SPARKLE RADIOPHARMACEUTICALS	Individual Study Table Referring to Part of the Dossier: Volume Page	(For National Authority Use only)
Name of Sponsor:	Sparkle srl Manufacturing site: Contrada Calò snc, Casarano (LE) Registered office: Contrada Cavallino snc, 62010-Montecosaro, (MC)	
Name of Finished Product:	64Cu(II)Cl2 (925MBq/ml) concentrate solution	
Volume:	From 1 to 3ml	
Name of Active Ingredient:	Copper64 Cu Cloride, concentrate for injectable solution	
Title of Study:	Technical and diagnostic performances of PET/CT with 64Cu(II)CL2 in localization of metastases from prostate carcinoma, in patients undergoing restaging for disease progression during ADT	
Investigators:	Dr. Rosa Sciuto *(Coordinator – Principal Investigator)*	
Study centre:	Dr. Rosa Sciuto *(Coordinator – Principal Investigator)* IRCCS - Istituto Nazionale Tumori Regina Elena (IRE) Istituti Fisioterapici Ospedalieri (IFO) *Via Elio Chianesi 53 – 00144 ROMA*	
Publication (reference):	none	
Studied period:	10 months date of first enrolment: 28.06.2016 date of last completed: 01.04.2017	
Phase of development:	Fase II	
Objectives:		
Main Objective:	Initial assesment of the diagnostic sensibility, on a per patient-basis, of whole body PET/CT after administration of 64Cu(II)Cl2, in the localization of metastatic lesions from PCa, of bones, lungs and lymph nodes (regional pelvic and/or lumbar and subfrenic nodes), preliminarly diagnosed on the basis of a Gold Standard surrogate, consisting of the integration of clinical and instrumental methods	
Secondary Objectives:	• Initial assessment of the diagostic sensibility, on a per lesion basis;	

	• Assessment of the technical performance of 64Cu(II)Cl2 PET/CT in terms of target to background contrast; • Assessment of the technical performance of 64Cu(II)Cl2 PET/CT in terms of intra observer diagnostic reproducibility; • Assessment of the technical performance of 64Cu(II)Cl2 PET/CT in terms of inter observer diagnostic reproducibility; • Assessment of optimization of post injection times in which to perform 64Cu(II)Cl2 PET/CT, in terms of per-patient and per lesion diagnostic sensibility, target to background contrast, intra observer diagnostic reproducibility; • Assessment of safety profile of the IMP in particular for the liver toxicity, deriving from the accumulation of the copper 64 in the liver; • Assessment of the kinetic of IMP in the tumour tissue and in the near health tissue.
Methodology:	monocentric, interventional, "open-label", "not first in human", cross-sectional, historical recruitment
Number of patients:	Planned: 50 enrolled: 51 drop-out: 1 analysed: 50
Diagnosis and main criteria for inclusion:	1. age>=50 at the time of enrolment (no upper age limit); 2. documented previous historical diagnosis of primitive prostate carcinoma; 3. subject treated with ADT (orchiectomy, and/or LHRH agonists, and/or androgens antagonists); 4. previous clinical diagnosis of metastatic disease on bone, and/or lung, and/or lymph node due to PCa (with involvement of pelvic region, and/or lumbar lymph node and/or sub phrenic), also documented with the restaging CT 5. recent disease progression (increase of PSA in serial determinations, and/or clinical progression and/or radiological), during ADT with clinical indication to restaging (also radiological) 6. availability of whole body CT examination (with or without contrast medium), performed for restaging during the 20 days before enrolment visit (slice thickness < 5mm) 7. availability of whole body CT examination (with and without contrast medium), performed within the eight months before the enrolment visit (technically comparable with the examination of restaging, particularly with slice thickness < 5mm) or

	at least one of the following imaging test relative to functional metabolic, performed for restaging on BSE clinically indicated, with 20days prior to enrolment visit: MRI(bone), 18F-FCH PET/CT; negative clinical history for other past or in progress neoplastic diseases, with the exception of non-melanoma skin cancers; 8. Karnofski's index >80%; 9. Absence of other co-morbidities (see: exclusion criteria); 10. Complete ability to understand the information reported in the trial informative leaflet for the subject 11. Complete ability to sign the valid informed consent
Test product, dose and mode of administration, batch number:	64Cu(II)Cl2/64-Copper Chloride Single intravenous administration of 64Cu (II) Cl2 with activity equal to: MBq = [20x body weight / 4 MBq] +/- 10%
Reference therapy, dose and mode of administration, batch number:	none
Duration of treatment:	one single dose
Criteria for evaluation: Efficacy:	For the verification of the sensitivity, three PET scans were provided after the administration of 64Cu (II) Cl2 (at 1, 4 and 24 hours). For each scan, a blind double reading was carried out by three independent observers who identified the positive sites of the disease ("positive" sites, according to the ad hoc diagnostic criteria). The correspondence between the diagnosis of positivity by each Observer and the "index lesions" previously identified by the Investigator was verified by the consensus of two external reviewers. A verification of the reproducibility of the result was foreseen by analysis of inter-observer and intra-observer reproducibility. A quantitative assessment of the target / fund captation ratio (T / B) was also performed in order to characterize the technical performance of the examination.
Safety:	Four safety modules were scheduled at 1h, 4h, 24h and 10 days after the administration of the 64Cu (II) Cl2 in order to monitor the patient by checking the vital parameters and the expected blood chemistry values.
SUMMARY - CONCLUSIONS	
EFFICACY RESULTS:	The results of the study regarding efficacy measures demonstrate: - High diagnostic sensitivity on a patient basis (94.7%)

	- High diagnostic sensitivity based on lesion (> 91%) - High intra and inter-observer reproducibility (100% and 90% respectively) - Overlapping diagnostic effectiveness in 1-hour and 4-hours detection - Poor diagnostic efficacy of 24-hour detection both in terms of sensitivity on a patient basis, on a lesion basis and in terms of the T / B ratio
SAFETY RESULTS:	The results of the study regarding safety measures show: - Excellent tolerability and absence of side effects / toxicity of any kind, - There were no deaths or adverse events of any kind. Dosimetry appropriate to the diagnostic applicability: the effective calculated doses are such that there is no toxicity due to the diagnostic administration.
Statistical methods:	Regarding the hypothesis testing related to the endpoint of the primary objective, the sample size was calculated at 50 Subjects. For an exact binomial test with a first type α error equal to 5%, a sample size equal to 50 subjects will be required to guarantee a test power of 80% to reject the null hypothesis that the sensitivity is <80% against the alternative hypothesis that sensitivity is> = 92.5%. At the end of the study, the null hypothesis can be rejected if at least 45 of the 50 patients will be correctly classified. A set of statistical analyzes were performed including: - sensitivity assessment and 95% confidence intervals - Student's parametric t test for paired data and ANOVA tests for repeated measurements - non-parametric tests of Mann-Whitney and Friedmann All multiple comparisons were adjusted with the Bonferroni correction.
CONCLUSION:	In conclusion, the results of the study show that PET with 64Cu (II) Cl2 is a diagnostic method characterized by a positive risk / benefit ratio in patients with metastatic prostate cancer and that can be proposed as a new method of investigation in different diagnostic questions related to prostate cancer as an alternative to current conventional methods (PET with F-choline, total-body TAC, skeletal scintigraphy). The study of the validity of PET with 64Cu (II) Cl2 is justified by Phase III studies to confirm the diagnostic accuracy on populations with different clinical characteristics.
Date of the report:	16.02.2018