

CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE

2^a EDIZIONE

Terapie di prima linea della malattia metastatica

Terapia di I linea



Focus on patient and disease

- ♀
- 60 years
- teacher
- obesity (130kg), arterial hypertension (controlled – ACE inhibitors), hypercholesterolemia and hypertriglyceridemia on treatment

July 2018:

- tenesmus, FOB +++, abdominal pain, obstructive symptoms

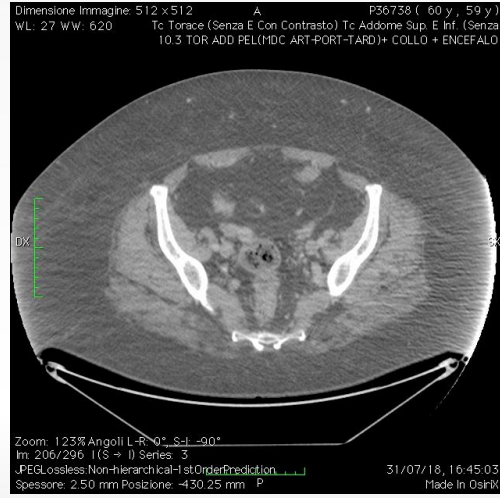
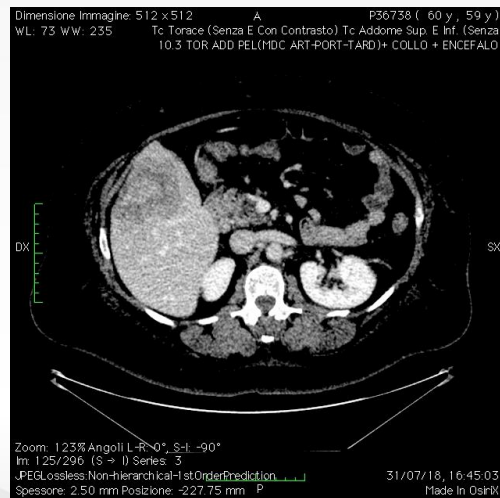
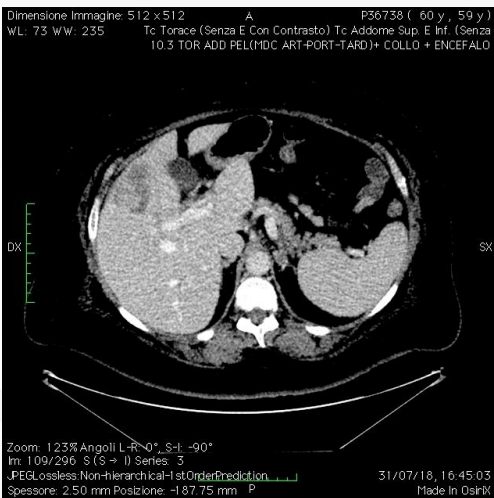
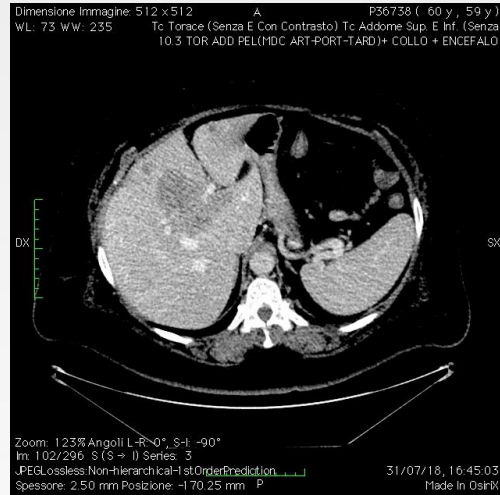
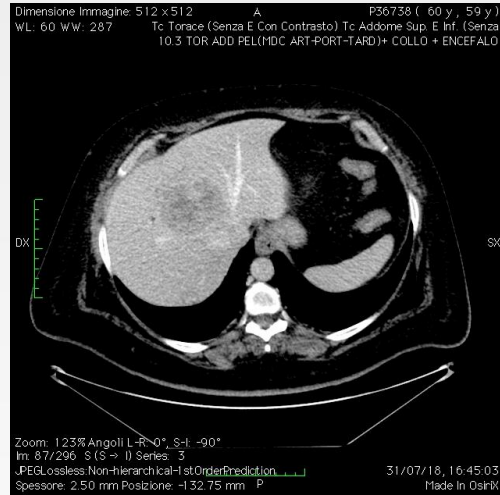
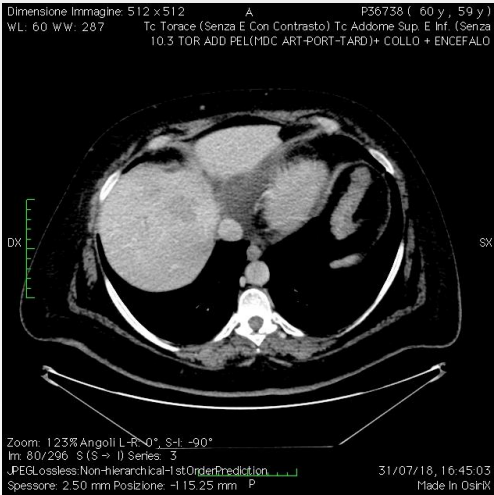
Instrumental examinations:

- Colonoscopy: obstructing heteroplastic tissue at sigma (30 cm from AV)
- CT scan: hepatic secondary lesions. Largest at: IVs (81x64mm) and Vs (76x51mm)
- MRI not possible for the patient's body volume
- Serum markers: CEA 745ng/mL; CA19.9 80U/L



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Endoscopy and CT scan





Focus on patient and disease

- No relevant comorbidities, FIT for chemotherapy
- Liver limited but **unresectable metastases** (localization, number, elevated serum markers)
- Tumor localization: LEFT
- **RAS and BRAF analysis: wild-type**

What treatment?



Prognostic and Predictive Relevance of Primary Tumor Location in Patients With *RAS* Wild-Type Metastatic Colorectal Cancer

Retrospective Analyses of the CRYSTAL and FIRE-3 Trials

Sabine Tejpar, MD; Sebastian Stintzing, MD; Fortunato Ciardiello, MD; Josep Tabernero, MD; Eric Van Cutsem, MD; Frank Beier, PhD; Regina Esser, MD

The relevance of primary tumour location in patients with metastatic colorectal cancer: A meta-analysis of first-line clinical trials

Julian Walter Holch^{a,b,*}, Ingrid Ricard^c, Sebastian Stintzing^{a,b},
Dominik Paul M...^{a,b}



Annals of Oncology 0: 1–17, 2017
doi:10.1093/annonc/mdx175
Published online 12 April 2017



SPECIAL ARTICLE

Prognostic and predictive value of primary tumour side in patients with *RAS* wild-type metastatic colorectal cancer treated with chemotherapy and EGFR directed antibodies in six randomized trials[†]

D. Arnold¹, B. Lueza², J.-Y. Douillard³, M. Peeters⁴, H.-J. Lenz⁵, A. Venook⁶, V. Heinemann⁷, E. Van Cutsem⁸, J.-P. Pignon², J. Tabernero⁹, A. Cervantes^{10,11} & F. Ciardiello^{12*}



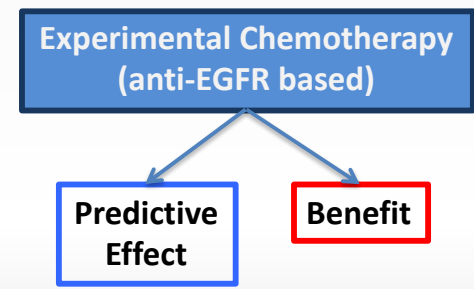
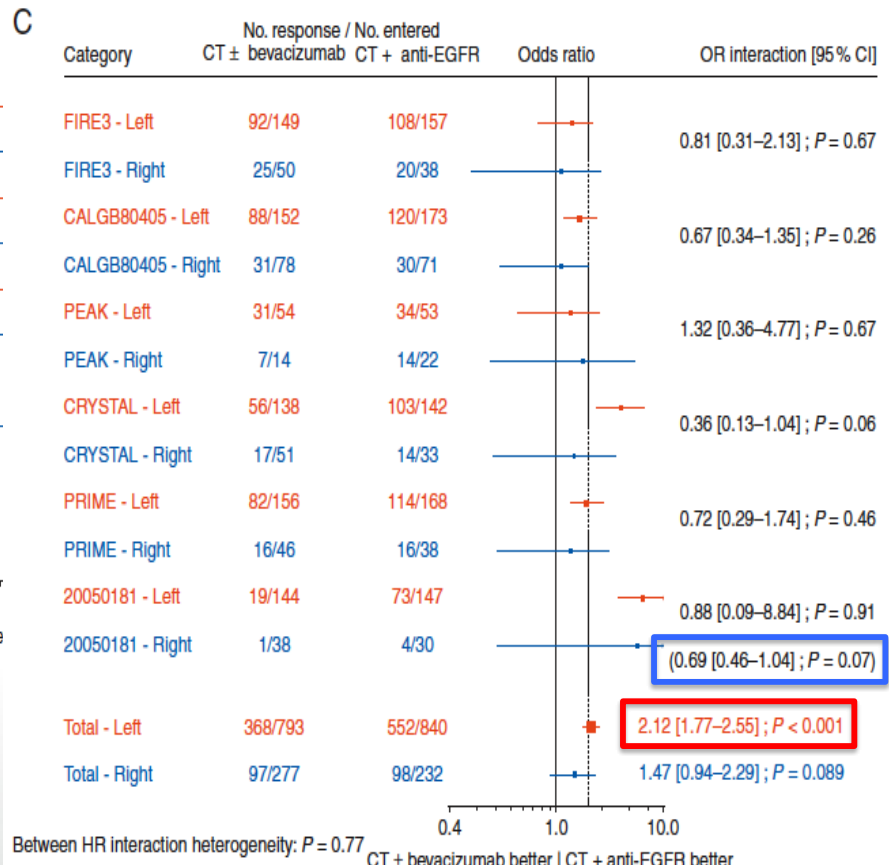
Pooled Analysis: OS



Pooled Analysis: PFS

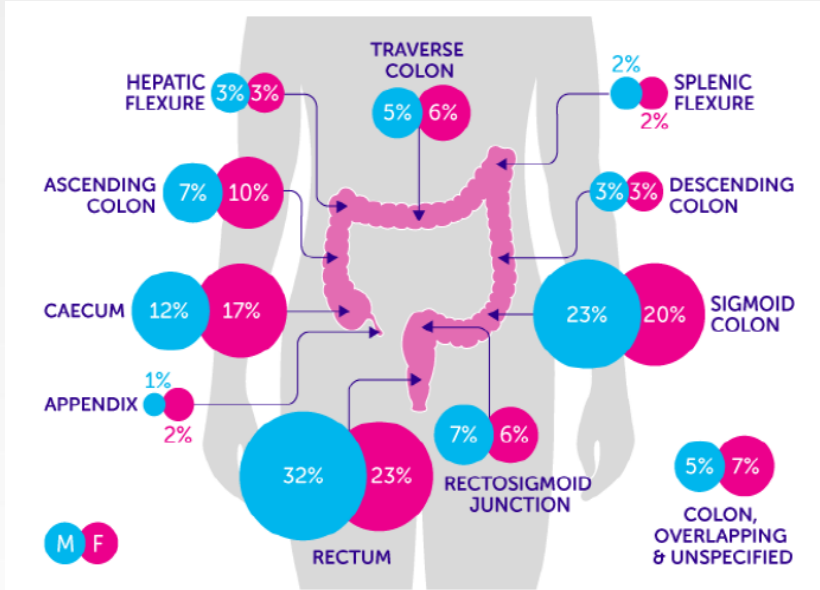


Pooled Analysis: ORR





Focus on treatment: rationale



In right side:

PFS: CT or CT/Bev > CT/EGFR
 OS: CT or CT/Bev > CT/EGFR
 ORR: CT/EGFR > CT or CT/Bev

In left side

PFS: CT/EGFR > CT or CT/Bev
 OS: CT/EGFR > CT or CT/Bev
 ORR: CT/EGFR > CT or CT/Bev

In RAS/BRAF wild-type patients with left primary tumor, first line therapy should be based on the combination anti-EGFR + chemotherapy independently from endpoint



Focus on patient and disease

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- Tumor localization: LEFT
- **RAS and BRAF analysis: wild-type**

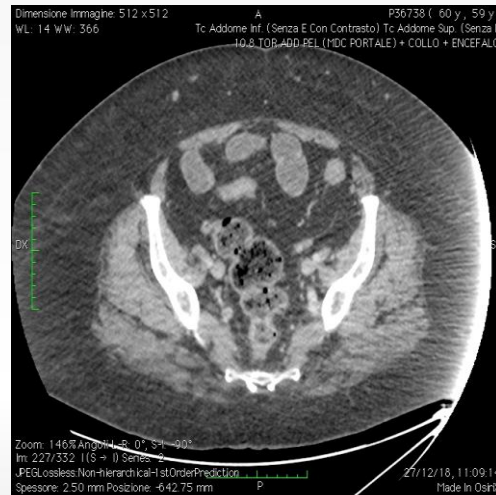
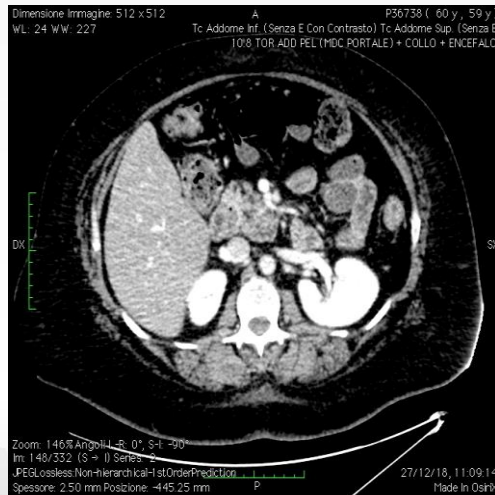
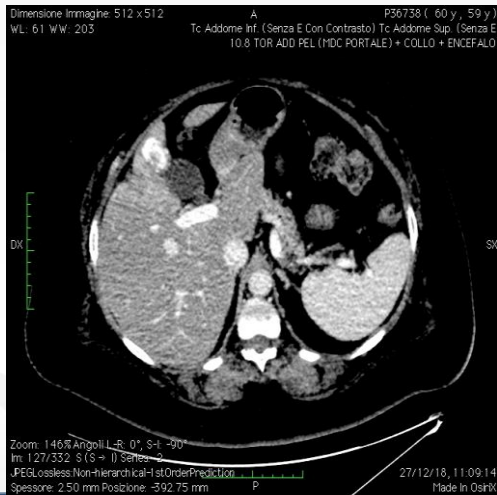
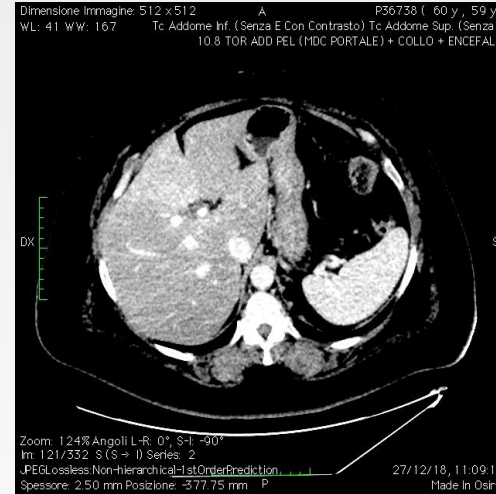
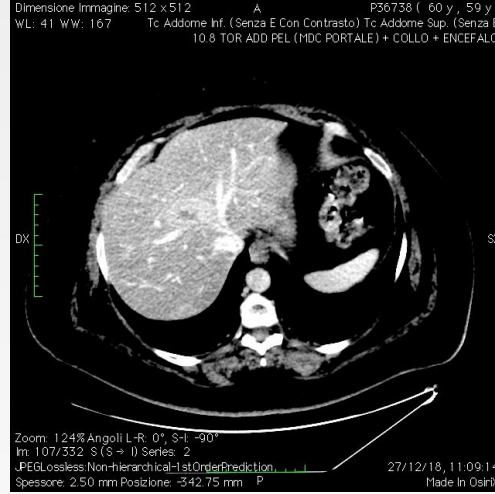
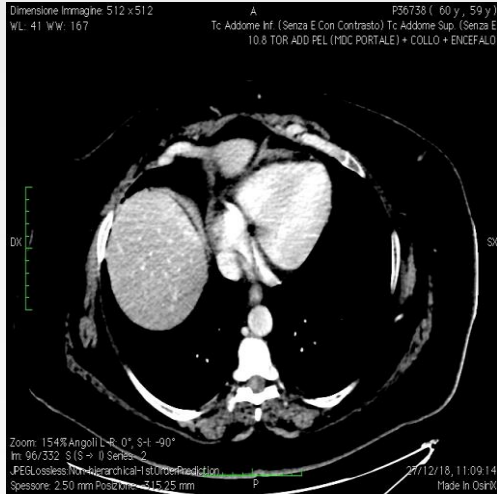
ChT + anti-EGFR

Stop and go strategy
FOLFIRI + panitumumab





Evaluation on treatment after 4 months (December 2018)



Reported side effects:

- G1 ocular conjunctivitis
- G2 skin rash
- G1 paronychia

STOP treatment

MDT: not indicated surgery



Management of skin toxicity

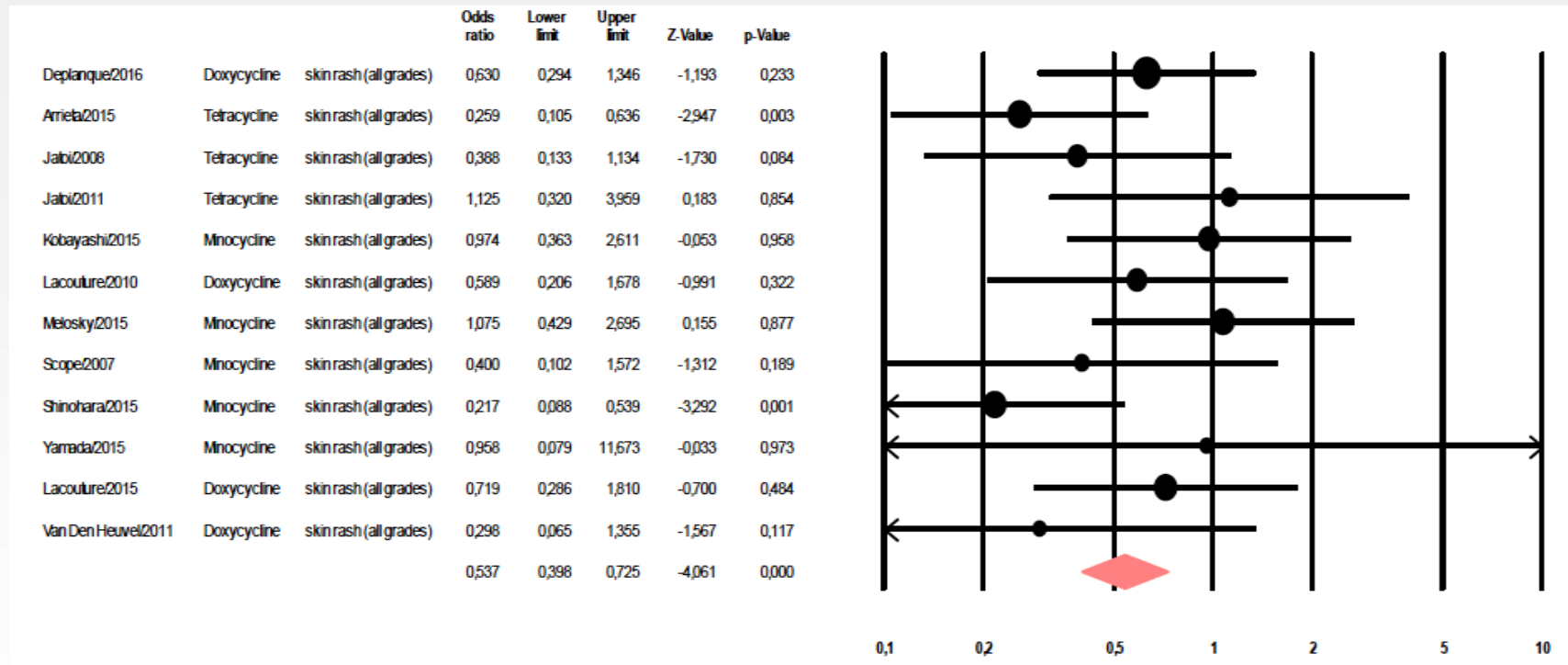
Pre-emptive skin treatment:

- Doxycycline 100 mg twice daily. During the assumption of doxycycline, the patient must be advised to drink plenty of liquids to reduce the risk of esophageal irritation and ulceration; he/she must take doxycycline in upright position and must not lie down for an hour after taking the drug. The patient should not take iron supplements, multivitamins, calcium supplements, antacids, or laxatives within 2 hours before or after taking doxycycline. Please remember that the absorption of tetracyclines is reduced when taken with foods, especially those containing calcium.
- Skin moisturizer applied to face, hands, feet, neck, back, and chest daily in the morning on rising





Management of skin toxicity: rationale for preemptive treatment



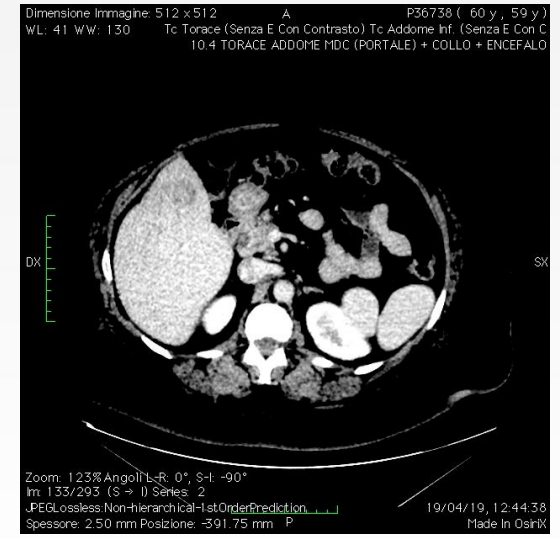
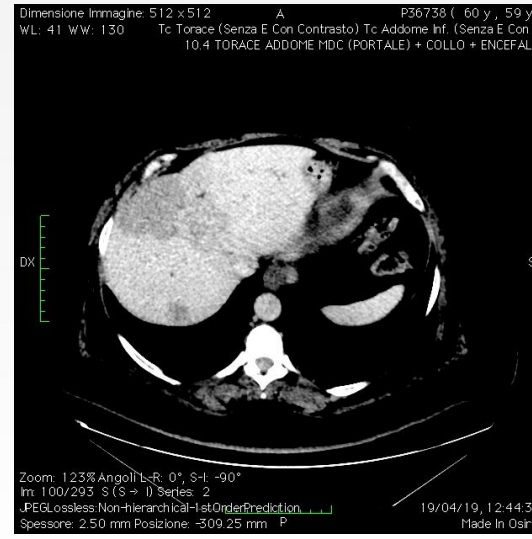
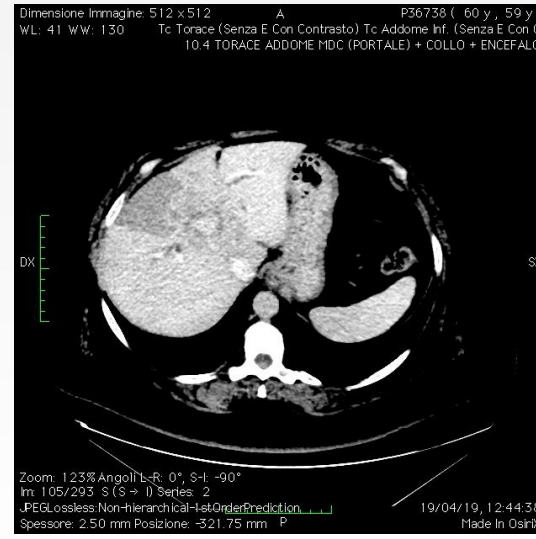
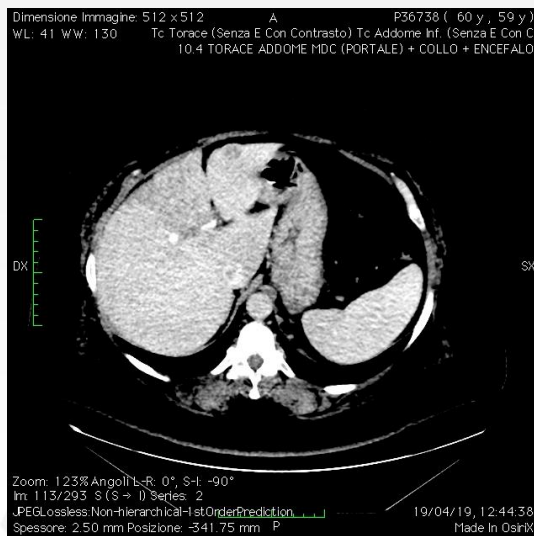
The results of this meta-analysis showed that the risk of skin rash after treatment with anti-EGFR agents for solid tumors was significantly lower in patients taking prophylaxis with antibiotics compared to those who were not



Focus on patient: relapse (April 2019)

CT scan: PD

Serum markers: CEA 124 ng/mL CA19.9 371 U/L



Reintroduction of FOLFIRI + panitumumab

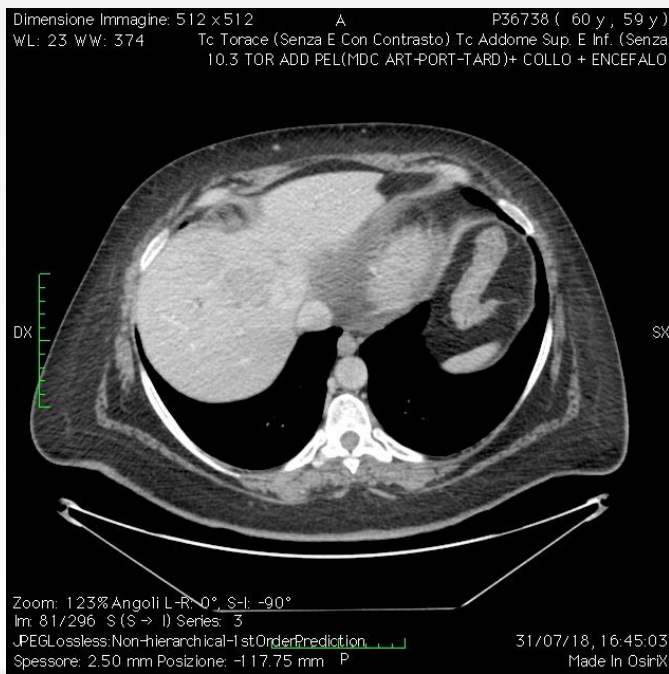


Evaluation of disease after 4 months

CT scan: response of liver lesions, reliable only in part

Serum markers: CEA 6 ng/mL CA19.9 17 U/L

Colonoscopy (08/2019): small residual disease, only partially ulcerated



How to proceed?



MDT evaluation

- Shrinkage of liver lesions
- Normal serum markers
- Response of primary tumor

- MDT decision: patient eligible for surgery
 - reverse approach





Surgery

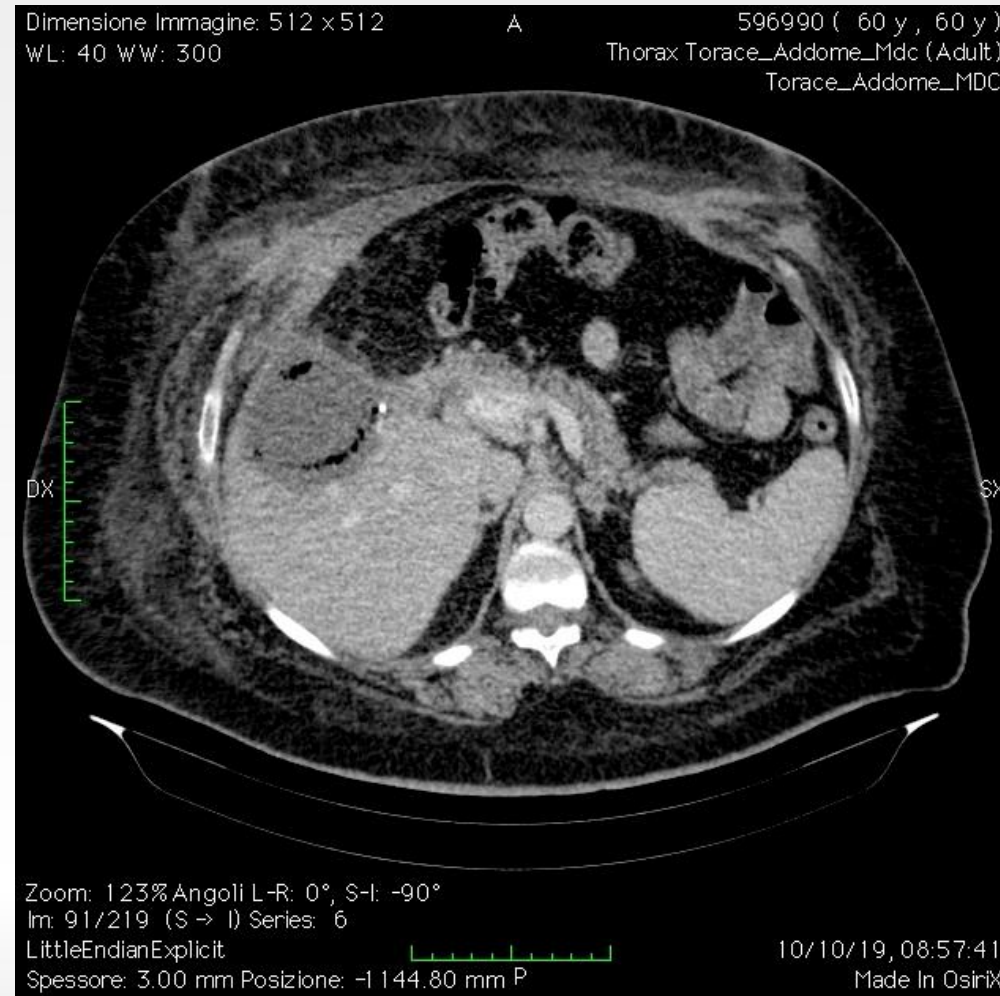
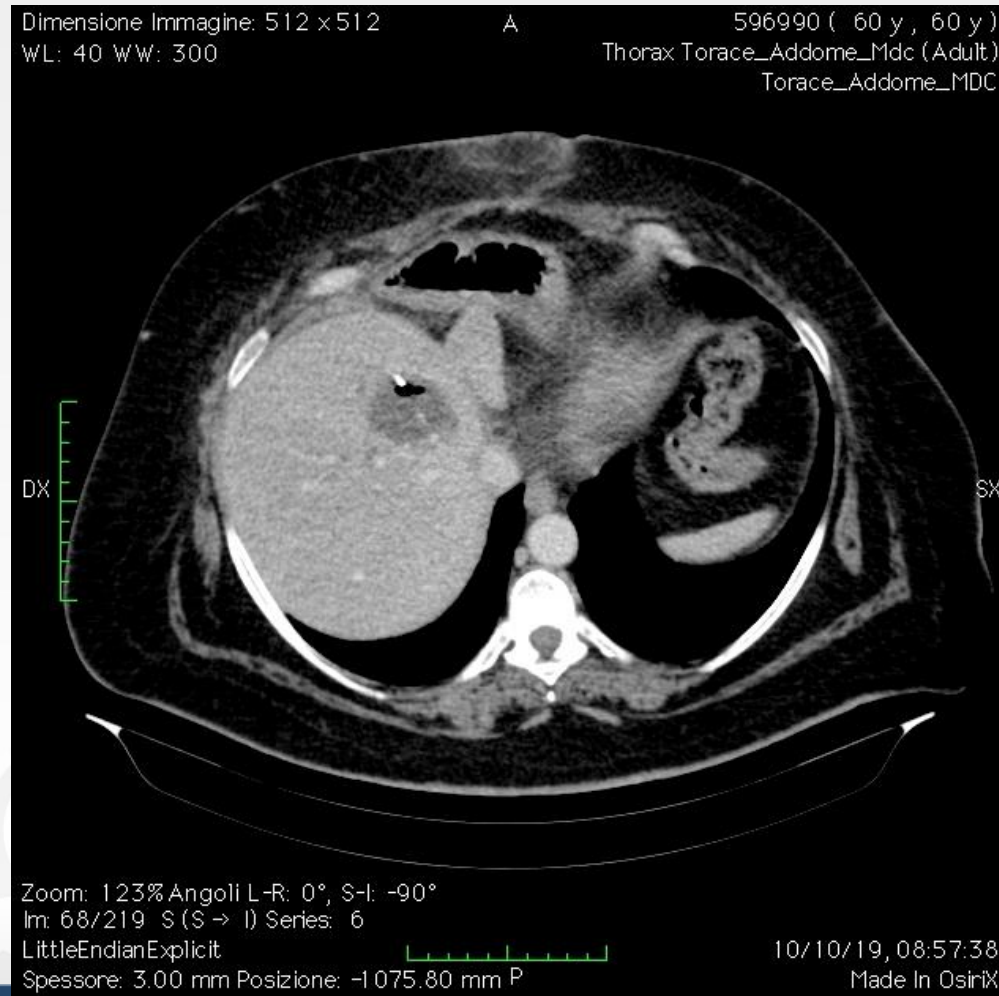
September 2019:

Resection of liver lesions (left hepatectomy): all lesions compatible for metastases from colon cancer





Post operative evaluation (40 days after surgery)





Surgery

December 2019

Resection of primary tumour: adenocarcinoma pT3pN1aG2 MSS

Follow up

April 2020

Liver relapse: chemotherapy (FOLFIRI + panitumumab) till March 2021

April 2021

Carcinomatosis: second-line chemotherapy (FOLFOX + bevacizumab)





Conclusions

- ✓ In our clinical practice molecular analysis of RAS/BRAF (...at least) is mandatory before beginning chemotherapy
- ✓ Patients with left primary tumor should be treated with anti-EGFR + chemotherapy whatever the endpoint
- ✓ Pre-emptive treatment of cutaneous toxicity should be considered before beginning an anti-EGFR based treatment
- ✓ The role of MDT confirms to improve prognosis of patients
- ✓ In this case operability was obtained only after reintroducing treatment



