FINAL SYNOPTIC CLINICAL STUDY REPORT

Study Title:	Immune Response to Influenza Vaccine in Subjects with B-cell Malignancies Treated with Idelalisib
Name of Test Drug:	Idelalisib (Zydelig®)
Dose and Formulation:	Idelalisib administered orally as indicated in the Gilead-sponsored parent study (100 mg or 150 mg twice daily)
Indication:	B-cell malignancies
Sponsor:	Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 USA
Study No.:	GS-US-313-4100
Phase of Development:	Phase 2
IND No.: **EudraCT No.:**	This is a non-IND study 2017-003055-30
ClinicalTrials.gov Identifier:	Not Applicable
Study Start Date:	23 October 2018 (First Subject Screened)
Study End Date:	24 January 2019 (Last Subject Last Observation for the Primary Endpoint) 24 January 2019 (Last Subject Last Observation for this Report)
Principal or Coordinating Investigator:	Name: Heidi Mocikova, MD Affiliation: PPD
Gilead Responsible Medical Monitor:	Name: Nishan Raj Telephone: PPD Fax: PPD
Report Date:	20 April 2020

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-313-4100
Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
USA

Title of Study: Immune Response to Influenza Vaccine in Subjects with B-cell Malignancies Treated with Idelalisib

Investigators: Multicenter study

Study Centers: 1 site in Czech Republic and 1 site in Spain

Publications: There were no publications at the time of this clinical study report.

Study Period:

23 October 2018 (First Subject Screened)
24 January 2019 (Last Subject Last Observation for the Primary Endpoint)
24 January 2019 (Last Subject Last Observation for this Report)

Phase of Development: Phase 2

Objectives:

The primary objective of this study was as follows:

- To assess the immune response to an influenza vaccine in subjects with B-cell malignancies who were being treated with idelalisib.

Methodology: This study assessed the immune response to an influenza vaccine in subjects who were receiving treatment with idelalisib (100 mg or 150 mg twice daily) in a Gilead-sponsored study (GS-US-313-1580, referring to as parent study throughout this document). Subjects who were to receive an influenza vaccination were invited to participate in this study. In order to be eligible, subjects must have received idelalisib for at least 7 consecutive days prior to receiving an influenza vaccine. Following informed consent, eligible subjects had a baseline blood sample taken (Day 1) and subsequently received the influenza vaccine administered per standard of care using a vaccine licensed and recommended in the site's country. The baseline blood sample was taken within 7 days prior to the administration of the influenza vaccine. Subjects returned to the clinic 28 days (± 7 days) after vaccination and had a second blood sample taken for testing for hemagglutination inhibition (HI) antibody titers against the vaccine.

Subjects in which idelalisib treatment had been interrupted for > 7 consecutive days during the period between vaccination and the second blood sample draw (28 days ± 7 days) were not considered evaluable for immune response.

Study GS-US-313-4100 was initially planned and conducted to fulfill a postmarketing clinical stipulation from Swissmedic to collect data on the investigation of the impact of idelalisib on the

immune system and to submit the study report by no later than 31 October 2020. On 01 October 2019, Swissmedic agreed with Gilead's request to be released from this stipulation as not enough patients were able to be recruited for this study. As a result, Gilead terminated Study GS-US-313-4100 early. A letter to investigators was issued globally on 09 October 2019 providing notification regarding study termination.
Number of Subjects (Planned and Analyzed): Planned: Approximately 22 subjects Analyzed: 2 subjects
Diagnosis and Main Criteria for Inclusion: Eligible subjects were ≥ 18 years of age, enrolled in a Gilead-sponsored study, receiving or scheduled to initiate treatment with idelalisib for at least 7 consecutive days prior to receiving an influenza vaccine, and would be receiving an influenza vaccine per standard of care. Subjects were not eligible to enroll in the study if they had acute disease or fever, had a history of severe allergic or hypersensitivity reaction to a component of the influenza vaccine, or had received any of the following medications or vaccinations within protocol-specified timeframes: systemic steroids, intravenous immunoglobulin therapy, cytotoxic chemotherapy, immunosuppressants, or vaccination against influenza or other vaccinations.
Duration of Treatment: The selected influenza vaccine was administered per standard of care on a single day within 7 days following the baseline blood sample. The expected duration of study participation was up to 42 days, not including the screening period of up to 7 days.
Test Product, Dose, and Mode of Administration: Influenza vaccine was commercially-available, licensed, and recommended influenza vaccine administered in an inpatient or outpatient medical setting, in accordance with the administration instructions described in the approved labeling and per standard of care. Influenza vaccine was not provided or administered by Gilead, per protocol. Idelalisib was supplied and administered as described in the Gilead-sponsored parent study.
Reference Therapy, Dose, and Mode of Administration: Not applicable
Criteria for Evaluation: **Efficacy:** No efficacy analyses were performed for this report. **Pharmacokinetics (PK)**: No PK assessments were performed for this report. **Safety:** Assessment of adverse events (AEs) and concomitant medications continued throughout the study. All AEs and serious adverse events (SAEs), regardless of cause or relationship, which occurred from the date of informed consent to participate in this study and throughout the duration of study (until the 28-day postvaccination visit has occurred or premature discontinuation from the study), were reported on the case report form of the Gilead-sponsored parent study. These data were exported from the Gilead-sponsored parent study and imported into the database for this study. **Other:** Pre- and post-vaccination HI antibody titers were evaluated prior to and 28 days [± 7 days] after vaccination.

Statistical Methods:

Because the study was terminated early and only 2 subjects were enrolled, no efficacy analyses and no summary analyses were conducted. The All Enrolled Analysis Set was defined and used as the primary analysis set in the final analysis. The Evaluable Analysis Set, the Per-Protocol Analysis Set, and the Safety Analysis Set were no longer needed and were not defined.

Efficacy: No efficacy analyses were performed for this report.

Pharmacokinetics: No PK assessments were performed for this report.

Safety: The following by-subject listings were provided for the All Enrolled Analysis Set: All AEs, SAEs, deaths, treatment-emergent AEs (TEAEs) leading to discontinuation of idelalisib, TEAEs leading to dose modification or temporary interruption of idelalisib, and TEAEs related to administration of influenza vaccine.

Other: Blood samples for HI antibody titers to each viral strain included in the selected influenza vaccine were collected at baseline (prior to vaccination), and again 28 days (± 7 days) postvaccination. A by-subject listing of HI antibody titers was provided by subject ID number in ascending order for the All Enrolled Analysis Set.

SUMMARY OF RESULTS:

Considering the small number of subjects enrolled as of study termination, only necessary analyses based on the limited data available are provided in this report.

Subject Disposition and Demographics: Two subjects were enrolled in the study before it was terminated early; both subjects received at least 1 dose of study drug and were included in the All Enrolled Analysis Set (Listing 16.2.5.1, Listing 16.2.5.2). Both subjects completed the study (Listing 16.2.1.3).

- Subject PPD received 100 mg idelalisib twice daily from PPD (Study Day 1) through PPD (Study Day 29) during this study. The subject received quadrivalent inactivated influenza vaccine on PPD (Study Day 7).
- Subject PPD received 150 mg idelalisib twice daily from PPD (Study Day 1) through PPD (Study Day 20) during this study. The subject received trivalent inactivated influenza vaccine on PPD (Study Day 1).

One subject was 64 years of age and one subject was 75 years of age. PPD (Listing 16.2.4.1). Subject medical history and prior and concomitant medications are presented in Listing 16.2.4.3 and Listing 16.2.4.4, respectively.

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

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

Safety Results: The 2 enrolled subjects experienced a total of 5 AEs during the study (Listing 16.2.7.1). Subject PPD experienced AEs of thrombocytopenia (Grade 2), cough (Grade 2), and neutropenia (Grade 3). Subject PPD AEs of diarrhea (Grade 2) and pyrexia (Grade 1). All AEs were assessed by the investigator as related to idelalisib except an AE of cough; none of these AEs were assessed by the investigator as related to influenza

vaccine.

The study drug was interrupted for Subject PPD from PPD (Study Day 21) to PPD (Study Day 28) due to an AE of Grade 2 diarrhea (Listing 16.2.7.5.2). The AE was resolved on PPD and the study drug was restarted on PPD.

No deaths, SAEs, or AEs leading to permanent discontinuation of idelalisib were reported (Listing 16.2.7.2.1, Listing 16.2.7.3, and Listing 16.2.7.5.1).

No AEs related to administration of influenza vaccine were reported (Listing 16.2.7.5.3).

Other Results: For Subject PPD, baseline (Day 1) and postvaccination visit (Day 29) HI antibody titers are provided in Listing 16.2.8.1.3. Subject PPD had idelalisib treatment interrupted for > 7 consecutive days during the period between vaccination and the visit for second blood sample (28 days ± 7 days), and was not considered as evaluable for immune response. HI titers data were unavailable for this subject.

CONCLUSIONS: No conclusions could be drawn given the limited number of subjects in the study. There were no new safety issues identified.