ESMO Preceptorship Programme

Gastric Cancer– Barcelona – 30-31 August

Fondazione Policlinico Universitario A. Gemelli
Università Cattolica del Sacro Cuore

Precision Medicine: a real new opportunity?

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DISCLOSURE OF INTEREST

”no conflicts of interest”.

Case History

- A 48 years, Caucasian young men, PS(ECOG): 0
- BMI: 20
- No co-morbidities
- **October 2018:** onset of anorexia, dyspepsia, weight loss and abdominal pain
- **November 2018:** Eco-endoscopy with biopsies: voluminous neoformation of the gastric corpus that affect the wall of the bowel to a full thickness, passing the serosa coming into contact with the hepatic parenchyma. Numerous lymphadenopaties along the small curve, the largest one of 16mm. Single lymphadenopathy (12 mm) near cholecyst and an other (7 mm) in anterior mediastinum.
- **TNM: cT4cN3, Stage III.** Histological exam: signet-ring cell carcinoma
- **CT total body**: no evidence of distal disease

- **December 2018:** Start pre-operative chemotherapy FLOT (5-FU, Folinic acid, Oxaliplatin, Docetaxel) for 4 cycles

- **PET/CT scan after 4 cycles**: Lymphadenopathy complete response and gastric partial response

- **12/02/2019:** Total Gastrectomy plus lymphadenectomy D2: Signet ring adenocarcinoma , **TNM**: pT4apN3b *(35/58)*, R0

- **March 2019:** PS(ECOG): 0, NRS: 0. Slight trembling and mild asthenia with laboratory test in range. He was enrolled in *Realflot clinical trial*: 4 cycles of adjuvant FLOT.

- **April 2019 t/b CT scan** : Linfonodal progression

AT THIS POINT WHAT TO DO ?

Multiple Options

- ✓ **FIRST OPTION: Ramucirumab** (Wilke H1 et *Lancet Oncol. 2014)*
- ✓ **SECOND OPTION: Folfiri** (Seo MD et al *Jpn J Clin Oncol. 2008*)
- ✓ **THIRD OPTION**: **Pembrolizumab 200 mg q21 in clinical trial** (based on MSI-H status)
- ✓ **FOURTH OPTION: HER-2 testing—>***Trastuzumab* (*Bang YJ et al, ToGA trial Lancet 2010)*

BACKGROUND

- Gastric cancer is genomically heterogeneous disease.

- No gene mutation was classified as Level_1 (FDA-recognized biomarker for an FDA-approved drug in that same indication).

- Few patients with actionable alterations received genomically matched therapy because of medical, logistical and economic considerations, a group of patients still had choice to participate in a clinical trial of matched targeted drugs, or try drugs in other indications (Hui Cai et al. *J Trans Med)*

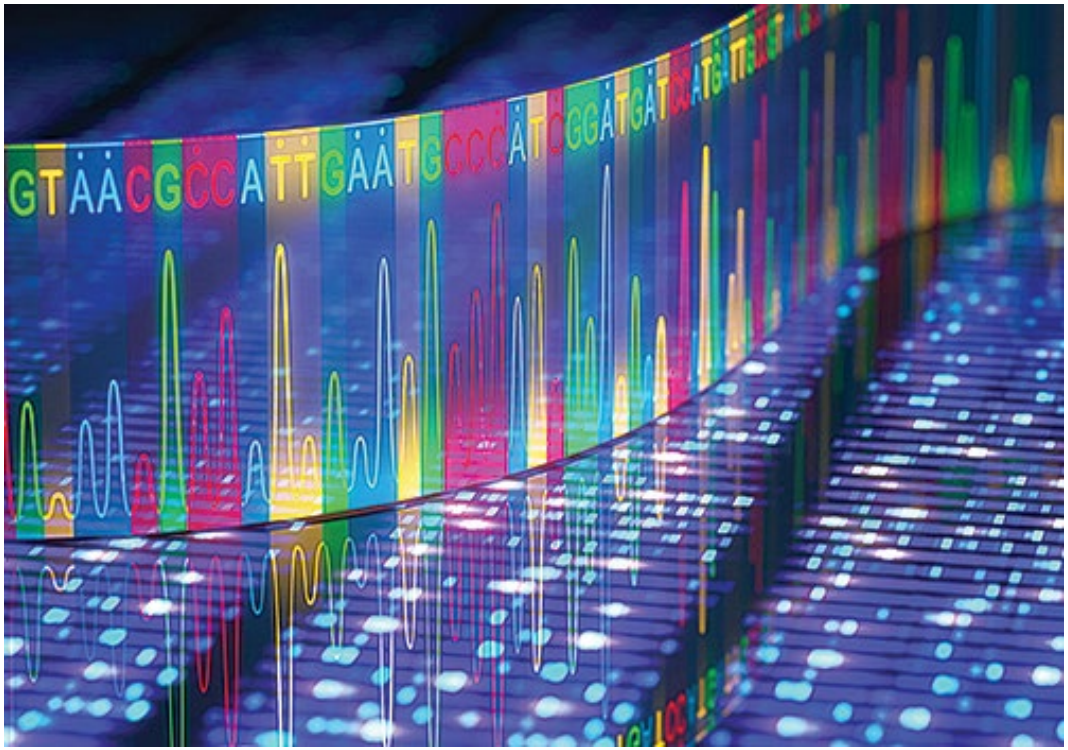
Access Protocol for Neratinib

Inclusion criteria:

"Patients with metastatic cancers with activating ERBB mutations, and/or EGFR amplifications who are refractory to standard or curative therapy does not exist or is not considered sufficient or appropriate by the Physician"

What to do to guide clinical management?

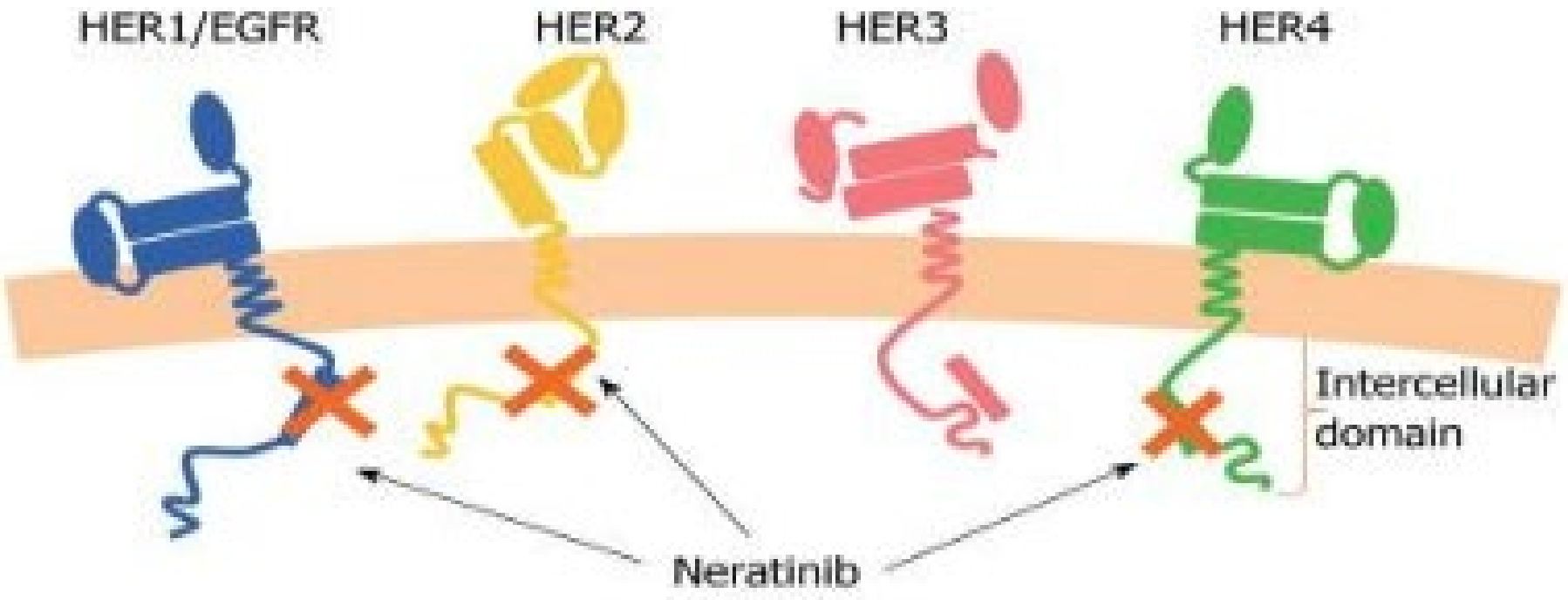
NEXT GENERATION SEQUENCING



Mutation analysis on gastric biopsy: **amplification of EGFR with *a fusion gene EGFR-SMAD4***

NERATINIB

Neratinib is an orally available irreversible tyrosin kinase inhibitor of ERBB1, ERBB2 and ERBB4. This drugs reduces ERBB1and ERBB2 autophosphorylation,downstream signaling, and the growth of ERBB1 and ERBB2 dependent cell lines (Rabindran et al. 2004).



Harpreet Singh, Amanda J. Walker et al U.S. Food and Drug Administration Approval*: Neratinib for the Extended Adjuvant Treatment of Early-Stage HER2-Positive Breast Cancer*

- **May 2019:**Start Neratinib 240 mg/die (OFF LABEL)
- **June 2019**: Decline of general conditions→Exitus

OS: *2 months*

Conclusions

"In clinical oncology precision medicine is a new scenario: in this case we have found a mutational driver for a target therapy as neratinib, but, in real life we have to challenge our practice between the opportunity of treatment, the patients performance, and the tumor itself"

Thank for your attention!