ESMO Preceptorship Programme

Colorectal – Valence – Date

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Gustave Roussy, Grand Paris, FRANCE

Adjuvant treatment of colon cancer
Disclosure

- Participation to advisory boards:
  - ROCHE
  - MERCK SERONO
  - AMGEN
  - SANOFI
  - BAYER
  - SIRTEX
  - LILLY
- Speaker in symposiums:
  - ROCHE
  - MERCK SERONO
  - SANOFI
  - TERUMO
- Research funding:
  - ROCHE
  - MERCK SERONO
  - PFIZER
Aims of the talk

- Adjuvant chemotherapy is indicated for stage III (N+)
  - FOLFOX / CapeOx
  - Capecitabine or (inf.) FU/LV as an option for some patients
  - FOLFOX / CapeOx for patients < 70y, use with caution for pts > 70y
- Antibodies (EGFR, VEGF) are not indicated
- The decision for an adjuvant treatment should balance the risk of cancer mortality and that of comorbidities
- Specific problems
  - Stage II
  - Elderly patients
  - Role of biological markers
STAGE III (N+)...
First positive study: 5FU + levamisole...

Moertel et al NEJM 1990

Sargeant D, J Clin Oncol 2009
X’Act trial (Capecitabine vs FuFol Mayo) Overall survival

Stage III colon
(n=1987)

Non infériority < 0.001
Superiority 0.05
2004 Polychemotherapy

FOLFOX new standard stage III

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MOSAIC study

Main endpoint: Disease-Free Survival (3-years)
Secondary endpoint: tolerance, overall survival (6-years)
(n=1123)

FOLFOX4
(LV5FU2 + oxaliplatin 85 mg/m²)

LV5FU2
(n=1123)

n=2246
Inclusion:
Oct 1998–Jan 2001 (146 centres; 20 countries)
• Colon cancer, complete resection
• Stage II, 40%; Stage III, 60%
• Age 18–75 years
• KPS ≥60
• No previous CT

A. de Gramont et al., ASCO 2003 / T. André et al. NEJM 2004
MOSAIC: Long-term results
Overall survival ITT

Evénements
FOLFOX4 243/1123 (21.6%)
LV5FU2 279/1123 (24.8%)
HR [95% CI]: 0.84 [0.71–1.00]

p=0.046

2.5%

Data cut-off: January 2007

ESMO PRECEPTORSHIP PROGRAM
A. de Gramont et al., ASCO 2007 / T. André et al. JCO 2009
Long-term Tolerance

Second cancer (% patients)

Peripheral Neuropathy

FOLFOX 5.5  
LV5FU2 6.1

Evaluable patients n=976  
4-year

Data cut-off: January 2007
Overall survival Stage II / III

- Stage II: HR [95% CI] = 1.00 [0.70–1.41], p=0.986
- Stage III: HR [95% CI] = 0.80 [0.65–0.97], p=0.023

Data cut-off: January 2007
FOLFOX OR XELOX ?
Stage III colon cancer
• No previous CT
• Resection ≤ 8 weeks n=1886

Main endpoint
Better DFS

ESMO PRECEPTORSHIP PROGRAM
Xelox, a valid option

HR = 0.80 (IC 95% : 0.69–0.93)  p=0.0045

Absolute difference at 3-year

Confirmed at 7 years : 63% vs 56%

Overall survival Xelox vs Fufol

HR = 0.87 (IC 95% : 0.72–1.05)  
p = 0.1486

Mean follow-up : 59 months

Confirmed with longer follow-up: 73 vs 67%

## The last 15 years

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>3-y DFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moertel 1990</td>
<td>Surveillance</td>
<td>52%</td>
</tr>
<tr>
<td>IMPACT 1993</td>
<td>Surveillance</td>
<td>44%</td>
</tr>
<tr>
<td>IMPACT 1994</td>
<td>FUFOL</td>
<td>62%</td>
</tr>
<tr>
<td>INT0089, 2005</td>
<td>FUFOL</td>
<td>63%</td>
</tr>
<tr>
<td>XELOXA, 2010</td>
<td>FUFOL ou RPMI</td>
<td>66%</td>
</tr>
<tr>
<td>André, 2003</td>
<td>LV5FU2</td>
<td>61%</td>
</tr>
<tr>
<td>MOSAIC 2004</td>
<td>LV5FU2</td>
<td>65%</td>
</tr>
<tr>
<td>X-ACT, 2005</td>
<td>Capecitabine</td>
<td>64%</td>
</tr>
<tr>
<td>MOSAIC 2004</td>
<td>FOLFOX4</td>
<td>73%</td>
</tr>
<tr>
<td>XELOXA, 2010</td>
<td>XELOX</td>
<td>71%</td>
</tr>
</tbody>
</table>
A LITTLE BIT MORE COMPLICATED…
## Fluoropyrimidine ± Oxaliplatin Stage III

<table>
<thead>
<tr>
<th></th>
<th>HR for DFS</th>
<th>P value</th>
<th>DFS (\Delta) (%)</th>
<th>HR for OS</th>
<th>P value</th>
<th>OS (\Delta) (%)</th>
</tr>
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<tbody>
<tr>
<td><strong>MOSAIC</strong></td>
<td>0.78</td>
<td>0.005</td>
<td>7.5% 58.9% vs 66.4% @ 5 year</td>
<td>0.80</td>
<td>0.023</td>
<td>4.2% 68.7% vs 72.9% @ 6 year</td>
</tr>
<tr>
<td><em>(FOLFOX)</em></td>
<td></td>
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<tr>
<td><strong>NSABP C-07</strong></td>
<td>0.78</td>
<td>0.0007</td>
<td>6.6% 57.8% vs 64.4% @ 5 year</td>
<td>0.85</td>
<td>0.052</td>
<td>2.7% 73.8% vs 76.5% @ 5 year</td>
</tr>
<tr>
<td><em>(FLOX)</em></td>
<td></td>
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<td><strong>XELOXA</strong></td>
<td>0.80</td>
<td>0.0045</td>
<td>4.4% 66.5% vs 70.9% @ 3 year</td>
<td>0.87</td>
<td>0.1486</td>
<td>3.4% ND (57 months FU)</td>
</tr>
<tr>
<td><em>(XELOX)</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 André T, J Clin Oncol. 2009  
2 Yothers G, J Clin Oncol 2011  
3 Haller D, J Clin Oncol 2011
# Fluoropyrimidine ± Oxaliplatin Stage III

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<thead>
<tr>
<th>Study</th>
<th>HR for DFS</th>
<th>P value</th>
<th>DFS ∆ (%)</th>
<th>HR for OS</th>
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<td>@ 5 year</td>
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<td>@ 5 year</td>
<td>57.8% vs 64.4%</td>
<td>CI, 0.72-1.00</td>
<td>@ 5 year</td>
<td>73.8% vs 76.5%</td>
</tr>
<tr>
<td><strong>XELOXA (XELOX)</strong></td>
<td>0.80</td>
<td>0.004</td>
<td>∆ 5%</td>
<td>0.83</td>
<td>0.04</td>
<td>∆ 3.0%</td>
</tr>
<tr>
<td></td>
<td>CI, 0.69-0.93</td>
<td>@ 5 year</td>
<td>62% vs 67%</td>
<td>CI, 0.70-0.99</td>
<td>@ 5 year</td>
<td>74% vs 77%</td>
</tr>
<tr>
<td><strong>X-ACT</strong></td>
<td>0.87</td>
<td>0.0528</td>
<td>∆ 3.6%</td>
<td>0.84</td>
<td>p=0.07</td>
<td>∆ 3.7%</td>
</tr>
<tr>
<td>FU/FA bolus vs. Capecitabine</td>
<td>CI, 0.75-1.00</td>
<td>@ 3y</td>
<td>60.6% vs. 64.2%</td>
<td>CI: 0.69–1.01</td>
<td>@ 3y</td>
<td>77.6% vs. 81.3%</td>
</tr>
</tbody>
</table>

1 André T, J Clin Oncol. 2009
2 Yothers G, J Clin Oncol 2011
3 Haller D, J Clin Oncol 2011
4 Schmoll HJ, J Clin Oncol 2016
Recurrence risk over time
ACCENT Database  N=12.233
Overall survival stage III pT3-4 N+

**N 1-3**

- FOLFOX4: 440 events, 117
- LV5FU2: 442 events, 132

Log-rank $P = .248$
HR, 0.864; 95% CI, 0.673 to 1.108

**N > 3**

- FOLFOX4: 229 events, 90
- LV5FU2: 231 events, 117

Log-rank $P = .012$
HR, 0.705; 95% CI, 0.535 to 0.928
Recurrence risk over time
ACCENT Database  N=12,233
International Duration Evaluation of Adjuvant Chemotherapy (IDEA) Folfox or Xelox: 6 months versus 3 months, stage III colon cancer

<table>
<thead>
<tr>
<th>Country</th>
<th>Trial</th>
<th>Group</th>
<th>Number of planned pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK, Australie, Nouvelle Zélande, Danemark, Espagne, Suède,</td>
<td>SCOT</td>
<td>CACTUS, OCTO</td>
<td>4000</td>
</tr>
<tr>
<td>Italie</td>
<td>TOSCA</td>
<td>GISCAD</td>
<td>2500</td>
</tr>
<tr>
<td>France</td>
<td>IDEA</td>
<td>GERCOR, PRODIDGE</td>
<td>2000</td>
</tr>
<tr>
<td>USA</td>
<td>80702</td>
<td>CALGB/SWOG</td>
<td>2500</td>
</tr>
<tr>
<td>Grèce</td>
<td>HORG</td>
<td>HORG</td>
<td>1000</td>
</tr>
<tr>
<td>Japon</td>
<td>ACHIEVE</td>
<td>JFMC</td>
<td>1200</td>
</tr>
<tr>
<td>Total</td>
<td>6 trials</td>
<td>16 groups</td>
<td>&gt;10,500</td>
</tr>
</tbody>
</table>

Statistical design of non-inferiority
- 2 sided 95% CI HR < 1.2
- DFS difference 2.7% at 3 years
A ROLE FOR TARGETED THERAPIES?
Bevacizumab

3 large negative studies (>6000 pts)
- NSABP- C08
- AVANT
- QUASAR 2
NSABP C-08 trial

- Stage II = 24.9%
- Main endpoint: 3-year DFS
- Median follow-up: 55 months

C. Allegra et al., ASCO 2011, A#3508
NSABP-C-08 (données actualisées) Pas d’intérêt bévacizumab adjuvant

mFF6  1341 Pts, 224 deaths
mFF6+Bev  1337 Pts, 218 deaths
HR=0.96, 95% CI (0.79-1.15)

\[ p = 0.64 \]

Allegra C et al 2013;31:359-64
AVANT study

DFS

<table>
<thead>
<tr>
<th></th>
<th>FOLFOX4 (N=955)</th>
<th>FOLFOX4 + Bev (N=960)</th>
<th>XELOX + Bev (N=952)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (95% CI)</td>
<td></td>
<td>1.17 (0.98, 1.39)</td>
<td>1.07 (0.90, 1.28)</td>
</tr>
</tbody>
</table>

T. Andre et al., ASCO 2011, A#3509
Cetuximab

2 large negative studies (>6000 pts)
- N0147
- PETACC 8
NO 147: Folfox +/- cetuximab

**KRAS WT**

<table>
<thead>
<tr>
<th>Arm</th>
<th>3 Year Rates (95% CI)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folfox n=902</td>
<td>75.8% (72.1%-79.6%)</td>
<td>1.2 (0.96-1.5)</td>
<td>0.22</td>
</tr>
<tr>
<td>Folfox + Cmab n=945</td>
<td>72.3% (68.5%-76.4%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**KRAS MT**

<table>
<thead>
<tr>
<th>Arm</th>
<th>3 Year Rates (95% CI)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folfox n=374</td>
<td>67.2% (61.4%-73.5%)</td>
<td>1.2 (0.9-1.6)</td>
<td>0.13</td>
</tr>
<tr>
<td>Folfox + Cmab n=343</td>
<td>64.2% (58.7%-70.2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Alberts et al. JAMA 2012;307:1383-93

ESMO PRECEPTORSHIP PROGRAM
PETACC8: PFS: Wt KRAS

<table>
<thead>
<tr>
<th>Years</th>
<th>FOLFOX4 + Cetuximab N = 791</th>
<th>FOLFOX4 N = 811</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>190</td>
<td>179</td>
</tr>
<tr>
<td>1</td>
<td>699</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>505</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>356</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>132</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S3-year PFS [95%CI], %
- FOLFOX4 + Cetuximab: 75.1 [71.7; 78.1]
- FOLFOX4: 78.0 [74.8; 80.8]

HR pour SSR [95% CI] p-value (log-rank)
- FOLFOX4 + Cetuximab: 1.047 [0.853; 1.286] p = 0.6562
- FOLFOX4: 0

NEW DATA: A CHANGE IN THE STANDARD OF CARE?
Prognostic role of tumour site

* 3% tumors of the transversum were excluded from further analysis

Schrag et al. ASCO 2016
Biological features: a prognostic role

KRAS/BRAF wt
KRAS mut
BRAFmut

<table>
<thead>
<tr>
<th>Mutated BRAF, nonmutated KRAS</th>
<th>66.6 (61.5–72.0%)</th>
<th>332 (114)</th>
<th>1.69 (1.31–2.20)</th>
<th>&lt;.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutated KRAS codon 12, nonmutated BRAF</td>
<td>74.3 (70.9–77.9%)</td>
<td>758 (185)</td>
<td>1.59 (1.29–1.93)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Mutated KRAS codon 13, nonmutated BRAF</td>
<td>73.8 (72.8–80.7%)</td>
<td>214 (50)</td>
<td>1.36 (0.99–1.83)</td>
<td>0.0538</td>
</tr>
</tbody>
</table>

Adjusted Wald P < .0001

Patients-at-risk

ESMO PRECEPTORSHIP PROGRAM

Interaction with MMR status

Overall $P$ value = .0142

<table>
<thead>
<tr>
<th>Category</th>
<th>5 yr DFS rate</th>
<th>95% CI</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non mutated $BRAF^{V600E}$ &amp; KRAS, pMMR</td>
<td>65.3%</td>
<td>60.3%</td>
<td>70.6%</td>
</tr>
<tr>
<td>Mutant KRAS, pMMR</td>
<td>57.7%</td>
<td>52.0%</td>
<td>63.9%</td>
</tr>
<tr>
<td>Mutant $BRAF^{V600E}$, pMMR</td>
<td>49.2%</td>
<td>33.6%</td>
<td>72.1%</td>
</tr>
<tr>
<td>Sporadic dMMR</td>
<td>71.0%</td>
<td>56.4%</td>
<td>89.1%</td>
</tr>
<tr>
<td>Familial dMMR</td>
<td>70.9%</td>
<td>60.1%</td>
<td>83.6%</td>
</tr>
</tbody>
</table>
Role of the 4 classes of molecular consensus???

<table>
<thead>
<tr>
<th>CMS1</th>
<th>CMS2</th>
<th>CMS3</th>
<th>CMS4</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSI Immune</td>
<td>Canonical</td>
<td>Metabolic</td>
<td>Mesenchymal</td>
</tr>
<tr>
<td>14%</td>
<td>37%</td>
<td>13%</td>
<td>23%</td>
</tr>
</tbody>
</table>

- **CMS1**
  - MSI, CIMP high, hypermutation
  - SCNA high
  - WORSE survival after relapse

- **CMS2**
  - Mixed MSI status, SCNA low, CIMP low
  - Metabolic deregulation
  - Worse survival and overall survival

- **CMS3**
  - SCNA high
  - Stromal infiltration, TGFβ activation, angiogenesis

- **CMS4**
  - SCNA high
  - Metabolic deregulation

---

*Figure 5. Proposed taxonomy of colorectal cancer reflecting significant biological differences in the gene expression-based molecular subtypes*

CIMP, CpG Island Methylator Phenotype; MSI, microsatellite instability; SCNA, somatic copy number alterations; TGF, transforming growth factor.

Guinney et al. Nat Med 2015
Beyond TNM system??

- 8904 patients
- TNM, clinico-pathological features and biological determination of Ras and Raf
- Training set: NO147 and PETACC 3
- Validation set: observational studies

Conclusion: Incorporation of MSI, BRAF and KRAS mutations improves the ability to prognosticate in stage II and stage III cc patients, but only modestly increases prediction accuracy in multivariate models that include clinicopathological features, particularly in chemotherapy-treated patients...
STAGE II DISEASE.... !!!!
Stage II

Small benefit (3%) with 5FU

No clear improvement with FOLFOX

Is it possible to define a subgroup that could benefit from FOLFOX?
Some Stage II disease with poor prognosis
QUASAR – a very small advantage...

Survival – Dukes stage B

- Chemotherapy
- Observation

Deaths
Chemotherapy: 224
Observation: 262
O-E: -22.1
Var: 121.5

p=0.04

Years from randomisation

% Survival
MOSAIC: FOLFOX vs LV5FU2, all stage II patients

Log-rank $P = .981$
HR, 1.004; 95% CI, 0.744 to 1.354
MOSAIC late follow-up and Stage II disease

![Graphs showing overall survival probabilities for low and high risk groups over time.](image-url)
High risk stage II and SEER
How to select high risk patients?

Overall 5-year survival

- 1950 colon cancer
  - Groupe 1, occlusion without perforation n=120 33%
  - Groupe 2, occlusion + perforation tumour n=35 50%
  - Groupe 3, occlusion + proximal perforation n=13 33%
  - Groupe 4, no occlusion, no perforation n=1682 51%

Fig 2. Five-year cancer-free survival.

Chen et al, 2000
Low number of lymph nodes remains not good...

- 134 567 pT3N0
- < 12 LN analysed
  - 23.3% of the patients
    • 46.8% in 2003 – 12.5% en 2012
  - 5-year overall survival : 66.8%
    • 69.8% > 12 LN versus 58.7% p< 0.001
  - 16.7% of adjuvant CT if less than 12 LN:
    • OS with CT 78.4% versus 54.7% without, p< 0.001

Wells KO et al. Dis Colon rectum 2017
Role of perineural invasion

- US National Database: 21,488 patients:
  - 55.2% T3, 23.1% T2, 14.4% T1, 7.3% T4 disease
  - 4.6% (n = 987) had PNI
  - 86.8% no PNI and no CT; 8.7% no PNI and CT; 3.7% (n = 785) PNI and no CT, and 0.9% (n = 202) PNI and CT
  - Patients with PNI who had CT: younger, private insurance, fewer comorbidities greater T stage
  - PNI and CT improved OS in T3-4 disease (P<0.001), but not in T1-2 disease.
  - Multivariate analysis: PNI greater HR mortality 1.38, CT decreased the hazard of mortality by 43%

Mirkin et al. Cancer Biol Ther May 2017
IHC pour protéines du MMR et PCR pour MSI détecte deux manifestations de la même biologie tumorale:
• MMR-D est synonyme de MSI-H
• MMR-P est synonyme de MSI-L/MSS
MSI + tumours, no benefit from 5FU based CT

Stage II

Stage III

MSI
(n=165)

MSS
(n=863)

No benefit in Stage III patients, could be even deleterious in stage II patients
ColoPrint, useful to select patients??
Immunoscore: an hope???
Immunoscore and stage II disease: DFS

ESMO PRECEPTORSHIP PROGRAM

Galon J. et al., ASCO 2016, OS 3500
AND ELDERLY???
Effect of age on efficacy of adjuvant CT

- SEER 1997-2000
- Colon Cancer stage III ≥ 66 years old CT with 5FU-FA during 6 months
- 3672 pts

- Benefit of CT in all the patients
- Decrease of the benefit with age, even with adjustment on socio-demographic and clinical features, ECOG PS

<table>
<thead>
<tr>
<th>Age</th>
<th>CT</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>66-69 y</td>
<td>81%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≥ 80 y</td>
<td>16%</td>
<td></td>
</tr>
</tbody>
</table>

Hazard Ratios for Colon Cancer Related death Chemotherapy vs. No Chemotherapy, by Age
Elderly patients Fu Lev, FuFol

n= 3351 (15% > 70y)  7 trials
Pooled analysis on individual data (C-08, Xeloxa, X-ACT, AVANT)

Univariable analysis

<table>
<thead>
<tr>
<th>Events, n (%)</th>
<th>HR</th>
<th>95% CI</th>
<th>P (Wald test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV5-FU &lt;70</td>
<td>472</td>
<td>0.62</td>
<td>0.54–0.72</td>
</tr>
<tr>
<td>XELOX/FOLFOX &lt;70</td>
<td>375</td>
<td>0.61</td>
<td>0.59–0.63</td>
</tr>
<tr>
<td>LV5-FU ≥70</td>
<td>162</td>
<td>0.78</td>
<td>0.61–0.99</td>
</tr>
<tr>
<td>XELOX/FOLFOX ≥70</td>
<td>112</td>
<td>0.78</td>
<td>0.61–0.99</td>
</tr>
</tbody>
</table>

Number at risk

| LV5-FU <70 | 1497 | 1454 | 1402 | 1350 | 1280 | 1207 | 1156 | 1106 | 1050 | 1012 | 931 | 781 | 581 | 201 | 38 | 4 | 0 |
| LV5-FU ≥70 | 424  | 407  | 398  | 379  | 358  | 334  | 321  | 307  | 284  | 267  | 245 | 198 | 142 | 56  | 13 | 1 | 0 |
| XELOX/FOLFOX <70 | 2418 | 2329 | 2267 | 2197 | 2098 | 1848 | 1426 | 1070 | 879  | 638  | 541 | 526 | 437 | 135 | 3  | 0 | 0 |
| XELOX/FOLFOX ≥70 | 480  | 450  | 431  | 414  | 399  | 344  | 274  | 208  | 173  | 130  | 117 | 110 | 88  | 35  | 3 | 0 | 0 |
Population-based data (real life..)

- 2920 patients: 1399 < 70y, 1521 ≥ 70y
  - 48% vs 81% adjuvant CT

**TABLE 2. Chemotherapy Regimens Delivered to Stage III Colon Cancer Patients in Ontario, 2002-2008 (n = 1861)**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>&lt;70 y (n = 1136)</th>
<th>70-74 y (n = 329)</th>
<th>75-79 y (n = 262)</th>
<th>≥80 y (n = 134)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-FU</td>
<td>200 (18)</td>
<td>73 (22)</td>
<td>51 (20)</td>
<td>19 (14)</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>32 (3)</td>
<td>66 (20)</td>
<td>88 (34)</td>
<td>57 (43)</td>
</tr>
<tr>
<td>FOLFOX</td>
<td>391 (34)</td>
<td>56 (17)</td>
<td>36 (14)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>FOLFIRI</td>
<td>166 (15)</td>
<td>29 (9)</td>
<td>10 (4)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>347 (31)</td>
<td>105 (32)</td>
<td>77 (29)</td>
<td>50 (37)</td>
</tr>
</tbody>
</table>

Abbreviations: 5-FU, 5-fluorouracil; FOLFIRI, folinic acid, fluorouracil, and irinotecan; FOLFOX, folinic acid, fluorouracil, and oxaliplatin. Percentages may add up to more than 100% because of rounding.

- Improved Cancer specific survival and OS: 0.53 and 0.56
- Effect smaller than that in younger patients

Merchant S et al Cancer 2017
Algorithm of decision in stage II disease

Stage II colon cancer

- Age < 70y
  - pT4
    - pMMR / MSS: Consider adj. CTx
    - dMMR / MSI-H: Additional marker: less than 12 LN / PNI? Gene signature / miRNA?
  - pT3: No adj. CTx
- Advanced age or comorbidities

ESMO PRECEPTORSHIP PROGRAM
Stage III disease

Complete resection

Adjuvant CT has to be discussed

Reference

Options

Folfox4 or Xelox

CI oxaliplatin: LV5FU2 or cap

> 70 y: Capecitabine or LV5FU2

DPD measure before tmt

ESMO PRECEPTORSHIP PROGRAM