Supplementary Materials

Table S1. Individual characteristics of 50 patients with the syndrome of inappropriate antidiuresis.

	Pat. #	Presumed cause of SIAD	Age [yr]	S-Na+ [mmol/l]	S-Osm [mOsm/kg]	U-Osm [mOsm/kg]	U-Na+ [mmol/l]	S-UA [mg/dL]	P-Copt. [pmol/l]	P-AVP [pmol/l]	DIU [L/T/–]	Spec. Treatment/ Chemotherapy
Ectopic Copeptin Excess ('Type A', 10%)	1	SCLC	74	122	255	698	92	4.1	228	5	–	Cisplatin, Etop.
	2	SCLC	74	113	248	676	160	2.9	251	5.6	–	Cisplatin, Etop.
	3	NSCLC	55	128	260	739	57	4.1	246	4.6	–	Cis., Gemcitabine
	4	NSCLC	70	129	264	712	58	3.8	188	2	–	Cis., Gemcitabine
	5	Renal Carc.	48	122	260	558	137	3.1	22.3	3.0	L	MTX
		Mean (SD)	64 (5)	123 (3)	257 (3)	676 (31)	101 (3)	3.6 (1)	135 (118)	4.0 (2)		
Shifted Osmotic Copeptin Response (Type B, 14%)	6	AML	66	128	260	339	57	4.1	12.4	3.0	–	Busulfan
	7	CLL, B-NHL	66	129	258	521	182	3.5	9.2	2.5	–	Flud., Cycloph, MTX
	8	NSCLC	53	126	265	558	178	2.1	6.2	2.4	–	Carbo., Docetaxel
	9	Idiopathic	57	129	266	445	98	3.4	6.2	1.9	–	-
	10	AML	76	125	260	333	128	3.2	9.7	1.2	–	Cytar., Clofarabin
	11	SLE	55	129	263	312	52	4	2.9	1.3	–	Decortin
	12	Renal Carc.	73	129	266	393	46	4.3	7.1	3.3	–	Sunitinib
		Mean (SD)	64 (3)	128 (1)	263 (1)	414 (37)	106 (22)	3.5 (0.3)	7.7 (3)	2.2 (0.8)		

	Pat. #	Presumed cause of SIAD	Age [yr]	S-Na+ [mmol/l]	S-Osm [mOsm/kg]	U-Osm [mOsm/kg]	U-Na+ [mmol/l]	S-UA [mg/dL]	P-Copt. [pmol/l]	P-AVP [pmol/l]	DIU [L/T/–]	Spec. Treatment/ Chemotherapy
Plateau-like/ missing osmotic Copeptin Response (Type C, 44%)	13	MM	75	129	263	326	62.8	3.8	16.7	0.9	T	Cycloph, Doxob
	14	CML	35	128	256	438	119.3	2.1	12.7	4.2	–	Imatinib
	15	Esophageal Ca.	66	126	260	385	75.5	4.4	5.8	0	–	Cisplatin, 5-FU
	16	Idiopathic	53	127	264	407	45.5	4.3	8.5	1.2	–	-
	17	Tuberculosis	70	118	248	386	122.1	2.6	1.7	3.3	–	Iso, Rifa, Eth, Pyr
	18	Esophageal Ca.	66	127	265	436	135.3	4.4	8.3	2.4	–	Cisplatin, 5-FU
	19	B-CLL	73	121	259	872	82.8	2.9	7.0	1.4	–	Flud, Cycloph
	20	B-NHL	58	123	256	543	147.9	2.8	4.5	1.5	–	R-CHOP
	21	B-NHL	68	121	256	613	154.7	6.1	11.2	8.4	–	R-CHOEP
	22	SCLC	57	127	264	312	69.3	3.2	4.5	4.4	L	Carbo, Etoposid
	23	Adeno-BC	50	121	253	411	79.1	1.7	2.5	2.0	–	Cis, Vino.
	24	HIV	54	117	245	366	128.9	2.9	5.6	3.1	–	Zidovudin, LPV/r
	25	Pancreatic Ca.	64	128	264	492	125	3.2	14.6	5.6	L	5-FU, Cis, a-INF
	26	MM	70	127	266	524	118	4.2	12.8	8.3	T	Bortezomib, DCEP
	27	MM	49	126	271	422	66.6	2.2	9.6	4.4	–	Bortezomib
	28	NSCLC	74	128	261	581	139	2.4	6.8	2.2	–	Dauno, Ara-C
	29	NSCLC	72	125	256	587	131.2	2.5	3.9	2.3	L	Cis, Etoposid
	30	CML	69	127	262	469	66.8	3.4	6.7	4.2	L	Cis, Etoposid
	31	B-CLL	67	127	259	576	108.3	4.4	4.7	8.2	–	Chlorambucil
	32	AML	42	123	255	521	136.2	2.5	4.9	2.3	–	Dauno, Ara-C
	33	Drug-induced	75	115	245	280	92.2	3.2	2.1	1.4	–	Carb
	34	AML	56	127	264	421	68.6	3.2	3.1	1.7	–	Dauno, Ara-C
		Mean (SD)	62 (2)	125 (1)	259 (1)	471 (28)	103 (7)	3.3 (0.2)	7.2 (4)	3.3 (2)		
Low Copeptin Anti-diuresis (Type D, 12%)	35	NSCLC	66	115	238	497	61.5	2.3	1.9	1.0	–	Carb, Decetaxel
	36	AML, MPS	46	126	265	296	63.5	3.1	1	2	–	allo-PBSCT, Eta.
	37	HIV, HepB,C	48	125	256	469	126.8	3.2	0.9	1.4	–	AZT/3TC/LPV/r
	38	MM	46	126	261	382	98.5	2.9	1.2	0.6	–	IEV
	39	HIV, tub. men.	24	128	262	451	91.1	3.6	1.4	1.2	–	Ritonavir
	40	Drug-induced	57	129	265	382	73.6	4.5	1.4	0.9	–	Quetiapine
		Mean (SD)	48 (5)	125 (2)	257 (4)	463 (56)	87 (7)	3.1 (0.3)	1.3 (0.1)	1.1 (0.5)		

	Pat. #	Presumed cause of SIAD	Age [yr]	S-Na+ [mmol/l]	S-Osm [mOsm/kg]	U-Osm [mOsm/kg]	U-Na+ [mmol/l]	S-UA [mg/dL]	P-Copt. [pmol/l]	P-AVP [pmol/l]	DIU [L/T/–]	Spec. Treatment/ Chemotherapy
Reverse Copeptin Response (Type E, 20%)	41	CML	48	117	245	691	66.4	3.4	50.5	14.9	–	Imatinib
	42	AML	67	111	231	712	88.2	2.6	42.8	10.7	L	Cyta, Clofarabin
	43	MM	53	126	259	656	80.4	4.7	27.6	4.5	T	IEV
	44	MM	60	129	268	761	261.1	4	188	22.4	–	Bortecomib, DCEP
	45	NSCLC	70	126	270	765	43.9	3.1	241	12.5	T	Carb, Decetaxel
	46	B-NHL	66	129	264	725	138	3.1	47.8	2.6	–	R-CHOP, Ritux.
	47	MCL	68	129	264	630	111.8	3.4	92.1	3.3	T	R-CHOP
	48	NSCLC	42	125	260	717	75.6	3.6	100.5	8.5	–	Palliative Radiatio
	49	B-NHL	50	129	260	871	96.9	3.2	28.9	4.9	–	Ritux, Flud
	50	AML	50	125	258	823	119	3.7	184	4.1	–	Dauno Ara-C
		Mean (SD)	57 (3)	125 (2)	258 (4)	735 (23)	108 (19)	3.5 (0.2)	100.3 (77)	8.8 (6)		

AVP, arginine-vasopressin; S-Na+, serum sodium; S-Osm, serum osmolality; U-Osm, urinary osmolality; U-Na+, urinary sodium; S-UA, serum uric acid; S-Crea, serum creatinine; S-Hct, serum hematocrit; P-Renin, plasma renin; P-Aldo, plasma aldosterone; DIU [L/T/-], diuretic use: loops, thiazides, none; n.a., not available.

AML, acute myeloid leukemia; B-NHL, B-cell non-Hodgkin lymphoma; NSCLC, non-small cell lung cancer; SLE, systemic lupus erythematosus; Ca., carcinoma; CML, chronic myeloid leukemia; MM, multiple myeloma; MCL, mantle cell lymphoma; MPS, myeloproliferative syndrome; CLL, chronic lymphatic leukemia; Carba, Carbamazepine; HIV, human immunodeficiency virus infection; SSRI, selective serotonine reuptake inhibitor; tub. men., tuberculous meningitis; SCLC, small-cell lung cancer. Cycloph, Cyclophosphamide; Doxo, Doxorubicin; 5-FU, 5-Fluoruracil; Eto, Etoposid; allo-PBSCT, peripheral blood stem cell transplant; Eta, Etanercept; AZT, Zidovidine; LPV/r, Lopinavir/Ritonavir; 3TC, Lamivudine; Flud, Fludarabin, MTX, Methotrexat; Iso, Isoniazid; Rifa, Rifampicin, Etha, Ethambutol; Pyr, Pyranizamid; R-CHOP, Rituximab/Cyclophosphamid/Hydroxydaunorubicin/Oncovin/Prednisolon; Carbo, Carboplatin; R-CHOEP, R-CHOP plus Etoposid; Cis, Cisplatin; Vino, Vinorelbin; a-IFN, alpha interferon; DCEP, Dexamethasone/Cyclophosphamide/Etoposide/Cisplatin; Dauno, Daunorubicin; Ara-C, Cytarabine; Ritux, Rituximab; IEV, Ifosfamid/Epirubicin/Etoposid; Cyta, Cytarabine.

Data are expressed as mean (SD).

Table S2. Individual hemodynamic responses to hypertonic saline load in controls and 50 patients with the syndrome of inappropriate antidiuresis.

	Subject	MAP		HR		U-Na+	B-Volume	S-Crea	S-UA	P-Renin	P-Aldosteron
	#	Baseline [mmHg]	Change [%]	Baseline [bpm]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]
Healthy Controls	1	75	11	62	13	16	13	-4	-9	-8	-19
	2	88	8	56	17	53	16	-12	-9	14	4
	3	80	12	66	12	29	21	0	-11	-13	-22
	4	82	7	72	11	127	18	-13	-8	-23	-13
	5	78	9	88	-11	63	21	2	-7	-6	-65
	6	74	10	64	9	-3	18	-9	-13	-13	-12
	7	82	-4	72	17	172	10	-12	-6	-4	-56
	8	86	-6	84	5	70	9	-7	-10	-2	23
	9	88	9	86	-2	79	16	0	-4	0	0
	10	72	10	74	11	107	19	0	-2	-37	0
	Median (quartiles)	72 (-12, 82)	9 (-4, 10)	72 (74, 84)	11 (3, 14)	67 (26, 112)	17 (12, 19)	-6 (-12, 0)	-9 (-10, -6)	-7 (-16, -2)	-13 (-31, 1)
Ectopic Copeptin Excess (Type A, 10%)	1	85	9	72	-6	39	5	0	-7	6	0
	2	72	22	84	-19	6	3	0	-3	-40	0
	3	93	-11	66	18	16	8	-9	-7	-39	-32
	4	88	10	80	-10	56	6	0	-3	-41	-50
	5	92	12	70	26	48	1	-14	6	-43	- 38
	Median (quartiles)	88 (79, 93)	10 (-1, 17)	72 (68, 82)	-6 (-15, 22)	39 (11, 52)	5* (2, 7)	0 (-12, 0)	-3 (-7, 7)	-40 (-42, -17)	-32 (-44, 0)

	Subject	MAP		HR		U-Na+	B-Volume	S-Crea	S-UA	P-Renin	P-Aldosteron
	#	Baseline [mmHg]	Change [%]	Baseline [bpm]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]
Shifted Osmotic Copeptin Response (Type B, 14%)	6	92	-10	65	17	1	4	17	-11	-65	-46
	7	64	44	95	-22	11	3	-25	-5	-48	-22
	8	79	-15	70	20	52	6	0	-6	-13	-7
	9	83	10	78	18	24	3	17	-44	-7	-6
	10	76	17	76	-16	25	8	0	-10	-68	-30
	11	90	-8	72	11	21	5	18	-2	-11	-15
	12	88	9	82	-20	35	4	-9	-7	-41	-22
	Median (quartiles)	83* (76, 90)	9 (-10, 17)	76 (70, 82)	11 (-20, 20)	24* (11, 35)	4* (3, 6)	0 (-9, 18)	-7 (-11, -2)	- 41* (-65, -7)	-22 (-30, -6)

	Subject	MAP		HR		U-Na+	B-Volume	S-Crea	S-UA	P-Renin	P-Aldosteron
	#	Baseline [mmHg]	Change [%]	Baseline [bpm]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]
Plateau-like/ missing osmotic Copeptin response (Type C, 44%)	13	91	-4	72	17	9	8	0	-5	0	0
	14	79	-13	64	13	-3	6	-14	0	-27	- 48
	15	85	9	66	12	32	9	33	-5	n.a.	-7
	16	94	-6	106	15	92	7	-13	n.a.	-14	0
	17	72	11	84	10	43	9	- 40	4	-26	-50
	18	76	11	92	-4	8	5	0	2	-33	-63
	19	92	7	60	17	7	7	0	-14	-8	-18
	20	96	17	76	21	-8	4	- 14	-7	-6	0
	21	88	-7	72	19	6	11	0	16	n.a.	n.a.
	22	92	-10	88	7	9	2	0	-13	-8	-9
	23	77	12	91	-6	20	8	0	6	-26	-7
	24	72	17	60	17	30	10	0	7	-4	-12
	25	88	11	88	9	9	17	0	-13	-14	-17
	26	100	7	64	13	-3	7	0	-5	-7	-12
	27	94	4	72	22	11	4	0	-32	-	n.a.
	28	88	-2	76	11	26	10	- 20	-21	-7	0
	29	94	6	68	6	29	4	-33	-24	-14	0
	30	92	7	66	15	-2	14	-14	-3	-10	-15
	31	75	-7	84	-14	66	2	-13	52	-2	-1
	32	86	13	82	-10	34	15	0	28	-4	0
	33	92	9	76	5	12	6	-22	-6	n.a.	-27
	34	64	31	95	-22	10	15	0	0	-10	-11
	Median (quartiles)	88** (77, 93)	7 (-5, 12)	76 (66, 88)	11 (3, 17)	11** (7, 31)	7.5* (5, 10)	0 (-13, 0)	-4 (-13, 5)	-9 (-17, -6)	-10 (-17, 0)

	Subject	MAP		HR		U-Na+	B-Volume	S-Crea	S-UA	P-Renin	P-Aldosteron
	#	Baseline [mmHg]	Change [%]	Baseline [bpm]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]	Change [%]
Low Copeptin anti-diuresis (Type D, 12%)	35	90	-7	62	16	6	1	0	13	-12	-8
	36	100	12	84	10	9	11	0	-13	- 43	-92
	37	88	-18	76	16	12	7	-17	3	-26	-39
	38	101	11	82	17	2	18	0	7	16	0
	39	94	-17	66	27	16	7	25	3	7	-17
	40	88	7	76	16	43	15	-8	-16	-27	-80
	Median (quartiles)	90** (88, 100)	7 (-17, 11)	76 (66, 82)	16 (10, 17)	12* (6, 16)	7* (6, 15)	0 (-8, 0)	3 (-13, 7)	-26 (-32, 7)	-39 (-80, -8)
Reverse Copeptin Response (Type E, 20%)	41	91	-9	62	16	8	6	0	-18	-34	-12
	42	86	19	74	19	1	4	-12.5	-4	-25	-19
	43	94	-13	72	15	-14	5	-20	-55	-31	-31
	44	92	7	62	19	-11	2	0	-3	n.a.	0
	45	76	-8	72	17	-20	1	0	-7	-22	-35
	46	66	17	76	17	-3	2	0	-7	-4	-19
	47	82	15	66	18	-21	8	25	-6	13	0
	48	100	8	70	23	5	6	-10	-8	17	-12
	49	79	-15	72	17	32	3	0	-3	-6	0
	50	91	-9	68	14	-20	4	-14	3	49	-15
	Median (quartiles)	89** (78, 93)	-1 (-10, 15)	71 (65, 73)	17 (16, 19)	-7** (-20, 6)	4* (2, 6)	0 (-13, 0)	-6 (-11, -3)	-6 (-28, 15)	-13 (-22, 0)

MAP, mean arterial pressure; HR, heart rate; U-Na+, urinary sodium; B-Vol, percent change in blood volume calculated by the method described in the text; S-Crea, serum creatinine; S-UA, serum uric acid; P-Ren, plasma renin; P-Aldo, plasma aldosterone; n.a., not available. Data are expressed as median (quartiles).
* $P<0.05$, ** $P<0.01$ for comparison of the respective SIAD subgroup with the healthy control group (Mann-Whitney U-test).