CLINICAL CASE

Young-onset gastric cancer

Maria Alsina, MD PhD

Hospital Universitario de Navarra

Navarrabiomed – IdiSNA

Pamplona, Spain

CLINICAL CASE

- 48 YO woman
- Married, with 2 children
- Currently working as a nurse in a Gynecological Center

- No toxic habits, no comorbidities, except from a surgery of an inguinal hernia when she was 2 YO

- Familiar history: paternal uncle with prostate cancer (75YO), paternal aunt endometrial cancer (65YO), maternal cousin thyroid cancer (39YO).

DIAGNOSIS

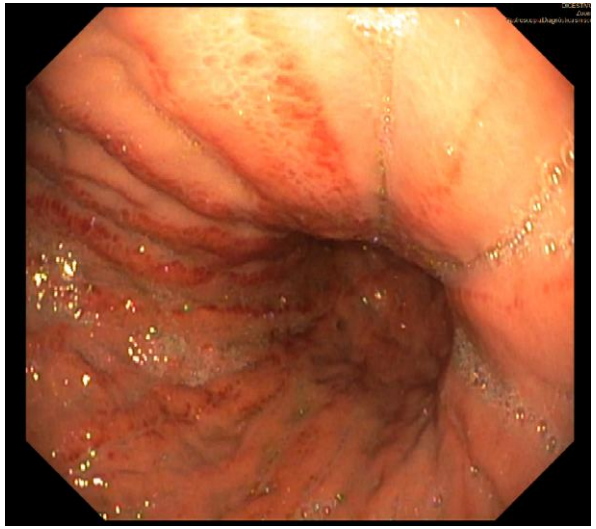
May 2023:

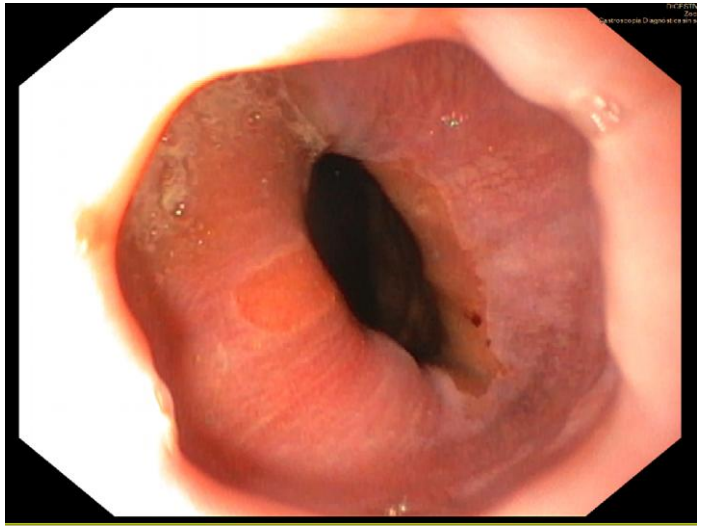
- The patient referred epigastric pain and a gastroscopy showed an erythematous area, which was reported as an intestinal metaplasia with H Pylori+. She realized H. Pylori eradication, but the pain didn't resolved and she started with constitutional syndrome.

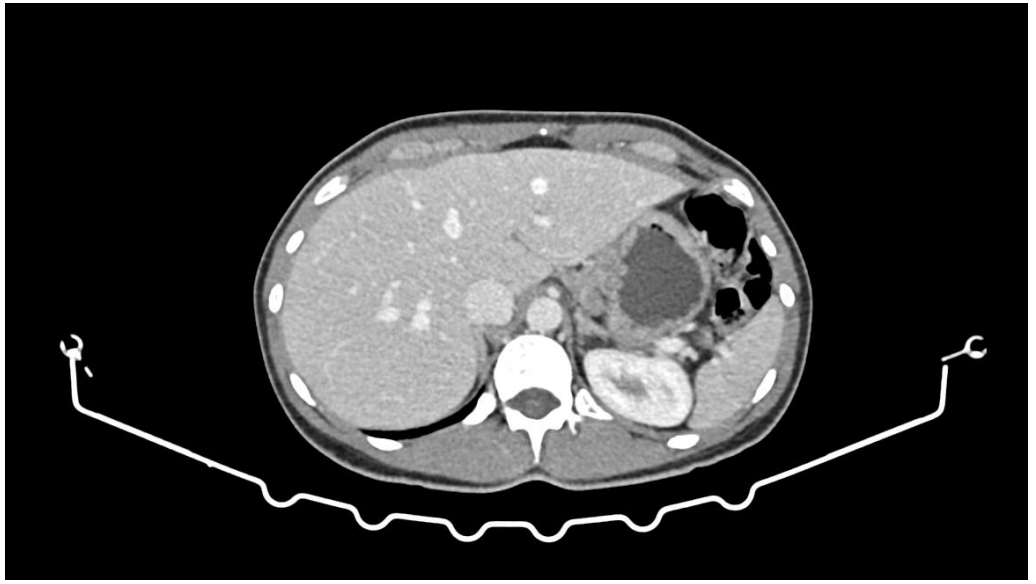
December 2023:

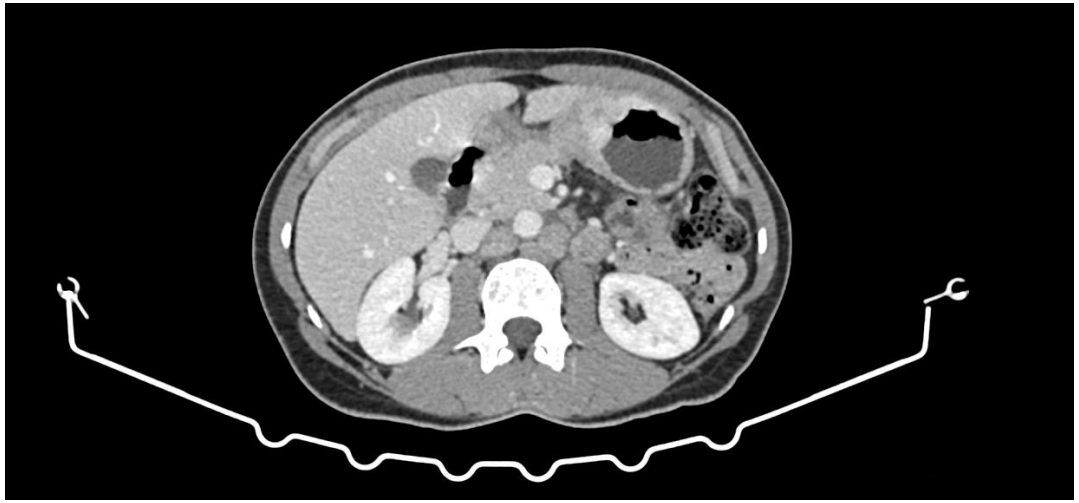
- (18th Dec 2023) A new gastroscopy was performed: lineal erosions in the lesser curvature and an ulcer in the distal zone.
- Pathology report: **diffuse carcinoma** with **signed ring cells**, **pMMR**, **HER2 negative**.
- (11th Jan 2024) CT scan:
  - Distended stomach without conclusive findings in the gastric Wall (certain thickening in a diffuse manner).
  - Lymph nodes in the gastrohepatic space and in the middle retroperitoneum, with presence of nodes that converge with each other and extend inferiorly to the iliac territory.
  - Possible mediastinal lymph node

DIAGNOSIS









DIAGNOSIS

- Laparoscopy (23 Jan 2024)
  - Minimal amount of ascites in the right hypochondria (aspired for cytology)
  - Gastric tumor on the anterior surface of the antrum that affects the serosa and ascends through the body with involvement of the lesser omentum.
  - Retroperitoneal lymph nodes, with an inter-aorto-cava conglomerate (biopsy)
  - Washing cytology
- Pathology report:
  - Cytology's: epithelial cells with atypia, CDX2-positive.
  - Biopsy: M1

DIAGNOSIS

- 1st Visit at the Medical Oncology Department (2 Feb 2024)

- The patient was almost asymptomatic (G1 asthenia and epigastric pain, G2 insomnia). ECOG 1.

48 YO woman, no comorbidities, diagnosed of a gastric cancer in the antrum (diffuse carcinoma wit signed ring cells, pMMR, HER2 negative) stage IV (retroperitoneal lymph nodes metastases)

HOW TO PROCEED?

- We asked for needed tests:
  - Blood test
  - PDL1 CPS
  - DPYD status

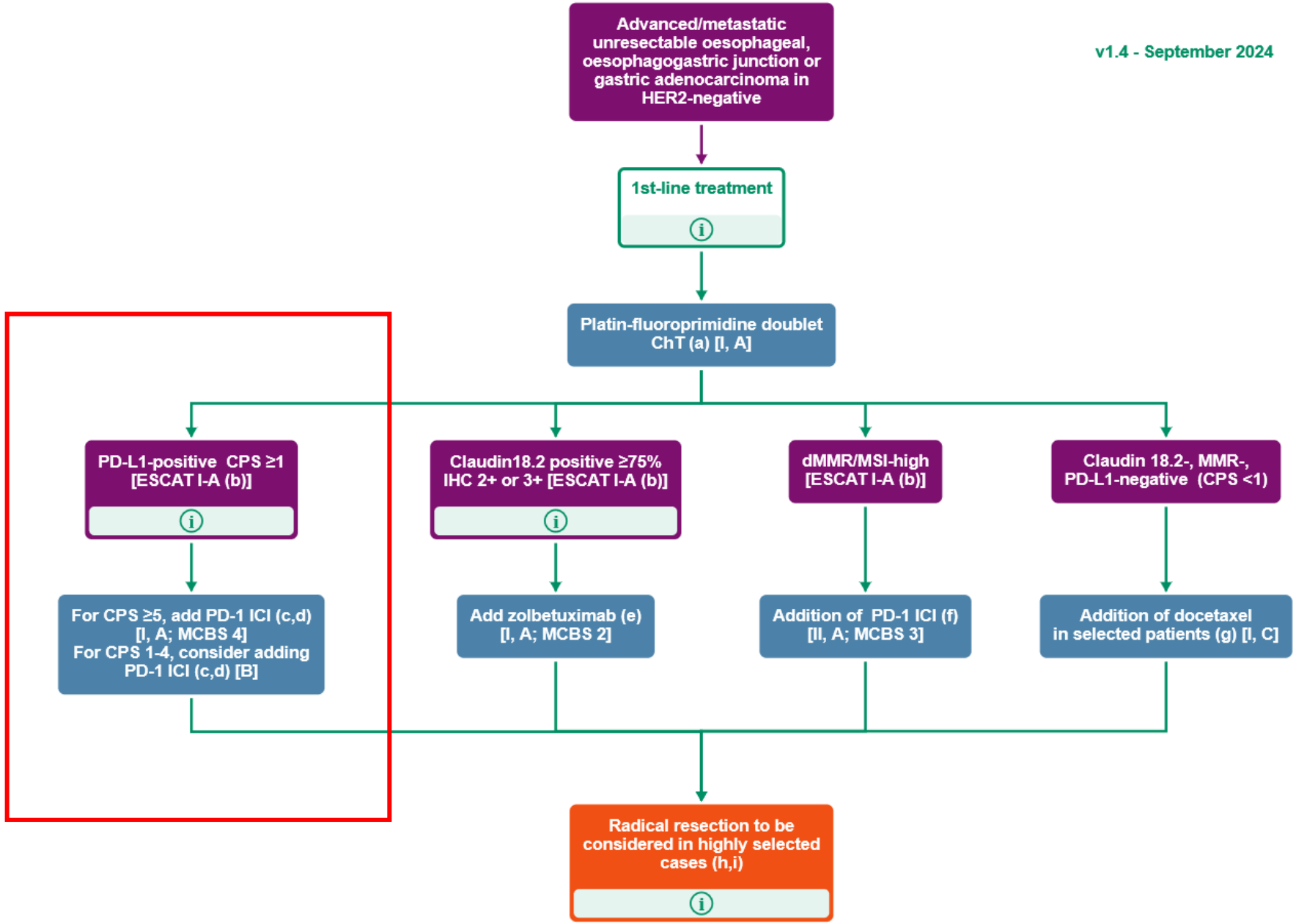
- She was referred to the Genetic Counseling

- Bone scan (5 Mar 2024): Multiple bone M1

- Alcaline phospatase 1545 U/L [40 – 150]
- CEA: 6 ng/mL, Ca19.9: 176 U/mL

- **PDL1 CPS = 5**

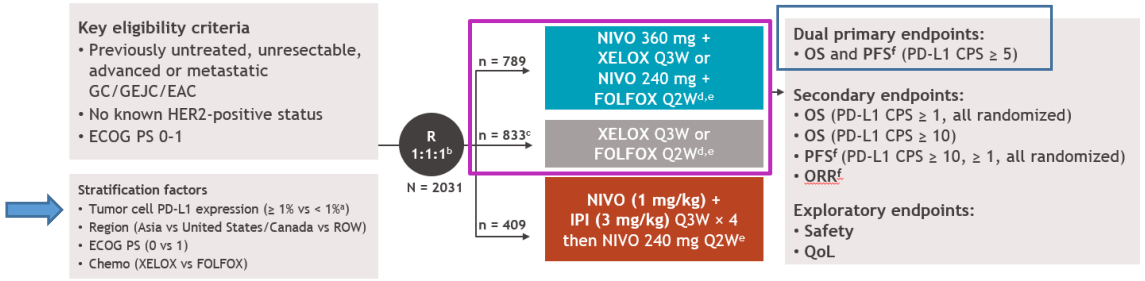
- No alterations in the DPYD


Advanced/metastatic unresectable oesophageal, oesophagogastric junction or gastric adenocarcinoma in HER2-negative
v1.4 - September 2024
1st-line treatment
Platin-fluoroprimidine doublet ChT (a) [I, A]
PD-L1-positive CPS ≥1 [ESCAT I-A (b)]
Claudin18.2 positive ≥75% IHC 2+ or 3+ [ESCAT I-A (b)]
dMMR/MSI-high [ESCAT I-A (b)]
Claudin 18.2-, MMR-, PD-L1-negative (CPS <1)
For CPS ≥5, add PD-1 ICI (c,d) [I, A; MCBS 4]
For CPS 1-4, consider adding PD-1 ICI (c,d) [B]
Add zolbetuximab (e) [I, A; MCBS 2]
Addition of PD-1 ICI (f) [II, A; MCBS 3]
Addition of docetaxel in selected patients (g) [I, C]
Radical resection to be considered in highly selected cases (h,i)

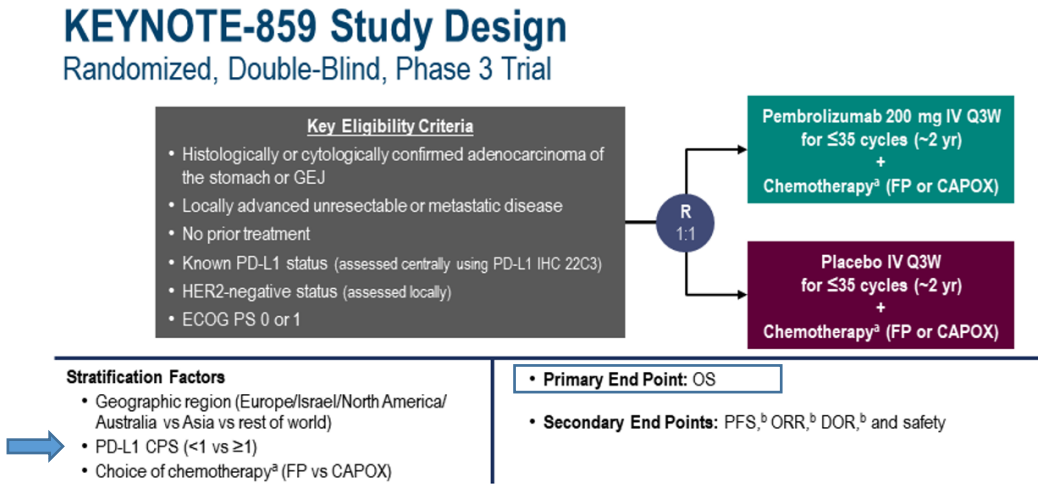
Checkmate649 and KEYNOTE-859

Checkmate-649

Figure 1. CheckMate 649 study design[5]

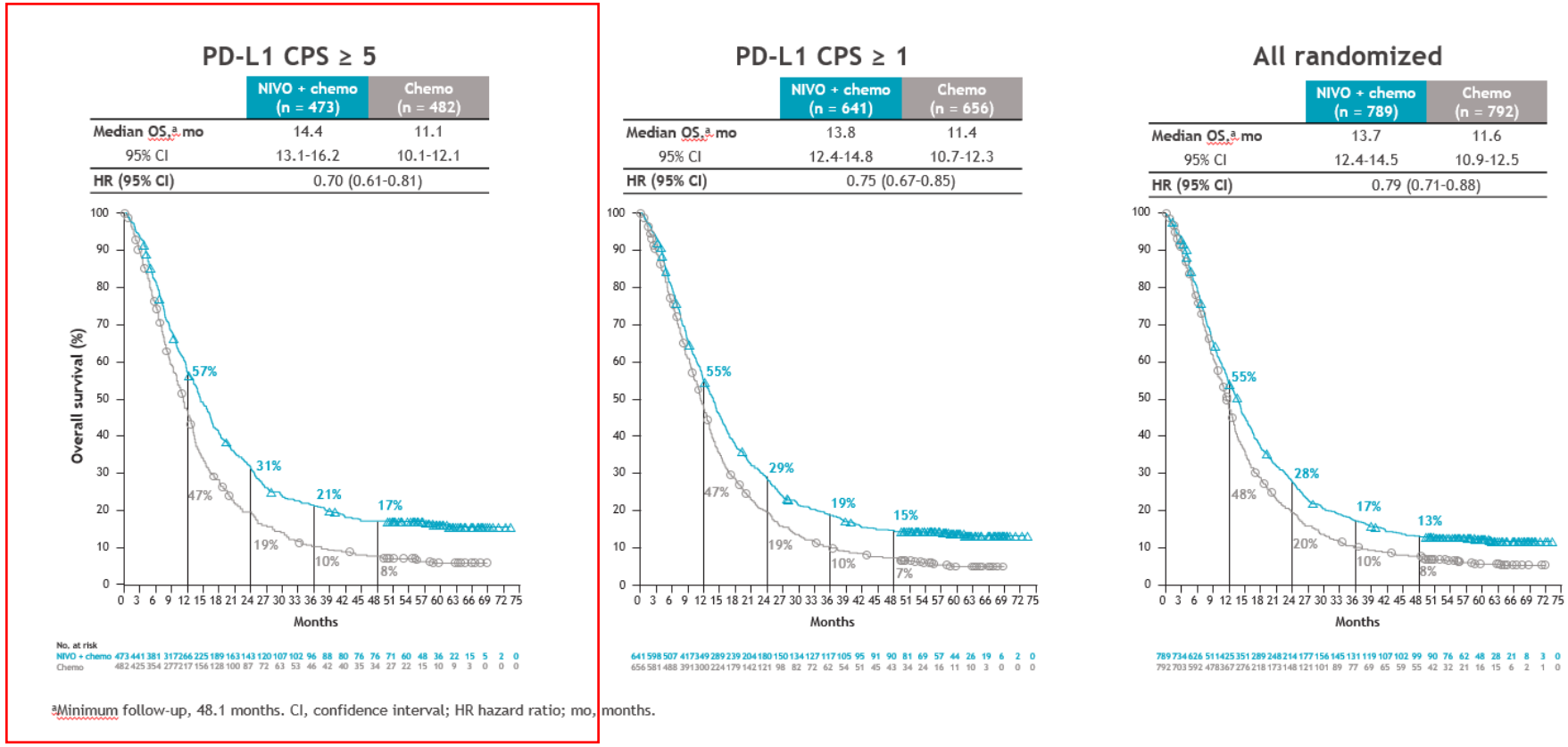


KEYNOTE-859



Checkmate649

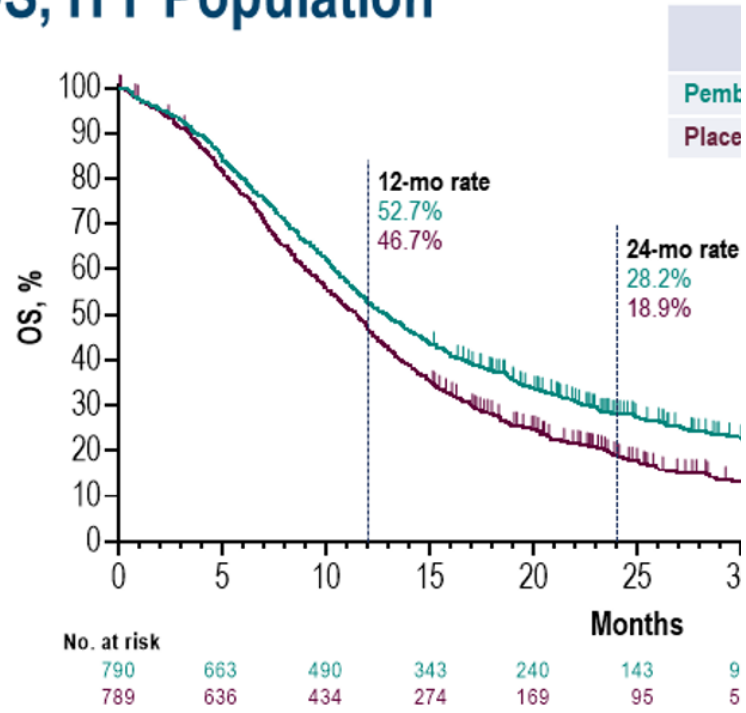
Figure 2. Overall survival



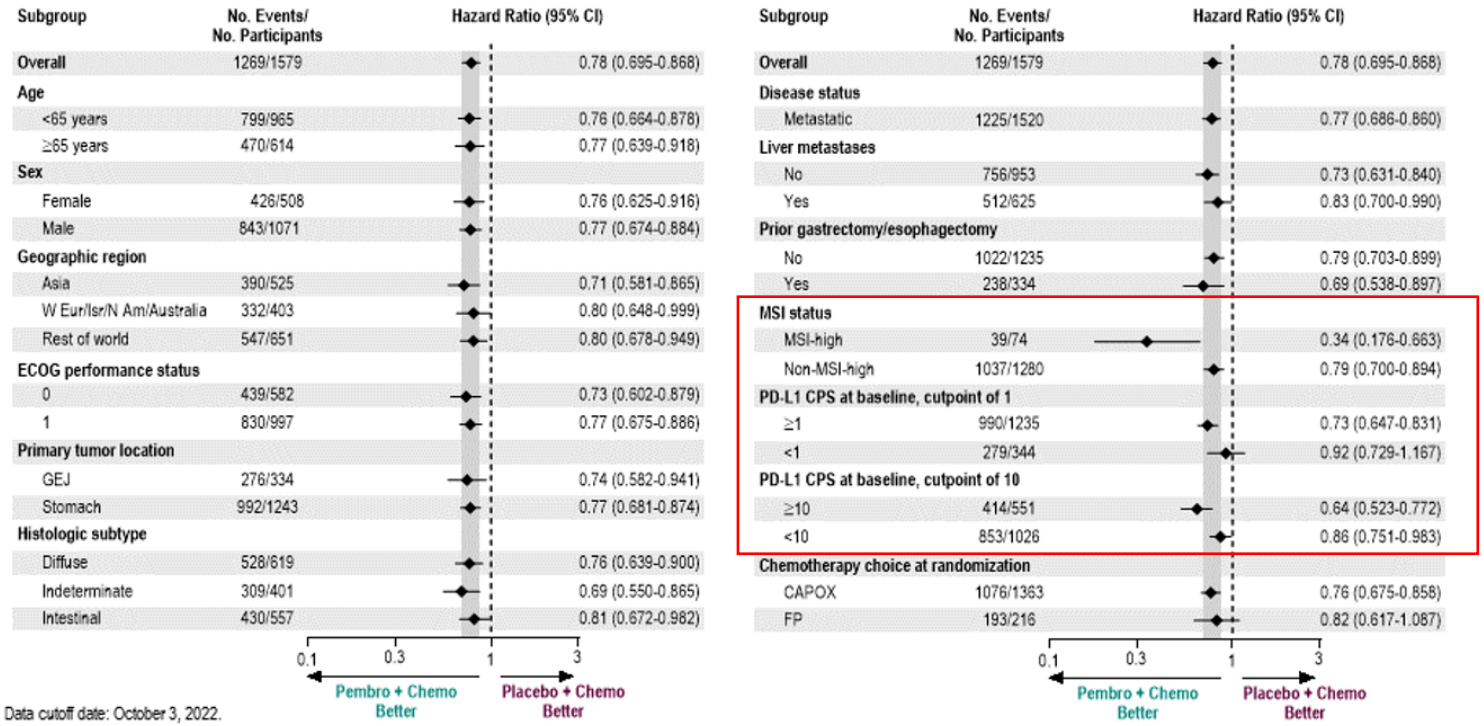
[a]Minimum follow-up, 48.1 months. CI, confidence interval; HR hazard ratio; mo, months.

KEYNOTE-859

OS, ITT Population



OS in Key Subgroups, ITT Population



Data cutoff date: October 3, 2022.

Rha ESMO Virtual Plenary feb 2023; Rha Lancet Oncol 2023

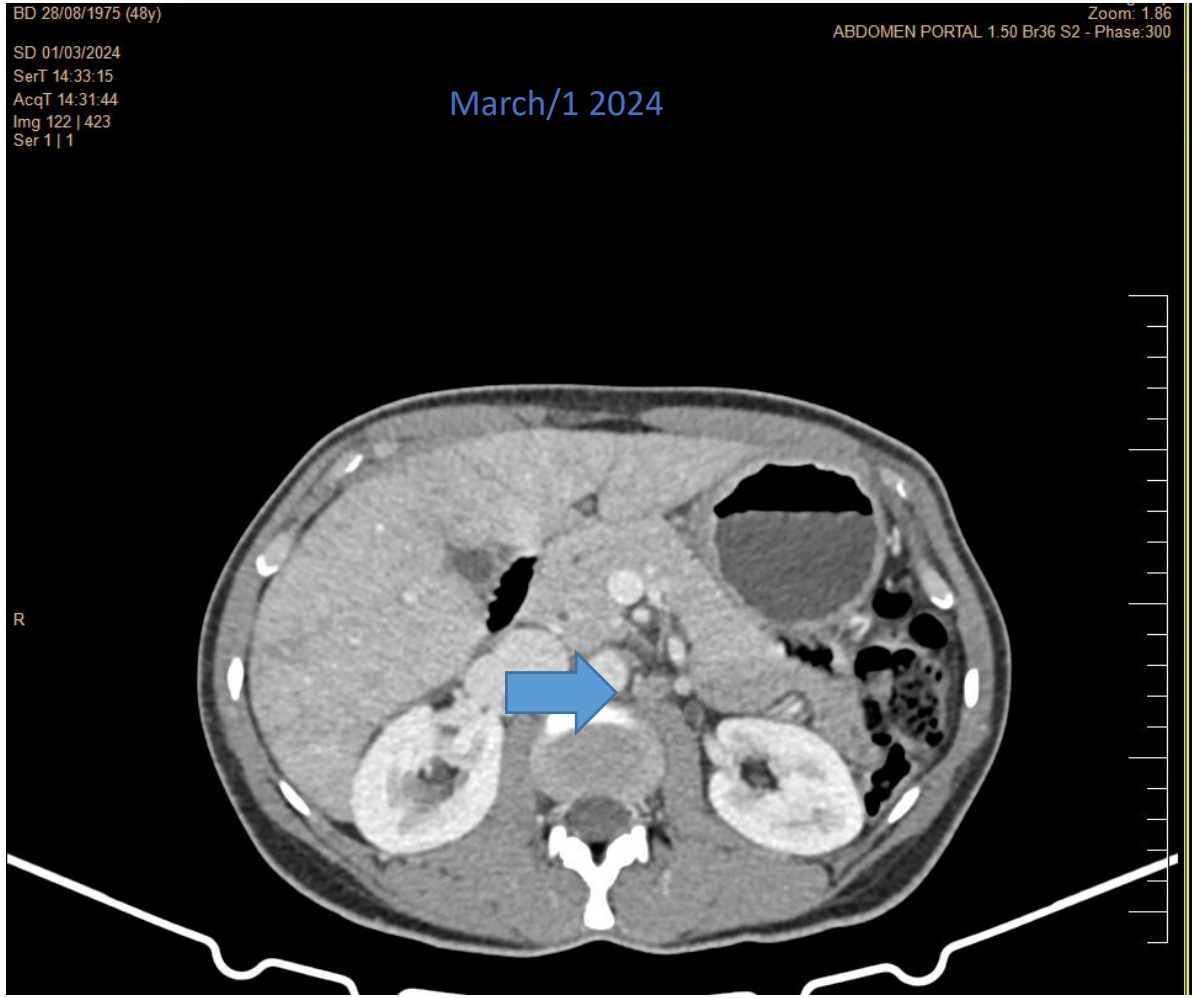
TREATMENT

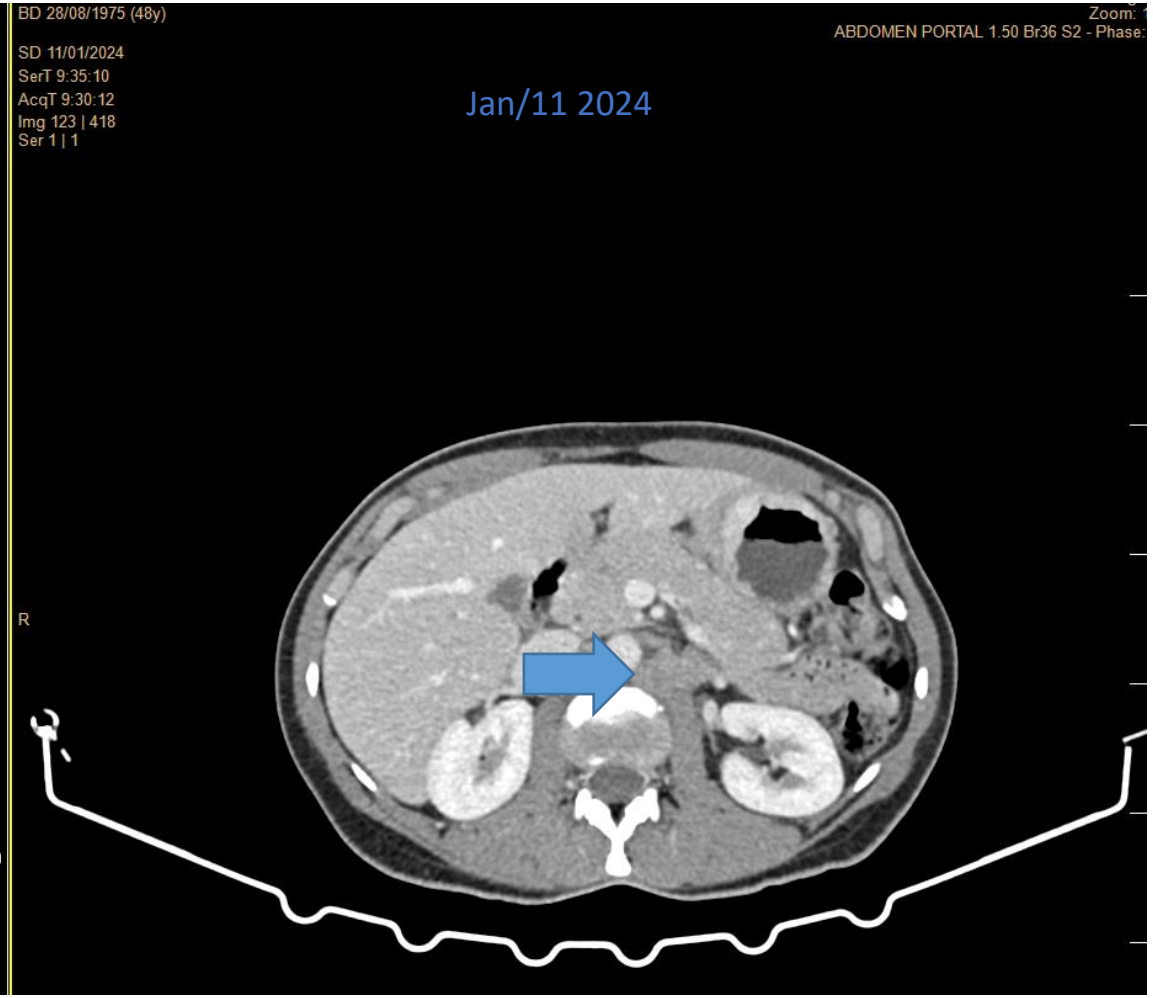
Feb – July 2024: **XELOX + Nivolumab** x 7 cycles.

- Toxicities:
  - G3 transaminase elevation after C1, related to capecitabine → delay/reduction
  - G1 hematological toxicity
  - G1 neurotoxicity

- Response: partial response

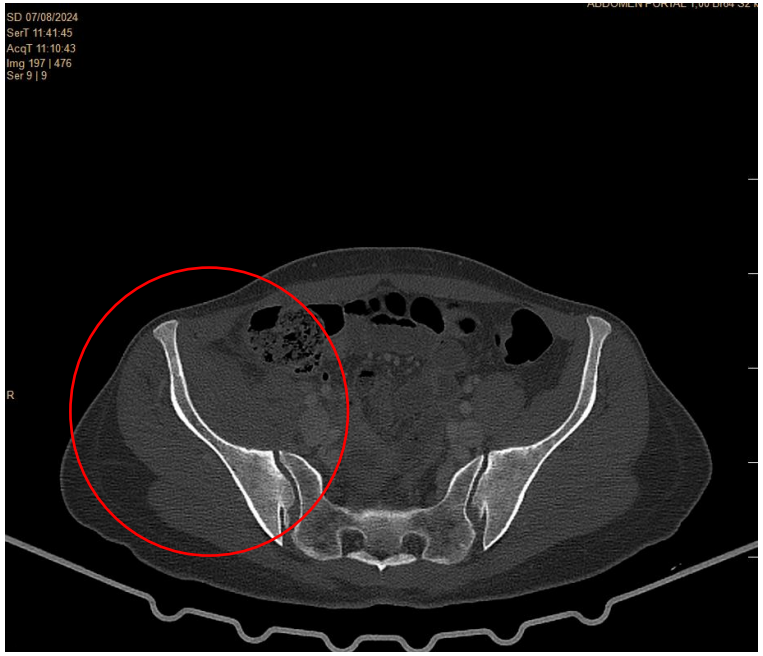
TREATMENT

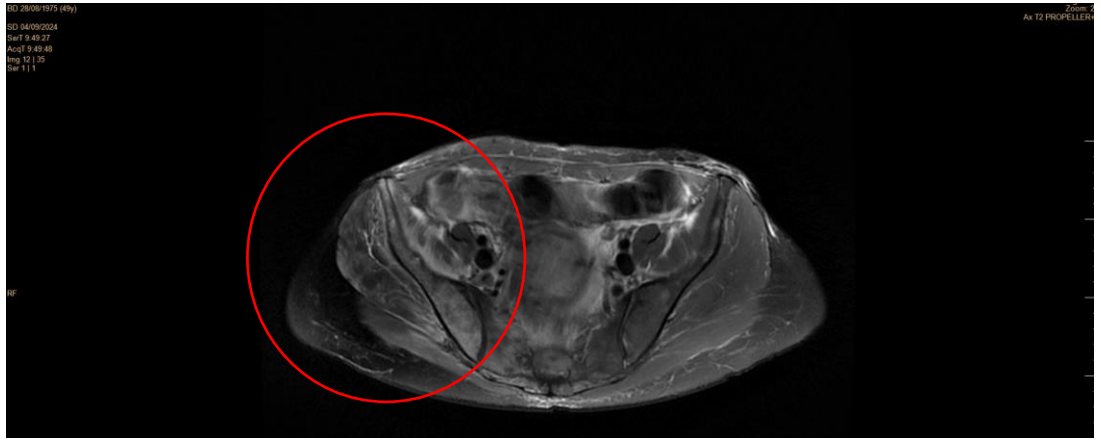

BD 28/08/1975 (48y)
SD 01/03/2024
SerT 14:33:15
AcqT 14:31:44
Img 122 | 423
Ser 1 | 1
Zoom: 1.86
ABDOMEN PORTAL 1.50 Br36 S2 - Phase:300
R
March/1 2024

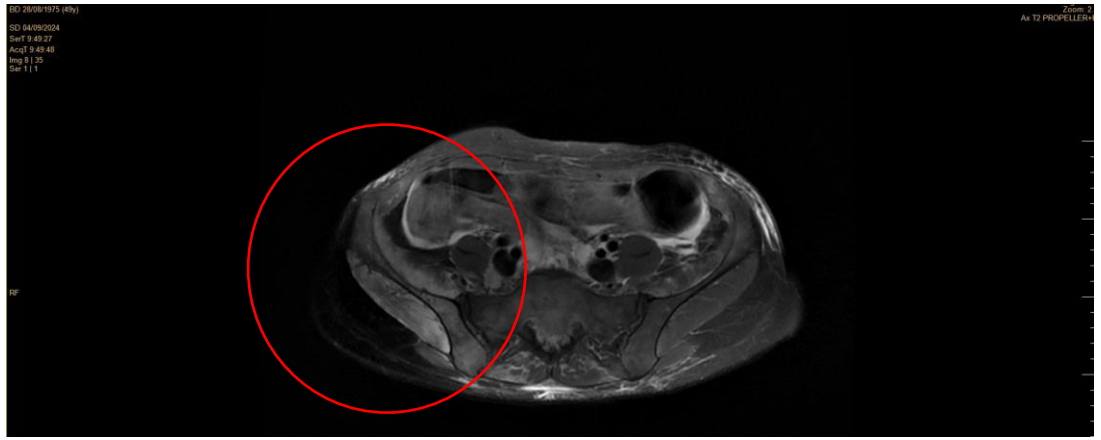

BD 28/08/1975 (48y)
SD 11/01/2024
SerT 9:35:10
AcqT 9:30:12
Img 123 | 418
Ser 1 | 1
ABDOMEN PORTAL 1.50 Br36 S2 - Phase:
R
Jan/11 2024

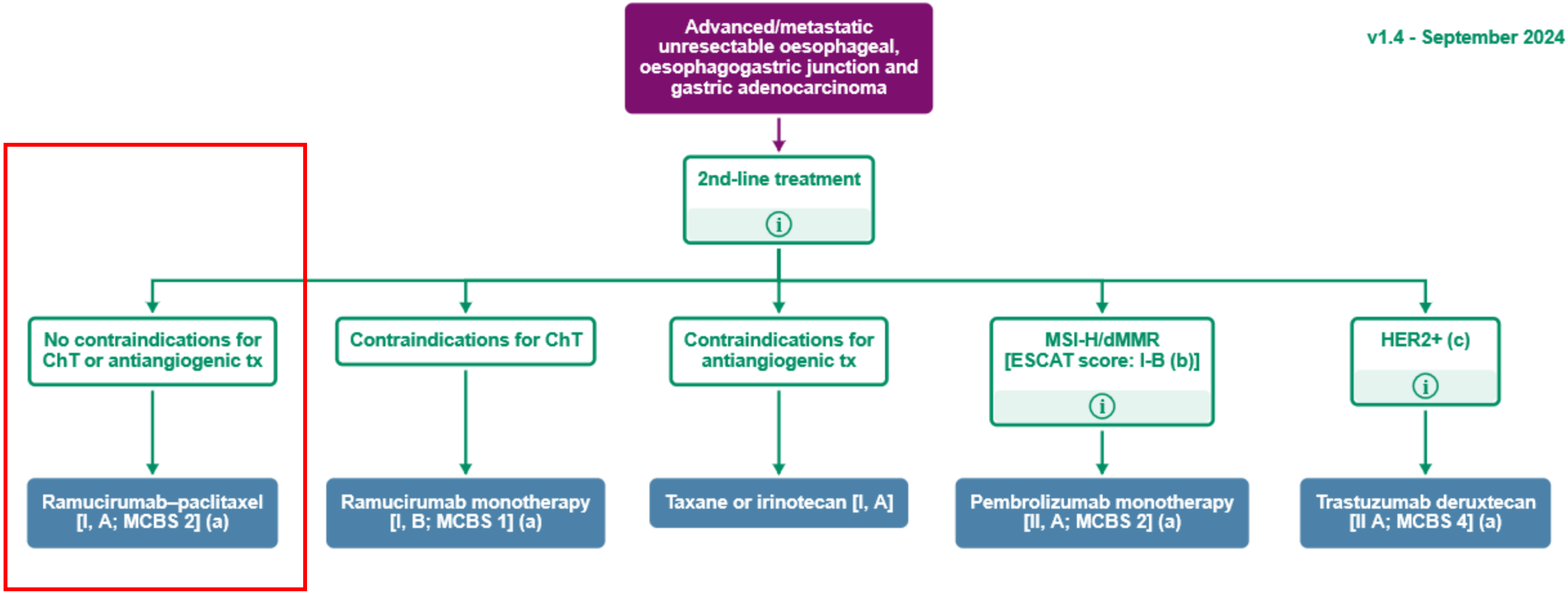
TREATMENT

August 2024: Patient started with new symptoms, with right inguinal pain and mild functional impotency of the right leg. The CT scan suggested an irregularity at the adjacent muscles to the iliac bone and ischiopubic remus, and tumor muscular infiltration was confirmed with an MRI.



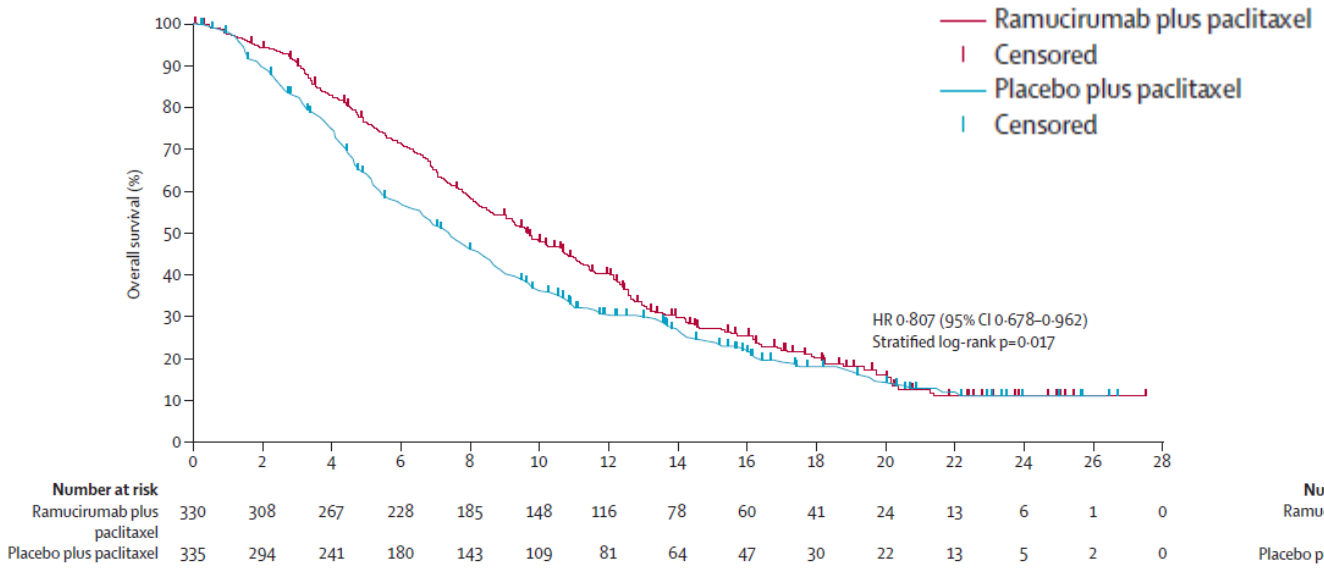




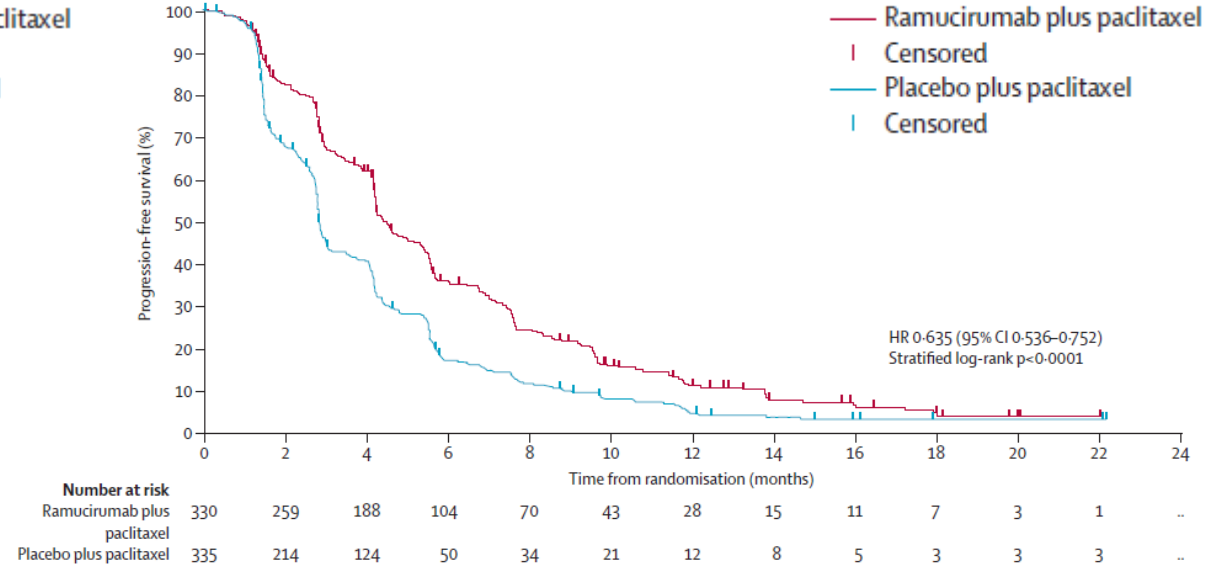

Advanced/metastatic unresectable oesophageal, oesophagogastric junction and gastric adenocarcinoma
v1.4 - September 2024
2nd-line treatment
No contraindications for ChT or antiangiogenic tx
Contraindications for ChT
Contraindications for antiangiogenic tx
MSI-H/dMMR [ESCAT score: I-B (b)]
HER2+ (c)
Ramucirumab–paclitaxel [I, A; MCBS 2] (a)
Ramucirumab monotherapy [I, B; MCBS 1] (a)
Taxane or irinotecan [I, A]
Pembrolizumab monotherapy [II, A; MCBS 2] (a)
Trastuzumab deruxtecan [II A; MCBS 4] (a)

The RAINBOW Trial (VEGFR2)

Median OS: 9.6 vs 7.4 months



Median PFS: 4.4 vs 2.9 months

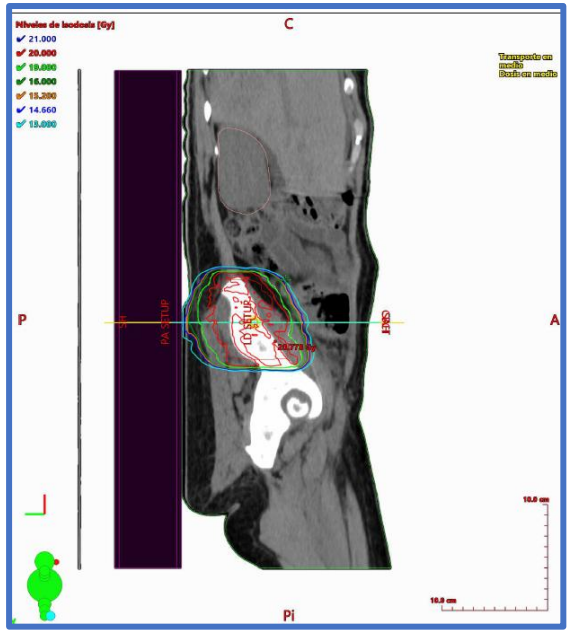


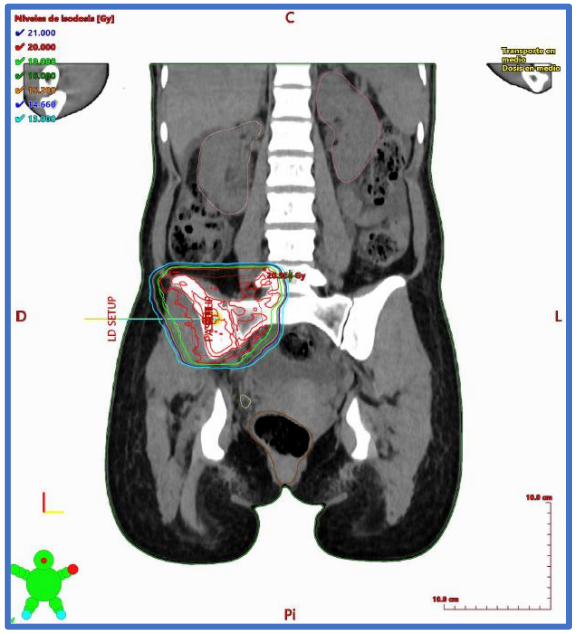
Wilke Lancet Oncol 2014

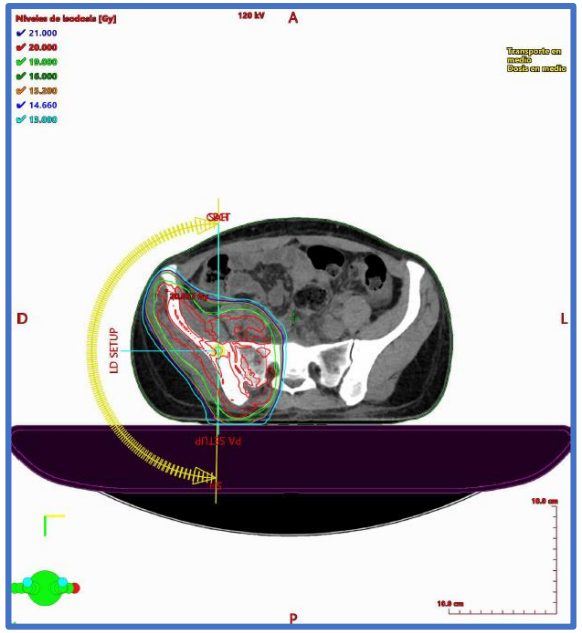
TREATMENT

In Aug/27, the patient started **a second line with paclitaxel – ramucirumab**, but she could only receive C1D1 and C1D8. C1D15 was omitted due to G2 neutropenia and G1 platelet count decrease.

Due to bad control of the paint, the patient received **palliative radiotherapy** 20 Gy (Sep/6-12)







TREATMENT

- In Sep/23, the patient came to the outpatients to start C2D1 referring mild dyspnea and severe asthenia. On top of that, the blood analyzes showed mild bicytopenia:

Técnica	Valor	Rango
Hemograma	:	
San-Hematíes, c	**2,5 x10^12/L**	**[4,1 - 5,2]**
San-Hemoglobina, g	**7,9 g/dL**	**[12 - 16]**
San-Hematocrito, w	**23,8 %**	**[34 - 47]**
San-Volumen corpuscular medio, v	96,2 µ^3	[80 - 100]
San-Hemoglobina corpuscular media, g	32 pg	[25 - 35]
San-Concentración Hb corpuscular media, g	33,2 g/dL	[32 - 36]
San-Ancho distribución eritrocitario, w	**22,6 %**	**[10,6 - 14,7]**
San-Leucocitos, c	**13,4 x10^9/L**	**[4 - 11]**
San-%Neutrófilos, w	61 %	[40 - 80]
San-%Linfocitos, w	**6 %**	**[20 - 50]**
San-%Monocitos, w	**0 %**	**[4,5 - 12]**
San-%Eosinófilos, w	1 %	[0,5 - 8]
San-%Basófilos, w	0 %	[0 - 2]
Cayados	**8 %**	**[0 - 0,1]**
Metamielocitos	**3 %**	**[0 - 0,1]**
Mielocitos	**9 %**	**[0 - 0,1]**
Eritroblastos	**12 %**	**[0 - 0,1]**
San-Neutrófilos, c	**8,2 x10^9/L**	**[1,8 - 7]**
San-Linfocitos, c	**0,8 x10^9/L**	**[1 - 4]**
San-Monocitos, c	**0 x10^9/L**	**[0,2 - 1]**
San-Eosinófilos, c	0,1 x10^9/L	[0 - 0,7]
San-Basófilos, c	0 x10^9/L	[0 - 0,2]
San-Plaquetas, c	**32 x10^9/L**	**[150 - 400]**
San-Volumen plaquetar medio, v	8,6 µ^3	[5,8 - 14]

Diagnosed of bone marrow infiltration

TREATMENT

We tried to keep on 2nd line treatment, offering chemotherapy with a close follow-up, but she presented a quick deterioration of her ECOG/PS status, thus impeding it.

Finally, the patient passed away in Oct/1 2024 (6 weeks after the last dose of chemotherapy)

DISCUSSION: Early-onset (Young-onset) GC

- Age: 25 to 50 YO
- Significant increase during the last decade (like for CRC, PDAC and BTC)
- Sporadic (lack hereditary or familiar background)
- Probably due to environmental factors, with distinct underlying molecular backbone

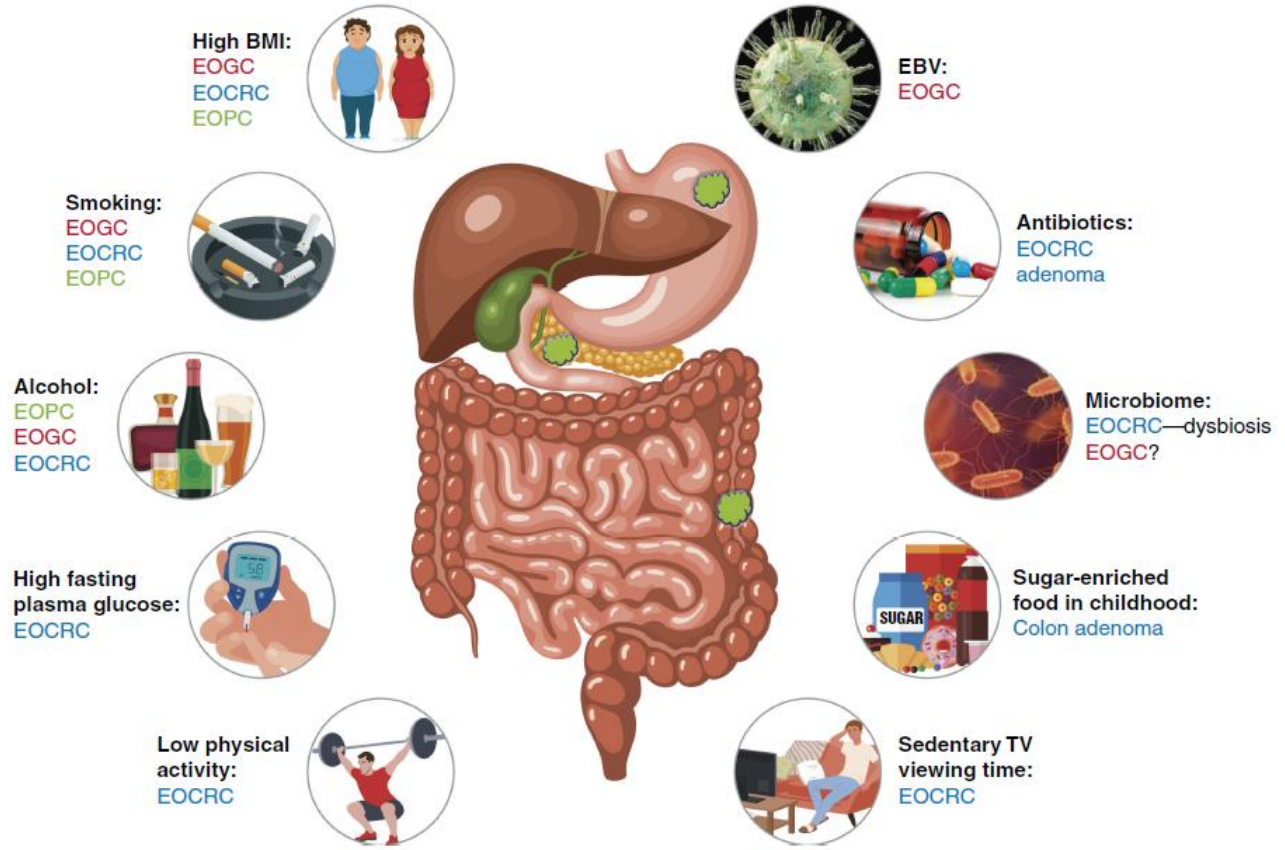


Figure 2. Potential environmental and behavioral factors for early-onset GI cancer. BMI, body mass index; EBV, Epstein–Barr virus; EOGC, early-onset gastric cancer; EOPC, early-onset pancreatic cancer.

Ben-Aharon et al. Cancer Discov 2023
Lumish et al. JNCI 2023

DISCUSSION: Early-onset (Young-onset) GC

- Young patients face unique challenges and unmeet needs
  - Early time in the patient life: social, economical and familiar expectancies
  - Late-term treatment toxicities

Early-onset (Young-onset) GC should be considered a **distinct entity**, and there is a clear unmeet need to clarify causes, molecular features and specific treatment algorithms

Ben-Aharon et al. Cancer Discov 2023

DISCUSSION

- Our patient presented high emotional distress, although a good familiar support
- She had 2 young children (10 and 12 YO), but she decided not to inform them until the “almost end” of the disease
- She suffered during all the entire oncology disease history

Young patients present high psycho-social needs

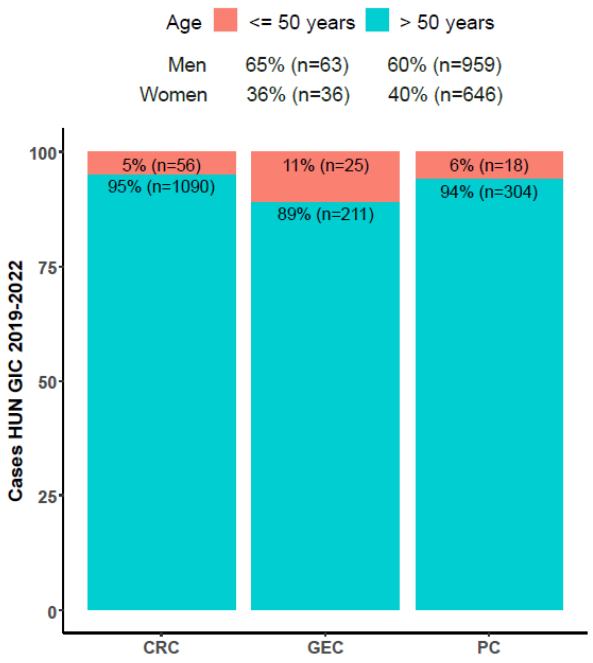
- As she was young, we flighted to keep her on treatment although, during the last 2 months, she presented an obvious ECOG deterioration

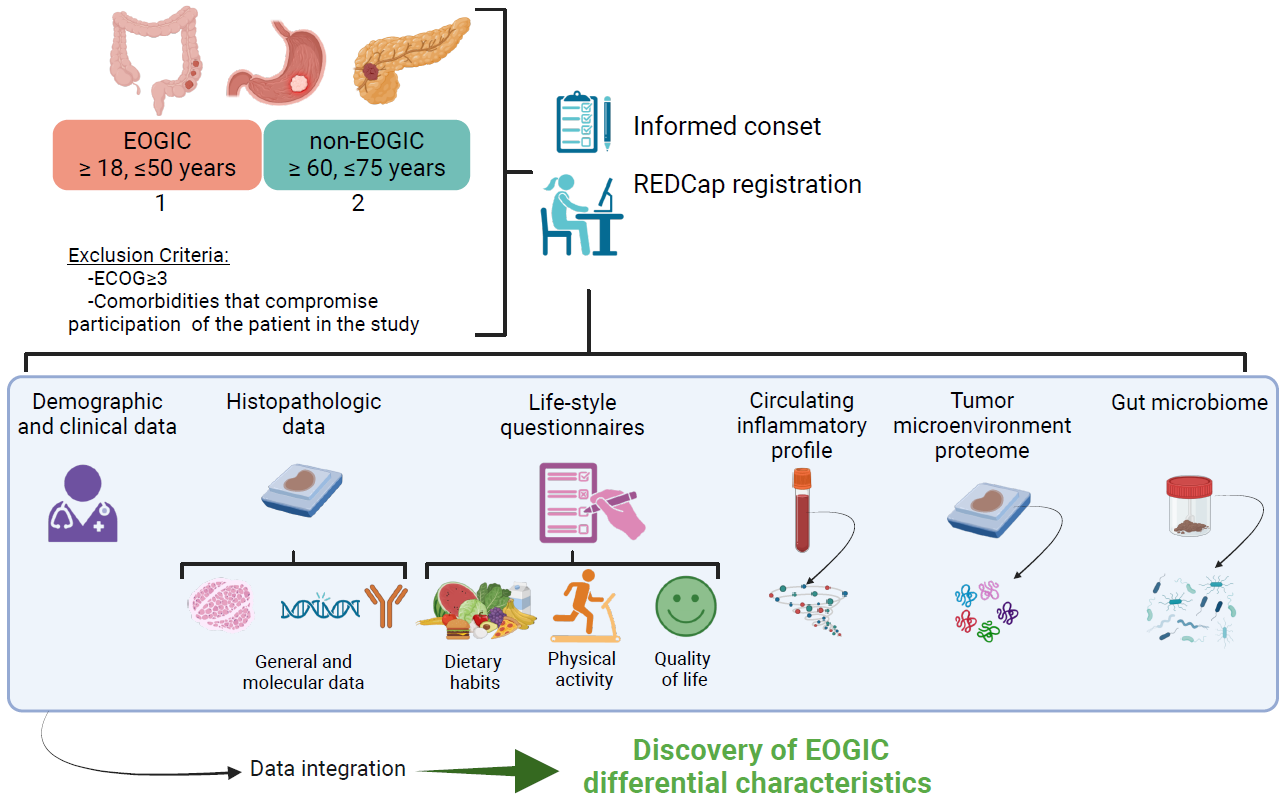
Oncologists need to learn how to be “objective” with young patients

DISCUSSION

Further research is urgently needed

- But our patient didn’t present any risk factor nor familiar history…





Vera, …., Alsina BMC Cancer 2024

Thank you for your attention

maria.alsina.maqueda@navarra.es