2. Protocol Synopsis

PROJECT TITLE	Dexamethasone for the treatment of established postoperative nausea and vomiting – a randomised, placebo-controlled, dose-finding study
BACKGROUND 10 lines max.	Postoperative nausea and vomiting (PONV) are frequent adverse effects of surgery and anaesthesia. Dexamethasone is widely used as antiemetic for the prophylaxis of PONV although the biological basis of its effect is still not fully understood. Little is known about the efficacy of antiemetic drugs for the treatment of established PONV symptoms. No single randomised trial has been published so far that tests the efficacy of dexamethasone for the treatment of established PONV symptoms.
PRIMARY OBJECTIVE(S)	To test in adults undergoing elective surgery under general anaesthesia the antiemetic efficacy of three different doses of IV dexamethasone for the treatment of established PONV symptoms, and to determine whether there is dose-responsiveness. In adjunct protocols we aim to establish a novel method to quantify the anti-nausea efficacy of an antiemetic drug, to study pharmacogenetics of PONV, and to further our understanding on the smoking status as a predictive factor of PONV.
INCLUSION/EXCLUSION CRITERIA	**Inclusion criteria:** Adults, age ≥18 to 80 years, scheduled for elective surgery, ASA status I to III. If the patient is female and of childbearing potential, she must have a negative pregnancy test. **Non-inclusion criteria:** Diabetes, GI ulcer, tonsillectomy, surgery requiring strict prevention of PONV, planned prolonged postoperative intubation or gastric tube postoperatively, outpatient surgery, patients receiving antiemetic drugs, with overt psychosis or taking antipsychotic treatment or drugs with known emetogenic potency (for instance, L-Dopa, COMT inhibitors).
RANDOMISATION/STUDY GROUPS/SAMPLE SIZE	Bi-centre (HUG, CHUV), placebo-controlled, randomised, stratified (for centre), double-blinded study. Sample 4x140=560 nauseous and/or vomiting patients to detect a 20% risk reduction in PONV (power 90%, alpha: 0.05, one-sided test).
INTERVENTION	IV single dose dexamethasone 3, 6, 12 mg or saline 0.9% (placebo).
FOLLOW-UP	Patients will be followed 24 hours after administration of study drug.
ENDPOINT(S)	Primary endpoint is complete absence of any nausea and/or vomiting (including retching) in a previously nauseated or vomiting patient within 24 hours after administration of the study treatment.
STATISTICAL ANALYSIS	The proportion of treatment success in each treatment group will be compared with the placebo group. OR (95%CI) will be computed using logistic regression. Departure from linear trend will be assessed by a likelihood ratio test.
TIME FRAME	The following milestones will apply: First patient randomized: April 2012; last patient randomized: March 2015; statistical analyses (main and adjunct projects) finished: June 2015; manuscript submission (main protocol): August 2015; final report: September 2015.
REQUESTED BUDGET	CHF (total for three years): CHF 538'629 TOTAL YEAR 2012: CHF 159'926 TOTAL YEAR 2013: CHF 147'926 TOTAL YEAR 2014: CHF 230'777