SYNOPSIS

Final Clinical Study Report for Study CA187016

TITLE OF STUDY: An Open-Label Randomized, Parallel, Two-Arm Phase II Study Comparing BMS-690514 + Letrozole with Lapatinib + Letrozole in Recurrent or Metastatic Breast Cancer Patients Who Are Hormone Receptor Positive Despite HER2 Status and Who Relapsed While Receiving or After Completing Adjuvant Antiendocrine Therapy.

PURPOSE: Breast carcinoma is the most common malignancy of women worldwide. Agents targeting epidermal growth factor receptor (EGFR) or HER1/ErbB1 and HER2 have been clinically validated for the treatment of solid tumors including breast cancer. However, responses to therapies vary with the expression of growth factor receptor signaling. In spite of all of the advances for early breast cancer especially with the use of antiendocrine therapy, many women still develop tumor relapse. Overall, the median survival of patients with breast cancer who develop recurrent disease while on antiendocrine therapy is only 2 to 3 years. In order to improve the response among patients with hormone-sensitive breast cancer, BMS-690514, a multiple tyrosine kinase inhibitor with targets against EGFR, HER2, HER4, and VEGFR1, 2, and 3, was developed.

The hypothesis was that BMS-690514 at a dose of 200 mg daily with letrozole at standard doses will confer a superior clinical benefit rate (CBR) when compared with lapatinib at a dose of 1500 mg daily with letrozole at standard doses for subjects who have locally recurrent or metastatic hormone receptor positive (HR+) breast cancer.

The BMS-690514 program was terminated due to the lack of superiority of BMS-690514 as compared with erlotinib in non-small cell lung cancer in study CA187017. Hence, the results of study CA187016 are being reported in a synoptic format with only safety data provided.

NUMBER OF SUBJECTS: One hundred and forty subjects were planned, 10 were enrolled, and 4 were randomized and treated.

DISPOSITION, DEMOGRAPHICS AND OTHER PERTINENT BASELINE CHARACTERISTICS: Subject disposition and pretreatment characteristics are presented in the following tables.

Subject Disposition: All Randomized Subjects

	BMS-690514 200 mg + 2.5 mg Letrozole	Lapatinib 1500 mg + 2.5 mg Letrozole	Total
N	1	3	4
Subjects treated, n (%)	1 (100)	3 (100)	4 (100)
Subjects discontinued, n (%)	1 (100)	3 (100)	4 (100)
Reason for discontinuation			
Administrative reason by sponsor, n (%)	-	1 (33)	1 (25)
Disease progression, n (%)	1 (100)	2 (67)	3 (75)

Pretreatment Subject Characteristics: All Treated Subjects

	BMS-690514 200 mg + 2.5 mg Letrozole	Lapatinib 1500 mg + 2.5 mg Letrozole	Total
N	1	3	4
Age, (years)			
Median	78	69	69.5
Min - Max	78 - 78	59 - 70	59 - 78
Race, n (%)			
White	1 (100)	2 (67)	3 (75)
Other	0	1 (33)	1 (25)
Ethinicity, n (%)			
Hispanic/ Latino	0	1 (33)	1 (25)
Not Hispanic/Latino	1 (100)	0	1 (25)
Not reported	0	2 (67)	2 (50)

Min: Minimum, Max: Maximum

SUMMARY OF SAFETY RESULTS: Adverse events (AEs) reported during the study are provided in the table below.

Overall Safety Summary: All Treated Subjects

	BMS-690514 200 mg + 2.5 mg Letrozole	Lapatinib 1500 mg + 2.5 mg Letrozole	Total
N	1	3	4
Deaths, n (%)	0	0	0
At least one AE, n (%)			
Any grade	1 (100)	3 (100)	4 (100)
Grade 3	1 (100)	0	1 (25)
Grade 4	0	0	0
At least one SAE, n (%)			
Any grade	1 (100)	0	1 (25)
Grade 3	1 (100)	0	1 (25)
Grade 4	0	0	0
AE leading to discontinuation, n (%)			
Any grade	0	0	0

AE: Adverse event, SAE: Serious adverse event

There were no deaths during the study. The one subject treated with BMS-690514 experienced 4 serious adverse events (SAEs): overdose (Grade 2), dehydration (Grade 3), hyponatremia (Grade 1), and renal failure (Grade 1). Of these SAEs, only dehydration was considered by the investigator to be related to BMS-690514. No SAEs were reported in subjects treated with lapatinib. No AEs leading to discontinuation were reported in the study subjects. All study subjects experienced at least 1 AE during the study. In the one subject treated with BMS-690514, 5 AEs were considered by the investigator to be related to BMS-690514. No clinically significant laboratory abnormalities were reported in the study subjects.

Disease progression was observed in the one subject treated with BMS-690514. In the lapatinib-treated subjects, disease progression was noted in 2 subjects, while 1 subject had stable disease.

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