2.0 Synopsis

<table>
<tr><td>AbbVie Inc.</td><td rowspan="3">Individual Study Table Referring to Part of Dossier:
Volume:

Page:</td><td rowspan="3">(For National Authority Use Only)</td></tr>
<tr><td>Name of Study Drug:
Navitoclax (ABT-263)</td></tr>
<tr><td>Name of Active Ingredient:
Navitoclax</td></tr>
<tr><td colspan="3">Title of Study:
An Extension Study of Navitoclax (ABT-263) in Subjects with Chronic Lymphocytic Leukemia (CLL)</td></tr>
<tr><td colspan="3">Coordinating Investigator:
Thomas Kipps, MD, PhD, University of California, San Diego, Moores Cancer Center.</td></tr>
<tr><td colspan="3">Study Sites:
15 sites in Australia, Israel, Poland, Ukraine, and the United States</td></tr>
<tr><td colspan="3">Publications:
None.</td></tr>
<tr><td colspan="2">Studied Period (Years):
First Subject First Visit: 18 June 2012
Last Subject Last Visit: 02 July 2013</td><td>Phase of Development: 2</td></tr>
<tr><td colspan="3">Objective:
The primary objective of this extension study was to continue evaluating the safety of navitoclax.</td></tr>
<tr><td colspan="3">Methodology:
This was an open-label, extension study to provide navitoclax treatment for subjects with CLL who had previously received navitoclax treatment in Arm C of Study ABT4710n and who may have derived treatment benefit as assessed by the investigator. The study enrolled subjects who had received navitoclax in Arm C of Study ABT4710n and had not discontinued for any reason prior to closure of Study ABT4710n.
If navitoclax treatment had been delayed or interrupted for ≥ 7 days prior to enrollment in the current study, a 7- to 14-day lead-in dose titration period was implemented prior to restarting the full dose of navitoclax the subject had been receiving in Study ABT4710n. If navitoclax treatment had not been interrupted or was delayed for < 7 days, the subject did not need to complete lead-in dosing and could continue with their defined dose. The defined dose was the last dose the subject received upon completion of Arm C in Study ABT4710n. Dose escalation could only occur upon consultation with the AbbVie Medical Monitor. No subject dose exceeded 250 mg.
This extension study continued to evaluate the safety of navitoclax until the subject experienced disease progression, experienced an adverse event (AE) that led to treatment discontinuation, or the subject chose another treatment regimen or withdrew consent. All subjects were to be discontinued from the study on or by 30 June 2013.</td></tr>
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Number of Subjects (Planned and Analyzed):

Approximately 40 subjects from Arm C of Study ABT4710n were planned for enrollment; 17 subjects actually enrolled.

Diagnosis and Main Criteria for Inclusion:

Each subject had been dosing in Arm C of the ABT4710n study, had not discontinued for any reason prior to study closure, and the investigator believed that continued treatment with navitoclax was in the best interest of the subject. Each subject met predefined hematology, coagulation, and chemistry laboratory criteria. Women of childbearing potential and men agreed to use adequate contraception prior to study entry, for the duration of study participation, and up to 90 days following completion of therapy. A subject was not eligible for study participation if he/she had discontinued navitoclax administration in Arm C of the ABT4710n study for reasons of disease progression, AE toxicity, withdrawal of consent, or principal investigator decision prior to study completion. Subjects who were pregnant or lactating or had any medical condition which, in the opinion of the investigator, placed the subject at an unacceptably high risk for toxicities were not eligible for study participation.

Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number:

Study Drug	Trademark	Formulation	Route of Administration	Manufacturer
Navitoclax	N/A	Tablets (25 mg)	Oral	AbbVie (Bulk Lot Numbers: 10-005254 11-003916)
Navitoclax	N/A	Tablets (100 mg)	Oral	AbbVie (Bulk Lot Numbers: 11-000822 11-003917)

N/A = not applicable.

Subjects self-administered navitoclax orally once daily. Each dose was to be taken with approximately 240 mL of water. All subjects were to self-administer navitoclax within 30 minutes after the completion of breakfast.

Duration of Treatment:

A subject could continue receiving navitoclax until the subject experienced disease progression, experienced an AE that led to treatment discontinuation, or the subject chose another treatment regimen or withdrew consent. All subjects were to be discontinued from the study on or by 30 June 2013.

Criteria for Evaluation

Efficacy:

Efficacy was not assessed in this study.

Safety:

The following safety evaluations were performed during the study: AE monitoring, vital signs, physical examination, platelet counts, and laboratory assessments.

Statistical Methods

The number and percentage of subjects having treatment-emergent AEs were tabulated by Medical Dictionary for Regulatory Activities system organ class and preferred term. The tabulations were also provided with further breakdowns by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v 4.0 toxicity grade and relationship to study drug. Serious adverse events (SAEs), events leading to discontinuation of treatment, and events leading to death were summarized. For the study as a whole, AEs were evaluated and summarized.

Laboratory test results and vital signs were summarized as appropriate. The baseline value (first value obtained in this study) was included in the statistical analysis and changes from baseline were addressed. Where applicable, clinical laboratory test determinations were categorized according to NCI CTCAE (Version 4.0) grades, and shifts from baseline NCI CTCAE grades to maximum and final postbaseline grades for each treatment group were assessed. Vital signs values were evaluated for possible clinical significance using criteria developed at AbbVie.

Summary/Conclusions

All 17 enrolled subjects were exposed to navitoclax during this study; the mean ± standard deviation length of exposure was 473.9 ± 204.24 days (median of 512 days; range of 126 to 730 days).

Of the 17 subjects who enrolled in the study, 15 (88.2%) experienced at least 1 AE; the most frequently reported AEs (in ≥ 10% of subjects) were thrombocytopenia (23.5%), and abdominal pain, diarrhea, hyperbilirubinemia, and bronchitis (11.8% each). Nine (52.9%) subjects experienced at least 1 related AE; the most frequently reported related AEs were thrombocytopenia (23.5%) and hyperbilirubinemia (11.8%). Six (35.3%) subjects experienced severe (NCI CTCAE Grade 3 or greater) AEs, the most common of which was thrombocytopenia (11.8%). Four (23.5%) subjects experienced Grade 3 or greater AEs considered by the investigator to have a reasonable possibility of being related to navitoclax; thrombocytopenia in 2 subjects, and hepatic steatosis, diabetes mellitus, metabolic syndrome, and colon neoplasm in 1 subject each.

There were no deaths reported during the study.

Five (29.4%) subjects reported a total of 11 SAEs. Of the 11 SAEs reported, only 1 (colon neoplasm) was considered by the investigator as having a reasonable possibility of being related to navitoclax. Eight SAEs reported by 4 subjects were severe (NCI CTCAE Grade 3 or greater); abdominal pain, fecal incontinence, large intestine perforation, femoral neck fracture, colon neoplasm, malignant neoplasm progression, quadriparesis, and urinary incontinence.

Four (23.5%) subjects experienced a total of 7 AEs that led to discontinuation of study drug; fecal incontinence, malignant neoplasm progression, quadriparesis, and urinary incontinence were all reported in 1 subject, and thrombocytopenia, colon neoplasm, and non-small cell lung cancer were reported in 1 subject each. No treatment-emergent AEs led to a dose reduction of navitoclax. One subject experienced an AE (femoral neck fracture) that led to interruption of navitoclax dosing.

The most notable change from Baseline hematology values was a decrease in platelet count values. Increases in mean alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and lactate dehydrogenase were noted; however, for all of these parameters, results were variable and median values either decreased from Baseline or increased to a lesser magnitude than the mean values. None of the mean changes in vital sign parameters from Baseline to the Final Visit were clinically meaningful.

Conclusions:

In this study in subjects with CLL who had completed Arm C of Study ABT4710n, navitoclax was dosed at 150 mg/day. A majority of subjects continued to tolerate navitoclax treatment and completed the study. The most frequently reported AEs were usually associated with thrombocytopenia and gastrointestinal events; thrombocytopenia and diarrhea are known side effects of navitoclax. No new safety signals were identified.