Study protocol

A Multicenter Randomized Trial, Comparing a 25G EUS Fine Needle Aspiration (FNA) Device with a 20G EUS ProCore Fine Needle Biopsy (FNB) Device

ASPRO trial (**ASP**iration versus **PRO**core)

ProCore study group

PROTOCOL TITLE

Protocol ID	ASPRO trial
Short title	Comparing a 25G EUS-FNA with a 20G EUS ProCore FNB Device
Version	Version 1
Date	13-10-2014
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Principal investigator ***(See paragraph 3.1 for a list of all principal investigators per site)***	Dr D.L. Cahen Department of Gastroenterology & Hepatology, Room H-337, Erasmus University Medical Center, Rotterdam, the Netherlands Email; djuna@cahen.nl
Sponsor	SLO (in Dutch: Stichting Lever Onderzoek, in English: Foundation for Liver and Gastrointestinal Research) on behalf of the Department of Gastroenterology and Hepatology of the Erasmus University Medical Center in Rotterdam, the Netherlands
Subsidising party of unrestricted grant	Cook Medical O'Halloran Road National Technology Park Limerick, Ireland www.cookmedical.com
Independent physician	Dr D. Sprengers Department of Gastroenterology & Hepatology, Erasmus University Medical Center, Rotterdam, the Netherlands Email; d.sprengers@erasmusmc.nl

Laboratory sites	Department of Clinical Pathology, Erasmus University Medical Center, Rotterdam, the Netherlands
Pharmacy	Not applicable

PROTOCOL SIGNATURE SHEET

Name	**Signature**	**Date**
For non-commercial research, Head of Department: Prof Dr M.J. Bruno, Head of Department of Gastroenterology & Hepatology, Erasmus University Medical Center, Rotterdam, the Netherlands		
Principal Investigator: Dr D.L. Cahen Department of Gastroenterology & Hepatology, Room H-337, Erasmus University Medical Center, Rotterdam, the Netherlands Email; djuna@cahen.nl		

1. STATISTICAL ANALYSIS

1.1 Descriptive statistics

Depending on distributional properties, outcome measures will be expressed as means ± standard deviations (SD) or as medians with interquartile ranges (IQR). Missing follow-up data will be considered to be missing at random. Statistical significance will be assessed with the use of Student's t-test for normally distributed continuous data; either the chi-square test for categorical data (with Yates' correction when appropriate) or Fisher exact test for categorical data; and the median test for non-normally distributed continuous data. Data will be analysed with SPSS, Statistical Package for the Social Sciences. SPSS Inc, Chicago, Illinois.

1.2 Univariate analysis

1.2.1 Primary endpoint

Overall diagnostic accuracy will be compared between the two groups, using the Pearson's chi-squared test. Additionally, the p-value, adjusted by strata, will be calculated.

1.2.2 Secondary endpoints

Technical success, pathological classification on which diagnosis was based, and safety (i.e. adverse events) will be compared between the two arms, using the Pearson's chi-squared test. Additionally, the p-value, adjusted by strata, will be calculated. Differences in quality and the presence of tissue cores of both arms will be tested using the non-parametric test for ordinal outcomes. Kappa values will be calculated to determine inter-observer variability among pathologists.

1.3 Multivariate analysis

To study the effect of the two methods on the different outcome measures, additional multivariate analysis will be applied, as described below.

Logistic regression will be applied to asses differences of accuracy between the two methods, adjusted for; age, indication, number of needle passes, vial number, and the presence of an on-site pathologist.

Ordinal logistic regression will be applied to asses differences of quality and presence of tissue cores between the two methods, adjusted for; age, indication, number of needle passes, vial number and the presence of an on-site pathologist.

1.4 Analysis Population

All analysis will be performed on an intention-to-treat (ITT), modified ITT, and per protocol population. The ITT population are patients that were randomised in the study. The modified ITT population is defined as all patients in whom a puncture resulted in the collection of a diagnostic tissue sample. Patients in which a puncture resulted in tissue collection, independent of the quality of the sample (diagnostic or not) are defined as the per protocol population.

1.5 Interim analysis

Not applicable.

1.6 Missing Data

Missing data will be reported, evaluated, and corrected if possible. When more than 30% of a variable is missing, the interpretation of this variable, as well as exclusion of this variable from the analysis, will be considered carefully. Prior to closure of the database, an official statistical analysis plan will be written.

Filename: Statistical plan ASPRO protocol.doc
Directory: /Users/Sil/Dropbox/ASPRO/METC EMC/C. Protocol
Template: /Users/Sil/Library/Group Containers/UBF8T346G9.Office/User Content.localized/Templates.localized/Normal.dotm
Title: Instructions for use ‘Template Research Protocol’
Subject:
Author: Carla Mellema
Keywords:
Comments:
Creation Date: 2/24/20 10:20:00 AM
Change Number: 2
Last Saved On: 2/24/20 10:20:00 AM
Last Saved By: Priscilla van Riet
Total Editing Time: 0 Minutes
Last Printed On: 2/24/20 10:20:00 AM
As of Last Complete Printing
Number of Pages: 5
Number of Words: 755 (approx.)
Number of Characters: 4.309 (approx.)