2. STUDY SYNOPSIS

Name of Sponsor/Company: Biogen Idec Inc.	**Individual Study Table Referring to Part <> of the Dossier** **Volume:** **Page:**	***(For National Authority Use only)***
Name of Finished Product: BIIB021	**Name of Active Ingredient:** BIIB021	**Study Indication:** Advanced metastatic breast cancer

Title of Study:

Phase IIa, Open-Label, Randomized, Non-Comparative Study of BIIB021 in Combination with Exemestane in Women with Hormone-Receptor Positive, Advanced Metastatic Breast Cancer Who Have Progressed on a Non-Steroidal Aromatase Inhibitor

Study Period: Date of First Treatment: 15 December 2009 Date of Last Treatment: 29 June 2011 End of Study Date: 31 October 2011 Date of Data Cut-Off: 19 July 2011	**Phase of Development:** Phase 2a

Study Objectives:

Primary objective:

The primary objective of this study was to assess the efficacy of 2 dosing regimens of BIIB021 in combination with exemestane in women whose hormone-receptor-positive (HR+) breast cancer had progressed following treatment with a non-steroidal aromatase inhibitor (AI).

Secondary objective:

The secondary objective of this study was to evaluate the safety and tolerability of BIIB021 in combination with exemestane in this study population.

Exploratory Objectives:

- To evaluate the pharmacokinetics of BIIB021 when combined with exemestane;
- To evaluate the effect of BIIB021 on pharmacodynamic biomarkers when combined with exemestane;
- To evaluate Quality of Life (QoL) for subjects receiving BIIB021 in combination with exemestane.

Overall Study Design (see the study protocol for details):

BIIB021 is a fully synthetic, orally available heat shock protein 90 (Hsp90) inhibitor. BIIB021 selectively and potently inhibits the molecular chaperone Hsp90, thereby inhibiting the proper assembly of multiple oncogenic proteins involved in tumor growth and survival.

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This Phase 2a randomized, open-label, noncomparative, multicenter study was designed to assess the efficacy and safety of 2 dosing regimens of BIIB021 in combination with exemestane. The definition of study treatment in this protocol was the investigational study drug, BIIB021 (formerly called CNF2024) in combination with exemestane.

Approximately 80 subjects with HR+ breast cancer who had progressed on a non-steroidal AI were to be stratified based on AI sensitivity or AI resistance. Subjects who were "AI sensitive" were defined as those who had a complete response (CR), partial response (PR), or stable disease (SD; SD was maintained for at least 6 months). All other subjects, including all those who received the non-steroidal AI as adjuvant therapy, were defined as "AI resistant." Within each stratum, subjects were randomized (1:1) to 100 mg BIIB021 twice daily (BID) (n = 40 subjects, BID regimen) or 450 mg BIIB021 three times weekly (TIW) (n = 40 subjects, TIW regimen) for continuous 28-day cycles. All subjects were to also take 25 mg exemestane once daily (QD).

Subjects were to be evaluated for safety, tolerability, efficacy, BIIB021 pharmacokinetics, pharmacodynamic biomarker data, and QoL. Subjects received study treatment until unacceptable toxicity, disease progression, death, or withdrawal of consent.

The study began with a 28-day assessment of dose-limiting toxicity (DLT) in up to 12 subjects randomized to the BID or TIW BIIB021 dosing regimen (up to 6 subjects per dosing regimen). Enrollment of the remaining subjects was to proceed according to the results of the DLT Assessment Period.

Subjects in the DLT Assessment Period who discontinued study treatment due to a non-DLT were replaced. Subjects who discontinued study treatment were not replaced.

DLT Assessment Period

Dose-limiting toxicities were assessed for up to 12 subjects randomized to the BID or TIW BIIB021 dosing regimens (up to 6 subjects per dosing regimen) in the beginning of the study. If ≤1 DLT was reported for 6 subjects during the first 28-day cycle, that BIIB021 dosing regimen continued to enroll. If ≥2 DLTs were reported during the first 28-day cycle, that dosing regimen did not continue to enroll.

The 4 possible outcomes of the 28-day DLT Assessment Period were as follows:

- If ≤1 DLT was reported for 6 subjects at 100 mg BID and ≤1 DLT was reported for 6 subjects at 450 mg TIW, 68 subjects could be randomized to either dosing regimen (n = 34 per regimen);
- If ≤1 DLT was reported for 6 subjects at 100 mg BID and ≥2 DLTs were reported for 450 mg TIW, 34 subjects could be enrolled into the BID dosing regimen only;
- If ≥2 DLTs were reported for 100 mg BID and ≤1 DLT was reported for 6 subjects at 450 mg TIW, 34 subjects could be enrolled into the TIW dosing regimen only;

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- If ≥2 DLTs were reported for 100 mg BID and ≥2 DLTs were reported for 450 mg TIW, the study would be terminated.

The DLT Assessment Period was reviewed and discussed during routine teleconferences with Biogen Idec and those Investigators who had enrolled subjects into the DLT Assessment Period. The outcome of these teleconference meetings determined which dosing regimens would continue to enroll subjects.

DLTs were defined as any of the following adverse events (AEs) if they were determined to be BIIB021 related:

- Any non-hematological toxicity Grade ≥3 according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), Version 4.0, with the following exceptions:
  - Nausea/vomiting and diarrhea were to be considered DLTs only if they reached Grade ≥3 for 3 days despite supportive care (ie, use of serotonin type 3 ($5HT_3$) antagonists such as ondansetron or palonosetron for nausea/vomiting);
  - Isolated laboratory abnormalities Grade ≥3 without clinical sequelae were not to be considered a DLT if they were not clinically significant in the opinion of the Investigator.
- Grade 4 neutrophil count decrease lasting >7 days;
- Febrile neutropenia (defined as an absolute neutrophil count [ANC] $<1 \times 10^3$ cells/mm^3 and fever ≥38.5°C) or documented infection Grade ≥3 with ANC $\leq 1 \times 10^3$ cells/mm^3;
- Grade 4 platelet count decrease;
- Delay >14 days for resumption of treatment due to toxicity.

Number of Subjects (Planned and Analyzed):

Up to 12 subjects were to be enrolled in the DLT Assessment Period (6 subjects per dosing regimen) and up to 68 subjects were to be enrolled if both regimens were deemed to be tolerable (34 subjects per dosing regimen), for a possible total of 80 subjects (40 subjects per dosing regimen).

A total of 53 subjects were enrolled in the study, 26 subjects in the BIIB021 100 mg BID regimen and 27 subjects in the BIIB021 450 mg TIW regimen. Enrollment was suspended at the decision of the Sponsor.

Efficacy and pharmacodynamics were not analyzed. All 53 subjects were analyzed for safety.

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Study Population:

Inclusion Criteria:

To be eligible to participate in this study, candidates must have met the following eligibility criteria at the time of enrollment or at the time point specified in the individual eligibility criterion listed:

1. Ability to understand the purpose and risks of the study and provide signed and dated informed consent and authorization to use protected health information in accordance with national and local subject privacy regulations;
2. Age ≥18 years at the time of informed consent or the age of consent in accordance with national regulations, whichever was higher;
3. Must have had histologically or cytologically confirmed estrogen receptor-positive or progesterone receptor-positive, incurable, locally advanced, or metastatic breast cancer
    - If available, pre-existing formalin-fixed and paraffin-embedded tumor tissue must have been submitted to Biogen Idec before study completion, but not necessarily prior to enrollment;
4. Must have had disease progression during treatment with a non-steroidal AI for locally advanced or metastatic disease, or relapsed during treatment or within 12 months of discontinuation of treatment in the adjuvant setting;
5. Must have been a postmenopausal female, defined as ≥60 years old, OR age ≥45 years with amenorrhea for ≥12 months with an intact uterus AND follicle stimulating hormone levels within postmenopausal range, OR prior bilateral oophorectomy;
6. Expected survival time of at least 3 months in the opinion of the Investigator;
7. Must have had measurable or evaluable disease
    - Measurable disease was defined as ≥1 lesion with a diameter of ≥10 mm (lesion must have been measurable in ≥1 dimension, with the longest diameter to be recorded);
    - Evaluable disease was defined as bone lesions evaluable by plain X-ray, computerized tomography (CT) scan, or magnetic resonance imaging (MRI). Lesions identified only by radionuclide bone scan were not allowed;
    - The target lesion(s) must not have been previously irradiated (newly arising lesions in previously irradiated areas were acceptable);
    - The following were not considered measurable or evaluable disease: leptomeningeal disease, ascites, pleural/pericardial effusion, inflammatory breast cancer, lymphangitis cutis/pulmonitis, cystic lesions, and abdominal masses that could not be reproducibly measured and followed by CT or MRI;

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8. One prior chemotherapy regimen for advanced metastatic breast cancer was allowed. Must have been at least 2 weeks since final treatment, and the subject must have recovered to baseline or Grade ≤1 toxicity from prior treatment
    - Prior chemotherapy in the adjuvant and/or neoadjuvant setting was allowed;
9. Prior radiotherapy was allowed. Must have been at least 2 weeks since treatment and the subject must have recovered to baseline or Grade ≤1 toxicity from prior treatment. Exceptions were as follows:
    - Strontium-90 (or other radiopharmaceutical) within previous 3 months was not allowed;
    - Sites of measurable disease must have been outside the radiotherapy port;
10. If the subject was taking bisphosphonates for bone metastases, bisphosphonate therapy must have been established for at least 3 months. Concurrent initiation of bisphosphonates was allowed if the subject had soft tissue or visceral metastases as the measurable or evaluable target lesion;
11. Must have been able to swallow and retain oral medication;
12. Eastern Cooperative Oncology Group (ECOG) performance status of ≤2;
13. Required laboratory values:
    - ANC ≥1 × 10^3 cells/mm^3, platelet count ≥75 × 10^3 cells/mm^3, hemoglobin ≥90 g/L (≥9 g/dL);
    - Bilirubin ≤3 × upper limit of normal (ULN) (unless due to Gilbert's syndrome), alanine aminotransferase (ALT), or aspartate aminotransferase (AST) ≤5 × ULN;
    - Serum creatinine ≤177 μmol/L (≤2.0 mg/dL);
    - International Normalized Ratio (INR) ≤1.5, except in subjects who were currently on anti-coagulation therapy and their most recent thrombotic event occurred >3 months prior to Day 1, then INR ≤3.5;
    - Glucose ≥3.3 mmol/L (≥60 mg/dL), sodium ≥130 mmol/L, calcium ≥2.0 mmol/L (≥8 mg/dL);
    - Plasma cortisol and adrenocorticotropic hormone (ACTH) levels that were not suggestive of adrenal insufficiency unless on replacement therapy for known adrenal insufficiency;
14. Electrocardiogram (ECG) with QTc of ≤470 msec and no clinically significant findings.

Exclusion Criteria:

Candidates were to be excluded from study entry if any of the following exclusion criteria existed at the time of enrollment or at the time point specified in the individual criterion listed:

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1. HER2 overexpressing tumor (immunohistochemistry [IHC] 3^+ or fluorescence in situ hybridization [FISH]$^+$);
2. Life-threatening metastatic visceral disease;
3. History of central nervous system (CNS) metastasis;
4. History of prior malignancies within the past 5 years with the exception of curatively treated basal or squamous cell carcinomas of the skin or carcinoma in situ of the cervix;
5. Previous treatment with exemestane;
6. Previous treatment with an Hsp90 inhibitor;
7. Other concurrent hormonal therapy except for the following: steroids for adrenal failure, hormones for non-disease-related conditions (ie, insulin for diabetes or Synthroid® for hypothyroidism), intermittent dexamethasone as an antiemetic;
8. Use of medications that may have affected the metabolism of BIIB021 within 14 days of the first dose of study treatment;

- Use of medications that may have affected the metabolism of exemestane, such as potent inducers of cytochrome p450 3A4 (CYP3A4), within 14 days of the first dose of the study treatment;
- Use of proton pump inhibitors within 7 days of the first dose of the study treatment. Use of H_2 antagonists, except cimetidine, was allowed;
- Active bacterial or viral infection requiring concurrent treatment;
- Known history of, or positive test result for, hepatitis B or C;
- Known history of, or positive test result for, human immunodeficiency virus (HIV);
- Uncontrolled, severe medical illness, which in the opinion of the Investigator and/or Sponsor could have compromised the protocol objectives;
- History of gastrectomy or major surgery to the small intestine;
- Chronic diarrhea (excess of 2 to 3 stools/day above normal frequency);
- Major surgery within 28 days of the first study treatment;
- Conditions that may have predisposed subjects to seizures:
- History of seizure, previous significant head trauma (eg, associated with loss of consciousness for more than 5 minutes), abrupt discontinuation of benzodiazepines, or use of potentially epileptogenic medications;
- Drug or alcohol abuse.

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Study Treatment, Dose, Mode of Administration, Batch Number(s):

100 mg BIIB021 BID Plus Exemestane:

Subjects randomized to this dosing regimen were to take 100 mg BIIB021 orally BID and 25 mg exemestane orally QD for continuous 28-day cycles. On Day 1 of Cycles 1 and 2, subjects were to take their first daily dose of BIIB021 while in the clinic. Exemestane and other doses of BIIB021 could be taken either at home or in the clinic.

450 mg BIIB021 TIW Plus Exemestane:

Subjects randomized to this dosing regimen were to take 450 mg BIIB021 orally TIW and exemestane orally QD for continuous 28-day cycles.

For Cycle 1, subjects were to take BIIB021 on Days 1, 3, 5, 8, 10, 12, 15, 17, 19, 22, 24, and 26. For Cycles 2 and beyond, TIW dosing days for BIIB021 could be adjusted. Subjects were to take BIIB021 3 times per week, with at least 1 day, but not more than 2 days, between doses (eg, a Monday-Wednesday-Friday or Tuesday-Thursday-Saturday dosing schedule).

On Day 1 of Cycles 1 and 2, subjects were to take BIIB021 while in the clinic. Exemestane and other doses of BIIB021 could be taken either at home or in the clinic.

BIIB021 lot numbers by subject are provided in Listing 16.2.5.1.1. Exemestane was purchased from commercial sources.

Duration of Treatment and Follow-Up:

The study period consisted of:

- Screening – within 14 days prior to the first dose of study treatment;
- Treatment – consisted of continuous 28-day cycles. All subjects continued to receive study treatment until unacceptable toxicity, disease progression, death, or withdrawal of consent;
- Final study visit – after discontinuation of study treatment. For the purposes of reporting, subjects who completed the final study visit were considered to have completed the study;
- Follow-up – the AE monitoring was to continue for 30 days after the last dose of study treatment or until all BIIB021-related toxicities had resolved, stabilized, or returned to baseline.

Criteria for Evaluation:

Efficacy:

No efficacy endpoints were summarized or evaluated.

Concentration Measurements:

The pharmacokinetics (PK) of BIIB021 and its metabolite(s) were to be analyzed for all subjects at prespecified time points to address the following:

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- To conduct a population PK analysis of BIIB021 and its metabolite(s) and to estimate population PK parameters;
- To evaluate the influence of population covariates on the PK of BIIB021;
- To assess whether BIIB021 drug accumulation occurs;
- If possible, to determine BIIB021 PK/pharmacodynamic correlations for toxicity and biomarker response.

Pharmacodynamics:

CYP2C19 polymorphisms were to be analyzed.

To assess the pharmacodynamic properties of BIIB021, whole blood and serum were to be collected to monitor the level of selected candidate biomarkers that may have reflected biologic activity of BIIB021. Additional analyses of candidate protein markers could be pursued.

- Peripheral blood mononucleatr cells (PBMC) biomarkers:
  - Hsp70 levels
  - MSD onco-signaling panel
- Serum Biomarkers:
  - HER2-ECD levels
- Breast cancer markers:
  - CEA
  - CA125
  - CA 27.29 or CA 15-3 per site practice
- CTC levels.

In addition, tumor tissue could have been analyzed for deoxyribonucleic acid (DNA), ribonucleic acid (RNA), or protein expression in an attempt to identify genetic signatures or mutations that may have correlated with a clinical response variable. Subjects who had consented to donate a tissue sample from a previously obtained biopsy/resection and agreed to genetic testing were required to sign and date a separate informed consent form (ICF).

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Quality of Life:

The QoL was to be assessed using the Functional Assessment of Cancer Therapy-Endocrine Subscale (FACT-ES) questionnaire. This is a patient-reported questionnaire that comprises the Functional Assessment of Cancer Therapy-Breast (FACT-B) questionnaire, and an endocrine symptom subscale. The FACT-B measures QoL in breast cancer. The ES for the FACT-B was developed and validated to assess benefits and side effects specific to women using hormonal treatments for breast cancer.

Safety:

Safety endpoints included: Incidence of AEs and serious adverse events (SAEs), concomitant therapy and procedure recording, physical examinations and vital sign measurements, weight, hematology parameters, blood chemistry parameters, creatine phosphokinase, urinalysis parameters, and ECG changes.

Statistical Methods:

Analysis Populations:

The Safety Population included all subjects who took at least 1 dose of BIIB021 or exemestane. All analyses of safety variables were performed for all subjects in the Safety Population.

The PK Analysis Population was to include all subjects who took any part of a dose of BIIB021 and had at least 1 sample collected for PK analysis.

General Methodology:

Descriptive statistics for continuous variables were tabulated and included the number of subjects, mean, standard deviation, median, minimum, and maximum. Descriptive statistics of categorical variables were tabulated by the number of subjects and percentages. Missing data were not imputed.

Adverse Events:

All AEs were graded using the adult NCI-CTCAE, Version 4.0. Adverse event terms were coded using the most current version of the Medical Dictionary for Regulatory Activities (MedDRA, Version 13.1).

The incidence of all AEs was summarized by System Organ Class (SOC) and Preferred Term and tabulated by dosing regimen for each dosing cycle and over the entire study period.

Subject listings for AEs, SAEs, AEs leading to discontinuation, and subject deaths are provided.

Laboratory Evaluations:

Hematology, blood chemistry, and urinalysis variables were graded on a scale of 1 to 5 according to the NCI-CTCAE, Version 4.0.

All laboratory results are provided in separate listings by laboratory test category. An abnormal laboratory result listing is provided.

Other Safety Assessments:

Subject listings of all vital sign measurements and ECG results are provided.

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Results:

Subject Disposition:

Subject disposition is provided in Listing 16.2.1.1. Study treatment administration by subject is provided in Listing 16.2.5.1 and detailed BIIB021 dosing information is provided in Listing 16.2.5.2.

A total of 53 subjects were enrolled in the study, 26 subjects in the BIIB021 100 mg BID regimen and 27 subjects in the BIIB021 450 mg TIW regimen.

Six subjects were continuing on treatment at the data cutoff, 2 subjects in the BIIB021 100 mg BID regimen and 4 subjects in the BIIB021 450 mg TIW regimen.

Forty-one subjects discontinued study treatment due to disease progression, 3 subjects due to withdrawal of consent, 2 subjects due to AEs, and 1 subject for "other" reasons ("patient refused to take IP due to AEs").

All 53 enrolled subjects were included in the Safety Population and analyzed for safety.

Demographics and Baseline Characteristics:

A summary of subject demographics and baseline characteristics is provided in Table 14.1.2. Concomitant medication use by subject is provided in Listing 16.2.9.2.

- All subjects were female;
- The mean (±standard deviation) age was 61.3 ± 9.90 years in the BIIB021 100 mg BID regimen (range: 41.0 to 84.0 years of age) and 62.7 ± 8.63 years in the BIIB021 450 mg TIW regimen (range: 42.0 to 79.0 years of age);
- Only 2 subjects were non-White, 1 subject was South African and 1 subject was Asian. Both non-White subjects were in the BIIB021 100 mg BID regimen.

Efficacy:

Not applicable.

Pharmacokinetics:

Not applicable.

Pharmacodynamics:

Not applicable.

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Safety:

Adverse events by SOC and Preferred Term are summarized in Table 14.3.1 and listed by subject in Listing 16.2.7.1. Serious AEs are presented in Table 14.3.2 and listed by subject in Listing 16.2.7.2. A by-subject listing of AEs leading to discontinuation of study treatment is provided in Listing 16.2.7.3. A listing of deaths is provided in Listing 16.2.7.4. Laboratory results are listed by subject in Listing 16.2.8.1 (hematology), Listing 16.2.8.2 (chemistry), Listing 16.2.8.3 (urinalysis), and Listing 16.2.8.4 (special chemistry, serology, and coagulation). Abnormal laboratory results are provided in Listing 16.2.8.5. Electrocardiogram results by subject are provided in Listing 16.2.9.1 and vital signs are provided in Listing 16.2.9.3.

In the BIIB021 100 mg BID group, 22 subjects (84.6%) experienced 1 or more AE and in the BIIB021 450 mg TIW regimen, 25 subjects (92.6%) experienced 1 or more AE. Adverse events reported by ≥10% of subjects in either dosing regimen are provided in Table 1.

Table 1 Summary of Adverse Events Reported by ≥10% of Subjects in Either Treatment Regimen (Safety Population)

System Organ Class Preferred Term[c]	Number of Subjects (%)[a,b] BIIB021 100 mg BID (N=26)	 BIIB021 450 mg TIW (N=27)
Subjects reporting at least 1 AE	22 (84.6)	25 (92.6)
Blood and Lymphatic System Disorders	1 (3.8)	4 (14.8)
Anaemia	1 (3.8)	3 (11.1)
Gastrointestinal Disorders	16 (61.5)	24 (88.9)
Abdominal pain	4 (15.4)	3 (11.1)
Abdominal pain upper	1 (3.8)	4 (14.8)
Constipation	0	4 (14.8)
Diarrhoea	6 (23.1)	10 (37.0)
Dyspepsia	2 (7.7)	3 (11.1)
Nausea	14 (53.8)	23 (85.2)
Vomiting	5 (19.2)	13 (48.1)
General Disorders and Administration Site Conitions	9 (34.6)	12 (44.4)
Fatigue	7 (26.9)	8 (29.6)
Infections and Infestations	3 (11.5)	10 (37.0)
Upper respiratory tract infection	0	3 (11.1)

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Table 1 Summary of Adverse Events Reported by ≥10% of Subjects in Either Treatment Regimen (Safety Population), Continued

System Organ Class Preferred Term[c]	Number of Subjects (%)[a,b] BIIB021 100 mg BID (N=26)	 BIIB021 450 mg TIW (N=27)
Metabolism and Nutrition Disorders	2 (7.7)	4 (14.8)
Decreased appetite	2 (7.7)	4 (14.8)
Musculoskeletal and Connective Tissue Disorders	9 (34.6)	13 (48.1)
Arthralgia	3 (11.5)	5 (18.5)
Back pain	4 (15.4)	5 (18.5)
Pain in extremity	3 (11.5)	0
Nervous System Disorders	12 (46.2)	20 (74.1)
Dizziness	8 (30.8)	15 (55.6)
Headache	5 (19.2)	7 (25.9)
Memory impairment	1 (3.8)	3 (11.1)
Psychiatric Disorders	7 (26.9)	8 (29.6)
Insomnia	5 (19.2)	7 (25.9)
Respiratory, Thoracic and Mediastinal Disorders	6 (23.1)	10 (37.0)
Dyspnoea	4 (15.4)	5 (18.5)
Skin and Subcutaneous Tissue Disorders	10 (38.5)	9 (33.3)
Hyperhidrosis	3 (11.5)	5 (18.5)
Vascular Disorders	11 (42.3)	13 (48.1)
Hot flush	11 (42.3)	11 (40.7)

[a] Percentages are based on the number of subjects in the Safety Population within each treatment regimen.
[b] Only AEs that occurred after the administration of the first study treatment (TEAEs) were included in this table.
[c] Subjects were counted only once within each SOC and each Preferred Term.
Abbreviations: AE = adverse event; SOC = System Organ Class.
Source: Table 14.3.1.

The 5 most frequently reported AEs by preferred term were: nausea, reported by 14 subjects (53.8%) in the BIIB021 100 mg BID regimen and 23 subjects (85.2%) in the BIIB021 450 mg TIW regimen; dizziness, reported by 8 subjects (30.8%) in the BIIB021 100 mg BID regimen and 15 subjects (55.6%) in the BIIB021 450 mg TIW regimen; hot flush, reported by 11 subjects (42.3%) in the BIIB021 100 mg BID regimen and 11 subjects (40.7%) in the BIIB021 450 mg TIW regimen; vomiting, reported by 5 subjects (19.2%) in the BIIB021 100 mg BID regimen and 13 subjects (48.1%) in the BIIB021 450 mg

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TIW regimen; and diarrhea, reported by 6 subjects (23.1%) in the BIIB021 100 mg BID regimen and 10 subjects (37.0%) in the BIIB021 450 mg TIW regimen.

One subjet died within 30 days of discontinuing study drug:

- [redacted]
  The death was assessed not to be related to an AE and not related to study drug.

One subject (3.8%) in the BIIB021 100 mg BID regimen reported 1 SAE and 6 subjects (22.2%) in the BIIB021 450 mg TIW regimen reported 7 SAEs within 7 days of discontinuing study treatment:

- [redacted]

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One subject discontinued study treatment due to a non-serious AE:

- [redacted]

Conclusion(s):

Both the BIIB021 100 mg BID regimen and the BIIB021 450 mg TIW regimen were well tolerated in combination with exemestane (25 mg daily) in this patient population.

Publication(s) Based on the Study:

None.

Date of Report:

12 October 2011