STAGE III COLORECTAL CANCER

CLINICAL DISCUSSION

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On behalf of the localized colorectal cancer guidelines panel
DISCLOSURE

Personal financial interests

Honoraria for advisory role, travel grants, research grants (past 5 years): Hoffman La-Roche, Bristol Myers Squibb, Bayer, Servier, Amgen, Merck Serono, Menarini

Institutional financial interests

Honoraria due to investigator contribution in clinical trials from: Bayer, Servier, Novartis, Boehringer Ingelheim, Boston Pharmaceuticals, Hoffman la Roche, Genentech
New Localised Colon Cancer Guidelines Coming

New guidelines expected for early 2020.


https://www.esmo.org/Guidelines/Gastrointestinal-Cancers/Early-Colon-Cancer/eUpdate-Early-Colon-Cancer-Treatment-Recommendations
Clinical portrait

• 61 y-o lady.

• Referral by GP due to fatigue and anaemia and change in bowel habit over the last 3 months.
Tumor diagnosis and staging

According to the staging performed, the patient has localised colon cancer without any distant metastatic lesions.
Consideration for Colon Cancer Diagnosis

• The only diagnostic test for localised colon cancer is colonoscopy with tumour biopsy.

• 3.6% rate of synchronic colonic tumours and much higher chances of premalignant lesions in the rest of the colon.
  • Complete colonoscopy or colono-tomography.

• 20% rate of synchronous metastasis:
  1. 95% liver
  2. 20% lung
  3. 20% peritoneum
  4. 15% lymph nodes
  • Thoracic-abdominal-pelvic CT scan recommended
    MRI for liver study and PET/CT for peritoneal study only when there is clinical doubt.

• High CEA preoperative levels accounts for higher chances of relapse


CEA, carcinoembryonic antigen; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography
Fibrocolonoscopy

No findings

Refer to screening program

Positive screening test

Suspicious clinical portrait

Fibrocolonoscopy

Polyp

Remove the polyp

Repeat in 1 to 2 years

Colorectal cancer

Diagnostic workout

• Complete lab test including CEA
• Chest, Abdominal, Pelvic CT scan
• Complete colonic examination

CEA, carcinoembryonic antigen; CT, computed tomography

Local staging:

Diagnosis

- According to the staging performed, the patient has localised colon cancer without any distant metastatic lesions.
- Following the decision of tumour board, the patient undergoes right hemicolecction.

Diagnosis

- The final results of the histology report establish the diagnosis of conventional adenocarcinoma of the colon invading the peri-colonic tissues.
- 15 lymph nodes are retrieved, two of them being positive for tumour invasion.
- Perivascular, perineural invasion are present while the result is negative for lymphatic invasion.
- Negative margins.
- Stage: pT3N1b, PN+, IV+
- Testing for MSI: microsatellite stable (MSS)

MSI, microsatellite instability
Stage III Colon Cancer Standard of Care

**NSABP-C07:**
- Standard of Care: 6 months therapy either FOLFOX or CAPOX

**MOSAIC:**

**XELOXA:**

Standard of Care: 6 months therapy either FOLFOX or CAPOX

Yothers JCO 2011 - André JCO 2009- Schmoll JCO 2015
IDEA initiative: International Duration Evaluation of Adjuvant Chemotherapy Collaboration

**Background and Rationale**

- Current standard of care for stage III colon cancer patients: six months of oxaliplatin-based treatment
  - FOLFOX, CAPOX
- Oxaliplatin is associated with cumulative dose-dependent neurotoxicity
  - 12.5% grade 3 neuropathy with 6 months of FOLFOX
- Shorter duration treatment without loss of efficacy would be of benefit to patients and health care resources

**Study Schema**

- Total planned accrual ≥ 10,500
- 3 months
- Investigator's choice: FOLFOX or CAPOX
- 6 months

R 1:1

FOLFOX: 5FU/LV + Oxaliplatin
CAPOX: Capecitabine + Oxaliplatin
IDEA initiative: International Duration Evaluation of Adjuvant Chemotherapy Collaboration

Primary DFS Analysis (mITT), cont.

Statistical Conclusions

3m TRT better
6m TRT better

DFS HR = 1.07
95% CI, 1.00 to 1.15

Not proven

DFS Comparison by Regimen, cont.

FOLFOX

DFS HR = 1.16
95% CI, 1.06 to 1.26
Inferiority

CAPOX

DFS HR = 0.95
95% CI, 0.85 to 1.06
Non-Inferiority

Interaction p-value = 0.0051

TRT: treatment

Barcelona ESMO Congress 2019

Presented by: Qian Shi, PhD on behalf of IDEA collaborators
IDEA initiative: International Duration Evaluation of Adjuvant Chemotherapy Collaboration

DFS Comparison by Stage, cont.

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Risk Group

- T1-3 N1: 3744, 3727, 1.01 (Favors 3m, Interaction P-value: 0.11)
- T4 or N2: 2634, 2622, 1.12 (Favors 6m)

DFS Comparison by Risk Group and Regimen

Risk Group: T1-3 N1
- Regimen: FOLFOX
- 3m TRT better: Not proven
- 6m TRT better: Non-Inferior
- DFS HR; 95% CI: 1.10; 0.96 to 1.26

Risk Group: T1-3 N1
- Regimen: CAPOX
- 3m TRT better: Non-Inferior
- 6m TRT better: Non-Inferior
- DFS HR; 95% CI: 0.85; 0.71 to 1.01
Considerations for colon cancer follow-up

- 30%-50% of patients with a localised colon cancer will eventually relapse

- Intensive follow up increase OS at 5 years

- 80% of relapses occur during the first 2 years

- Less than 5% relapse after the 5th year
Algorithm for follow up after curative resection

0 months to 3 years after surgery
- Clinical and CEA assessment every 3 to 6 months
- Chest-Abdominal-Pelvic CT scan every 6 months
- Fibrocolonoscopy every 2 years starting 1 year after surgery

3 years to 5 years after surgery
- Clinical and CEA assessment every 6 to 12 months
- Chest-Abdominal-Pelvic CT scan every 12 months
- Fibrocolonoscopy every 2 years in if no findings

End of follow up

Second primary tumour
- See therapeutic algorithm for localized mCRC

Relapse
- See guidelines for mCRC

Screening program


CEA, carcinoembryonic antigen; CT, computed tomography; mCRC, metastatic colorectal cancer