

SUPPLEMENTAL DIGITAL CONTENT

Supplementary Table 1. Summary of propensity score parameters of MARS, unmatched standard medical therapy, and matched standard medical therapy treated patients.

Matched Parameter	MARS (N=104)	Unmatched SMT (N=1544)	Matched SMT (N=416)
APAP Etiology	51 (49.0%)	748 (48.4%)	197 (47.4%)
Age	39.4 (14.9)	42.1 (15.4)	42.5 (15.4)
Sex (male)	39 (37.5%)	542 (35.1%)	137 (32.9%)
RRT	32 (30.8%)	232 (15.0%)	114 (27.4%)
Vasopressor Support	43 (41.3%)	207 (13.4%)	110 (26.4%)
Mechanical Ventilation	56 (53.8%)	408 (26.4%)	198 (47.6%)
Grade 3/4 HE	55 (52.9%)	378 (24.5%)	192 (46.2%)
INR	4.7 (2.8)	3.2 (1.9)	3.8 (2.3)
Bilirubin (μmol/L)	213.4 (206.2)	164.0 (166.6)	180.6 (187.2)
Creatinine (μmol/L)	171.5 (129.1)	156.7 (141.9)	179.5 (132.6)
KCC were met	52 (50.0%)	338 (21.9%)	142 (34.1%)

Data presented as n (%) or mean (standard deviation), where appropriate.

Abbreviations: *APAP*, acetaminophen; *HE*, hepatic encephalopathy; *INR*, international normalized ratio; *KCC*, King's College Criteria; *MARS*, molecular adsorbent recirculating system; *SMT*, standard medical therapy; *RRT*, renal replacement therapy.

Supplementary Table 2. Additional non-matched baseline (pre-MARS/admission) characteristics of MARS and matched standard medical therapy treated patients.

Parameter	MARS (N=104)		SMT (N=416)	
	N	n (%) or Median (IQR)	N	n (%) or Median (IQR)
Etiology	104		416	
APAP		51 (49.0%)		197 (47.4%)
Viral Hepatitis		5 (4.8%)		32 (7.7%)
Drug-Induced (Non-APAP)		17 (16.3%)		37 (8.9%)
Autoimmune Hepatitis		4 (3.8%)		30 (7.2%)
Wilson's Disease		3 (2.9%)		5 (1.2%)
Indeterminant		10 (9.6%)		35 (8.4%)
Other		14 (13.4%)		80 (19.2%)
MELD	104	38.0 (30.5-42.5)	416	32.0 (26.0-39.0)
Biochemistry				
Hemoglobin (g/L)	104	100.5 (88.0-116.0)	412	107.0 (92.0-122.0)
White Blood Cells (10 ⁹ cells/L)	104	10.0 (7.3-14.5)	412	10.2 (6.7-14.3)
Platelets (10 ⁹ cells/L)	104	98.5 (62.5-151.5)	411	122.0 (75.0-182.0)
ALT (units/L)	104	3079.5 (1003.5-5677.5)	415	2087.0 (616.0-4417.0)
AST (units/L)	104	3040.5 (561.0-7775.5)	414	1814.0 (463.0-5167.0)
Lactate (mmol/L)	98	4.0 (2.7-7.5)	242	3.7 (2.3-7.2)
Ammonia (μmol/L)	87	125.0 (80.0-252.0)	270	103.0 (68.0-176.0)
PaO ₂ /FiO ₂ Ratio	100	370.7 (286.1-453.8)	191	325.0 (189.5-430.0)

Abbreviations: *ALT*, alanine aminotransferase; *APAP*, acetaminophen; *AST*, aspartate aminotransferase; *FiO₂*, fraction of inspired oxygen; *INR*, international normalized ratio; *IQR*, interquartile range; *MARS*, molecular adsorbent recirculating system; *PaO₂*, partial pressure of oxygen (arterial); *SMT*, standard medical therapy.

Supplementary Table 3. Summary of MARS therapy parameters (n=104).

MARS Therapy Parameter	n (%) or Median (IQR)
Sessions	3.0 (1.5-4.0)
Total Duration (hours)	24.0 (9.0-33.1)
Maximum Blood Flow (mL/min)	180.0 (180.0-200.0)
Maximum Albumin Flow (mL/min)	180.0 (180.0-180.0)
Anticoagulation ^a	
Heparin	13 (12.5%)
Citrate	58 (55.8%)
None	33 (31.7%)

^a Patients receiving citrate regional anticoagulation were monitored closely for citrate toxicity. This was defined as a total calcium (mg/dL) to ionized calcium (mmol/L) ratio >2.5 for >48 hours.

Note: All participating institutions utilised PRISMAFLEX (Baxter International Inc., Deerfield, Illinois) renal replacement therapy system as part of MARS setup.

Abbreviations: IQR, interquartile range; MARS, molecular adsorbent recirculating system.

Supplementary Table 4. Predictors of 21-day transplant-free survival: *main model*
(MARS: n=104; standard medical therapy: n=416).

Parameter	OR	95% OR Confidence Interval		P-value
MARS treatment^a	1.90	1.07	3.39	0.030
APAP Etiology	5.21	3.00	9.07	<0.001
Propensity Score^b	<0.001	<0.001	0.36	0.027
Age	0.99	0.97	1.01	0.234
Vasopressor Support	0.67	0.28	1.59	0.363
INR	0.91	0.79	1.05	0.201
KCC were met	0.66	0.31	1.40	0.278

^a Reference group: standard medical therapy.

^b Per 1% increase in propensity score value.

Note: Model adjusts for covariates with standardized mean difference >0.2 (absolute value).

Abbreviations: *APAP*, acetaminophen; *INR*, international normalized ratio; *KCC*, King's College Criteria; *MARS*, molecular adsorbent recirculating system; *OR*, odds ratio.

Supplementary Table 5. Predictors of 21-day transplant-free survival: *model 2* (MARS: n=104; standard medical therapy: n=416).

Parameter	OR	95% OR Confidence Interval		P-value
MARS treatment^a	1.86	1.05	3.31	0.033
APAP Etiology	6.21	3.75	10.29	<0.001
Propensity Score^b	<0.001	<0.001	<0.001	<0.001

^a Reference group: standard medical therapy.

^b Per 1% increase in propensity score value.

Abbreviations: APAP, acetaminophen; MARS, molecular adsorbent recirculating system;

OR, odds ratio.

Supplementary Table 6. Predictors of 21-day transplant-free survival: *model 3* (MARS: n=104; standard medical therapy: n=416).

Parameter	OR	95% OR Confidence Interval		P-value
MARS treatment^a	1.91	1.07	3.41	0.029
APAP Etiology	5.41	3.08	9.48	<0.001
Propensity Score^b	<0.001	<0.001	0.21	0.019
Age	0.99	0.97	1.01	0.211
Vasopressor Support	0.74	0.30	1.84	0.521
Mechanical Ventilation	0.66	0.35	1.22	0.183
Grade 3/4 HE	1.46	0.80	2.67	0.216
INR	0.91	0.79	1.05	0.213
KCC were met	0.70	0.33	1.48	0.346

^a Reference group: standard medical therapy.

^b Per 1% increase in propensity score value.

Note: Model adjusts for covariates with standardized mean difference >0.1 (absolute value).

Abbreviations: APAP, acetaminophen; HE, hepatic encephalopathy; INR, international normalized ratio; KCC, King's College Criteria; MARS, molecular adsorbent recirculating system; OR, odds ratio.

Supplementary Table 7. Unadjusted outcomes at 21 days following treatment with MARS or standard medical therapy.

Outcome	MARS (N=104)	SMT (N=416)
Listed for Transplant	31 (29.8%)	98 (23.6%)
Received Transplant	23 (22.1%)	78 (18.8%)
Survived	74 (71.2%)	292 (70.2%)
Transplant-free Survived	54 (51.9%)	220 (52.9%)

Note: The above summary statistics are unadjusted and do not take into account residual differences between molecular adsorbent recirculating system and standard medical therapy treated patients following matching.

Abbreviations: MARS, molecular adsorbent recirculating system; SMT, standard medical therapy.

Supplementary Table 8. Distribution and modality of renal replacement therapy with MARS or standard medical therapy.

	MARS (n=114)	SMT (n=416)
RRT any (pre MARS)	32 (30.8%)	114 (27.4%)
IHD only	1 (1%)	19 (4.5%)
CRRT only	31 (30%)	84 (20.1%)
IHD and CRRT	0	11 (2.6%)
No RRT	72 (69.2%)	302 (72.6%)

Abbreviations: *MARS*, molecular adsorbent recirculating system; *SMT*, standard medical therapy.