These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert in the country of prescription.

Sponsor / Company: Sanofi **Drug substance(s):** SAR240550 (iniparib)	**Study Identifiers:** NCT00677079 **Study code:** ARD11489
Title of the study: A Phase 2, Single Arm Study of BSI-201 in Patients with BRCA-1 or BRCA-2 Associated Advanced Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer	
Study center(s): 1 study center in US	
Study period: Date first patient enrolled: 17/Jun/2008 Date last patient completed: 29/Dec/2008	
Phase of development: Phase 2	

Objectives: The primary objective was to evaluate the response rate (per the Response Evaluation Criteria in Solid Tumor [RECIST]) to iniparib when administered at 8 mg/kg intravenously twice weekly in patients with breast cancer genes 1- or 2- (BRCA1- or BRCA2-) associated advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer.

The secondary objectives were:

- To evaluate the clinical benefit rate (CBR) (overall response rate [ORR] and stable disease [SD]) of iniparib when administered at 8 mg/kg intravenously twice weekly in patients with BRCA1- or BRCA2-associated advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer.
- To evaluate progression-free survival (PFS) and overall survival in patients receiving iniparib.
- To evaluate response as measured by CA125 level in patients receiving iniparib.
- To evaluate the safety and tolerability of iniparib when administered at 8 mg/kg intravenously twice weekly.

The exploratory objectives were:

- To assess the extent of poly (ADP-ribose) polymerase (PARP) inhibition in peripheral blood mononuclear cells.
- To assess PARP1 gene expression in tumor samples and correlate expression levels to response to iniparib.
- To identify secondary intragenic mutations and correlate with response to iniparib.
- To collect ascites fluid from patients when it was clinically necessary for tumor banking.

Number of patients**:**	Planned: Maximum 35 (Simon's 2-stage design: 1st stage, 12 patients; 2nd stage, 23 patients)
	Treated: 12
Evaluated:	
	Efficacy: 12
	Safety: 12

Diagnosis and criteria for inclusion:

- Female, age 18 or older.
- Histologically or cytologically confirmed advanced epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer (Stage III or IV).
- Patients must have received at least 1 regimen of platinum/taxane therapy.
- Confirmed BRCA1 or BRCA2 mutation.
- One or more measurable lesions, at least 10 mm in longest diameter by spiral computed tomography (CT) scan or 20 mm in longest diameter when measured with conventional techniques (palpation, plain x-ray, CT, or magnetic resonance imaging [MRI]).
- Karnofsky Performance Status ≥70%.
- Estimated life expectancy of at least 16 weeks.

Study treatments

Investigational medicinal product(s): Iniparib (BSI-201, SAR240550)

Dose: Iniparib (8 mg/kg; Days 1 and 4 weekly; 8-week cycle)

Route(s) of administration: Intravenous [IV] infusion (1 hour)

Duration of treatment: Patients were treated for 8-week cycles, with additional cycles as long as they had stable or responding disease (per RECIST criteria) and wished to remain on study.

Duration of observation: All patients had a final follow-up visit within 4 weeks following the last dose of iniparib, after which time they were contacted by study staff every 3 months for the first year and every 6 months thereafter to assess disease status and survival.

Criteria for evaluation: The following safety criteria were evaluated at designated intervals throughout the study and summarized using descriptive statistics and/or listings: adverse events (AEs), physical examination, Karnofsky Performance Status, height, weight, vital signs (blood pressure, respiration rate, pulse, temperature), and electrocardiogram (ECG). Clinical assessment of disease status was performed via radiographic assessment (CT scan or MRI) of disease as baseline (within 28 days of Day 1) and during Week 8 of each cycle and blood CA-125 level at baseline (within 14 days of Day 1), during Week 8 of each cycle, and at final visit (within 4 weeks after the last dose of iniparib). Efficacy data are tabulated or listed. Descriptive statistics are presented.

Statistical methods:

All patients who received at least 1 dose of iniparib were included in the safety analysis.

Demographic and baseline disease characteristics were summarized using descriptive statistics.

Safety: Treatment-emergent adverse events (TEAEs) were defined as AEs that occurred after the first dose of iniparib through 30 days after the last dose. The number and percentage of patients with TEAEs were tabulated by system organ class (SOC) and preferred terms (PT, all and related). All deaths and serious adverse events (SAEs) were listed.

Hematology and biochemistry results were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 3.0, when applicable. The number and percentage of patients with laboratory abnormalities (ie, all grades and Grade 3-4) using the worst grade during the on-treatment period were provided.

Efficacy: Best overall response was listed for each patient.

Summary:

Overall, 12 patients received at least 1 cycle of iniparib at a dose of 8 mg/kg.

All patients had been heavily pretreated, having received a median of 7 prior chemotherapeutic regimens (range, 3 to 14, per clinical review). Only 3 of the 12 patients were considered to have possibly platinum-sensitive disease at the time of enrollment.

The median exposure was 7.5 weeks (range, 4 to 17 weeks). One or more doses were omitted in 5 (41.7%) patients. Dose reductions were not allowed.

All 12 (100%) patients experienced at least 1 TEAE of any grade. The most commonly reported TEAEs of any grade (incidence ≥50.0%) were hypoalbuminemia (100%); hyperglycemia (91.7%); asthenia and decreased hemoglobin (PT: hemoglobin [each 83.3%]); increased activated partial thromboplastin time (PT: activated partial thromboplastin time; 66.7%); constipation, hyperbilirubinemia, increased aspartate aminotransferase (PT: aspartate aminotransferase), increased alkaline phosphatase (PT: blood alkaline phosphatase), and increased international normalized ratio (PT: international normalized ratio [each 58.3%]); and hyponatremia and abdominal pain (each 50.0%).

The most commonly reported treatment-related TEAEs were in the Gastrointestinal Disorders and the General Disorders and Administration Site Conditions SOCs. Treatment-related TEAEs of any grade occurring in ≥10% of patients included asthenia (83.3%), constipation (25.0%), diarrhea (25.0%), nausea (25.0%), abdominal pain (16.7%), and decreased hemoglobin (PT: hemoglobin [16.7%]).

Grade 3 or higher TEAEs were observed in 7 (58.3%) patients. These events included increased alanine aminotransferase (PT: alanine aminotransferase), increased alkaline phosphatase (PT: blood alkaline phosphatase), and increased international normalized ratio (PT: international normalized ratio [each 16.7%]) and malignant pleural effusion, lymphopenia, hyponatremia, hypertension, diarrhea, hyperbilirubinemia, death, increased activated partial thromboplastin time (PT: activated partial thromboplastin time), and increased aspartate aminotransferase (PT: aspartate aminotransferase [each 8.3%]). Two treatment-related Grade 3 or higher TEAEs were reported (diarrhea and hypertension).

Five (41.7%) patients experienced 5 treatment-emergent SAEs (ie, 1 SAE per patient). Four SAEs, which included Grade 2 hematuria, Grade 3 hyperbilirubinemia, Grade 3 malignant pleural effusion, and death due to disease progression, were reported as unrelated to study drug. One SAE of Grade 3 hypertension was reported as related to study drug. No TEAEs led to permanent treatment discontinuation.

Eleven of the 12 patients died. One of the 11 deaths was reported during the treatment period (within 30 days after the last dose of iniparib) as a fatal serious TEAE due to disease progression, assessed by the Investigator as not related to study drug. The remaining 10 deaths occurred after 30 days after the last dose of iniparib; information regarding the relationship to study drug was not available for these deaths.

A Grade 3-4 hematologic laboratory abnormality of lymphopenia was observed in 1 (8.3%) patient. Grade 3-4 liver function abnormalities included elevations in aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin, each in 1 (8.3%) patient, and alkaline phosphatase in 2 (16.7%) patients. Renal function abnormalities were observed in 3 (25.0%) patients.

Among the 12 patients who received study drug, no complete or partial responses were demonstrated. One patient had SD that lasted 2 cycles, and the remaining 11 patients had progressive disease. Therefore, the study was discontinued at Stage 1 of the Simon's 2-stage design due to lack of observed responses; no safety concerns were noted.

Issue date: 19-Jan-2016