SUPPLEMENTAL FILE

Evaluation of the Bioequivalence and Food Effect on the Bioavailability of CC-486 (Oral Azacitidine) Tablets in Adult Patients with Cancer

Hani M. Babiker, MD; Mohammed Milhem, MBBS; Joseph Aisner, MD; William Edenfield, MD; Dale Shepard, MD, PhD; Michael Savona, MD; Swaminathan Iyer, MD, PhD; Maen Abdelrahim, MD, PhD; CL Beach, PharmD; Barry Skikne, MD; Eric Laille, MS; Kao-Tai Tsai, PhD; Thai Ho, MD, PhD

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Corresponding author: Hani M. Babiker, M.D.
University of Arizona Comprehensive Cancer Center
hanibabiker@email.arizona.edu

Ethics Committees and Institutional Review Boards for the CC-486-CAGEN-001 Study

Site No.	Investigator Name	Name/Address of IEC/IRB	Name of Chairperson(s)
001	William Edenfield	Greenville Health System (GHS) Institutional Review Board, Committee C 701 Grove Road Greenville, SC 29605	James Hayes, MD
002	Vivek Khemka	Western Institutional Review Board – WIRB 1019 39th Avenue SE, Suite 120 Puyallup, WA 98374	Erin Brower, MS, CIP
005	Thai Ho	Mayo Clinic Institutional Review Board 200 First Street SW Rochester, MN 55905	Ouellette Yves, MD
007	Michael Savona	Vanderbilt University Institutional Review Board 1313 21st Avenue South 504 Oxford House Nashville, TN 37232-4315	James A.S. Muldowney, MD
009	Maen Abdelrahim	The Methodist Hospital Research Institutional Review Board 1130 John Freeman MS: MJG6-014 Houston, TX 77030 Former Address: The Methodist Hospital Research Institutional Review Board 6565 Fannin Street Houston, TX 77030	Susan Miller, MD, MPH

Supplementary Table 1. Baseline demographic and disease characteristics

	Bioequivalence Cohort (Stage 1) (N = 30)	Food Effect Cohort (Stage 2) (N = 57)
Age, median (range)	68.5 (46, 86)	62.0 (31, 88)
Race, n (%)		
White	27 (90)	53 (93)
Other[a]	2 (6)	2 (4)
Not Collected or Reported	1 (3)	2 (4)
Sex, n (%)		
Male	20 (67)	34 (60)
Female	10 (33)	23 (40)
BMI, median (range)	27.8 (16, 44)	26.6 (19, 47)
Malignancy type, n (%)		
Metastatic or inoperable solid tumors	27 (90)	57 (100)
Myelodysplastic syndromes	1 (3)	0
Acute myeloid leukemia	1 (3)	0
Multiple myeloma	1 (3)	0
Time since diagnosis (years), median (range)	3.5 (0.1, 19.2)	4.8 (0.2, 27.1)
ECOG performance status score, n (%)		
0	7 (23)	20 (35)
1	23 (77)	34 (60)
2	0	3 (5)

[a]Black or African-American, Asian, American Indian or Alaskan Native

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.

Supplementary Table 2. Plasma pharmacokinetic parameters for two formulations of CC-486 (2 x 150-mg tablets [Formulation A] and 1 x 300-mg tablet [Formulation B])

Treatment	Statistics	AUCt (ng*h/mL)	AUC_∞ (ng*h/mL)	C_{max} (ng/mL)	T_{max} (h)	$t_{1/2}$ (h)	CL/F (L/h)	Vz/F (L)
2 x 150 mg tablets	N	30	30	30	30	30	30	30
	Geometric Mean	225.0	228.5	143.0	NA	0.544	1313	1031
	Geometric %CV	63.7	62.6	53.1	NA	32.0	62.6	67.4
	Median	226	232	149	1.0	0.52	1300	922
	Min, Max	71.8, 555	76.4, 557	34.5, 362	0.48, 3.0	0.34, 1.1	538, 3930	389, 3860
1 x 300 mg tablet	N	30	30	30	30	30	30	30
	Geometric Mean	239.1	241.6	145.1	NA	0.492	1242	881.1
	Geometric %CV	65.2	64.5	63.7	NA	26.9	64.5	67.4
	Median	236	237	148	1.0	0.46	1270	900
	Min, Max	93.0, 640	94.5, 642	46.7, 362	0.50, 2.5	0.33, 0.87	468, 3170	317, 2790

PK Parameter	Treatment	N	Geometric Mean	Ratio (%) of Geometric Means	90% CI of Ratio (%) of Geometric Means	Intra-patient %CV
AUCt (ng*h/mL)	2 x 150 mg	30	225.0	106.27	(95.21, 118.62)	25.4
	1 x 300 mg	30	239.1			
AUC_∞ (ng*h/mL)	2 x150 mg	30	228.5	105.71	(95.01, 117.62)	24.7
	1 x 300 mg	30	241.6			
C_{max} (ng/mL)	2 x 150 mg	30	143.0	101.52	(89.87, 114.68)	28.3
	1 x 300 mg	30	145.1			

PK Parameter	Condition	N	Median	Median Difference	90% CI of Median Difference (Fed – Fasted)	*P*-value
T_{max} (h)*	Fasted	30	1.0	-0.017	(-0.25, 0.03)	<0.710
	Fed	30	1.0			

N patients = the total number of patients for which the PK parameter could be calculated

*Median and median difference (Test vs. Reference), and 90% CI of the median difference, are from Hodges-Lehmann estimate. The P value is from Wilcoxon signed-rank test.

AUC_∞, area under the plasma concentration-time curve from time 0 extrapolated to infinity; C_{max}, maximum plasma concentration; T_{max}, time to C_{max}; $t_{1/2}$, terminal half-life; CL/F, apparent total clearance; Vz/F, volume of distribution; NA, not applicable.