

SUPPLEMENTARY DATA

Supplementary Table 1. Cases of SGLT2i-associated ketoacidosis identified.

Case #	Summary or Average (when known)	1	2		3			4	5
Timing of episodes	8% with >1 episode		first	+2 days	first	+4 days	+32 days		
Age (years)	54.0	67	56	56	48	48	48	53	26
M/F	46% M, 54% F	F	F	F	F	F	F	M	F
T1/T2	13% T1, 74% T2, 13% unknown	T2	T2	T2	T2	T2	T2	T2	T1
BMI (kg/m ²)	31.5	30	35	35	51	51	51	34	22
Duration (years)		?	?	?	?	?	?	23	14
SGLT2i (C/D/E, mg)	82% C, 15% D, 3% E	C, 100	D, 5	D, 5	C, 300	C, 300	C, 300	E, 10	C, 100
Insulin	59%	no	MDI	MDI	no	no	no	no	CSII
Metformin (mg)	38%	2000	2000	2000	no	no	no	500	no
Sulfonylureas	15%	no	yes	yes	no	no	no	no	no
Incretin therapy	38%	no	GLP-1	GLP-1	GLP-1	GLP-1	GLP-1	no	GLP-1
TZD	10%	no	no	no	no	no	no	yes	no
Most recent A1c	10.0%	?	10.9%	10.9%	9.9%	9.9%	9.9%	?	6.8%
A1c (mmol/mol)	86	?	96	96	85	85	85	?	51
Initial glucose (mg/dl)	328	231	536	389	167	246	209	199	218
pH	7.12	?	?	?	?	Ve 7.13	Ve 6.99	?	Ve 7.15
pCO ₂ mm/Hg	29	?	?	?	?	Ve 21	Ve 17	?	Ve 26
Bicarbonate (mEq/L)	14	19	21	13	15	6	<5	21	10
Anion Gap (mmol/L)	20	13	20	22	26	23	?	18	21
Ketones (U/P)	97% present, 3% unknown	U	U	U	U	U	P	U	U
Potential contributors noted	49% Nausea/Vomiting	Acute colitis x2 days with fever and incontinence	N/V/D x1 day	N/V/D x3 days	N/V x1 day, epigastric pain, primary biliary cirrhosis	chest pain, N/V, primary biliary cirrhosis	chest pain, N/V, primary biliary cirrhosis	acute N/V (<1 day)	Acute N/V (<1 day)
Insulin dose missed or reduced	28%	NA	Held glipizide	Held glipizide	NA	NA	NA	NA	no
Where treated	91% In	ED, In	ED	ED	UC	ED, In	ED, In	ED, In	ED, In
SGLT2 added within 1 month	28%	?	no	no	no	no	no	no	no
DKA type (Glucose <=300 mg/dL or hyperglycemic (glucose >300 mg/dL))	72% with glucose <=300 mg/dL	<=300 mg/dL	hyperglycemic	hyperglycemic	<=300 mg/dL	<=300 mg/dL	<=300 mg/dL	<=300 mg/dL	<=300 mg/dL

SUPPLEMENTARY DATA

Case #	6	7	8	9	10	11	12	13	14
Timing of episodes									
Age (years)	58	44	44	72	37	69	53	77	29
M/F	M	F	M	M	F	F	M	F	M
T1/T2	T2	?	?	T2	T2	T2	T2	T2	T1
BMI (kg/m ²)	29	18	28	24	morbid obesity	24	38	31	29
Duration (years)	?	?	?	?	?	?	?	?	?
SGLT2i (C/D/E, mg)	C, ?	C, ?	D, 10	D, 5	C, 150	C, 300	C, 300	C, 300	C, ?
Insulin	no	MDI	MDI	no	PMI	PMI	MDI	no	MDI
Metformin (mg)	no	no	no	500	2000	2000	500	1000	no
Sulfonylureas	yes	no	no	no	yes	no	no	yes	no
Incretin therapy	no	no	no	DPP4	no	no	no	no	no
TZD	no	no	no	no	no	no	no	yes	no
Most recent A1c	9.5%	14.1%	7.6%	9.7%	?	10.5%	?	?	9.5%
A1c (mmol/mol)	80	131	60	83	?	91	?	?	80
Initial glucose (mg/dl)	299	769	216	904	162	419	205	186	198
pH	Ve 7.2	?	7.34	7.37	7.12	Ve 7.29	7.23	7.17	?
pCO ₂ mm/Hg	Ve 28	?	39	42	11	Ve 50	31	36	?
Bicarbonate (mEq/L)	10	14	17	17	9	21	11	18	13
Anion Gap (mmol/L)	29	28	17	21	19	15	16	15	16
Ketones (U/P)	U	U+P	U+P	U+P	P	P	U	U	U+P
Potential contributors noted	Chemotherapy initiated, N/V x3 days	N/V x4 days	pain treated with narcotics, N/V x5 days	Non-adherence, mental status change, seizure, steroid injection	Gastric bypass surgery same day	Husband died 3 weeks earlier, hematochezia x1 day	4 days post-gastric bypass, weakness, new Afib	N/V x2 days, ureteral stone, septic shock	N/V x1 day
Insulin dose missed or reduced	NA	yes	no	NA	no	?	yes	NA	yes
Where treated	ED, In	ED, In	ED, In	ED, In	In	ED, In	ED, In	ED, In	ED, In
SGLT2 added within 1 month	no	?	?	yes	?	?	no	?	?
DKA type (Glucose <=300 mg/dL or hyperglycemic (glucose >300 mg/dL))	<=300 mg/dL	hyperglycemic	<=300 mg/dL	hyperglycemic	<=300 mg/dL	hyperglycemic	<=300 mg/dL	<=300 mg/dL	<=300 mg/dL

SUPPLEMENTARY DATA

Case #	15	16	17	18	19		20	21	22	23
Timing of episodes					first	+2 weeks				
Age (years)	45	28	49	68	60	60	48	55	66	49
M/F	F	F	F	M	M	M	F	M	F	M
T1/T2	T2	T1	T2	T2	T2	T2	T2	T2	T1	T2
BMI (kg/m ²)	29	29	39	27	unknown	unknown	30	20.66	16	36.12
Duration (years)	3	?	?	?	26	26	4	12	25	10
SGLT2i (C/D/E, mg)	C, 300	C, 300	C, 300	C, 100	C, 300	C, 300	C, ?	C, 100	C, ?	C, 100
Insulin	no	MDI	no	MDI	BI	BI	no	MDI	MDI	MDI
Metformin (mg)	?	no	2000	2000	2000	2000	2000	no	no	?
Sulfonylureas	no	no	no	no	no	no	no	no	no	no
Incretin therapy	DPP4	no	GLP-1	no	GLP-1	GLP-1	no	no	no	no
TZD	no	no	no	no	no	no	no	no	no	no
Most recent A1c	?	9.1%	9.3%	?	?	?	15.1%	11.0%	?	8.6%
A1c (mmol/mol)	?	76	78	?	?	?	142	97	?	70
Initial glucose (mg/dl)	292	289	312	249	182	168	630	282	337	346
pH	Ve 7.01	Ve 6.95	?	?	7.25	7.04	6.7	7.13	7.16	7.5
pCO ₂ mm/Hg	Ve 23	Ve 19	?	?	29	24	24.7	37	26	21.9
Bicarbonate (mEq/L)	6	<5	?	15	15	8	3.3	15	20	15
Anion Gap (mmol/L)	29	?	17	21	16	18	24	20	21	18
Ketones (U/P)	P	P	U	U	U	U+P	U+P	U+P	U	U+P
Potential contributors noted	N/V x1 day	N/V/D x4 days	acute stroke	N/V x1 day, family also affected	Poor oral intake	Starvation, clonazepam overdose	No	No	Hip surgery within 1 month	Chronic pancreatitis, recent but not current alcohol binge, cocaine +
Insulin dose missed or reduced	NA	no	NA	no	no	yes	NA	yes	yes	yes
Where treated	ED, In	ED, In	ED, In	ED, In	ED	ED, In	ED, In	ED, In	ED, In	ED, In
SGLT2 added within 1 month	yes	?	no	?	?	?	?	yes	yes	?
DKA type (Glucose <=300 mg/dL or hyperglycemic (glucose >300 mg/dL))	<=300 mg/dL	<=300 mg/dL	hyperglycemic	<=300 mg/dL	<=300 mg/dL	<=300 mg/dL	hyperglycemia	<=300 mg/dL	Hyperglycemic	hyperglycemic

SUPPLEMENTARY DATA

Case #	24	25	26	27	28	29	30	31	32	33
Timing of episodes										
Age (years)	62	43	59	48	80	45	62	70	58	33
M/F	M	M	M	M	F	F	F	M	M	F
T1/T2	T2	T2	T2	T2	T2	T2	?	T2	?	T1
BMI (kg/m ²)	33.69	34.72	22.12	33.27	20.55	36.88	29.1	24.6	32.2	26.2
Duration (years)	?	8	12	16	?	10	?	?	?	?
SGLT2i (C/D/E, mg)	C, 300	C, ?	C, ?	C, 300	C, 100	D, 5	C, 600	C, 300	C, 300	D, 10
Insulin	BI	no	no	BI	no	MDI	MDI	no	MDI	BI
Metformin (mg)	500	?	no	2000	1000	?	?	?	?	?
Sulfonylureas	no	no	no	no	no	no	no	no	no	no
Incretin therapy	no	no	no	GLP-1	DPP4	DPP4	no	DPP4	DPP4	no
TZD	no	no	no	no	yes	no	no	no	yes	no
Most recent A1c	14.2%	12.5%	10.2%	6.9%	?	9.9%	8.4%	?	11.9%	11.6%
A1c (mmol/mol)	132	113	88	52	?	85	68	?	107	103
Initial glucose (mg/dl)	453	172	800	125	318	131	413	250	524	596
pH	7.36	7.32	7.24	7.3	?	?	7.155	7.157	6.9	7.02
pCO ₂ mm/Hg	28	29	39.4	40	?	?	28.3	45	24.4	11
Bicarbonate (mEq/L)	18	15	17	21	12	16	8	12	29	3
Anion Gap (mmol/L)	22	18	23	15	16	16	28	20	14	21
Ketones (U/P)	U+P	U+P	U+P	U+P	U+P	U+P	U+P	U	U+P	U
Potential contributors noted	no	Acute weight loss of 15 pounds	no	Canagliflozin dose increased within the week	Acalculous cholecystitis	no	Colonoscopy prep with N/V	Possible digoxin toxicity, acute renal failure, intubated	alcohol abuse, recurrent acute pancreatitis	N/V/D, abdominal pain, dyspnea x3 days
Insulin dose missed or reduced	yes	NA	NA	yes	NA	no	?	NA	?	yes
Where treated	ED, In	ED, In	ED, In	ED, In	ED, In	ED, In	In	In	In	In
SGLT2 added within 1 month	yes	yes	?	no	yes	yes	yes	yes	no	?
DKA type (Glucose <=300 mg/dL or hyperglycemic (glucose >300 mg/dL))	hyperglycemia	<=300 mg/dL	hyperglycemic	<=300 mg/dL	hyperglycemic	<=300 mg/dL	hyperglycemic	<=300 mg/dL	hyperglycemic	hyperglycemic

SUPPLEMENTARY DATA

Case #	34	35	36	37	38	39
Timing of episodes						
Age (years)	53	63	35	56	60	69
M/F	F	M	F	F	F	M
T1/T2	T2	T2	T2	T2	?	T2
BMI (kg/m ²)	31	38.4	43.5	37.5	26.9	30.9
Duration (years)	16	?	?	5	12	5
SGLT2i (C/D/E, mg)	C, 300	C, 300	D, 10	C, 300	C, 300	C, 300
Insulin	MDI	PMI	no	no	MDI	no
Metformin (mg)	?	no	no	?	?	?
Sulfonylureas	no	yes	no	yes	no	no
Incretin therapy	no	no	GLP-1	DPP4	no	DPP4
TZD	no	no	no	no	no	no
Most recent A1c	8.5%	10.9%	?	7.9%	7.7%	6.5%
A1c (mmol/mol)	69	96	?	63	61	48
Initial glucose (mg/dl)	400's	380	215	328	244	167
pH	Ve 7.172	7.27	Ve 7.265	?	7.348	?
pCO ₂ mm/Hg	Ve 19.8	26.1	Ve 30.7	?	20.4	?
Bicarbonate (mEq/L)	8	13	14	24	8	20
Anion Gap (mmol/L)	34	16	18	13	24	16
Ketones (U/P)	P	P	U+P	U	U	?
Potential contributors noted	N/V/D, abdominal pain x 2 days, severe dehydration, gastroparesis	Fournier gangrene, septic shock	Marijuana use, N/V/D x1 day, gastroparesis	N/V/D	N/V, malaise x1 day, recent stressors, decrease urine output	N/V/D x 3 days
Insulin dose missed or reduced	no	?	NA	NA	yes	NA
Where treated	In	In	In	In	In	In
SGLT2 added within 1 month	no	?	?	?	yes	no
DKA type (Glucose <=300 mg/dL or hyperglycemic (glucose >300 mg/dL))	hyperglycemic	hyperglycemic	<=300 mg/dL	hyperglycemic	<=300 mg/dL	<=300 mg/dL