

SUPPLEMENTAL MATERIAL

Antibiotic and antifungal prophylaxis in Liver transplant recipients

Standard antibiotic prophylaxis for LT is performed with ev cefotaxime (Cefotaxime, Mylan Generics, Italy) 2 gr plus ev ampicillin (Ampicillina, Biopharma, Italy) 2 gr at anesthetic induction, with a supplementary dose administration after 3 and 6 hours during the surgical procedure and then every 8 hours for 3 days) . For patients allergic to penicillin standard prophylaxis is ev ciprofloxacin (ciprofloxacin, Mylan Generics, Italy) 400 mg at anesthetic induction, then every 6 hours during the procedure and then every 12 hours, plus ev clindamycin (Dalacin, Pfizer, Italy) 600 mg at anesthetic induction, then every 6 hours during the procedure and then every 8 hours, both for 3 days.

Patients with a pre-LT surveillance rectal swab positive for a pathogen resistant to standard prophylaxis (either MDR gram negative or VRE) received an individualized peri-operative anti-bacterial prophylaxis for 3 days, based on the bacteria susceptibility test.

Other prophylaxis

All patients received a PCP prophylaxis consisting in trimethoprim 160 mg and sulfamethoxazole 800 mg (Bactrim, Eumedica Pharmaceuticals, Germany) three times a week, as soon as oral administration could be tolerated and for the first 6-12 months after transplantation.

All patients with at least two risk factors for candidiasis received anti-fungal prophylaxis with fluconazole (Flucanazolo Kabi, Fresenius Kabi, Italy) (6mg/kg for a week). All patients with at least one risk factor for *Aspergillus* received liposomal amphotericin B (Ambisome, Gilead, Italy) 3mg/kg/die or anidulafungin 100 mg/die for a week.

LT recipients who were seronegative for CMV and received an organ from a CMV seropositive donor (D+/R-) had anti-viral prophylaxis with ganciclovir (Cymevene, Recordati, Italy) 5mg/kg/die or valganciclovir (Valganciclovir, Teva, Italy) 900mg/die for 3 months as soon as oral administration was possible. All the other patients received acyclovir as antiviral prophylaxis.

Table S1: Microorganisms causing infections in the first 30 days after OLT in patients treated and not treated with IgM enriched preparation.

	TOTAL	NO IgM	IgM	p
Microorganisms causing infections 30 days after OLT (n, %)	38	23	15	
Gram-positive microorganisms (n, %)	17 (0,45)	10 (0,43)	7 (0,46)	0,847
<i>Enterococcus spp. (n)</i>	7	4	3	
<i>Coagulase-negative staphylococci (n)</i>	5	3	2	
<i>Others (n)</i>	5	3	2	
Gram-negative microorganisms (n, %)	14 (0,37)	8 (0,35)	6 (0,40)	0,749
<i>Pseudomonas aeruginosa (n)</i>	5	3	2	
<i>Klebsiella spp (n)</i>	2	2	0	
<i>Escherichia coli (n)</i>	3	1	2	
<i>Others (n)</i>	4	2	2	
Fungal infections (n, %)	7 (0,18)	5 (0,22)	2 (0,14)	0,514
<i>Candida spp</i>	4	3	1	
<i>Aspergillus Fumigatus</i>	3	2	1	

Abbreviations: IgM, IgM-enriched polyclonal immunoglobulins preparation

Table S2: Demographics, severity score and pre-transplantation infective condition, in a subpopulation of 66 patients obtained by propensity score based matching, treated and not treated with IgM enriched preparation.

	TOTAL (n=66)	NO IgM (n=33)	IgM (n=33)	p-value
Age (years; median- IQR)	56 (52-62)	57 (53-61)	55 (51-63)	0,437
Female (n, %)	17 (25,8)	9 (27,3)	8(24,2)	0,778
MELD score (median-IQR)	21 (12-29)	22 (12-29)	16 (11-27)	0,284
Causes of ESLD (n, %)				
<i>Hepatocellular carcinoma</i>	15 (22,7)	9 (27,3)	6 (18,2)	0,378
<i>HBV-related</i>	7 (10,6)	6 (18,2)	1 (3)	0,046
<i>HCV-related</i>	18 (27,3)	11 (33,3)	7 (21,2)	0,269
<i>Alcoholic</i>	27 (40,9)	13 (39,4)	14 (42,4)	0,802
<i>Other causes</i>	26 (39,4)	9 (27,3)	17 (51,5)	0,044
Non -standard antibiotic prophylaxis (n, %)	83 (92,2)	29 (87,9)	31 (93,9)	0,392
Anti-fungal prophylaxis (n, %)	39 (43,3)	14 (42,4)	11 (33,3)	0,432
Risk Factors for post-operative infections (n, %)				
<i>Ongoing Infections</i>	37 (41,1)	13 (3339,4)	14 (42,4)	0,802

<i>Infections 30 days before OLT</i>	53 (58,9)	21 (63,6)	17 (51,5)	0,319
<i>Colonization MDR 30 days before OLT</i>	59 (65,6)	23 (69,7)	21 (63,6)	0,602
<i>ICU admission 30 days before OLT</i>	18 (20)	6 (18,2)	8 (24,2)	0,547

Abbreviations: n, number; IQR, interquartile range; OLT, orthotopic liver transplantation; MELD, model of end stage liver disease; ESLD: end stage liver disease; HBV, hepatitis B virus; HCV, hepatitis C virus; IgM, IgM-enriched polyclonal immunoglobulins preparation; ICU, intensive care unit; MDR: multidrug resistance micro-organisms. Other causes included: autoimmune diseases, re-transplant for complications, hemochromatosis, Budd- Chiari syndrome.

Table S3: New bacterial infections in the first 30days after transplantation, intensive care unit and hospital free days, and mortality at day 30 and 90 after transplantation, in a subpopulation of 66 patients obtained by propensity score based matching, treated and not treated with IgM enriched preparation, treated and not treated with IgM enriched preparation.

	TOTAL (n=66)	NO IgM (n=33)	IgM (n=33)	p-value
New Infections 30 days after-OLT (n, %)	25 (37,9)	16 (48,5)	9 (27,3)	0,067
MDR infections 30 days after OLT (n, %)	10 (15,2)	5 (15,2)	5 (15,2)	1
New colonization by MDR 30 days after OLT (n, %)	16 (24,2)	10 (30,3)	6 (18,2)	0,251
New Pneumonia 30 days after-OLT (n, %)	12 (18,8)	6 (18,2)	6 (18,2)	0,176
New abdominal infections 30 days after-OLT (n, %)	11 (16,7)	8 (24,2)	3 (9,1)	0,198
New primary blood stream infections 30 days after-OLT (n, %)	0 (0)	0 (0)	0 (0)	
New other infections 30 days after-OLT (n, %)	3 (4,5)	2 (6)	1 (3)	0,269
New fungal infections 30 days after-OLT (n, %)	5 (22,7)	5 (15,2)	0 (0)	0,020
New septic shock 30 days after-OLT (n, %)	1 (1,5)	1 (3)	0 (0)	0,321
ICU free days at day 30 after OLT (median, IQR)	27 (24-28)	26 (25-27)	27 (24-28)	0,424
New AKI requiring CRRT 30 days after-OLT (n, %)	3 (4,5)	1 (3)	2 (6)	0,534
Re-laparotomy 30 days after-OLT (n, %)	7 (10,6)	4 (12,1)	3 (9,1)	0,722
Hospital free days at day 90 (median, IQR)	66 (24-77)	68 (44-76)	66 (24-78)	0,928
Mortality at day 30 post OLT (n, %)	3 (4,5)	2 (6,1)	1 (3)	0,555

Mortality at day 90 post OLT (n, %)	7 (10,6)	5 (15,2)	2 (6,1)	0,230
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Abbreviations: n, number; OLT, orthotopic liver transplantation; MDR, multi drug resistant; IgM, IgM-enriched polyclonal immunoglobulins preparation; ICU, intensive care unit.