ESMO Clinical Practice Guidelines

Treatment strategies in Gastric Cancer: Applying the ESMO Guidelines - Discussion -

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Disclosures

Yung-Jue Bang has declared no potential conflicts of interest

Case: Resectable GEJ cancer

- 48-years old man
- Presents with gastric pain, dysphagia, weight loss, and anemia
- GEJ adenocarcinoma, HER2 (-)

Q1: Staging investigations

What else is undoubtly needed before decision making ?

1. Nothing more - information are complete
2. Endoscopic ultrasound (EUS)
3. EUS plus diagnostic laparascopy
4. EUS plus PET
5. all of the above (EUS, Lap, PET)

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Procedure	Purpose
Routine blood tests	• Check for evidence of iron-deficiency anaemia • Check hepatic and renal function to determine appropriate therapeutic options
Endoscopy + biopsy	• Obtain tissue for diagnosis, histological classification and molecular biomarkers, e.g. HER-2 status.
CT thorax + abdomen ± pelvis	• Staging of tumour—particularly to detect local/distant lymphadenopathy and metastatic disease sites
Endoscopic ultrasound (EUS)	• Accurate assessment of T and N stage in potentially operable tumours • Determine proximal and distal extent of the tumour
Laparoscopy + washings	• To exclude occult metastatic disease involving the diaphragm/peritoneum
Positron emission tomo-graphy (PET, if available)	• May improve detection of occult metastatic disease in some cases

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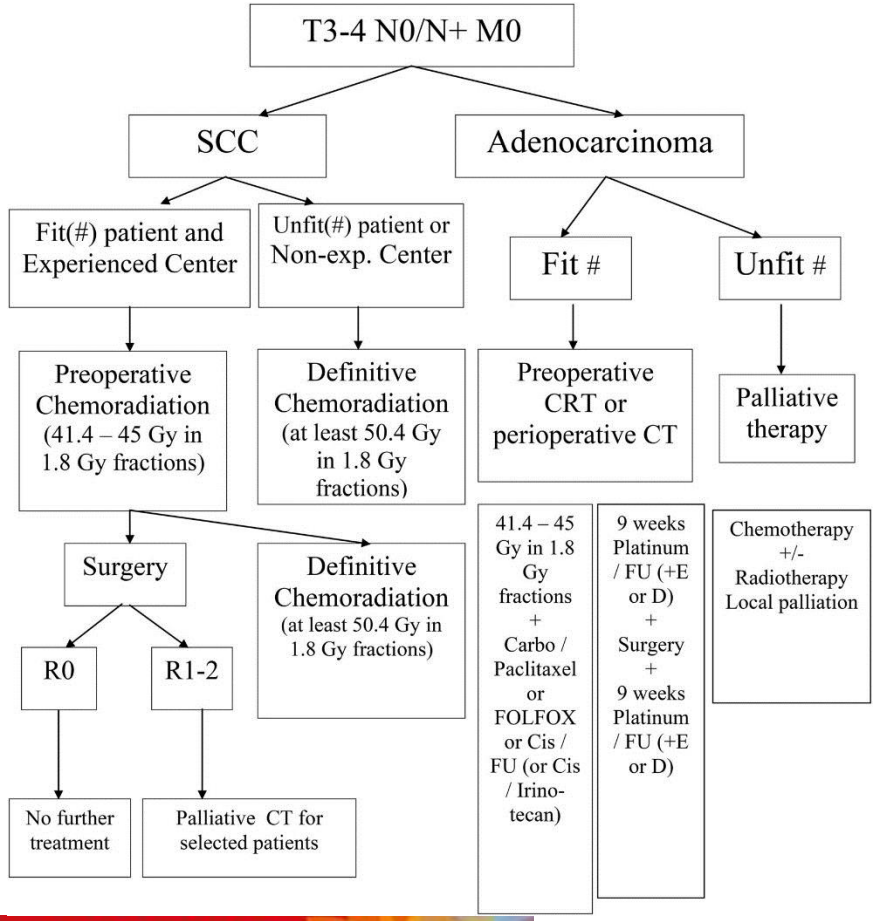
Question 2: Approach to operable, but locally advanced GEJ cancer (cT3N1)

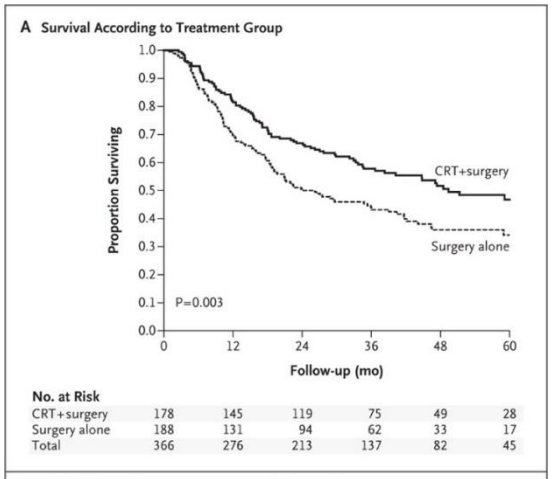
1. Surgery alone
2. Surgery plus adjuvant Rtx* / CRtx* (if N+)
3. Preoperative CRtx*
4. Pre- / perioperative ECF / ECX / EOX /...
5. Pre- / perioperative other regimen

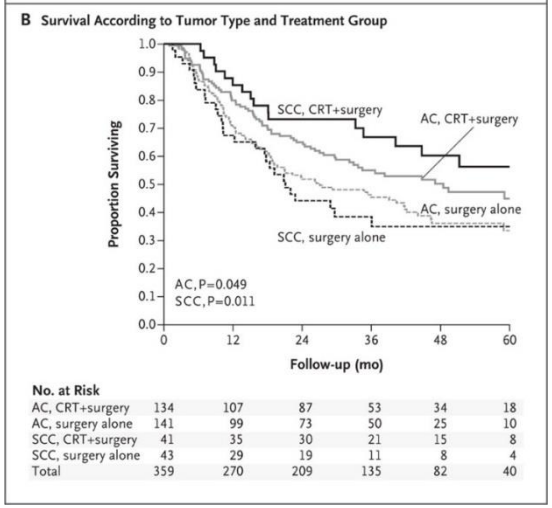
ESMO Clinical Practice Guidelines for esophageal cancer

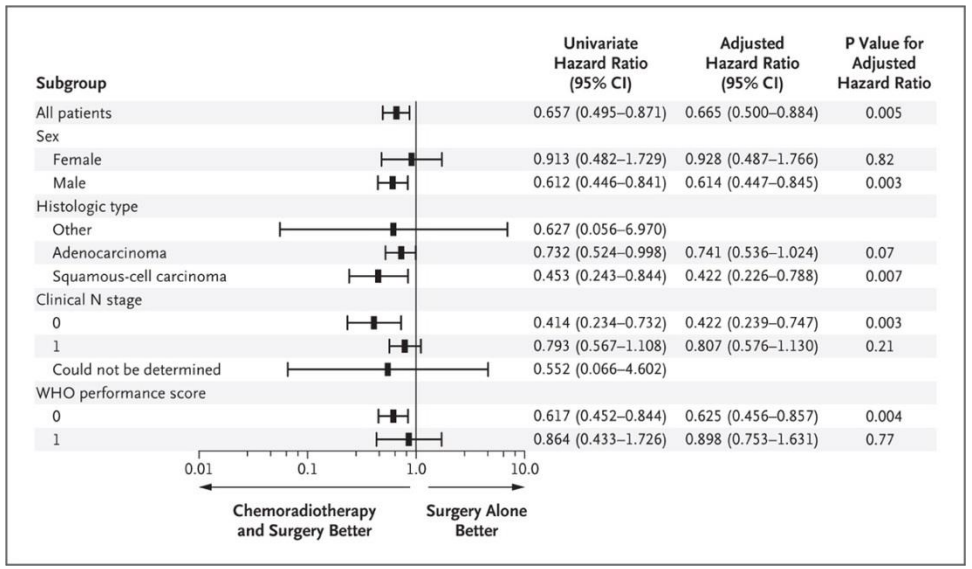


M. Stahl et al. Ann Oncol 2013;24:vi51-vi56

Phase III trial of preoperative CRT for esophageal or EGJ cancer







- Overall survival was significantly better in the chemoradiotherapy-surgery group (HR, 0.657; 95% CI, 0.495 to 0.871; P=0.003)

van Hagen P et al. N Engl J Med 2012;366:2074-84

Q2: What would be your suggestion?

1. Surgery alone
2. Surgery plus adjuvant Rtx* / CRtx* (if N+)
3. Preoperative CRtx*
4. Pre- / perioperative ECF / ECX / EOX /...
5. Pre- / perioperative other regimen

* Rtx = radiotherapy; CRtx = chemo-radiotherapy

In Asia, other option includes

- Surgery
  - Total gastrectomy (D2 resection)
  - Abdominal approach (for Siewert II-III)
- Followed by adjuvant chemotherapy
  - XELOX for 6 months
  - S-1 for 1 year

Follow-up: relapse

- Treated with preop CRT with carbo/paclitaxel
- Followed by R0 surgery; ‘near CR’

- However, 4.5 months later, CEA 122 ng/mL
  - Relapse with a single liver metastasis

Question 3: chemotherapy of HER2-negative disease

1. Re-biopsy of liver lesion (HER2,...)
2. Start Ctx with FP* alone
3. Start Ctx with FP*/platinum
4. Start Ctx with FP*/ Platinum / Docetaxel
5. Start other treatment (Irinotecan, Ramucirumab,...)

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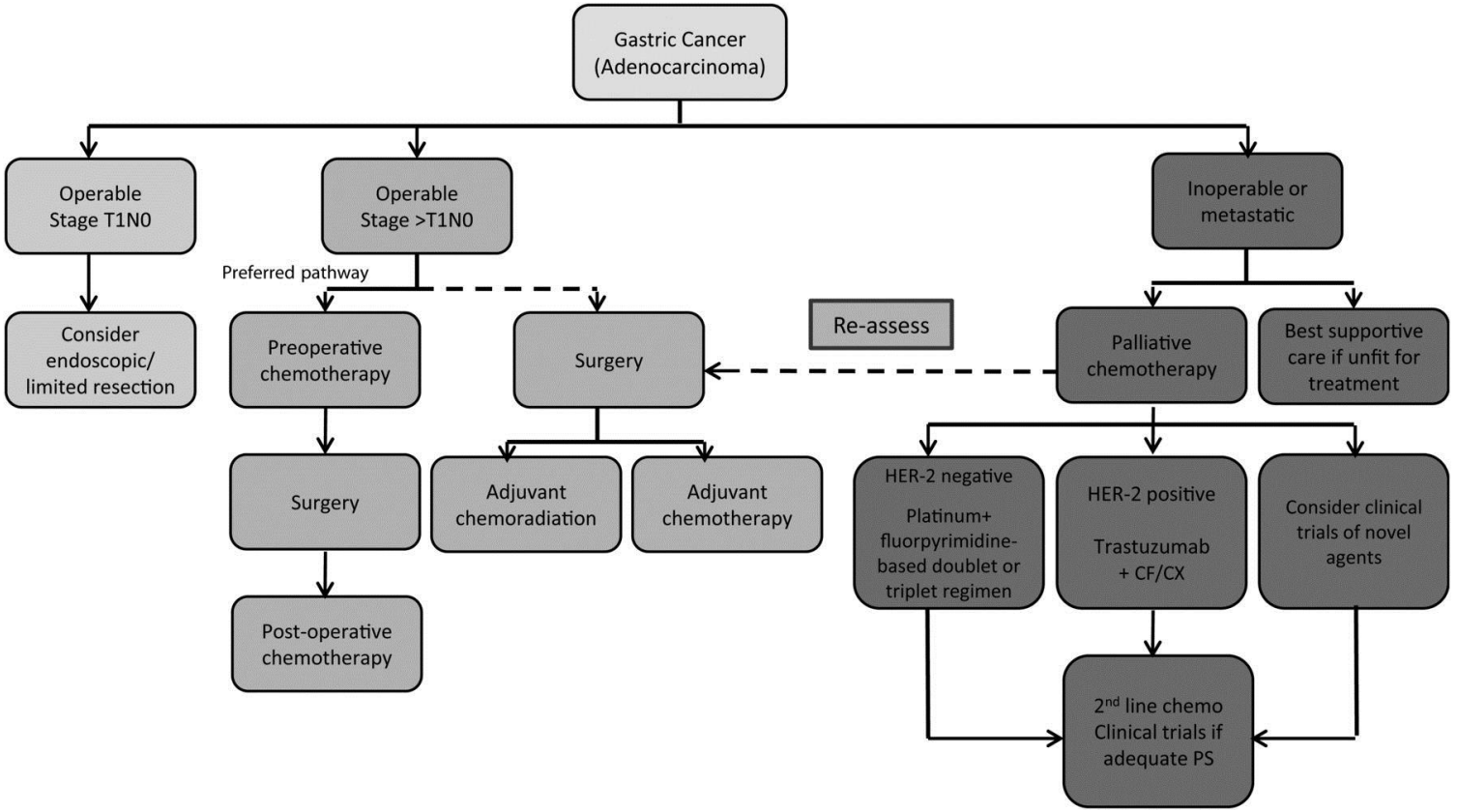
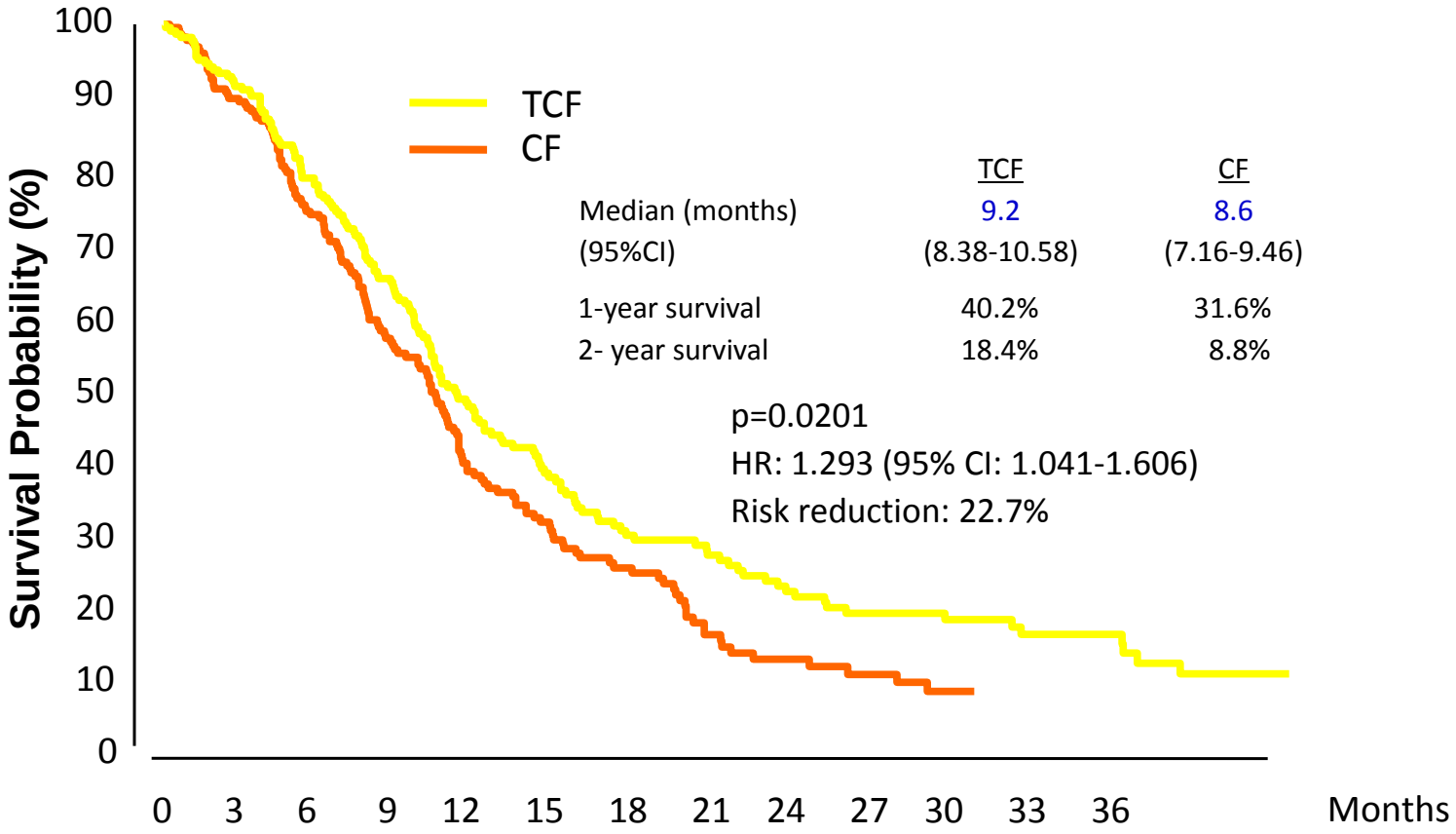


Q3: What is your suggestion now?

1. Re-biopsy of liver lesion (HER2,...)
2. Start Ctx with FP* alone
3. Start Ctx with FP*/platinum
4. Start Ctx with FP*/ Platinum / Docetaxel
5. Start other treatment (Irinotecan, Ramucirumab,...)

* FP = *any* Fluoropyrimidine (inf. 5FU, Capecitabine, S1, others)

V-325 trial: Overall survival

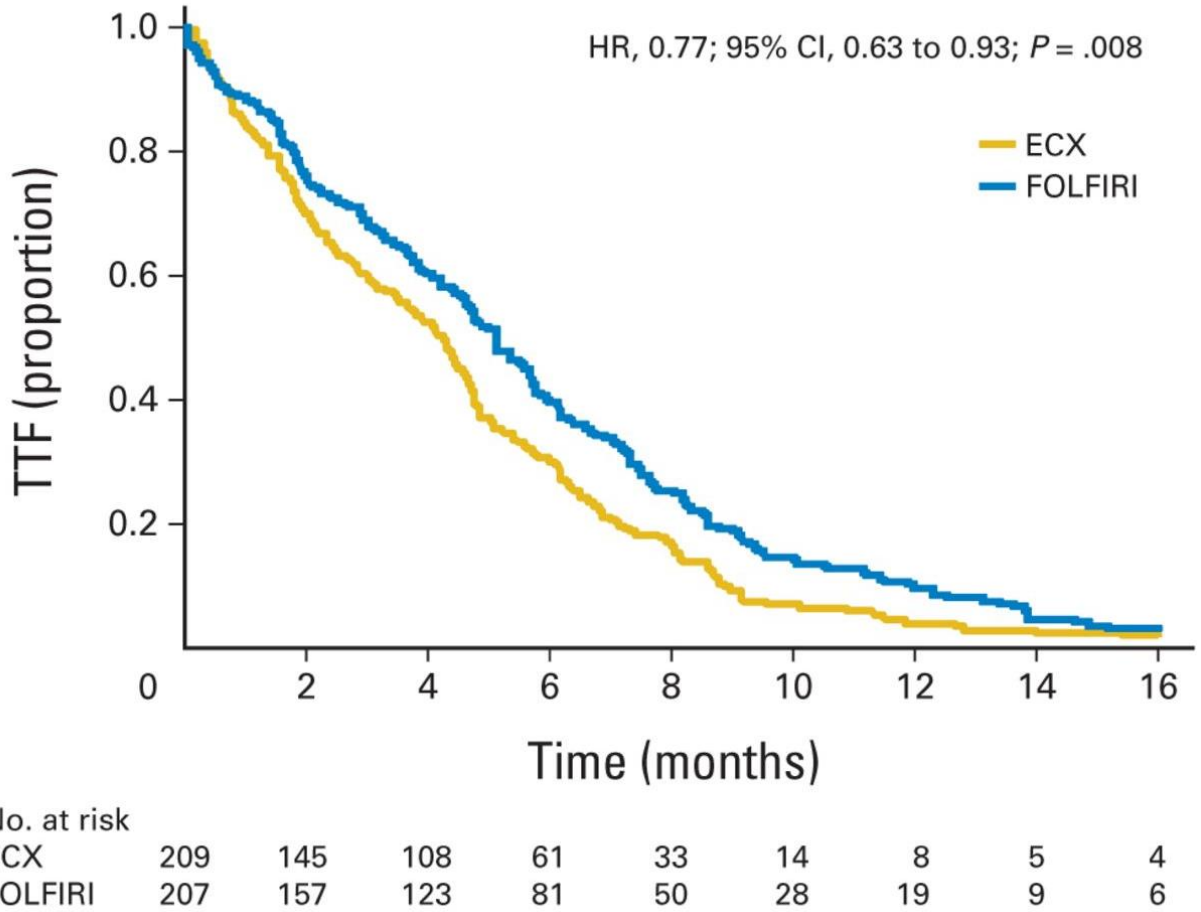


- DCF was associated with higher incidence of grade ¾ neutropenia with fever and/or infection 29% *vs* 12%), and grade ¾ diarrhea (19% *vs* 8%)

Van Cutsem E, et al JCO 2006;24:4991-7

FOLFIRI vs. ECX: French study

Primary endpoint: TTF



	FOLFIRI	ECX	HR	P
TTF	5.08 m	4.24 m	0.77	0.008
PFS	5.75 m	5.29 m	0.99	0.96
OS	9.72 m	9.49 m	1.01	0.95
ORR	37.8%	39.2%		

Guimbaud R et al. JCO 2014;32:3520-26

Follow-up: 2nd relapse

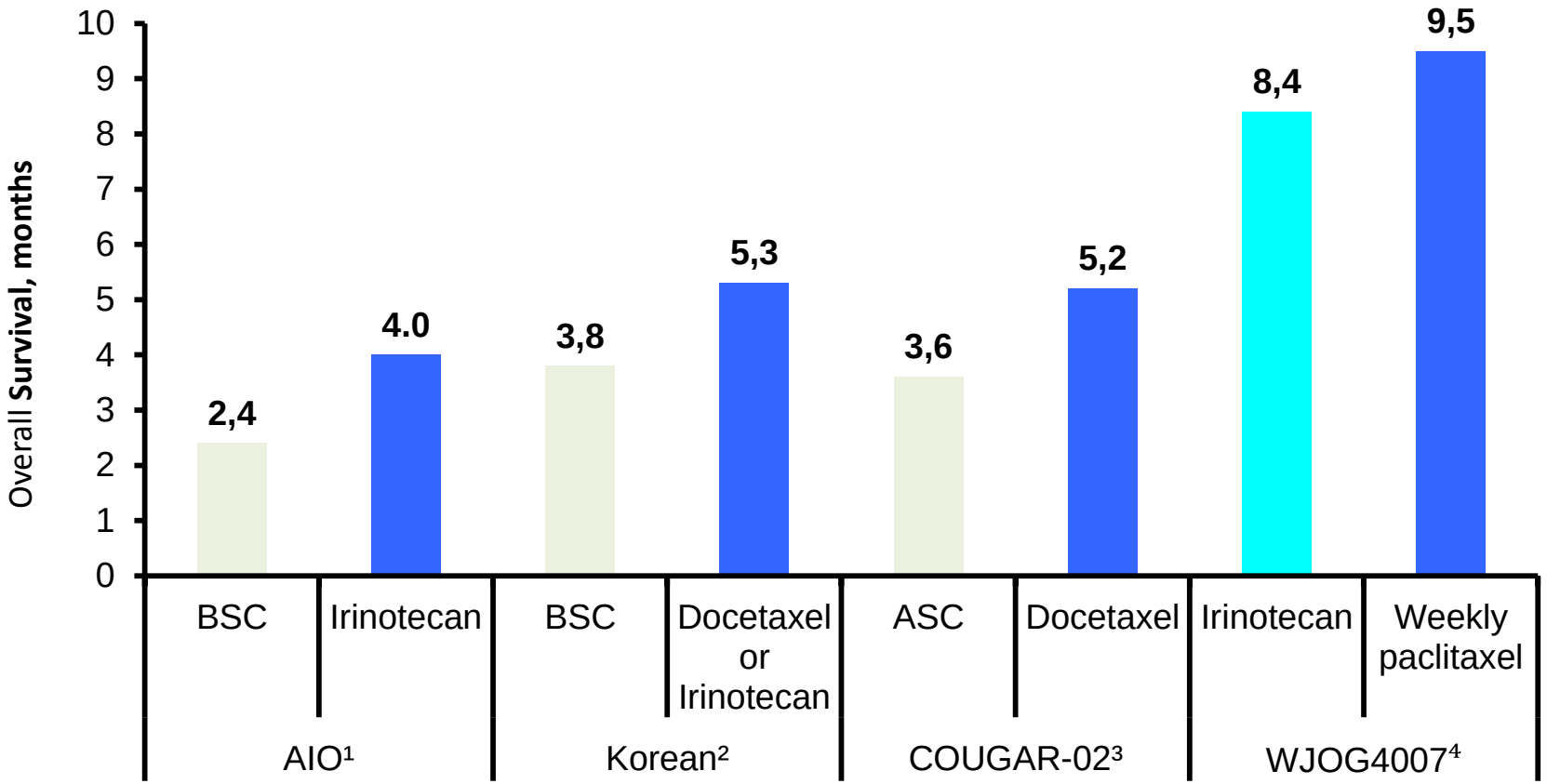
- Treated with FLOT → PR (for 4.5 months)
  → Capecitabine d/t neuropathy (for 4 months)
  → Observation

- 4 months later, increased pre-existing lesion without any new lesions

Question 4: 2nd-line treatment

1. Re-Induce FP +/- Oxaliplatin +/- Taxane
2. Start „2nd line“ Taxane
3. Start „2nd line“ Taxane plus Ramucirumab
4. Start „2nd line“ Ramucirumab
5. Start „2nd line“ Irinotecan (+/- FP)
6. Consider ablative treatment to the liver met (surgery, RFTA, etc.)

2nd-Line chemotherapy trials



[1]Thuss-Patience PC et al. Eur J Cancer 2011;47:2306, [2]Kang JH et al. J Clin Oncol 2012;30:1513, [3]Ford H, et al. Lancet Oncol 2014, [4]Hironaka S et al. JCO 2013

Q4: What is your suggestion now?

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Other option includes

- Chemotherapy
  - Resume fluoropyrimidine/platinum doublet only if, neuropathy < Grade II
  - Paclitaxel + ramucirumab
  - FOLFIRI or others

- Clinical trial
  - PARP inhibitor, STAT3 inhibitor etc
  - Immune check-point blocking agents