

# AN ACUTE AND SEVERE EVENT IN A PATIENT TREATED WITH RAMUCIRUMAB



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**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 m<sup>2</sup> BMI 27.2 kg/m<sup>2</sup>

#### Abbreviations

- ACS: acute coronary syndrome
  BMI: body mass index

- CRT: chemoradiotherapy
- CT: chemotherapyDOCp: Docetaxel+Oxaliplatin+Capecitabine
- 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

# **Oncology Medical record**

April 2012 Gastric Adenocarcinoma (uT4N+)

Jun 2012 CRT 45Gy + DOCp

Aug 2012 Gastrectomy

**Periodic reviews** 

Locoregional progression

Jul 2014

Radiological & biochemical

Jun 2015

#### Notable response FOLFOX x 6 cycles (pT1a N1 M1) progression (uT3) DOCp x 3 cycles + 5-FU/LV x 3 cycles PFS 23 months PFS 10 months 29 total RAMU doses (4 with TXL + 25 as monotherapy) April 2017 Jul 2017 75 years old Radiological March 2016 Jul 2016 Oct 2017 Dic 2017 Angina on progression 74 years old Maintenance GMB+Ox+BVZ Maintenance TXL + BVZ Biweekly x 4

TXL+RAMU x 4 cycles TXL 80 mg/m<sup>2</sup> days 1.8.15 RAMU 8 mg/kg days 1,15

RAMU 8 mg/kg biweekly

Good

Stop RAMU quality of life

exertion

TXL 80 mg/m<sup>2</sup> days 1,8,15 BVZ 5 mg/kg days 1,15 Follow-up

BVZ 7,5 mg/kg every 3 weeks

24 months

March 2018

PFS 16 months

OS from beginning of Ramucirumab

April 2017 Cardiovascular event

Pain in the left forearm that radiates to left hemithorax. These discomforts were triggered upon exertion.

ECG: discrete ascent of the ST in inferior leads and ST on the lateral side

Elevation of troponins

cycles

**STEMI** Killip I\* Normal EF

catheterization

Lesions at the origin of the distal third and a critical lesion at the origin of the posterior descending. Angioplasty and implantation of a drug-eluting stent were performed on both lesions with good angiographic results

# 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
Enalapríl	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	ίν	22/03/16	7/04/17	Gastric adenocarcinoma
Dexamethasone	8 mg	ίν	7/04/17	7/04/17	Premedication ramucirumab
Dexchlorpheniramine	5 mg	ίν	7/04/17	7/04/17	Premedication ramucirumab
Metoclopramide	10 mg	ίν	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

Improbable

Probable Definite

# Naranjo

Doubtful Probable Definite

# WHO-UMC Certain

Unclassifiable

Probable **Possible** Unlikely

# 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<sup>2,3</sup>

#### **Bibliography**

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