Errata to the FDA Briefing Document

Oncologic Drugs Advisory Committee Meeting (ODAC)

April 12, 2016

Rociletinib

Applicant: Clovis Oncology, Inc.

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Page 13, row 2

Clovis requested accelerated approval under 21 CFR 314 Subpart H for rociletinib 500 mg BID based on ORR of **42.1% (95% CI: 30.9, 54.0)** ~~38.2% (95% CI 25.4, 52.3)~~ as assessed by investigator using RECIST v1.1.

Page 16, Paragraph 1

For study CO-1686-019, the first patient was enrolled on 17 June 2014 in and the study is currently ongoing with 42 enrolled patients **as of the enrollment cut-off date for analysis of this trial**.

Page 17

- ECOG Performance Status (PS) 0-**1** ~~2~~ **for CO-1686-008** (0-1 for CO-1686-019)

Page 18, Section 4.3, first paragraph

The efficacy measurement assessment was conducted by computed tomography (CT) scans of the chest, abdomen, and pelvis according to RECIST version 1.1 criteria, and repeated every 8 weeks (Cycle 2, 4, 6) **in Study CO-1686-019 and every 6 weeks in Study CO-1686-008** and every 3 cycles thereafter.

Page 21, Table 7 (data missing under "Black/African American")– 500 mg dose

Table 7 Demographic and Disease Characteristics of the Efficacy Analysis Population

	500 mg (N=79)	**625 mg (N=170)**	**750 mg (N=76)**	**Pooled^ (N=325)**
Race, n (%)				
American Indian/Alaska Native		1 (1)		1 (0)
Asian	15 (19)	42 (25)	19 (25)	76 (23)
Black/African American	**3(4)**	7 (4)	1 (1)	11 (3)

Page 23, Section 4.5.2, first paragraph

The primary outcome measure of objective response rate (ORR) as assessed by central radiologic review (IRR)**, as agreed-upon during the 09 June 2015, pre-NDA meeting,** is 22.8% (95% CI 14.1, 33.6) for patients who received rociletinib 500 mg BID~~, as agreed upon during the 09 June 2015, pre-NDA meeting~~.

Page 24, Table 8

In this pooled analysis, the ORR is 30.2% (95% CI **25.2**~~22.5~~, 35.5).

Table 8 Objective Response by IRR

Analysis Value	500mg (N=79)	625mg (N=170)	750mg (N=76)	Pooled^ (N=325)
	n/N(%)	n/N(%)	n/N(%)	n/N(%)
95% Confidence Interval	[14.1, 33.6]	[25.4, 39.9]	[22.5, 44.6]	[**25.2**~~22.5~~, 35.5]

Page 27, Table 10

Table 10 Overview of Adverse Events Safety Analysis Population ~~**019**~~ **(n= 400)**

	500 N= 90 n (%)	**625 N = 209 n (%)**	**750 N = 95 n(%)**	**1000 N = 6 n (%)**	**Total N= 400 n (%)**
≥ 1 SAE	40 (44)	97 (46)	45(47)	5 (83)	187~~9~~ (47)

Page 29, Section 4.5.3.4

The most common adverse reactions leading to dose interruption in 5% or more patients are hyperglycemia (22%), QT interval prolongation (**10**~~41~~%), nausea (10%), fatigue (8%), diarrhea (7%), vomiting (6%).

Page 35, Section 5.3.5.12

Five deaths were attributed to pneumonia, and one death each to sepsis and **aspiration** ~~acute respiratory distress syndrome~~.

Table 24

Table 24 Narratives of On-Study Sudden Deaths

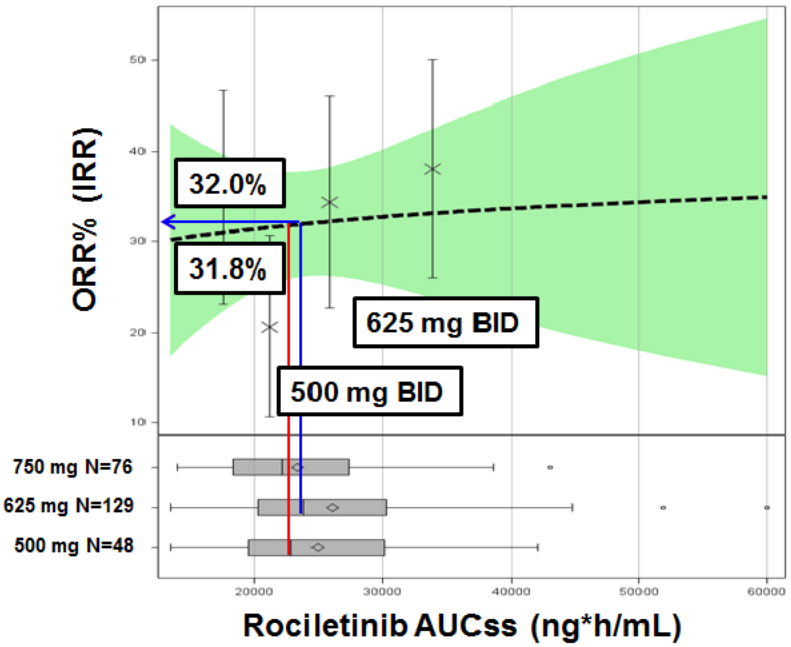
USUBID Dose	**AE-Preferred Term**	**Study Day**	**Clinical Summary**
008-117705[A] **750 mg**	Sudden death	13	… Patient was found dead at home on study Day 1~~2~~3. ….

Page 37, Section 5.1.2

Using this modeling, the predicted ORRs (95% CI) for the 500 mg and 625 mg dose cohorts are **31.8% (26.0 to 37.7%) and 32.0% (26.2 to 37.8%)** ~~28.7% (23.4 to 34.0%) and 29.5% (24.0 to 34.9%)~~, respectively.

Page 38, Figure 4

Replaced with new figure below:



Note: … The box plots at the bottom represent the distribution of rociletinib $AUC_{ss,}$ at each dose group **(500, 625, 750 BID HBr formulation)** ~~(500, 625, 750, 1000 mg BID HBr formulation; and FB formulation)~~.

Page 40

Analyses of change in the QTcF interval based on electrocardiograms obtained in patients enrolled in Studies CO-1686-008 and CO-1686-019 indicate that prolongation in the QTc interval increases with **M460 exposure** ~~dose~~ (**Figure 6**).

Page 41, footnote to Figure 6

Note: … The black dots and bars represent the median and 95% CI of the **change in QTcF (ms) from baseline** ~~observed response rate~~ in each quantile of the **M460 concentration** ~~rociletinib~~ ~~AUC_{ss}~~.

Page 42, Table 25

Table 25 Frequency of NAT2 Phenotypes across Racial and Ethnic Populations

NAT2 phenotype frequency %	Rapid acetylator	Intermediate acetylator	Slow acetylator
Chinese [A]	23–30 [A]	~~21–~~45 [A]	25 [A] ~~–52~~
U.S. Hispanic	14	~~32–~~**54**	~~54~~**32**