DiSCHARGE

Diagnostic Imaging Strategies for Patients with Stable Chest Pain and Intermediate Risk of Coronary Artery Disease: Comparative Effectiveness Research of Existing Technologies

Annual Meeting 2016

Agenda of Steering Committee (SC) Meeting

Thursday, 18 February 2016, 3:00-4:30pm (CET, Budapest Time)

DISCHARGE Coordinator and Project Management: Marc Dewey (MD), Adriane Napp (AN)

Meeting Minutes: Christoph Katzer and Sarah Feger

DISCHARGE Steering Committee:

Dr. Jacob Geleijns (JG), Dr. Christine Kubiak (CK), Dr. Iñaki Gutiérrez-Ibarluzea (GI), Prof. Jacqueline Müller-Nordhorn (JMN), Prof. Peter Schlattmann (PS), Prof. Klaus Kofoed (KK), P Christian Delles (CD), Prof. Teodora Benedek (TB), Prof. Marco Francone (MF), Dr. Ligita Zvaigzne (LZ), Prof. Matthias Gutberlet (MG), Prof. Marc Dewey (MD)

Present:

Dr. Christine Kubiak (CK), Dr. Iñaki Gutiérrez-Ibarluzea (GI), Prof. Jacqueline Müller-Nordhorn (JMN), Prof. Peter Schlattmann (PS), Prof. Klaus Kofoed (KK), Prof. Christian Delles (CD), Prof. Teodora Benedek (TB), Prof. Marco Francone (MF), Adriane Napp (AN), Prof. Marc Dewey (MD)

Absent: Dr. Jacob Geleijns (JG), Dr. Ligita Zvaigzne (LZ), Prof. Matthias Gutberlet (MG),

Nr.	Issues	Outcomes	ID
1	**Welcome**		
2	**Recruitment**		
	How to improve recruitment rate		
	a) 1/3 of sites are recruiting. Currently 300 patients after 4 months. In case, other sites recruited at the same rate, recruitment would be sufficient. Delay of 6-8 months due to missing eCRFs. Patient recruitment has to be finished before deadline (to have enough time for Follow-up.	→ Additional compensation of 25% for patients being included until 1 July 2016 (Heavy Recruitment). Already decided 7.12.2015. → Compensation is taken from budget for patients being recruited afterwards. Clarification of decision from 7.12.2015. All agreed. . → Outreach to public will be pushed.	

	b) Responsibility of regional clinical site representatives concerning outreach activities	→ All regional clinical site representatives will be contacted by project management and will be given contact details of clinical sites. Region representatives will support outreach activities of the respective local sites.	
	c) Publication of results	→ Pilot study results will be published as soon as possible. PRCT results: Idea to publish first results after recruitment termination about procedural complications to have influence on the development of guidelines and politics. All agreed.	
3	**Participation Annual Meetings**		
	Non-participating partners		
	a) Repeated absence of clinical site representative.	→ Recommendations of DC are accepted i. DC co-chair JD will contact respective site. ii. Any potential budget loss will be covered by violating site only. iii. Decision will be sent to all sites in form of a formal procedure by DC chair.	
4	**Monitoring-Manual /SOPs**		
	Definition of cut-off values for protocol deviations		
	a) Handout and presentation of SOP "Definition of critical protocol violations and their handling" for discussion of thresholds (Appendix 1)	→ All agreed	
	b) Screening Log Patients, about 2000 in PRCT should be considered with about 20 Euros per patient. To stay within the budget, the amount will be reflected in the payment for the recruitment.	→ All agreed	
	c) Presentation of *"Payment Border Sheet"* (Appendix 2) to address the statistical value of patients	→ All agreed	
	d) Informed consent not signed by some patients	→ will be reported to local IRB → without consent, patients will be classified as withdrawals and do not count for the main study → CK and AN: the above can be avoided with a form for the patient to sign that he/she would have provided consent on the day of inclusion. All agreed.	

5	**Other**		
	b) Monitoring Visits	→ Planned after 6 months and immediately in case of serious protocol violations Note from AN: Details are in the Monitoring Manual about the visit frequency and items to be monitored.	
	c) First Results: Only 2 minor AE and one SAE reported. 20 AE expected	→ 48h Follow-up needs to be better documented. Note from AN: A 48h Follow-up worksheet for the phone call has been prepared and will be sent to the clinical sites.	

Appendix 1: Definition of critical protocol violations and their handling

Every finding recorded through the on-site and remote monitoring should be corrected. If there is no way of correcting a finding a note to file (NTF) has to be created by the monitor. This NTF should contain all information necessary to explain how this finding could occure and what was done to prevent it in the future. The NTF will be filed by the monitor in DISCHARGE folder (\\141.42.17.44\Klinische Studien\DISCHARGE\Monitoring). The site will receive an email with the NTF and needs to file it in the ISF under "12. Miscellaneous, 12.1 Note to files". Additional actions are listed below. The overview of thresholds are the responsibility of the remote/central monitoring. On-site monitors include all findings in their report, regardless of their category and follow them. Decisions on further actions will be made centrally. Actions already take place upon detection before the thresholds are reached.

Signal	Description	Relevant for On-Site Monitoring	Relevant for Remote Monitoring	Consequence Corrective and preventive actions
Red critical	• Unacceptable procedures and findings with the informed consent	x	x	Increased frequency of on-site monitoring; training; closure of study site; legal consequences. Increased frequency central site contact.
	• Inclusion of patients against in- and exclusion criteria	x	x	
	• Inclusion of patients without ICA referral		x	
	• Fraud or misconduct (falsifying data or patients); no reliable data	x		
	• No or insufficient SAE/MACE/AE documentation or reporting	x	x	
	• No follow up of patients		x	
	• Withdrawal after randomisation and before diagnostic procedure for 5% of patients (Patient rejects to undergo CT or ICA, no test at all)		x	
	• Withdrawal after procedure for 5% of patients (Patient rejects to undergo Follow-up)		x	
	• 1. Randomisation deviation (>2 %): ○ 1.1 Patients received ICA instead of CT ○ 1.2 Patients received CT instead of ICA	x	x	
	• 2. Protocol deviations/CT based management (>1% for each item/on a per patient basis): ○ 2.1 Patients received ICA even though CT was negative ○ 2.2 Patients received ICA even though CT was < 20% stenosis ○ 2.3 Patients received ICA even though CT was 20 – 50% stenosis ○ 2.4 Patients received ICA even though CT was ≥ 50% stenosis and no high risk anatomy ○ 2.5 Patients received ICA even though CT was NDX no high risk anatomy		x	

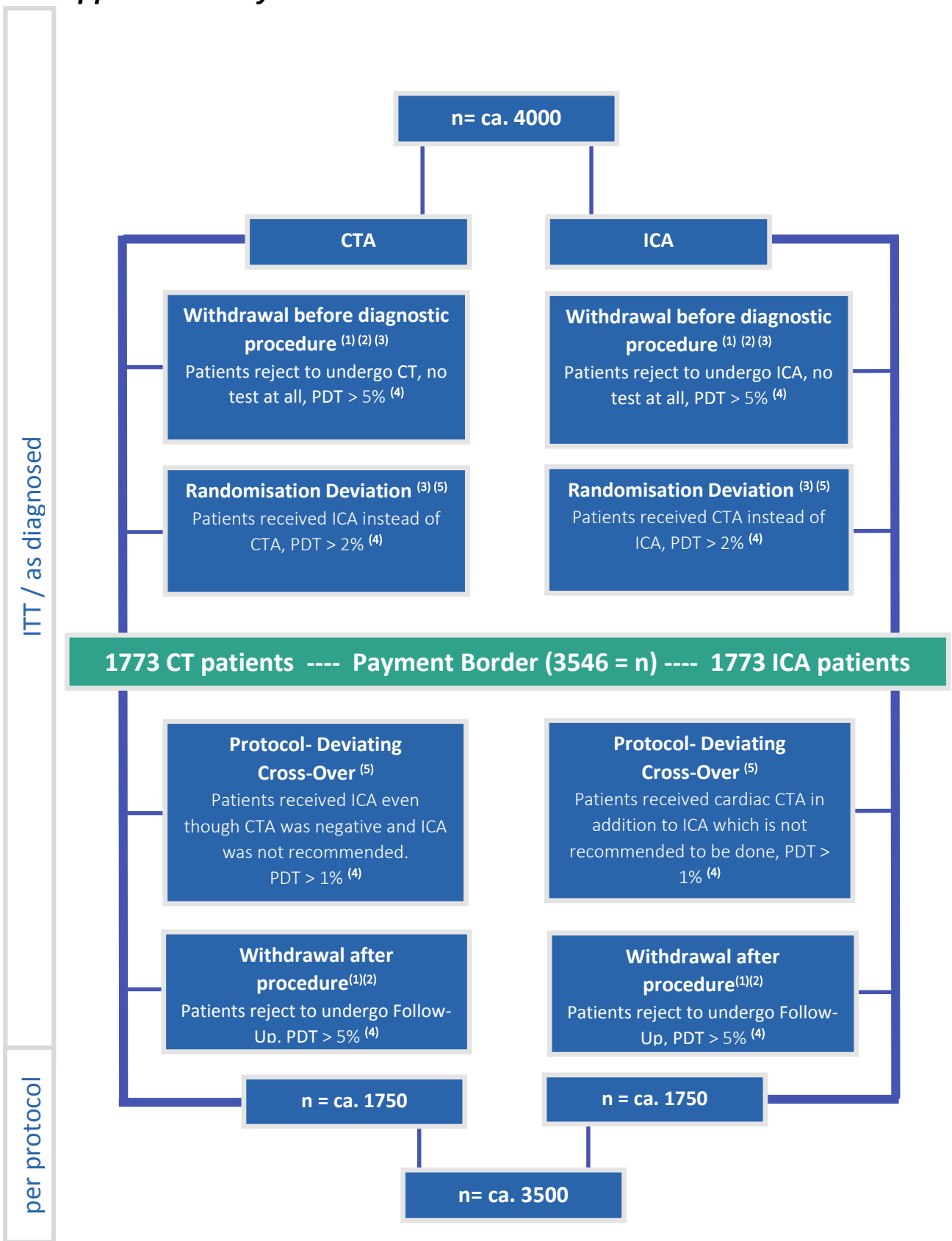
	○ 2.6 Patients received ICA even though CT was ≥ 50% stenosis, no high risk anatomy and ischemia < 10 % ○ 2.7 Patients did not receive ICA even though CT was ≥ 50% stenosis and high risk anatomy ○ 2.8 Patients did not receive ICA even though CT was NDX and high risk anatomy ○ 2.9 Patients did not receive ICA even though CT was ≥50%, no high risk and ischemia >10% ○ 2.10 CT management recommendation wasn´t followed in CT decisions and no reason was given ○ 2.11 ICA management recommendation wasn´t followed in ICA decisions and no reason was given			
	• 3. Violation of the 10-step guide (>10% for each item or >10% on a per patient basis) ○ 2.1 No oral beta blockade or alternative medication though HR >50 bpm ○ 2.2 No second dose of betablockers though HR >60 bpm ○ 2.3 No i.v. betablockers though HR >55 bpm or HR variability >10% and no contraindications ○ 2.4 Z-axis CTA < coronaries on CACS +2*15mm ○ 2.5 No administration of nitroglycerin though systolic blood pressure >100mmHg		x	
	• Violations of scanner specific protocols (to be added)		x	
	• Accumulation of red major protocol deviations	x	x	
Red major	• no, very late or insufficient documentation (no source data); late follow up of patients		x	Increased frequency of on-site monitoring; training. Increased frequency central site contact.
	• Late documentation (Accumulation of late documentation / No correction of late documentation)		x	
	• Late SAE reporting: later than 7 days	x	x	
	• Late documentation: later than 10 working days for documents concerning the CT/ICA procedure, results and management recommendations and decisions after the planned procedure. All other entries later than 20 working days.		x	
	• Accumulation of yellow minor protocol deviations	x	x	
	• Problems with the traceability of data	x		
	• Violations of the the QoL_SES_Lifestyle completion strategy (before procedure)		x	

	• Violations of the lung nodule flowchart (to be added)		x	
	• Withdrawal after procedure (>5%): ○ Patients reject to undergo Follow-up		x	

	• Reconstructions
	  ○ CACS not performed at 120kV and FBP, small field of view, slice thickness 3mm and slice increment 3mm
	  ○ CTA not performed at FOV ≤180mm, slice thickness ≤0.8mm and slice increment ≤0.5mm, no reconstruction at the automatic best phase (auto best systole and diastole) and further reconstructions in 5% intervals of RR
	  ○ Noncardiac structures not reconstructed on large FOVs with slice thickness of 1 mm and slice increment of 1mm
			x	

Yellow minor	• Late documentation: later than 5 working days for documents concerning the CT/ICA procedure, results and management recommendations and decisions after the planned procedure. All other entries later than 10 working days (e.g., Patient Acceptance after Procedure)		x	Depending on the nature of findings: more training; increased frequency of site contact (and on-site monitoring)
	• Protocol deviations with no further impact on patient‘s safety or the reliability of the data	x	x	
Green Minor	• No or only few minor findings	x	x	If applicable training or increased site contact

Appendix 2: Payment Border Sheet



1) Withdrawal = patient withdrew or was withdrawn by PI from Clinical Study
2) Ask these patients if they will be available for Follow-Up
3) Patients need to be replaced by repeated recruitment to match pre-planned patient number
4) PDT: Protocol Deviation Threshold; If the given percentage is exceeded in one or more years, risk monitoring of the clinical site will be performed
5) These patients need to be in the Follow-Up