Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients: Manipur, India

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Study Protocol

Version 1.2, April 2017

Ammendement to Version 1.1, February 2017 and version 1.0, November 2016

In partnership with:

National AIDS Control Organization, Ministry of Health and Family Welfare, New Delhi

and

Regional Institute of Medical Sciences, Imphal, Manipur.

Médecins Sans Frontières / Doctors Without Borders, India
C-106 Defence Colony, New Delhi, India, 110024

CONTENTS

Abbreviations

Ag S	Antigen S
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
APRI	Aminotransferase/platelet ratio index
ART	Antiretroviral therapy
CD4	Cluster of differentiation 4
CHC	Chronic Hepatitis C
CRF	Case Report Form
DAAs	Directly Acting Antivirals (drug)
EASL	European Association for the Study of the Liver
EOT	End of treatment
ERB	Ethical Review Board
FBC	Full blood count
FDA	Food and Drug Administration (US)
GT1	HCV Genotype 1
HBV	Hepatitis B virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IFN	Interferon
INR	International normalized ratio
ITT	Intent to Treat
MDR	Multi-Drug Resistance
MoH	Ministry of Health
MSF	Médecins Sans Frontières
MSM	Men who have Sex with Men
NAAT	Nucleic Acid Amplification Test
NACO	National AIDS Control Organization
OCA	Operational Center Amsterdam
OST	Opioid substitution therapy
PCR	Polymerase Chain Reaction

PEG-IFN	Pegylated interferon
PEG-RBV	Pegylated interferon plus ribavirin
PLWHA	People living with HIV/ AIDS
PWIDs	People who inject drugs
RBV	Ribavirin
RDT	Rapid Diagnostic Test
RNA	Ribonucleic acid
SVR 12	Sustainable Viral Response at 12 weeks
TB	Tuberculosis
VL	Viral load
WHO	World Health Organization

ADMINISTRATIVE DETAILS

1. Title of the Project	Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients: Manipur, India
2. Name and Address of Lead Research Institute	Médecins Sans Frontières / Doctors Without Borders, India C-106 Defence Colony, New Delhi, India, 110024
3. Name, Address of Participating Research Institute/s	National AIDS Control Organisation, Department of AIDS Control, Ministry of Health and Family Welfare, Government of India. 6th Floor, Chandralok Building, Janpath, New Delhi, 110001
4. Protocol version **Preceding version(s)**	1.2, Apr 2017 1.1, Feb 2017. 1.0, Nov 2016
5. Points of amendment Feb 2017	a. Change in Principal and Co-investigators b. Explanation to inclusion criteria (page 6) c. Additions to patient information sheet d. Inclusion of patient information sheet and consent forms in five languages.
6. Points of amendment, April 2017	a. Inclusion of project site details b. Inclusion of adverse event monitoring plan c. Explaination of study outcomes d. Eloboration of data management e. Revision of study timeline

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Information about MSF:

Médecins Sans Frontières / Doctors Without Borders, India has been collecting, analysing and reporting experience from their treatment activities in Manipur since 2004. Within the existing project, experienced medical, biomedical and data management staff have managed a large and comprehensive de-identified database to follow the progress of over 3000 patients being treated for HIV, TB and/or MDRTB. MSF has regularly provided data reports to NACO and RNTCP in accordance with our respective agreements and expectations of the collaborations.

SECTION B: PROJECT DETAILS

1. ***TITLE OF PROJECT***

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients: Manipur, India

2. PROJECT SITES

a. Doctors without Borders Clinic, Thangjam Road, Churachandpur, Manipur 795128.
b. Doctors without Borders Clinic Primary Health Centre, Chakpikarong, Chandel District, Manipur 795102
c. Doctors without Borders Clinic, ward No. 3, P.O & P.S Moreh, Moreh Sub-Division, Chandel District, Manipur, 795131

3. ***BACKGROUND & RATIONALE FOR THE STUDY AND ITS APPLICATION WITH RESPECT TO THE PROGRAMME PRIORITIES UNDER NACP-IV.***

INTRODUCTION

Médecins Sans Frontières (MSF) has been active in Manipur state since 2004. MSF has ART centres in Churachandpur, Moreh and Chakpikarong providing care and treatment to over 1600 people living with HIV/AIDS (PLWHA). MSF has a Public Private Partnership (PPP) with the National AIDS Control Organisation (NACO). Both parties signed an MOU in which it was agreed to set up a collaborative ART project between NACO and MSF that would seek to be a model for high quality provision of ART and associated healthcare and medical management of PLWHAs in its sites in India. As part of this commitment to care, MSF commenced hepatitis C (HCV) treatment for HIV co-infected individuals in July 2015 in Churachandpur.

The rapidly evolving HCV landscape, including new DAA based regimens, provides novel treatment options and opportunities to treat patients successfully, with fewer side effects and simplified surveillance in low resource settings. The aim of this study is to assess the effectiveness and safety of chronic HCV treatment amongst HIV positive co-infected patients

receiving treatment in accordance with current WHO and other International treatment protocols and guidelines, within real world settings.

A prospective longitudinal cohort study was chosen to support the monitoring of the introduction of these new regimens and contribute to post licensure surveillance. An important caveat to note is that this study is in no way a Phase four clinical trial or a pharmaco-vigilance study. The methodology described is in accordance with an observational study of a cohort of patients under HCV treatment in the MSF ART centres and analysis of routinely collected clinical data.

This study falls within the national targets outlined by the National Aids Control Program (NACP-IV), Component 3 of which highlights the importance of comprehensive care, support and treatment programs for people living with HIV/AIDS. Included within this component is the recognition of the management and treatment of concurrent infections that have an adverse impact on morbidity and mortality.

4. OBJECTIVES

Primary objective

The primary objective of this study is to assess the effectiveness of HCV curative treatments in patients with chronic hepatitis C (CHC), co-infected with HIV in Manipur, India.

Secondary objectives

a. To describe the demographic, clinical and biological characteristics of patients with chronic hepatitis C and HIV co-infection
b. To assess the effectiveness of HCV curative strategies in patients with chronic HCV, co-infected with HIV stratified by regimen and by site
c. To identify risk factors associated with differing virological responses
d. To assess the safety of HCV treatment
e. To monitor the safety of HCV treatment in HIV co-infected patients
f. To document the clinical and biological tolerance of the HCV treatment
g. To assess the feasibility of HCV treatment
h. To assess comparative performance of elastography (Fibroscan®) and APRI (AST to Platelet Ration Index), to evaluate liver fibrosis among HIV/HCV co-infected individuals
i. To describe causes of non-eligibility for treatment
j. To describe the clinical and biological evolution of co-infected patients, not eligible for HCV treatment
k. To assess treatment adherence

5. PRESENT KNOWLEDGE AND RELEVANT BIBLIOGRAPHY INCLUDING FULL TITLES OF ARTICLES RELATING TO THE PROJECT

The burden of hepatitis C worldwide is now being recognized as a major public health problem. An estimated 180 million people (≈3% of the world's population) are chronically infected with the hepatitis C virus (HCV), responsible for 500,000 deaths each year (1, 2). Two thirds of those infected by Hepatitis C live in Africa or in Asia.

Approximately 4-5 million people are estimated to be co-infected with HIV and HCV, representing 16% of people living with HIV globally (3, 4). Co-infection of HIV and HCV has negative and reciprocal clinical implications for patients. First, HIV accelerates the progression of HCV. Those with co-infection progress to significant liver disease and cirrhosis faster and more often than those only infected with HCV alone, with nearly 80% developing liver damage (5-8). Despite patients taking anti-retroviral therapy (ART), patients with HIV-HCV co-infection remain at significantly increased risk of overall mortality compared to their HIV mono-infected peers (9). Furthermore, co-infection with HCV in the era of ART is associated with worse HIV-related outcomes including weaker immune recovery with ART (lower mean CD4 counts), more rapid progression to AIDS, higher levels of HIV virus in the blood, poorer virological control on ART (11% loss of ART efficacy in co-infected patients) and more common neurocognitive deficits (10-12). In order to maximize the benefits from increased ART use globally, interventions designed to address the growing burden of HCV in PLWHA must be rapidly rolled out.

Nationwide, 2,100,000 people are estimated to be living with HIV (13) and 18,216,000 people have been infected with HCV in India (4). HCV screening is included in the HIV national protocol, but only for individuals with history of drug use and individuals with multiple blood and blood product transfusion (14-16). Treatment is not widely available in India.

Within India, the true prevalence and clinical evolution of hepatitis and hepatitis related liver disease is unknown. Although the World Health Organisation (WHO) estimates an overall HCV prevalence of 12 million within India (≈ 1% of Indian population), reported infection rates are much higher among at risk populations. Solomon et al. conducted a multisite study involving 15 cities and 14481 IDUs in 11 states of India. Within Manipur state, the reported HCV prevalence within this high risk group was 60.3% with a HIV-HCV co-infection prevalence of 24.5% (17)

There is a significant knowledge gap regarding the experiences of treating Hepatitis C infection among HIV-infected patients, especially in programmatic settings in resource-constrained countries. Treatment effectiveness needs to be properly reported, treatment challenges need to be systematically documented and the experiences and the needs of HIV/HCV co-infected patients need to be widely communicated and shared.

6. DETAILED RESEARCH PLAN

METHODOLOGY

I. Study Design

The study will be a prospective longitudinal cohort study, which will monitor the diagnosis, treatment and follow-up of the HIV patients identified with a chronic hepatitis C within 3 clinic sites in Manipur; Churachandpur, Chakpikarong and Moreh.

The analysis of routinely collected clinical data will facilitate the assessment of the effectiveness of HCV treatment among patients with chronic hepatitis C, co-infected with HIV, from time of confirmation of their HCV Viral load until SVR12, death, lost to follow up, medical decision to exit the study or transfer out, whichever comes first.

The study will assess implementation of new recommended HCV-curative regimens in real world settings, not specific new drugs. The specific treatment regimens used, including new DAAs, will be selected in accordance with current WHO, international and national recommendations and protocols (18-20). Of the new DAA's, only drugs registered and available in India will be used in accordance with international and national recommendations and protocols.

II. Study population

The study population will include HIV infected patients from Manipur state diagnosed with chronic hepatitis C (viral load HCV positive) meeting eligibility criteria. These patients will be directly identified in the MSF sites.

III. Sample size

The sample will exhaustively include all patients meeting the inclusion criteria in each site for a period of two years. Currently MSF, in collaboration with NACO has approximately 1600 adult patients being actively followed up for HIV care within Manipur. The overall rate of HIV-HCV co-infection, based on HCV serological screening performed to date is approximately 27%. Assuming 80% of serologically positive patients have chronic hepatitis C, the minimum sample size expected for this study will be 345 patients.

IV. Sampling design

The sample will exhaustively include all patients meeting the inclusion criteria in each site for a period of two years.

Inclusion and Exclusion criteria:

When the results of VL tests become available, all patients over 18 years will be invited to participate in the study, if they fulfill eligibility criteria. Inclusion is not linked with eligibility for HCV or HIV *treatment.* A criterion of non-eligibility to treatment is not considered as inclusion or exclusion criteria for study participation[1].

The individual may withdraw consent at any point during the study with no impact on treatment and care.

[1] Eligibility for study inclusion and HCV treatment are different. The study will also include HCV positive patients who do not receive treatment either due to non-priority of treatment or presence of clinical contraindications. (These patients may receive treatment at a later date). This is intended to fulfil secondary objectives 'i' and 'j'. However patients will receive standard HCV treatment and care in the event of non-eligibility to the study or refusal to participation in the study.

Table 1: Study participant eligibility criteria

	Eligibility criteria for study inclusion	***Eligibility criteria for HCV treatment***
Inclusion criteria	• *HIV/HCV co infection independent of the stage of liver disease* • *Over 18 years of age* • *HCV viral load greater than 12UI/mL* • *HIV positive status confirmed by the national and MSF algorithm* • *Able and willing to provide informed consent* • *Willing to comply with all study procedures*	***Clinical Review*** • *Confirmed HCV infection* • *HIV infection controlled on ART or asymptomatic HIV infection with CD4 count>500/ µL in the absence of ART* • *Controlled drug use* • *Controlled opportunistic infections* • *Hemoglobin threshold: 9 g/dL* ***Psychosocial Review*** • *Adherent to HIV treatment and appointments* • *Controlled use of substances (if relevant)* • *No evidence of uncontrolled psychiatric disorder*
Exclusion criteria	• *Individual aged less than 18 years* • *Individual does not consent to be part of the study.*	***Clinical Review*** • *Evidence of hepatocarcinoma* • *Advanced/terminal heart or pulmonary or renal or other disease* • *Active, uncontrolled opportunistic Infections* • *First 3 months of a new ART regimen (unless minor ARV change for toxicity);* • *Pregnancy or planning pregnancy in following months, unwillingness to use contraception* *Breastfeeding women.*
		Psychosocial Review
		• *Unwillingness of the patient to adhere to HCV treatment & ART* • *Uncontrolled severe psychiatric disorder.* • *Unstable substance use*

V. Statistical methods to be used

Demographic and baseline characteristics of the patients will be described using summary statistics (mean with their 95% CI or median with inter-quantile intervals for continuous data; frequency and proportion for categorical data). It will include (but not be restricted to): - age - sex – treatment received - clinical signs at inclusion, haemoglobin and other biological measures at inclusion.

Depending of the distribution of the data, different tests and reports of results will be provided. Distributions of categorical variables between two groups will be compared with the Fisher's exact test or chi-squared. Comparisons of continuous variables will be performed with a 2-sample t-test when the variable shows a normal distribution; otherwise, a Wilcoxon rank sum test will be performed.

Risk factors associated with the different outcomes will be assessed using univariate and multivariate models. Epidemiological and clinical relevant variables will be included in the multivariate model to obtain an adjusted measure of association.

To assess the APRI performance, compared to Fibroscan®, for assessment of liver fibrosis among HIV/HCV coinfected individuals, sensitivity, specificity, negative predictive value, positive predictive value will be computed, across liver fibrosis scores.

We will use an alpha level of 5% for all statistical tests. All statistical tests will be two-sided. All efficacy endpoints will be analyzed on the intent-to-treat (ITT) population during the cohort study (every year). The ITT population will include all subjects who were initiated under treatment (at least one prescription of HCV treatment).

Analyses will be performed using STATA, version 13 (StataCorp, College Station, Texas).

VI. Tools

Demographic and clinical data is currently collected via case reporting forms (CRFs) and laboratory forms. Data is collected on: individual baseline information, clinical evaluation information, laboratory results and treatment information. The CRFs are presented in Appendix 1-4. (All forms are currently being used for recording clinical management of new HCV patients entering treatment). De-identified data is entered in to an electronic database and used for reporting and monitoring and evaluation of HCV treatment activities.

Study participants will be linked through unique study numbers assigned to study participants. Personal identifier information will be recorded only on CRFs, and will be kept separately to maintain confidentiality.

Question 21 on CRF1 (Appendix 2) will identify patients who have consented to be part of the cohort study.

21_Did the patient sign an informed consent for the cohort study ☐ Yes ☐ No ☐ DK

In the event of a serious adverse event occurring, the Indian national "Suspected Adverse Drug Reaction Reporting Form" will be completed. This can be found at the following web link:

http://www.ipc.gov.in/PvPI/ADRReportingForm.pdf

VII. Implementation / Operational Plan

As outlined within the introduction, MSF has been active in Manipur since 2004 and now has ART centres in Churachandpur, Chakpikarong and Moreh providing care and treatment for over 1600 patients living with HIV/AIDS (PLWHA). As part of MSF's commitment to provide high quality care to PLWHA, treatment of HCV for HIV co-infected individuals was commenced in 2015. As such, the treatment activities, on which this prospective observational study will be based, are a part of MSF's on-going routine operational activities.

The following describes these current operational activities in addition to supplementary activities which will be incorporated for the conduct of a scientifically rigorous prospective observational study.

Participant's recruitment

Serological screening for HCV has been routinely undertaken on all confirmed HIV positive patients entering within the MSF facility since 2012. Serological rapid tests, approved by Indian regulatory authorities have been used for this purpose. During 2015 confirmation of active HCV infection was commenced within the program with Real time PCR for virology on a Roche platform within Babina private laboratory, Imphal.

Patients with a HCV viral load detectable and a co-infection with HIV will be proposed to join the study, if they fulfil eligibility criteria for the study. Patients eligible to participate in the study will receive comprehensive information about the treatment regimen and the study, its risks and benefits, the study's objectives and procedures.

In addition to the verbal information, a Patient Information Sheet concerning the study will be provided, with contact information (Appendix 5).

For individuals who are eligible and interested in participating, the health staff will obtain informed consent from the individual to participate to the study (Appendix 5) Consent form and Patient Information Sheets will be translated and back translated in the local languages most adapted to the patients, where possible.

Patients will be informed that they will be free to withdraw from the study at any time with no impact on access to care and treatment.

The procedures concerning the study information and the informed consent will be performed by trained study staff, with a background in nursing or counselling, and who are not directly involved in the patient's care.

Patient initial interview

Following the consent process, a structured initial interview will be administered by trained study staff to each patient to collect background information. The questionnaire will include closed questions and will take approximately 30 minutes.

Issues addressed during the interview will be:

- Socio-demographic information: age, sex, marital status, occupation

- Medical background and comorbidities
- Screening for depression
- HIV status, care and treatment history
- HBV history including tests and vaccination history
- Potential substance consumption abuse (alcohol, other drugs)
- Additional important health problems and treatments
- Behavioral risk factors for HCV infection

The data will be collected through standardized case report form (CRF1), see Appendix 1.

Initial interview will be performed at the inclusion visit.

For the follow-up consultations, a second questionnaire (CRF 2, Appendix 2) will collect information on the day of the consultation. In addition, during this consultation, questions will be asked on new comorbidities or new complaints.

Clinical examination

Each patient included will undergo a clinical exam, conducted by trained medical staff and findings will be recorded on standardized questionnaires (CRF2, Appendix 2). The assessment will include clinical signs of liver decompensation and investigation of potential clinical adverse drug reactions. In the case where adverse events have led to a change in treatment or treatment interruption, a specific CRF will be filled (CRF AE, Appendix 4).

Laboratory Procedures

All laboratory tests are performed using universal precautions and all specimens labelled with patient unique I.D and date of collection.

a). HCV viral load

HCV viral load is used to confirm diagnosis of chronic HCV infection. It is also used to evaluate patients' eligibility for treatment. Finally, viral load is the key measure to assess response to antiviral treatment.

b). HCV Genotyping

A HCV Genotype determination is performed to help determine the appropriate length and type of treatment in accordance with the most current WHO, Indian or other International guidelines. Genotyping has been performed by RT-PCR and sequencing with specimens sent to Babina laboratory in Imphal, Manipur. Due to concerns regarding the ability for this laboratory to differentiate between Genotype 1 and Genotype 6 with the given genotyping platform being used, further DBS samples will be sent to a Reference laboratory for quality control of genotype determination.

c). Other laboratory tests

The pre-treatment assessment and the follow-up of patients during treatment will require other laboratory tests at different time points, according also to the treatment regimen. The minimum schedule is presented in Table 3.0 of Appendix 3.

Laboratory tests are performed on site in Churachandpur with specimens sent to a reference laboratory in Babina for genotyping and viral load determination. Results of the different tests are collected on a specific CRF (CRF Lab results Form Appendix 3).

Elastography

Staging of the liver fibrosis and the calculation of the Metavir score will be determined by the elastography, using Fibroscan® 402 (Echosens, Paris) Training of field doctors in the use of this machine was conducted by trainers from Echosens during December of 2015.

The results will be interpreted according to the manufacturer recommendations. Results, including the validity score of the procedures which will be registered on the CRF Bio.

Plasma storage

Manipur will store plasma from consenting patients. Plasma is required in order to differentiate resistance profiles of the new DAA regimes, of which little is known. Additional tests on the plasma may be conducted in the case of failure of treatment, comparing viral profile before treatment to latter ones. In addition, as the transmission pathways are unclear, tests may be needed to differentiate relapse from re-infection during or after treatment. Therefore, the storage of samples will give the possibility to adapt medical care to the patients and adapt further the treatment regimen if indicated. Plasma will be stored for a period of five years.

Consent for the storage of plasma is included on the main consent form with a separate permission required. The patient will be explained the purpose of the plasma storage and asked to sign and additional section of the consent form if they agree for their plasma to be stored.

Disposal of samples

The disposal of hazardous waste will be in accordance with national regulations[2]. Infectious waste will be packaged in an approved manner for transfer to a facility with incineration capacity. Steam autoclaving is the preferred method of decontamination. Waste will be placed in autoclavable plastic bags and color coded according to whether it is to be autoclaved and /or incinerated. As per Schedule-I of the national guidelines, samples for disposal will be safely transported to a bio-medical waste treatment facility for final treatment, processing and disposal.

Counselling Support

Counselling is part of routine medical care for all participants in the study. The MSF project sites in Manipur already have a strong counselling service as part of the HIV/ART program. Counsellors have received additional training on HCV related issues and offer regular support to patients receiving HCV treatment. Additionally counselling staff have been trained on qualitative and quantitative indicators to assist in the monitoring of adherence.

[2] Bio-medical waste management rules, 2016. http://pibphoto.nic.in/documents/rlink/2016/mar/p201632701.pdf

HIV follow-up

The HIV follow up is included with the schedule of the HCV care visit. The ART and other necessary treatment are prescribed during these common consultations. Biological follow up concerning the HIV status of the patients is followed. The ART and HCV treatments may be adapted due to potential drug interactions. HIV follow-up and ART prescription are done following the national and international protocols.

Treatment

HCV treatment is being provided for HIV co-infected patients meeting the treatment eligibility criteria. The observational study will assess and monitor the use of recommended HCV treatment regimens consisting of medications registered and available within India. In the absence of a current Indian national protocol containing the new DAA drugs, the treatment regimens will follow the current recommendations of WHO and equivalent national or international expert advisory body such as the INASL and EASL.

The choice of regimen will be made, in accordance with recommendations after considerations of the patient's characteristics (genotype, liver staging etc.), history of past treatment, associated co-morbidities, current medications and any relative or absolute contraindications.

The currently recommended treatment regimens that will be used are as follows:

Table 2: Treatment regimen for patients without cirrhosis

	Sofosbuvir + Daclatasvir	Sofosbuvir + Ledipasvir	Sofosbuvir + Ribavirin
Genotype 1	12 weeks	12 weeks	
Genotype 3	12 weeks		24 weeks
Genotype 6	12 weeks	12 weeks	

Table 3: Treatment regimen for patients with cirrhosis

	Sofosbuvir + Daclatasvir	Sofosbuvir + Daclatasvir + Ribavirin	Sofosbuvir + Ledipasvir	Sofosbuvir + Ledipasvir+ Ribavirin
Genotype 1	24 weeks	12 weeks	24 weeks	12 weeks
Genotype 3		24 weeks		
Genotype 6	12 weeks		24 weeks	12 weeks

Treatment regimens to be used will be reviewed and adjusted to remain consistent with international guidelines which may be released after the commencement of the study. Additionally, only DAA's registered and available for use in India will be used within any treatment regimens prescribed. Although Pegylated interferon remains available in India, this will not be used in any treatment regimens.

Although none of the three currently available DAA's are contra-indicated for use with any Antiretroviral therapy currently being used in India, some combinations are known to require dosage adjustments. All doses of DAA's prescribed will be in accordance with last

recommendations of the experts and of the manufacturers. It is not anticipated that ART regimens will be required to be altered as a result of the use of new DAA medications

Response to treatment and toxicity are monitored by regular laboratory testing as outlined in table 3.0 of Appendix 3 in this research protocol.

Follow-up

HCV follow up visits will follow laboratory schedule as outlined in appendix 3. HCV follow up visits will be integrated into the HIV clinic visit schedule as to minimize the number of visits to the clinic. Patients will be educated about side effects & should return to the clinic at any time if problems arise. In the event of non-adherence to a scheduled visit, the particiapant will be contacted through means concented by the participant at the time of enrolment.

Drugs

All drugs to be used are pre-qualified by WHO, MSF and licensed for use in India by Indian regulatory authorities. In case of generics, only drugs from MSF-prequalified maufactures will be used. MSF's qualification of pharmaceutical products follows WHO norms. Procurement of the drugs will follow the MSF standard, in accordance with the national regulations. All products will be stored in a secured area, under storage conditions recommended by the manufacturer and in accordance with applicable regulatory requirements. Following are manufacturer details of drugs to be used for the study

Safety assessment

The study will collect and report on standardized forms Adverse Events (AE) and Adverse Reactions (AR) leading to death, modification or discontinuation of treatment (See CRF AE and Appendix 4). As recommended, tolerance and monitoring for adverse events associated with the use of the proposed regimen will be searched for at each visit through clinical and laboratory examination (i.e. alanine transaminase, creatinine, haemoglobin). Monitoring of adverse events will follow the manufacturer recommendation. Treatment will be adjusted according to the recommendations of the manufacturers and of the national and international institutions or MSF medical guideline. The study team will notify immediately and within 48 hours all AE that led to treatment modification, to the study site principal investigators through a specific form (CRF AE, Appendix 4). In case of serious adverse event or reaction, the study principal investigators will be informed within 48 hours and then inform within seven days to the study Scientific Committee and the local Ethical Review Board. In the event of a serious adverse event occurring, the Indian national "Suspected Adverse Drug Reaction Reporting Form" will be completed. This can be found at the following web link: http://www.ipc.gov.in/PvPI/ADRReportingForm.pdf. All AE or AR considered as serious AE or leading to a change in the treatment, from the date the patient starts the HCV treatment, during the entire treatment follow-up, and up to four weeks after the intake of the last regimen drug should be reported. In addition, serious AE that occur after this period and during the post-treatment follow-up should be reported if the event is suspected to be related to any of the drugs included in the regimen. The decision to postpone, modify or to interrupt/discontinue the regimen will be left at the discretion of the clinical team following discussion with the study principal investigators and with the medical HCV referent of the

section. For all AEs, patients will receive the best care available and will be followed up until resolution.

List of potential adverse events and their management are provided in appendix 6

Medical advisory panel
The study is supported by a medical co-ordinator, study principal investigator, based in the Delhi Co-odination of MSF. Regular program committees will be held to discuss medical or program issues. The program committee also has a access to a team of experts, including clinicians and virologists specialized on HCV treatment, who will advise on the individual patient management and treatment decisions in case of specific conditions. The program committee and the experts will have access to coded clinical and biological data collected during the study, as appropriate, from patients requiring specialized care.

Standardized documents with the required information will be used. The review and patient decision will also involve closely the MSF medical team and medical coordinator in each study site. Recommendations will be based on patient's records data, on current international and national recommendations and on the availability of access to drugs in the country.

VIII. Study Outcome Measures

The primary endpoint is the proportion of patients with sustainable viral response at 12 weeks, among patients who initiated HCV treatment (irrespective of regimen).
The endpoint will be plasma HCV-RNA response at week 12 after end of treatment (EoT). Treatment success is defined as viral load as either undetectable or below a concentration of 12UI/mL Treatment failure is defined as either a detectable viral load 12 weeks after cessation of treatment, death or loss to follow-up, medical decision to exit the study or transfer-out.

The following definitions will be considered:
In case of viral load detectable 12 weeks after end of treatment, the outcome will be considered as treatment failure.

- Deaths will be recorded by the medical teams, notified by a close relative or friend or reported by a tracing team (for programs implementing such strategy).
- Loss to follow-up is defined as two months after a planned date of appointment withoutcontact, among patients who were not dead or transferred out.
- Transfer out is defined as a patient who has been transferred to another medical facility or consultation and for whom the treatment outcome is not known, without the possibility to continue the HCV follow up in the study site. Patients that require to be transferred out will be informed that it is very unlikely that they can continue HCV treatment. In case of possible return to the study site, the patient may be proposed again to enter in the study and informed consent will be sought again. The same identification number will be used.
- Exit due to medical reason is defined as a cessation of follow decided by the clinicians, in collaboration with the patients, due to other more urgent medical needs.

Secondary endpoints:

- Proportion of patients included in the cohort by socio-demographic characteristics: age group, sex, occupation, marital status, risk factors of HCV exposition

- Proportion of patients included in the cohort by clinical and biological characteristics: genotype, HCV viral load, liver fibrosis staging, presence of ascites, HIV WHO staging at baseline, CD4 count and HIV viral load prior to HCV treatment, HBV status, Child pugh score, hematology, biochemistry
- Proportion of patients with HBV infection defined as a positive RDT with HBV AgS diagnosis
- Distribution of liver fibrosis stage among included population
- Proportion of patients with HCV treatment initiated
- Proportion of SVR 12 among the patients having completed HCV treatment.
- Proportion of patients with SVR 12 stratified by regimen and by genotype
- Proportion of patients with SVR 12 stratified by site
- Mortality among the patients in the HCV cohort overall, and among patients who initiated treatment or among patients without treatment initiation
- Proportion of defaulters during before, during and after treatment
- Proportion of patients transferred out, and for whom medical decision to interrupt HCV follow up has been taken
- Frequency and type of demographic, clinical and biological risk factors associated with treatment outcomes: age , sex, liver fibrosis stage, child pugh score, genotype, clinical symptoms, comorbidities with HBV infection , addiction
- Concerning the safety of HCV treatment: Frequency and type of treatment-related side effects or events that cause modification of dosage of the HCV treatment
- Frequency and type of treatment-related side effects that cause permanent interruption (discontinuation) of the HCV treatment
- Concerning the feasibility of HCV treatment: Proportion of patients included in the cohort but non eligible to treatment at the first assessment, by clinical and biological characteristics, over time (yearly eligibility assessment): HCV viral load, liver fibrosis stage, child pugh score, presence of ascites,HIV viral load
- Frequency and type of demographic, clinical and biological risk factors associated with non-eligibility to treatment: age , sex, fibrosis stage, child pugh score, genotype, clinical symptoms, biological anomalies, comorbidities with HBV infection, addiction
- Frequency of reporting of missed doses by patients

IX. Data management

Data Collection Tools

Paper based questionnaires and lab forms will be used for collection of individual baseline information, clinical evaluation information, laboratory results and treatment information. The different CRFs are presented in Appendix 1 and 2. Other data collection tools may be used in the laboratory. Questionnaires will be pre-tested prior to initiation of data collection. Study forms will be linked through unique study numbers assigned to study participants. Personal identifier information will be recorded on separate forms, and will be kept separately to maintain confidentiality.

Listing of data collection questionnaire (Appendix 1 & 2):

- Baseline information
- Consultation form
- Comorbidities form
- Biological form

- Adverse Events form

In case of adverse events, specific reports will be filled, initial and follow up reports (Appendix 3).

Prior to the inclusion in this cohort, the patient may be under medical follow up for his HIV and / or HCV care. These data are collected on different tools. Some information would be used for this study. As example, the CD4 count at enrolment will be found in the HIV database used in the HIV care facility. The source of the data is specific to each site. The data will be reported to the HCV database.

Data Management and Monitoring

The site investigators are responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. The investigators will maintain adequate case histories of study subjects, including accurate case report forms (CRFs) and source documentation. Data will be collected, stored, cleaned and analyzed by study staff. Participant names will not be entered in the database. Data from the CRFs will be entered on the database designed by MSF/Epicentre for the management of patients with HCV. Coded data will be exported from the different site's sources and merged into a single dataset in Stata for statistical analysis. The original CRF could be retrieved from unique identification numbers.A copy of the database will be sent and kept at New Delhi coordination and password protected. Datamanipulation and analyses will be performed using Stata® (College Station, Texas, USA).

Data Quality Control

For each study participant, all data collected during the study will be recorded into individual patient case report forms (CRFs). Data entry will incorporate consistency, range and other checks. In each study site, a minimum of 50 patient files per month will be reviewed to assess accordance with the data entry in the database. The site investigator will run regular additional checks. The quality of data collection and study record keeping will be routinely monitored by the site investigator. Unanticipated problems and adverse events must be reviewed by the site investigators and actions taken accordingly. A Report on data quality will be produced by the site investigators and shared with Principle Investigator. Study investigators, staff and laboratory personnel will all be appropriately trained regarding the protocol requirements and a standard operations manual will be available.

Data sharing

Data are the property of the patients and of the Ministry of Health, Govt. of India. MSF is willing to make these data (anonymized coded / anonymized as applicable) available to MoH if they want to perform further research on them. MSF's large repository of research data, with routinely collected data can potentially be of value to public health researchers. MSF recognizes the ethical imperative it has to share its data transparently, and in a timely manner for the greater public-health good.

For external partners, any request of access to data will be assessed and will follow the ethic and regulatory procedures of India.

Quality Assurance and Quality Control Protocols

X.

- All staff within project site have received comprehensive training on the care and management of HCV infection.
- All staff directly involved in the recruitment, consenting, data collection and data management for this study will receive comprehensive training in the conduct of research in full compliance with the Declaration of Helsinki (21) and International Ethical Guidelines for Biomedical Research Involving Human Subjects (22).
- The quality of data collection and management will be routinely monitored by the onsite data manager and cross-checked by the MSF epidemiologist based in Delhi.
- Data management, monitoring, quality control, data sharing and data analysis in the Manipur sites will be in accordance with ethical standards of confidentiality and anonymity. Data will be collected, stored, cleaned and analyzed by study staff. Participant names will not be entered in the database. Data will be stored securely and password protected, with de-identified data made available to NACO on request. Regular reporting of study progress and patient outcomes will be provided to NACO at an agreed interval.
- In addition to the performance of internal and external quality control procedures set up by each laboratory and to ensure quality control of the different HCV tests, a proficiency testing will be proposed to the laboratories using characterized samples. This procedure will be repeated on a regular basis, and will include panels of samples with different viral concentration and different genotypes.

XI. Ethical considerations & respondent protection measures

This protocol, recruitment materials, informed consent forms and questionnaires, contained in Annexes have been submitted for ethical review to the MSF Ethical Review Board and received ethical clearance. The protocol has also received ethical clearance from Regional Institute of Medical Sciences, Lamphelpat, Imphal, India on 23rd March 2016. This study has been approved by National Aids Control Organization, New Delhi (nodal body of Ministry of health, Govt. of India) on 3rd Nov 2016

a). Risks to participants

Study participation is not expected to convey any major risks to patients. The specific procedures of the study only concern data collection and their coded use. The interview to assess treatment adherence and to identify potential risk factors associated with treatment failure are conducted as part of the patient clinical management, the researches will access thecoded data of those consenting to be part of the study. There is no additional data to be collected that is already not part of the clinical management of these patients.

Similar to blood taking during routine clinical care, blood taking for the current care or for storage may cause a slight discomfort.

b). Direct Benefits for participants

HCV care and treatment are not yet available in the MoH structures. Each study participant will benefit from diagnosis and treatment for the HCV infection. Participants will receive direct feedback on the success of their current treatment.

c). Indirect Benefits for participants

The study results are expected to support optimization of HCV patient management, co-infected by HIV and inform optimization of treatment regimens, in limited resource settings. Participants will indirectly benefit from the expected effects of the study findings on future HCV care and follow-up.

d). Protection from risk

There will be no electronic link between the Identification number and the name of the patient as names will not be entered in the database.

e). Consent form

Consent form has been approved by the MSF Ethics review Board (ERB) and will be translated into the 5 main local languages in Manipur State, as deemed possible.

A trained clinician/counselor will administer the information sheet verbally, encouraging questions. When it is deemed the subject has a good understanding they will be asked to sign the consent form. The subject will sign the informed consent document prior to any study-related analysis of their data. Subjects will be given the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The participant, if functionally illiterate, may sign the consent by marking with a thumbprint on the signature line. The presence of a witness who will also have to sign the document will also be encouraged. The subject may withdraw consent at any time throughout the course of the study. A copy of the signed informed consent document will be given to subjects for their records. The rights and welfare of the subjects will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline to participate in this study.

XII. Timelines

The study has an estimated start date of December 2016, and with the end of inclusions being December 2018. Table 2 provides a breakdown of the study timetable for the Manipur sites.

Table 4: Study Timeframe

Activities	Time
Protocol development and submission to MSF Ethical Committee	Jan 2016-April 2017-
National Protocol developments and submission to NACO	April 2016 – Nov 2016
Field preparation and pilot study	Nov-Dec 2016
Recruitment	May 2017 to May 2019
Follow-up patients	May2017 toAug 2019
Field data management	May 2017 to Aug 2019
Regular Data analysis and Monitoring_ interim reports	May 2016 to Aug 2019
Final report (including outcomes)	Dec 2019
External communication	Jan 2020

7. FACILITIES IN TERMS OF EQUIPMENT, ECT, AVAILABLE AT THE INSTITUTION / ORGANISATION FOR THE PROPOSED INVESTIGATION

The treatment activities on which this observational study will be performed are on-going programmatic activities within the MSF clinics located in Churachandpur, Chakpikarong and Moreh. Within these locations MSF in partnership with NACO, operate as outpatient facility with associated on-site laboratory capacity. Each of these laboratories is capable of performing routine biochemistry, haematology, CD4 counts, serological testing HIV / HCV / HBV / Syphilis and Microscopy. Each also has a GeneXpert machine. In addition a mobile Fibroscan machine is present and can be moved between these sites.

Each clinic is computerised with password protected access to currently used data collection tools

No additional equipment will be required to conduct the observational cohort study

8. BUDGET REQUIREMENT WITH DETAILED ITEM-WISE BREAK-UP AND FULL JUSTIFICATION

As the study is a prospective observational study of MSF's comprehensive package of care currently being provided for people living with HIV / AIDS within Manipur, minimal additional costs outside of MSF's normal operational costs will be required.

There will be no requirement for additional funding from NACO

A. BUDGET FOR PERSONNEL: **Nil budget requirement**

Justification:
The coordinating team at Delhi will be responsible for the preparatory activities, training, conduct of meetings and monitoring of the study. They would be responsible for coordinating the research activities, data management and report writing.

The investigators appointed at the site will enroll the participants, collect data, organize local meetings, follow-up cases and conduct the study activities at each site in conjunction with the coordination team.

All of the coordinating staff and field staff, who will be involved in the conduct of this study, are currently full time employees of MSF OCA India responsible for the conduct of MSF's routine programmatic care and treatment activities. There will be no further additional staff requirements for the conduct of this study.

B. BUDGET FOR MEETINGS AND TRAINIGS: **Nil budget requirement**

Justification:
All of protocols, tools, IEC material and counselling materials have been developed by current members of the coordinating and field teams to support routine programmatic activities. Similarly trainings have been delivered in study sites by coordinating team members and senior field team members to support routine programmatic activities. Additional trainings for team members involved in the conduct of the study have been incorporated into the routine field trainings.

C. BUDGET FOR CONSUMABLE MATERIALS: **Total requirement: 1,00,000 Rs**

Table 5: Proposed budget for consumables

Printer Toners, Software, Stationeries including printing of forms and IEC material	BUDGET (In Rupees)			
	Year 1	Year 2	Year 3	Total
For two sites	50000 (25,000 for each site)	50000 (25,000 for each site)	50000 (25,000 for each site)	1,50,000

Justification:
Budget for printing of informed consent and data collection forms, IEC material and Counseling flip charts and other essential stationeries needed for functioning of the project.

D. BUDGET FOR TRAVEL: ***Nil budget requirement***

Justification:
The coordinating team in Delhi regularly conducts supervisory visits to the sites to monitor the conduct and quality of our routine care and treatment activities. The regular monitoring of the study conduct and data collection will be incorporated into these routine visits. The field team including the LRI co-investigator lives within the area of the study sites and as such no additional travel costs will be incurred.

The Principle investigator and coordinating team are located within Delhi and such no travel costs will be incurred for the conduct of required meetings with NACO during the course of the study.

E. BUDGET FOR OTHER COSTS: **Total requirement : 2,50,000 Rs**

Table 6: Proposed budget for dissemination costs

Item wise by category	BUDGET (In Rupees)			
	Year 1	Year 2	Year 3	Total
Printing of report and research brief			50,000	50,000
Dissemination of study findings			1,00,000	1,00,000
Publication or by presenting data in Conferences and Seminars on the subject			1,00,000	1,00,000
total	Nil	Nil	2,50,000	2,50,000

Justification:

This budget involves cost towards developing and printing of the final report, the draft of which would be shared with the investigators and coordinators of the study. For dissemination of information in the scientific community, the data will be presented in workshop attended by collaborators, researchers, policy makers, programme managers and PLHA group representatives. Cost that would be incurred by investigators to attend conferences/seminars or publish the manuscript based on data collected is budgeted under this head.

TOTAL COSTS FOR LRI

Table 7: Proposed total budget

Item wise by category	BUDGET (In Rupees)			
	Year 1	Year 2	Year 3	Total
A	0	0	0	Nil
B	0	0	0	Nil
C	50,000	50,000	50,000	1,50,000
D	0	0	0	Nil
E	0	0	2,50,000	2,50,000
total	50,000	50,000	3,00,000	4,00,000
5% OVERHEADS	2,500	2,500	15,000	20,000
Total	52,500	52,500	3,15,000	4,20,000

REFERENCES

1. Hanafiah KM, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: New estimates of age-specific antibody to hepatitis C virus seroprevalence. Hepatology. 2012;(Cdc):1–48.

2. WHO. Global policy report on the prevention and control of viral hepatitis in WHO Member States. Geneva; 2013.

3. Sands A, Harmanci H, Easterbrook P. Challenges and Priorities in the Management of HIV/HBV and HIV/HCV Coinfection in Resource-Limited Settings. Seminars in Liver Disease. 2012. p. 147–57.

4. Lavanchy D. Evolving epidemiology of hepatitis C virus. Clin Microbiol Infect. 2011 Feb;17(2):107–15.

5. Deng L-P. Impact of human immunodeficiency virus infection on the course of hepatitis C virus infection: A meta-analysis. World J Gastroenterol. 2009;15(8):996.

6. Limketkai BN, Mehta SH, Sutcliffe CG, Higgins YM, Torbenson MS, Brinkley SC, et al. Relationship of liver disease stage and antiviral therapy with liver-related events and death in adults coinfected with HIV/HCV. JAMA. 2012;308(4):370–8.

7. Anderson JP, Tchetgen Tchetgen EJ, Lo Re V, Tate JP, Williams PL, Seage GR, et al. Antiretroviral therapy reduces the rate of hepatic decompensation among HIV- and hepatitis C virus-coinfected veterans. Clin Infect Dis. 2014 Mar;58(5):719–27.

8. Hadigan C, Kottilil S. Hepatitis C virus infection and coinfection with human immunodeficiency virus: challenges and advancements in management. JAMA. 2011 Jul 20;306(3):294–301.

9. Chen T-YY, Ding EL, Seage Iii GR, Kim AY. Meta-analysis: increased mortality associated with hepatitis C in HIV-infected persons is unrelated to HIV disease progression. Clin Infect Dis. 2009 Nov 15;49(10):1605–15.

10. Greub G, Ledergerber B, Battegay M, Grob P, Perrin L, Furrer H, et al. Clinical progression, survival, and immune recovery during antiretroviral therapy in patients with HIV-1 and hepatitis C virus coinfection: the Swiss HIV Cohort Study. Lancet. 2000 Nov 25;356(9244):1800–5.

11. Vivithanaporn P, Nelles K, DeBlock L, Newman SC, Gill MJ, Power C. Hepatitis C virus coinfection increases neurocognitive impairment severity and risk of death in treated HIV/AIDS. J Neurol Sci. 2012 Jan 15;312(1-2):45–51.

12. Pulido F, Hill A, van Delft Y, Moecklinghoff C. Impact of hepatitis C co-infection on response to antiretroviral treatment. AIDS Rev. 14(2):124–31.

13. UNAIDS/WHO. Global report: UNAIDS report on the global AIDS epidemic 2013. Geneva; 2013.

14. NACO/ Department of AIDS Control Ministry of Health & Family Welfare. Annual Report 2011-

2012. New Delhi; 2011.

15. NACO/ Department of AIDS Control Ministry of Health & Family Welfare. Antiretroviral therapy guidelines for HIV -infected adults and adolescents. 2013.

16. NACO/ Department of AIDS Control Ministry of Health & Family Welfare. Annual report 2013 [Internet]. 2014 [cited 2014 Sep 24]. Available from: http://www.naco.gov.in/upload/2014 mslns/NACO_English 2013-14.pdf

17. Solomon et el. Burden of hepatitis C virus disease and access to hepatitis C virus services in people who inject drugs in India: a cross-sectional study: Sunil Solomon et al. Lancet Infectious _SJDisease: December 2014

18. WHO: Guidelines for the screening, care and treatment of persons with chronic Hepatitis C; Policy Brief: February 2016

19. Indian National Association for Study of the Liver (INASL) Guidance for Antiviral Therapy Against HCV Infections in 2015: journal of Clinical and Experimental Hepatology: September 2015

20. EASL Recommendations on Treatment of Hepatitis C 2015: Journal of Hepatology; March 2015

21. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects [Internet]. 2013 [cited 2014 Sep 25]. Available from: http://www.wma.net/en/30publications/10policies/b3/index.html

22. CIOMS. International Ethical Guidelines for Biomedical Research Involving Human Subjects. Geneva; 2016.

Appendix 1: Filled on enrolment in HCV Cohort
CRF 1 _Interview: Baseline information

1_Surname: _____ 2_Forename: _____(**not to enter in the database**)
Patient's file N° _____

3_**Identification cohort Number**: __ __ __ __ __ 4_ID Key __ __ (to be filled by data clerk)

10_Date of enrolment: ____ -____ -_____ *(dd-mm-yyyy)* 11_Site of Enrolment: _____	12_Name of interviewer: _____ 13_Doctor / Clinical Officer / Nurse / Others	14_Data clerk initials: _____ 15_Date of data entry: ____ -____ -_____ *(dd-mm-yyyy)*

Instructions: *Complete all the questions, considering the skips, next to the answers*

If the answer is unknown, tick the box DK (don't know) or use DK for missing day, month or value

NURSE: Consent & Registration (go thru the tracing form in back of patient file and update with patient)

21_Did the patient sign an informed consent for the cohort study ☐ Yes ☐ No ☐ DK

Did the patient:
- 22_ Consent to be contacted by phone ☐ Yes ☐ No ☐ DK
- 23_Consent to be visited at home ☐ Yes ☐ No ☐ DK
- 24_Consent to contact relatives ☐ Yes ☐ No ☐ DK

Is the patient enrolled?

25_ In an HIV cohort? Name of HIV register FUCHIA 26_ FUCHIA number _____

27_ Other cohort? Name of register Patient's File 28_ pt file number (data clerk refer to top of form)

NURSE: Hepatitis C Status *(from Fuchia summary sheet in front of patient file)*

Result of the HCV **serologic test**: 101_Date of the test: _____ -_____ -_____ *(dd-mm-yyyy)*

102_Type of Test: ☐ ORAQUICK ☐ TRI-DOT ☐ ELISA Laboratory ☐ Others ☐ DK

103_Result: ☐ Positive ☐ Negative ☐ DK

Result of the **HCV virology test** 104_Date of the test: _____ -_____ -_____ *(dd-mm-yyyy)*

105_HCV Viral Load _____ IU/ mL

NURSE: Demographic Information

110_Date of birth____ -____ -_____*(dd-mm-yyyy)* **OR** 111_If don't know date of birth: Age _____Years

112_Gender at birth ☐ Female ☐ Male

113_Nationality ☐ Indian ☐ Burmese ☐ Other (specify) _____ ☐ DK

114_What kind of work does the patient do most of the time? *From PSA Form*

☐ Employed ☐ Housework ☐ Pensioner ☐ Student
☐ Unemployed ☐ Other (Specify) _____ ☐ DK

115_What is the current patient's marital status?

☐ Single ☐ Married ☐ Living together ☐ Widowed
☐ Divorced/separated ☐ Other (Specify) _____ ☐ DK

Patient's initials: _____ **Pt file N°** _____/_____ Name of interviewer: _____	Data clerk Initials: _____ Date data entry: ___ -___ -_____ *(dd-mm-yyyy)*

NURSE: Medical baseline information: *(Patient's file or interview)*

120_Height: _____ *(in cm)*

121_Previous HCV treatment: ☐ Yes ☐ No ☐ DK *If No, skip to question 131*

122_Date of the end of the previous treatment (completed or interrupted): ___ -_____*mm-yyyy)*

123_Previous HCV treatment received:

PEG - IFN ☐ Yes ☐ No Boceprevir ☐ Yes ☐ No

Ribavirin ☐ Yes ☐ No Other (Specify) _____

Telaprevir ☐ Yes ☐ No Other (Specify) _____ ☐ DK

124_Outcome of previous treatment:

☐ Completed & cured ☐ Discontinued because of non-response

☐ Completed (unsuccessful) ☐ Discontinued for other reasons ☐ DK

Hepatitis B Status: (*(from Fuchia summary sheet), if no record in file then ask patient*)

131_Received HBV **vaccination**: ☐ No dose ☐ 1 dose ☐ 2 doses

☐ Completed (3 doses or additional boosters) ☐ DK

132_**HBV serologic test**

(Antigen S): ☐ Yes ☐ No ☐ DK *→If No or DK, skip to question 140*

133_ Date of the test: ____ - _____ *(mm-yyyy)*

134_ Result of the HBV tests: ☐ Positive ☐ Negative ☐ DK

NURSE: Comorbidities *(From Fuchia summary sheet in front of patient file)*

HIV status:

140_Previous HIV Tests ☐ Yes ☐ No ☐ DK *→ If No or DK, skip to question 160*

141_Year of the last HIV test: _____ *(yyyy)*

142_Result of the HIV tests: HIV Status: ☐ Positive ☐ Negative ☐ Intermediate ☐ DK

→If HIV status negative, indeterminate or DK, skip to question 160

143_Is the patient followed in MSF HIV cohort? ☐ Yes ☐ No ☐ DK *→If No, skip to question 146*

CD4 count at HIV care enrolment

144_Date of the CD4 count: ___ -_____ *(mm-yyyy)*

145_Result: _____cells /µL ☐ DK

146_WHO HIV staging at HIV care enrolment**)** ____ ☐ DK

147_HIV Treatment: ☐ Yes ☐ No ☐ DK *→ If No or DK, skip to question 160*

148_Date of the **first received** ART treatment: ___ -_____ *(mm-yyyy)*

149_Date of start of the **current** ART regimen: ___ -_____ *(mm-yyyy)*

150_Current HIV treatment: ☐ DK

Drug _____ Daily Dosage _____☐ DK **(dosage not entered**

Drug _____ Daily Dosage _____☐ DK **in the database)**

Drug _____ Daily Dosage _____☐ DK

Drug _____ Daily Dosage _____☐ DK

Patient's initials: _____ **Pt file N°** _____/_____ Name of interviewer: _____	Data clerk Initials: _____ Date data entry: ___ -___ -_____ *(dd-mm-yyyy)*

DOCTOR: Does the patient have one of these comorbidities? *(Patient's file or interview)*

160_Current Tuberculosis		☐ Yes	☐ No	☐ DK
161_History of sickle cell or thalassemia		☐ Yes	☐ No	☐ DK
162_Flukes (Site)		☐ Yes	☐ No	☐ DK
163_Renal impairment	☐ Yes on Dialysis	☐ Yes not on Dialysis	☐ No	☐ DK
164_Diabetes	☐ Yes IDDM	☐ Yes NIDDM	☐ No	☐ DK

DOCTOR: Risk factors of liver complications (present or past) or reinfection *(Patient's interview)*

Does/ Did the patient have one or several of these risk factors:

170_History of Invasive medical procedures (surgery, biopsy, endoscopy…)		☐ Yes	☐ No	☐ DK
171_History of blood transfusion		☐ Yes	☐ No	☐ DK
172_Health care worker (current or past)		☐ Yes	☐ No	☐ DK
173_Prisoner	☐ Current	☐ Past	☐ No	☐ DK
174_Partner with HCV positive status	☐ Current	☐ Past	☐ No	☐ DK

CRF1: To be filled by the Counsellor

Pt file N° _____/_____ Name of interviewer: _____ Date of interview: _____	Data clerk Initials: _____ Date data entry: ___ -___ -_____ *(dd-mm-yyyy)*

To evaluate the risk of depression of the patient: *(from PSA form)* *(data clerk take note of numbering)*

166_Screening Depression PHQ9 Score _____ *(Refer to the specific assessment tool)*

Risk factors of liver complications (present or past) or reinfection *(Patient's interview)*

Is the patient ….?

175_Transgender ☐ Yes ☐ No ☐ DK

176_Man who has ever had sex with a man (MSM) ☐ Yes ☐ No ☐ DK

177_Sex worker ☐ Current ☐ Past ☐ No ☐ DK

Addiction *(Patient's interview)*

180_ To evaluate the alcohol consumption of the patient: **AUDIT** score _____ ***Refer to the specific tool***

190_Has the patient ever used any drug /substance?

☐ Current ☐ Past ☐ No ☐ DK →*If No or DK, skip to the end of the questionnaire*

Which type of drug does the patient use or have they used in the past?

191_Opioids: heroin, morphine, opium…. ☐ Current ☐ Past ☐ No ☐ DK

192_Cocaine: coke, crack… ☐ Current ☐ Past ☐ No ☐ DK

193_Amphetamine: speed, meth….. ☐ Current ☐ Past ☐ No ☐ DK

194_others ☐ Current ☐ Past ☐ No ☐ DK

195_How has the patient use the drug?

☐ Injecting ☐ Smoking ☐ Injecting and smoking combined ☐ Others

198_ Opiods consumption of the patient: Opiods **ASSIST** score _____ ***Refer to the specific tool***

Is the patient attending a harm reduction program? ☐ Yes ☐ No ☐ DK

196_an opioid substitution program or oral substitution treatment (OST)

☐ Current ☐ Past ☐ No ☐ DK

197_a syringe exchange program ☐ Current ☐ Past ☐ No ☐ DK

Appendix 2: Follow up visit form CRF2 _N° Visit: _____

CRF2 _N° Visit: _____

1_Surname: _____ 2_ Forename: _____ (not to enter in the database)

Patient's file N° _____

3_ **Identification cohort Number**: __ __ __ __ __ 4_ ID Key __ __ (to be filled by data clerk)

10_ Date of consultation: ____ -____ -_____ *(dd-mm-yyyy)* 11_ Site of consultation: _____	12_ Name of interviewer: _____ 13_ Doctor / Clinical Officer / Nurse / Others	14_ Data clerk initials: _____ 15_ Date of data entry: ____ -____ -_____ *(dd-mm-yyyy)*

Instructions: *Complete all the questions (one answer per question), considering the skips*

If the answer is unknown, tick the box DK (don't know) or use DK for missing day, month or value.

NURSE : **Follow-up** (only weight to be entered in the database)

Body temp: _____[C°] Blood Pressure: ____/_____ [mmHg] Pulse : ____/min O2 sat : ___ [%]

210_ Weight: _____ *(in kg)*

DOCTOR: **Medical baseline information:**

Liver dysfunction at the clinical examination

220_Presence of ascites ☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ DK

221_ Presence of hepatic encephalopathy ☐ None ☐ Grade I-II ☐ Grade III-IV ☐ DK

Free text for consultation

_____

_____

_____

_____

_____

_____

_____

DOCTOR: 241_ Other or NEW comorbidities ☐ Yes ☐ No ☐ DK if No, skip to question 250

242_ HIV infection ☐ Yes ☐ No ☐ DK (new test done during the current follow up)

243_ HBV infection ☐ Yes ☐ No ☐ DK (new test done during the current follow up)

244_Tuberculosis (new diagnosis) ☐ Yes ☐ No ☐ DK

245_Diabetes ☐ Yes ☐ No ☐ DK

246_ Malaria ☐ Yes ☐ No ☐ DK

247_Dengue ☐ Yes ☐ No ☐ DK

248_Other ☐ Yes ☐ No ☐ DK

249_If yes: specify _____

250_ **New Test results (bio or others)** ☐ Yes ☐ No ☐ DK **if Yes: To fill the Lab Form**

Pt file N° _____ **Visit N°:** ___ Name of interviewer: _____	Data clerk Initials: _____ Date data entry: ___ -___ -___*(dd-mm-yyyy)*

DOCTOR: **HIV Care follow-up**

260_**Is the patient HIV positive** ☐ Yes ☐ No ☐ DK *If No or DK, skip to question 270*

261_CURRENT WHO staging (Site) _____ ☐ DK

262_**HIV consultation outcome**:

☐ Pre ART *(skip to 270)* ☐ ART Initiation

☐ Continuation same dose/ regimen *(skip to 270)* ☐ Modification dose/regimen

☐ Discontinuation due to adverse event *(skip to 270)* ☐ Stop for other reasons ☐ *(skip to 270)*

263_ If HIV Treatment initiation or modification, complete with name and dosage of the new regimen.

☐ DK

Drug _____ Dosage _____ ☐ DK *(dosage not entered*

Drug _____ Dosage _____ ☐ DK *in the database)*

Drug _____ Dosage _____ ☐ DK

Drug _____ Dosage _____ ☐ DK

DOCTOR: **CONSULTATION DECISION**

270_**Is the patient eligible for the HCV treatment or currently under treatment?**

☐ Not assessed /pending results (skip to 280) ☐ Eligible /or already under treatment (skip to 272)

☐ Not eligible ☐ Follow up after treatment (skip to 280)

271_ **Reasons** not eligible currently for treatment (after skip to 280)

☐ Due to ineligible liver stage ☐ Patient's unwillingness to start

☐ Due to liver decompensation ☐ Contraindication to treatment

☐ Pregnancy/breastfeeding ☐ Others**: (Clinical Case Review priority)**

_____

272_ **Decision for treatment or continuation of care**

☐ Waiting List (skip to 280) ☐ Initiation (skip to 274)

☐ Continuation same dose ☐ Modification dose due to weight change

☐ Adverse event/pregnancy leading to Modification ☐ or Discontinuation of treatment(+ fill CRF AE)

☐ Stop for other reasons (skip to 280) ☐ Treatment Finished (skip to 280)

273_If under HCV treatment: How many doses have been missed for the last three days? _____ ☐ DK

(dose = all pills taken at the same moment during the day)

274_ **Treatment** if ***initiation*** or ***modification*** *(do not fill if continuation of same regimen)*

Drug _____ Dosage _____ mg per day / per week

Drug _____ Dosage _____ mg per day / per week

Drug _____ Dosage _____ mg per day / per week

280_ **End of follow up:** ☐ Yes ☐ No *if Yes, skip to question 290*

281_**Date of the next consultation** (***for HCV care***) ___ -___ -_____ *(dd-mm-yyyy)* (go to next page)

290 _Reasons of End of Follow up in HCV care *(end of questionnaire)*

☐ Cured ☐ Transfer out ☐ Medical decision to stop HCV Follow up

☐ Death ☐ Loss of Follow up

To be filled by the COUNSELLOR

Pt file N° _____ **Visit N°:** _____ Name of interviewer: _____	Data clerk Initials: _____ Date data entry: ___ -___ -_____ *(dd-mm-yyyy)*

COUNSELLOR:	**Addiction Follow-up**		
230_ Drug use since last visit	☐ Yes	☐ No	☐ DK
231_ Opioid substitution program (or OST)	☐ Yes	☐ No	☐ DK
232_Alcohol use since last visit	☐ Yes	☐ No	☐ DK

COUNSELLING SESSION (Information entered in Hepa-MUD)

300_Counselling Focus (only one answer is possible, **mark ONLY the main focus of the session**

- ☐ Enhanced Coping
- ☐ Enhanced Motivation
- ☐ Practical Support
- ☐ Family related issues
- ☐ Adherence issues
- ☐ Alcohol use
- ☐ Lifestyle changes
- ☐ Drug Use / Harm reduction
- ☐ Mild/moderate depression
- ☐ Other Mental Health issues
- ☐ Regular follow-up
- ☐ Pretreatment adherence counselling ☐ 1 ☐ 2 ☐ 3
- ☐ DK
- ☐ NS

301_Function rating score _____ (0-10 score) ☐ DK ☐ NS

Complaint rating score **(not entered into database)** _____ (0-10 score) ☐ DK ☐NS

302_Adherence - % of pills taken since last visit _____ ☐ DK ☐ NS

303_PHQ-9 Score **(only if PHQ-9 done at this visit)** _____ (0-27 score) ☐ DK ☐ NS

Validated Depression (score ≥5) **(not entered into database)** ☐ Yes ☐ No

☐ PSA ☐ Start Treatment ☐ End Treatment ☐ SVR-12 ☐ SOS

304_Mental Health or psychosocial issues: _____

Other information (Not entered in Hepa-MUD)

Remarks _____

_____

_____

_____

_____

_____

_____

Special attention_____

_____

_____

Pt file N° _____ **Visit N°:** _____ Name of interviewer: _____	Data clerk Initials: _____ Date data entry: ___ -___ -_____ *(dd-mm-yyyy)*

Review of life style

Alcohol _____

Drugs _____

Were you able to avoid tobacco _____

_____

Remarks_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Special attention_____

_____

_____

DOCTOR : 199_ **Clinical Case Review Priority**

(ONLY ONE ANSWER – *prioritize the main concern*)

- ☐ Alcohol Abuse
- ☐ OST
- ☐ Counselling
- ☐ Depression
- ☐ HCV Rx
- ☐ HIV Adherence
- ☐ Opportunistic Infections
- ☐ MH Review
- ☐ Psychiatric Referral
- ☐ DK
- ☐ NS

Comments_____

_____

Appendix 3: Laboratory Results Form _Visit N°: ____ (Attach results to the form)

Patient's initials: _____ Pt file N° _____ **Visit N°: ____** Name of interviewer: _____	Data clerk Initials: _____ Date data entry: ____ -____ -_____*(dd-mm-yyyy)*

Hepatitis C Test

420_**HCV Viral Load** __ __ .__ __ __. __ __ __ IU/ mL 421_DATE ___ -___ -_____ *(dd-mm-yyyy)*

421_ ☐ *If HCV VL undetectable*

422_**Genotype** _____ Sub-type _____ 423_DATE ___ -___ -_____ *(dd-mm-yyyy)*

424_**Fibroscan** kPA . __ __.__ __ 425_DATE ___ -___ -_____ *(dd-mm-yyyy)*

426_ Validity % __ __ __ 427_ Staging Category F _____

428_**Liver Biopsy** Metafavir score __ __ __ 429_ DATE ___ -___ -_____ *(dd-mm-yyyy)*

430_ **APRI score**: _____ calculated by clinician (*calculated also in the database*)

431_ **Child Pugh score**: _____ calculated by clinician (*calculated also in the database*)

HIV associated tests

432_ CD4 count __ __ __ __ cells/µL 433_ DATE ___ -___ -_____ *(dd-mm-yyyy)*

434_ Viral Load __ __. __ __ __. __ __ __ copies/mL 435_ DATE ___ -___ -_____ *(dd-mm-yyyy)*

☐ *If HIV VL undetectable*

436_ **HIV diagnosis tests** (According to national guidelines) 437_ DATE ___ -___ -_____ *(dd-mm-yyyy)*

☐ Positive ☐ Negative ☐ Indeterminate

Miscellaneous Tests

438_ **Pregnancy Test**

☐ Positive ☐ Negative 439_ DATE ___ -___ -_____ *(dd-mm-yyyy)*

440_ **Proteinurie**

Results : ☐ + ☐ ++ ☐ +++ ☐ ++++ 441_ DATE ___ -___ -_____ *(dd-mm-yyyy)*

442_ **HBV test** Ag HbS

☐ Positive ☐ Negative 443_ DATE ___ -___ -_____ *(dd-mm-yyyy)*

1_Surname: _____ 2_Forename: _____(not to enter in the database) **Patient's file N°** _____ 3_**Identification cohort Number**: __ __ __ __ __ 4_ID Key __ __

5_Date of consultation: ____ -____ -_____ *(dd-mm-yyyy)* 6_Site of consultation: _____	7_Name of interviewer: _____	9_Data clerk initials: _____ 10_Date of data entry: ____ -____ -_____ *(dd-mm-yyyy)*

Instructions: *Complete only for the received results. Circle the correct Unit.*
If the answer is unknown, tick the box DK (don't know)
*The requested date is the **date of the blood taken**.*
*Please refer carefully to the laboratory results and **mark the laboratory results form with the Visit N°***

Hematology			401_DATE ____ -____ -_____ *(dd-mm-yyyy)*
402_Erythrocytes (RBC)	__, __	10^6 / µL	
403_Leukocytes (WBC)	__ __ ,__	10^3 / µL	
404_Neutrophils	__ __ __	10^3 / µL	or Neutrophils __ __ __ %
405_Platelets	__ __ __	10^3 / µL	
406_Haemoglobin	__ __ ,__ __	g/dL	

Coagulation tests		407_ DATE ____ -____ -_____ *(dd-mm-yyyy)*
408_Quick Test	__ __ __ %	409_INR __. __ __ (no unit)

Biochemistry			410_ DATE ___ -___ -_____ *(dd-mm-yyyy)*
411_ALT __ __ __	IU/L		*Circle the correct Unit.*
412_AST	__ __ __	IU/L	417_ Glucose __ __ __ mg/dL
(413_AST upper limit reference	__ __ __	IU/L)	418_Creatinine (serum) __ __ __ mg /dl
414_Albumin	__ __ __	g/dl	419_TSH __ __ __ µU/ml
415_Total Bilirubin	__ __ __	mg/dL	
416_Direct Bilirubin (conjugated)	__ __ __	mg/dL	

Minimum laboratory follow-up schedule

Table 3.0 Schedule of consultation and of laboratory follow-up

Examination	Baseline	Pre-treatment[3]	Ongoing Monitoring (weeks of Treatment)								12 wks after
			1	2	3	4	8	12	16	20	24	Rx
Clinical Evaluation	X	X	X[5]	X	X[6]	X	X	X	X[6,7]	X[6,7]	X[7]	X
HBsAg	X											
Complete blood count	X	X		X[8]		X[8]	X[8]	X[8]				
Haemoglobin				X		X	X	X	X[7]	X[7]	X[7]	
CD4 count	X							X[9]			X[9]	
INR[1]	X											
ALT	X	X		X		X		X			X[7]	X
AST[1]	X	X										
Creatinine, Creatinine clearance		X		X		X		X			X[7]	
Bilirubin total[1]	X	X						X			X[7]	
Albumin[1]	X	X				X		X				
Glucose	X					X						
TSH[2]	X							X[2]				
HCV Viral Load	X	X[4]				X[6]		X[9]			X[9]	X
HCV Genotype	X											
HIV Viral Load	X							X[9]			X[9]	
Pregnancy Test		X				X	X	X	X[10]	X[10]	X[10]	
FibroScan	X											

[1] required if METAVIR F4, APRI cut-off for cirrhosis;
[2]applies to PEG-INF containing therapy only;
[3]all biochemical tests should be repeated if longer than three months from baseline examinations;
[4]ONLY if longer than six months from baseline examination;
[5]clinical evaluation during first month of treatment- additionally after 1st and 2nd week of treatment;
[6]optional ;
[7]if treatment duration more than 12 weeks;
[8]if PEG-INF containing regimen or decompensated cirrhosis (Child Pugh B-C) otherwise Hb alone is sufficient;
[9] if end of treatment;

Appendix 4: Adverse Events Reporting Form

CRF AE_ **N° Visit: _____**

1_Surname: _____ 2_Forename: _____ (not to enter in the database)

Patient's file N° _____

3_**Identification cohort Number**: __ __ __ __ __ 4_ID Key __ __

10_Date of consultation: ___ /___ /_____ *(dd/mm/yyyy)* 11_Site of consultation: _____	12_Name of interviewer: _____ 13_Doctor / Clinical Officer / Nurse / Others	14_Data clerk initials: _____ 15_Date of data entry: ___ /___ /_____ *(dd/mm/yyyy)*

Instructions: **Only for the <u>events leading to a change in the HCV treatment</u>: change of drugs, change of dosage or interruption of treatment.**

Fill all the questions. *If the answer is unknown, tick the box DK (don't know)*

Neurologic / Psychiatric

501_Depression ☐ Yes ☐ No ☐ DK
502_Mania ☐ Yes ☐ No ☐ DK
503_Headache ☐ Yes ☐ No ☐ DK

Ocular / visual / hearing (from baseline)

504_Eye disorders ☐ Yes ☐ No ☐ DK
505_Hearing Loss ☐ Yes ☐ No ☐ DK

Gastrointestinal

506_Increase jaundice- hepatitis flare ☐ Yes ☐ No ☐ DK
507_Diarrhea ☐ Yes ☐ No ☐ DK
508 Nausea/ vomiting ☐ Yes ☐ No ☐ DK

Skin – Dermatological

509_Rash ☐ Yes ☐ No ☐ DK
510_Photosensitivity ☐ Yes ☐ No ☐ DK
511_Hair loss ☐ Yes ☐ No ☐ DK

Musculoskeletal/ respiratory

512_Cough/Respiratory Tract symptoms ☐ Yes ☐ No ☐ DK
513_Arthralgia/myalgia ☐ Yes ☐ No ☐ DK
514_Cardiologic problem ☐ Yes ☐ No ☐ DK

Endocrine / metabolic

515_Diabetes Mellitus ☐ Yes ☐ No ☐ DK
516_Thyroid dysfunction ☐ Yes ☐ No ☐ DK

Biology anomaly

517_Anemia ☐ Yes ☐ No ☐ DK ☐
518_Neutropenia ☐ Yes ☐ No ☐ DK ☐
519_ Thrombocytopenia ☐ Yes ☐ No ☐ DK ☐
520_ Increase of ALT/AST ☐ Yes ☐ No ☐ DK ☐

521_ **Other**: specify _____

522_**Pregnancy** ☐ Yes ☐ No ☐ DK *If yes, fill the specific report form*

523_ Is the Adverse event is considered as **Serious Adverse Event**: ☐ Yes ☐ No ☐ DK
If yes, fill the specific report form

Signature of the clinician _____

Transfer to Site Investigator (PI) ☐ Yes ☐ No ☐ DK ☐

Date received by study PI ___ /___ /_____ **Signature study PI** _____

Appendix 5:

Patient Information and Consent Form

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients

Manipur, 2017

Language: English Original language: English

Madam / Sir,

You have been recently diagnosed with chronic hepatitis C infection.

You are being invited to take part in a study. Before you decide whether or not to take part in the study, it is important for you to understand why the study is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Ask us if there is anything that is not clear or if you would like more information. If you don't want today to take this decision, you will have a further opportunity to decide if you wish to take part to the study.

What is Hepatitis C (HCV) and how is it treated?

Hepatitis C is a virus that can cause liver disease. Hepatitis C can be a serious disease. It may take many years for the liver damage to become a problem that needs medical help. Until now the care has not been available because the treatment was very difficult to take and expensive. New medicines are now available that are safer and cheaper.

Not everybody infected with HCV infections needs to be treated straight away. The type of treatment and the number of days it takes to treat the HCV infection is different depending on many factors. We will check whether you need treatment at this time and whether you are ready to receive treatment. According to the results, a treatment plan will be made by your Doctor.

At the moment there treatment for Hepatitis C is not commonaly available in India. But, MSF will provide you with standard treatment recommended by World Health Organization free of cost All drugs provided by MSF are approved and registered for use by Government of India. No experimental medicine is used.

What is the study?

This study is organized by the medical team of MSF and of the national partner, NACO. This study has been approved by National AIDS Control Organization, New Delhi, Research Ethics Board of the Regional Institute of Medical Sciences, Lamphelpat, Imphal. and the MSF ethics review board..

The aim of the study is to assess the effectiveness of the different care for hepatitis C. Any adult (older than 18 years), who has HIV and is diagnosed with chronic hepatitis C will be assessed and asked to join this study.

Why I have been proposed to participate?

You are invited to join this study because you are an adult and you have been diagnosed with chronic Hepatitis C.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to stop being part of the study at any

time and you don't have to give a reason. If you decide not to be part of the study, or to withdraw your consent, this will not affect the care you receive or your access to HCV treatment.

What will happen to me if I take part?

If you accept to be part of the study, you will sign a consent form, this gives the study staff permission to use information about you and your treatment. At no point will we use your name.

We will record information about you such as age, marital status, other illnesses and clinical examination results. But this information will not be linked with your name. A number will be used instead of your name so that no-one knows the information is about you, except your doctor and team looking after you. The researchers will not have access to your name. Results of blood tests or other exams will be recorded under your number.

Your name, address or any other information that can identify you will not be recorded on the computer, only the number. It is this number that will allow us to match the different information collected. Some information may be very personal such as HIV status, drug or alcohol use. You can discuss any concerns with the medical staff. It is important that you know that all the information collected will be kept following strict confidentiality and anonymity procedures.

What do I have to do?

There is no difference for you regarding the clinical care you will receive. You must come to clinic to have a medical consultation and to receive the medicine according to the treatment. If you miss a scheduled appointment for consultation, we can contact you to remind you about the appointment. Adherence to medical consultation is vital for effective treatment of hepatitis C However, you may choose not to be contacted as well.

If you are a woman who is under HCV treatment and becomes pregnant, you must inform your doctor immediately. HCV Treatment may have to be discontinued if you become pregnant but your follow up will continue and adapted. Your participation in the study will continue.

What are the risks and advantages?

All the different procedures are part of your medical treatment. The study does not include any extra treatment. Being part of the study means we use the data about you and your treatment and compare this to other people receiving HCV treatment.

You will receive regularly information on how you are progressing on your treatment. Your doctor will meet with you regularly and answer any of your questions.

The results of this study will help us to increase our knowledge about the treatment of HCV and help develop better treatment plans, and therefore benefit all of society.

How we will the data, that we collect, be treated we collect?

Your medical record will be kept safe and only your medical and study teams can see it. We will not use your name in any study report.

The study will take about 3 years to complete. When the study is finished a poster with the main findings will be posted in the health centre so that you can see the results of the study. We will also publish the results in a scientific journal.

What happens when the follow up stops?

After the treatment has been completed, it is hoped, but not certain, that your HCV will be cured. You will be invited to follow your HIV care as before. However, if your symptoms return or you think you may have been infected again with HCV, you should see your doctor immediately.

Storage of specimen

If you give us your permission, we would like to store a small sample of your blood for up to 5 years (8ml or 2 tea spoons). We plan to use this blood sample to better understand the outcome of any treatment you may have received. We will store the blood sample with some information about you, your age and sex. We will not put your name on the blood samples. There will be no way to know the blood sample is yours. Your sample will not be sold.

What if there is a problem?

If you have questions, or if you are having any problem from any medicines, you should talk to your nurse or doctor.

Important contacts:

For questions regarding study, treatment, care, adverse events and treatment of adverse events and/or any associated illness;
Dr. Jeetesh Shougrakpam, Co-investigator
Medical Doctor, MSF Churachandapur, Manipur
Tel: +91 841 302 8978

Supervision of treatment and care
Dr. Sabrina Sharmin, Co-investigator
Medical Coordinator, MSF / Doctors Without Borders, India
C-106 Defence Colony, New Delhi
Tel: + 91 9810556410

Supervision of the study
Dr.Himanshu M., Principle Investigator
Medical Coordinator, MSF / Doctors Without Borders, India
C-106 Defence Colony, New Delhi
Tel: + 91 7042297536

Ethical oversight
Research Ethics Board
Regional Institute of Medical Sciences, Lamphelpat, Imphal, 795004
Tel: +91 385 2414750.

STATEMENT OF CONSENT

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients Manipur, 2017

Language: English Original language: English

Copies:2 – one for the participant (patient) and other for participant's confidential personal file.

I have read this form or someone has read it to me. I was encouraged to ask questions and given time to ask questions. I agree to be in this study. I know that after choosing to be in this study, I may stop being part of the study at any time for any reason. My participation is voluntary.

I understand that the study might need to contact me.

☐ *I agree to be contacted.* ☐ *I **do not** agree to be contacted.*

I prefer to be contacted by (check all that apply).

1. *Through (Mobile) phone*
2. *Coming to my house*
3. *Contacting my relatives*
4. *Other method (specify)* _____

STORAGE OF SPECIMENS:

In case you are HCV positive and willing to provide a blood sample, we would like to store a small sample of your blood.

☐ *I agree to have the blood samples stored.* ☐ *I **do not** agree that these blood samples will be stored.*

I agree to participate to this study

Participant's Name: (Print)		Participant's signature:		Date:	

If patient illiterate

Witness's Name: (Print)		Witness's signature:		Date:	

I have explained the purpose of this research to the volunteer. To the best my knowledge, he/she understands the purpose, procedures, risks and benefits of this research.

Investigator's Name: (Print)		Investigator's signature:		Date:	

Patient Information and Consent Form

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients
Manipur, 2017

Language: Mizo Original language: English

Ka Pu/Pi

Tun hnai deuh khan Hepatitis C benvawn natna I vei tih hmuhchhuah a ni a.

Hemi kaihhnawih zirchiannaah tel ve la kan ti a. Thutlukna I siam hmain he zirchianna hi eng vanga neih nge tih leh eng thilte nge ni dawn tih hrechiang hmasa phawt la kan ti a ni. He thuziak hi uluk taka chhiar hmasa turin kan ngen a che. He zirchianna chungchang hi I duh chuan midangte pawh sawipui la. Hriatthiam loh I neihte leh hriat belh duh I neih chuan min zawt bawk dawn nia. He zirchianna thu-ah tunah thuthlukna I siam nghal thei lo a nih pawhin ni dangah pawh I tel thei tho bawk a nia.

HEPATITIS C (HCV) HI ENGNGE NI A, ENGTIA ENKAWL TUR NGE?

Hepatitis C chu Thin natna thlentu natna hrik (virus) chikhat a ni a. Natna hlauhawm tak a ni thei. Kum tam tak liam hnu chauhah te mithiamte enkawl ngai a ni thei bawk. Tunhma chuan enkawl a har bakah inenkawl man a to hle a ni. Tunah chuan damdawi thar tha zawk leh man tlawm zawk a awm tawh a ni.

HCV natna nei nazawng hi chutianga damdawi nena enkawl nghal an ngai vek kher lo a. Treatment(Enkawlna) pek dan leh a tihdam hun chhung pawh chhan hrang hrang vangin a inang lo bawk a ni. Nangpawh treatment(enkawlna) pek nghal I ngaih dawn leh dawn loh te leh treatment(enkawlna) la turin I inpeih leh peih lohte pawh kan en dawn a ni. I result a zirin doctor-in I treatment(enkawlna) lak dan tur a sawi dawn a ni.

Tunah hrih chuan he natna damdawi thar hi India ramah hian a pek (chawh) dan tur kalphung felfai a la awm lova, amaherawhchu tuna doctor-in a hrilh tur che hi World Health Organization leh Indian Natioinal Association for the Study of Liver-ten an pawm ve ve a ni. Heng damdawi thar hi sawrkar pawmpui tawh emaw pawmpui tura kalpui mek a ni a, rinthu damdawi a ni lo a ni.

ZIRCHIANNA CHU ENGNGE?

He zirchianna hi MSF medical team leh India rama kan thawhpui NACO te tangruala kan buatsaih a ni a. NACO leh MSF ethical committee tena an pawmpui a ni bawk a ni.

He zirchiannain a tum chu hepatitis C natna enkawlna tangkai dan hriatchian a ni. Puitling tupawh, kum 18 aia upa HIV natna hrik pai leh hepatitis C natna benvawn veite chu zirchian turin ngen an ni dawn a ni.

ENG VANGIN NGE HE ZIRCHIANNAA TEL TURA MIN SAWM?

Puitling I nih vang leh hepatitis C benvawn vei I nih avangin he zirchiannaa tel tur hian sawm I ni.

KA TEL VE KHER A NGAI EM?

Intihluihna a awm lova, tel I duh leh duh loh athu a ni e. Tel I duh chuan he lehkha hi pek I ni ang a, tel remtihna form (consent form) sign tura ngen I ni ang. I duh hun hunah he zirchianna atang hian I inhnukdawk thei a, a chhan leh vang pawh sawi kher a ngai lovang. He zirchiannaah tel duh lo mah la, consent form I thehluh pawh la kir leh pawh ni la enkawlna I dawn mek hi chu I la dawng zui zel tho dawn a ni.

TEL DUH TA ILA KA CHUNGAH ENGNGE THLENG ANG?

He zirchiannaah hian tel ve I duh a nih chuan consent form i sign ang. Staff ten nangma chungchang leh enkawlna I dawn dan te an en thei ang. I hming erawh thupsak tlat I ni ang.

I kum, nupui-pasal I neih leh neih loh te, natna dang I neih leh neih loh te leh I clinical examination result te kan la ang. Mahse heng hi I hming nen khawiah mah kan ziak kawp lovang. Doctor leh nangmah enkawltute tih loh midang tumahin nangma chungchang a ni tih an hriat loh nan I hming aiah number pakhat dah a ni thung dawn a ni. Researcher-te pawh I hming hi hrilhhriat an ni dawn lo a ni. Thisen test leh thil dang test result te pawh I number-ah zel chhinchhiah a ni ang.

I hming, address emaw nangmah I ni tih hriatchhuah theihna thil dang hrim hrim pawh computer-ah record a ni bawk lovang a, I number chauh chhinchhiah a ni ang. Chu I number hmang chuan kan thil hmuhchhuahte chu kan chhuizawm zel dawn a ni. Thil thenkhat chu sawi a nuam lo maithei, entirnan HIV hrik I pai leh pai loh te, ruihhlo I tih leh tih loh te leh zu I in leh in loh chungchang te pawh a ni ang. Harsatna I neih engpawh kan medical staff te I sawipui thei ang. He zirchianna atanga information kan lak reng reng chu a putchhuak dawn lova, uluk takin nangma chungchang a ni tih hriat loh turin thup tlat a ni dawn a ni tih hi hrechiang la kan duh a ni.

ENGNGE KA TIH VE TUR?

Enkawlna I dawn mek hi a ngaiin a kal reng tho ang. Clinic-ah inenkawl tur leh damdawi ei turin I rawn kal ziah ang.

Hmeichhia I nih a hepatitis C inenkawl mek I nih a I rai a nih chuan doctor I hrilh vat ang. Chutianga I lo rai a nih chuan HCV treatment chu tihtawp a ngai maithei a, amaherawhchu enkawl zui reng I la ni tho ang a, a tul dan azirin inenkawl dan pawh her danglam hret a ngai maithei. He zirchiannaah hian I la tel zui zel tho ang.

FIMKHUR A NGAIHNA LEH HE ZIRCHIANNAA TEL A THATNA TE ENGNGE?

Inenkawl dan chi hrang hrangte hi medical treatment I lakna chhung ami vek a ni. He zirchianna hian enkawlna I lak mek piah lam engmah a khawih tel lovang. Nangma dinhmun leh enkawlna I dawn dan an la dawn tihna a ni mai a, enkawlna dawng mek midangte nen in dinhmun kan khaikhin mai dawn a ni.

Enkawlna I dawn chungchanga hma I sawn dan hriattir thin I ni ang a. Doctor-in a en fo dawn che a, harsatna engpawh a lo hrilhfiah zel ang che.

He zirchianna atanga kan thil hmuhchhuah hian HCV enkawl danah nasa takin min pui dawn a, tih dan thar tha zawk te kan lo hmuhchhuah phah ang a, khawtlang tan pawh malsawmna a ni dawn a ni.

ENGTIN NGE INFORMATION KAN LAK KHAWM HI KAN TIH DAWN?

I medical record hi uluk takin kan vawnghim dawn a, nangmah enkawltu medical team leh zirchiangtu team te chauhin an en thei ang. Thil dang, zirchianna dang engah mah I hming kan hmang lovang.

He zirchianna hian kum 3 vel a awh dawn a. Chumi zawhah kan thil hmuhchhuahte chu poster-ah siamin nangmah pawhin I lo hmuh ve theih turin health centre hrang hrangah tarchhuah a ni dawn a ni. Kan thil hmuhchhuah hi scientific journal-ah pawh kan chhuah bawk ang.

FOLLOW-UP ZAWHAH ENGTIN ZEL?

Treatment(enkawlna) zawhah hi chuan HCV natna atangin I dam vek ang tih chu kan tiam thei lo che a, mahse I dam ngei kan ring tlat a ni. HIV inenkawlna dawng chhunzawm zel turin sawm I ni ang. Amaherawhchu HCV natna a lo langchhuak leh emaw HCV hrik I lo kai thar leh palh hlauh a nih chuan doctor pan vat ang che.

THISEN DAH THAT

I phal chuan kum 5 thleng vel chu I thisen tlemte (8ml/fiante 2 vel) chu vawn that kan duh a ni. He I thisen sample hi treatment I lakna result zirchian nan kan duh a ni. I thisen sample-ah chuan nangma chungchang, I kum leh mipa/hmeichhia I nihna te chhinchhiah kan duh a. I hming erawh kan ziak lang lovang. Chuvangin nangma thisen a ni tih a hriat dawn loh a ni. I thisen sample hi zawrh a ni bawk dawn lo a ni.

HARSATNA ENG EMAW LO AWM TA SE ?

Zawhna engpawh I nei a nih chuan, emaw, I damdawi ei chungchangah harsatna engpawh I lo nei a nih chuan nurse emaw doctor te hi hriattir dawn nia.

ZAWHNA ZAWHNA TUR

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STATEMENT OF CONSENT

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients Manipur, 2017

Language: Mizo Original language: English

Copies:2 – one for the participant (patient) and other for participant's confidential personal file.

HRIAT TIRNA LEH PHALNA

He lekha thu hi ka hrethiam ani. Ka hriatthiam loh thil te zawh fiahna hun pek kani e. He zirna ah hian tel ka inhuam e. Tin, he zirna chung chang ah hian eng hunah pawh ka in hnukdawk thei tih hriattir ka ni bawk e. Keima duh thlanna ngeia tel kani e.

He zirna atan hian min rawn biak fo -

☐ *Ka pawm e.*
☐ *Ka **pawm lo** e.*

Heng a hnuaia hmanrua hmangte hian min rawn biak ka pawm e.

1. *Mobile Phone*
2. *Ka Chenna Inah min rawn pan thei.*
3. *Ka chungte an rawn be thei.*
4. *Hanraw dang*_____

THIL DAH THATNAN

Hep C positve I nih a, he kan zirna tanpuitu atan I thisen tlem a zawng mamawh anih a, chu thisen(tlemte) chu

☐ *In zirna atan dahthat ka phal e*
☐ *In zirna atan dahthat **ka phallo e.***

He zirna ah hian telve ka pawm e.

Hming (Damlo)		Signature		Date	

Ziak thiamlo tan

Hriatpuitu Hming		Hriatpuitu Signature		Date	

He lekha chunga thu hi damlo hnenah ka hrilfiah tawh a. Damlo pawh in he zirna atana pawimawh leh a kaih hnawih tinreng hriattir tawh ani e.

Dawngsawngtu Hming		Dawngsawngtu Signature		Date	

Patient Information and Consent Form

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients

Manipur, 2017

Language: Hamar Original language: English

Pi/ Pu……..

Chronic Hepatitis C a na inih ti hmusuok a ni a inchukna (study) a thang ve dinga fiel I nih. Ami ruokchu, hi inchukna a thang dinga thuthlukna I siem hmain, hi study hi iengtita thaw am a ni a ti le ieng iem a tul ding ana tikai I hriet a tha a Hieng a hnuoia thukai hi ingun taka tiem dinga ngen I nih. I nuom chun mi dang le khawm hi inchukna thu hi I hril thei, Thil fie lo deu Amani thil hrietsa tula I ngaihai I min dawn thei bawk a. Vawisun khera thuthlukna I siem theinaw ani khawmin, hmatienga khawm hi inchuknaa hin I thang thei zing a nih.

HEPATITIS C (HCV) hi iem ana, iengtin am inkawl a ni a ? Hepatitis C hi virus (natna hrik) chikhat, thin natna inthun thei tu a nih, Hepatitis C hi natna tium tak a ni thei bawk. Thin thalo ta dinga buoina inthun dingin kum tamtak a lak el thei. Vawisunni chen hin hi enkawlna hi hmu thiin ala um nawa, asanchu a treatment (enkawlna) hi an tak leiin le a man a tam em leiin.Damdawi thar, man tlawm le tha lem tu ruok hin chu a um tah.

Hepatitis C a na phawt hi enkawl nghal an ngai vawng kher nawh. A treatment dawn gang le HCV infection enkawlna dinga ni tul zat khawm an ang vawng naw thei, Hieng huna hin treatment thaw nhai in ni le in ni naw enfel kan ta, chu result dungzuiin dontor in treatment plan a hung siem dinga nih. Tulak hin chu India ramag damdawi tharhai hmanga treatment plan siem ala ni hri nawh, I doctor in plan a siempek che chu WHO le Indian National Assn. for the study of Live haiin an recommend a nih. Damdawi tharhai hi pawm le zieklut le a then zieklut ding mek an nit tawl.

INCHUKNA HI IEM?

Hi inchukna hi MSF medical team le a national partners NACO hai buolsai a nih. Hi inchukna hi NACO le MSF ethnical committee haiin an pawmpui a nih.

Hi inchukna thiltum chu hepatitis C enkawlna chi dang dang, mi dang dangin an dawng haiah ieng anga enkawlna pek, him thatak ata ti a nih. Puitling (kum 18 le a chungtieng) HIV a na le HCV nei ti hmusuok hai chu tha deuva enkawlin hi inchuknaa thang dinga fiel ning an tih.

IENG LEIA THANG DINGA FIEL AM KA NA?

Mi puitling I ni a, chronic hepatitis C inei ti hmusuok a ni leia thang dinga fiel i nih.

HMA KA LO LAK VE KHER A NGAI A NI?

Awiah, hma lak le lak naw chu nanga thu thu a nih, I lo nuom chun, information sheet pek ning I ta, chun consent form ah suoi I kei ngai a fih, Hi inchukna a hin I nuom hun hunah I thang naw theia, a san hril kher khawm ngai kher naw nih, Hi inchuknaa I thang ta naw khawmin enkawlna I dawn ding le HCV treatment thua I hriet ding pop o chu la dawng zing tho i tih.

THANG VE LANG IEM CHANG KA TA?

Hi inchuknaa thang ve dinga I pawm chun, consent form ah suoi I kei ngai a ta, chu chun an chuklu staff haiin nang le I enkawlna dawnghai inhrietlirna dingin hmang thei an tih. Amiruokchu, I hming ruok chu hmang ni naw nih.

I kum, nuhmei/Pasal nei le nei lo le I natna danghai le clinical examination results hai sinsie ning a ta, amiruokchu, hi thil a hin I hming suk lang ni naw nih. I hming aiin number hmang ning a ta, hi thil hi nang a ta a nih tukhawmin hre naw nihai, I doctor le a enkawltu che team ti lo chu, Inchuktuhai kuomah I hming inhrietlir ni naw nih.Thisen test le exam dang danghai chu I number hnuoiah inchik ning a tih.

I hming umna le chanchin, nang an sui dawk theina ding hrim hrim chu khawla thun ni naw nih, number chau lo chu , Hi number a hin thil hmusuoka umhai chu inchikin an um ding a nih. Hmusulka umhai hi mimal thil deu, hieng HIV, drugs le zua inhnel hai chen a ni thei a. Chuonghaia ngaituo nuom inei hai chu medical staff hai le hrittlang thei ning a tih.Thil hmusuoka um pop o hi hril suok ni naw ni a, ip tlat ning tih.

IEM KA THAW NGAI A TA?

Clinical care I dawng ding hi danglam chuong sawt naw nih, Clinic a mi damdawi tienga thurawn le damdawi la dingin treatment dungzuiin I hung ngai a tih.

Nuhmei, HCV treatment thaw lai ini a, in rai chun, I doctor inrang deuvin hril nghal rawh. I lo inrai a ni chun HCV treatment chu la suktawp hri phawt a ngai el theia, amiruok chu a hnungah sunzawm nawk ning a tih. Inchuknaah thang ve zing itih.

A THATNA LE THAT LONA IEM ANA?

Enkawlna (treatment) dang danghai hi I medical treatment a thang vawng a nih. Inchuknaa hin extra treatment a thang nawh. Hi inchuknaa I thang ve hin nanga kan thil hmusuok hai le mi dang HCV treatment la hai inthawka kan hmusuok hai kan enkhi hlak a nih.

I treatment dawnga I h masawn danhai inhrietlirna pek zing ning I tih. I doctor in inhmupui deu zing chea, zawna I nei hai po po dawn a tih.

Hi inchuknaa kan thil hmuhai hin HCV treatment thaw dan ding vel kan hrietna suk zau ata, chun, hieng neka treatment thalem thaw dan ding ngaituoin, khaw mipui hai chenin hlawkpui an tih.

DATA KAN LAKKHAWM HI IENGTIN AM ENKAWL NING ATA?

I medical record hi sie that ning a ta, I medical le study teams hai Chauvin en thei an tih, study report hai le I hming hmang nawng kan tih.

Hi inchukna hin kum 3 vel awng a tih. Hi inchukna zoa hin poster ah thil hmusuoka umhai ziek lang ning a ta, chu chu health centre ah tar ning a tih. Nang khawmin chu taka hmusuoka umhai chu hmu thei I tih. Chun, scientific journal ah hmusuoka umhai hi insuo ni bawk a tih.

FOLLOW UP TAWP PHAT IENTIN AM NING A TA?

Treatment zo hnung hin I HCV chu a dam beisei a nih a, amiruokchu chieng taka hril thei a ni nawh. HIV enkawlna tieng sunzawm ding a hril ning a tih. Amiruokchu, a hmaa I natna hai bawk a hung kir nawk chun, annawleh HCV a na nawka in nai chun I doctor I pan vat ding a nih.

STORAGE OF SPECIMEN:

I phalna imi pek chun, I thisen tlawmte hi kum 5 sung siethat kan nuom a (8ml/thir haihaw hni). Enkawlna I lo dawng ta hai kakhawk/rasuok hai tha nawk zuola kan en na dingin hmang kan nuom a nih. Hi thisen a hin sinsiena dingin I kum le I nina (nuhmei/pasal) kan sie sa bawk ding a

nih. I hming ruok chu thang naw nih. Nang ita ngei a nih ti chu tukhawmin hre naw nihai. Hi thisen hi zawr naw bawk kan tih.

BUOINA LO UM SIEN THE:
Zawna inei Amani damdawi I fak haiah buoina I nei chun I nurse Amani doctor rawn/inbiekpui rawh.

Zawna inei chun a hnuoia hming ziek hi bie rawh

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INHRIETTIRNA LE PHALNA:

Hi thuziek hi ka hrielthiem a nih. Ka hrietthiem lo thil hai indawn fel hun pek ka nih. Hi inchukna a hin thang kan zuom chun, hi inchukna chungchang a hin ieng huna khawm kan hnukdawk thei ti inhriettir ka ni bawk. Ka ditthlangna ngiea thang ka nih.

Hi inchuknaa hin an mi biek

- ☐ Ka pawm ie
- ☐ Ka pawm naw ie

Hieng a hnuoia hmangruohai hmangin an mi biek ka pawm ie

1. Mobile Phone
2. Ka umna in ngeia mi hung panin.
3. Ka sunghai an hung biek thei
4. Hmangruo dang _____

THIL SIE THAT DAN

Hep C positive I ni a, hi kan inchukna thangpiutu dingin I thisen tlawm a zawng mamaw a ni a, Chu thisen thawmte chu

- ☐ Inchuk dinga sie that ka phal
- ☐ Inchuk dinga sie that ka phat nawh

Hi inchukna a hin thang ve ka nuom

Hming (Damlo)		Signature:		Date:	

Ziek theilo hai ta dingin

Hrietpuitu Hming		Hrietpuitu Signature		Date	

Hi lekha chungthu hi damlo kuomah ka hrilfie tha a. Damlo khawm hi inchuknaa dinga pawimaw le tul hai in hriettir a nit ah:

Dawngsawngtu Hming		Dawngsawngtu Signature		Date:	

Patient Information and Consent Form

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients

Manipur, 2017

Language: Thangpi (Burmeese) Original language: English

Hepatitis C နှင့် HIV ရောဂါသည်များအတွက် နေထိုင်နည်း နည်းလမ်းကောင်းများ

မိတ်ဆွေ သင့်တွင် Hepatitis C ရှိ မရှိ သေချာအောင် စစ်ဆေးပါ။ အကယ်၍ ဤပိုး သင့်တွင် ကူးစက်နေပါက ဆွေးနွေးတိုင်ပင်အောင် ဖိတ်ဖော်ပါသည်။ ဤဆွေးနွေးမှုတွင် သင့်တွင် ပိုးရှိ မရှိ မသိသ၍ ဘာကြောင့် ဤဆွေးနွေးလေ့လာမှု ပြုပါသလဲ၊ ဘာတွေလိုအပ်လဲဆိုတာ သင်ကိုယ်တိုင် နားလည်စေလိုခြင်း ဖြစ်ပါတယ်။ ဒါကြောင့် အောက်တွင်သိသင့်သောအချက်များကို သေချာဖတ်စေချင်သည်။ သင်နားမလည်သည်များ ရှိခဲ့သော်လည်းကောင်း ပိုမိုသိရှိနားလည် လိုလျှင်သော်လည်းကောင်း ဆွေးနွေးတိုင်ပင်နိုင်ပါသည်။

Hepatitis C နှင့် HIV ဆိုတာ ဘာပါလဲ၊ ဘယ်လိုနေထိုင်ရပါမလဲ။

Hepatitis C ဟာ ကူးစက်ရောဂါပိုးတစ်မျိုးပါ။ ဒီရောဂါဟာ ကြောက်စရာရောဂါပါ။ ဤပိုးဟာ အသည်းကိုဖျက်ဆီး အသိနောက်ကျပါက နှစ်များစွာကြာ ကုသရတတ်ပါသည်။ ပျောက်ကင်းအောင်ကုသစရိတ်များစွာ လိုအပ်သည့်အတွက် လူတိုင်း မကုသနိုင်သေးပါ။ သို့သော် ယခု ဈေးသက်သာ၍ ပျောက်ကင်းအောင် ကုသပေးနိုင်သော ဆေးကောင်းများပေါ်လာပါပြီ၊ C ပိုး ကူးစက်ခံရသူတိုင်း ချက်ချင်း ကုသဆေးသောက်ရန် မဆိုလိုပါ။ ကုသပျောက်ကင်းရန်အတွက် အချက်အလက်များစွာ ကြိုတင်လေ့လာပြီးမှ ကုသချိန် ဘယ်လောက်ကြာမည်ကို သိရမှာပါ။ စစ်ဆေးမှုများပြုလုပ်ပြီးမှ မည်သို့ ကုသရမည်ကို သိရပါမည်။ ဤစစ်ဆေးမှု ရလဒ်ကို ကြည့်ပြီး ဆရာဝန်မှ မည်သို့ကုသနေထိုင်ရမည်ကို ပြောပြနိုင်မည်ဖြစ်ပါသည်။ သို့သော် ယခုလက်ရှိတွင် အိန္ဒိယနိုင်ငံတွင် ဤရောဂါ ပျောက်ကင်းစေသော ဆေးဝါးများမရှိသေးပါ။ သို့သော်ကျန်းမာရေးဌာနမှ ကမ္ဘာ့ကျန်းမာရေး (WHO) နှင့် (India National Association for Study of Liver) အဖွဲ့တို့ ပူးပေါင်း၍ ကြိုးစားနေချိန်ဖြစ်ပါသည်။ ရောဂါပျောက်ကင်းစေသော ဆေးဝါးများ ရှာဖွေသုတေသနပြုလုပ်နေဆဲဖြစ်ပါသည်။

ကျွန်တော်တို့ ဘာတွေ ဆွေးနွေးတိုင်ပင်လေ့လာသင့်ပါသလဲ။

ဤရောဂါအကြောင်း MSF medical team နှင့်အတူ လက်တွဲသော NACO နှင့် MSF ethical committee တို့မှ ဆွေးနွေးလေ့လာကြရန် အကြံပြုနှိုးဆော်ထားပါသည်။ ဤဆွေးနွေးလေ့လာ တိုင်ပင်ခြင်းအားဖြင့် ဤရောဂါ ကုသပျောက်ကင်းအောင် နည်းလမ်းကောင်းများ တတ်စေလိုခြင်းဖြစ်ပါသည်။

၁၈ နှစ်အထက် အရွယ်ရောက်ပြီး HIV နှင့် Hepatitis C ရောဂါသည်များ ဤရောဂါများအကြောင်း ဆွေးနွေးတိုင်ပင်လေ့လာနိုင်အောင်လည်း ဖိတ်ခေါ်ပါသည်။

ဘာကြောင့် ကျွန်ုပ်ကို ဆွေးနွေတိုင်ပင်လေ့လာရန် ဖိတ်ခေါ်ရပါသလဲ။

ဤဆွေးနွေးတိုင်ပင်လေ့လာခြင်းတွင် သင့်အားဖိတ်ခေါ်ရခြင်းမှာ သင့်တွင် (Cronic) Hepatitis C ရောဂါပိုး ကူးစက်ခံနေရလို့ဖြစ်ပါသည်။

ဤဆွေးနွေးတိုင်ပင်လေ့လာခြင်း၌ ကျွန်ုပ်ဘာကြောင့် ပါဝင်သင့်သလဲ။

ဤဆွေးနွေးတိုင်ပင်လေ့လာခြင်းတွင် သင်ပါဝင်၊ မပါဝင်ခြင်းသည် သင်၏ ဆုံးဖြတ်ချက်ပေါ်တွင်မူတည်ပါသည်။ သင်ပါဝင်ဆွေးနွေးလိုလျှင် ဤစာစောင်၌ လက်မှတ်ထိုး အတည်ပြုပေးရန်ဖြစ်ပါသည်။ ပါဝင်ဆွေးနွေးလိုခြင်း မရှိတော့လျှင် အချိန်မဆွေး ရပ်နားနိုင်ပါသည်။ သင်ဆွေးနွေးတိုင်ပင်ခြင်းမှ ရပ်နားပြီးလျှင် ဤရောဂါအကြောင်း ဆက်၍ တိုင်ပင်ဆွေးနွေးရန် မလိုတော့ပါ။ သင်၏ကုသမှုနှင့် ရှေ့ဆက်ကုသမှုကိစ္စအတွက် ပြဿမရှိပါ။

ကျွန်ုပ်တို့ဆွေးနွေးတိုင်ပင် လေ့လာခြင်းတွင် ပါဝင်လိုလျှင် ကျွန်ုပ်မည်သို့ပြုလုပ်ရမည်နည်း။

ဆွေးနွေးတိုင်ပင်လေ့လာခြင်းတွင် ပါဝင်လိုလျှင် ပါဝင်လိုကောင်း လက်မှတ်ထိုးပေးပါ။ ဤသို့ လက်မှတ်ထိုးပေးခြင်းအားဖြင့် သင့်အချက်အလက်များအား (Staff) များသိရှိခွင့် ပြုလုပ်ခြင်းဖြစ်သည်။ သင်၏ အချက်အလက်ဆိုသည်မှာ သင်၏ရောဂါများ၊ စစ်ဆေးမှုအဖြေများအား သိမ်းဆည်းထားမည်ဖြစ်သည်။ ဤအချက်အလက်များအား သင်၏အမည်နှင့် သိမ်းဆည်းထားမည်မဟုတ်ဘဲ သင့်အတွက် လျှို့ဝှက်နံပါတ်နှင့် သိမ်းဆည်းထားမည်ဖြစ်ပါသည်။ အကြောင်းမှာ သင့်အချက်အလက်များ ပြင်ပသို့ မပေါက်ကြားရန်ဖြစ်သည်။ သင့်ဆရာဝန်အဖွဲ့နှင့် သင်သာလျှင် သိရှိမည်ဖြစ်ပါသည်။ Research ပြုလုပ်သောသူများသာလျှင် သင့်ကို မသိဘဲ သင်၏ လျှို့ဝှက်နံပါတ်သာ သိမည်ဖြစ်သည်။ သင်၏နာမည် လိပ်စာများအား သီးသန့်ကွန်ပျူတာဖိုင်တွင် သိမ်းထားမည်ဖြစ်သည်။ သင့်လျှို့ဝှက်နံပါတ်သာလျှင် အသုံးပြုရမည်ဖြစ်ပါသည်။ အကြောင်းမှာ သင်၏ HIV (status) နှင့် သင်သုံးစွဲသော မူးယစ်ဆေးများအား အပြင်လူ မသိစေလိုခြင် ဖြစ်ပါသည်။

ကျွန်ုပ်ဘာတွေလုပ်ရမလဲ။

သင်သောက်နေကျဆေးဝါးများ ပြောင်းသောက်ရန်မလိုပါ။ ပုံမှန်ကုသရန်ဖြစ်သည်။

ကောင်းကျိုးနှင့် ဆိုးကျိုးများ။

အချင်းအရာအားလုံးတို့သည် သင့်ကုသမှုများအတွက် ထိရောက်ရန်ဖြစ်သည်။ ဤလေ့လာတိုင်ပင်ဆွေးနွေးခြင်းတွင် တမူထူးခြားသောအရာ မရှိပါ။ ဤဆွေးနွေးခြင်းတွင် ပါဝင်ခြင်းသည် သင့်နှင့် HIV ရောဂါသည်များ မည်သို့ နေထိုင်ကုသရမည်ကို သိရှိရန်ဖြစ်သည်။ ထို့ပြင် သင်၏ဆရာဝန်နှင့်အမြဲတွေ့၍ သိရှိလိုသော အချက်များအား အချိန်မရွေး ဆွေးနွေးအကြံတောင်းနိုင်မည်ဖြစ်သည်။ ဤသို့ဆွေးနွေးခြင်းအားဖြင့် အကြံကောင်း ဉာဏ်ကောင်းများအား လူနာနှင့် လူနာပြုစုသူတို့တွင် နေထိုင်ပြုစုနည်းများ တိုးတက်လာမည်ဖြစ်သည်။ အများအတွက်လဲ အကျိုးရှိလာမည်ဖြစ်သည်။

တွေ့ရှိသော ဒေတာများအား မည်သို့အသုံးချပါသလဲ။

သင်၏ဆေးစစ်မှုမှတ်တမ်းများအား လုံခြုံစွာ သိမ်းဆည်းထားပြီး သင်နှင့် သင်၏ Medical Team နှင့် Study Team တို့သာလျှင် ကြည့်ခွင့်ရမည်ဖြစ်သည်။ သင်၏ အမည်ဖော်ပြမည်မဟုတ်ပါ။ ဤ study ပြီးဆုံးအောင် (၃)နှစ်ကြာမည်ဖြစ်သည်။ ဤဆွေးနွေးတိုင်ပင်လေ့လာခြင်းပြီးဆုံးလျှင် တွေ့ရှိသော လေ့လာမှုများအား Health Center တွင်ချိတ်ဆွဲဖော်ပြပေးမည်ဖြစ်သည်။ ဆွေးနွေးမှုရလဒ်ကောင်းများ သင်မြင်တွေ့ရမည်ဖြစ်သည်။ Scientific Journal တို့တွင်လည်း ဖော်ပြသွားမည်ဖြစ်သည်။

သင်၏ကုသမှုများအား ရပ်နားပါက မည်သို့ဖြစ်မည်နည်း။

သင်၏ကုသမှုများသည် ဆေးပတ်မှန်အောင် သောက်သုံးချိန်တွင် အမှန်ရောဂါပျောက်ရန် နှစ်သိမ့်မှုလဲ ပေးနိုင်မည်ဖြစ်သည်။ လုံးဝပျောက်ရန် အာမမခံနိုင်ပါ။ ရောဂါပိုးရှိ မရှိပြန်လည်စစ်ဆေးရမည်ဖြစ်သည်။ HIV ပိုး ကုသမှုပြီးဆုံးသော်လည်း ဆက်၍ကျန်းမာရေးထိန်းသိမ်းထားရမည်ဖြစ်သည်။ သင့်တွင် ရောဂါပြန်ဖြစ်ပြီဟု ထင်လျှင် သင်၏ဆရာဝန်နှင့် အမြန်တွေ့ဆုံရမည်။

<u>သင်၏ သွေးနမူနာအား သိမ်းထားမည်။</u>

သင်၏ခွင့်ပြုချက်ဖြင့် သွေးနမူနာ 8ml ထုတ်ယူပြီး (၅)နှစ်သိမ်းဆည်းထားမည် ဖြစ်သည်။ ဤနမူနာ သိမ်းဆည်းထားခြင်းသည် သင်၏ ရောဂါကုသမှု ရှိမရှိ သိနိုင်ရန်ဖြစ်သည်။ ဤသွေးနမူနာကို သင်၏အသက်၊ ကျား၊ မ စသဖြင့်သာ မှတ်သားပြီး မည်သူဖြစ်သည်ကို ဖော်ပြမည်မဟုတ်ပါ။ သင်သွေးအားလည်း ရောင်းချမည် မဟုတ်ပါ။

<u>သင်ဆေးသောက်စဉ် အခက်အခဲရှိပါက မည်သို့လုပ်ရမည်။</u>

သင်ဆေးသောက်စဉ် ဆေးမတည့်သည့်ပြဿနာ၊ အဆင်မပြေမှုများ ကြုံပါက ဆရာဝန်၊ ဆရာမများအား ချင်ခြင်းအသိပေးပါ။

သင်ပိုသိရှိလိုပါက အောက်ပါလိပ်စာများသို့ မေးမြန်းနိုင်သည်။

Dr. Jeethesh Shougrakpam, Medical Doctor

MSF, Churachanpur, Manipur,

ဆက်သွယ်ရန်ဖုန်းနံပါတ် +၉၁၈၄၁၃၀၂၈၉၆၈

STATEMENT OF CONSENT

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients Manipur, 2017

Language: Burmeese (script – English) Original language: English
Copies:2 – one for the participant (patient) and other for participant's confidential personal file.

Ngarsai i ponehcan ko hpaat pye shoetmahote taithcone tait u k ngarko mha hpaat hkaesai . ngar mayyhkwannmyarrko mayy raan aarrpayy aarr myahaout nhaint mayyhkwannmyarrko mayy raan aahkyanepayy htarrhkaesai . ngarsai i laelarmhu hpyit sabhawtuu sai . ngarsai i laelarmhu hpyithphoet shayy hk yyaya pwee naw kya, ngar so aakyaunggpyahkyet myarraatwat mai sany aahkyanetwin laelarmhu eat aahcateaapine hpyithkyinn ko rautt an hcay hkyinn nghaar ngar sieat. a kyahanyaupyaeat parwainmhu mimi sand aalyawwat hpyitpartaal .

Ngar laelarmhu ngarko saatswal par raan loaautpartaal aan saw nghaar narrlaipartaal .

0 ng ngar saatswalmayymyanrar hkanr hphoet sabhawtuu sai .
0 ng ngar saatswalmayymyanrar hkanr hphoet sabhawtuu kya parbhuu .

Ngar (shouthtarr sawsuu aapaunggthoet sai hc hcya sayy) k saatswalmayymyan hkanr hphoet lolarr kyapartaal.
1. ngar aainlar
2. hpone ko tasaint(mobhine)
3. a kyahanyaupyaeat swaymyoe sarr hkyinnsaatswal
4. aahkyarrnaeelam (saatmhaat) _____

Namuunar solhaawinmhu: s ngya sanyya HCV aapyusabhaw nhaint swaynamuunar myarrko lololarrlarr shi a mhu , ngarthoetsai sainthoet eata sway sai eat sayy ngaal tae namuunar twayko saimsaee hphoet lopartaal .

0 ng aasway ko ngar namuunar saimsaee htarr shisai hphoet sabhawtuu sai .
0 ng de swaynamuunar saimsaee htarr mai ko sabhawmatuu parbhuu .

ngarsai i laelarmhu parwainsaungrwat raan sabhawtuu

Parwainsuu rae aamai:		parwain suueat laatmhat:		nae hchaell	

luunarhcarmataatsuu aakaal.

s kya s hkayan		s kya s hkayan		nae hchaell	

rae aamai		eat laatmhat			

ngar hcaytanarwaanhtam i sutaysan eat rairwalhkyet shinnpyahkaesai kya pye . aakaunggsone ko ngar panyar a taat hcayraan, suu / suu m rairwalhkyet, lotehtonelotenaeemyarr, aantararalmyarr nhaint i sutaysan eat aakyoekyaayyjuumyarr ko narrlai sai .

hconehcamhcaitsayyrayymhauurae aamai:		hconehcamhcaitsayyrayymhauu laatmhaat		nae hchaell	

Patient Information sheet

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients

Manipur, 2017

Language: Kuki Original language: English

Consent form yet to be validated

Pu/Pi,

Hepatitis c na nei leh neilou naki vetsah in nana neitai.

hichi thu ahin kihoulim pi dia kou nahi.Hichi kihoukhom(study) na akhun napan napanlou naki gellhah masang akhun ipijeh ahichii study kibol aipi pi poimaw ahitikhu nangman nahet ngai ahi.Hijeh chun anoija hetdia kilawm hochu phatechan anasimlha in. Akisei ho hi nahet them lou auma chuleh nahetbe nom aumjongleh neidoh thei u ahi. Hiche a hi najao nom najaonom lou seinaphat namube ding ahie.

Hepatitis c (hcv) hi ipiham chuleh iti kijen ham?

Hepatitis C hi hit chikhat thin natna hinpolut hit khat ahie. Hiche hi natna khohtah khat hithei ahie. Hiche natna hin thin ahin suhset a chuleh jentei ahung hi nadinga chu kum tampitah ahin lahthei ahie.Tuchan a hi ajenna hi sum tamtah lut ahijeh in koijouse akijenjounaipoi. Tuthah ahin lout hah tampi hiche natna jen nadin ahung sohdoh tan chuleh aman jong ahung nem in hoi jong ahoi tai e.

Hiche natna hit neijouse chu kijen peipei ngal di ti ahideh poi e. Akijen dingdan chuleh ni ijat lutding ham tihi thil tamtah ho lahkhom tadia a chujouleh kisei thei penbep ding ahinalai e.Test chom chom kibol intin jen pat thein ahi nahilou kikhol ding ahinalai e. Hiche test results dungjui achu nakijen panding dan na Doctor pan nahin seipeh ding ahi.

Tutu dinmun hin India ah hiche natna jen nadin louthah aumnaipoi e.Doctor in nakijen nadin ahin guon ding hi World Health Organisation(WHO) toh Indian National Association for Studyof Liver in aphatsah pa ahie. Hiche louthah ho hi jahdinga phatsah ahilou leh jahthei ham ti hi achelhah jing laitah ahinalai e.experimental lou vang akijang poi.

Sikhom/study ding hi ipiham?

Hiche simkhomding hi ahin MSF medical team hotoh atohkhom piu NACO tohguon ahin chuleh NACO leh MSF ethical committee in aphatsah ahie.

Hiche study tup leh doi hi Hepatitis C kijen naho alolhin na ichan gei a lolhing ham ti ahie. Mi pilhing koi hile kum 18 apat achung lam HIV toh Hepatitis neikop hochu hiche study ahi jaodia ki kouding ahi.

Ipijeh a keihi ajao dia eikikou ham?

Hiche simkhom/study a naki kouna jeh chu nangjong chronic Hepatitis C nei nahi akimatdoh jeh ahie.

Hiche a hi kajao ngai ham?

Ahipoi, pan leh panlou chu nangkhut a kingam ahie. Napan di leh vang hiche lekha hi nakipe a nanop na soi nakai ngaiding ahie. Kajaonom poi natileh nanop phat phat a na ngah thei ahie chuleh ajeh jong nasei angaipoi e. Najao tahlou vanga nakijen nading hihen nakijen nasa ho ima abuoi ding aumpoi e.

Hiche ahi kajao leh i kati tadem?

Ajaoding nahitah leh, nanopna soi nakai ding, hiche chun staff ho nagn chung chang thu ho jah nathei phalna napeh hiding ahi. Namin tah vang itih hijong leh kijang louding ahi.
Nang chungchang tichu nakum,jinei neilou,natna dang naneiho,chuleh na kivetsah na results ho ki chingtup di ahie. Hiche hohi naming toh kikoi khom lou ding ahi. Number khatjoh naming lheng a kijang ding ahi koiman nang nahi ahetlou nadinga.Na Doctor pa toh aloi atoh khompi hobou toh nangin nahetdiu ahi. Research bolhon na number bou ahet diu koi nahi ahetloudiu ahitai.
Naming chuleh na kho naveng ho chu computer chom khat a nakikoi pehding, Number nakipe bou chu lhangphonga kimang ding ahie. Mihetdia nadei lou tichu, na natna, na HIV status, Khamnathei nabol, Ju nadon tiho hi mihetding nadeilou ding jeh a naming kisel ahi.

Ipi kabol ngai ham?

Angeina bang a Clinic a lou nakisan chuleh nakivetsah jiho ima a lamdang ding aumpoi e.Na kijen nangei bang a chelha jing ding ahinai e.
Numei nahi a HCV kijen nahi a nao navop khah tah leh aging lamthei pen a na Doctor nahetsah ding ahi. Na HCV kijen chu chomkhat ngah ngai ding ahi, ahinla na hung kivetsah jing toh hiche study a napan na hi angei bang a na sutjom ding ahie.

Ipi ham a risks chuleh aphatchomna ho (advantages)?

Thil akibol jouse hi nakijen natoh kisai ahi.Hiche study hin achombeh a akibolbe aumdeh poi e, study a najao jeh hi nagma kijen dan thil hohi midnd HCV kijen hotoh tekah na kibol ahie.
Nakijen amachal dan ho nakihetsah jingding chuleh na Doctor in nakimu pi jinga doh nom hetnom ho ama kom a nadoh a aman nahilchen jing ding tina ahi.
Hiche study akon a kimudoh leh kihedoh hohin ajen ho hetna apehbe a chuleh kijen dan hi ahoijo cheh a semphat ding ti hi ahie. Hiche hin midang dand adia jong phatchom na ahin pohdoh ding ahie.

Data kichomkhom hohi ipi a kajah ding uham?

*N*a medical record kilakhom jouse hi hoisel a kikoitup a nangma toh na medical toh na study team hobou in avet thei ding ahi.Namin tah hoima a kitahlang louding ahi.
Hiche study hi ajochen nadia kum 3 lutding ahie. Hiche hi akichai teng poster khat a akihedoh chuleh akimudoh jouse health centre a kitahdoh ding ahie hiche a chu a study results jouse namu thei ding ahi. Hiche results ho jonghi Scientific journal khat a kisuo ding ahie.

Navetsah jingding nikho leh phat hochu najom lou leh itiding ham?

Na kijensah hi akichai a lou naneh ding phatsung alhin tengleh, aki kinepna chu nadam chending ti ahin, ahinla nadam lheng mong mong ding ahitai tivang akisei thei naipoi hichedia chu a hit aum aumtah lou vetkitngaiding ahi. HCV treatment akichai teng na HIV kijen na chu najom jing nahlai ding ahi. Hiche kah lah ahi HCV veikit dia nakiginmo a ahileh na Doctor aganglam theipen a nakimu pi ngai ahi.

Na thisan lah a koichingding?

Nang in phalna neipeh uleh, na thisan 8ml hi lah a kum 5 sung koitup di kiti ahin, hiche kibol lo napen chu hiche nathisan hi treatment na lah naho a aphatchom naho het chen nading kiti ahi.Hiche na thisan hi nangchung chang thu themkhat toh, nakum chuleh pasal numei nahi bou kikoi ding naming jao louding koi nahi kihelouhel ding ahie.Na thisan jong kijoh louhel di ahie.

Na louneh na a boina aumleh itiding?

Thudoh ding nanei a, ahilouleh nalouneh a kona boina tichu nalouneh nakituopi lou aum khah leh, na doctor toh nurse koma nasei ngal ding ahie.

Doh Nom Seinom Na Neileh Koi Na Contact Ding Anuoi Ahin Akipe E

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Patient Information sheet

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients

Manipur, 2017

Language: Zou Original language: English

Consent form yet to be validated

Hepatitis C, HIV oh neikhom te adia loching tah a kikepthei nadia lampi siemtupna

Pu/pi

Hepatitis c nanei leh nneilou naki ensah a nanei tahi. Tami thu ah kihoulim pidia chial nahi. Tami ki houkhawmna study akhun,napanleh napanlou thupuahna nalaah masang in ,bangjiah a tami study ki bawl a,bangbang poimaw ahiai chikhu nangman nathei ngai ahi. Tuajieh in aneilam a theidia kibawl tekhu hoideu in simkhia in. Akigen tekhu natheisiamlou aum a,na theibe ut aum lehjong nadoh thei nading hunlem nanei a,tualeh napan utsih lejong na utlou thujong nagenthei hi.

Hepatitis C (HCV) bang ahia,bangchi kikep ahiai ?

Hepatitis C khu natna chikhat ahi. Tami natna khu natna jauhuai khat hing hithei ahi. Tami natna in sin angsuhsiat a,kep ahing ngai chiang in hunsawtpi khat alathei hi. Tuatan akhu akikepna nadia sum tampi lut ahijiah in mijousia akikem jousih hi. Hinaleh tukhang in damdawi tha ahingsuoh ta a,tuami damdawi pen hoijong ahoi a,amanjong atawm hi.

Tami natna hit neijousie khu,kijen peingalding china hilou in,aki kepdidan leh nibangjat lutding chi siltampi laahkhawm phot a tuajou chieng a kigenthei panding ahi. Test tuomtuom hing kibawl photding,tuajou chieng a jenthei nahileh nahilou kingaituo nalai ding ahi. Tami test dungjui a na doctor pan anghil theipan ding ahi.

Tuleh tu dinmun in india gam ah,tami natna jen nading damdawi (jatui) aum naisih hi. Doctor in angjen nading damdawi khu **world health organisation (who)** tawh **indian national association for study of liver** in aphal pieh pen ahi. Tami damdawi khu jahthei ahidiei ahisih diei chi akisui khiet laitah ahi. Experimental damdawi vang akijang sih dinghi.

Simkhawm (study) dingkhu bang ahiei ?

Tami simkhawm dingkhun msf medical team te tawh asep khawmpi naco leh msf ethical committee n aphatsah uh ahi. Tami study tupleh ngiimkhu hepatitis c kikep na a alawchinna bang ahiai chikhu ahi. Mi piching kum 18 apat atunglam hiv tawh hepatitis c neikhawm te chial ahi.

Bangdia kei ajau dia hing kihan e ?

Tami simkhawm (study) adia ahing kihat nakhu nangjong chronic hepatitis nei nahijieh ahi.

Tamna kapan angai ei ?

Hilou e,panding leh panlouding pen nangma khut a kinga ahi. Napan ding levang tami laipeh hing kipie a na utna suai na bawl ngai ahi. Napan utsih lejong nangma uthunhun in natawp thei hi ualeh ajiehjong nagen ngailou ding ahi. Napan nonlou ding vang a nakikep nasa te ah bangma buoina aum vawtsih dinghy.

Tamna kapan leh bang kachi tadiai ?

Apang ding nahi taleh na utna suai nakai ding hi. Tammi khun staff te kung a nangma tungtang athei thei nadia phalna napieh china ahi. Namin pen bangchih hunlai injong kijang louding ahi. Nang tungtang chipen ji nanei leh na neilou,natna dang nanei te tualeh na kietsahna result te kikoi tup ding ahi. Tualeh tamte khu naming tawh kikawi khawm louding ahi. Nambat khatkhu naming tang a kijang ding ahia,ajiehpen koiman nang nahilam ang theilou nading ahi. Na doctor paleh asep khawmpite leh nangchauh in nathei ding uh ahi. Research bawltenjong na nambat chauh athei ding ua,nangopen koi nahijong angthei sih ding uhi.
Namin tualeh nakhua naveng tepen computer tuomkhat a hing kikoi piehding ahi. Nambat hing kipepen khu langhtang tah a kijang ding ahi. Mithei dia nadeilou natna,hiv status,khamthei nabawl zu nadawn tekhu mithei dia andeilou dingjieh ahi.

Bang ka bawl angai ei ?

Angaina banga clinic a jatui (damdawi)na kisan tekhu bangma akilamdang ding aumsih hi. Na kijen napen angai bang a peilel ding ahi.

Bang e ajauhuai naleh aphat tuamna

Sil akibawl jousia khu nakikep natawh kisai ahi. Tami study khu atuamdeu a kibawlbe aum diehsih hi. Tami study a napanjieh pen nangma kikepna midang hcv kijenna tetawh ki enkhawm a kibawl ahi. Nakikep nain amasawn dante hing kitheisah jingding,dohnuam theibe nuam nanei a nadohleh aman anghil ding china ahi.
Tami study apat aki mube leh akimube te in,ang kemte pat theina kibelap naleh kikep dingdan ahoijawsem a siemphat ding china ahi. Tuajieh in tamikhu midang adding ajong phattuamna hing hiding ahi.

Data kiktom khawmte bang a kajah ding uh a hiei ?

Na medical record kila khawm jousie hoideu a kikoitup a,nangma leh na medical team te tawh na study team te chauh in a etthei ding ahi. Naming pen akitaah lang sih ding ahi.
Tami study pen akijaw nading in kum 3 alut ding hi. Tami abei chiang in poster khat a kitaah dawh a,tualeh akimudoh jousie **health centre** a kitaahdoh ding ahi. Tuajou chieng in study result jousie namuthei tading ahi. Tami result jousie khu **scientific journal** khat a kisuo ding ahi.

Naki etsah jing nading nileh hunte najop lou leh bang chiding ?

Na kietsah khu najaneh ding hun achinchieng in leh,kinepna khu nadamchien ding china ahi. Ahin na damsieng ngeingei ding chipen aki genthei naisih hi. Tuajieh in natna hit nanei leh naneilou etkia angai ding hi.hcv kikepna akijaw chieng ajong hiv natna kikepna napen peijom

jing veve ding ahi. Tuaban ah hcv vei kitdia naki ginmaw a ahileh na doctor pa akin theilam pen a nava kimupi ding ahi.

Na sisan laah a koitup ding

Nangma apat phalna aum leh na sisan 8ml laah a kum 5 koitup ding kichi ahi. Tami kibawl napen na sisan khu treatment kijen na apat naphat tuamna te theichian nading kichi ahi. Tami na sisan pen nag tungtangthu themkhat tawh ,nakum tualeh pasal nahileh hilou numei nahileh hilou chauh kikoiding namin jaulou ding,koi nahi hing kithei louding ahi. Tualeh na sisan jong kijuah louding ahi.

Naja nehna a buaina aumleh bangchi ding ?

Thudoh ding nanei a,ahisihleh naja neh na apat buaina,ban ah najaneh nakituahpi sihleh na doctor pa kungleh nurse te kung ah nagen pei ngal dinghi.

Dohnuam gennuam nanei leh koi na contact ding anei ah ahing kipie hi.

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STATEMENT OF CONSENT

Longitudinal cohort to evaluate Hepatitis C treatment effectiveness in HIV co-infected patients Manipur, 2017

Language: Pythe Original language: English

Copies:2 – one for the participant (patient) and other for participant's confidential personal file.

Patient information sheet yet to be validated

CONSENT PIAKNA THUPUAN

Hiai lai a kigelh thu te ka sim, ahihkeileh min ka theih dingin hon simsak hi. Dotna bawltheih dingin hanthawn in ka om a, dotna bawl dingin hun piakin le ka om hi. Study apang dingin phalna ka pia hi. Study a pangdia phalna ka piak nung a le bangziak hiam a ka kizuk kik ut leh pang nawnlou thei kahi chih ka thei hi. Keimah deihtelna le ut na ziak liauliau a pang kahi.

Apoimoh leh thuzak in le ka omthei chih ka thei hi.

☐ A hon thuzak uh ***ka ut*** A hon thuzak uh ***ka utkei***

Thuzakna dia ka deihte:

1. Mobile phone
2. Ka inn ua hong
3. Ka tanau te tungtawn a
4. Adang dang *(genchian in)* _____

STORAGE OF SPECIMEN

HCV hepatitis C positive bang na hih khak leh, na sisan tamlou ka kem nuam uh hi.

☐ Sisan kep di ***ka phal*** Sisan kep di ***ka phal kei***

Study ah pang dingin ka phalna ka pia.

Pangtu Min:		Pangtu Suai:		Ani:	

Damlou lai theilou bang ahihleh

Theihpihtu Min:		Theihpihtu Suai:		Ani:	

Apangtu di kiang ah thilsui (research) na ziak ka hilhchian hi. Ka theih tannin, hiai thilsuina (research) toh kisai, mipa/minu in a ziak, akibawldan, asia apha leh a phattuamna di a theikim vek hi.

Investigator's Min:		Investigator's Suai:		Ani:	

Appendix 6

Management of the adverse effects

The main side effects associated with sofosbuvir are: Sofosbuvir+ ribavirin - fatigue, headache, anaemia

Table 1. Treatment –emergent adverse events (all grades) reported in (> or = 15% of subjects in any treatment arm (Source Sovaldi package insert p.6)

Symptom	***Interferon free regimen***		
	Placebo 12 weeks N=71	*SOF+RBV 12 weeks N=650*	*SOF+RBV 24 weeks N=250*
Fatigue	*24%*	*38%*	*30%*
Headache	*20%*	*24%*	*30%*
Nausea	*18%*	*22%*	*13%*
Insomnia	*4%*	*15%*	*16%*
Pruritus	*8%*	*11%*	*27%*
Anemia	*0%*	*10%*	*6%*
Asthenia	*3%*	*6%*	*21%*
Rash	*8%*	*8%*	*9%*
Decreased appetite	*10%*	*6%*	*6%*
Chills	*1%*	*2%*	*2%*
Influenza Like Illness	*3%*	*3%*	*6%*
Pyrexia	*0%*	*4%*	*4%*
Diarrhea	*6%*	*9%*	*12%*
Neutropenia	*0%*	*<1%*	*<1%*
Myalgia	*0%*	*6%*	*9%*
Irritability	*1%*	*10%*	*10%*

Table 2: Management of adverse effects

Side effect	Comments	Suggested Management Strategies
GENERAL		
Fatigue	Fatigue is very common in patients with HCV and is probably increased on treatment with ribavirin. The following are not helpful in management of fatigue: dose reduction,	1. Check haemoglobin 2. Screen for depression 3. Suggest behavioural strategies to conserve energy e.g. rest periods, napping, planning ahead 4. Adequate fluid intake
Injection site reaction	Redness and induration are common. Occasionally painful nodules or ulceration may develop	1. Review technique for injection 2. Avoid painful or ulcerated areas

Side effect	Comments	Suggested Management Strategies
OTHER		
Respiratory Tract symptoms including shortness of breath	Ribavirin may be associated with cough.	1. Check haemoglobin (shortness of breath can occur with anemia); 2. CXR may be useful for persistent symptoms.
Rash	Itchy, dry, flaky skin is the most common abnormality due to treatment. It may resolve with time but will require treatment if severe.	1. Avoid powerful skin detergents and use regular non-perfumed skin moisturizers and sunblock during HCV treatment 2. If symptoms persist a low potency steroid cream (1% hydrocortisone) and antihistamine may be used (e.g. loratadine 10mg) 3. If severe and persistent a temporary reduction in the dose of RBV should be trialled.
Hearing Loss	Sudden loss of hearing and tinnitus have been described on treatment with ribavirin. The mechanism is unclear.	Hearing loss may not fully resolve after discontinuation of therapy but continuation of therapy may also not worsen symptoms.
AUTOIMMUNE DISEASES		
Diabetes Mellitus	Worsening of blood sugar control may occur on treatment for HCV	1. Counsel patients about the possibility of disturbances in glucose levels during treatment for HCV. 2. Advise to monitor blood sugar levels closely and medication dose adjustment may be required
increase of ALT/AST and/or jaundice-hepatitis flare	liver toxicity of all drugs in use	1. Consider liver toxicity of all drugs in use (record all drugs & doses in use + all drugs used last 7 days, plus alcohol consumption); 2. investigate HCV treatment failure with HCV VL & adherence; 3. investigate acute HEV infection (IgM & IgG; consider PCR if available) & HAV infection (IgM & IgG), 4. HBV treatment failure (check HBV viral load & treatment adherence); 5. HDV disease among HBsAg(+) including acute infection. Discuss all cases with HIV/TB/HCV advisor.
HAEMATOLOGICAL		
Anemia	Ribavirin causes haemolytic anemia and bone marrow suppression Usually occurs within 1-2 weeks of starting treatment in about 10% patients.	1. Management depends on baseline Hb and local normal range, availability of growth factors (e.g. erythropoietin), and whether patient has heart disease as anemia may worsen cardiac disease 2. If significant anemia occurs, the dose of ribavirin should be adjusted downwards by 200mg increments. 3. With improvements in Hb an attempt should be made to re-

Side effect	Comments	Suggested Management Strategies
		increase the dose. 4. To avoid dose reductions associated with anemia, growth factors may be used if available.
Neutropenia	No clear evidence exists that neutropenia during therapy has an adverse effect, nor that the use of G-CSF reduces rate of infections and/or improves SVR rates	Management depends on baseline neutrophil count, population normal range and the presence of other factors increasing the susceptibility to infection e.g. cirrhosis or HIV infection See below
Thrombocytopenia		Management depends on baseline platelet count and population normal range, See below