**Appendix A:**

**EUROALF group participants**

1. Mark A Aldersley, Department of Hepatology, St. James’s University Hospital, Leeds, UK.
2. Jonathan Cohen, The Department of General Intensive Care, Rabin Medical Center, Campus Beilinson, Petah Tikva, Israel.
3. Angels Escorsell, Liver Unit, Hospital Clinic, University of Barcelona, Barcelona, Catalunya, Spain.
4. János Fazakas, Clinic of Transplantation and Surgery, Semmelweis University, Budapest, Hungary.
5. Valentin Fuhrmann, Department of Intensive Care Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.
6. Bernard Goubaux, Department of Anaesthesia and Intensive Care, Hôpital l'Archet, Centre Hospitalo-Universitaire de Nice, Nice, France
7. Aya D Hollmann, Critical Care Department, Vall d'Hebron University Hospital, Barcelona, Spain.
8. Eric Hoste, Department of Critical Care Medicine, Ghent University and Ghent University Hospital, Ghent, Belgium.
9. Mark Hudson, Liver Unit, Freeman Hospital, Newcastle upon Tyne, UK.
10. Philippe Ichai, Centre Hépato-Biliaire, AP-HP Hôpital Paul Brousse, Villejuif, France; Unit 785, Inserm, Villejuif, France; Faculté de Médecine, Univ Paris-Sud, Le Kremlin-Bicêtre, France.
11. Yaron Ilan, Liver Unit, Hebrew University-Hadassah Medical Center, Jerusalem, Israel.
12. Hadem Johannes, Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany.
13. Constantine J Karvellas, Division of Critical Care Medicine, Division of Hepatology,University of Alberta, Edmonton, Alberta, Canada.
14. Pierre-Francois Laterre, Critical Care Department, St Luc University Hospital, Université Catholique de Louvain, Brussels, Belgium.
15. Fin S Larsen, Department of Hepatology, University Hospital of Copenhagen, Copenhagen, Denmark.
16. Antoni Mas, Liver Unit, Hospital Clinic, University of Barcelona, Barcelona, Catalunya, Spain.
17. Pablo Monedero, Department of Anesthesia and Critical Care, Clinica Universidad de Navarra, Pamplona, Spain.
18. James O’Beirne, UCL Institute of Liver & Digestive Health, Royal Free Hospital, London, UK.
19. Marija Ribnikar, Department of Gastroenterology, University Medical Centre, Ljubljana, Slovenia.
20. Concha Ruiz-Villén, Department of Anesthesia, Hospital Universitario “Reina Sofía”, Córdoba, Spain.
21. Didier Samuel, Centre Hépato-Biliaire, AP-HP Hôpital Paul Brousse, Villejuif, France; Unit 785, Inserm, Villejuif, France; Faculté de Médecine, Univ Paris-Sud, Le Kremlin-Bicêtre, France.
22. Kenneth J Simpson, Scottish Liver Transplantation Unit, Royal Infirmary of Edinburgh, Edinburgh, UK.

**Appendix B:**

**European ALF Consortium Practice Questionaire**

|  |  |
| --- | --- |
| Name |  |
| Specialty |  |
| Country |  |
| Institution |  |

**Institution and activity**

|  |  |
| --- | --- |
| 1. What is the nature of your institution? | □ University Teaching hospital □ Non-teaching hospital □ Other |
| 2. How many inpatient beds does it have? | □ <100 □ 100-300 □ 300-500 □ 500-1000 □ >1000 |
| 2. Is it a liver transplantation centre? | □ Yes □ No |
| 3. How many elective and emergency liver transplants are performed annually? | □ <20 □ 20-50 □ 50-100 □ >100 |
| 4. How many transplants for ALF are performed annually? | □ <10 □ 10-20 □ 20-40 □ >40 |
| 5. How many patients with ALF do you admit annually? | □ <10 □ 10-20 □ 20-40 □ 40-60 □ >60 |

**Standards of Care**

**General issues**

|  |  |
| --- | --- |
| 6. Who takes external referrals with ALF to your hospital | □ Hepatologist □ Surgeon □ Intensivists □ Other (Specify) |
| 7. What is the average time from external referral to admission | □ <1 day □ 1-2 days □ 2-5 days □ Other (Specify) |
| 8. What proportion of patients do you think would have benefited from earlier referral? | □ <25% □ <50% □ >50% □ >75% □ 100% |
| 9. In those who are initially admitted to the ward environment – do you have any difficulty in arranging admission to an intensive care unit area? | □ Yes □ No |
| 10. How frequently will the patient be reviewed by a ‘consultant' or senior doctor? | □ >1/Day □ Daily □ Alternate days □ Weekly □ Other |

**Ward based care**

**What proportion of ward ALF patients?**

|  |  |
| --- | --- |
| 11.   Receive antibiotics? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 12. Receive systemic antifungals? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 13. Have abdominal ultrasound? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 14. Have abdominal CT or MR? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 15. Have Volumetric CT? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 16. Have transjugular liver biopsy? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 17. Receive terlipressin? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 18. Receive intravenous albumin? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 19. Receive lactulose? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 20. Receive ammonia lowering drugs (LOLA, benzoate etc)? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 21. Receive intravenous n-acetyl cysteine? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 22. Do you administer n-acetyl cysteine to patients with non-paracetamol ALF? | □ Yes □ No |

**Nutrition Support**

**What proportion of ward ALF patients:**

|  |  |
| --- | --- |
| 23. Take unmodified normal diet only? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 24. Are given dietary supplements? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 25. Are fed by nasogastric tube? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 26. Receive intravenous feeding? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 27. Receive branched chain amino acids? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |

**Coagulation**

|  |  |
| --- | --- |
| 28. Which coagulation parameters do you measure | □ Prothrombin time □ APTR □ INR □ Fibrinogen  □ Factor V □ Thromboelastography □ Other (Specify) |
| 29. Do you administer routine coagulation support (FFP/Cryoprecipitate)? | □ Yes □ No |
| 30. What proportion will be given coagulation support as part of standard care? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 31. Do you administer coagulation support prior to procedures (eg central lines/paracentesis)? | □ Yes □ No |
| 32. Do you administer routine platelet support? | □ Yes □ No |
| 33. At what level do you supplement platelets? | □ <20 □ 20-50 □ 50-75 □ 75-100 |

**ICU Based Care**

|  |  |
| --- | --- |
| 34. Who is in charge of care of ALF patients who require ICU/HDU care? | □ Hepatologists □ Surgeons □ Intensivists □ Shared care □ Other (Specify) |
| 35. What level of encephalopathy triggers ICU/HDU admission? | □ Grade 0 □ Grade 1 □ Grade 2 □ Grade 3 □ Grade 4 |
| 36. How frequently will the patient be reviewed by a ‘consultant' or senior doctor? | □ >1 X Daily □ Daily □ Alternate days □ Weekly □ Other (Specify) |

**What proportion of patients?**

|  |  |
| --- | --- |
| 37.   Receive antibiotics? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 38. Receive systemic antifungals? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 39. Have abdominal ultrasound? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 40. Have abdominal CT or MR? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 41. Have Volumetric CT? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 42. Have transjugular liver biopsy? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 43. Receive terlipressin? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 44. Receive intravenous albumin? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 45. Receive lactulose? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 46. Receive ammonia lowering drugs (LOLA, benzoate etc)? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 47. Receive intravenous n-acetyl cysteine? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 48. Take standard diet only? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 49. Are given dietary supplements? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 50. Are fed by nasogastric tube? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 51. Receive intravenous feeding? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 52. Receive branched chain amino acids? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 53. Do you administer n-acetyl cysteine to patients with non-paracetamol ALF? | □ Yes □ No |

**Coagulation**

|  |  |
| --- | --- |
| 54. Which coagulation parameters do you measure | □ Prothrombin time □ APTR □ INR □ Fibrinogen  □ Factor V □ Thromboelastography □ Other (Specify) |
| 55. Do you administer routine coagulation support (FFP/Cryoprecipitate)? | □ Yes □ No |
| 56. What proportion will be given routine coagulation support? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 57. Do you administer coagulation support prior to procedures (eg central lines/paracentesis)? | Central line insertion: □ Yes □ No  Paracentesis: □ Yes □ No  Transjugular biopsy: □ Yes □ No |
| 58. Do you administer routine platelet support? | □ Yes □ No |
| 59. At what level do you supplement platelets? | □ <20 □ 20-50 □ 50-75 □ 75-100 |

**Cardiovascular support**

|  |  |
| --- | --- |
| 60. What is your first-line vasopressor? | □ Norepinephrine □ Epinephrine □ Dopamine □ Other |
| 61. Do you use corticosteroids for cardiovascular support? | □ Yes □ No |
| 62. Do you perform synacthen (ACTH) testing? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 63. What form of cardiovascular monitoring do you use | □ Pulmonary artery catheter □ PICCO □ LIDCO □ Other (Specify) |
| 64. What is your preferred site of central venous catheterization? | □ Femoral □ Jugular □ Subclavian |

**Neurological Support**

|  |  |
| --- | --- |
| 65. What level encephalopathy precipitates intubation and ventilation? | □ Grade 0 □ Grade 1 □ Grade 2 □ Grade 3 □ Grade 4 |
| 66. What proportion of ventilated patients with encephalopathy do you administer sedation to? | □ 0-25% □ 25-50% □ 50-75% □ 75-100% |
| 67. What are your preferred sedative agents for patients with ALF (Please check one or more boxes as required) | □ Opiates □ Benzodaizepines □ Propofol □ Other (Specify) |
| 68. What proportion of ventilated patients receives muscle relaxants? | □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 69. Do you use intra-cranial pressure monitoring? | □ Yes □ No |
| 70. If yes, what are your triggers to ICP monitor insertion? | Elevated ammonia: □ Yes □ No  Cardiovascular instability: □ Yes □ No  Pupillary abnormalities: □ Yes □ No  Young age: □ Yes □ No  Severity of coagulopathy: □ Yes □ No  Renal failure: □ Yes □ No  Other (Specify) |
| 71. In what proportion of patients with HE of grade 3 and above do you insert ICP monitors? | □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |
| 72. With which agents do you correct coagulation with prior to ICP monitoring? | □ Fresh Frozen plasma □ Cryoprecipitate □ Platelets □ Novo 7 □ Other (Specify) |
| 73. Do you support coagulation daily once an ICP bolt has been placed | □ Yes □ No |
| 74. What is the ICP pressure that will trigger treatment? | □ 10-15 □ 15-20 □ 20-25 □ 25-30 □ >30 |
| 75. With which first line interventions do you treat raised intracranial pressure? | Mannitol: □ Yes □ No  Hypertonic saline: □ Yes □ No  Indomethacin: □ Yes □ No  Barbiturates: □ Yes □ No  Hyperventilation: □ Yes □ No  Increased sedation: □ Yes □ No  Other (Specify) |
| 76. Which agents do you use for raised ICP not responding to first-line therapy? | Mannitol: □ Yes □ No  Hypertonic saline: □ Yes □ No  Indomethacin: □ Yes □ No  Barbiturates: □ Yes □ No  Hyperventilation: □ Yes □ No  Increased sedation: □ Yes □ No  Other (Specify) |
| 77. Do you target a specific cerebral perfusion pressure? | □ Yes □ No |
| 78. If yes, what CPP? | □ 40-50 □ 50-60 □ 60-70 □ >70 |

**Renal Support**

|  |  |
| --- | --- |
| 79. What primary form of renal replacement therapy do you use for patients with ALF? | □ Continuous Hemofiltration or hemodialysis □  Intermittent hemodialysis □ Other (Specify) |
| 80. Do you use a specified 'dose' of continuous hemofiltration? | □ Yes □ No  If yes, what dose |
| 81. What are your triggers for renal replacement therapy? | Hyperkalemia: □ Yes □ No  Fluid overload: □ Yes □ No  Acidosis: □ Yes □ No  Elevated ammonia: □ Yes □ No  Oliguria: □ Yes □ No  Elevated Lactate: □ Yes □ No |

**Transplantation**

|  |  |
| --- | --- |
| 82. Who makes decisions in relation to Transplantation? | □ Hepatologists □ Surgeons □ Intensivists □ Multi-disciplinary team □ Other |
| 83. Do you have an age limit in relation to transplantation? | □ Yes □ No |
| 84. If yes, what is the age above which transplantation is not considered? | □ >30 years □ >40 years □ >50 years □ >60 years |
| 85. What transplantation criteria do you apply? | □ Clichy □ Kings College □ Other |
| 86. What proportion of patients listed undergoes Transplantation? | □ 0-25% □ 25-50% □ 50-75% □ 75-100% |
| 87. What is the average wait-time before surgery? | □ 0-1 day □ 1-2 days □ 2-3 days □ >3 days |
| 88. What would you estimate the survival rate to be in patients who fulfill transplantation criteria but do not undergo surgery? | □ 0% □ 0-25% □ 25-50% □ 50-75% □ 75-100% □ 100% |

**89. What do you think are the pivotal areas we need to address in the future for ALF research?**