SYNOPSIS

Name of Sponsor/Company	Daiichi Sankyo Co., Ltd.
Name of Finished Product	SONAZOID® 16 μL vial for injection
Name of Active Ingredient	perflubutane
Title of Study	DD-723 Phase II Clinical Trial - Dose-response study in patients with suspected prostate cancer -
Investigators	4 investigators
Study Centre(s)	4 centers
Publication (reference)	Uemura H, Sano F, Nomiya A, et al. Usefulness of perflubutane microbubble-enhanced ultrasound in imaging and detection of prostate cancer: phase II multicenter clinical trial. World Journal of Urology, 2013, 31(5): 1123-1128.
Studied Period	9 months (March 2009 -December 2009)
Phase of Development	Phase II
Objectives	Examination of the recommended dose based on the dose-response relationship, by assessing the contrast effect, as well as safety of DD-723 in subjects with suspected prostate cancer.
Methodology	Multicenter, randomized, and single-blind controlled trial: Dose-response study on three doses, parallel group, and blinded assessment by three independent blinded reviewers with respect to images that were randomized the order of assessment.
Number of Patients (planned and analyzed)	Planned: 75 subjects（60 subjects for efficacy assessment, 15 subjects for training and inter-rater reliability confirmation） Treatment: 75 subjects Analyzed: 58 subjects Training and inter-rater reliability confirmation : 15 subjects
Diagnosis and Main Criteria for Inclusion	1) Subjects with suspected prostate cancer 2) Subjects whose most recent PSA level is between 4.0 ng/mL and 20 ng/mL 3) Subjects aged between 20 and 80 years at the time of

	informed consent
Test Product, Dose and Mode of Administration, Batch Number	A single dose of 0.024 μL MB/kg, 0.12 μL MB/kg, or 0.36 μL MB/kg delivered via a forearm vein Lot number: DD723L0S08T01A
Duration of Treatment	Single injection
Reference Therapy, Dose and Mode of Administration, Batch Number	N.A.
Criteria for Evaluation	Rate showed enough imaging effect by blinded reviewers: Results of multiple evaluations by three blinded reviewers were used to assess as the primary endpoint.
Statistical Method	The main target groups for the efficacy analysis was PPS, and the dose-response relationship of the efficacy rate of the overall contrast effect was evaluated in contrast-enhanced ultrasonography in PPS by Cochran-Armitage test using contrast coefficient (-2,1,1).
Summary - Conclusion	The primary endpoint was assessed in the efficacy analysis set, which comprised 58 (low dose group: 20 subjects, intermediate dose group: 20 subjects, high dose group: 18 subjects) of the 75 patients (low dose group: 27 subjects, intermediate dose group: 25 subjects, high dose group: 23 subjects). The efficacy rates in the overall contrast effect were 35.0% (7/20, 95%CI: 14.1 - 55.9) in the low dose group, 95.0% （19/20, 95%CI: 85.4 -100.0） in the intermediate dose group, and 77.8%（14/18, 95%CI:58.6 - 97.0） in the high dose group, respectively. That means that the highest efficacy rate was showed in the intermediate dose of 0.12 μL MB/kg and also it was saturated in the intermediate dose [Cochrane–Armitage test using contrast coefficients (-2, 1, 1): P<0.001]. Analysis of safety revealed no dose-dependence in terms of the incidence of adverse events, and all of the adverse events that occurred were mild.
Date of Report	Sep, 2014