Standard Operating Procedure for Acute on Chronic Liver Failure (ACLF) Liver Transplantation Tier.

ACLFLTSOP V1.3

Background

a. The Acute on Chronic Liver Failure Liver Transplantation Tier (ACLFLT) provides a mechanism by which select patients with cirrhosis who are may be waitlisted in a prioritised waitlist tier that recognises both their high likelihood of death without liver transplantation and that of deterioration such that transplantation is not possible if they follow the standard process for elective transplantation.

b. The ACLFT is below that of Super-urgent priority and that of Hepatoblastoma, split-able grafts and critically ill paediatric recipients.

1.1 ACLFLT Candidate Selection.

1.1a Potential candidates will be selected by individual transplantation centre after local multi-disciplinary team review. Cases will be reviewed by a team including Hepatologist, Intensivist and Transplant Surgeon and accepted by consensus as meeting the ACLFLT entry criteria and the having physical reserve sufficient to survive transplantation.

1.1b Candidates may have already been waitlisted for LT under standard mechanisms and deteriorated whilst on the waitlist (WL), or may have presenting with ACLF without having had previous consideration for LT. Use of the ACLFLT is currently restricted only to patients with cirrhosis who have not undergone previous LT.

1.1c Each Transplant centre will have a local ACLF LT lead who may be consulted for advice and information on the practical use of the Tier.

1.2 Entry Criteria

A checklist for case inclusion is attached in appendix 1.

1.2a All patients considered for expedited transplantation under this scheme should have cirrhosis, significant liver failure as manifest by jaundice and coagulopathy and thus an illness that will be corrected by restoration of liver function by LT.

1.2b All patients should also have physiologic instability and organ dysfunction or failure that mandates care in a critical care (HDU or ICU) setting and is of severity such that a 28-day survival is consistently expected to be below 50%. This would most often be patients who

fulfil EASL-CLIF criteria for ACLF of Grade 3 (appendix 2). ACLF score and grade may be determined using the online tool at https://www.efclif.com/scientific-activity/score-calculators/clif-c-aclf.

1.2c Where cases with alcohol-related liver disease are being considered the standard guidance for acceptance of such cases will apply.

1.3 Exclusion Criteria

1.3a Cases will not be eligible for consideration for ACLFLT if they have chronic co-morbidity which would preclude them from LT under standard mechanisms.

1.3b Other exclusion criteria are:

- Age >60 years.
- Previous liver transplantation.
- Active bacterial or fungal sepsis.
- CMV viraemia.
- Severe irreversible brain injury.
- MOF of such a severity and/or with adverse trajectory precluding successful LT.
- Use of ECMO.
- Gross frailty and likely inability to rehabilitate.
- Active malignancy.
- Severe acute pancreatitis or intestinal ischemia.

1.3c It is recognised that some exclusion criteria – particularly those relating to assessment of severity of multi-organ failure or frailty – are not binary and may require subjective assessment. The opportunity to discuss these cases will be available at the point of case proposal prior to registration for ACLFLT.

1.4 Candidate Proposal

1.4a Following local multidisciplinary team review, confirmation of fulfilment of entry criteria and review of exclusion criteria. First contact will parallel the initial stages of the current national appeals process and the local proposing clinician will email LAG Chair and/or Deputy Chair (Doug Thorburn / John Isaacs; douglas.thorburn@nhs.net/ John.Isaac2@uhb.nhs.uk) who will then contact the ACLFLT Working Group lead (William Bernal: william.bernal@nhs.net). Cases will be discussed with the proposer by email and/or telephone to ensure that entry criteria are fulfilled and that exclusion criteria are not present.

1.4b If after review the LAG Chair and ACLFLT Working Group lead accept the patient onto the ACLFLT tier then the candidate may be registered as such with NHSBT.

1.4c This service will initially operate only during working hours and Monday to Friday. Once contact has been made with NHSBT, the assessment process with or without registration should be completed on the same working day.

1.5 Candidate Registration

When a candidate is accepted onto the ACLFLT tier, processes will differ according to whether the candidate is or is not already waitlisted for LT.

1.5a Where the candidate **is not** already waitlisted:

1. Complete the electronic Standard Elective Liver Registration Form (FRM4332/3) and return to ODT information services at as per standard processes.
2. Complete the ACLFLT Tier Registration Form (ACLFTFRM1) sections A and B and through standard processes and via email at XXX and to the ACLFLT Working Group lead (XXX).

1.5b Where the candidate **is** already waitlisted:

1. Complete the ACLFLT Tier Registration Form (ACLFTFRM1) sections A and C and return through standard processes and via email at XXX and to the ACLFLT Working Group lead (XXX).

2. Candidate Follow-up

Following registration under the ACLFLT Tier additional information supplementary to that submitted for standard follow-up to NHSBT will be returned to NHSBT and the ACLFLT Working Group lead whether or not the candidate undergoes LT. Data required is specified in Appendix 3 and it is the responsibility of the Centre ACLFLT lead to ensure that this is submitted in a timely fashion.

2.1 In Transplant Recipients:

Supplemental information will be required at the following time points:

1. At time of transplant
2. At hospital discharge
3. At 3 months post-transplant (coincident with standard NHSBT follow-up)
4. At 12 months post-transplant (coincident with standard NHSBT follow-up)

2.2 In Candidates not undergoing Transplantation

1. At hospital discharge
2. At 3 months post waitlisting

Appendix 1

Entry and Exclusion Checklist for ACLF Liver Transplantation Tier

Entry:

- Age >17 years / fulfilling criteria for adult LT.
- Cirrhosis with liver failure as manifest by jaundice and coagulopathy.
- Inpatient in Critical Care Unit (ICU or HDU) for organ support
- Expected 28-day survival <50%; ACLF grade ≥2, usually ACLF grade 3.

Exclusion:

- Age >60 years
- Previous Liver Transplantation
- Active bacterial or fungal sepsis
- CMV viraemia
- Severe irreversible brain injury
- MOF of such a severity and/or with adverse trajectory precluding successful LT.
- Use of ECMO
- Gross frailty and likely inability to rehabilitate
- Active malignancy
- Severe acute pancreatitis or intestinal ischemia

Appendix 2

Definitions for Classification of ALF Grade.

Table 9. CLIF-Sequential Organ Failure Assessment (SOFA) score (adapted from Ref. n° 3).

The CLIF-Sequential Organ Failure Assessment (SOFA) score					
Organ/system	**0**	**1**	**2**	**3**	**4**
Liver (bilirubin mg/dl)	<1.2	≥1.2–<2.0	≥2.0–<6.0	≥6.0–<12.0	**≥12.0**
Kidney (creatinine, mg/dl)	<1.2	≥1.2–<2.0	**≥2.0–<3.5**	**≥3.5–<5.0**	**≥5.0**
Cerebral (HE grade)	No HE	Grade I	Grade II	**Grade III**	**Grade IV**
Coagulation (INR and PLT count)	<1.1	≥1.1–<1.25	≥1.25–<1.5	≥1.5–<2.5	**≥2.5 or PLT ≤ 20.000/mm^3**
Circulation (MAP, mmHg and vasopressors)	≥70	<70	**Dopamine ≤5* or dobutamine or terlipressin**	**Dopamine >5* or E ≤0.1* or NE ≤0.1***	**Dopamine >15* or E >0.1* or NE >0.1***
Lungs					
PaO_2/FiO_2, or	>400	>300–≤400	>200–≤300	>100–≤200	**≤100**
SpO_2/FiO_2	>512	>357–≤512	>214–≤357	>89- ≤214	**≤89**

E, epinephrine; FiO_2, fraction of inspired oxygen; HE, hepatic encephalopathy; NE, norepinephrine; PaO_2, partial pressure of arterial oxygen; SpO_2, pulse oximetric saturation. The bold text indicates the diagnostic criteria for organ failures.
* µg/kg/min.

Table 10. Classification and grades of ACLF (adapted from Ref. 3).

Grades of ACLF	Clinical characteristics
No ACLF	No organ failure, or single non-kidney organ failure, creatinine <1.5 mg/dl, no HE
ACLF Ia	Single renal failure
ACLF Ib	Single non-kidney organ failure, creatinine 1.5–1.9 mg/dl and/or HE grade 1–2
ACLF II	Two organ failures
ACLF III	Three or more organ failures

ACLF, acute-on-chronic liver failure; HE, hepatic encephalopathy.

Source: EASL Clinical Practice Guidelines for the management of Patients with decompensated Cirrhosis Journal of Hepatology 2018 69 (2) 406-460

The Online Scoring Tool is at:

https://www.efclif.com/scientific-activity/score-calculators/clif-c-aclf.

Appendix 3

Supplementary Follow-up Data Required

Candidates Transplanted:

At time of Transplant

Laboratory values

HB (g/dl)
WBC ($x10^9$/l)
Neutrophil ($x10^9$/l)
Leucocyte ($x10^9$/l)
Platelets ($x10^9$/l)
Ur (mMol/l)
Cr (µmol/l)
Alb (g/dl
INR
Bilirubin (µmol/l)
Na (mMol/l)
K (mMol/l)
PO_2 (KPa)
FiO_2 (%)
Lactate (mMol/l)

Clinical State

Level of Care (1-3)
Ventilated (Y/N)
Renal Replacement therapy (RRT)
HE Grade (0-4)
Vasopressors Y/N
Mean Arterial Pressure (mmHg)

At Hospital Discharge:

Date of Hospital Discharge
Days ventilated
Days in ITU
Days RRT
Days in hospital
Renal status at D/C (Normal/impaired/RRT dependent)
Performance status at D/C (as per Standard Liver Dataset)

At 3 and 12 months post-LT (additional to existing NHSBT follow-up data)

Alcohol use Y/N
Units/week