Categorization of liver limited mCRC and its approaches (neoadjuvant, conversion, palliative)

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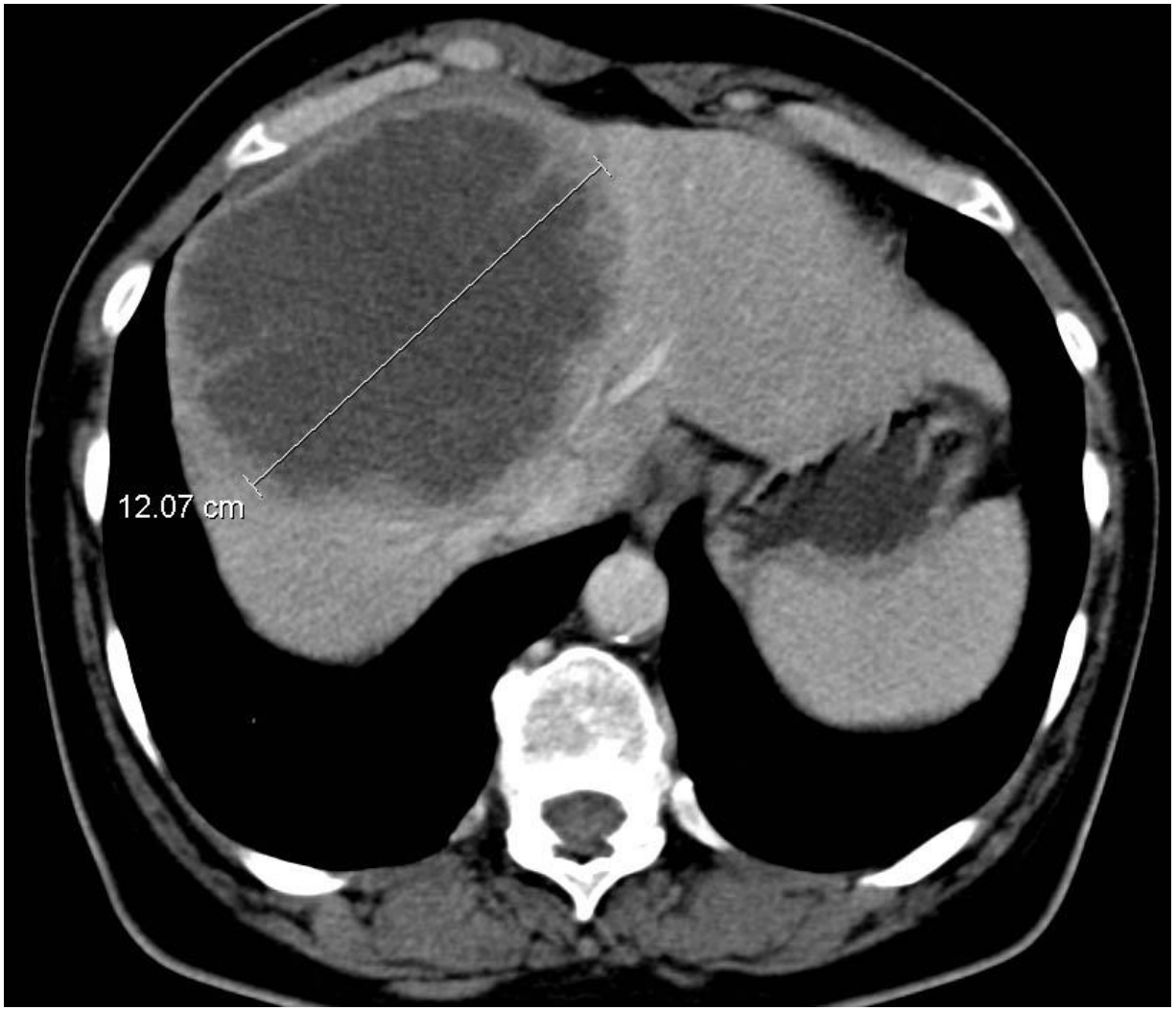
Disclosures

Research funding, speakers Bureau, Advisory role:

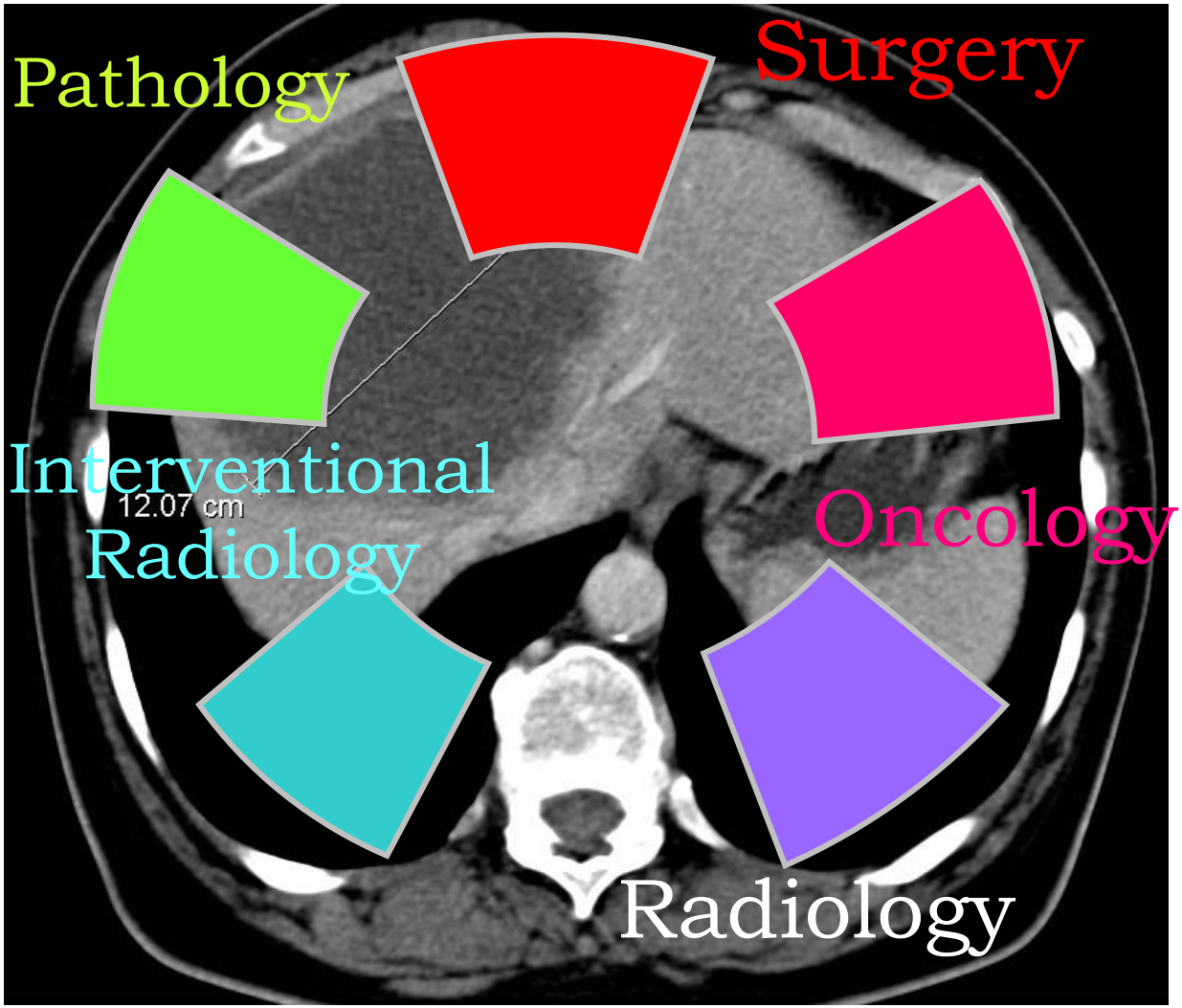
- Roche
- Merck-Serono
- Bayer
- Sanofi-Aventis
- Amgen

Requirements



Requirements

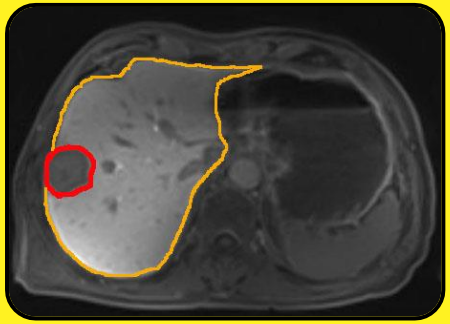
The MDT meeting



Criteria to define resectability in mCRC

Upfront resectable (10%)

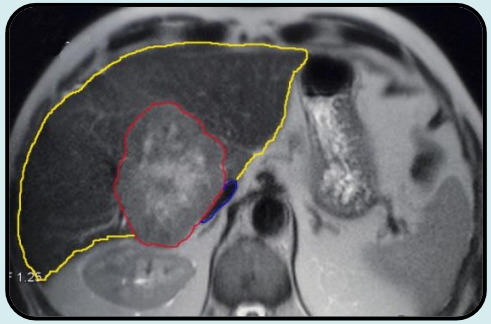
- Sufficient remnant liver (30% of healthy liver volume)
- Possibility of upfront R0 resection



Neoadjuvant Therapy

Borderline resectable (20%)

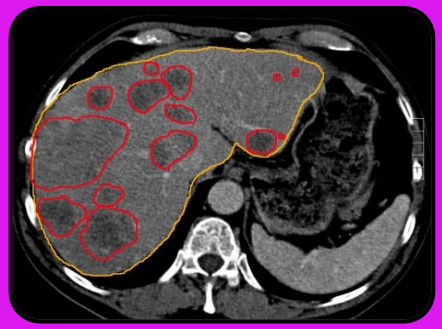
- Requirement of tumour downsizing to achieve resectability
- Invasion or contact of metastases with preservable vascular structures



Conversion Therapy

Unresectable (70%)

- Multiple disease sites
- All liver segments infiltrated by metastases
- Poor patient performance status



Palliative Therapy

Assessment of individual cases by multidisciplinary teams (MDTs) is critical

Nordlinger et al, AnnOncol 2009

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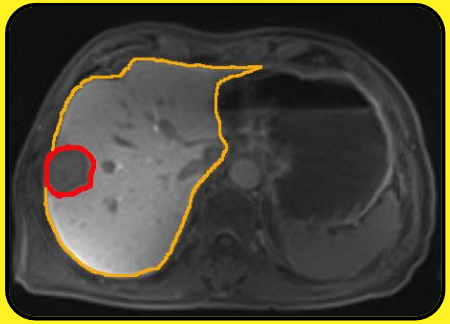

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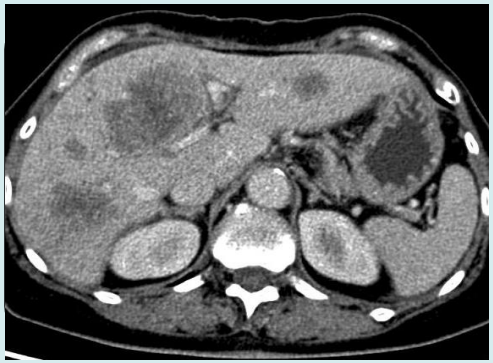

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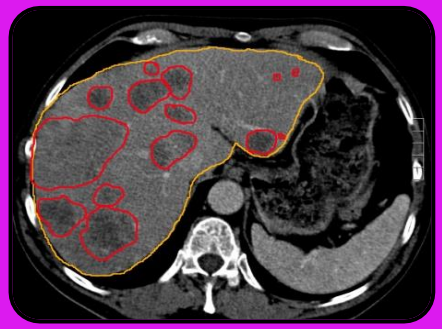

Palliative Therapy

Assessment of individual cases by multidisciplinary teams (MDTs) is critical

Nordlinger et al, AnnOncol 2009

Unresolved issues

- How can we best agree upon resectability
- What place do biologics have in the neoadjuvant/conversion setting
- Which treatment combination leads to the best ORR
- How long should we treat prior to attempted surgery
- Value of radiological compared to pathological response
- How should we evaluate liver function and liver damage
- What should we do with the primary in synchronous mCRC
- Who is the ideal candidate for a potential curative approach

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Upfront resectable CRLM

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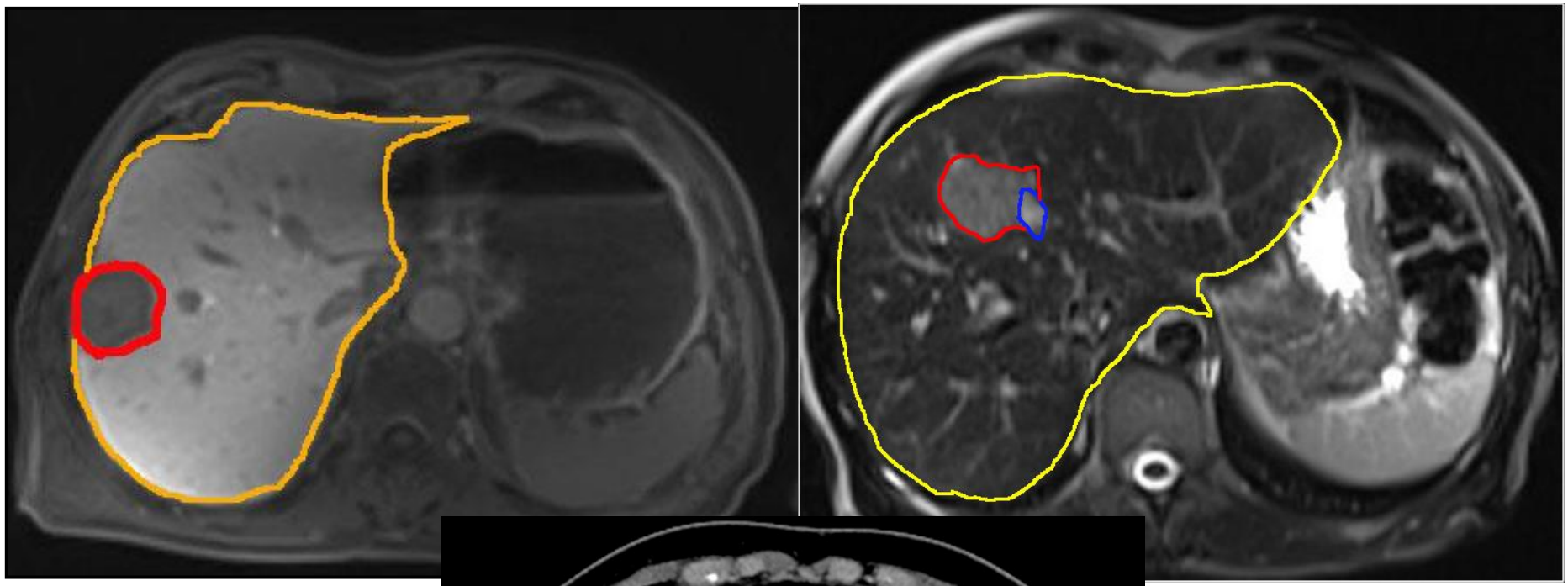

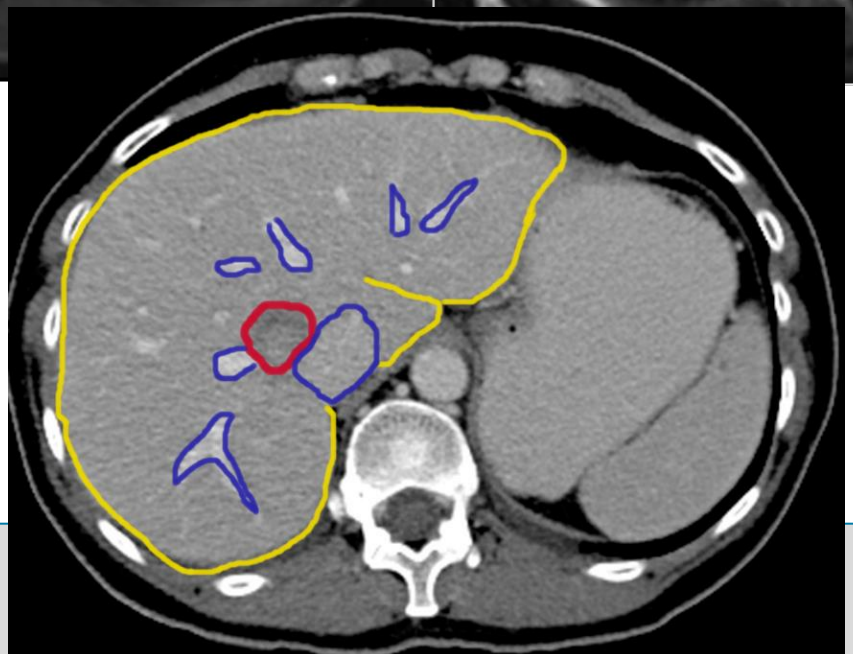

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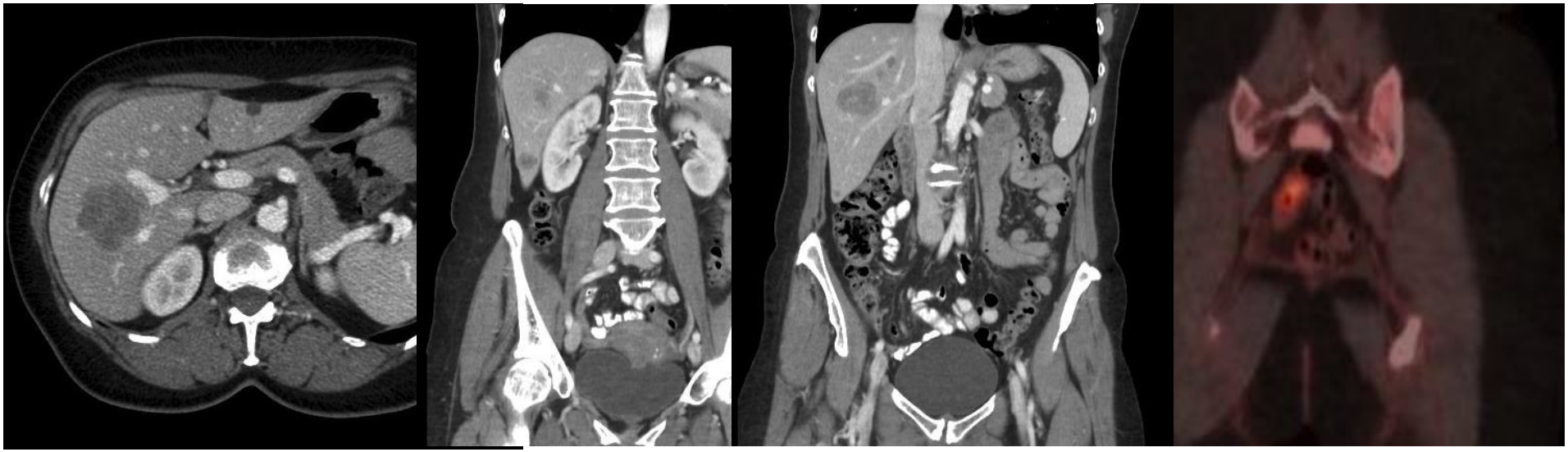
Neoadjuvant CTx approach (LLD)

Study	CTx	n	ORR, (%)	LR rate (%)	mPFS (mts)	mOS (mts)
EORTC 40983[1]	FOLFOX 4 vs Surgery alone	364	43	83 vs 84	20 vs 12 (*0.041*)	64 vs 55
New EPOC [2]	FOLFOX6+ Cetuximab vs FOLFOX6	260	70 vs 62	87 vs 93	14 vs 21 (*0.030*)	39 vs n.r.
BOS [3]	FOLFOX+Cetux vs FOLFOX+Cetux+Bev	43	68 vs 57	91 vs 76	15 vs 14	n.r. vs 48

[1] *Nordlinger Lancet 08, LancetOnc 13* ,[2] *Primrose LancetOnc 14,*
[3] *personal communication*

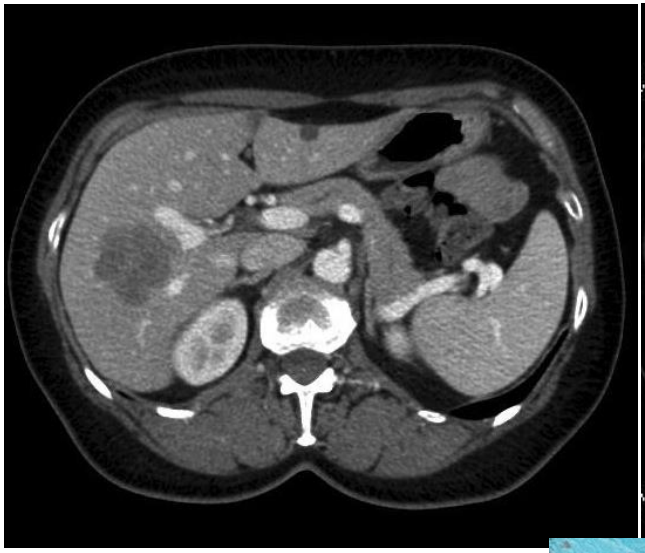
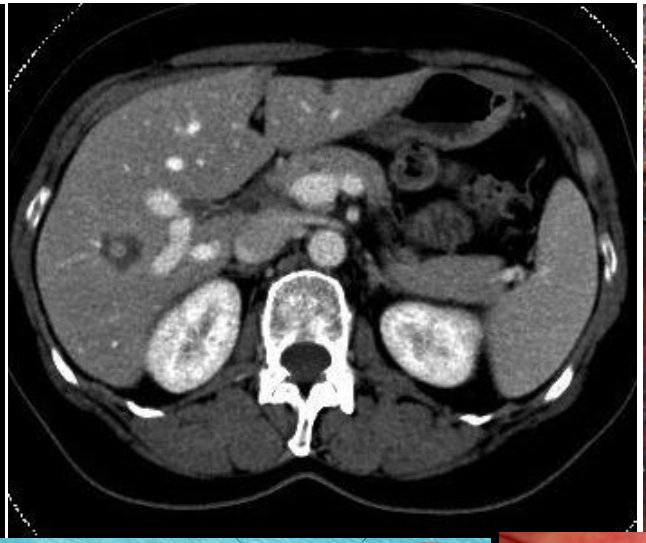
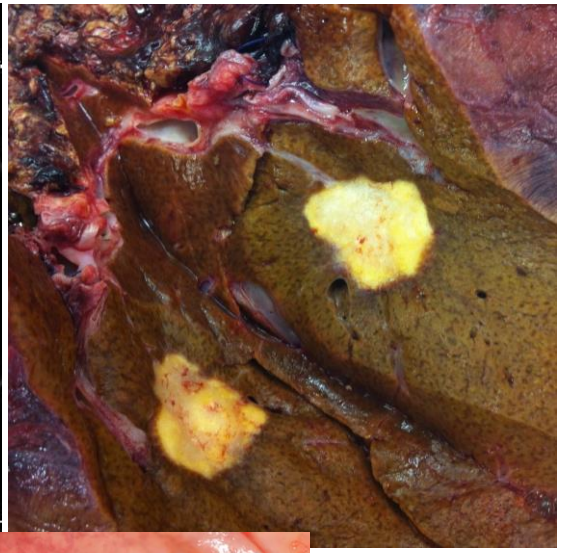
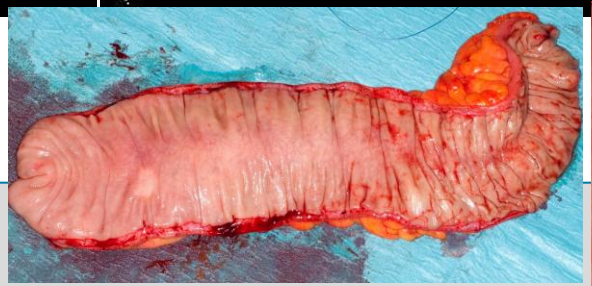
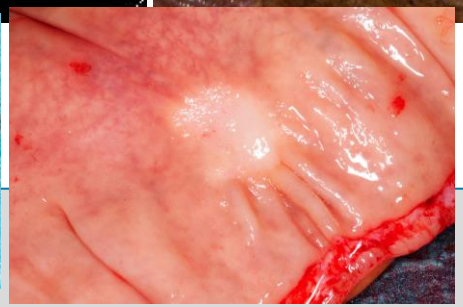
mCRC

- 58a female, ECOG 0
  - Diagnosis of mCRC during follow-up of her known liver haemangiomas
  - 3 rigth sided CRLM, asymptomatic primary; CEA 7

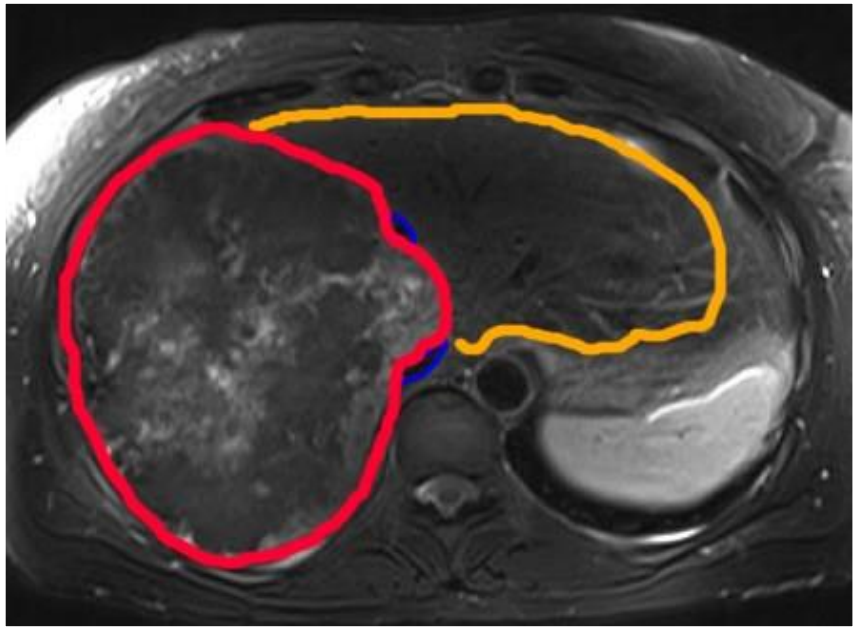


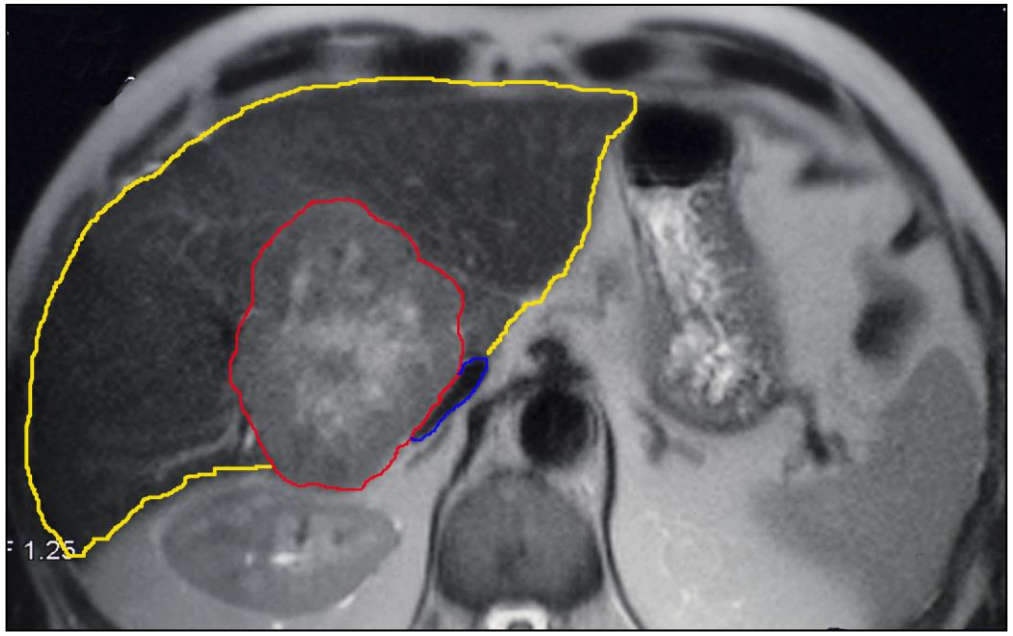
mCRC

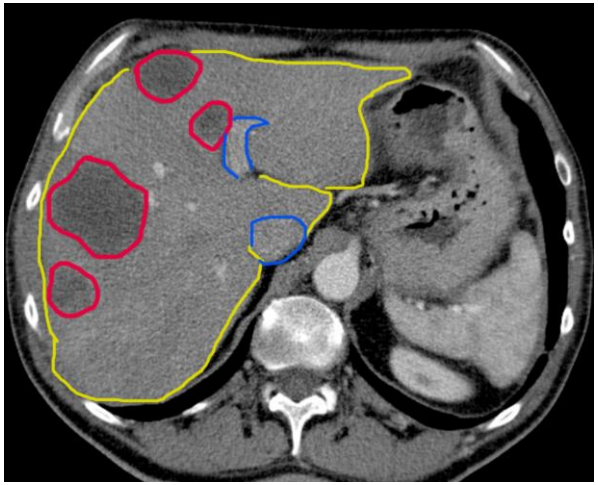
- 58a female, ECOG 0
  - Neoadjuvant Xelox + Bevacizumab over 2 months
  - Radiologic PR; CEA 2; pathologic MhR

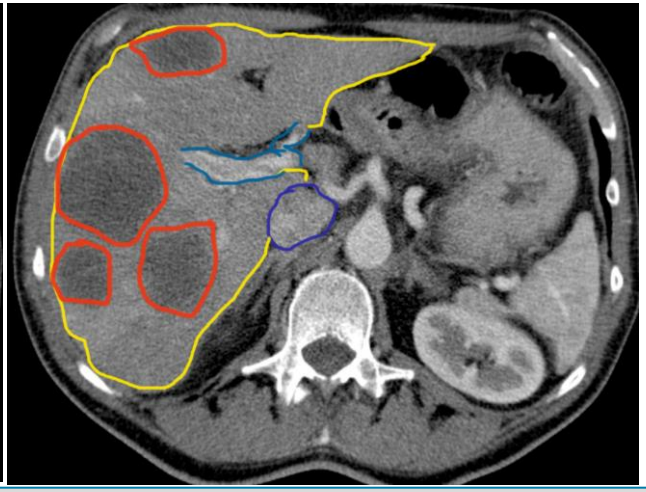






Borderline resectable CRLM







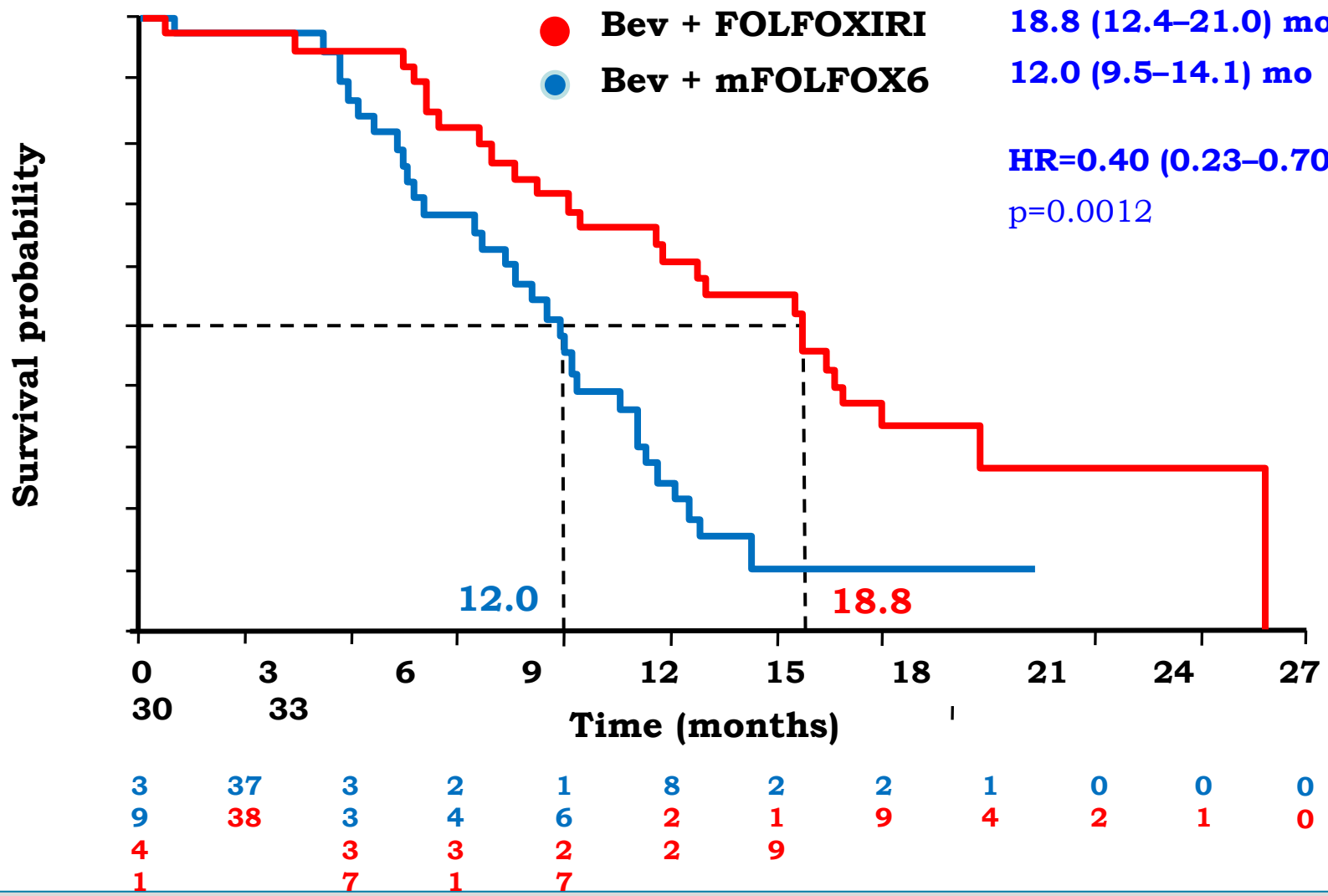


Conversion CTx approach (LLD)

Study	CTx	Controlled study	n	RR, (%)	liver resection rate, (%)
Vie-LM-Bev [1]	Xelox + Bevacizumab	No	56	73	93
GONO [2]	Folfoxiri + Bevacizumab	No	30	80	40
Boxer [3]	Xelox + Bevacizumab	No	45	78	40
Olivia[4]	Folfoxiri + Bev vs Folfox + Bev	yes	80	81 vs 62	49 vs 23 (R0)
CELIM [5]	FOLFOX6/FOLFIRI + Cetuximab	No	106	70	33
POCHER [6]	Chrono-IFLO + Cetuximab	No	43	79	60
Ye[7]	Folfiri/Ox +/- Cetux	yes	116	57 vs 29	26 vs 7 (R0)

[1] Gruenberger JCO 08, [2] Masi LancetOnc 10, [3] Wong AnnOnc 11, [4] Gruenberger ASCO 13, [5] Folprecht LancetOnc 09, [6]Garufi, BJC 10, [7]Ye, JCO 13

Progressions-free survival: ITT



Median (95% CI)

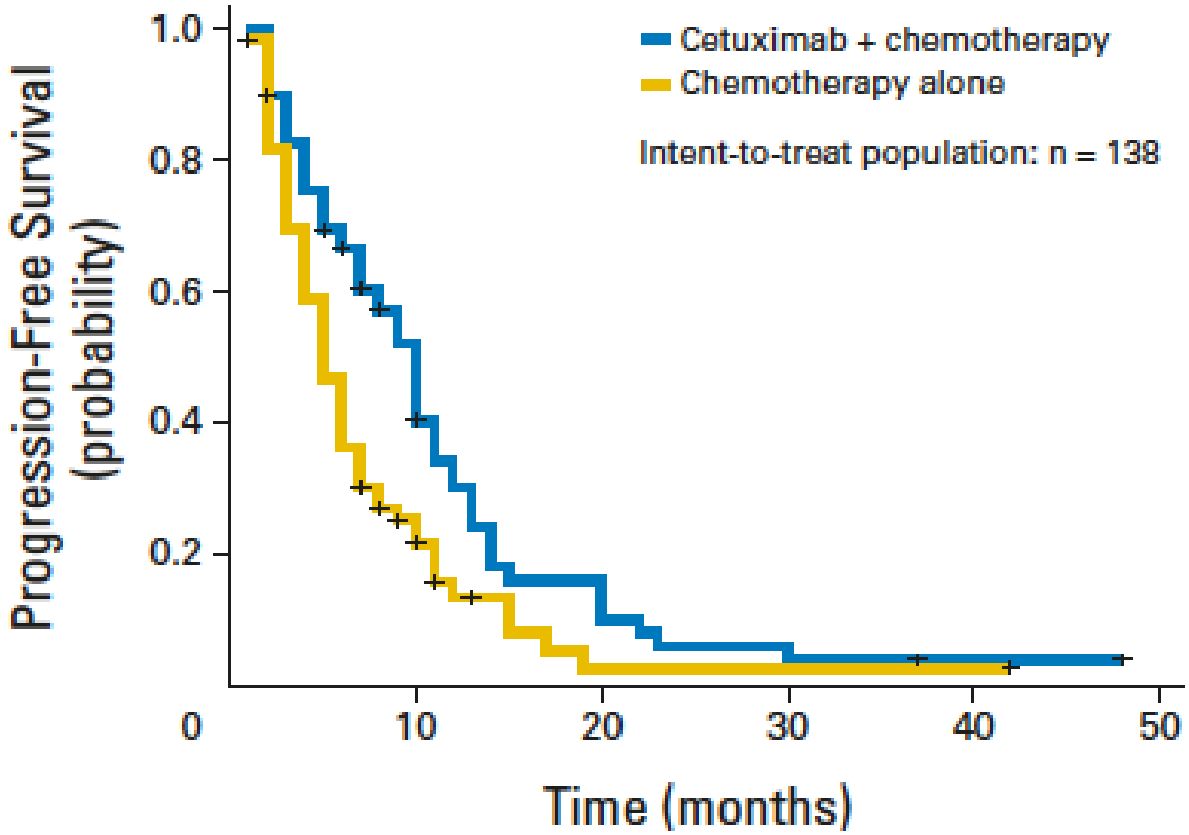
18.8 (12.4–21.0) mo

12.0 (9.5–14.1) mo

HR=0.40 (0.23–0.70)

p=0.0012

Progressions-free survival: ITT



No. at risk						
Cetuximab + chemotherapy	70	31	8	3	1	0
Chemotherapy alone	68	14	1	1	1	0

Median (95% CI)

10.2 (8.6–11.4) mo

5.8 (3.9–6.1) mo

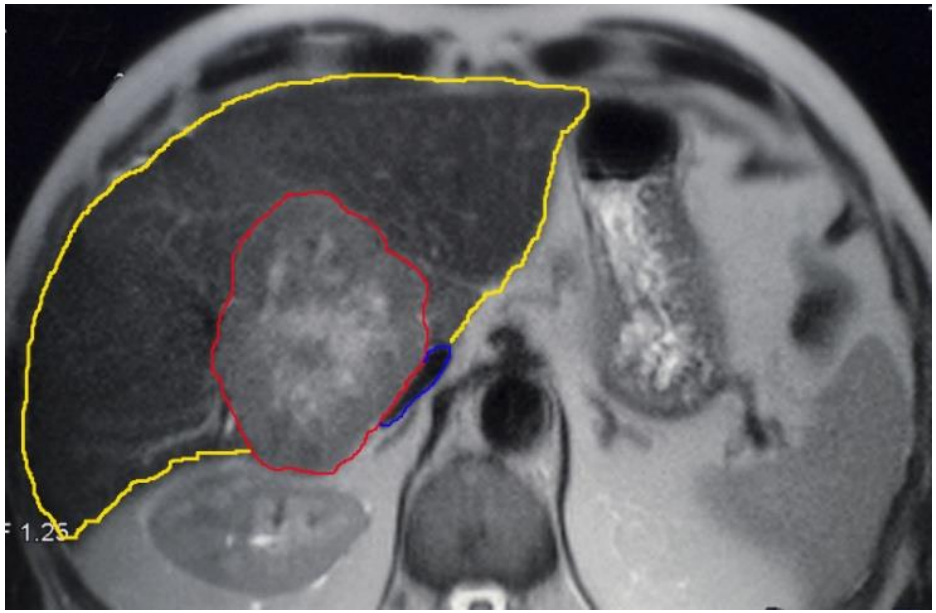
HR=0.60 (0.41–0.87)

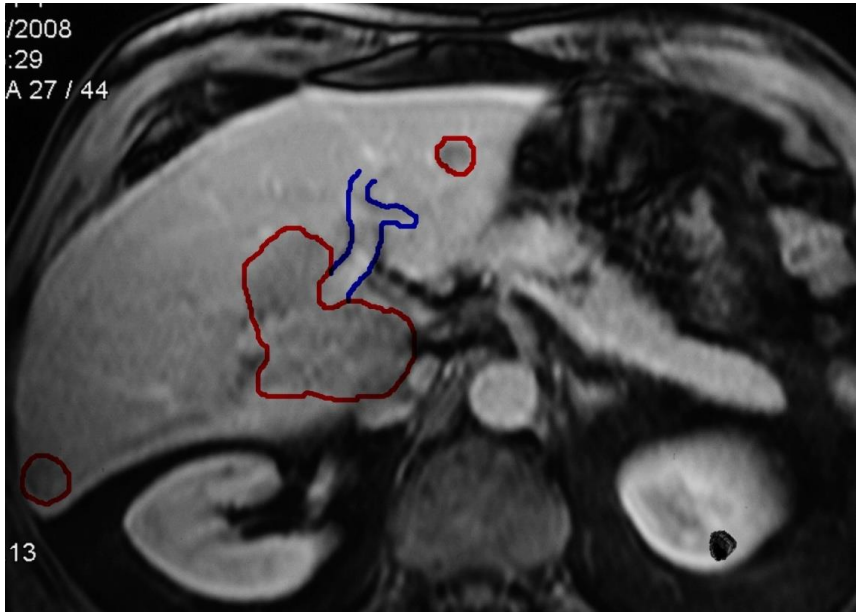
p=0.004

Ye et al; JCO 2013

Borderline resectable CRLM

- 62a male, ECOG 0
  - Diagnosis of metachronous initially borderline resectable CRLM (LLD)
  - 1 central CRLM, 1 additional lesions in each lobe ; CEA 143





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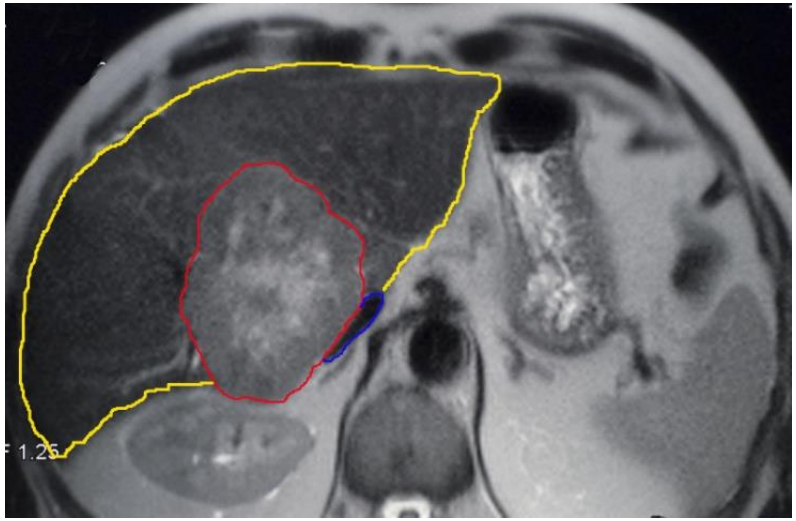
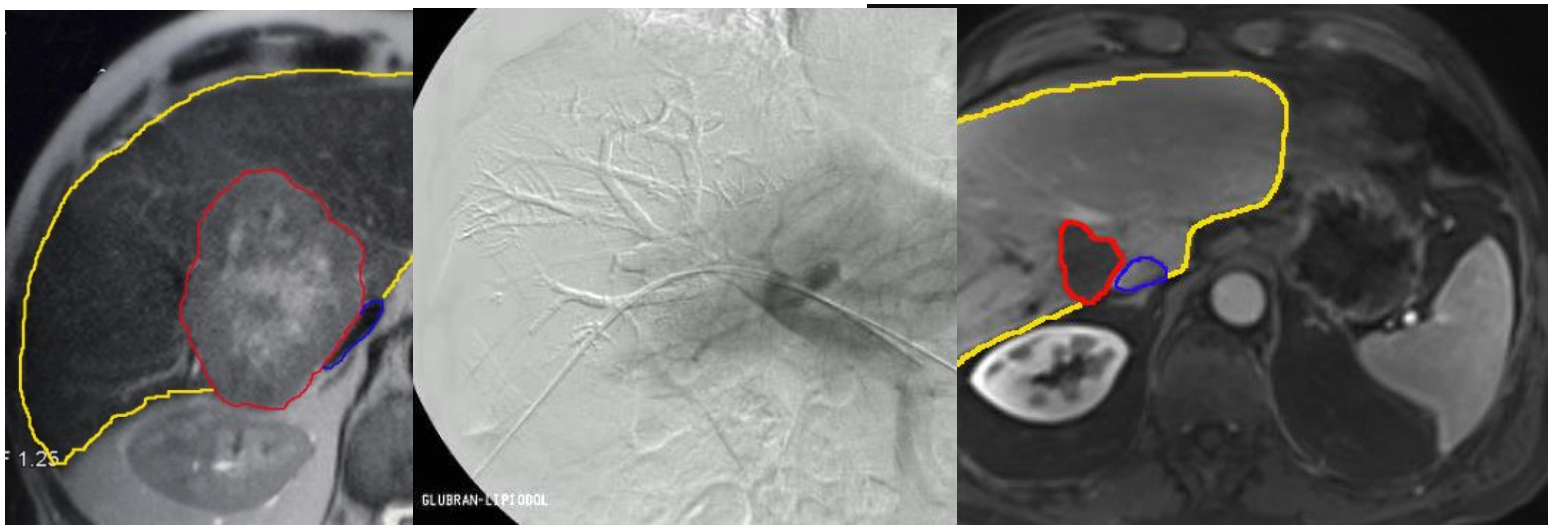


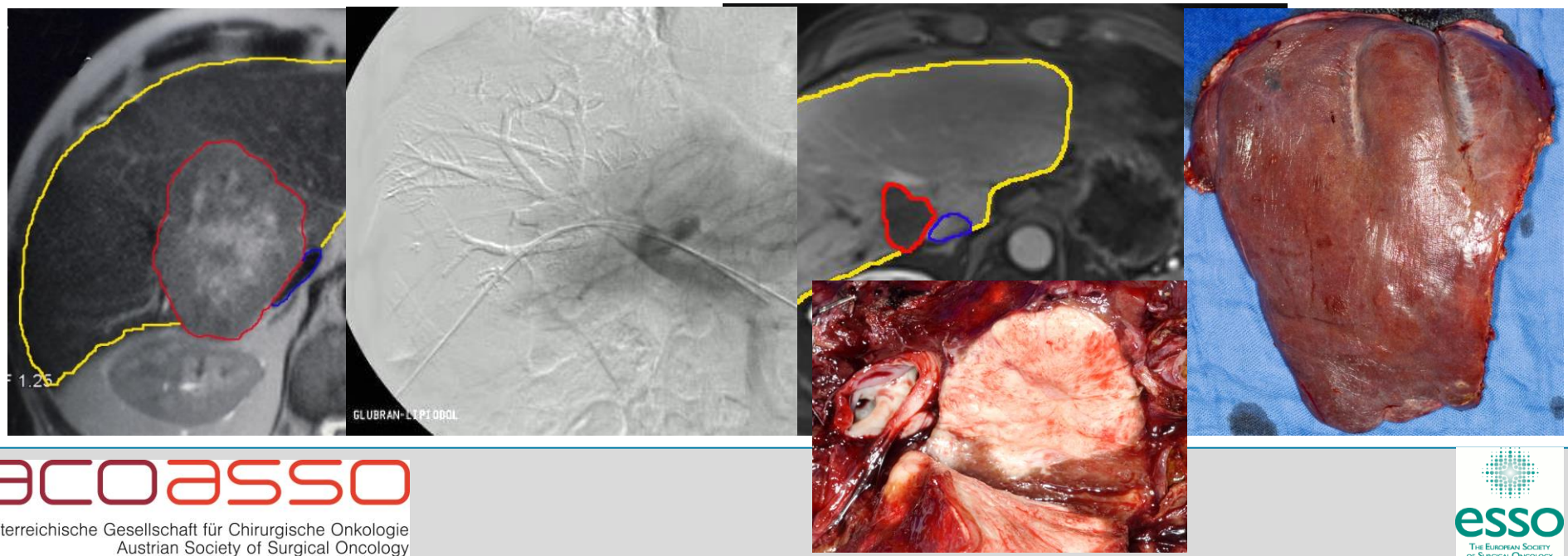
Borderline resectable CRLM

- 62a male, ECOG 0
  - Diagnosis of metachronous initially borderline resectable CRLM (LLD)
  - 3 months FOLFOXIRI + Bevacizumab with rad PR



Borderline resectable CRLM

- 62a male, ECOG 0
  - Diagnosis of metachronous initially borderline resectable CRLM (LLD)
  - 3 months FOLFOXIRI + Bevacizumab with rad PR
  - rPVE, extended r hemihepatectomy
  - Pathological complete response (0% viable tumor cells)



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Unresectable CRLM

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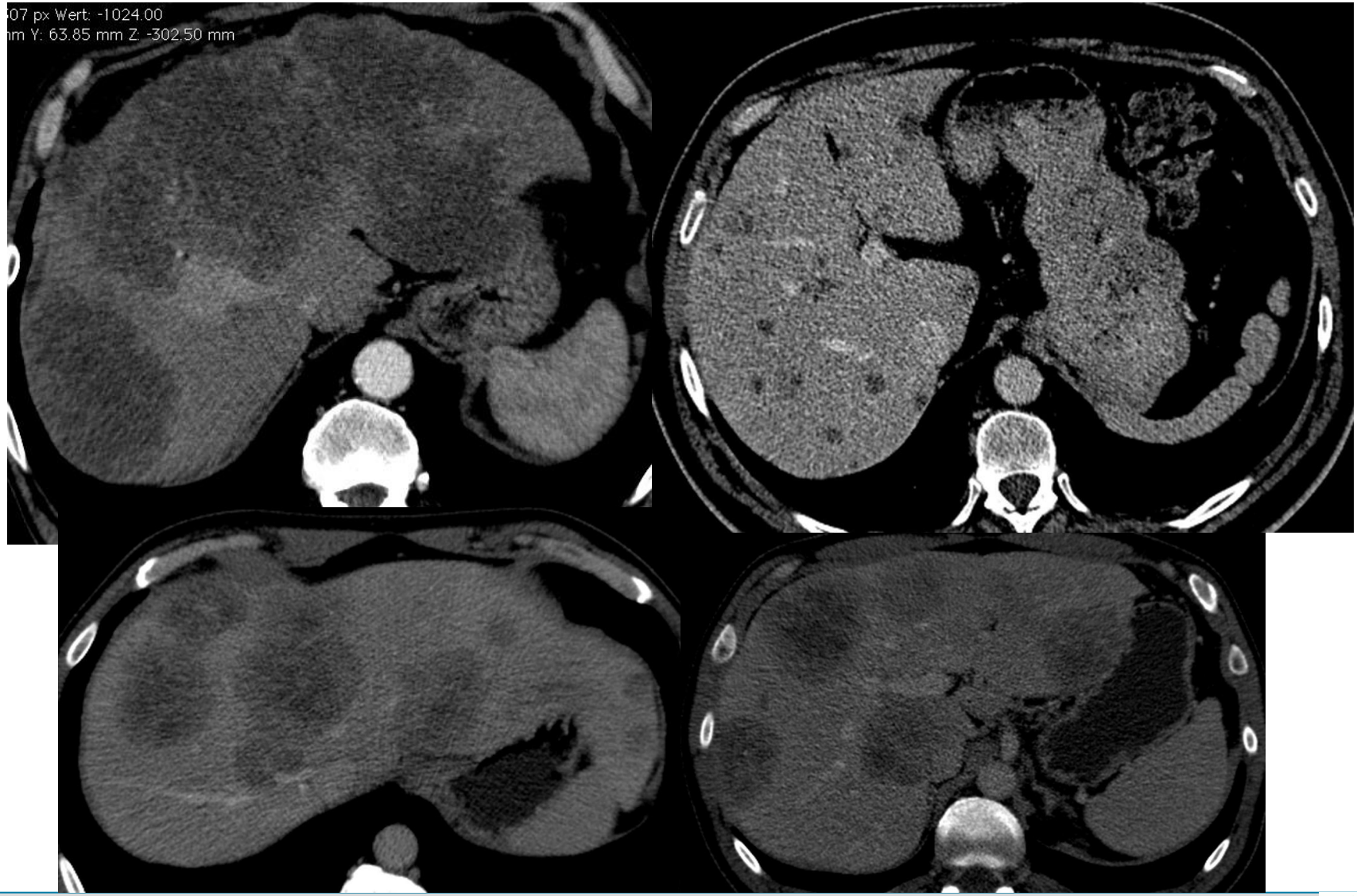

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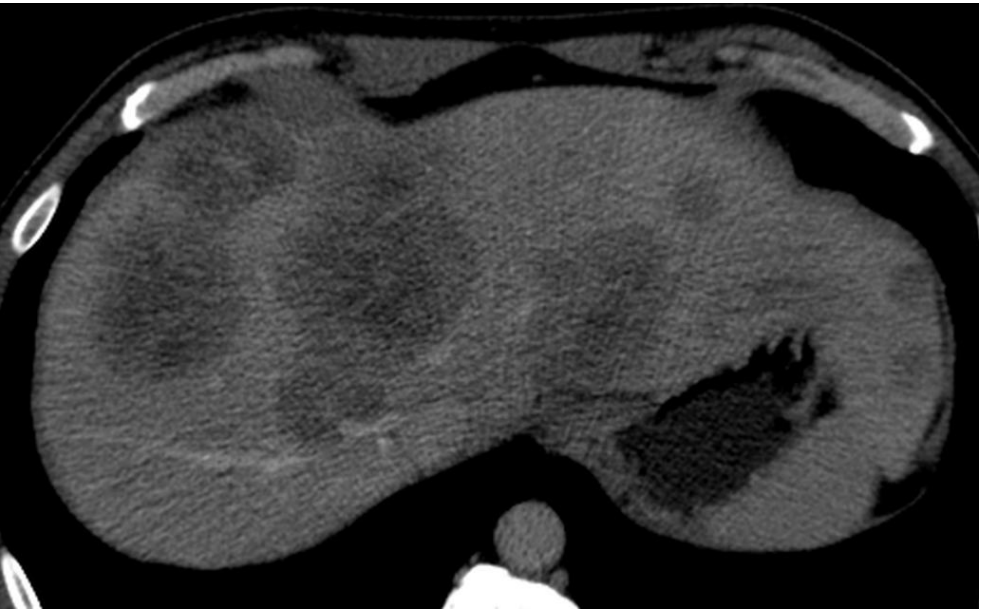
Palliative CTx approach

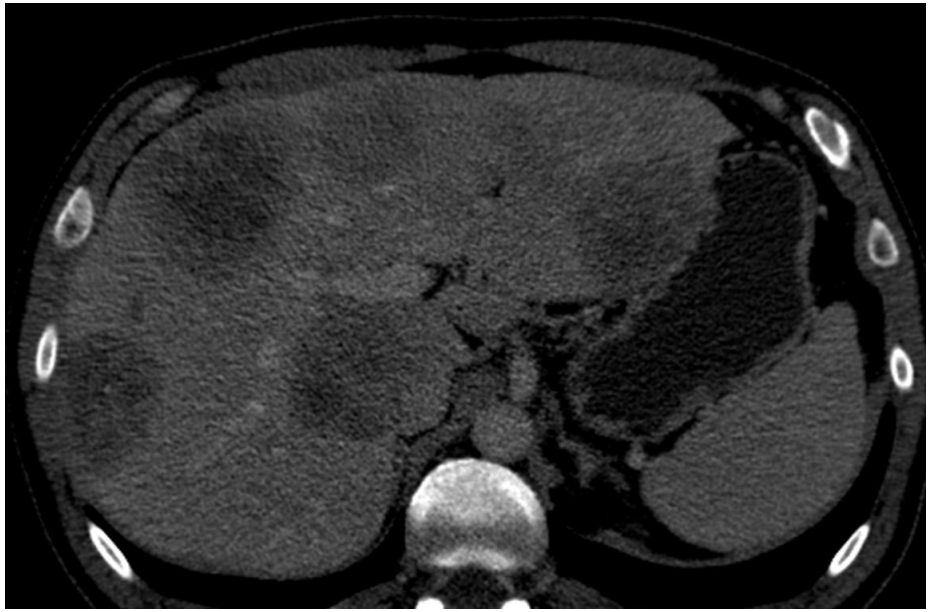
Study	CTx	n (all wt)	ORR, (%)	LR rate (%)	mPFS (mts)	mOS (mts)
CALGB 80405 [1]	FOLFOX/FOLFIRI +Cetux vs FOLFOX/FOLFIRI +Bev	1137 *(Kras only)*	?	12%	10 vs 11	30 vs 29 *(0.34)*
FIRE 3 [2]	FOLFIRI +Cetux vs FOLFIRI+Bev	342	66 vs 60	?	10 vs 10	33 vs 26
TRIBE [3]	FOLFOXIRI+Bev vs FOLFIRI +Bev	129	65 vs 53 (ITT)	?	13 vs 11	42 vs 34

[1] Venook ASCO 14, [2] Stinzing ECC 13, [3] Loupakis ASCO 14

Strategies CLM

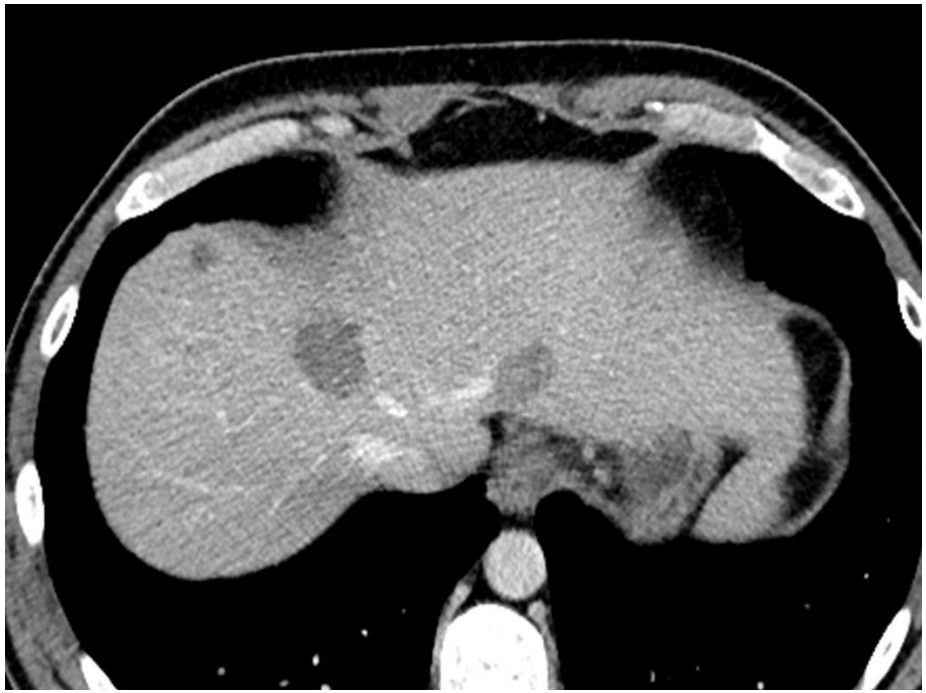
- 45a male, ECOG 0
  - Diagnosis of synchronous unresectable mCRC 12/13 (Ras, Braf wt)

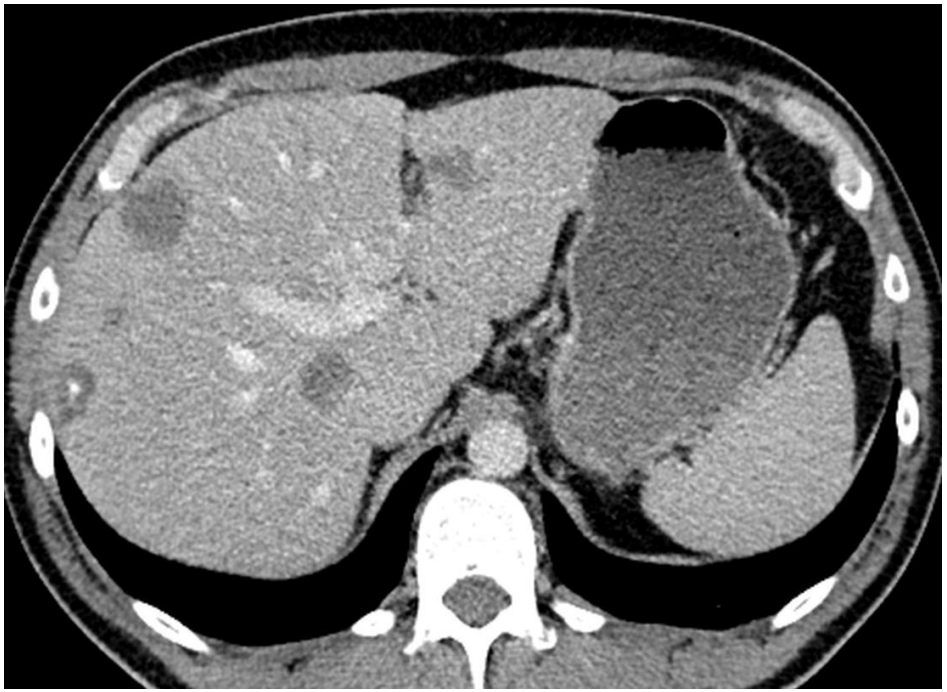




Strategies CLM

- 45a male, ECOG 0
  - Diagnosis of synchronous unresectable mCRC 12/13 (Ras, Braf wt)
  - 4 months FOLFOX + Panitumumab with rad PR





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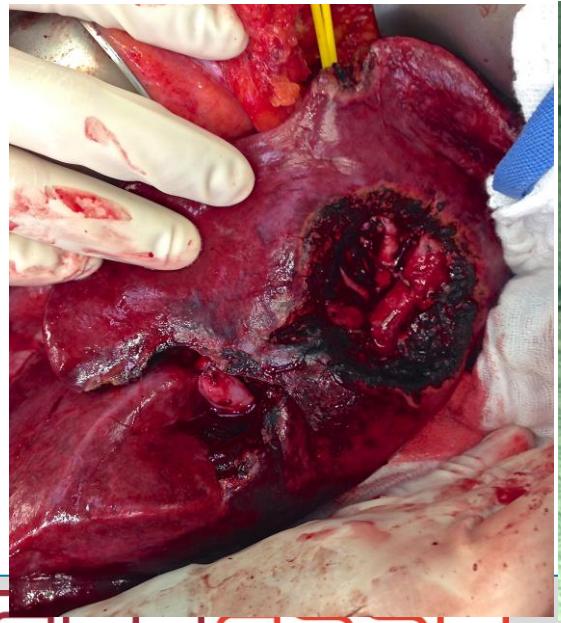
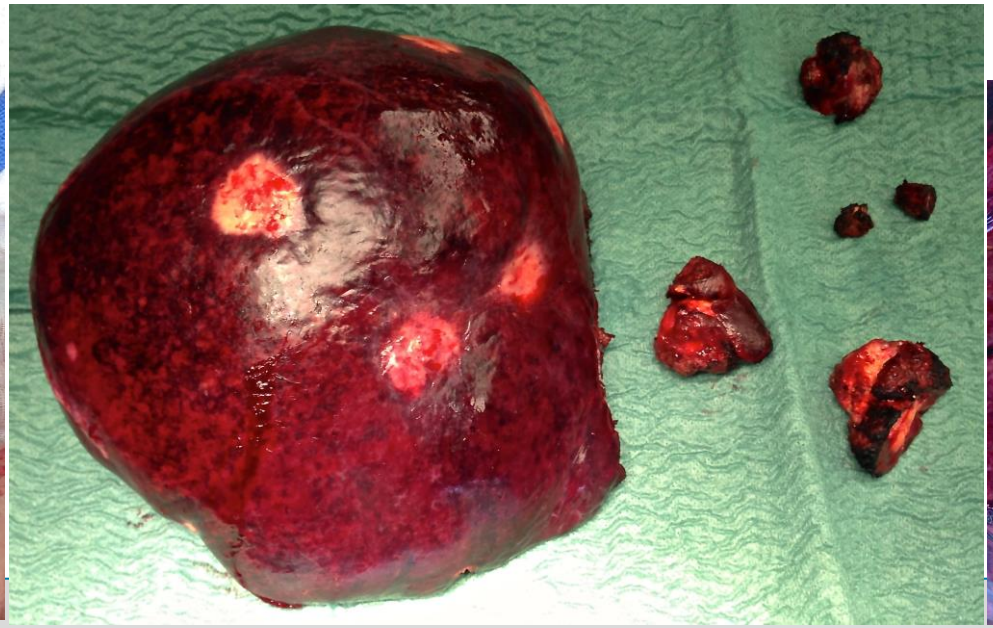
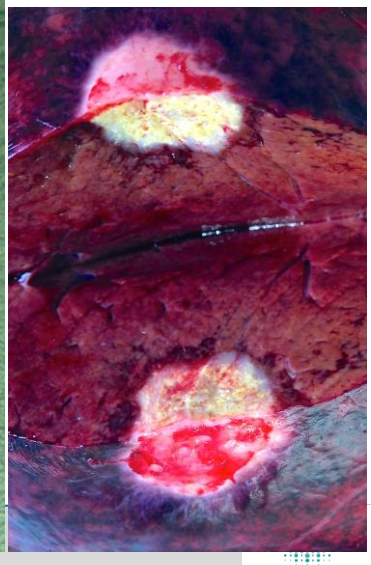
  - extended r hemihepatectomy, atypical resections left lobe







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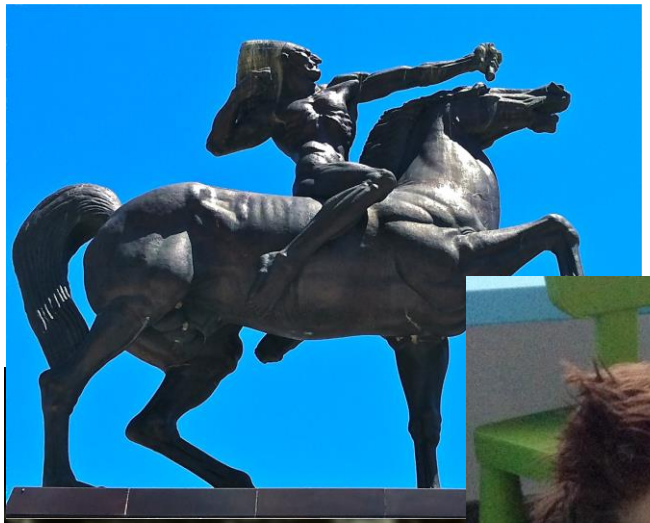
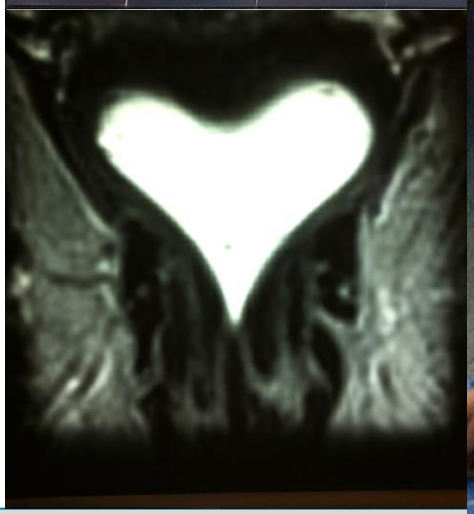
  - 4 months FOLFOX + Panitumumab with rad PR
  - extended r hemihepatectomy, atypical resections left lobe
  - Pathological partial response (10-50% viable tumor cells)
  - Anterior resection after 4 wks (pT3, pN1 (1/50), G2, L1, V1)

Summary

- Multidisciplinary process and decision-making is essential in mCRC setting
- General agreement upon resectability criteria
- Definition of treatment aim during MDT meeting
- Regular follow-up and rediscussion (e.g. 2 months)
- Surgical intervention: planned, intentional, accidental
- Important NEW issues: pathological assessment of response; avoidance of normal liver tissue damage
- The majority of patients with mCRC require long-term disease control
- Improved survival in patients undergoing secondary resection with curative intent

thanks





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