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# Clinical Study Protocol

# SASL 34

# TREATMENT OF NON-ALCOHOLIC STEATOHEPATITIS (NASH) PATIENTS WITH VITAMIN D [TopSIDe Study] – A randomized, double blind, placebo-controlled multicenter phase II trial in patients with fatty liver disease


**Sponsor-Investigator and Principal Investigator:**

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**Study Product:** **Vitamin D3 (Burgerstein Vitamine)**

**Amended Protocol:** **Version 4.0, date 16.10.2012**
**(Includes: Amendment 1: 16.10.2012)**

## STUDY SYNOPSIS

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| **Sponsor-Investigator** | Prof. Dr. med. Andreas Geier, UniversitätsSpital Zürich |
| **Study Title:** | **Treatment of non-alcoholic steatohepatitis (NASH) patients with vitamin D** |
| **Short Title/ Study ID:** | **TopSIDe Study**<br>**SASL 34** |
| **Protocol Version and Date:** | Version 4, 16.10.2012 |
| **Clinical Phase:** | Phase 2 |
| **Methodology:** | randomized, doubleblind, placebo-controlled, multicenter |
| **Study Duration:** | 73 weeks (1 week Screening, 48 weeks treatment period, 24 weeks Follow-up) |
| **Study Center(s):** | Multicenter study - The study will be conducted in about 7 Swiss centers (in the German, French and Italian part of Switzerland) |
| **Main Principal Investigator(s):** | Prof. Dr. Jean-Francois Dufour, Inselspital Bern<br>Prof. Dr. Beat Müllhaupt, UniversitätsSpital Zürich |
| **Laboratory Investigator(s):** | Prof. Dr. med. Arnold von Eckardstein, Zürich (Clinical Chemistry)<br>Prof. Dr. med. Heike Bischoff-Ferrari, Zürich (Vitamin D Physiology)<br>Dr. med. Oliver Tschopp, Zürich (Endocrinology & Diabetology)<br>Dr. med. E. Marques Maggio, Zürich (Pathology) |
| **Statistician:** | Prof. Dr. B. Seifert, Zürich (Biostatistics) |
| **Objective(s)/ Outcome(s):** | To test the efficacy of vitamin D to improve non-alcoholic steatohepatitis with regard to biochemical and histological parameters |
| **Number of Subjects:** | 60 patients, 30 patients for each treatment group (30 patients Vitamin D3, 30 patients placebo) |
| **Diagnosis and Main Inclusion Criteria:** | Patients with 25-OH vitamin D insufficiency, elevated alanine aminotransferase level and a diagnosis of definite or possible steatohepatitis (NASH) from a liver biopsy, obtained within 12 months preceding entry |
| **Main Exclusion Criteria:** | Cirrhosis, present liver disease other than NASH, serious diseases limiting life expectancy, breast-feeding or pregnant women, unhealthy alcohol consumption, drug abuse or substitution therapy, regular use of vitamin preparations within the previous 6 months and during the study, weight loss >5% within 12 months before study entry, newly diagnosed Diabetes mellitus requiring medical treatment within 12 months before study entry, use of anti-obesity drugs, previous or current hypercalcemia, chronic renal disease |
| **Study Product, Dose, Route, Regimen:** | Vitamin D3 (Burgerstein Vitamine) 2.100 IU (7 tablets), oral administration |
| **Duration of administration:** | 48 weeks treatment period |
| **Reference therapy, Dose, Route, Regimen:** | Placebo (7 tablets), oral administration |

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| **Study Schedule:** | First-Subject-In April 2012 (planned)<br>Last-Subject-Out October 2015 (planned) |
| **Statistical Methodology:** | Comparison of group characteristics at entry: Mann-Whitney U test and $Chi^2$ or Fisher`s exact test.<br>Effect on serum alanine aminotransferase level [primary end point]: Unpaired t-test.<br>Comparison of changes in histological steatosis, changes in the NASH activity score (NAS) and individual component scores of the NAS (steatosis, lobular inflammation, ballooning, fibrosis) [secondary end points]: Mann-Whitney U test. |
| **GCP Statement:** | This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, and ICH-GCP as well as all national legal and regulatory requirements. The study will also follow the respective SAMW Guideline regarding the collection of human biological material (Biobanking). |