RADIOLOGY	**US Scan – X-ray**
Study code **56DX** - [_0_|_0_|_3_] - [___|___|___]	Initials [__|__|__|__|__|__]

1. US Scan (The general US scan is performed for all patients between day 5 and day 6 of illness)

a. Was a general ultrasound performed? ○ Yes ○ No

b. If Yes, date and time of US scan: [__|__]/[__|__]/[__|__] – [__|__]:[__|__]

c. Result:

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Ascites	○ Yes ○ No	○ Small ○ Moderate ○ Massive
Pleural effusion	○ Yes ○ No	□ Right [__|__].[__|__] cm □ Left [__|__].[__|__] cm
Pericardial effusion	○ Yes ○ No	[__|__].[__|__] cm
Liver size*		[__|__].[__|__] cm
Gallbladder wall**		[__|__].[__|__] cm
Others, please describe: [_____]		

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2. Was a chest X-ray performed? ○ Yes (Choose the worst) ○ No

a. If so, date and time of x-ray: [__|__]/[__|__]/[__|__] - [__|__]:[__|__]

b. Result: □ normal □ pleural effusion □ pulmonary edema □ pneumonia

□ other, please describe: [_____]

Signature: [_____] [___|___|___|___]

Other ultrasounds performed (if different results)

a. If so, date and time of US : [__|__]/[__|__]/[__|__] - [__|__]:[__|__]

b. Result: □ normal □ pleural effusion □ Ascites □ Pericardial effusion

□ hepatomegaly □ Gallbladder thickening

□ other, please describe: [_____]

Parameters	**Definition**
*Liver enlargement	Liver size exceeds 15cm
**Gallbladder wall thickening	Thickness of gallbladder wall exceeds 0.35cm on ultrasound scan

STUDY DRUG	**STDR**
Study code **56DX** - [_0_|_0_|_3_] - [___|___|___]	Initials [__|__|__|__|__|__]

	Administration of study drug	**Staff**	**Vomit within 30 mins after study drug intake**	**Administration of replacement dose**	**Staff**
Cohort: [___]					
Day 1	**[__|__]/[__|__]/[__|__]**				
AM	Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)		○ Yes ○ No	○ Yes ○ No Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)	
PM	Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)		○ Yes ○ No	○ Yes ○ No Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)	
Day 2	**[__|__]/[__|__]/[__|__]**				
AM	Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)		○ Yes ○ No	○ Yes ○ No Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)	
PM	Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)		○ Yes ○ No	○ Yes ○ No Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)	
Day 3	**[__|__]/[__|__]/[__|__]**				
AM	Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)		○ Yes ○ No	○ Yes ○ No Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)	
PM	Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)		○ Yes ○ No	○ Yes ○ No Time: [__|__]:[__|__] Metformin: ○ 500mg ○ 850mg Number: [___] tablet(s)	

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STUDY DRUG	**STDR**
Study code **56DX** - [_0_|_0_|_3_] - [___|___|___]	Initials [__|__|__|__|__|__]

	Administration of study drug	**Staff**	**Vomit within 30 mins after study drug intake**	**Administration of replacement dose**	**Staff**
Day 4 [__|__]/[__|__]/[__|__]					
AM	Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)		O Yes O No	O Yes O No Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)	
PM	Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)		O Yes O No	O Yes O No Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)	
Day 5 [__|__]/[__|__]/[__|__]					
AM	Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)		O Yes O No	O Yes O No Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)	
PM	Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)		O Yes O No	O Yes O No Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)	
Day 6 [__|__]/[__|__]/[__|__] **(For patients in cohort 2 only. These patients start the first dose of metformin in the afternoon of study day 1)**					
AM	Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)		O Yes O No	O Yes O No Time: [__|__]:[__|__] Metformin: O 500mg O 850mg Number: [___] tablet(s)	

Changes to the study drug regimen

1. Was the study drug stopped early? O Yes O No

If yes, date stopped [___|___]/[___|___]/[___|___] time: [___|___]:[___|___]

2. Reason for stopping drugs

AE/SAE(s) O Yes O No Number of AE related to the cessation [__]

Patient's withdrawal from the trial O Yes O No Other, specify [_____]

Signature: [_____] [___|___|___|___] **Date: [___|___]/[___|___]/[___|___]**

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ADVERSE EVENT **AE**

Study code
56DX - [_0_|_0_|_3_] - [___|___|___]

Initials
[__|__|__|__|__|__]

1. Adverse event (AE) number: [__|__]
Please fill in a new AE form for each event and number events sequentially (first AE should be '01')

2. Date of AE onset: [___|___]/[___|___]/[___|___] time: [___|___]:[___|___]

3. Specify New AE: [___]
Please fill in a code specifying the event as below

1- Worsening level of consciousness (fall in GCS ≥ 2 points)
2- Change in blood pressure (PP < 20 mmHg, SBP < 90 mmHg or unmeasurable BP)
3- Vomiting (patient vomits within 30 mins after metformin replacement dose, or vomit is recorded as ++ or +++ during 24h – eg ≥ 3 episodes separated by 15 mins during 24h)
4- Epigastric abdominal pain
5- Diarrhoea (≥ 5 episodes/day)
6- Mucosal bleeding
7- Rash, urticaria
8- Increased lactate (≥ 3 mmol/L)
9- Episode of hypoglycaemia (Glycemia < 3.9 mmol/L or < 70 mg/dL)
10- Increased liver enzyme (AST or ALT > 400 U/L)
11- Acute kidney injury (eGFR < 60 ml/mn/1,73m^2; Plasma creatinin >2 x above upper baseline)
12- Thrombocytopenia (Platelet < 20.000/uL)
13- *Other event, specify: [_____]*

4. Abnormal value (unit): [_____] [_____]
(If appropriate, please fill in the abnormal value used to determine the AE above).

5. Grade the event (What grade was the event at its worst moment?)
○ Mild: Discomfort noticed but no disruption of normal daily activities
○ Moderate: Discomfort sufficient to reduce or affect daily activity
○ Severe: Inability to perform daily activity

6. Is the event a serious adverse event (SAE)? ○ Yes ○ No
Please complete the SAE reports as soon as possible

7. Relatedness of the AE
a. Specify the relatedness to study drug:
○ Related to study drug ○ Probably related to study drug ○ Possibly related to study drug
○ Unlikely to be related to study drug ○ Not related to study drug
b. Specify the relatedness to dengue disease:
○ Related to dengue disease ○ Probably related to dengue disease ○ Possibly related to dengue disease
○ Unlikely to be related to dengue disease ○ Not related to dengue disease

8. Is the event a suspected unexpected serious adverse reaction? ○ Yes ○ No

9. Summary of treatment for the AE: [_____]

10. Date of END of AE: [___|___]/[___|___]/[___|___] (not clinically relevant anymore)

11. What was the final outcome of this AE?
○ AE recovered ○ Patient died ○ Condition on-going at end of study

Signature: [_____] [___|___|___|___] **Date:** [___|___]/[___|___]/[___|___]

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FOLLOW-UP-1	**FU-1**
Study code **56DX** - [_0_|_0_|_3_] - [___|___|___]	Initials [__|__|__|__|__|__]

AROUND DAY 21-28 OF ILLNESS: Indicate one option: ○ A ○ B ○ C

A. The patient attends the study clinic for assessment: please complete this form, and obtain the final blood sample.

B. The patient doesn't attend the study clinic and the information is gathered by phone: please complete this form as far as possible.

C. The patient doesn't attend the study clinic and cannot be contacted by phone. Leave this form blank.

Date of collecting information [__|__]/[__|__]/[__|__|__|__] (dd/mm/yyyy)

1. Temperature: [__|__]. [__] °C ○NA
2. Pulse: [__|__|__]/min ○NA
3. BP: [__|__|__]/[__|__|__] mmHg ○NA
4. Respiratory rate: [__|__]/min ○NA
5. Weight: [__|__|__].[__] kg ○NA
6. Arm circumference: [__|__|__] cm ○NA
7. Waist circumference: [__|__|__] cm ○NA

8. Has the patient been completely well since the last visit during the acute illness? ○ Yes ○ No
   a. If no, describe any new/significant problems:
   [_____]
   [_____]
   b. If no, is there any abnormality on examination:
   [_____]
   [_____]
9. Has the patient had fever since the last visit? ○ Yes ○ No
   [_____]
   [_____]
10. Did the patient take any antibiotics/other treatment from a doctor since the last visit? ○ Yes ○ No
    a. If yes indicate which drug and the reason (if the patient knows)?
    [_____]
    [_____]
11. Did the patient attend any other clinic or hospital since the last visit? ○ Yes ○ No
    a. If yes, give the name and reason?
    [_____]
    [_____]
12. Main summary diagnosis (probable) for any problems identified above:
    [_____]
13. Final blood sample taken (FBC, Biochemistry and Research Samples): ○ Yes ○ No

Signature: [_____] [___|___|___|___]

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FOLLOW-UP-2	**FU-2**
Study code **56DX** - [_0_|_0_|_3_] - [___|___|___]	Initials [__|__|__|__|__|__]

BEFORE/AFTER THE ACUTE FEBRILE ILLNESS

14. Before the acute febrile illness, did you ever have mental health problems (feeling down, depressed, hopeless, anxiety, severe mood disorder)?
    ○ Yes ○ No ○ I do not remember

If Yes, please describe the problem: [_____]

PERSISTING PROBLEMS AFTER THE ACUTE FEBRILE ILLNESS

15. For how long did the patient need to stay at home before being back to work (school): [__|__] days
16. Was the patient back to work (school): ○ Fulltime ○ Part-time
17. Was the patient able to resume the same "normal" daily activities compared to before the acute illness episode? ○ YES ○ NO

If NO, go to the next part of this form. If YES, skip the below questions and sign your name at the end of this form

PERSISTENT SYMPTOMS If YES, please continue to the right and estimate the duration of the persisting problem. If NO, please go directly to the next question			**DURATION** (days) *
18. Persistent headaches	○ YES	○ NO	[___]
19. Muscle and/or joint pain	○ YES	○ NO	[___]
20. Skin problems If Yes – please describe: **[**_____**]**	○ YES	○ NO	[___]
21. Loss of appetite	○ YES	○ NO	[___]
22. Problems with eye sight If Yes – please describe: **[**_____**]**	○ YES	○ NO	[___]
23. Sleeping problems:			
a. Trouble falling or staying asleep	○ YES	○ NO	[___]
b. Sleeping too much	○ YES	○ NO	[___]
24. Alteration of concentration at work (at school)	○ YES	○ NO	[___]
25. Feeling of tiredness or no energy	○ YES	○ NO	[___]
26. Mental health problems:			
a. Little interest or pleasure in doing things	○ YES	○ NO	[___]
b. Excessive anxiety	○ YES	○ NO	[___]
c. Feeling irritated	○ YES	○ NO	[___]
d. Feeling depressed, hopeless	○ YES	○ NO	[___]
27. OTHER – please describe [_____]			[___]

Signature: [_____**] [**___|___|___|___**]**

*Round up the duration. If the symptoms still persist up until the FU visit, fill "88"

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TRIAL COMPLETION	**TC**
Study code **56DX** - [_0_|_0_|_3_] - [___|___|___]	Initials [__|__|__|__|__|__]

Date of Completion: [___|___]/[___|___]/[___|___]

1. Patient completed the entire trial? *(followed up for 21 -28 days)* ○ Yes ○ No
2. Date of last clinical assessment: [___|___]/[___|___]/[___|___]
3. Lost to follow-up: ○ Yes ○ No

If yes, last date of follow-up: [___|___]/[___|___]/[___|___]

4. **If lost to follow-up, check ONE box that applies for this participant**

○ Withdrawal of consent for study participation by the participant

○ Unable to contact

○ Sponsor terminated the trial

○ Death

○ Other, specify [_____]

5. ***IF Withdrawal of consent for study participation by the participant***

a. Date of withdrawal of consent: [___|___]/[___|___]/[___|___]

6. ***IF unable to contact***

a. Last date of being able to contact: [___|___]/[___|___]/[___|___]

7. ***IF Sponsor terminated the trial***

a. Last date of assessment: [___|___]/[___|___]/[___|___]

8. ***IF Death***

a. Date of death [___|___]/[___|___]/[___|___]

b. Place of death: ○ Hospital ○ Home ○ Other

c. In your opinion, based on the information available to you, was the patient's death caused directly by dengue disease? ○ Yes ○ No ○ Unknown

d. If "No", OR "Unknown", what, in your opinion, caused the death?

[_____]

[_____] [_____] [___|___]/[___|___]/[___|___]

Printed Name Signature