

**Table S1.** Inclusion and exclusion criteria.

<p><b>Inclusion criteria</b></p>	<ul style="list-style-type: none"> <li>- Age <math>\geq</math> 65</li> <li>- General condition WHO <math>\leq</math> 2</li> <li>- Metastatic rectal or colon adenocarcinoma, histologically-proven on the primary tumour or a metastasis</li> <li>- Metastases non-resectable and/or patient inoperable</li> <li>- Metastases not or little symptomatic</li> <li>- At least one measurable target according to RECIST v1.1 criteria, not previously irradiated</li> <li>- No previous treatment of the metastatic disease. Previous chemotherapy in an adjuvant situation completed 6 months or more before diagnosis of the metastasis is authorized</li> <li>- Adequate biological examination: Hb <math>\geq</math> 9 g/dl, polynuclear neutrophils <math>\geq</math> 1,500/mm<sup>3</sup>, creatinine clearance &gt; 50 mL/mn (Cockcroft and Gault formula), platelets <math>\geq</math> 100,000/mm<sup>3</sup>, total bilirubin <math>\leq</math> 1.5 x UNL, creatininemia &lt; 1.5 x UNL, ALP &lt; 5 x UNL, AST and ALT <math>\leq</math> 5 x UNL, GGT &lt; 5 x UNL</li> <li>- Proteinuria (strip) &lt; 2+; if <math>\geq</math> 2, test proteinuria over 24 hours which must be <math>\leq</math> 1 g.</li> <li>- Patients treated with anticoagulants (coumadin, warfarin) can be included if the INR can be closely monitored. A change in anticoagulant treatment for low molecular weight heparin is preferable in order to respect indications.</li> <li>- Central genotyping of thymidylate synthase (TS) in blood DNA</li> <li>- Informed consent signed</li> </ul>
<p><b>Exclusion criteria</b></p>	<ul style="list-style-type: none"> <li>- Patients with in situ primary tumour, and presenting clinical symptoms (occlusion, haemorrhage)</li> <li>- Macronodular peritoneal carcinomatosis (risk of perforation)</li> <li>- Cerebral metastases</li> <li>- Uncontrolled hypercalcemia</li> <li>- Uncontrolled hypertension (SBP &gt; 150 mmHg and DBP &gt; 100 mmHg) or history of hypertensive attack or hypertensive encephalopathy</li> <li>- Any uncontrolled progressive disease over the past 6 months: hepatic insufficiency, renal insufficiency, respiratory insufficiency</li> <li>- Subsequent complications in the 6 months prior to inclusion: myocardial infarction unstable/severe angina, coronary artery bypass, congestive cardiac insufficiency NYHA III or IV, stoke or transient ischemic attack</li> <li>- The following conditions in the 3 months prior to inclusion: Grade 3 or 4 gastrointestinal, treatment-resistant peptic ulcer, ulcerative esophagitis or gastritis, infectious or inflammatory bowel disease, diverticulitis, pulmonary embolism or other uncontrolled thromboembolic event, unconsolidated bone fractures</li> <li>- Major surgery during the 28 days preceding the start of treatment</li> <li>- Known acquired immune deficiency syndrome (AIDS related illnesses) or known HIV infection requiring antiretroviral therapy</li> <li>- Anti-cancer treatments other than the trial treatments (chemotherapy, targeted therapy, immunotherapy)</li> <li>- History of haematological malignancies or cancer except those treated for more than 5 years and considered cured, in situ carcinomas of the cervix and skin cancers treated (melanoma excluded)</li> <li>- Any contraindication to the treatments used in the trial</li> <li>- Deficiency of DPD</li> <li>- Patient treated with new oral anticoagulants (such as rivaroxaban XARELTO®, apixaban ELIQUIS®, dabigatran PRADAXA®) except if relayed by K antivitamin</li> <li>- Pregnant or breast-feeding woman, no effective contraception in patients of child-bearing age</li> <li>- Impossibility of undergoing medical monitoring during the trial for geographic, social or psychological reasons</li> </ul>