| | |
|---|---|
| APPLICANT/ COORDINATING INVESTIGATOR | Prof. Dr. med. Gunnar Folprecht<br>University Hospital Carl Gustav Carus<br>University Cancer Center / Medical Department I<br>Fetscherstr. 74, 01307 Dresden, Germany |
| CONDITION | Colon cancer UICC stage II without microsatellite instability |
| OBJECTIVE(S) | The study evaluates the value of postoperative circulating tumor DNA (ctDNA) as selection criterion in patients with colon cancer UICC stage II.<br>Primary:<br>- To determine the disease free survival (DFS) in patients (pts) with stage II colon cancer who are positive for ctDNA after the resection of the primary with vs. without chemotherapy<br>Secondary:<br>- To determine the overall survival (OS) in pts with stage II colon cancer who are positive for ctDNA after the resection of the primary with vs. without chemotherapy<br>- To determine the DFS and OS in pts with stage II colon cancer without adjuvant chemotherapy who are positive vs. who are negative for ctDNA after the resection of the primary |
| INTERVENTION(S) | Patients with resected colon cancer stage II and III treated at approx. 180 colon cancer centers are enrolled in the AIO COLOPREDICT screening platform and screened for micro satellite instability (MSI) - and for this project for frequent tumour mutations (i.e. TP53, KRAS, APC…) in the formaline fixed paraffin embedded (FFPE) primary tumor material. For patients with colon cancer stage II, the patient specific mutation will be analysed in postoperative plasma samples by ultra-deep sequencing to determine the presence of the patient specific mutation (i.e. TP53, KRAS, APC…). Patients who are positive for postoperative ctDNA and microsatellite stable (MSS) are randomized (2:1) to adjuvant chemotherapy or to follow up. All patients negative for postoperative ctDNA are not randomized but followed up.<br>Experimental intervention: Chemotherapy (oxaliplatin / fluoropyrimidine, in pts who are positive for postoperative ctDNA; elderly pts: fluoropyrimidine)<br>Control intervention: Follow up (no chemotherapy)<br>Duration of intervention per patient: 6 months (chemotherapy cohort)<br>Follow-up per patient: 5 years |
| KEY INCLUSION AND EXCLUSION CRITERIA | Key inclusion criteria:<br>- Histologically proven colon cancer stage II, microsatellite stable<br>- Resection of the primary 3 – 8 (max.12) weeks before randomization<br>- Age > 18 years<br>Key exclusion criteria:<br>- Clinical high risk situation, if it is regarded as certain indication for adjuvant therapy by the treating physician and the patient<br>- Contraindication to chemotherapy (inadaequate bone marrow, hepatic, renal function)<br>- Comorbidity influencing the prognosis of the patients (i.e. secondary cancer)<br>- Participation at another interventional study for postoperative therapy |
| OUTCOME(S) | Primary efficacy endpoint:<br>- DFS of patients with positive postoperative ctDNA at study enrolment by treatment arm<br>Key secondary endpoint(s):<br>- OS of pts with positive postoperative ctDNA by treatment arm<br>- DFS and OS of untreated pts by postoperative ctDNA<br>Assessment of safety:<br>- Toxicity |
| STUDY TYPE | Investigator intiated, prospective, controlled, randomized, confirmatory study |

| | |
|---|---|
| STATISTICAL ANALYSIS | Efficacy:<br>- DFS in pts positive for postoperative ctDNA by treatment arm<br>Description of the primary efficacy analysis and population:<br>- Stratified log rank test for DFS in all randomized pts positive for postoperative ctDNA treated with or without chemotherapy<br>Safety:<br>Descriptive safety data for both arms will be reported in detail for per protocol treated pts by treatment arm. Further, numbers of grade 3-5 events and rates of pts with grade 3-5 events will be compared according to system organ classes following the intent to treat principle<br>Secondary endpoint(s):<br>- Overall survival by treatment arm<br>- DFS and OS of untreated pts by presence/absence of postoperative ctDNA |
| SAMPLE SIZE | To be assessed for eligibility: n = 3500 (screened for ctDNA, MSI)<br>To be allocated to trial: n = 231 (randomized pts)<br>To be analysed: n = 231 |
| TRIAL DURATION | Time for preparation of the trial (months): 9<br>Recruitment period (months): 36<br>First patient in to last patient out (months): 60<br>Time for data clearance and analysis (months): 8 (primary analysis)<br>Duration of the entire trial (months): 77 (including preparation);<br>plus 3 years long term follow-up for overall survival |