Proposed

Colorectal cancer systemic anti-cancer therapy (chemotherapy) regimens: Draft definitions for review

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# Introduction

**Tēnā koutou katoa**

**We are seeking your clinical review of proposed colorectal systemic anti-cancer therapy (chemotherapy) regimen definitions.**

The Ministry and the Systemic Anti-Cancer Therapy (SACT) NZ Colorectal Work Group have developed a set of regimen definitions for colorectal cancer. Driven primarily by the Medical Oncology Work Group (MOWG), the intention of this work is to implement consistent and agreed naming conventions for all common regimens in use for the treatment of colorectal cancer across the New Zealand public and private sector. Having consistent definitions provides the foundation for the collection and synthesis of this data into actionable intelligence and supports the improvement of outcomes for people with cancer.

It is important to make clear that this project is not about mandating specific treatments for specific cancers; it is not about telling oncologists how to prescribe. This project is about ensuring that whatever regimen an oncologist chooses to prescribe is named according to an agreed nomenclature and that (sometimes subtly) different regimens are appropriately labelled and differentiated through this nomenclature.

|  |
| --- |
| **What feedback are we seeking?**We are providing an opportunity for all professionals involved in medical oncology services to provide feedback on this set of regimen definitions. In particular, we would like to know;* if you think these definitions are accurate and reflective of current practice
* if these definitions cover the range of regimens in common use across the New Zealand public and private sector.

**Who are we seeking feedback from?**Primarily we are seeking feedback from medical oncologists, pharmacists and nurse specialists, who provide and support SACT treatment services for people with colorectal cancer in New Zealand. Other DHB staff may also wish to comment on the regimens definitions. We expect individuals will assess the regimens in areas that relate to their specialist knowledge and they may review as many regimens as they wish. **How can you provide your feedback?**You can provide feedback, comments and any queries about the regimens or regimen development process to,SACTNZ@health.govt.nz**When do we need feedback by?**Please complete your review of these definitions and submit any other feedback by **Friday 6 December 2019.** |

### Background

**SACT NZ project purpose**

Systemic Anti-Cancer Therapy (SACT) refers to a group of cancer treatments comprising chemotherapy agents alongside targeted therapies, immunotherapy and supportive care medicines to reduce side effects. SACT is delivered in regimens, often containing combinations of multiple anticancer agents and supportive medications.

The purpose of this project is to deliver key components to address existing information gaps in monitoring SACT variation, quality, access and performance in New Zealand. These include development of:

1. Standardised data definitions, regimens and other nomenclature.
2. SACT measures and indicators that include the capability to determine complexity, quality and consistency of service provision, including specifying the data items to support this.
3. A centralised data repository and associated reporting cycle to regularly collect, validate and store SACT data items (analogous to the Radiation Oncology Collection).
4. An analysis and presentation layer to regularly update and disseminate key information and intelligence derived from SACT data.

Successful delivery of these components will require that opportunities for capturing additional data relating to quality, consistency of access and treatment variation are identified, with suggestions for improving the analysis and interpretation of SACT data and information. Close alignment with the Cancer Health Information Strategy (CHIS) work streams and other IT projects within the sector is crucial. This data standardisation, collection and analytics project will serve as a key enabler of the wider SACT NZ work programme, and aims to drive performance and efficiencies that result in improved outcomes and reduced inequities for people with cancer. This document relates to number 1 above and presents proposed standardised regimen definitions for colorectal cancer.

**What is a regimen?**

A regimen is a combination of one or more drugs given together at specific doses and according to a pattern that often repeats (known as a cycle). There is agreement with the Medical Oncology Work Group (MOWG) to initially define the following for all regimens in common use across New Zealand:

* regimen name (eg, Colorectal metastatic FOLFOX6)
* constituent anticancer drugs (eg, Capecitabine)
* doses and dose unit for each drug (eg, 50 mg/m2)
* dose frequencies for each drug (eg, day 1 and 8)
* cycle length (eg, 21 days)
* route of administration for each drug (eg, IV)
* max duration over which each dose should be delivered (eg, 2 hours).

**Guiding principles in the development of regimen definitions**

The following key principles have guided the development of the definitions in this document:

1. Use existing NSW eviQ definitions as the starting point for our own New Zealand definitions <https://www.eviq.org.au/medical-oncology>.
2. Each regimen should be supported by evidence in the medical oncology literature.
3. Each regimen name should be clearly labelled with the indication it is intended to treat (eg ‘Colorectal’) and whether it is an adjuvant, metastatic or combined chemo/radiation regimen.
4. This work is about developing definitions for commonly prescribed or ‘standard’ regimens. Providers must always retain the ability to rapidly create new regimens not on this list in response to patient need.
5. Specific supportive care regimens will be developed as a separate work stream; although each regimen will be allocated a rating on at least the four dimensions of:
	1. emetogenicity
	2. hypersensitivity
	3. growth factor support
	4. anti-diarrhoeals.

These ratings will guide the choice of which supportive care regimens are paired with each anticancer regimens. Definitions of these dimensions and ratings are included in Appendix 2.

1. Total agreement on all regimen elements is not a prerequisite for inclusion on this list. This work is about clearly defining the range of regimens in use across New Zealand and is not about debating their validity as treatment options or restricting the choice of regimens available to oncologists.

**How did we come up with these regimen definitions?**

The development process for these regimens followed the following process:

1. We collected all regimens in use across the public sector and most or all regimens in use across the private sector. See Appendix 1 for a table of centres whose regimens have been sourced and documented.
2. Each of the centres using their own unique set of colorectal regimens were asked to nominate a colorectal oncology representative to participate in a half day workshop to develop a national set of colorectal regimen definitions. See Appendix A for list of representatives.
3. Each regimen from each centre was compared against the equivalent regimen from the New South Wales eviQ library of SACT regimens (<https://www.eviq.org.au/medical-oncology/colorectal>). Any regimen item (drugs, doses etc) that did not align precisely with the eviQ definition was flagged as a difference.
4. Each centre representative was provided with a list of the differences between their regimens and the equivalent eviQ definition and were asked whether they were willing to align with the eviQ definition and whether they felt this was a difference that required discussion within a workshop. Representatives were asked to consult with their teams, including pharmacists and nurse specialists prior to responding.
5. A half day workshop with centre representatives was held to discuss unresolved variations and develop a draft national list of colorectal regimen definitions. If there were unresolved disagreements on the exact definition of a particular regimen then two versions were created. An example of this is the inclusion of both high and low dose folinic acid versions of FOLFOX6. These draft definitions are presented in this document below for review and feedback.

**What will happen next?**

Your feedback will be presented and considered by the SACT Colorectal Working Group. Feedback will be incorporated into an agreed final set of colorectal regimen definitions. Centres will be requested to update their local regimen definitions to align with those presented in the finalised set. At present, an annual review and update process for these regimens is planned with the working group.

### Key outcomes of workgroup meeting (5 July 2019)

* Agreement to adopt eviQ naming convention but exclude individual drug names in brackets as part of name. Reason for this is limited field size in e-prescribing systems.
* Use generic drug names and exclude references to trade names within regimen definitions.
* Definitions should specify a ‘max duration’ over which each drug should be given. This reflects small differences in how drugs are delivered (eg, 3 min IV push vs 15 min IV small bag)
* Doses of folinic acid assume the less bioavailable d-isomer is used as is generally the case in New Zealand at the time of writing. Centres should check the folinic acid isomer they are using and adjust the dose if necessary.
* This list includes all regimens currently in use across the public sector and most regimens in the private sector. Inclusion of a regimen in this list does not therefore indicate whether a regimen’s drugs are all fully funded or not. Please refer to PHARMAC for guidance on funding and eligibility criteria [www.pharmac.govt.nz](http://www.pharmac.govt.nz).

# Colorectal regimen definitions

Adjuvant regimens

1. Colorectal adjuvant capecitabine

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Capecitabine | 1,250 mg/m2 TWICE a day  | Oral | 1 to 14 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Twelves, C., W. Scheithauer, J. McKendrick, et al. 2012. "Capecitabine versus 5-fluorouracil/folinic acid as adjuvant therapy for stage III colon cancer: final results from the X-ACT trial with analysis by age and preliminary evidence of a pharmacodynamic marker of efficacy." Ann Oncol 23(5):1190-1197.
2. Twelves, C., A. Wong, M. P. Nowacki, et al. 2005. "Capecitabine as adjuvant treatment for stage III colon cancer." N.Engl.J.Med. 352(26):2696-2704.
3. Colorectal adjuvant CAPOX

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Capecitabine | 1,000 mg/m2 TWICE a day  | Oral | 1 to 14 | - |
| Oxaliplatin | 130 mg/m2  | IV | 1 | 120m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Grothey, A., A. Sobrero, A. Shields, et al. 2018. "Duration of Adjuvant Chemotherapy for Stage III Colon Cancer". N Engl J Med 2018;378:1177-88
2. Haller, D. G., J. Tabernero, J. Maroun, et al. 2011. "Capecitabine plus oxaliplatin compared with fluorouracil and folinic acid as adjuvant therapy for stage III colon cancer." J Clin Oncol 29(11):1465-1471.
3. Cassidy, J., S. Clarke, E. Diaz-Rubio, et al. 2008. "Randomized phase III study of capecitabine plus oxaliplatin compared with fluorouracil/folinic acid plus oxaliplatin as first-line therapy for metastatic colorectal cancer." J Clin Oncol 26(12):2006-2012.
4. Schmoll, H. J., T. Cartwright, J. Tabernero, et al. 2007. "Phase III trial of capecitabine plus oxaliplatin as adjuvant therapy for stage III colon cancer: a planned safety analysis in 1,864 patients." J Clin Oncol 25(1):102-109.
5. Colorectal adjuvant de Gramont (modified) (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic Acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 3,000 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Andre, T., P. Colin, C. Louvet, et al. 2003. "Semimonthly versus monthly regimen of fluorouracil and leucovorin administered for 24 or 36 weeks as adjuvant therapy in stage II and III colon cancer: results of a randomized trial." J.Clin Oncol 21(15):2896-2903.
2. Colorectal adjuvant de Gramont (modified) (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 3,000 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Andre, T., P. Colin, C. Louvet, et al. 2003. "Semimonthly versus monthly regimen of fluorouracil and leucovorin administered for 24 or 36 weeks as adjuvant therapy in stage II and III colon cancer: results of a randomized trial." J.Clin Oncol 21(15):2896-2903.
2. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
3. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
4. Colorectal adjuvant FOLFOX6 (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 85 mg/m2  | IV | 1 | 120m |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump  | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Grothey, A., A. Sobrero, A. Shields, et al. 2018. "Duration of Adjuvant Chemotherapy for Stage III Colon Cancer". N Engl J Med 2018;378:1177-88
2. Andre, T., C. Boni, L. Mounedji-Boudiaf, et al. 2004. "Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer." N.Engl.J.Med. 350(23):2343-2351.
3. Andre, T., C. Boni, M. Navarro, et al. 2009. "Improved overall survival with oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment in stage II or III colon cancer in the MOSAIC trial." J Clin Oncol 27(19):3109-3116.
4. Colorectal adjuvant FOLFOX6 (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 85 mg/m2 | IV | 1 | 120m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Grothey, A., A. Sobrero, A. Shields, et al. 2018. "Duration of Adjuvant Chemotherapy for Stage III Colon Cancer". N Engl J Med 2018;378:1177-88
2. Andre, T., C. Boni, L. Mounedji-Boudiaf, et al. 2004. "Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer." N.Engl.J.Med. 350(23):2343-2351.
3. Andre, T., C. Boni, M. Navarro, et al. 2009. "Improved overall survival with oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment in stage II or III colon cancer in the MOSAIC trial." J Clin Oncol 27(19):3109-3116.
4. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
5. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
6. Colorectal adjuvant QUASAR

**7 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 370 mg/m2  | IV | 1 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. QUASAR Collaborative Group. 2000. "Comparison of flourouracil with additional levamisole, higher-dose folinic acid, or both, as adjuvant chemotherapy for colorectal cancer: a randomised trial." Lancet. 355(9215):1588-1596
2. Patel, K., D. A. Anthoney, et al. 2004. "Weekly 5-fluorouracil and leucovorin: achieving lower toxicity with higher dose-intensity in adjuvant chemotherapy after colorectal cancer resection." Ann.Oncol 15(4): 568-573.
3. Colorectal adjuvant Roswell Park (low dose folinic acid)

**56 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 50 mg | IV | 1, 8, 15, 22, 29, 36 | 2m |
| Fluorouracil | 500 mg/m2  | IV | 1, 8, 15, 22, 29, 36 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Wolmark, N., H. Rockette, B. Fisher, et al. 1993. "The benefit of leucovorin-modulated fluorouracil as postoperative adjuvant therapy for primary colon cancer: results from National Surgical Adjuvant Breast and Bowel Project protocol C-03." J.Clin Oncol. 11(10):1879-1887.
2. Kuebler, J. P., H. S. Wieand, M. J. O'Connell, et al. 2007. "Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07." J Clin Oncol 25(16):2198-2204.
3. Kuebler, J. P., H. S. Wieand, M. J. O'Connell, et al. 2007. "Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07." J Clin Oncol 25(16):2198-2204.

1. Colorectal adjuvant Roswell Park (high dose folinic acid)

**56 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 400 mg/m2 | IV | 1, 8, 15, 22, 29, 36 | 120m |
| Fluorouracil | 500 mg/m2  | IV | 1, 8, 15, 22, 29, 36 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Wolmark, N., H. Rockette, B. Fisher, et al. 1993. "The benefit of leucovorin-modulated fluorouracil as postoperative adjuvant therapy for primary colon cancer: results from National Surgical Adjuvant Breast and Bowel Project protocol C-03." J.Clin Oncol. 11(10):1879-1887.
2. Kuebler, J. P., H. S. Wieand, M. J. O'Connell, et al. 2007. "Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07." J Clin Oncol 25(16):2198-2204.
3. Kuebler, J. P., H. S. Wieand, M. J. O'Connell, et al. 2007. "Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07." J Clin Oncol 25(16):2198-2204.
4. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
5. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
6. Colorectal adjuvant MAYO

**28 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 50 mg | IV | 1 to 5 | 2m |
| Fluorouracil | 425 mg/m2 | IV | 1 to 5 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. International Multicentre Pooled Analysis of Colon Cancer Trials (IMPACT) investigators.1995."Efficacy of adjuvant fluorouracil and folinic acid in colon cancer. " Lancet. 345(8955):939-44
2. Rectal locally advanced capecitabine chemoradiation (5 day dosing)

**7 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Capecitabine | 825 mg/m2 TWICE a day  | Oral | 1 to 5 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Roh, M., GA Yothers, MJ O'Connell, et al. 2011. "The impact of capecitabine and oxaliplatin in the preoperative multimodality treatment in patients with carcinoma of the rectum: NSABP R-04." J. Clin. Oncol 29(18 Suppl):3503.
2. Hofheinz, R. D., F. Wenz, S. Post, et al. 2012. "Chemoradiotherapy with capecitabine versus fluorouracil for locally advanced rectal cancer: a randomised, multicentre, non-inferiority, phase 3 trial." Lancet Oncol 13(6):579-588.
3. Rectal locally advanced capecitabine chemoradiation (continuous dosing)

**7 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Capecitabine | 825 mg/m2 TWICE a day  | Oral | 1 to 7 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Roh, M., GA Yothers, MJ O'Connell, et al. 2011. "The impact of capecitabine and oxaliplatin in the preoperative multimodality treatment in patients with carcinoma of the rectum: NSABP R-04." J. Clin. Oncol 29(18 Suppl):3503.
2. Hofheinz, R. D., F. Wenz, S. Post, et al. 2012. "Chemoradiotherapy with capecitabine versus fluorouracil for locally advanced rectal cancer: a randomised, multicentre, non-inferiority, phase 3 trial." Lancet Oncol 13(6):579-588.
3. Rectal locally advanced fluorouracil chemoradiation

**7 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Fluorouracil | 1,575 mg/m2 (equivalent to 225 mg/m2/day) | CIV via pump | 1 | 7 days |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Bosset, J. F., G. Calais, A. Daban, et al. 2004. "Preoperative chemoradiotherapy versus preoperative radiotherapy in rectal cancer patients: assessment of acute toxicity and treatment compliance. Report of the 22921 randomised trial conducted by the EORTC Radiotherapy Group." Eur J Cancer 40(2):219-224.
2. Bosset, J. F., L. Collette, G. Calais, et al. 2006. "Chemotherapy with preoperative radiotherapy in rectal cancer." N.Engl.J Med. 355(11):1114-1123.
3. O'Connell, M. J., J. A. Martenson, H. S. Wieand, et al. 1994. "Improving adjuvant therapy for rectal cancer by combining protracted-infusion fluorouracil with radiation therapy after curative surgery." N.Engl.J.Med. 331(8):502-507.
4. Sauer, R., H. Becker, W. Hohenberger, et al. 2004. "Preoperative versus postoperative chemoradiotherapy for rectal cancer." N.Engl.J.Med. 351(17):1731-1740.

Metastatic regimens

1. Colorectal metastatic capecitabine (1000)

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Capecitabine | 1,000 mg/m2 TWICE a day  | Oral | 1 to 14 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Van Cutsem, E., P. M. Hoff, P. Harper, et al. 2004. "Oral capecitabine vs intravenous 5-fluorouracil and leucovorin: integrated efficacy data and novel analyses from two large, randomised, phase III trials." Br J Cancer 90(6):1190-1197.
2. Cassidy, J., C. Twelves, E. Van Cutsem, et al. 2002. "First-line oral capecitabine therapy in metastatic colorectal cancer: a favorable safety profile compared with intravenous 5-fluorouracil/leucovorin." Ann.Oncol 13(4):566-575.
3. Colorectal metastatic capecitabine (1250)

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Capecitabine | 1,250 mg/m2 TWICE a day  | Oral | 1 to 14 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Van Cutsem, E., P. M. Hoff, P. Harper, et al. 2004. "Oral capecitabine vs intravenous 5-fluorouracil and leucovorin: integrated efficacy data and novel analyses from two large, randomised, phase III trials." Br J Cancer 90(6):1190-1197.
2. Cassidy, J., C. Twelves, E. Van Cutsem, et al. 2002. "First-line oral capecitabine therapy in metastatic colorectal cancer: a favorable safety profile compared with intravenous 5-fluorouracil/leucovorin." Ann.Oncol 13(4):566-575.
3. Colorectal metastatic capecitabine and bevacizumab

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Bevacizumab | 7.5 mg/kg  | IV | 1 | 90 minutes |
| Capecitabine | 1,250 mg/m2 TWICE a day  | Oral | 1 to 14 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Tebbutt, N. C., K. Wilson, V. J. Gebski, et al. 2010. "Capecitabine, bevacizumab, and mitomycin in first-line treatment of metastatic colorectal cancer: results of the Australasian Gastrointestinal Trials Group Randomized Phase III MAX Study." J Clin Oncol 28(19):3191-3198.
2. Colorectal metastatic capecitabine and mitomycin

**42 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Mitomycin | 7 mg/kg  | IV | 1 | 90 minutes |
| Capecitabine | 1,000 mg/m2 TWICE a day  | Oral | 1 to 14 and 22 to 35 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Chong, G., J. L. Dickson, D. Cunningham, et al. 2005. "Capecitabine and mitomycin C as third-line therapy for patients with metastatic colorectal cancer resistant to fluorouracil and irinotecan." Br J Cancer 93(5):510-514.
2. Vrdoljak, E., T. Omrcen, M. Boban, et al. 2008. "Capecitabine and mitomycin-C in the therapy of pretreated patients with metastatic colorectal cancer: single center retrospective study with 36 patients." J B. U. ON. 13(4):513-518.
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6. Colorectal metastatic CAPIRI

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 240 mg/m2  | IV | 1 | 90m |
| Capecitabine | 800 mg/m2 TWICE a day  | Oral | 1 to 14 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Xu RH, Muro K, Morita S *et al*. Modified XELIRI (capecitabine plus irinotecan) versus FOLFIRI (leucovorin, fluorouracil, and irinotecan), both either with or without bevacizumab, as second‐line therapy for metastatic colorectal cancer (AXEPT): A multicentre, open‐label, randomised, non‐inferiority, phase 3 trial. *Lancet Oncol* 2018; 9: 660– 71.
2. Colorectal metastatic CAPIRI (modified) (200 irinotecan fractionated)

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 100 mg/m2 | IV | 1,8 | 90m |
| Capecitabine | 800 mg/m2 TWICE a day  | Oral | 1 to 14 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Xu RH, Muro K, Morita S *et al*. Modified XELIRI (capecitabine plus irinotecan) versus FOLFIRI (leucovorin, fluorouracil, and irinotecan), both either with or without bevacizumab, as second‐line therapy for metastatic colorectal cancer (AXEPT): A multicentre, open‐label, randomised, non‐inferiority, phase 3 trial. *Lancet Oncol* 2018; 9: 660– 71.
2. Colorectal metastatic cetuximab

**7 day cycle**

**Cycle 1**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Cetuximab | 400 mg/m2 (loading dose only)  | IV | 1 | 120m |

**Cycle 2 and further cycles**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Cetuximab | 250 mg/m2 (subsequent doses)  | IV | 1 | 60m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Minimal | High | Secondary | Yes |

**References**

1. Nott, L., M. Khattak, T. Price, et al. Cancer Council Australia Colorectal Cancer Guidelines Working Party. [Version URL: https://wiki.cancer.org.au/australiawiki/index.php?oldid=173114, cited 2018 Apr 16]. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal\_cancer/Systemic\_therapy\_molecular\_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party. Cl
2. Jonker, D. J., C. J. O'Callaghan, C. S. Karapetis, et al. 2007. "Cetuximab for the treatment of colorectal cancer." N Engl J Med 357(20):2040-2048.
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5. Van Cutsem, E., H. J. Lenz, C. H. Kohne, et al. 2015. "Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and RAS Mutations in Colorectal Cancer." J Clin Oncol 33(7):692-700.
6. Heinemann, V., L. F. von Weikersthal, T. Decker, et al. 2014. "FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial." Lancet Oncol 15(10):1065-1075.
7. Douillard, J. Y., K. S. Oliner, S. Siena, et al. 2013. "Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer." N Engl J Med 369(11):1023-1034.
8. Colorectal metastatic cetuximab (weekly) and irinotecan (two weekly)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Cetuximab | 400 mg/m2 (loading dose only)  | IV | 1 | 120m |
| Cetuximab | 250 mg/m2  | IV | 8 | 60m |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |

**Cycle 2 and further cycles**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Cetuximab | 250 mg/m2 | IV | 1 and 8 | 60m |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | High | Secondary | Yes |

**References**

1. Nott, L., M. Khattak, T. Price, et al. Cancer Council Australia Colorectal Cancer Guidelines Working Party. [Version URL: https://wiki.cancer.org.au/australiawiki/index.php?oldid=173114, cited 2018 Apr 16]. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal\_cancer/Systemic\_therapy\_molecular\_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party. Cl
2. Van Cutsem, E., H. J. Lenz, C. H. Kohne, et al. 2015. "Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and RAS Mutations in Colorectal Cancer." J Clin Oncol 33(7):692-700.
3. Heinemann, V., L. F. von Weikersthal, T. Decker, et al. 2014. "FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial." Lancet Oncol 15(10):1065-1075.
4. Douillard, J. Y., K. S. Oliner, S. Siena, et al. 2013. "Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer." N Engl J Med 369(11):1023-1034.
5. Clarke, S. J., S. Yip, C. Brown, et al. 2011. "Single-agent irinotecan or FOLFIRI as second-line chemotherapy for advanced colorectal cancer; results of a randomised phase II study (DaVINCI) and meta-analysis [corrected]." Eur J Cancer 47(12):1826-1836.
6. Sobrero, A. F., J. Maurel, L. Fehrenbacher, et al. 2008. "EPIC: phase III trial of cetuximab plus irinotecan after fluoropyrimidine and oxaliplatin failure in patients with metastatic colorectal cancer." J Clin Oncol 26(14):2311-2319.
7. Cunningham, D., Y. Humblet, S. Siena, et al. 2004. "Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer." N.Engl.J.Med. 351(4):337-345.
8. Wilke, H., R. Glynne-Jones, J. Thaler, et al. 2008. "Cetuximab plus irinotecan in heavily pretreated metastatic colorectal cancer progressing on irinotecan: MABEL Study." J Clin Oncol 26(33):5335-5343.
9. Colorectal metastatic cetuximab and irinotecan (two weekly)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Cetuximab | 500 mg/m2  | IV | 1 | 120m |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | High | Secondary | Yes |

**References**

1. Nott, L., M. Khattak, T. Price, et al. Cancer Council Australia Colorectal Cancer Guidelines Working Party. [Version URL: https://wiki.cancer.org.au/australiawiki/index.php?oldid=173114, cited 2018 Apr 16]. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal\_cancer/Systemic\_therapy\_molecular\_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party. Cl
2. Van Cutsem, E., H. J. Lenz, C. H. Kohne, et al. 2015. "Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and RAS Mutations in Colorectal Cancer." J Clin Oncol 33(7):692-700.
3. Heinemann, V., L. F. von Weikersthal, T. Decker, et al. 2014. "FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial." Lancet Oncol 15(10):1065-1075.
4. Douillard, J. Y., K. S. Oliner, S. Siena, et al. 2013. "Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer." N Engl J Med 369(11):1023-1034.
5. Martin-Martorell, P., S. Rosello, E. Rodriguez-Braun, et al. 2008. "Biweekly cetuximab and irinotecan in advanced colorectal cancer patients progressing after at least one previous line of chemotherapy: results of a phase II single institution trial." Br J Cancer 99(3):455-458.
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7. Clarke, S. J., S. Yip, C. Brown, et al. 2011. "Single-agent irinotecan or FOLFIRI as second-line chemotherapy for advanced colorectal cancer; results of a randomised phase II study (DaVINCI) and meta-analysis [corrected]." Eur J Cancer 47(12):1826-1836.
8. Sobrero, A. F., J. Maurel, L. Fehrenbacher, et al. 2008. "EPIC: phase III trial of cetuximab plus irinotecan after fluoropyrimidine and oxaliplatin failure in patients with metastatic colorectal cancer." J Clin Oncol 26(14):2311-2319.
9. Cunningham, D., Y. Humblet, S. Siena, et al. 2004. "Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer." N.Engl.J.Med. 351(4):337-345.
10. Wilke, H., R. Glynne-Jones, J. Thaler, et al. 2008. "Cetuximab plus irinotecan in heavily pretreated metastatic colorectal cancer progressing on irinotecan: MABEL Study." J Clin Oncol 26(33):5335-5343.
11. Tabernero, J., F. Ciardiello, F. Rivera, et al. 2010. "Cetuximab administered once every second week to patients with metastatic colorectal cancer: a two-part pharmacokinetic/pharmacodynamic phase I dose-escalation study." Ann Oncol 21(7):1537-1545.
12. Colorectal metastatic CAPOX

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 130 mg/m2  | IV | 1 | 120m |
| Capecitabine | 1,000 mg/m2 TWICE a day  | Oral | 1 to 14 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Cassidy, J., S. Clarke, E. Diaz-Rubio, et al. 2008. "Randomized phase III study of capecitabine plus oxaliplatin compared with fluorouracil/folinic acid plus oxaliplatin as first-line therapy for metastatic colorectal cancer." J Clin Oncol 26(12):2006-2012.
2. Arkenau, H. T., D. Arnold, J. Cassidy, et al. 2008. "Efficacy of oxaliplatin plus capecitabine or infusional fluorouracil/leucovorin in patients with metastatic colorectal cancer: a pooled analysis of randomized trials." J Clin Oncol 26(36):5910-5917.
3. Cassidy, J., J. Tabernero, C. Twelves, et al. 2004. "XELOX (capecitabine plus oxaliplatin): active first-line therapy for patients with metastatic colorectal cancer." J.Clin Oncol 22(11):2084-2091.
4. Colorectal metastatic CAPOX and bevacizumab

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 130 mg/m2  | IV | 1 | 120m |
| Capecitabine | 1,000 mg/m2 TWICE a day  | Oral | 1 to 14 | - |
| Bevacizumab | 7.5mg/kg | IV | 1 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Saltz, L. B., S. Clarke, E. Diaz-Rubio, et al. 2008. "Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: a randomized phase III study." J Clin Oncol 26(12):2013-2019.
2. Colorectal metastatic de Gramont (modified) low dose folinic acid

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 3,000 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. de Gramont, A., J. F. Bosset, et al. 1997. "Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study" J.Clin Oncol. 15(2): 808-815.
2. Cheeseman, S. L., S. P. Joel, J. D. Chester, et al. 2002. "A 'modified de Gramont' regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer." Br J Cancer 87(4):393-399.
3. Limat, S., C. H. Bracco-Nolin, C. Legat-Fagnoni, et al. 2006. "Economic impact of simplified de Gramont regimen in first-line therapy in metastatic colorectal cancer." Eur J Health Econ 7(2):107-113.
4. de Gramont A., A. Figer, M. Seymour, et al. 2000. "Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer." J.Clin Oncol 18(16):2938-2947.
5. Colorectal metastatic de Gramont (modified) high dose folinic acid

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 5m |
| Fluorouracil | 3,000 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. de Gramont, A., J. F. Bosset, et al. 1997. "Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study" J.Clin Oncol. 15(2): 808-815.
2. Cheeseman, S. L., S. P. Joel, J. D. Chester, et al. 2002. "A 'modified de Gramont' regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer." Br J Cancer 87(4):393-399.
3. Limat, S., C. H. Bracco-Nolin, C. Legat-Fagnoni, et al. 2006. "Economic impact of simplified de Gramont regimen in first-line therapy in metastatic colorectal cancer." Eur J Health Econ 7(2):107-113.
4. de Gramont A., A. Figer, M. Seymour, et al. 2000. "Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer." J.Clin Oncol 18(16):2938-2947.
5. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
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7. Colorectal metastatic FOLFIRI (modified) (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Tournigand, C., T. Andre, E. Achille, et al. 2004. "FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study." J.Clin Oncol 22(2):229-237.
2. Colucci, G., V. Gebbia, G. Paoletti, et al. 2005. "Phase III randomized trial of FOLFIRI versus FOLFOX4 in the treatment of advanced colorectal cancer: a multicenter study of the Gruppo Oncologico Dell'Italia Meridionale." J.Clin Oncol 23(22):4866-4875.
3. Colorectal metastatic FOLFIRI (modified) (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Tournigand, C., T. Andre, E. Achille, et al. 2004. "FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study." J.Clin Oncol 22(2):229-237..
2. Colucci, G., V. Gebbia, G. Paoletti, et al. 2005. "Phase III randomized trial of FOLFIRI versus FOLFOX4 in the treatment of advanced colorectal cancer: a multicenter study of the Gruppo Oncologico Dell'Italia Meridionale." J.Clin Oncol 23(22):4866-4875.
3. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
4. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
5. Colorectal metastatic FOLFIRI (modified) and bevacizumab (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Bevacizumab | 5 mg/kg | IV | 1 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Ackland, S. P., S. Clarke, R. Perez-Carrión, et al. 2008. "Updated efficacy data from AVIRI: A large phase IV trial of first-line bevacizumab plus FOLFIRI in patients with mCRC." ASCO 2008 Gastrointestinal Cancers Symposium.
2. Hurwitz, H., L. Fehrenbacher, W. Novotny, et al. 2004. "Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer." N.Engl.J Med. 350(23):2335-2342.
3. Colorectal metastatic FOLFIRI (modified) and bevacizumab (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Bevacizumab | 5 mg/kg | IV | 1 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Ackland, S. P., S. Clarke, R. Perez-Carrión, et al. 2008. "Updated efficacy data from AVIRI: A large phase IV trial of first-line bevacizumab plus FOLFIRI in patients with mCRC." ASCO 2008 Gastrointestinal Cancers Symposium.
2. Hurwitz, H., L. Fehrenbacher, W. Novotny, et al. 2004. "Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer." N.Engl.J Med. 350(23):2335-2342.
3. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
4. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
5. Colorectal metastatic FOLFIRI (modified) and cetuximab (low dose folinic acid)

**14 day cycle**

**Cycle 1**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Cetuximab (Loading dose) | 400 mg/m2 | IV | 1 | 120m |
| Cetuximab (subsequent doses) | 250 mg/m2 | IV | 8 | 60m |

**Cycle 2 and further cycles**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Cetuximab  | 250 mg/m2 | IV | 1,8 | 60m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | High | Secondary | Yes |

**References**

1. Nott, L., M. Khattak, T. Price, et al. Cancer Council Australia Colorectal Cancer Guidelines Working Party. [Version URL: https://wiki.cancer.org.au/australiawiki/index.php?oldid=173114, cited 2018 Apr 16]. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal\_cancer/Systemic\_therapy\_molecular\_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party. Cl
2. Van Cutsem, E., C. H. Kohne, E. Hitre, et al. 2009. "Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer." N Engl J Med 360(14):1408-1417.
3. Van Cutsem, E., H. J. Lenz, C. H. Kohne, et al. 2015. "Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and RAS Mutations in Colorectal Cancer." J Clin Oncol 33(7):692-700.
4. Heinemann, V., L. F. von Weikersthal, T. Decker, et al. 2014. "FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial." Lancet Oncol 15(10):1065-1075.
5. Douillard, J. Y., K. S. Oliner, S. Siena, et al. 2013. "Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer." N Engl J Med 369(11):1023-1034.
6. Van Cutsem, E., C. H. Kohne, I. Lang, et al. 2011. "Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status." J Clin Oncol 29(15):2011-2019.
7. Colorectal metastatic FOLFIRI (modified) and cetuximab (high dose folinic acid)

**14 day cycle**

**Cycle 1**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Cetuximab (Loading dose) | 400 mg/m2 | IV | 1 | 120m |
| Cetuximab (subsequent doses) | 250 mg/m2 | IV | 8 | 60m |

**Cycle 2 and further cycles**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Cetuximab  | 250 mg/m2 | IV | 1,8 | 60m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | High | Secondary | Yes |

**References**

1. Nott, L., M. Khattak, T. Price, et al. Cancer Council Australia Colorectal Cancer Guidelines Working Party. [Version URL: https://wiki.cancer.org.au/australiawiki/index.php?oldid=173114, cited 2018 Apr 16]. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal\_cancer/Systemic\_therapy\_molecular\_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party. Cl
2. Van Cutsem, E., C. H. Kohne, E. Hitre, et al. 2009. "Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer." N Engl J Med 360(14):1408-1417.
3. Van Cutsem, E., H. J. Lenz, C. H. Kohne, et al. 2015. "Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and RAS Mutations in Colorectal Cancer." J Clin Oncol 33(7):692-700.
4. Heinemann, V., L. F. von Weikersthal, T. Decker, et al. 2014. "FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial." Lancet Oncol 15(10):1065-1075.
5. Douillard, J. Y., K. S. Oliner, S. Siena, et al. 2013. "Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer." N Engl J Med 369(11):1023-1034.
6. Van Cutsem, E., C. H. Kohne, I. Lang, et al. 2011. "Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status." J Clin Oncol 29(15):2011-2019.
7. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
8. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
9. Colorectal metastatic FOLFIRI (modified) and cetuximab (two weekly) (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Cetuximab  | 500 mg/m2 | IV | 1 | 120m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | High | Secondary | Yes |

**References**

1. Nott, L., M. Khattak, T. Price, et al. Cancer Council Australia Colorectal Cancer Guidelines Working Party. [Version URL: https://wiki.cancer.org.au/australiawiki/index.php?oldid=173114, cited 2018 Apr 16]. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal\_cancer/Systemic\_therapy\_molecular\_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party. Cl
2. Van Cutsem, E., C. H. Kohne, E. Hitre, et al. 2009. "Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer." N Engl J Med 360(14):1408-1417.
3. Van Cutsem, E., H. J. Lenz, C. H. Kohne, et al. 2015. "Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and RAS Mutations in Colorectal Cancer." J Clin Oncol 33(7):692-700.
4. Heinemann, V., L. F. von Weikersthal, T. Decker, et al. 2014. "FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial." Lancet Oncol 15(10):1065-1075.
5. Douillard, J. Y., K. S. Oliner, S. Siena, et al. 2013. "Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer." N Engl J Med 369(11):1023-1034.
6. Hubbard, J. M. and S. R. Alberts. 2013. "Alternate dosing of cetuximab for patients with metastatic colorectal cancer." Gastrointest Cancer Res 6(2):47-55.
7. Cheng, Ann-Lii, Gerardo Cornelio, Lin Shen, et al. 2013. "First-line Cetuximab with FOLFOX or FOLFIRI Every 2 Weeks In KRAS Wild-Type Metastatic Colorectal Cancer: phase II APEC Study." Annals of oncology 24 (suppl 4):iv34-iv35. Abstract No:PD-0028
8. Brodowicz, T., T. E. Ciuleanu, D. Radosavljevic, et al. 2013. "FOLFOX4 plus cetuximab administered weekly or every second week in the first-line treatment of patients with KRAS wild-type metastatic colorectal cancer: a randomized phase II CECOG study." Ann Oncol 24(7):1769-1777.
9. Martin-Martorell, P., S. Rosello, E. Rodriguez-Braun, et al. 2008. "Biweekly cetuximab and irinotecan in advanced colorectal cancer patients progressing after at least one previous line of chemotherapy: results of a phase II single institution trial." Br J Cancer 99(3):455-458.
10. Tabernero, J., F. Ciardiello, F. Rivera, et al. 2010. "Cetuximab administered once every second week to patients with metastatic colorectal cancer: a two-part pharmacokinetic/pharmacodynamic phase I dose-escalation study." Ann Oncol 21(7):1537-1545.
11. Pfeiffer, P., D. Nielsen, J. Bjerregaard, et al. 2008. "Biweekly cetuximab and irinotecan as third-line therapy in patients with advanced colorectal cancer after failure to irinotecan, oxaliplatin and 5-fluorouracil." Ann Oncol 19(6):1141-1145.
12. Van Cutsem, E., C. H. Kohne, I. Lang, et al. 2011. "Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status." J Clin Oncol 29(15):2011-2019.
13. Colorectal metastatic FOLFIRI (modified) and cetuximab (two weekly) (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 180 mg/m2  | IV | 1 | 90m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Cetuximab  | 500 mg/m2 | IV | 1 | 120m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | High | Secondary | Yes |

**References**

1. Nott, L., M. Khattak, T. Price, et al. Cancer Council Australia Colorectal Cancer Guidelines Working Party. [Version URL: https://wiki.cancer.org.au/australiawiki/index.php?oldid=173114, cited 2018 Apr 16]. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal\_cancer/Systemic\_therapy\_molecular\_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party. Cl
2. Van Cutsem, E., C. H. Kohne, E. Hitre, et al. 2009. "Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer." N Engl J Med 360(14):1408-1417.
3. Van Cutsem, E., H. J. Lenz, C. H. Kohne, et al. 2015. "Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and RAS Mutations in Colorectal Cancer." J Clin Oncol 33(7):692-700.
4. Heinemann, V., L. F. von Weikersthal, T. Decker, et al. 2014. "FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial." Lancet Oncol 15(10):1065-1075.
5. Douillard, J. Y., K. S. Oliner, S. Siena, et al. 2013. "Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer." N Engl J Med 369(11):1023-1034.
6. Hubbard, J. M. and S. R. Alberts. 2013. "Alternate dosing of cetuximab for patients with metastatic colorectal cancer." Gastrointest Cancer Res 6(2):47-55.
7. Cheng, Ann-Lii, Gerardo Cornelio, Lin Shen, et al. 2013. "First-line Cetuximab with FOLFOX or FOLFIRI Every 2 Weeks In KRAS Wild-Type Metastatic Colorectal Cancer: phase II APEC Study." Annals of oncology 24 (suppl 4):iv34-iv35. Abstract No:PD-0028
8. Brodowicz, T., T. E. Ciuleanu, D. Radosavljevic, et al. 2013. "FOLFOX4 plus cetuximab administered weekly or every second week in the first-line treatment of patients with KRAS wild-type metastatic colorectal cancer: a randomized phase II CECOG study." Ann Oncol 24(7):1769-1777.
9. Martin-Martorell, P., S. Rosello, E. Rodriguez-Braun, et al. 2008. "Biweekly cetuximab and irinotecan in advanced colorectal cancer patients progressing after at least one previous line of chemotherapy: results of a phase II single institution trial." Br J Cancer 99(3):455-458.
10. Tabernero, J., F. Ciardiello, F. Rivera, et al. 2010. "Cetuximab administered once every second week to patients with metastatic colorectal cancer: a two-part pharmacokinetic/pharmacodynamic phase I dose-escalation study." Ann Oncol 21(7):1537-1545.
11. Pfeiffer, P., D. Nielsen, J. Bjerregaard, et al. 2008. "Biweekly cetuximab and irinotecan as third-line therapy in patients with advanced colorectal cancer after failure to irinotecan, oxaliplatin and 5-fluorouracil." Ann Oncol 19(6):1141-1145.
12. Van Cutsem, E., C. H. Kohne, I. Lang, et al. 2011. "Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status." J Clin Oncol 29(15):2011-2019.
13. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
14. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
15. Colorectal metastatic FOLFOX6 (modified) (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 85 mg/m2 | IV | 1 | 120m |
| Folinic acid | 50 mg  | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. de Gramont A., A. Figer, M. Seymour, et al. 2000. "Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer." J.Clin Oncol 18(16):2938-2947.
2. Maindrault-Goebel, F., Gramont A. de, C. Louvet, et al. 2000. "Evaluation of oxaliplatin dose intensity in bimonthly leucovorin and 48-hour 5-fluorouracil continuous infusion regimens (FOLFOX) in pretreated metastatic colorectal cancer. Oncology Multidisciplinary Research Group (GERCOR)." Ann.Oncol. 11(11):1477-1483.
3. Tournigand, C., T. Andre, E. Achille, et al. 2004. "FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study." J.Clin Oncol 22(2):229-237..
4. Colorectal metastatic FOLFOX6 (modified) (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 85 mg/m2 | IV | 1 | 120m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. de Gramont A., A. Figer, M. Seymour, et al. 2000. "Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer." J.Clin Oncol 18(16):2938-2947.
2. Maindrault-Goebel, F., Gramont A. de, C. Louvet, et al. 2000. "Evaluation of oxaliplatin dose intensity in bimonthly leucovorin and 48-hour 5-fluorouracil continuous infusion regimens (FOLFOX) in pretreated metastatic colorectal cancer. Oncology Multidisciplinary Research Group (GERCOR)." Ann.Oncol. 11(11):1477-1483.
3. Tournigand, C., T. Andre, E. Achille, et al. 2004. "FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study." J.Clin Oncol 22(2):229-237..
4. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
5. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
6. Colorectal metastatic FOLFOX6 (modified) and bevacizumab (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 85 mg/m2 | IV | 1 | 120m |
| Folinic acid | 50 mg  | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Bevacizumab | 5 mg/kg  | IV | 1 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Saltz, L. B., S. Clarke, E. Diaz-Rubio, et al. 2008. "Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: a randomized phase III study." J Clin Oncol 26(12):2013-2019.
2. Colorectal metastatic FOLFOX6 (modified) and bevacizumab (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 85 mg/m2 | IV | 1 | 120m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Bevacizumab | 5 mg/kg  | IV | 1 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Saltz, L. B., S. Clarke, E. Diaz-Rubio, et al. 2008. "Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: a randomized phase III study." J Clin Oncol 26(12):2013-2019.
2. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
3. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
4. Colorectal metastatic FOLFOX6 (modified) and cetuximab (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 85 mg/m2 | IV | 1 | 120m |
| Folinic acid | 50 mg  | IV | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump | 1 | 46h |
| Cetuximab | 500 mg/m2 | IV | 1 | 120m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | High | Secondary | Yes |

**References**

1. Venook, A.P., D. Niedzwiecki, H. Lenz et al. 2017. "Effect of first-line chemotherapy combined with cetuximab or bevacizumab on overall survival in patients with KRAS wild-type advanced or metastatic colorectal cancer". JAMA. 2017 june 20; 317(23): 2392-2401
2. Nott, L., M. Khattak, T. Price, et al. Cancer Council Australia Colorectal Cancer Guidelines Working Party. [Version URL: https://wiki.cancer.org.au/australiawiki/index.php?oldid=173114, cited 2018 Apr 16]. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal\_cancer/Systemic\_therapy\_molecular\_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party. Cl
3. Colorectal metastatic FOLFOX6 (modified) and cetuximab (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 85 mg/m2 | IV | 1 | 120m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 2,400 mg/m2  | CIV via pump over 46 hours | 1 | 46h |
| Cetuximab | 500 mg/m2 | IV | 1 | 120m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | High | Secondary | Yes |

**References**

1. Venook, A.P., D. Niedzwiecki, H. Lenz et al. 2017. "Effect of first-line chemotherapy combined with cetuximab or bevacizumab on overall survival in patients with KRAS wild-type advanced or metastatic colorectal cancer". JAMA. 2017 june 20; 317(23): 2392-2401
2. Nott, L., M. Khattak, T. Price, et al. Cancer Council Australia Colorectal Cancer Guidelines Working Party. [Version URL: https://wiki.cancer.org.au/australiawiki/index.php?oldid=173114, cited 2018 Apr 16]. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal\_cancer/Systemic\_therapy\_molecular\_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party. Cl
3. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
4. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
5. Colorectal metastatic FOLFOXIRI (modified) (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 165 mg/m2  | IV | 1 | 90m |
| Oxaliplatin | 85 mg/m2  | IV | 1 | 120m |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 3,200 mg/m2  | CIV via pump | 1 | 48h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| High | Low | Secondary | Yes |

**References**

1. Souglakos, J., N. Androulakis, K. Syrigos, et al. 2006. "FOLFOXIRI (folinic acid, 5-fluorouracil, oxaliplatin and irinotecan) vs FOLFIRI (folinic acid, 5-fluorouracil and irinotecan) as first-line treatment in metastatic colorectal cancer (MCC): a multicentre randomised phase III trial from the Hellenic Oncology Research Group (HORG)." Br J Cancer 94(6):798-805.
2. Falcone, A., S. Ricci, I. Brunetti, et al. 2007. "Phase III trial of infusional fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFOXIRI) compared with infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI) as first-line treatment for metastatic colorectal cancer: the Gruppo Oncologico Nord Ovest." J Clin Oncol 25(13):1670-1676.
3. Montagnani, F., A. Chiriatti, G. Turrisi, et al. 2011. "A systematic review of FOLFOXIRI chemotherapy for the first-line treatment of metastatic colorectal cancer: improved efficacy at the cost of increased toxicity." Colorectal Dis 13(8):846-852.
4. Colorectal metastatic FOLFOXIRI (modified) (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 165 mg/m2  | IV | 1 | 90m |
| Oxaliplatin | 85 mg/m2  | IV | 1 | 120m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 3,200 mg/m2  | CIV via pump | 1 | 48h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| High | Low | Secondary | Yes |

**References**

1. Souglakos, J., N. Androulakis, K. Syrigos, et al. 2006. "FOLFOXIRI (folinic acid, 5-fluorouracil, oxaliplatin and irinotecan) vs FOLFIRI (folinic acid, 5-fluorouracil and irinotecan) as first-line treatment in metastatic colorectal cancer (MCC): a multicentre randomised phase III trial from the Hellenic Oncology Research Group (HORG)." Br J Cancer 94(6):798-805.
2. Falcone, A., S. Ricci, I. Brunetti, et al. 2007. "Phase III trial of infusional fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFOXIRI) compared with infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI) as first-line treatment for metastatic colorectal cancer: the Gruppo Oncologico Nord Ovest." J Clin Oncol 25(13):1670-1676.
3. Montagnani, F., A. Chiriatti, G. Turrisi, et al. 2011. "A systematic review of FOLFOXIRI chemotherapy for the first-line treatment of metastatic colorectal cancer: improved efficacy at the cost of increased toxicity." Colorectal Dis 13(8):846-852.
4. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
5. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
6. Colorectal metastatic FOLFOXIRI (modified) with bevacizumab (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 165 mg/m2  | IV  | 1 | 90m |
| Oxaliplatin | 85 mg/m2  | IV  | 1 | 120m |
| Folinic acid | 50 mg | IV  | 1 | 2m |
| Fluorouracil | 3,200 mg/m2  | CIV via pump | 1 | 48h |
| Bevacizumab | 5mg/kg | IV | 1 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| High | Low | Secondary | Yes |

**References**

1. Loupakis, F., C. Cremolini, G. Masi, et al. 2014. "Initial therapy with FOLFOXIRI and bevacizumab for metastatic colorectal cancer." N Engl J Med 371(17):1609-1618.
2. Cremolini C., F. Loupakis, G. Masi, et al. 2015. " FOLFOXIRI plus bevacizumab (bev) versus FOLFIRI plus bev as first-line treatment of metastatic colorectal cancer (mCRC): Updated survival results of the phase III TRIBE trial by the GONO group." ASCO GI Meeting Abstract. J Clin Oncol 33 (suppl 3; abstr 657)
3. Colorectal metastatic FOLFOXIRI (modified) with bevacizumab (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 165 mg/m2  | IV  | 1 | 90m |
| Oxaliplatin | 85 mg/m2  | IV | 1 | 120m |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 3,200 mg/m2  | CIV via pump | 1 | 48h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| High | Low | Secondary | Yes |

**References**

1. Loupakis, F., C. Cremolini, G. Masi, et al. 2014. "Initial therapy with FOLFOXIRI and bevacizumab for metastatic colorectal cancer." N Engl J Med 371(17):1609-1618.
2. Cremolini C., F. Loupakis, G. Masi, et al. 2015. " FOLFOXIRI plus bevacizumab (bev) versus FOLFIRI plus bev as first-line treatment of metastatic colorectal cancer (mCRC): Updated survival results of the phase III TRIBE trial by the GONO group." ASCO GI Meeting Abstract. J Clin Oncol 33 (suppl 3; abstr 657)
3. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
4. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
5. Colorectal metastatic irinotecan three weekly

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 350 mg/m2 | IV | 1 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Cunningham, D. and B. Glimelius. 1999. "A phase III study of irinotecan (CPT-11) versus best supportive care in patients with metastatic colorectal cancer who have failed 5-fluorouracil therapy. V301 Study Group." Semin.Oncol. 26(1 Suppl 5):6-12.
2. Van Cutsem, E. and G. H. Blijham. 1999. "Irinotecan versus infusional 5-fluorouracil: a phase III study in metastatic colorectal cancer following failure on first-line 5-fluorouracil. V302 Study Group." Semin Oncol 26(1 Suppl 5):13-20.
3. Lal, R., J. Dickson, D. Cunningham, et al. 2004. "A randomized trial comparing defined-duration with continuous irinotecan until disease progression in fluoropyrimidine and thymidylate synthase inhibitor-resistant advanced colorectal cancer." J Clin Oncol 22(15):3023-3031.
4. Fuchs, C. S., M. R. Moore, G. Harker, et al. 2003. "Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer." J Clin Oncol 21(5):807-814.
5. Colorectal metastatic irinotecan three weekly (250 fractionated)

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 125 mg/m2 | IV | 1,8 | 90m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

1. Colorectal metastatic QUASAR (modified)

**7 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 50 mg | IV | 1 | 2m |
| Fluorouracil | 370 mg/m2  | IV | 1 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Cassidy, J., C. Twelves, E. Van Cutsem, et al. 2002. "First-line oral capecitabine therapy in metastatic colorectal cancer: a favorable safety profile compared with intravenous 5-fluorouracil/leucovorin." Ann.Oncol 13(4):566-575.
2. Van Cutsem, E., C. Twelves, J. Cassidy, et al. 2001. "Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: results of a large phase III study." J Clin Oncol 19(21):4097-4106.
3. QUASAR Collaborative Group. 2000. "Comparison of flourouracil with additional levamisole, higher-dose folinic acid, or both, as adjuvant chemotherapy for colorectal cancer: a randomised trial." Lancet. 355(9215):1588-1596
4. Patel, K., D. A. Anthoney, et al. 2004. "Weekly 5-fluorouracil and leucovorin: achieving lower toxicity with higher dose-intensity in adjuvant chemotherapy after colorectal cancer resection." Ann.Oncol 15(4): 568-573.
5. Colorectal metastatic Roswell Park (modified) (high dose folinic acid)

**56 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 400 mg/m2 | IV | 1,8,15,22,29,36 | 120m |
| Fluorouracil | 500 mg/m2  | IV | 1,8,15,22,29,36 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
2. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
3. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
4. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
5. Colorectal metastatic Roswell Park (modified) (low dose folinic acid)

**56 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 50 mg | IV | 1,8,15,22,29,36 | 2m |
| Fluorouracil | 500 mg/m2  | IV | 1,8,15,22,29,36 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. Cassidy, J., C. Twelves, E. Van Cutsem, et al. 2002. "First-line oral capecitabine therapy in metastatic colorectal cancer: a favorable safety profile compared with intravenous 5-fluorouracil/leucovorin." Ann.Oncol 13(4):566-575.
2. Van Cutsem, E., C. Twelves, J. Cassidy, et al. 2001. "Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: results of a large phase III study." J Clin Oncol 19(21):4097-4106.
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5. Colorectal metastatic de Gramont (modified) (low dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic Acid | 50 mg | IV bolus | 1 | 2m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 3,000 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. de Gramont, A., J. F. Bosset, et al. 1997. "Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study" J.Clin Oncol. 15(2): 808-815.
2. Cheeseman, S. L., S. P. Joel, J. D. Chester, et al. 2002. "A 'modified de Gramont' regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer." Br J Cancer 87(4):393-399.
3. Limat, S., C. H. Bracco-Nolin, C. Legat-Fagnoni, et al. 2006. "Economic impact of simplified de Gramont regimen in first-line therapy in metastatic colorectal cancer." Eur J Health Econ 7(2):107-113.
4. de Gramont A., A. Figer, M. Seymour, et al. 2000. "Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer." J.Clin Oncol 18(16):2938-2947.
5. Colorectal metastatic de Gramont (modified) (high dose folinic acid)

**14 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Folinic acid | 400 mg/m2 | IV | 1 | 120m |
| Fluorouracil | 400 mg/m2  | IV | 1 | 15m |
| Fluorouracil | 3,000 mg/m2  | CIV via pump | 1 | 46h |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Low | Low | Secondary | Yes |

**References**

1. de Gramont, A., J. F. Bosset, et al. 1997. "Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study" J.Clin Oncol. 15(2): 808-815.
2. Cheeseman, S. L., S. P. Joel, J. D. Chester, et al. 2002. "A 'modified de Gramont' regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer." Br J Cancer 87(4):393-399.
3. Limat, S., C. H. Bracco-Nolin, C. Legat-Fagnoni, et al. 2006. "Economic impact of simplified de Gramont regimen in first-line therapy in metastatic colorectal cancer." Eur J Health Econ 7(2):107-113.
4. de Gramont A., A. Figer, M. Seymour, et al. 2000. "Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer." J.Clin Oncol 18(16):2938-2947.
5. Petrelli N, Douglass HO Jr, Herrera L, et al: The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: A prospective randomized phase III trial—Gastrointestinal Tumor Study Group. J Clin Oncol 7::1419,1989-1426,
6. de Gramont A, Bosset JF, Milan C, et al: Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 15::808,1997-815,
7. Colorectal metastatic FLOX

**56 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 85 mg/m2  | IV  | 1, 15, 29 | 120m |
| Folinic acid | 20 mg | IV  | 1, 8, 15, 22, 29, 36 | 2m |
| Fluorouracil | 500 mg/m2  | IV | 1, 8, 15, 22, 29, 36 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Kuebler, J. P., H. S. Wieand, M. J. O'Connell, et al. 2007. "Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07." J Clin Oncol 25(16):2198-2204.
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3. Kato T, Nagata N, Fujii M *et al*. Multi‐center phase II study of FLOX for advanced colorectal cancer patients in Japan: SWIFT 3 study. *Anticancer Res* 2011; 31: 4657– 64.
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5. Colorectal metastatic IrOX

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Irinotecan | 200 mg/m2  | IV | 1 | 90m |
| Oxaliplatin | 85 mg/m2  | IV | 1 | 120m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

1. Becouarn Y, Gamelin E, Coudert B,et al. Randomized multicenter phase II study comparing a combination of fluorouracil and folinic acid and alternating irinotecan and oxaliplatin with oxaliplatin and irinotecan in fluorouracil-pretreated metastatic colorectal cancer patient. J Clin Oncol 2001;19:4l95–201.
2. Colorectal metastatic raltitrexed and oxaliplatin

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Oxaliplatin | 130 mg/m2  | IV | 1 | 120m |
| Raltitrexed | 3 mg/m2 | IV | 1 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| High | Low | Secondary | Yes |

**References**

1. Cascinu S, Graziano F, Ferrau F, Catalano V, Massacesi C, Santini D, Silva RR, Barni S, Zaniboni A, Battelli N, Siena S, Giordani P, Mari D, Baldelli AM, Antognoli S, Maisano R, Priolo D, Pessi MA, Tonini G, Rota S, Labianca R: alitrexed plus oxaliplatin (TOMOX) as first-line chemotherapy for metastatic colorectal cancer. A phase II study of the Italian Group for the study of gastrointestinal tract carcinomas (GISCAD). Ann Oncol. 2002, 13: 716-720. 10.1093/annonc/mdf091.
2. Colorectal metastatic raltitrexed

**21 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Raltitrexed | 3 mg/m2 | IV | 1 | 15m |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Moderate | Low | Secondary | Yes |

**References**

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7. Colorectal metastatic regorafenib

**28 day cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Drug** | **Dose** | **Route** | **Day** | **Max Duration** |
| Regorafenib | 160 mg ONCE daily | Oral | 1 to 21 | - |

|  |  |  |  |
| --- | --- | --- | --- |
| **Emetogenicity** | **Hypersensitivity** | **Growth Factor Support** | **Anti-diarrhoeals** |
| Minimal | Low | Secondary | Yes |

**References**

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# Appendix 1: Working group members

The SACT Colorectal Working Group members in 2019/2020 are:

|  |  |  |
| --- | --- | --- |
| Chair | Dr Chris Jackson | Medical Oncologist, Southern DHBClinical Director, Mercy Cancer Care |
| Members | Dr Richard NorthDr Ian KennedyDr Kate ClarkeDr Michelle VaughanDr Rebecca CarrollDr Anna WojjtachaDr Amanda AshleyElaine RogersSimon Pointer | Chair MOWG, Bay of Plenty DHB, Canopy Cancer CareMedical Oncologist, Waikato DHBMedical Oncologist, Capital and Coast DHBMedical Oncologist, Canterbury DHB and St Georges Cancer Care CentreMedical Oncologist, MidCentral DHBMedical Oncologist, Nelson Marlborough DHBMedical Oncologist, Auckland DHBNurse specialist, Auckland DHBPharmacist, Southern DHB |

# Appendix 2: Supportive care dimensions

**Emetogenicity:** The degree to which a drug or regimen can induce nausea and vomiting (emesis)

|  |  |
| --- | --- |
| **Rating** | **Description** |
| High | >90% risk of emesis\* |
| Moderate | 30 to 90% risk of emesis\* |
| Low | 10 to 30% risk of emesis\* |
| Minimal | <10% risk of emesis\* |

\*percentage of patients who experience emesis in the absence of effective antiemetic prophylaxis

**Hypersensitivity:** Hypersensitivity is an adverse reaction to administration of a drug with features of an anaphylactic (antibody mediated) or anaphylactoid (not antibody mediated) reaction.

|  |  |
| --- | --- |
| **Rating** | **Description** |
| Low | Low risk of hypersensitivity |
| Moderate | Moderate risk of hypersensitivity |
| High | High risk of hypersensitivity |

**Growth factor support:** Growth factor support is an essential component of therapy for several of the most commonly used adjuvant chemotherapy regimens that frequently cause substantial myelosuppression and anemia.

|  |  |
| --- | --- |
| **Rating** | **Description** |
| Primary | >20% chance of febrile neutropenia. Primary growth factor prophylaxis recommended. |
| Secondary | <20% chance of febrile neutropenia. Primary growth factor prophylaxis not recommended. |
| Not applicable | Growth factor not applicable for this regimen. |

**Anti-diarrhoeals:** Treatment-induced diarrhoea is an increased frequency, and decreased consistency, of bowel motions, or ostomy output as a result of medical treatment.

|  |  |
| --- | --- |
| **Rating** | **Description** |
| Yes | Anti-diarrhoeal prophylaxis recommended |
| No | Anti-diarrhoeal prophylaxis not recommended |