**Supplementary Table 1.**

**Regimens and doses of first-line chemotherapy**

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| --- | --- | --- | --- |
| **Regimens** | **Drug** | **Dose** | **Frequency** |
| Capecitabine | Capecitabine | 2000 mg/m² PO daily for 14 days | Every 3 weeks \* |
| 5-FU | 5-FU  Calcium folinate | Bolus: 400 mg/m² i.v.  Infusion 46 h: 2400 mg/ m² i.v.  400 mg/m² i.v. | Every 2 weeks \*\* |
| Capeox | Capecitabine  Oxaliplatin | 2000 mg/m² p.o. daily for 14 days  130 mg/m² i.v. | Every 3 weeks \* |
| Folfox | 5-FU  Calcium folinate  Oxaliplatin | Bolus: 400 mg/m² i.v.  Infusion 46 h: 2400 mg/ m² i.v.  400 mg/m² i.v.  85 mg/m² i.v. | Every 2 weeks \*\*\* |
| Irinotecan | Irinotecan | Bolus: 180 mg/m² i.v. | Every 2 weeks \*\*\*\* |
| Capiri | Capecitabine  Irinotecan | 1600 mg/m² p.o. daily for 14 days  200 mg/m² i.v. | Every 3 weeks \* |
| Folfiri | 5-FU  Calcium folinate  Irinotecan | Bolus: 400 mg/m² i.v.  Infusion 46 h: 2400 mg/ m² i.v.  400 mg/m² i.v.  180 mg/m² i.v. | Every 2 weeks \*\*\*\* |
| Irox | Irinotecan  Oxaliplatin | 165 mg/m² i.v.  85 mg/m² i.v. | Every 2 weeks \*\*\*\* |

i.v. intravenous, p.o. per os

\*optional addition of bevacizumab 7.5 mg/m² i.v.

\*\*optional addition of bevacizumab 5 mg/m² i.v.

\*\*\*optional addition of bevacizumab 5 mg/m² i.v., irinotecan 165 mg/m² i.v., cetuximab 500 mg/m² i.v., or panitumumab 6 mg/kg i.v.

\*\*\*\* optional addition of bevacizumab 5 mg/m² i.v., cetuximab 500 mg/m² i.v., or panitumumab 6 mg/kg i.v.

5-FU, oxaliplatin, irinotecan and bevacizumab were used as standard regimens in first-line treatment during the whole period. Cetuximab was added as a standard in first-line therapy in 2014.