AGMT | ARBEITSGEMEINSCHAFT MEDIKAMENTÖSE TUMORTHERAPIE

Pilotstudy:

Biomarker directed treatment in metastatic colorectal cancer

Protocol Number: AGMT_ERCC1
EudraCT Number: 2011-003217-41

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Protocol Synopsis:

Indication: Untreated wt RAS metastatic colorectal cancer

Study design: Pilot study, non-randomized, open, phase II

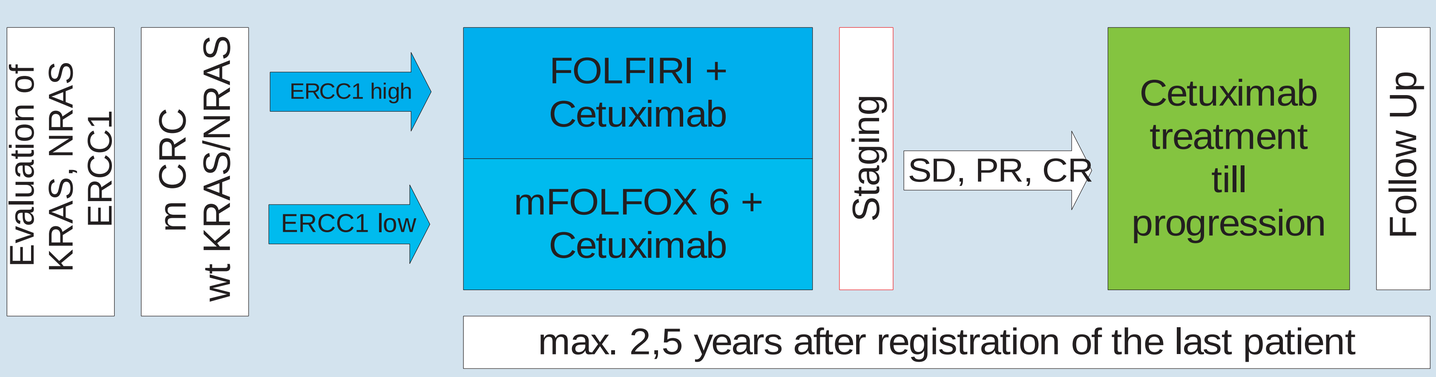
Planned sample size: 50 patients

Recruitment:
First patient in (FPI): Q3 2012
Last patient in (LPI): Q3 2017
Last patient out (LPO): March 2018 (expected)

Primary objective
Assessment of response in patients with previous untreated wt RAS advanced colorectal cancer using mFOLFOX6 or FOLFIRI and Cetuximab with therapy chosen using ERCC-1 gene expression assessment.

Secondary objectives
- PFS and OS
- Description of group differences between ERCC-1 low and ERCC-1 high patients with respect to response rate, PFS and OS and also with respect to KRAS and NRAS status
- Secondary resection rate
- Toxicity

Study Design:



This pilot study will investigate ERCC-1 (Excision-Repair Cross-Complementing) as a predictive marker for treatment with platinum based regimens in mCRC patients. In a Pre-Screening phase the RAS mutation status and ERCC-1 gene expression will be assessed at the CLIA approved laboratory Response genetics in Los Angeles, California, USA. RAS wt patients will then be treated with 6 cycles of one of the following regimens chosen for optimization based on patient characteristics:

- Patients with ERCC-1 gene expression < 1.7 (ERCC-1 low):
  mFOLFOX6 in combination with Cetuximab
- Patients with ERCC-1 gene expression > 1,7 (ERCC-1 high):
  FOLFIRI in combination with Cetuximab

ERCC1 low	*ERCC1 high*
Modified FOLFOX6 (mFOLFOX6)	**FOLFIRI**
Oxaliplatin 85 mg/m^2 on day 1, 15 q d29 for 6 cycles	Irinotecan 180 mg/m^2 on day 1, 15 q d29 for 6 cycles
Folinic acid (FA) 400 mg/m^2 on days 1 and 15 q d29 for 6 cycles	Folinic acid (FA) 400 mg/m^2 on days 1 and 15 q d29 for 6 cycles
Fluorouracil (5-FU) 400 mg/m^2 bolus day 1 and 16 2400 mg/m^2 46-hour infusion on days 1, 2 and 15, 16 q d29 for 6 cycles	Fluorouracil (5-FU) 400 mg/m^2 bolus day 1 and 16 2400 mg/m^2 46-hour infusion on days 1, 2 and 15, 16 q d29 for 6 cycles
Cetuximab: 500 mg/m^2 Cetuximab will be administered on day 1 and then biweekly	

Inclusion Criteria (selected):

- Untreated advanced wt RAS metastatic colorectal cancer patients
- Adequate tissue to evaluate for genotyping
- Age ≥ 18 years
- Previous adjuvant therapy must have been completed ≥ 1 months before therapy initiation on this study
- ECOG performance status of 0-2
- Adequate organ function
  - Hematologic: Absolute neutrophil count > 1.500/µL
    Hemoglobin >9 mg/dl
    Platelet count >100.000 /µl
  - Renal: Serum creatinine <1x5 x ULN
  - Hepatic: Serum bilirubin <1,5 mg/dl

Recruitment:

No	*Site*	*Screened patients*	*Eligible pat. (RAS wt)*
01	LKH Feldkirch / Interne E	14	8
02	PMU Salzburg / III Med.	14	9
03	UK Graz / Onkologie	8	8
04	Kepler UK, Med Campus III./ Interne 3	5	3
05	KH Kufstein / Interne II	1	1
06	LKH Bludenz / Innere Med.	2	0
07	BHS Linz / Interne I	16	6
08	LKH Bregenz / Innere Med.	1	1
09	KH Dornbirn / Innere Med.	3	2
10	LKH Hohenems / Intensivmed.	1	0
11	LKH Steyr / Med. II	5	4
12	AKH MUW / Med. I Hämatologie	7	5
	TOTAL	**77**	**47**

Status March 2017

An academic clinical trial
Sponsor: Arbeitsgemeinschaft medikamentöse Tumortherapie gemeinnützige GmbH, Clinical-Scientific Director: R. Greil