FINAL SYNOPTIC CLINICAL STUDY REPORT

Study Title:	An Open Label, Roll Over Study to Provide Idelalisib to Subjects Previously Treated with the Investigational PI3Kδ Inhibitor, GS-9820
Name of Test Drug:	Idelalisib (Zydelig®)
Dose and Formulation:	150-mg tablets twice daily 100-mg tablets for subjects requiring dose reduction
Indication:	Lymphoid Malignancies
Sponsor:	Gilead Sciences, Inc. 199 East Blaine Street Seattle, WA 98102 USA Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 USA
Study No.:	GS-US-313-2120
Phase of Development:	Phase 4
IND No.: **EudraCT No.:**	Not Applicable 2015-005766-39
ClinicalTrials.gov Identifier:	NCT02739360
Study Start Date:	04 May 2016 (First Subject Screened)
Study End Date:	28 December 2017 (Last Subject Last Observation)
Principal or Coordinating Investigator:	Name: Arnon Kater, MD, PhD Affiliation: PPD
Gilead Responsible Medical Monitor:	Name: Pankaj Bhargava, MD Telephone: PPD Fax: PPD
Report Date:	05 June 2018

CONFIDENTIAL AND PROPRIETARY INFORMATION

This study was conducted in accordance with the guidelines of Good Clinical Practice, including archiving of essential documents.

STUDY SYNOPSIS
Study GS-US-313-2120

Gilead Sciences, Inc.
199 East Blaine Street
Seattle, WA 98102 USA

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404 USA

Title of Study: An Open Label, Roll Over Study to Provide Idelalisib to Subjects Previously Treated with the Investigational PI3Kδ Inhibitor, GS-9820

Investigators: PPD Arnon P. Kater, MD, PhD

Study Centers: 2 sites in the Netherlands

Publications: There were no publications at the time of this CSR.

Study Period:

04 May 2016 (First Subject Screened)
28 December 2017 (Last Subject Last Observation)

Phase of Development: Phase 4

Objectives:

The primary objective of this study was as follows:

- To provide idelalisib, a marketed PI3Kδ inhibitor, in lieu of GS-9820, an investigational second generation PI3Kδ inhibitor, to subjects receiving GS-9820 in Study GS-US-315-0102 at the time of study closure who had objective evidence of clinical benefit defined as at least stable disease on imaging assessed by the independent review committee (IRC) and no toxicities prior to enrollment in this study that would preclude initiating therapy with idelalisib. Idelalisib and GS-9820 are both in the class of agents that inhibit PI3Kδ and as such this exchange of class for class agent was warranted and acceptable.

Methodology: This study was an open-label, rollover study to provide idelalisib to subjects receiving GS-9820 in Study GS-US-315-0102 at the time of study closure. All subjects received idelalisib 150 mg taken orally twice daily continuously.

This study was closed by Gilead Sciences, Inc. (Gilead) once all subjects who chose to continue to receive idelalisib treatment were transitioned to commercially-available idelalisib.

Number of Subjects (Planned and Analyzed):
Planned: 6 subjects
Analyzed: 3 subjects

Diagnosis and Main Criteria for Inclusion and Exclusion:

To be eligible, subjects must have received GS-9820 in Study GS-US-315-0102 with objective evidence of clinical benefit at the time of Study GS-US-315-0102 closure. Subjects with a known hypersensitivity or intolerance to any of the active substances or excipients in the formulation of idelalisib, ongoing toxicities that precluded initiating therapy with idelalisib, or concurrent participation in another therapeutic clinical trial were excluded from participation.

Duration of Treatment:

Treatment continued until unacceptable toxicity, disease progression, study discontinuation, or death occurred.

Idelalisib administration was only to be continued in subjects with a positive benefit-risk profile assessment as per the investigator.

Test Product, Dose, Mode of Administration, and Batch No.:

- Idelalisib 150 mg twice daily (1 × 150-mg oral tablet twice daily, batch no. THSP)
- Idelalisib 100 mg twice daily (1 × 100-mg oral tablet twice daily for subjects requiring dose reduction, batch no. NSZP)

Reference Therapy, Dose, Mode of Administration, and Batch No.: None

Criteria for Evaluation:

Efficacy: No efficacy analyses were performed for this report.

Pharmacokinetics (PK): No PK assessments were performed for this report.

Safety: Overall safety profile was evaluated by the type, frequency, severity, timing of onset, duration, and relationship to study treatment of adverse events (AEs), serious adverse events (SAEs), and deaths.

Statistical Methods:

Safety was assessed using data collected from subjects who received at least 1 dose of idelalisib. All the analyses were limited to descriptive summaries.

Efficacy: No efficacy analyses were performed for this report.

Pharmacokinetics: No PK analyses were performed for this report.

Safety: Clinical and laboratory AEs were coded using the current version of Medical Dictionary for Regulatory Activities (MedDRA), Version 20.1. System organ class (SOC), high-level group term (HLGT), high-level term (HLT), preferred term (PT), and lower-level term (LLT) were provided in the AE dataset. The severity of AEs were graded using the Common Terminology Criteria for Adverse Events (CTCAE), Version 4.03. All AEs and laboratory abnormalities presented in this report were treatment emergent and are referred to as AEs and laboratory abnormalities throughout this report. Additionally, the relationship of AEs to study drug was investigator assigned. Listings of individual subject laboratory results were provided and all AEs were listed based on the Safety Analysis Set.

SUMMARY OF RESULTS:

Subject Disposition and Demographics: Six subjects previously enrolled in Study GS-US-315-0102 were offered screening for enrollment into this study. One subject did not provide consent for screening and 2 subjects did not meet the inclusion/exclusion criteria. A total of 3 subjects were enrolled and received study treatment (150 mg idelalisib twice daily) in this study. All 3 subjects discontinued the study: 1 discontinued due to an AE (lung disorder; reported as: "drug-induced pulmonary disease, unknown diagnosis"), and 2 discontinued due to study termination by the sponsor. The subject ages ranged from 76 to 84 years and 2 of the 3 were female. Subject race and ethnicity were not permitted to be reported due to local regulations.

Efficacy Results: No efficacy analyses were performed for this report.

Pharmacokinetics Results: No PK assessments were performed for this report.

Safety Results:

Exposure: Exposures to idelalisib for the 3 subjects were 175, 589, and 602 days. One subject had a 2-day idelalisib dose interruption due to a Grade 3 SAE (cholangitis) and was rechallenged with idelalisib 150 mg twice daily.

Adverse events: All 3 subjects experienced at least 1 AE and a total of 24 preferred terms for distinct AEs were reported during the study. The majority of the AEs were Grade 1 or Grade 2 in severity. One subject experienced the following Grade 3 AEs: cholangitis, delirium, and lung disorder. The only AE occurring in more than 1 subject was Grade 2 urinary tract infection, which occurred in all 3 subjects.

Two subjects experienced AEs assessed by the investigator as related to idelalisib, which included the following: bronchitis chronic, lung disorder, anemia, aspartate aminotransferase increased, and influenza like illness. Of these, only the AE of lung disorder was Grade ≥ 3 in severity.

One subject experienced 2 SAEs (cholangitis and lung disorder). The subject's idelalisib treatment was interrupted due to cholangitis; however, the cholangitis resolved despite prior resumption of idelalisib dosing. The SAE of lung disorder, reported as related to idelalisib by the investigator, led to the permanent discontinuation of idelalisib. There were no other SAEs reported and no deaths occurred during the study.

No subjects had liver-related laboratory abnormalities of aspartate aminotransferase (AST) > 3 × the upper limit of normal (ULN), alanine aminotransferase (ALT) > 3 × ULN, or total bilirubin > 1.5 × ULN. One subject had Grade 1 AST increased and 1 subject had Grade 1 ALT increased.

CONCLUSIONS:

Safety data in this study do not warrant changes to the safety profile of idelalisib.