

Objective

To describe the consequences of an acute coronary syndrome (ACS) on the pharmacotherapeutic treatment of a patient with gastric adenocarcinoma receiving Ramucirumab.

Material & Methods

- ✓ The data were obtained by reviewing the electronic medical records
- ✓ Karch-Lasagna, Naranjo and WHO-UMC algorithms have been used

Results

Male
Former smoker
Hypertension
Hyperlipidemia

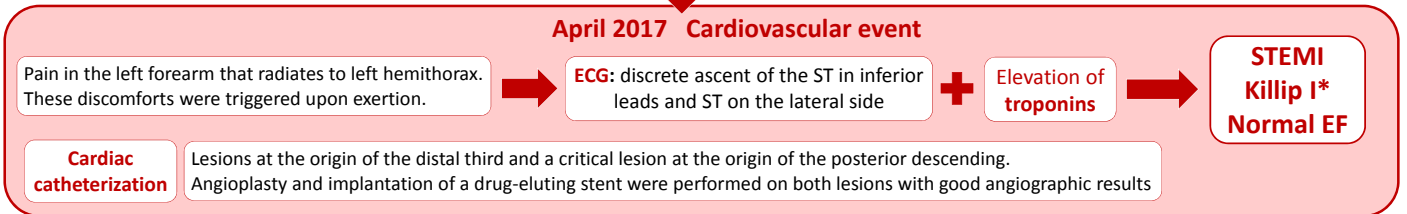
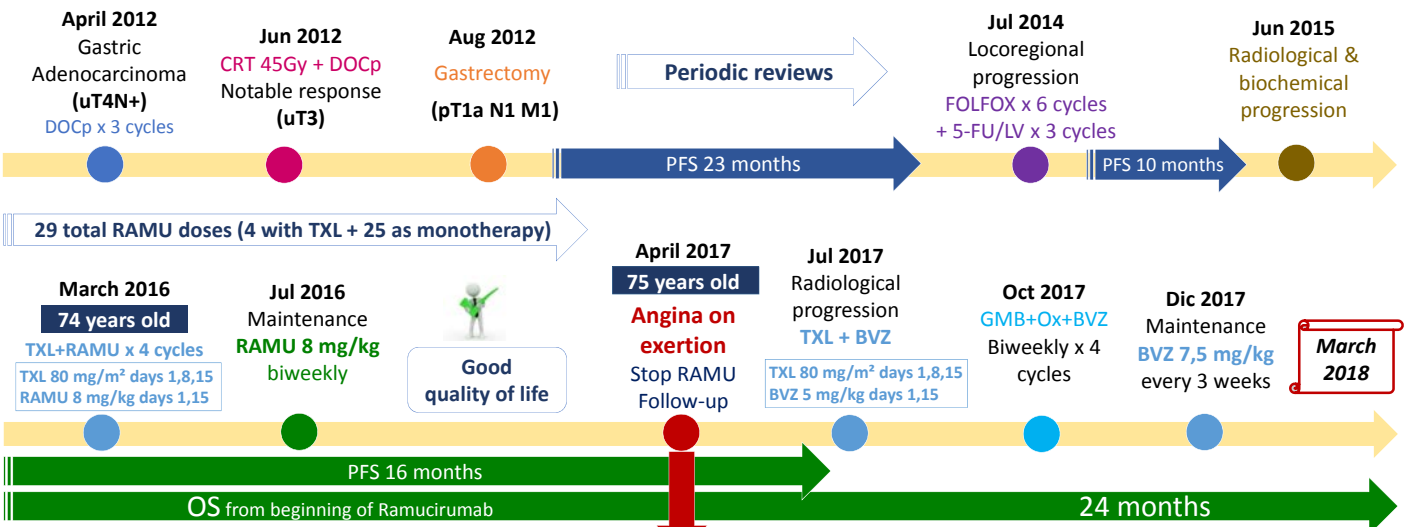
April 2012
Gastric adenocarcinoma (uT4N+)

72 years old
82.5 kg
174 cm
1.97 m²
BMI 27.2 kg/m²

Abbreviations

- 5-FU/LV: 5-Fluorouracil/Leucovorin
- ACS: acute coronary syndrome
- BMI: body mass index
- BVZ: Bevacizumab
- CRT: chemoradiotherapy
- CT: chemotherapy
- DOCp: Docetaxel+Oxaliplatin+Capecitabine
- ECG: electrocardiogram
- EF: ejection fraction
- FOLFOX: oxaliplatin+5-FU/LV
- GMB: gemcitabine
- OS: overall survival
- Ox: oxaliplatin
- PFS: progression free survival
- RAMU: ramucirumab
- STEMI: ST-elevation myocardial infarction
- TXL: paclitaxel

Oncology Medical record



***Killip Classification for Heart Failure**

- Killip-I: No signs of congestion
- Killip-II: S3 and basal rales on auscultation
- Killip-III: Acute pulmonary edema
- Killip-IV: Cardiogenic shock

Yellow Card April 2017

Drugs	Dose/day	Route	Date started	Date stopped	Used for
Enalapril	40 mg	oral	* before 2012	-	Hypertension
Hydrochlorothiazide	25 mg	oral	6/04/2016	-	Hypertension
Amlodipine	5 mg	oral	6/04/2016	-	Hypertension
Ramucirumab	500 mg	iv	22/03/16	7/04/17	Gastric adenocarcinoma
Dexamethasone	8 mg	iv	7/04/17	7/04/17	Premedication ramucirumab
Dexchlorpheniramine	5 mg	iv	7/04/17	7/04/17	Premedication ramucirumab
Metoclopramide	10 mg	iv	7/14/17	7/04/17	Premedication ramucirumab
Ranitidine	150 mg	oral	7/04/17	7/04/17	Premedication ramucirumab

Causality assessment between Ramucirumab and ACS

Karch-Lasagna <1 Improbable 1-3 Conditional 4-5 Possible 6-7 Probable ≥8 Definite 1	Naranjo 0 Doubtful 1-4 Possible 5-8 Probable ≥9 Definite 2	WHO-UMC Certain Probable Possible Unlikely Conditional Unclassifiable Possible
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Cardiovascular risk factors for ACS

- > 55 years ✓
- Male ✓
- Hypertension ✓
- Former smoker ✓
- Hyperglycaemia ✗
- Hypertriglyceridemia ✗

Causality algorithms show an uncertain correlation between the drug and the acute coronary syndrome while the patient presented four of the six risk factors related to cardiovascular events

Conclusions

- The appearance of an ACS has caused the suspension of an effective drug as Ramucirumab despite the doubtful causal relation between them if we take into account the cardiovascular risk factors of the patient
- The PFS (16 months) was much higher than that observed in the pivotal trial (median=4.4 months) and even higher than overall survival (median=9.6 months)¹
- It would be advisable a cardiovascular assessment before treatment with an anti-angiogenic monoclonal antibody^{2,3}

Bibliography

1. Wilke H, Muro K, Van Cutsem E, et al. 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;1224-1235.

2. Totzeck M, Mincu RI & Rassaf T. Cardiovascular Adverse Events in Patients With Cancer Treated With Bevacizumab: A Meta-Analysis of More Than 20000 Patients. *J Am Heart Assoc* 2017;6:e006278.

3. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines. Zamorano J, Lancellotti P, Rodriguez Muñoz D et al. *Eur Heart J* 2016; 37:2768-2801.