid Tumours (RECIST) and were stratified by performance status and number of prior chemotherapy regimens for advanced disease (1 vs 2).

‡This multicentre, phase III study was conducted in 30 sites across the United Kingdom and evaluated OS in patients >18 years old who experienced progression within 6 months on a platinum-fluoropyrimidine combination chemotherapy regimen. Patients (N=168) were randomised to receive either docetaxel + ASC, or ASC only (n=84 in each arm). Patients in the docetaxel arm received 75 mg/m^2 every 3 weeks for up to 6 cycles. Patients were stratified by disease status, disease site, duration of response to prior chemotherapy and ECOG status.

§This multicentre, phase III study was conducted in 37 centres across Japan and evaluated efficacy (OS, progression-free survival, response rate), toxicity and the proportion of patients receiving subsequent chemotherapy in patients with metastatic or recurrent gastric adenocarcinoma. Patients (N=223) refractory to a fluoropyrimidine + platinum-based regimen were randomised to receive 4-week infusion cycles with either paclitaxel 80 mg/m^2 (n=111) on days 1, 8 and 15, or irinotecan 150 mg/m^2 (n=112) on days 1 and 15, until disease progression, unacceptable toxicities or consent withdrawal. Patients were randomised according to institution, ECOG status and by the presence or absence of measurable lesions.

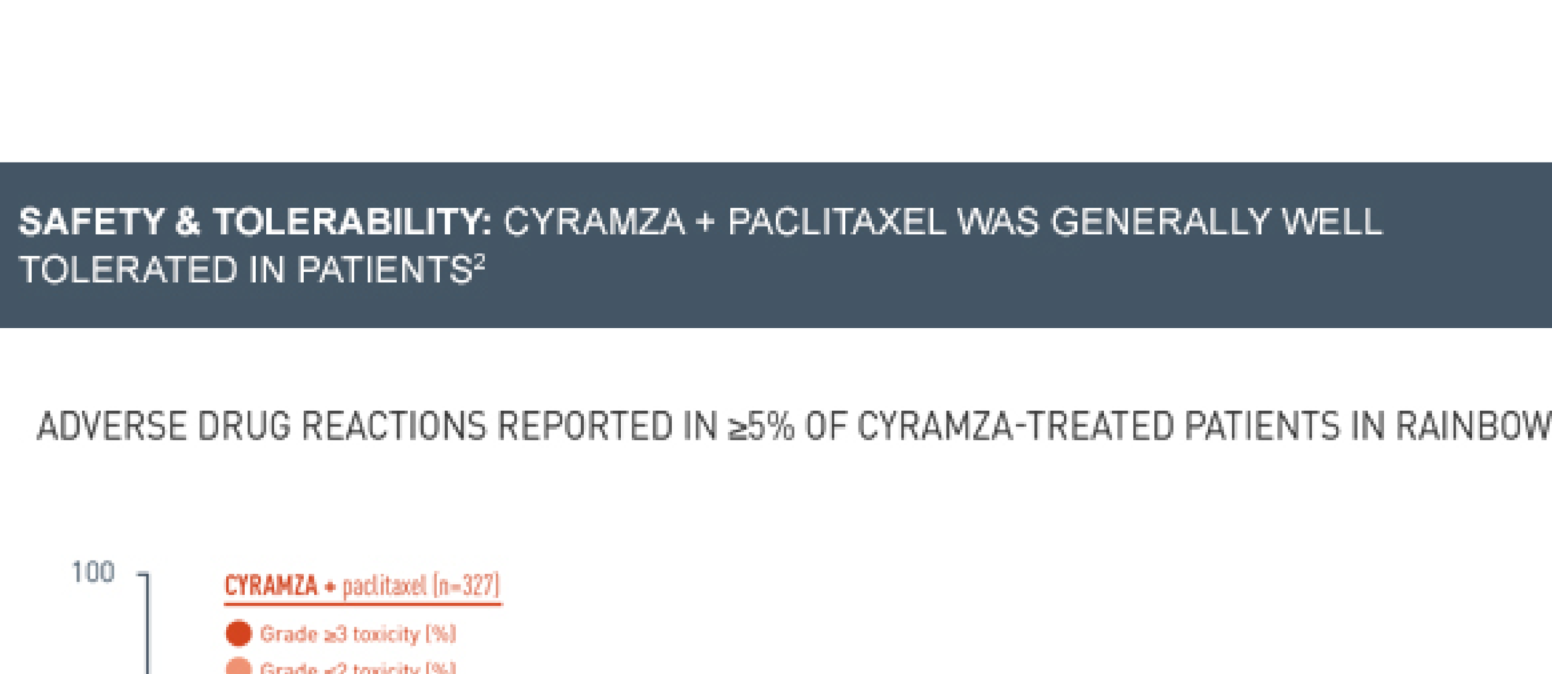
STUDY DESIGN: A ROBUST 2ND-LINE TRIAL IN mGC/GEJ[2]

RAINBOW (N=665) was a robust placebo-controlled, multicentre, double-blind, international, randomised phase III study in 2nd-line mGC/GEJ



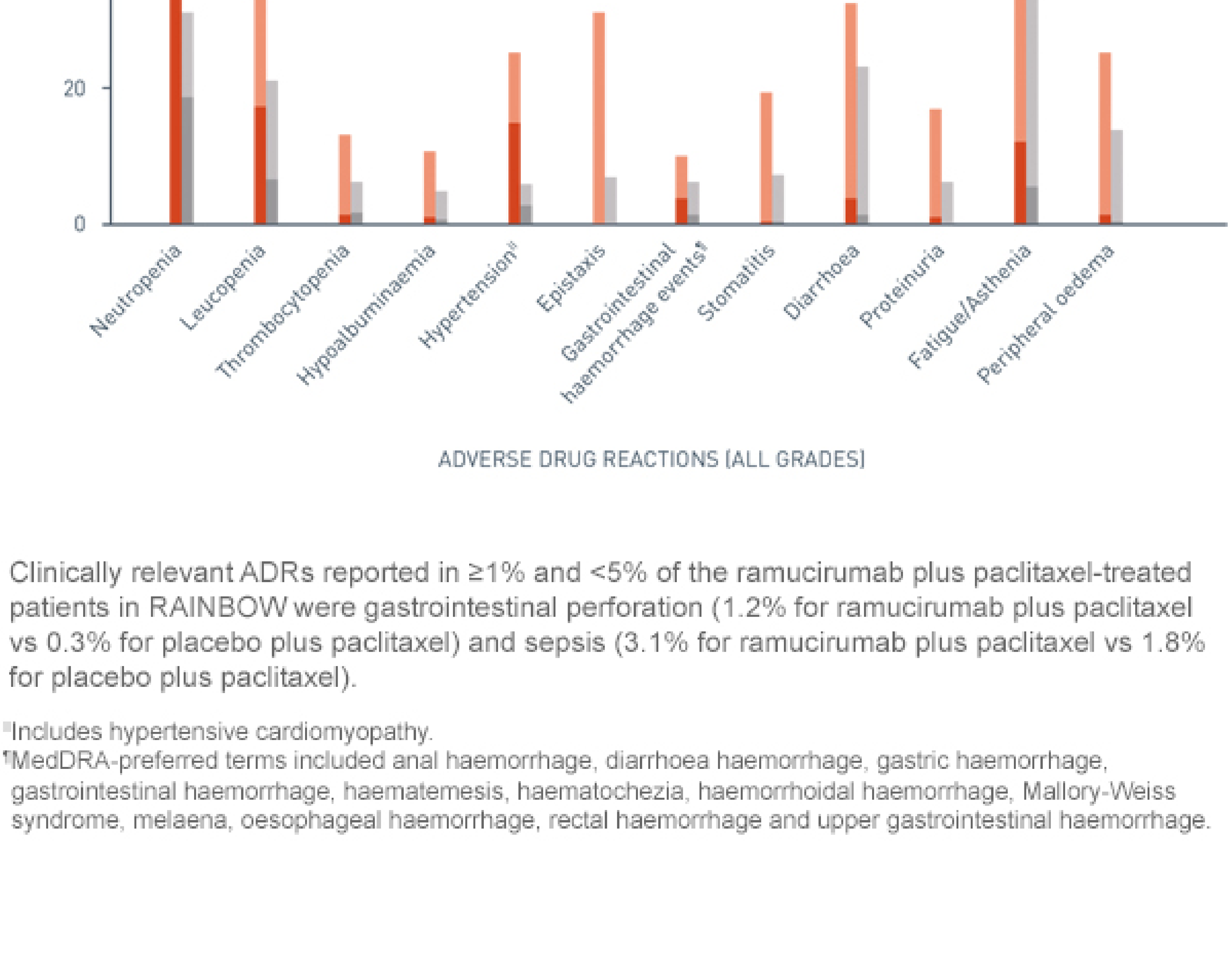
DISCONTINUATION RATE: TREATMENT DISCONTINUATION RATES DUE TO ADVERSE EVENTS WERE SIMILAR ACROSS BOTH TREATMENT ARMS[2]

In RAINBOW, CYRAMZA + paclitaxel was generally well tolerated in patients and had similar discontinuation rates across both treatment arms (12% vs 11% with placebo + paclitaxel)



SAFETY & TOLERABILITY: CYRAMZA + PACLITAXEL WAS GENERALLY WELL TOLERATED IN PATIENTS[2]

ADVERSE DRUG REACTIONS REPORTED IN ≥5% OF CYRAMZA-TREATED PATIENTS IN RAINBOW



Clinically relevant ADRs reported in ≥1% and <5% of the ramucirumab plus paclitaxel-treated patients in RAINBOW were gastrointestinal perforation (1.2% for ramucirumab plus paclitaxel vs 0.3% for placebo plus paclitaxel) and sepsis (3.1% for ramucirumab plus paclitaxel vs 1.8% for placebo plus paclitaxel).

‖Includes hypertensive cardiomyopathy.
¶MedDRA-preferred terms included anal haemorrhage, diarrhoea haemorrhage, gastric haemorrhage, gastrointestinal haemorrhage, haematemesis, haematochezia, haemorrhoidal haemorrhage, Mallory-Weiss syndrome, melaena, oesophageal haemorrhage, rectal haemorrhage and upper gastrointestinal haemorrhage.

To learn more about the RAINBOW trial,

please visit www.XXXXXX.com.

You can also contact your Lilly Oncology sales representative.

CYRAMZA in combination with paclitaxel is indicated for the treatment of adult patients with advanced gastric cancer or gastro-oesophageal junction adenocarcinoma with disease progression after prior platinum and fluoropyrimidine chemotherapy.

mGC=metastatic gastric cancer; GEJ=gastro-oesophageal cancer; HR=hazard ratio; CI=confidence interval; 5-FU=5-fluorouracil; FA=folinic acid; ECF=epirubicin, cisplatin and 5-fluorouracil; BSC=best supportive care; ECOG=Eastern Cooperative Oncology Group; ASC=active symptom control; ADR=adverse drug reaction; MedDRA=Medical Dictionary for Regulatory Activities.

References: 1. Wilke H, Muro K, Van Cutsem E, et al; for the RAINBOW Study Group. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. *Lancet Oncol*. 2014;15(11):1224-1235. **2.** CYRAMZA Summary of Product Characteristics. Eli Lilly Nederland B.V. December 2015. **3.** Thuss-Patience PC, Kretzschmar A, Bichev D, et al. Survival advantage for irinotecan versus best supportive care as second-line chemotherapy in gastric cancer—a randomised phase III study of the Arbeitsgemeinschaft Internistische Onkologie (AIO). *Eur J Cancer*. 2011;47(15):2306-2314. **4.** Kang JH, Lee SI, Lim DH, et al. Salvage chemotherapy for pretreated gastric cancer: a randomized phase III trial comparing chemotherapy plus best supportive care with best supportive care alone. *J Clin Oncol*. 2012;30(13):1513-1518. **5.** Ford HER, Marshall A, Bridgewater JA, et al. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. *Lancet Oncol*. 2014;15(1):78-86. **6.** Hironaka S, Ueda S, Yasui H, et al. Randomized, open-label, phase III study comparing irinotecan with paclitaxel in patients with advanced gastric cancer without severe peritoneal metastasis after failure of prior combination chemotherapy using fluoropyrimidine plus platinum: WJOG4007 trial. *J Clin Oncol*. 2013;31(35):4438-4444.

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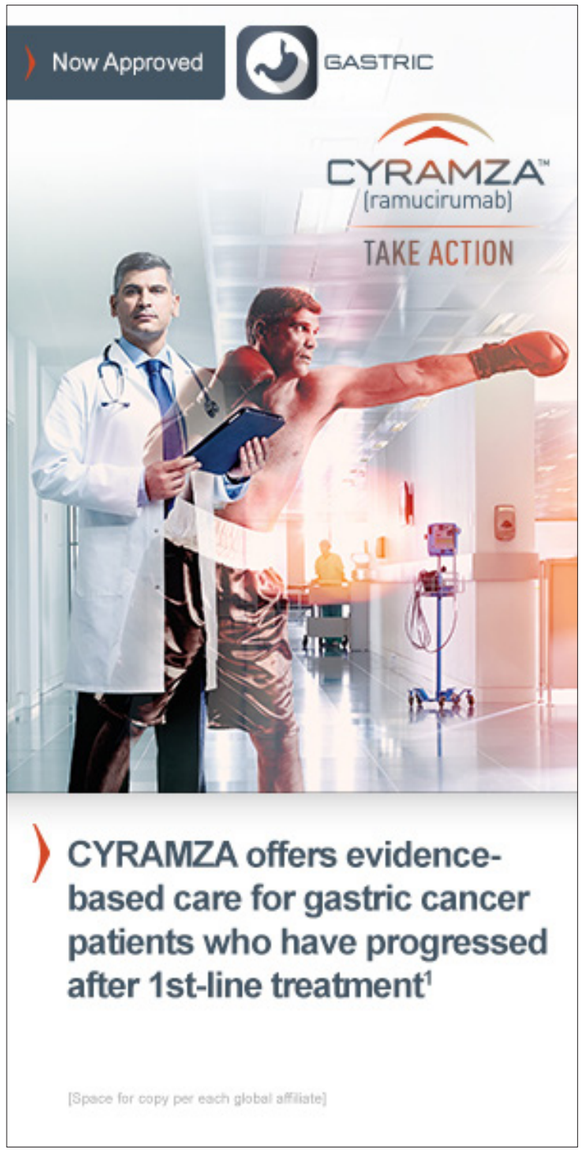

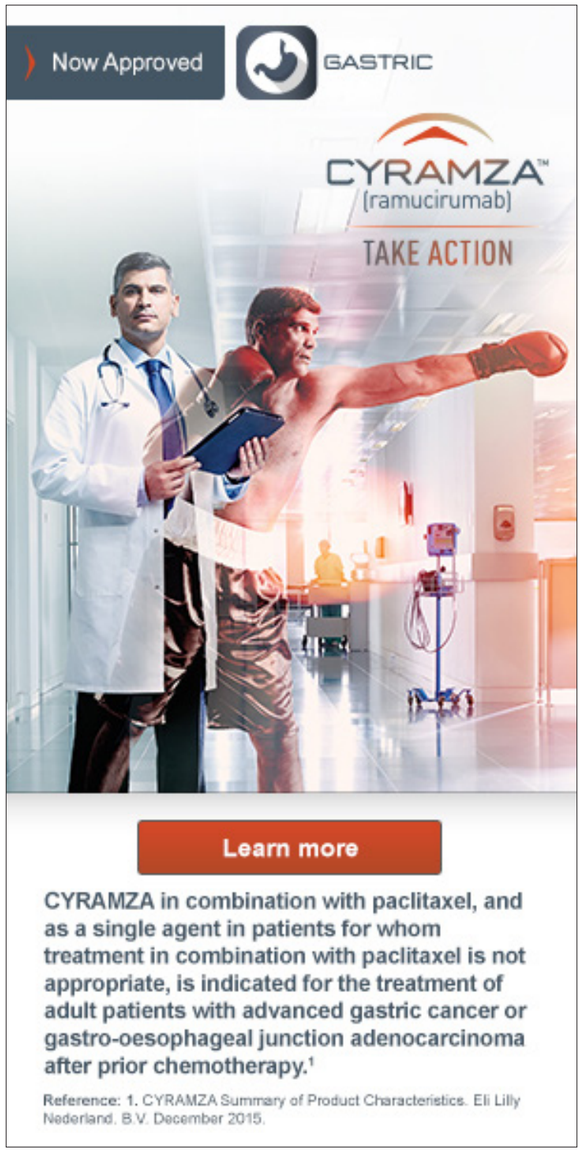

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