



Fondation du Centre  
Pluridisciplinaire d'Oncologie

## Fondation du Centre Pluridisciplinaire d'Oncologie

CHUV BH 06 - Rue du Bugnon 46 - 1011 Lausanne

### ZOOM SAKK 77/09 and SASL 30

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| <b>Indication</b>                   | <b>Carcinome hépatocellulaire, stade B</b>  |
| <b>Title</b>                        | A phase I open label/phase II randomized, double-blind, multicenter trial investigating the combination of everolimus and TransArterial ChemoEmbolisation (TACE) with doxorubicin in patients with hepatocellular carcinoma.  |
| <b>Protocol ID</b>                  | <b>SAKK 77/09 and SASL 30</b>   |
| <b>Phase</b>                        | Phase I/II  |
| <b>Sponsor</b>                      | SAKK (Swiss Group for Clinical Cancer Research)   |
| <b>Local Principal Investigator</b> | Dr A. Dorothea WAGNER   |
| <b>Primary Objective</b>            | <p><b>Objective of phase I</b><br/>The main objective of the phase I is to determine the recommended dose (RD) of everolimus in patients with HCC treated with TACE.</p> <p><b>Objective of phase II</b><br/>The main objective of phase II is to determine the efficacy and tolerability of everolimus in patients with HCC treated with TACE as compared to TACE alone.</p>   |
| <b>Inclusion/exclusion criteria</b> | <p><b>Inclusion Criteria include the following:</b></p> <ul style="list-style-type: none"> <li>○ Diagnosis of HCC based on the EASL's criteria</li> <li>○ HCC stage B according to the Barcelona Clinic Liver Cancer (BCLC) staging classification</li> <li>○ Candidate for transarterial chemoembolization (TACE) after multidisciplinary discussion (tumor board).</li> <li>○ Child-Pugh score &lt; 8</li> <li>○ Local therapies have been interrupted for at least 4 weeks (e.g. transarterial embolization/chemoembolization [limited to 5 treatments], radiofrequency ablation, kryoablation, radiation therapy or percutaneous ethanol injection).</li> <li>○ WHO performance status 0-1.</li> <li>○ Adequate haematologic, liver and renal functions.</li> <li>○ Adequate coagulation parameter: INR ≤ 2</li> <li>○ Age ≥ 18 years.</li> <li>○ Patient compliance and geographic proximity allow proper staging and follow-up.</li> </ul> <p><b>Exclusion criteria include the following:</b></p> <ul style="list-style-type: none"> <li>○ BCLC advanced stage, i.e. either portal invasion (segmental portal obstruction), extrahepatic spread.</li> <li>○ Treatment with Sorafenib within 4 weeks prior to start of trial drug.</li> <li>○ More than five prior TACE.</li> </ul> |

- Contraindication for hepatic embolization procedure:
  - Complete portal vein thrombosis.
  - Large arterio-portal or arterio-venous fistula within the liver.
  - Allergy to contrast media.
  - Contraindication to hepatic artery catheterisation, such as severe peripheral vascular disease precluding catheterisation.
- Previous or concurrent malignancy that is distinct in primary site or histology from HCC, EXCEPT cervical carcinoma in situ, treated non-melanoma skin cancer, superficial bladder tumor (Ta, Tis, T1). Any cancer curatively treated > 3 years prior to entry is permitted.
- Tumor involvement (> 50% whole liver).
- Presence or history of metastatic disease (imaging, chest X-ray, required only if clinical evidence) [**in presence of metastases, please consider the SAKK 77/08**].
- Concurrent treatment with other experimental drugs or other anti-cancer therapy, treatment in a clinical trial within 30 days prior to trial entry.
- Concurrent use of biologic response modifiers (G-CSF and other hematopoietic growth factors) within 30 days prior to trial entry.
- Any serious underlying medical condition (at the judgment of the investigator) which could impair the ability of the patient to participate in the trial (e.g. active autoimmune disease, uncontrolled diabetes).
- Contraindication to have MRI (e.g. pacemaker).
- Active heart disease defined as congestive heart failure >NYHA class 2; active coronary artery disease (myocardial infarction more than 6 months prior to trial entry is allowed); cardiac arrhythmias requiring anti-arrhythmic therapy (beta-blockers or digoxin are permitted) or uncontrolled hypertension.
- Hypertension defined as systolic blood pressure greater than 150 mmHg or diastolic pressure greater than 90 mmHg despite optimal medical management.
- Thrombotic or embolic events within the past 6 months such as a cerebrovascular accident (including transient ischemic attacks), pulmonary embolism, or deep vein thrombosis (DVT).
- Serious non-healing wounds (including wounds healing by secondary intention), acute or non-healing ulcers, or bone fractures within 3 months of fracture.
- Evidence of bleeding diathesis.
- Any clinically serious infection (> grade 2 NCI CTCAE Version 3.0) except for HBV and HCV infection.
- Major surgery within 4 weeks prior to start of trial drug.
- Radiotherapy during trial or within 3 weeks prior to start of trial drug.

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|  | <ul style="list-style-type: none"><li>○ Known HIV infection.</li><li>○ Impairment of swallowing that would preclude administration of everolimus.</li><li>○ History of hemoptysis or surgery within the past 28 days.</li><li>○ Organ allograft.</li><li>○ Patient on a waiting list for liver transplantation.</li></ul> |
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