Preliminary results of the Transarterial Chemoembolization Treatment with idarubicin (TACTida) study

Final results will be presented as scientific articles over the coming years.

Study design:
The Transarterial Chemoembolization Treatment with idarubicin (TACTida) study has been conducted at Uppsala University (EudraCT number: 2021-001257-31) by a cross-disciplinary team of experienced specialists in pharmacology, cell biology, pathology, multi-omics analyses, imaging and clinical hepatology. The study protocol has been published.[1] Consecutive patients with hepatocellular carcinoma (HCC) scheduled for transarterial chemoembolization (TACE) were included. In addition to routine clinical management, a positron emission tomography/magnetic resonance imaging (PET/MRI) examination was performed, and liver biopsies were taken from the tumour and tumour-surrounding liver parenchyma before and after the first TACE treatment. Patients who tolerated 10 mg Idarubicin at first TACE, received 15 mg Idarubicin at the following TACE.

The study consists of 2 parts, where study part A constitutes the clinical trial comparing the two doses of Idarubicin (10 mg and 15 mg), and study part B has a follow up design where patients are followed regardless of whether treatment is continued or not.

Results:
After approval from the regional ethical review board and written informed consent 30 consecutive patients were included between January 2022 and October 2024. One patient was excluded because of occurring comorbidity that made him unsuitable for TACE. The remaining 28 patients (9 women, 19 men, mean age 78 years) constitute the study population.

6 patients only received one TACE (with 10 mg Idarubicin), and the remaining have now received a mean number of 5 TACE treatments (range 2-10). 4 patients are scheduled for continued treatment according to clinical routine. In the remaining 24, treatments were discontinued due to disease remission, disease progression, or death.

Tolerance and safety:
86 % of the patients (n=24/28) tolerated the 10 mg dose well and were accepted for dose increase to 15 mg at their second TACE. 50% (n=14/28) of the patients are still alive.

There were no major adverse events during or following TACE. Safety will be further evaluated and compared between the 2 doses regarding biochemical markers, liver function/toxicity, and quality of life (self-evaluation by patients before and after every TACE using the Short-Form Health Survey (SF-36)).

Other analyses to be made:
Plasma has been sampled from a peripheral vein before and during 24 hours after TACE and will be used for quantification and population plasma pharmacokinetics (PK) of idarubicin and its active metabolite idarubicinol.

Tumour response is being evaluated on PET/MRI and computed tomography (CT) performed before and after TACE.

Tissue from tumour and tumour-surrounding liver parenchyma will be used for histopathology, molecular biology and multiomics analyses (metabolomics, lipidomics, proteomics). Multiomics analyses will also be performed on liquid biopsy material (plasma).

Organoids have been cultured from tumour[2] and tumour-surrounding liver parenchyma, analysed and exposed to different concentrations of idarubicin or vehicle-control for 6, 24, 48 and 72 hours, measuring cell growth and viability to quantify if ex vivo drug response correlates to the patient's response to TACE treatment. RNA and protein samples have been taken from treated and untreated organoids for further molecular and multiomics assays to define underlying mechanisms that contribute to response and resistance.

All analyses have been performed blinded to each other and without knowledge of the clinical outcome.

The results from these analyses will be used to compare the effects of the two doses and to identify potential non-invasive biomarkers for drug response.

1. Nyman SS, Ahlstrom H, Creusen AD, et al. Study protocol for locoregional precision treatment of hepatocellular carcinoma with transarterial chemoembolisation (TACTida), a clinical study: idarubicin dose selection, tissue response and survival. *BMJ Open* 2022; **12**(11): e065839.
2. Kopsida M, Clavero AL, Khaled J, et al. Inhibiting the endoplasmic reticulum stress response enhances the effect of doxorubicin by altering the lipid metabolism of liver cancer cells. *Mol Metab* 2024; **79**: 101846.