## Supplementary TABLE A.1: Treatments used in the XELAVIRI/ AIO KRK0110 trial.

| Therapy arm               | Induction                                                                 | Escalation                                                                 |
|---------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------|
| **Sequential**            | oral capecitabine 1250 mg/m² twice daily, days 1-14 plus infusional       | capecitabine 800 mg/m² twice daily days 1-14, intravenous                  |
| **therapy arm**           | bevacizumab 7.5 mg per kg of body weight on day 1, repeated every 3 weeks | irinotecan 200 mg/m² on day 1 plus bevacizumab at a dose of 7.5 mg per kg | |
|                           | intravenous on day 1: racemic folinic acid with 400 mg/m², 5-FU bolus    | body weight infused on day 1, repeated every 3 weeks                      |
|                           | of 400 mg/m², fluorouracil over 46 hours of 2400 mg/m² bevacizumab 5 mg  |                                            | |
|                           | per kg body weight; repeated every 2 weeks                                |                                            | |
| **Combination**           | capecitabine 800 mg/m² twice daily, days 1-14, intravenous                | oral capecitabine 1250 mg/m² twice daily, days 1-14 plus infusional       |
| **therapy arm**           | irinotecan 200 mg/m² on day 1 plus bevacizumab at a dose of 7.5 mg per kg | bevacizumab 7.5 mg per kg of body weight on day 1, repeated every 3 weeks |
|                           | body weight infused on day 1, repeated every 3 weeks                      |                                            | |
|                           | intravenous on day 1: irinotecan 180 mg/m², racemic folinic acid with     |                                            | |
|                           | 400 mg/m², 5-FU bolus of 400 mg/m², fluorouracil over 46 hours of 2400   |                                            | |
|                           | mg/m² bevacizumab 5 mg per kg body weight; repeated every 2 weeks        |                                            | |
|                           | intravenous on day 1: irinotecan 180 mg/m², racemic folinic acid with     |                                            | |
|                           | 400 mg/m², 5-FU bolus of 400 mg/m², fluorouracil over 46 hours of 2400   |                                            | |
|                           | mg/m² bevacizumab 5 mg per kg body weight; repeated every 2 weeks        |                                            | |
Supplementary FIGURE A.1: Consort diagram of study population.

Legend: FP- fluoropyrimidine; BEV- bevacizumab; IRI- irinotecan; WT- wildtype; MT- mutant.
Supplementary FIGURE A.2: Best response in the trial.

Legend: Blue images display response assessments of the sequential treatment arm (fluoropyrimidine plus bevacizumab), red images show response assessments of the initial combination treatment arm (fluoropyrimidine, bevacizumab, and irinotecan) in (from top to bottom) groups: BRAF mutant, female patients, male patients.