

## Meta-analysis comparing maintenance strategies with continuous therapy and complete chemotherapy-free interval strategies in the treatment of metastatic colorectal cancer

### Supplementary Materials

#### Chemotherapy regimens in the trials included in the pool analysis

##### (1) XelQuali :

###### Induction:XELOX

Oxaliplatin 130 mg/m<sup>2</sup> IV over 2 hours day 1  
 Capecitabine 1000 mg/m<sup>2</sup> twice daily PO days 1–14  
 (total daily dose 2000 mg/m<sup>2</sup>)  
 Repeated every 3 weeks

###### Maintenance:Capecitabine

Capecitabine 1,250 mg/m<sup>2</sup> twice daily PO days 1–14  
 every 3 weeks until PD

##### (2) CCOG-0704:

###### Induction:mFOLFOX6

Oxaliplatin 85 mg/m<sup>2</sup> IV over 2 hours day 1  
 1-LV 200 mg/m<sup>2</sup> IV over 2 hours days 1  
 5-FU 400 mg/m<sup>2</sup> IV bolus days 1  
 5-FU 2,400 mg/m<sup>2</sup> IV over 46 hours days 1  
 Repeated every 2 weeks.

###### Maintenance: S-1

80 mg for patients with body surface area (BSA) < 1.25 m<sup>2</sup>;  
 100 mg for patients with BSA 1.25–1.5 m<sup>2</sup>  
 120 mg for patients with BSA ≥ 1.5 m<sup>2</sup>  
 (total daily dose was administered orally in two divided doses for 28 days, followed by a 14-day treatment-free interval)

##### (3) GERCOR DREAM; OPTIMOX3:

Induction:

###### BEV+FOLFIRI:

Irinotecan 180 mg/m<sup>2</sup> 90 minutes infusion day 1  
 Folinic acid 400 mg/m<sup>2</sup> racemic form day 1  
 or 200 mg/m<sup>2</sup> levo form 2-h infusion  
 5-FU 400 mg/m<sup>2</sup> 15-min infusion day 1  
 5-FU 2400 mg/m<sup>2</sup> 46-h continuous infusion day 1  
 BEV: 5 mg/kg IV over 90 minutes day 1  
 Repeated every 2 weeks

###### BEV+mFOLFOX7:

Oxaliplatin 100 mg/m<sup>2</sup> 2-h infusion day 1  
 Folinic acid 400 mg/m<sup>2</sup> racemic form or 200 mg/m<sup>2</sup> levo form 2-h infusion day 1

Fluorouracil 2400 mg/m<sup>2</sup> 46-h continuous infusion day 1  
 BEV: 5 mg/kg IV over 90 minutes day 1  
 Repeated every 2 weeks

###### BEV+mXELOX:

Oxaliplatin 100 mg/m<sup>2</sup> 2-h infusion day 1  
 Capecitabine 1250 mg/m<sup>2</sup> twice daily PO day 1  
 (total daily dose 2500 mg/m<sup>2</sup>)  
 Repeated every 3 weeks.

###### Maintenance:

Arm1: BEV 7.5 mg/kg IV over 90 minutes day 1  
 Repeated every 3 weeks  
 Arm2: BEV+ Erlo  
 BEV 7.5 mg/kg IV over 90 minutes day 1  
 Repeated every 3 weeks  
 Erlo 150 mg once daily

##### (4) Nordic Act:

Induction:

###### BEV+ XELOX

Oxaliplatin 130 mg/m<sup>2</sup> IV over 2 hours day 1  
 Capecitabine 1000 mg/m<sup>2</sup> twice daily PO days 1–14  
 (total daily dose 2000 mg/m<sup>2</sup>)  
 BEV 7.5 mg/kg IV over 30 minutes or according to local practice day 1  
 Repeated every 3 weeks

###### BEV+ XELIRI:

Irinotecan 180 mg/m<sup>2</sup> 90 minutes infusion day 1  
 Capecitabine 1000 mg/m<sup>2</sup> bid on days days 1–14  
 (total daily dose 2000 mg/m<sup>2</sup>)  
 BEV 7.5 mg/kg IV over 30 minutes or according to local practice day 1  
 Repeated every 2 weeks

###### BEV+ FOLFOX:

Oxaliplatin 85 mg/m<sup>2</sup> IV 2 hours day 1  
 Leucovorin 200 mg/m<sup>2</sup> IV 2 hours day 1  
 5-FU 400 mg/m<sup>2</sup> iv bolus day 1  
 5-FU 2400 mg/m<sup>2</sup> iv over 44 hours, day 1  
 BEV 5.0 mg/kg IV over 30 minutes or according to local practice day 1  
 Repeated every 2 weeks

Maintenance:?

**(5) CAIRO3**

Induction:CAPOX-B:

Capecitabine 1000 mg/m<sup>2</sup> orally twice daily days 1–14

Oxaliplatin 130 mg/m<sup>2</sup> intravenously day 1

Bevacizumab 7.5 mg/kg intravenously day 1,

Repeated every 3 weeks

Maintenance:Capecitabine

Capecitabine 625 mg/m<sup>2</sup> orally twice daily days 1–14

Bevacizumab 7.5 mg/kg intravenously days 1

Repeated every 3 weeks

**(6) OPTIMOX1**

Induction:

**FOLFOX4:**

Oxaliplatin 85 mg/m<sup>2</sup> 2-hour infusion days 1

Leucovorin isomers 1-LV 100 mg/m<sup>2</sup> or dl-LV 200 mg/m<sup>2</sup> 2-hour infusion day 1

5-FU 400 mg/m<sup>2</sup> iv bolus

5-FU 600 mg/m<sup>2</sup> iv over 23 hours days 1–2

Repeated every 2 weeks

**FOLFOX7:**

Oxaliplatin 130 mg/m<sup>2</sup> 2-hour infusion day 1

Leucovorin isomers 1-LV 200 mg/m<sup>2</sup> or dl-LV 400 mg/m<sup>2</sup> 2-hour infusion day 1

5-FU 2400 mg/m<sup>2</sup> 46-hour infusion day 1

Repeated every 2 weeks

(s) LV5FU2:

L-LV 200 mg/m<sup>2</sup> or dl-LV 400 mg/m<sup>2</sup> 2-hour infusion

5-FU 400 mg/m<sup>2</sup> iv bolus

5-FU 3,000 mg/m<sup>2</sup> 46-hour infusion

Repeated every 2 weeks

**(7) AIO 0207**

**CAPOX:**

Capecitabine 1000 mg/m<sup>2</sup> twice daily PO days 1–14, 22–35

(total daily dose 2000 mg/m<sup>2</sup>)

Oxaliplatin 70 mg/m<sup>2</sup> IV over 2 hours days 1, 8, 22, 29

Cycle repeated day 43

Bevacizumab 7.5 mg/kg IV over 90 minutes, days 1, 22

if tolerated subsequently over 60 and 30 minutes

Repeated day 43

**XELOX:**

Capecitabine 1000 mg/m<sup>2</sup> twice daily PO days 1–14, 22–35

(total daily dose 2000 mg/m<sup>2</sup>)

Oxaliplatin 130 mg/m<sup>2</sup> IV over 2 hours days 1, 22

Cycle repeated day 43

Bevacizumab 7.5 mg/kg IV over 90 days 1, 22 minutes, if tolerated subsequently over 60 and 30 minutes

Repeated day 43

**FOLFOX6:**

Oxaliplatin 100 mg/m<sup>2</sup> IV over 2 hours days 1, 15, 29

(dl-)Folinic acid 400 mg/m<sup>2</sup> IV over 2 days 1, 15, 29 hours

5-FU 400 mg/m<sup>2</sup> IV bolus days 1, 15, 29

5-FU 2400 mg/m<sup>2</sup> IV over 46 hours days 1, 15, 29

Cycle repeated day 43

Bevacizumab 5 mg/kg IV over 90 minutes days 1, 15, 29

if tolerated subsequently over 60 and 30 minutes

Repeated day 43

**FOLFOX4:**

Oxaliplatin 85 mg/m<sup>2</sup> IV over 2 hours days 1, 15, 29

(dl-)Folinic acid 200 mg/m<sup>2</sup> IV over 2 days 1, 2, 15, 16, 29, 30 hours

5-FU 400 mg/m<sup>2</sup> IV bolus days 1, 2, 15, 16, 29, 30

5-FU 600 mg/m<sup>2</sup> IV over 22 hours days 1, 2, 15, 16, 29, 30

Cycle repeated day 43

Bevacizumab 5 mg/kg IV over 90 minutes days 1, 15, 29

if tolerated subsequently over 60 and 30 minutes

Repeated day 43

**Modified FOLFOX7:**

Oxaliplatin 100 mg/m<sup>2</sup> IV over 2 hours days 1, 15, 29

(dl-)Folinic acid 400 mg/m<sup>2</sup> IV over 2 days 1, 15, 29 hours

5-FU 3000 mg/m<sup>2</sup> IV over 46 hours days 1, 15, 29

Cycle repeated day 43

Bevacizumab 5 mg/kg IV over 90 minutes days 1, 15, 29

if tolerated subsequently over 60 and 30 minutes

Repeated day 43

**Modified FOLFOX4:**

Oxaliplatin 85 mg/m<sup>2</sup> IV over 2 hours days 1, 15, 29

(dl-)Folinic acid 400 mg/m<sup>2</sup> IV over 2 days 1, 15, 29 hours

5-FU 3000 mg/m<sup>2</sup> IV over 46 hours days 1, 15, 29

Cycle repeated day 43

Bevacizumab 5 mg/kg IV over 90 minutes days 1, 15, 29

if tolerated subsequently over 60 and 30 minutes

Repeated day 43

**Simplified FOLFOX4:**

Oxaliplatin 85 mg/m<sup>2</sup> IV over 2 hours days 1, 15, 29  
(dl-)Folinic acid 400 mg/m<sup>2</sup> IV over 2 days  
1, 15, 29 hours  
5-FU 400 mg/m<sup>2</sup> IV bolus days 1, 15, 29  
5-FU 2400 mg/m<sup>2</sup> IV over 46 hours days 1, 15, 29  
Cycle repeated day 43  
Bevacizumab 5 mg/kg IV over 90 minutes, days  
1, 15, 29  
if tolerated subsequently over 60 and 30 minutes  
Repeated day 43

**(8) OPTIMOX2****Modified FOLFOX7:**

Oxaliplatin 100 mg/m<sup>2</sup> 2-hour infusion day 1  
LV 400 mg/m<sup>2</sup> 2-hour infusion day 1  
5-FU 3000 mg/m<sup>2</sup> 48-hour infusion day 1  
Repeated every 2 weeks

**Simplified LV5FU2:**

LV 400 mg/m<sup>2</sup> 2-hour infusion day 1  
5-FU 400 mg/m<sup>2</sup> IV bolus day 1  
5-FU 3000 mg/m<sup>2</sup> 48-hour infusion day 1  
Repeated every 2 weeks

**(9) MACRO**

Induction:

**XELOX:**

Oxaliplatin 130 mg/m<sup>2</sup> day 1  
Capecitabine 1,000 mg/m<sup>2</sup> twice daily days 1–14  
Bevacizumab 7.5 mg/kg day 1  
Repeated every 3 weeks

**(10) Yalcin 2013**

Induction:

**XELOX:**

Oxaliplatin 130 mg/m<sup>2</sup> IV on day 1  
Capecitabine 1,000 mg/m<sup>2</sup> orally twice daily days  
1–14  
bevacizumab 7.5 mg/kg day 1  
Repeated every 3 weeks

**(11) NORDIC VII****Arm A: FLOX**

Regimen 23 was administered every 2 weeks as  
Oxaliplatin 85 mg/m<sup>2</sup> over 1 hour (30 to 90 minutes)  
day 1  
5-FU 500 mg/m<sup>2</sup> IV bolus (<5 minutes) day 1 and 2  
FA 60 mg/m<sup>2</sup> IV bolus (<10 minutes) days 1 and 2  
Repeated every 2 weeks

**Arm C: FLOX+Cetuximab**

Cetuximab was administered every week as an  
initial dose of 400 mg/m<sup>2</sup> and there after 250 mg/m<sup>2</sup>.