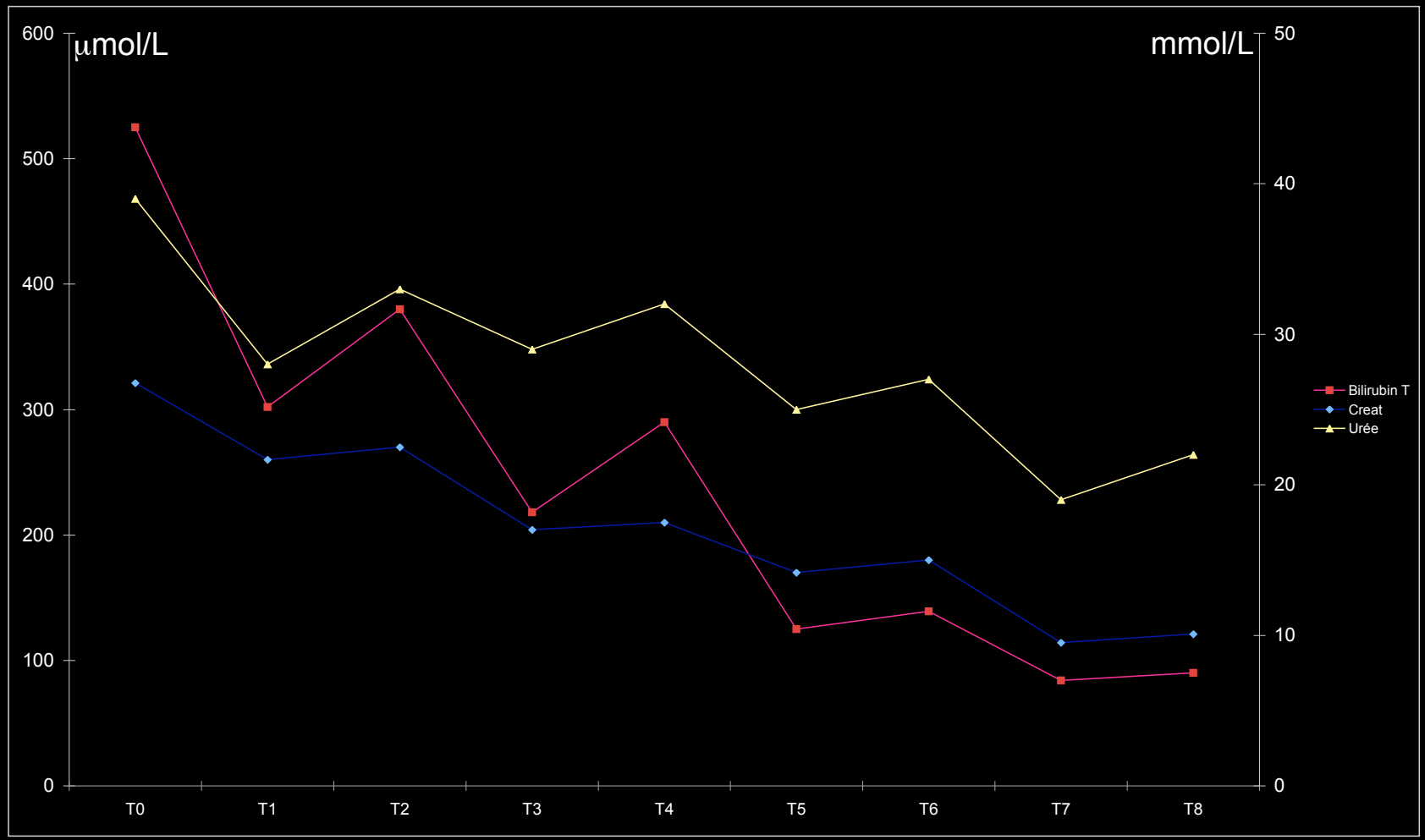
Ictères cholestatiques

JM Constantin

Actualités sur les supports hépatiques artificiels
Dialyse à l'albumine par le système MARS®
6 Fevrier 2008

Expérience Clermontoise
9 Patients

- Indications : Ictère cholestatique
  - 2 ALF
  - 5 AoCLF
  - 2 ALF post TH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Bilirubin T
Creat
Urée

	SAPSII	VM	IRA	Choc	Sepsis	nMars	TH	Devenir
HF	54	Oui	Oui	Oui	Oui	4	Oui	S
HF	29	Oui	Oui	Non	Non	2	Oui	DC (J3)
VHC	32	Non	Non	Oui	Non	5	Non	S
VHC	58	Oui	Oui	Oui	Oui	4	Oui	S
Ci.OH	64	Oui	Non	Oui	Non	6	Oui	S
Ci.OH	34	Oui	Oui	Oui	Oui	5	Non	DC
Ci.OH	42	Oui	Oui	Oui	Oui	8	Non	DC
NRFG	64	Oui	Oui	Oui	Non	4	Oui	S
VHCr	38	Non	Ouil	Oui	Non	11	Oui	S
Total	46 ± 14	7/9	7/9	8/9	4/9	5±3	6/9	6/9

Table 1. Demographic data of eight patients with acute exacerbation of chronic liver disease treated with the molecular adsorbent recycling system (MARS)

Patient No.	Age	Sex	Liver Disease	Precipitating Event	APACHE II Score	Encephalopathy Stage	No. of MARS Treatments	Outcome
1	56	M	Alcohol, HCV	SBP	30	III/IV	5	Death (30 d)
2	45	M	Alcohol, HCV	Upper GI bleeding Acute hepatitis	21	III/IV	8	Death (60 d)
3	24	F	HCV	Upper GI bleeding	18	II/III	2	OLT
4	67	F	Cryptogenic cirrhosis	SBP	27	II/III	2	Death (1 d)
5	60	M	Alcohol	Unknown	28	IV	1	Recovered
6	37	F	Alcohol	UTI	17	III	3	Recovered
7	29	F	Amyloidosis, FMF	Sepsis	19	II/III	2	Recovered
8	61	M	Alcohol	Upper GI bleeding	20	III	2	Recovered

APACHE II, Acute Physiology and Chronic Health Evaluation II; HCV, hepatitis C virus; FMF, familiar Mediterranean fever; SBP, spontaneous bacterial peritonitis; GI, gastrointestinal; UTI, urinary tract infection; OLT, orthotopic liver transplantation.

Parameters	Pre-MARS	Post-MARS	*p* Value
Ammonia, mg/dL	280 ± 67	65 ± 6	<.005
Lactate, mmol/L	6.5 ± 1.2	2.8 ± 0.7	<.02
Albumin, g/dL	3.9 ± 0.4	4 ± 0.9	ns
Blood urea nitrogen, mg/dL	29 ± 3.2	10 ± 1	<.03
Creatinine, mg/dL	2.3 ± 0.2	1.2 ± 0.7	<.04
Glucose, mg/dL	145 ± 10	134 ± 10	ns
Total bilirubin, mg/dL	25 ± 6	12 ± 2	<.03
Direct bilirubin, mg/dL	17 ± 3.6	8 ± 1.7	<.03
Aspartate aminotransferase, U/L	937 ± 305	584 ± 305	ns
Alanine aminotransferase, U/L	836 ± 448	518 ± 230	ns
Alkaline phosphatase, U/L	128 ± 10	121 ± 12	ns
Prothrombin time, secs[a]	21 ± 2	20 ± 3	ns
Platelets, 1000/μL	78 ± 16	81 ± 11	ns
Hematocrit, %	28 ± 2	30 ± 1	ns

Sorkine *CritCareMed* 2001

Patient ID	Age	Sex	Etiology (Precipitating event)	SAPS	MELD	UNOS	HRS	HE	N. MARS
1	28	F	NASH (Sepsis)	55	30	2a	No	II	4
2	23	F	WD (WD crisis)	59	35	2a	No	IV	2
3	45	M	HBV (Upper GI bleeding)	44	49	2a	No	II	6
4	49	M	ETOH (SBP)	61	50	2a	Yes	I	2
5	71	M	HBV (SBP)	33	43	no status	Yes	I	4
6	44	F	WD (WD crisis)	32	35	1	No	II	2
7	28	F	HBV (SBP)	39	38	1	No	IV	1

	Pre-MARS	Post-MARS	*P*
Total bilirubin (mg/dl)	42.4 ± 13.6	30.4 ± 7.3	0.0000009
Conjugated bilirubin (mg/dl)	29.4 ± 9	19 ± 6	0.000000
Unconjugated bilirubin (mg/dl)	13.1 ± 7.5	11.1 ± 4.4	0.07
Albumin (g/dl)	3.2 ± 0.5	3.3 ± 0.5	0.0009
Bile acids (mmol/L)	190.9 ± 133.5	131.5 ± 92.5	0.0001
BUN (mg/dl)	61.5 ± 37.05	43.9 ± 25.57	0.00001
Creatinine (mg/dl)	2.97 ± 2.07	2.23 ± 1.44	0.00004
PT (%)	36.1 ± 13.7	38.6 ± 13.4	0.05

BUN indicates blood urea nitrogen; PT: prothrombin time.

Patient ID	Bridge time (days)	Complications	Outcome (3 months)
1	22	—	OLTx, alive
2	—	Multi organ failure	Death
3	36	Fungal pneumonia	OLTx, alive
4	—	Multi organ failure	Death
5	—	Bacterial pneumonia	Death
6	5	Respiratory failure	OLTx, alive
7	—	Sepsis	Death

DiCampli *Artif organ* 2003

An Australian Experience With the Molecular Adsorbents Recirculating System (MARS)

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Kurtovic *Ther Aph Dial* 2006

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (years)	71	43	32	40	46	48
Gender	Male	Male	Female	Male	Female	Male
APACHE II	33	30	34	25	31	28
Diagnosis	AoCLF 2o sepsis Grade 4 HE HRS	Liver damage 2o sepsis ATN	Liver damage 2o sepsis ATN	AoCLF 2o sepsis Grade 3 HE HRS	AoCLF 2o sepsis Grade 3 HE HRS	AoCLF 2o sepsis Grade 4 HE HRS controlled on terlipressin
Background	Cirrhosis (NASH)	Post-hemi hepatectomy	Post-renal transplant	Cirrhosis (HCV, alcohol)	Cirrhosis (HCV)	Cirrhosis (HCV, alcohol)
Child-Pugh	Class C	N/A	N/A	Class C	Class C	Class C
Other Treatment	Ventilated CVVHD Norepinephrine	Ventilated CVVHD Norepinephrine	Ventilated CVVHD	Ventilated CVVHD Norepinephrine	Ventilated CVVHD Norepinephrine	Ventilated

		Patient 1		Patient 2		Patient 3		Patient 4		Patient 5		Patient 6	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Norepinephrine	(μg/kg/min)	0.22	0.02	0.06	0.16	0	0	0.22	0.10	0.32	0.06	0	0
Creatinine	60–110 μmol/L	307	142	132	239	171	234	241	144	164	107	110	74
Urea	2.9–7.1 mmol/L	21	13	16	22	1	6	11	9	15	7	11.3	9.4
Ammonia	15–50 μmol/L	67	47										
HE Grade		4	3	0	0	0	0	3	1	3	2	4	3
Bilirubin	<25 μmol/L	161	210	654	528	260	182	484	137	510	326	766	512
Bile acids	0–6 μmol/L	75	75					27	16	202	67	353	205
AA/β-OH-But		4.2	6.8					1.3	8.0	4	4.5	1.1	1.4
PDR ICG	>16%/min	4.4	5.5	4.3	5.2	4.3	5.4	5.6	5.2			5.9	5.8
Duration of treatment (h)		24, 16		15, 13		5, 6		12, 16, 20		6, 6, 6		8, 8	
Outcome		ICU discharge Died in ward		Died in ICU		ICU discharge Died on ward		ICU discharge Discharged home		Died in ICU		ICU discharge Died on ward	

Kurtovic *Ther Aph Dial* 2006

	ECAD n = 39	SMT n = 31	*P* Value
Age†	49 (20-67)	56 (32-76)	0.019
Sex	24 Males 15 Females	15 Males 16 Females	NS
HE grade 3	20 (51%)	19 (61%)	NS
HE grade 4	19 (49%)	12 (39%)	
	5 None 22 Mild, moderate	3 None 20 Mild, moderate	
Ascites	12 Severe	8 Severe	NS
Creatinine† (0.5-1.5 mg/dL)	1.7 (0.4-5.6)	1.7 (0.6-5.0)	NS
Total bilirubin† (<1.2 mg/dL)	15.8 (1.8-54.5)	12.2 (2.3-58.9)	NS
Albumin† (3.5-5.0 g/dL)	2.4 (1.3-4.1)	3.0 (1.8-4.5)	0.004
INR†	2.1 (1.2-5.9)	1.9 (1.3-5.4)	NS
Primary liver disease (cirrhosis)			
Alcoholic liver disease (ALD)*	15 (39%)	12 (39%)	NS
Viral hepatitis (HCV/HBV)	11 (28%)	10 (32%)	
ALD/viral hepatitis	6 (15%)	3 (10%)	
Cryptogenic cirrhosis	4 (10%)	3 (10%)	
AIH/PSC	3 (8%)	2 (6%)	
Drug induced	0 (0%)	1 (3%)	
HE precipitating factor			
Infection	10 (26%)	10 (32%)	NS
Bleeding	6 (15%)	3 (10%)	
Electrolyte imbalance	3 (8%)	6 (19.3%)	
Other	7 (18%)	6 (19.3%)	
Unknown	13 (33%)	6 (19.3%)	
CTP score	13 (10-15)	12 (10-15)	NS
MELD score	33 (11-49)	28 (15-50)	NS
SOFA score ≥ 9	88%	81%	NS
SIRS score · 2	51%	45%	NS
Glasgow coma score†	6 (3-12)	8 (3-15)	NS

Hassanein *Hepatology* 2007

Clinical Studies

Liver International
DOI: 10.1111/j.1478-3231.2006.01293.x

Molecular adsorbent recirculating system treatment for patients with liver failure: the Hong Kong experience

Chui Liver Intern 2006

Case	Age	Sex	Pathology	Indication	Cr µmol/l	Bili µmol/l
1	59	F	HBV cirrhosis	AoCLF	210	520
2	52	M	HBV cirrhosis	AoCLF	480	890
3	62	M	HCC	Posthepatectomy	256	676
4	42	M	Acute HBV hepatitis	ALF	86	512
5	33	M	HBV cirrhosis	AoCLF	250	798
6	51	M	Wilson's disease	AoCLF	186	1029
7	59	M	HBV cirrhosis	AoCLF	513	707
8	56	F	PBC	AoCLF	100	578
9	52	F	Posttransplant	Graft dysfunction	112	1030
10	47	M	HCC	Posthepatectomy	589	167
11	68	M	HCC	Posthepatectomy	319	83
12	50	M	HBV cirrhosis	AoCLF	193	706
13	48	M	HBV cirrhosis	AoCLF	120	576
14	47	M	Posttransplant	Graft dysfunction	56	956
15	42	M	HBV cirrhosis	AoCLF	424	684
16	34	M	Drug-induced ALF	ALF	75	811
17	57	M	Posttransplant	Graft dysfunction	594	702
18	46	M	HBV cirrhosis	AoCLF	243	764
19	55	M	HBV cirrhosis	AoCLF	190	652
20	39	M	Posttransplant	Graft dysfunction	344	643
21	66	M	Cholangiocarcinoma	Posthepatectomy	392	713
22	54	M	HBV cirrhosis	AoCLF	464	355

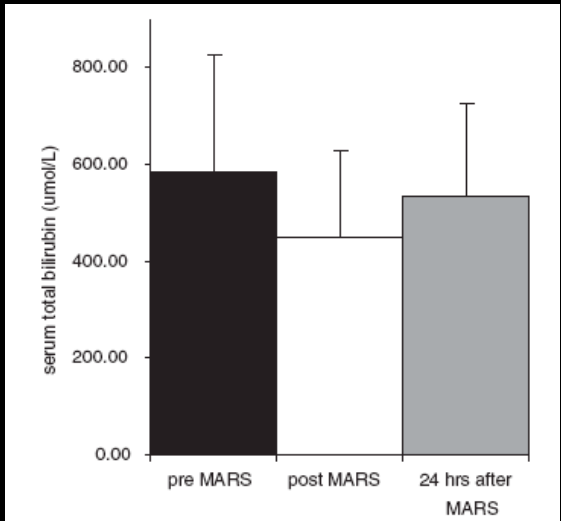


Fig. 1. Serum bilirubin changes before, after and 24 h after molecular adsorbent recirculating system.

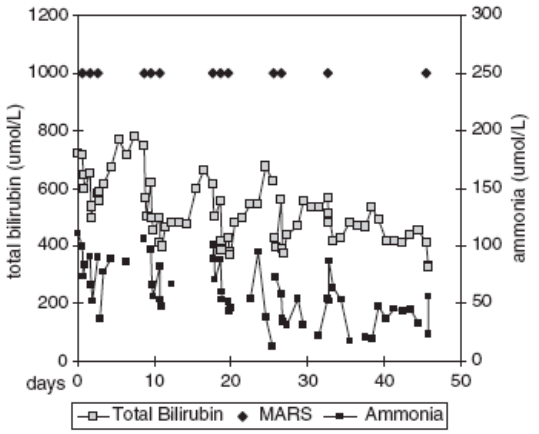


Fig. 2. Serum bilirubin and blood ammonia changes with repeated molecular adsorbent recirculating system treatment.

Chui Liver Intern 2006

?

Case	Age	Sex	Pathology	Indication	Cr μmol/l	Bili μmol/l	HRS	HE	VB	Sepsis	Total number of MARS	Outcome
1	59	F	HBV cirrhosis	AoCLF	210	520	–	+	–	–	1	Died
2	52	M	HBV cirrhosis	AoCLF	480	890	+	–	+	–	2	Died
3	62	M	HCC	Posthepatectomy	256	676	–	–	–	+	2	Died
4	42	M	Acute HBV hepatitis	ALF	86	512	–	+	–	–	1	Alive
5	33	M	HBV cirrhosis	AoCLF	250	798	+	+	–	–	1	Died
6	51	M	Wilson's disease	AoCLF	186	1029	+	–	+	–	3	Died
7	59	M	HBV cirrhosis	AoCLF	513	707	–	+	–	–	2	Died
8	56	F	PBC	AoCLF	100	578	+	+	–	–	2	Died
9	52	F	Posttransplant	Graft dysfunction	112	1030	–	–	–	–	2	Transplant, died
10	47	M	HCC	Posthepatectomy	589	167	–	–	–	–	3	Died
11	68	M	HCC	Posthepatectomy	319	83	–	–	–	–	2	Died
12	50	M	HBV cirrhosis	AoCLF	193	706	+	–	–	–	5	Transplant, alive
13	48	M	HBV cirrhosis	AoCLF	120	576	+	+	–	–	6	Transplant, died 12 months
14	47	M	Posttransplant	Graft dysfunction	56	956	–	–	–	–	2	Transplant, died 4 months
15	42	M	HBV cirrhosis	AoCLF	424	684	+	–	–	–	9	Died
16	34	M	Drug-induced ALF	ALF	75	811	–	+	–	–	2	Transplant, alive
17	57	M	Posttransplant	Graft dysfunction	594	702	–	+	–	+	6	Died
18	46	M	HBV cirrhosis	AoCLF	243	764	+	+	–	–	13	Died
19	55	M	HBV cirrhosis	AoCLF	190	652	–	+	–	+	3	Died
20	39	M	Posttransplant	Graft dysfunction	344	643	–	+	+	–	2	Died
21	66	M	Cholangiocarcinoma	Posthepatectomy	392	713	–	–	–	–	3	Died
22	54	M	HBV cirrhosis	AoCLF	464	355	+	+	–	–	2	Died

Chui Liver Intern 2006

Mr jean B. 51 ans

- Cryoglobulinémie (Ag froide)
- Voyage à Saint-Petersbourg
- Pyocholécyste
- Défaillances d’organes en post-opératoire
- Transfert en Réanimation en France.

Mr jean B. 51 ans

- Etat de choc : noradrenaline 0.5 µ/kg.min
- VM : FiO2 0.5, PEP 10cm.H_2O
- Dysfonction hépatique :
  - Bilirubine tot : 1580 µ/L
  - Cytolyse : ASAT: 450, ALAT: 422
- Dysfonction Rénale : D.U < 0.5 mL/kg/min
- Dysfonction neurologique : nécessité d'une sédation

Mr jean B. 51 ans

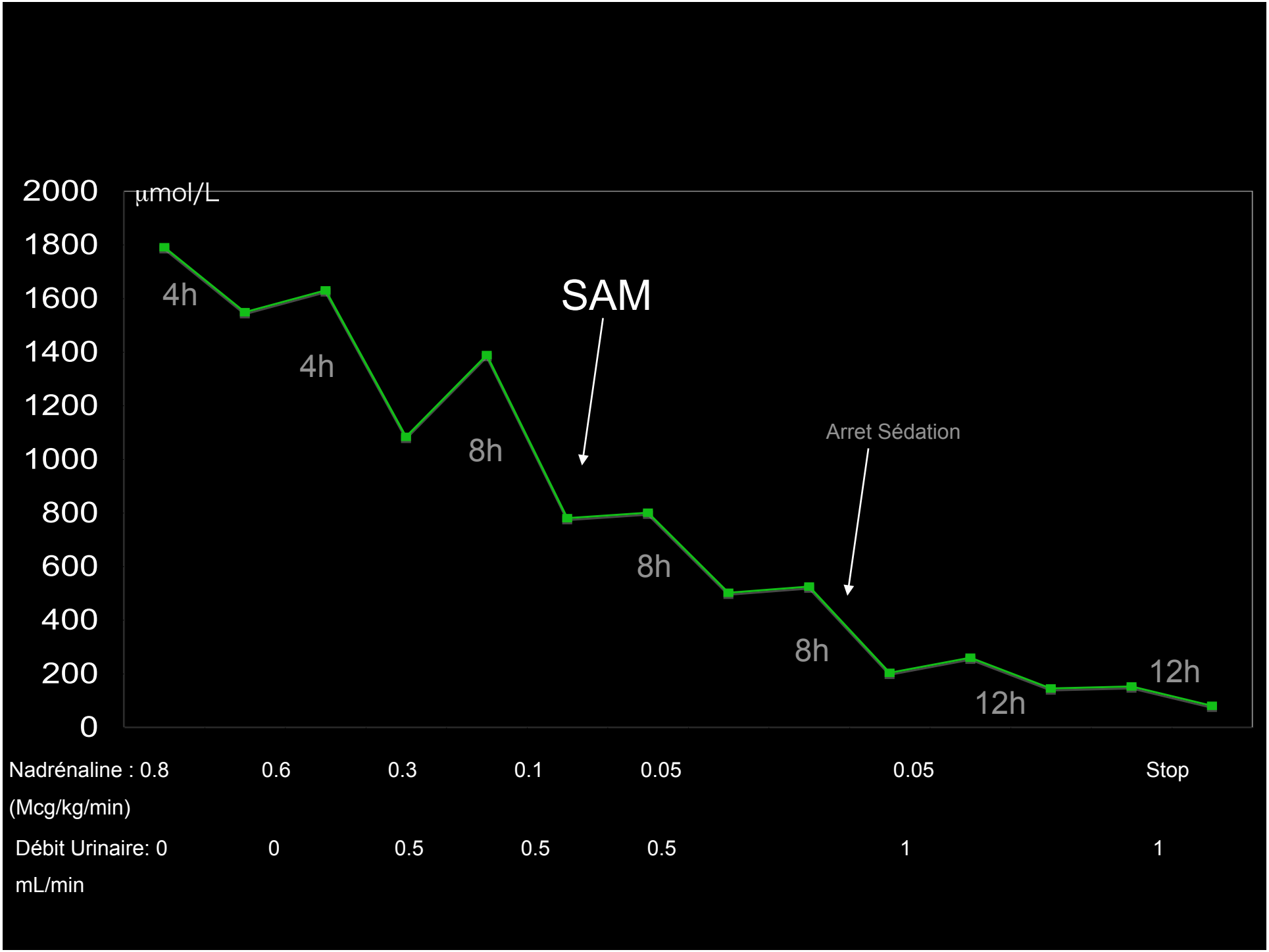
- Bloc opératoire :
  - Hématome sous hépatique modéré
  - Pas de compression des VB
  - Pas de signe septique

  - Réalisation d’une biopsie hépatique.

Mr jean B. 51 ans

- H 24 :
  - Bilirubine Tot : 1795 µmol/L
  - Anurie
  - Choc
  - …

MARS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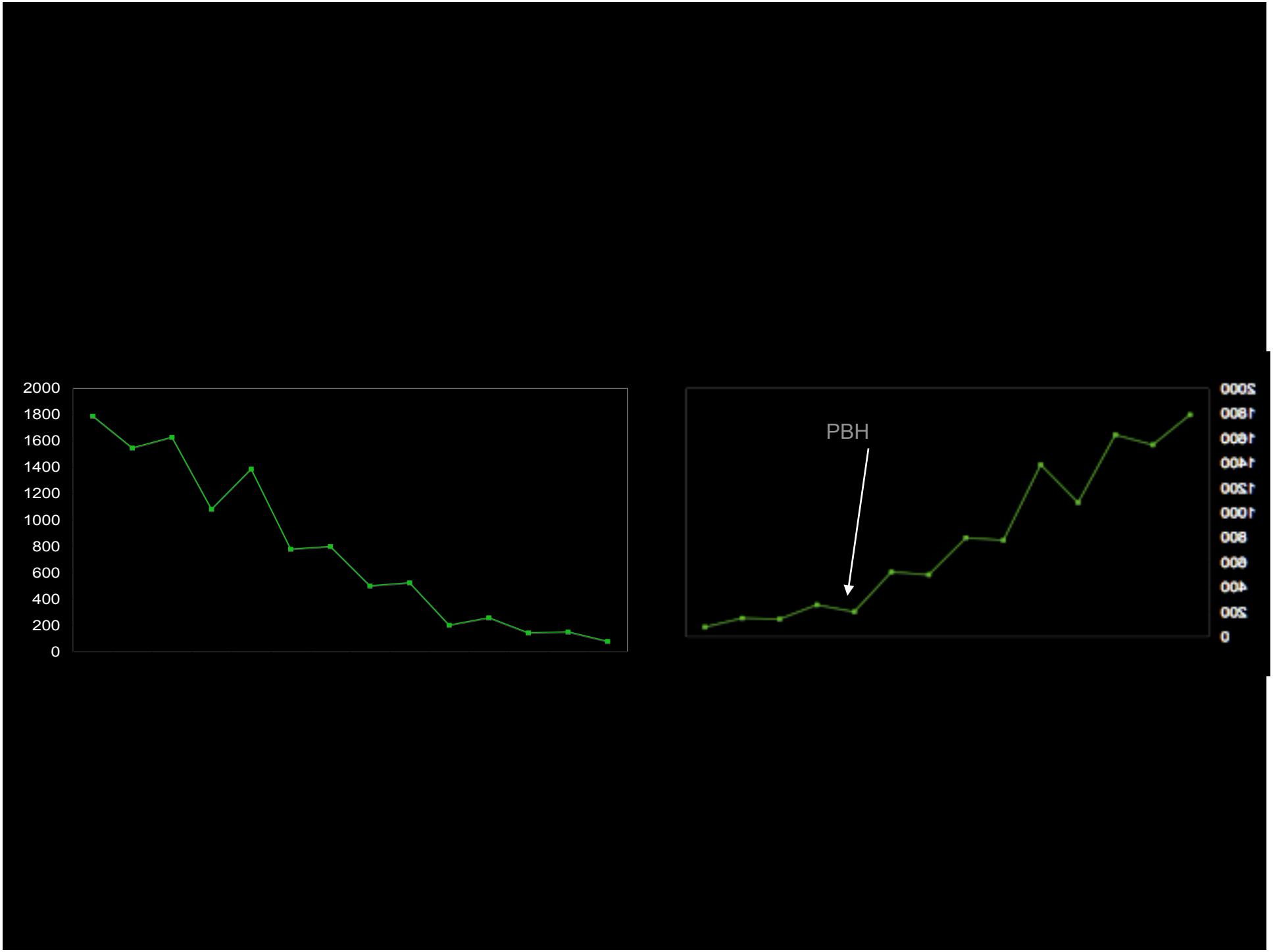
12h
Nadrénaline : 0.8 0.6 0.3 0.1 0.05 0.05 Stop
(Mcg/kg/min)
Débit Urinaire: 0 0 0.5 0.5 0.5 1 1
mL/min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Indication et Résultats de MARS dans l'ictère cholestatique ?

Molecular adsorbent recycling system treatment has proved to be a promising technology in the treatment of patients with acute exacerbation of chronic liver disease.

Sorkine *CritCareMed* 2001

Ictère Cholestatique

- A partir de quel niveau de bilirubine ?
- Pour quels Patients ?
- Si le patient n'est pas « Transplantable» ?
- Quels Objectifs ?

Voltaire

Candide ou l'Optimisme

folio classique

Merci de Votre attention …

Think Different …