

EASL 2010 Highlights

Artificial liver support

- HELIOS trial (Rifai #6)
 - Prometheus+SMT vs. SMT in acute-on-chronic liver failure
 - N=145
 - Kein survival benefit (28d: 66% vs. 63%)
 - Survival benefit in Subgruppe mit MELD >30 (p=0.02)
- MARS RELIEF trial (Banares #184)
 - MARS+SMT vs. SMT in acute-on-chronic liver failure
 - N=189
 - Kein survival benefit (28d: 59% vs. 60%)
 - „There is no life on MARS“
- High-volume plasmapheresis in acute liver failure (Larsen, EASL-CLIF)
 - N=160
 - Signifikante Verbesserung des transplant-free survival
- Albumindysfunktion bei chron. Leberversagen (Öttl et al., BBA 2008; Jalan et al., Hepatology 2009) → neues Therapiekonzept?

EASL 2010 Highlights

Alcoholic liver disease

- PNPLA3/adiponutrin gene polymorphism in alcoholic liver cirrhosis (Stickel #1183)
 - Erstbeschreibung Romeo et al. Nature Genetics 2008
 - Zahlreiche Publ. zu NAFLD Pathogenese
- Liver transplantation in patients with alcoholic hepatitis (Duclos-Vallee, EASL-ESBRA)
 - case-control study
 - 20 Pat mit schwerer AH (Nonresponse auf 7d Steroide) → early liver transplantation
 - Survival 75% vs. 35% (historische Kontrollen)
 - Alkoholrezidiv 1/20
 - Delay bis zur Listung median 23d
 - Delay Listung → LTX median 35d

6-Months Abstinence Rule??

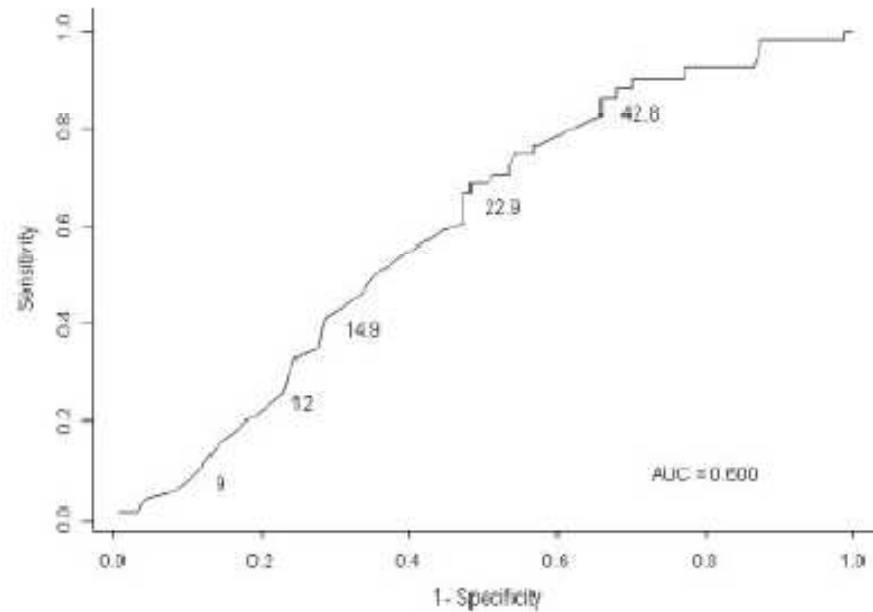


Figure 3. ROC curve for the prediction of relapse (single use) within 18 months of transplant using months sober prior to transplant (selected points on curve labeled with corresponding months sober pre-LTX). *The numbers on the curve are months of pre-LTX sobriety.

DiMartini et al., Liver Transplantation 2006

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Hepatitis C

- IL-28 Polymorphismen
 - Ansprechen auf Peg-IFN/Ribavirin
 - Spontanclearance bei akuter Hepatitis C
- Silibinin rescue therapy (Biermer #36)
 - 11 Pat mit suboptimaler Response auf Standardtherapie
 - geringe Virämie (15-2000 IU/ml) 8 Wochen lang (Wo. 16-30)
 - 1400 mg Silibinin (4A Legalon) an 2 aufeinanderfolgenden Tagen
 - 8/11 Patienten nach 1 Woche virusfrei
- Vitamin D Supplementation (Abu Mouch #55)
 - Vitamin D wirkt immunmodulatorisch (T_{reg}), antifibrotisch, ...
 - Vitamin D Spiegel bei CHC ↓, korreliert invers mit Fibrose (Petta et al., Hepatology 05/2010)
 - Pilotstudie (n=58)
 - Gruppe A: Vortherapie mit Vit. D 1000-4000 E/d 4 Wo.
 - EVR 96% vs. 48%
 - SVR 86% (13/15) vs. 41% (5/12)

EASL 2010 Highlights

Cholestatic Liver Diseases

1. **Autotaxin but not bile salts correlate with itch intensity in cholestasis (Kremer et al.)**

Methods:

Autotaxin activity was measured enzymatically in diluted serum samples of patients with intrahepatic cholestasis of pregnancy, PBC, PSC

In mice, scratch activity after intradermal pruritogen injection was quantified.

Results:

Serum bile salts, histamine, tryptase and μ -opioids did not show any correlation with itch intensity. ATX activity highly correlated with intensity of pruritus and was markedly increased in sera from cholestatic patients with vs. without pruritus

In PBC patients who underwent nasobiliary drainage, itch intensity as well as ATX activity decreased. Serum bile salts show no correlation

Conclusion:

ATX and its product LPA, play a key role in cholestatic pruritus

Future therapy in case of pruritus?

- ATX inhibitors
- LPA receptor blockers

2. Farnesoid-X Receptor Agonists: A new class of drugs for the treatment of PBC? An international study evaluating the addition of INT-747 to UDCA (D. Shapiro)

INT-747: 6-ethyl chenodeoxycholic acid is a novel derivate of the primary human bile acid CDCA (natural ligand of FXR receptor, a nuclear hormone receptor); 100x more potent than FXR agonist than CDCA

Methods:

- international double blind placebo controlled multicenter study
- effects of INT 747 on AP, other liver enzymes

Results:

- INT 747 10 mg: $-23,7 \pm 17,8$ %AP
- INT 747 25 mg: $-24,7 \pm 17,9$ %AP
- INT 747 50 mg: $-21,9 \pm 27,6$ %AP
- vs. Pbo $-2,6 \pm 12,5$ %AP

INT 747 10 mg: -28 ± 27 %ALT
INT 747 25 mg: -35 ± 22 %ALT
INT 747 50 mg: -21 ± 49 %ALT
vs. Pbo -0 ± 35 %ALT

EASL 2010 Highlights

Postgraduate Course

- Adrenal dysfunction in acute-on-chronic liver failure
 - Relative adrenal insufficiency (RAI) häufig bei Zirrhotikern mit septischem Schock
 - Hydrocortison 4x50 mg bei pathologischem Synacthen-Test (68%) → Überleben 64% vs. 32% (Fernandez et al., Hepatology 2006)
- Early TIPS in variceal bleeding (Garcia-Pagan et al., NEJM in press)
- Primary prophylaxis of variceal bleeding
 - Propranolol nach wie vor first-line
 - Carvedilol: zu wenig Daten