## Patient eligibility

## **Inclusion criteria**

Patients need to meet all the following inclusion criteria for anticipating this study

- 1. Provide a signed informed consent document
- 2. Age between 18 and 75 at time of informed consent;
- 3. Histologically confirmed gastrointestinal cancer excluding gastric cancer. For colorectal caner, the RAS (*KRAS* exon 2, 3, 4 and *NRAS* exon 2,3,4) and *BRAF* gene (exon 16) should be wild-type by PCR assays.
- 4. Presence of HER2 positivity determined by qualified pathologists of participating center. The HER2 positivity criteria of ToGA<sup>a)</sup> study was used in this study.
- 5. Metastatic disease and evidence of measurable lesion per RECIST v1.1 should be radiologically confirmed.
- 6. ECOG PS of 0 or 1
- 7. Progression of disease after at least one prior regimen
- 8. Adequate bone marrow, hepatic and renal function by the following at screening:
  - a. Absolute neutrophil count  $\geq 1,500/\text{mm}^3$
  - b. Platelets  $\geq 90 \times 10^3 / \text{mm}^3$
  - c. Hemoglobin  $\geq 9 \text{ g/dL}$
  - d. Serum total bilirubin  $\leq 1.5 \times$  upper limit of normal (ULN)
  - e. Alanine aminotransferase and/or aspartate aminotransferase  $\leq$  2.5× ULN, or  $\leq$  5× ULN in presence of liver metastases
  - f. serum creatinine  $\leq$  1.5× ULN, or calculated by Cockcroft-Gault formula or directly measured creatinine clearance  $\geq$  40 mL/min
- 9. Permitted contraceptive methods should be taken for female of childbearing age during treatment and within 7 months of the last treatment.

## **Exclusion criteria**

Patients meeting any of the following criteria will not be included in this study:

- 1. allergic to medication received
- 2. Left ventricular ejection fraction < 50% as determined by ECHO of MUGA
- 3. Prior treatment with any HER2-targeted therapy
- 4. Systemin immunotherapy, biological therapy or any clinical trial treatment within two weeks before informed consent
- 5. Operative treatment within 3 weeks before treatment of this trial
- 6. Symptomatic brain metastasis or epilepsy that require medical treatment
- 7. History of other malignancies in the last 5 years except for basal cell carcinoma and cervical carcinoma *in situ*
- 8. History of symptomatic coronary heart disease, myocardiopathy or heart failure; uncontrolled hypertension defined as persistent systolic blood pressure ≥ 180 mmHg or diastolic blood pressure ≥ 100 mmHg; symptomatic cardia valve disease, myocardial infarction or high-risk arrhythmia
- 9. Use of long-term or high-dose corticosteroids (inhaled corticosteroids and short-term oral corticosteroids for resisting vomiting or promoting appetite are permitted)
- 10. Persons without legal capacity; with medical or ethical reasons affecting the continuation of the study
- 11. Pregnant and lactating or planning to to get pregnant during treatment
- 12. Concurrent jaundice, ascites, alkaline phosphatase ≥3× ULN, ≥ grade 3 continuous proteinuria, urine albumin-creatinine ratio > 3.5 g/24 hr or renal failure requiring hemodialysis or peritoneal dialysis

- 13. Concurrent ≥ grade 3 persistent infection or unhealed wound or ulceration or fracture; history of organ transplantation
- 14. Concurrent ≥ grade 3 bleeding event or known history of coagulation disorders
- 15. Known history of HIV or HBV or HCV infection
- 16. Residual CTCAE > grade 1 toxicity from any prior anticancer therapy (except for alopecia, anemia or hypothyroidism)
- 17. Any conditions that investigators consider that is not suitable to participate in this study
- 18. Prior exposure to anthracycline: doxorubicin > 500 mg/m² or epirubicin > 720 mg/m² CTCAE, Common Terminology Criteria for Adverse Events; ECHO, echocardiography; ECOG PS, Eastern Cooperative Oncology Group performance status; HBV, hepatitis B virus; HCV, hepatitis C virus; HER2, human epidermal growth factor receptor 2; HIV, human immunodeficiency virus; MUGA, multigated radionuclide angiography; PCR, polymerase chain reaction; RECIST, Response Evaluation Criteria in Solid Tumor. <sup>a)</sup>A phase 3, randomised controlled trial (registration number: NCT01041404).