1 TRIAL OVERVIEW

PROTOCOL TITLE

SAKK 77/06 and SASL 23. Continuous sunitinib treatment in patients with unresectable hepatocellular carcinoma. A multicenter phase II trial.

OBJECTIVES

The primary objective of this trial is to demonstrate antitumor activity of continuous sunitinib (Sutent®) treatment in patients with unresectable hepatocellular carcinoma (HCC).
The secondary objective is to evaluate the safety of sunitinib treatment.

ENDPOINTS

Primary endpoint:

- Progression free survival (PFS) at 12 weeks

Secondary endpoints:

- Objective response
- Disease stabilization (DS)
- Duration of DS
- Progression free survival (PFS)
- Time to progression (TTP)
- Overall survival (OS)
- Adverse events (AEs)
- Serum alpha fetoprotein (AFP) level

SUBPROJECTS

Pharmacology

The objective of this subproject is the measurement of trough plasma concentrations of sunitinib and its primary metabolite (SU012662) after 2 weeks of continuous treatment with sunitinib in 15 patients.

Serum cobalamin level

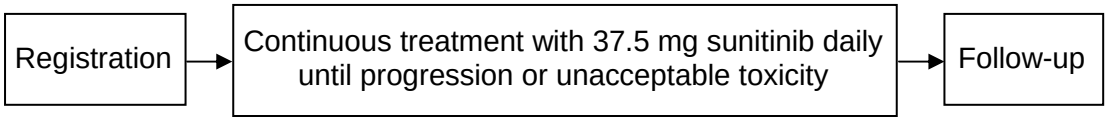
The objective of this subproject is the measurement of serum cobalamin level during sunitinib treatment in order to investigate the relationship between sunitinib treatment and cobalamin deficiency.

Tumor density

The objective of this subproject is to investigate whether changes in tumor density could be used as a criterion for tumor response in future trials.

TRIAL DESIGN

Multicenter phase II trial.



SELECTION OF PATIENTS (MOST IMPORTANT CRITERIA)

- Histologically, cytologically or radiologically diagnosed hepatocellular carcinoma, localized but surgically unresectable or metastatic
- Measurable disease according to RECIST
- Child-Pugh class A or mildly decompensated Child-Pugh class B liver dysfunction
- No prior systemic anti-cancer treatment for HCC

STATISTICAL CONSIDERATIONS

The trial is designed to detect 40% of patients without progression at 12 weeks. Simon's two-stage optimal design with a power of 90%, a significance level of 5% and a sample size of 45 is chosen.

TRIAL DURATION

The inclusion of patients is planned to start in Q3 2007 and will stop after the inclusion of 45 patients, which is expected in Q4 2008.

TRIAL TREATMENT

Sunitinib: 37.5 mg p.o. daily until progression or unacceptable toxicity

22.7 List of participating centers/investigators

Institution	Oncology Fax, Phone, E-mail	Hepatology/ Gastroenterology Fax, Phone, E-mail	Patient accrual per year
SAKK centers			
Basel: KSB	Dr. Viviane Hess Fax : +41 61 265 53 16 Phone: +41 61 265 57 14 vhess@uhbs.ch	Prof. Dr. Markus H. Heim Fax: +41 61 265 53 52 Phone: +41 61 328 63 62 markus.heim@unibas.ch	3
Bern: Inselspital	Prof. Dr. Markus Borner Fax: +41 31 382 12 37 Phone: +41 31 632 41 14 markus.borner@insel.ch	Prof. Dr. Jean Francois Dufour Fax: +41 31 632 49 97 Phone: +41 31 632 87 29 jf.dufour@ikp.unibe.ch	5
Genève: HCUG	PD Dr. Arnaud Roth Fax: +41 22 372 77 45 Phone: +41 22 372 77 44 arnaud.roth@sim.hcuge.ch	PD Dr. Pietro E. Majno Fax: +41 22 372 76 89 Phone: +41 22 372 77 10 pietro.majno@hcuge.ch	4-5
Lausanne: CHUV	Dr. Michael Montemurro Fax: +41 21 314 07 37 Phone: +41 21 314 45 30 michael.montemurro@hospvd.ch	Prof. Dr. Darius Moradpour Fax: +41 21 314 07 07 Phone: +41 21 314 47 23 Darius.Moradpour@chuv.ch	3-4
St. Gallen: KSSG	Dr. Dieter Köberle Fax: +41 71 494 63 25 Phone: +41 71 494 11 11 dieter.koeberle@kssg.ch	PD Dr. Jan Borovicka Fax: +41 71 494 28 62 Phone: +41 71 494 11 11 jan.borovicka@kssg.ch	2-5
Ticino: IOSI	Dr. Piercarlo Saletti Fax: +41 91 811 67 80 Phone: +41 91 811 67 72 pcsaletti@bluewin.ch	not applicable	3-4
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Foreign centers			
Budapest, Hungary: St. László Teaching Hospital	Prof. Dr. György Bodoky Fax: +36 1 455 8261 Phone: +36 1 455 8107 bodokygy@hungarnet.hu	not applicable	5-6
Total accrual expected per year			~32