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 2015

Thursday 11. February 2015, 08:30 – 18:00h

Participants:

P01: Marc Dewey (MD) (Coordinator), Adriane Napp (AN) (Project Manager),Robert Haase, Michael Laule, Jacqueline Müller-Nordhorn (JMN) (WP Leader), Nina Rieckmann (NR), Olaf Bender, Felix Frömel (FF), Corinna Meier-Windhorst (CMW), Florian Specht, Anja Bärrn, Lisa Timm, Paolo Ibes, Simon Drees, Sascha Priem, Viktoria Wieske, Christoph Katzer (CKa), Florian Michallek, Denise Sengül,
P02: Fabian Plank
P04: Vojtech Suchanek (VS) (PI CT), Cyril Stechvosky
P05: Klaus Kofoed (KK)(PI CT - WP Leader), Kirsten Thrysoe
P06: -
P07: Borek Foldyna
P08: Pál Maurovich-Horvath (PMH)(PI CT), Mihaly Karoly , Csilla Celeng
P09: Peter Ball (PB)(PI CT), Michele Crawford Jefferson
P10: Jonathan Dodd (JD) (PI CT), Siobhan Quinlan, Ali Abdi
P11: Gildo Matta (GM), Maurizio Porcu (PI ICA)
P12: Marco Francone (MF) (PI CT), Iacopo Carbone
P13: Ligita Zvaigzne (LZ)(PI CT), Marina Berzina
P14: Gintare Sakalyte (GS) (PI ICA), Antanas Jankauskas (AJ) (PI CT)
P15: Ewa Zdunczyk
P16: Rita Faria
P17: Teodora Benedek (TB) (PI CT), Sebastian Condrea
P18: Nada Čemerlić Ađjić (NCA) (PI ICA), Milovan Petrovic, Tatjana Miljkovic
P19: Jose Rodriguez Palomares (JRP) (PI CT), Filipa Valente
P22: Christian Delles (CD)(PI CT), Katriona Brooksbank
P23: Gershan Davis (GD)(PI CT/ICA), Erica Thwaite
P24: Christoph Schumacher (CS), Anke Strenge-Hesse (ASH)
P25: Koos Geleijns (KG)(WP Leader)
P26: Iñaki Gutiérrez-Ibarluzea (IGI)(WP Leader), Gaizka Benguria
P27: Vladimir Rogalewicz (VR)(WP Leader), Ivana Juřičková, Vojtěch Kamenský
P28: Peter Schlattmann (PS)(WP Leader), Mario Walther
P29: Antti Saraste, Heli Ylikoski
P30: Cezary Kepka (PI CT)
P31: represented through P17
P32: Radosav Vidakovic (PI CT)
P33: Inigo Sans Ortega
Clinical Site interested in participating: Ladislav Pavic (Croatia)
EAB: Harold Sox (HS)
DSMB: Danilo Fliser, Tim Friede

Nr.	Issues	Outcomes	
2.	**Welcome and Round of Introduction**		
	2.1 Welcome by Marc Dewey **2.2 Round of Introduction**		
3.1	**Status of the DISCHARGE Trial** (Marc Dewey)		
	HS: What about patients who refuse to be randomised?	MD: If a patient refuses to participate in the study, a field in the eCRF form will be added to report the reason of withdrawal. The patient will be informed about his benefit in terms of outcome by participating in the study. The CT reconstructions at 70%, 75% and 80% must be evaluated as well as the automatically chosen phase.	
	Q. Comparison of scanner specific protocols of Siemens and Toshiba; Siemens recommends sharp scanner/kernel for CTA, for Toshiba not, so soft kernel used. Why is recommendation missing? Differences in protocol might lead to different results, e.g. in CACS	MD: scanner specific protocols will be checked and updated	
	Q.P04: If many reconstructions are done all of them need to be reviewed otherwise if you miss something it counts as fault. All coronary arteries have to be reviewed in all phases.	MD: when automatic motion in the silent phase does not work then review several phases for the reconstructions you are happy with. Not just use automatic motion phase, good for reducing work load and finding the silent phase. Still the recommendation is to do phases 70%, 75%, 80% and compare it. Also iterative reconstruction is good to be used. Situation might be different with full cardiac coverage in retrospective gating but covered by tube current modulation. Do more phases in patients with higher heart rate (40%-80%) and review those. But do not send us all the phases you finally used for reading	
	JD: Will Video be available for download?	MD: Yes, the video files can be downloaded from the member's area on the DISCHARGE website. It is mandatory to retain the same contrast agent throughout the study. The CT contrast agent can be ordered and is paid by DISCHARGE.	

	GM: Is it mandatory to use the same contrast agent throughout the whole trial?	MD: Yes, do not change CT contrast agent, especially the concentrations needs to be consistent in order to full fill a certain method protocol. AN: Consumables like contrast agent can be paid by DISCHARGE	
3.2	**Patient Management in DISCHARGE Part I** (Marc Dewey, Jonathan Dodd Robert Haase)		
	No further discussion		
3.3	**Patient Management in DISCHARGE Part II** (Marc Dewey, Robert Haase)		
		Scanograms will be send to Corelab in order to not overlook lung cancer, will be updated in the 10-step guide	
		Authorships: First authorship position: site with highest recruitment. Second authorship position: site with second highest recruitment	
	AJ: Are there the same rules for borderlines stenosis (just above 50%) and occlusions?	RH: same rule, measurement of lesion length is mandatory in eCRF MD: chronic total occlusions were a big discussion in one of the telephone conferences. Measurement of lesion length can help to define the length of stent which should cover the entire lesion. No definition because there is no evidence to base it upon. Clinical sites can use information from CTA for ICA but not forced to since communication at sites might be different.	
	MD: Who is using the 'worst view' feature?	Information of worst view could be given to Cathlab, but no big feedback in telephone conference	
	Question: CTA and SPECT, for example, not matching. What should we do?	MD: Use the best locally available ischemia test when an ischemic region does not match a stenotic lesion. Maybe perform a third test.	

	KK: „Borderline“stenosis (between 20-50 %) → more aggressive approaches concerning risk factor modification and optimal medical therapy? How to teach physicians how to proceed in case of 20-50% findings? HS: It might be important to describe the process of decision making, especially for patients who underwent a CTA.	MD: Both sides are responsible. Refers to summary of Joep Perk et.al (see meeting folder) → intense risk factor modification →high dose statins (great discussions in last year's meeting) based on CT high-risk plaque features eCRFs will give you suggestions concerning measures that should be taken There is a minimum set of actions that are needed: - try to get patient of smoking - get lipids down - treat hypertension Do not do anything against the guidelines In individual cases, local heart team decisions may differ from eCRF. It is ok, but you have to give reasons and try to treat high-risk plaques aggressively.	
3.4	**Clinical Site Efforts to Prepare for DISCHARGE** (All clinical sites)		
	HS: Recommends to write method section of study before PRCT starts in order to allow different insights, e.g. when probability is going to be estimated	MD: There will be many different method papers due to complexity of the study and amount of topics, it will be objective of this spring to summarise, get approved and submit methods papers. Probability estimated in the eCRF	
	KK: Will there be rules of who is in charge for referring the patients to ICA?	The indication for ICA should optimally be established externally, at least it should not be done by the investigators themselves. It is required to upload the referral form with the indication for ICA (e.g. as pdf or jpeg file) in the eCRF.	
	HS: Is there a list of clinical relevant criteria for referring to ICA to give readers of articles the chance to see to which population the results might apply?	MD: A list of medical indications for ICA will not be explicitly established in order to pragmatically depict the clinical routine patient collective. However, in the resulting paper an appendix table will be supplied to explain the origin of the patients, e.g. prior imaging test. It will be established by Teodora Benedek, Klaus Kofoed and Rita Faria	
		All PR activity will need approval of coordinating site, this needs to be reported to the EU since it is a deliverable. Please e-mail to discharge.eu@charite.de Each site will set up a summary of all dissemination efforts locally taken (e.g. announcements in public media, leaflets, Christmas or birthday cards etc.). This summary will also be submitted to the EU.	

		It is required in the eCRF to name both a reader and a supervisor to perform the CT readings yielding two investigators in total for this task. It is not appropriate to have the CT examinations read by one investigator only.	
		In order to correctly perform the CT examination, a scanner specific protocol is required which is already established for the accepted scanners. Two sites declared the use of scanners not accepted in advance. These sites need to contact coordinating site and the manufacturer in order to develop an appropriate protocol If scanner specific protocol does not work sites need to contact coordinating site and people who developed protocol in order to change it. Without scanner specific protocol approved by MD no start of study.	
	HS: What about patients with the pretest probability just below the lower threshold but with positive family history for CAD Q.: Still CT scan for patients with a lower pretest probability (under ten)?	The pretest probability is calculated within the eCRF and requires patient‘s age, gender and angina symptom classification. The latter features 4 discrete categories and it is at the exclusive assessment by a physician. (The pretest probability must not be included in the patient information.) Patients that are included in the study will receive ICA independent from their pretest probability. Patients with a pretest probability inappropriate for randomization will be recorded in the screening log. No CT for those patients outside the 10-60% pretest probability. ICA results of these patients will be submitted to the coordinator‘s site. They will not receive follow-up.	

	KK: Recording and comparison of malpractice in ICA as well as in CTA	Clinical practice features the fact that guidelines are not in all cases perfectly applied. In order to correctly depict this, data about both ICA and CT procedures that are performed at each site will be recorded including radiation dose applied. Data of patients participating in the pilot study will be compared to those not taking part. This additional effort enables anticipating potential criticism concerning a study design putatively aiming at minimizing false negative results in CT, thus preventing patients to receive ICA. Due to three sites declaring issues in collecting these data, strategies will be developed in cooperation with these sites. Excluding patients with high pretest probabilities is not an alternative option to deal with this issue due to the intention of the DISCHARGE study to establish CT as the primary procedure for patients within the range of 10-60% pretest probability.	
3.5	**Pilot Study: Status and Main Result** (Florian Specht, Lisa Timm, Anja Bärrn)		

	Working groups:	QoL: Jacqueline Müller-Nordhorn, Nina Rieckmann, Inaki Gutiérrez-Ibaluzea, Peter Schlattmann, Paolo Ibes, Christoph Katzer, Paolo Ibes, Marc Dewey Micro-costing: Vladimir Rogalewicz, Christoph Katzer, Ivana Jurickova, Marc Dewey Acceptance of the time trade-off question: Elke Zimmermann? A psychologist or experienced person may be needed to perform the interviews: Jacqueline Müller-Nordhorn, Nina Rieckmann European differences e.g. in regards to city vs. rural lifestyle: Jonathan Dodd, Peter Schlattmann, Peter Ball. Question: Will it be appropriate to record ZIP code of the patient? Validation and comparison of the different questionnaires (SF-12 self-rated health item, SF-12 physical component summary score, EuroQol 5d-3L and Hospital Anxiety and Depression Scale, Mac New): Not yet declared. Differences in patient consent process of sites: Gershan Davis, Theodora Benedek, Antanas Jankauskas, Iacopo Carbone, Jonathan Dodd?? Influence in timeframe from CT to ICA and then to therapy: Jose Palomares, Marco Francone, Rita Faria, Vojtech Suchanek Comparison of radiation dose in ICA and CT Pilot study versus non-study patients: Jose Palomares, Marco Francone, Koos Gelejins, Cyril Stechvosky, Pál Maurovich-Horvath, Theodora Benedek, Marc Dewey	
3.6	**Pilot Study: Quality of Life and TTO-Results** (Jacqueline Müller-Nordhorn, Nina Rieckmann)		
	Q: What is the ideal time point to fill out QoL questionnaire?	Hand out questionnaires after pretest probability calculation, but BEFORE randomization Avoid informing patients about their randomized arm before you hand out the questionnaires	

	MF: 25 % of patients never had chest discomfort? Maybe further analysis needed, e. g. local or cultural differences?	NR: remembers big discussion at last year's meeting of how to define and rephrase the terms chest pain and chest discomfort, may be and translation and wording issue? Solution: ask the patients concerning that contradiction.	
3.7	**Pilot Study: Micro-costing Results** (Christoph Katzer)		
	VR: doubts possibility to collect precise and concrete data for society perspective during the two follow-ups → to big error in data	MD: it was a strategic decision not putting the society perspective in the proposal to the EU since the EU demands explicitly the patient's perspective and the health care provider perspective. Conclusion after comparison to National Lung Screening Trial publication on cost effectiveness that data could be easily collected in DISCHARGE based on major cost drivers. Drafts for follow-up in eCRF do exist to meet those purposes. Data will not be perfect due to PRCT. But society perspective should be included in order to be published in high impact journals.	
	GI: Difficult to collect that data. Too many assumptions will be made VR: suggests diary for patients	MD: there will be estimations due to incorrect or invalid patient data. It is very important to engaging patients to collect data themselves e.g. in a special folder for copies of reports of visits, no diary due to PRCT	
	HS: suggests to laying out a model of events happening after the procedure, sort it by likelihood and change numerator or denominator	MD: correct, focus will lie on major cost drivers	
		CK: population of DISCHARGE trial will be in part old with a considerable amount of patients already retired. Will be difficult to collect data about informal work. Suggests to take published data and base a model on those MD: good experience with the MC Williams calculator. Proposes to contact first or corresponding author of analysis and ask about experiences and if they might be interested to join	
3.8	**Review of Radiation Exposure of Cardiac CT** (Koos Geleijns)		

	Schlattman: How big was the drop of reading quality?	KG: Refers to the gold standard to measure the drop. MD: Regards to the importance of diagnostic quality due to the fact of the importance of a good identification of CAD. MF: Says that DISCHARGE is not a low dose study. Important is the identification of the disease. MD: Plaques will be lost if the dose gets reduced too much.	
3.9	**Systematic Review of MACE Definitions** (Iñaki Gutiérrez-Ibarluzea)		
	PS: Sees a potential of reporting bias and inconsistency of patients answers. HS: subjectiveness?	MD: Agrees, refers to standardised gathering of data. MACE definitions are based on literature research. Stresses importance of telling the patient to collect copies of results and keep copies. This is particularly needed by the Clinical Events Committee (CEC) which will review all MACE.	