

## OBJECTIVE

TO ESTIMATE DOWNSTREAM MEDICAL COSTS FROM ADVERSE EVENTS (AES) & POOR PATIENT OUTCOMES ASSOCIATED WITH MAJOR TYPE-2 DIABETES DRUGS.

## BACKGROUND

- PRE-APPROVAL CLINICAL TRIALS DO NOT PREDICT MANY REAL WORLD AES
- ~1,500,000 POST-MARKETING AE REPORTS SUBMITTED TO FDA ANNUALLY
- TYPE 2 DIABETES PATIENTS HAVE MULTIPLE COMORBIDITIES PUTTING THEM AT HIGHER RISK OF AES
- AES ASSOCIATED WITH DIABETES DRUG USE ARE IMPORTANT TO UNDERSTAND BECAUSE STRICT MEDICATION ADHERENCE IS VITAL
- AES ARE A SIGNIFICANT SAFETY & COST BURDEN TO THE HEALTHCARE SYSTEM.
- THEREFORE, UNDERSTANDING WITHIN- & ACROSS-CLASS SAFETY DIFFERENCES OF DIABETES DRUGS IS OF GREAT INTEREST

## METHODS

WE ANALYZED 99,195 "PRIMARY SUSPECT" FAERS TYPE 2 DRUG CASE REPORTS.

PART ONE MEASURED DISPROPORTIONAL REPORTING RATES ACROSS NUMEROUS AES THAT REPRESENT SIGNIFICANT SAFETY & MEDICATION ADHERENCE ISSUES.

PART TWO ESTIMATED DOWNSTREAM MEDICAL COSTS FOR EACH DRUG:

- 1) AE & OUTCOME COSTS WERE DERIVED FROM AHRQ'S HCUP SURVEY,
- 2) ONLY "IMPORTANT MEDICAL EVENTS" (EUDRAVIGILANCE) WERE INCLUDED,
- 3) NON-SERIOUS AES & OUTCOMES WERE NOT INCLUDED,
- 4) ONLY THE HIGHEST AE OR OUTCOME COST WAS USED FROM EACH REPORT,
- 5) RESULTING CASES COUNTS WERE DIVIDED BY DRUG USAGE DATA TO ESTIMATE DIRECT MEDICAL COST BURDEN PER EXPOSURE.

## RESULTS

PART ONE - DISPROPORTIONAL REPORTING (REPORTING ODDS RATIO - ROR)

- "PANCREATITIS," "PANCREATITIS ACUTE," & "PANCREATIC CARCINOMA" SHOWED ELEVATED REPORTING FOR MOST MEMBERS OF THE DPP-4 AND GLP-1 CLASSES (NUMEROUS RORS IN THE 20-80 RANGE).
- ELEVATED RORS FOR HYPOGLYCEMIA WERE OBSERVED FOR ALL DPP-4 DRUGS BUT ONLY NOTED IN SELECT GLP-1 & SGLT2 DRUGS.
- WHILE ALL DRUG CLASSES HAD MEMBERS WITH ELEVATED REPORTING FOR DIABETIC KETOACIDOSIS, THE SGLT2 INHIBITORS HAD MUCH HIGHER RORS THAN THE OTHER TWO CLASSES.
- AS EXPECTED, ELEVATED REPORTING FOR GENITAL RELATED INFECTIONS WAS ONLY EVIDENT IN THE SGLT2 CLASS (NOT SHOWN).

## DISPROPORTIONAL REPORTING RESULTS OF NOTE (ROR, 95% CONFIDENCE INTERVAL, & CASE COUNT)

ADVERSE EVENT	BYDUREON	BYETTA	TANZEUM	VICTOZA	NESINA	TRADJENTA	ONGLYZA	KOMBIGLYZ E XR	JANUVIA	JANUMET	JANUMET XR	FARXIGA	INVOKANA	JARDIANCE
PANCREATITIS	6.03 (5-7) (175)	11.85 (11-12) (1,920)	3.12 (2-6) (10)	22.00 (21-23) (1,281)	7.75 (5-13) (14)	18.90 (16-22) (219)	14.05 (12-16) (166)	10.47 (8-14) (39)	22.79 (22-24) (1,462)	23.71 (21-27) (296)	15.61 (10-24) (23)	1.13 (1-2) (10)	2.99 (2-4) (79)	1.46 (0-5) (3)
PANCREATITIS ACUTE	2.97 (2-4) (30)	12.49 (12-13) (705)	2.73 (1-9) (3)	20.56 (19-23) (432)	38.43 (25-59) (23)	13.38 (10-17) (56)	12.42 (9-16) (52)	6.10 (3-12) (8)	13.18 (12-15) (315)	17.05 (14-21) (78)	3.76 (1-15) (2)	1.33 (1-4) (4)	0.66 (0-1) (6)	1.42 (0-10) (1)
PANCREATIC CARCINOMA	4.50 (3-7) (28)	25.07 (23-27) (811)	1.47 (0-10) (1)	28.54 (26-32) (365)	31.63 (18-56) (12)	17.00 (13-23) (44)	15.85 (12-22) (41)	7.40 (3-17) (6)	68.55 (64-74) (863)	79.15 (69-91) (208)	6.10 (2-24) (2)	1.62 (1-5) (3)	0.53 (0-2) (3)	9.31 (3-25) (4)
HYPOGLYCAEMIA	1.53 (1-2) (41)	3.31 (3-4) (527)	2.76 (1-6) (8)	1.56 (1-2) (93)	4.84 (2-10) (8)	7.80 (6-10) (86)	6.41 (5-8) (71)	3.75 (2-6) (13)	10.85 (10-12) (678)	5.80 (5-7) (71)	8.74 (5-16) (12)	3.42 (2-5) (27)	2.55 (2-3) (61)	1.07 (0-4) (2)
DIABETIC KETOACIDOSIS	0.82 (0-2) (5)	1.64 (1-2) (60)	0 (0) (0)	4.65 (4-6) (62)	0 (0) (0)	0.78 (0-3) (2)	0.39 (0-3) (1)	0 (0) (0)	1.74 (1-3) (26)	2.84 (1-6) (8)	0 (0) (0)	34.15 (26-44) (59)	38.36 (33-44) (195)	29.38 (17-52) (12)

RED BOXES INDICATE RORS WITH LOWER BOUND 95% CONFIDENCE INTERVALS ABOVE 5

## PART TWO - ESTIMATED DOWNSTREAM MEDICAL COSTS

DRUG NAME	TOTAL COSTS (2010-2015)	COSTED CASES	DOWNSTREAM COSTS PER RX	DRUG NAME	TOTAL COSTS (2010-2015)	COSTED CASES	DOWNSTREAM COSTS PER RX
BYETTA (GLP-1)	\$51,758,165	3,295	\$21.05	INVOKANA (SGLT2)	\$19,704,043	1,218	\$3.48
FARXIGA (SGLT2)	\$12,019,595	652	\$18.71	KOMBIGLYZE XR (DPP-4)	\$2,190,901	174	\$3.07
NESINA (DPP-4)	\$3,871,389	280	\$13.97	JARDIANCE (SGLT2)	\$1,668,599	91	\$2.42
TRADJENTA (DPP-4)	\$15,982,400	1,141	\$4.80	JANUVIA (DPP-4)	\$84,746,431	5,099	\$2.09
BYDUREON (GLP-1)	\$14,778,810	1,020	\$4.07	JANUMET (DPP-4)	\$27,810,445	1,671	\$1.59
VICTOZA (GLP-1)	\$50,055,817	3,877	\$3.58	ONGLYZA (DPP-4)	\$11,709,752	895	\$1.40

## CONCLUSIONS

THIS STUDY PROVIDED: DISPROPORTIONAL REPORTING TRENDS FOR KEY AES & ESTIMATED DIRECT MEDICAL COSTS FROM POST-MARKETING AES & POOR PATIENT OUTCOMES ASSOCIATED WITH MAJOR TYPE 2 DIABETES DRUGS.

### WHAT IS ALREADY KNOWN:

- PRE-APPROVAL TRIALS CANNOT PREDICT MANY AES OBSERVED IN REAL WORLD PATIENTS.
- TYPE 2 DIABETES PATIENTS ARE ESPECIALLY PRONE TO AES & REQUIRE STRICT MEDICATION ADHERENCE FOR SUCCESSFUL BLOOD SUGAR CONTROL, THEREFORE, REAL WORLD SAFETY DATA IS OF GREAT IMPORTANCE.

### WHAT THIS STUDY ADDS:

- ELEVATED REPORTING RATES FOR PANCREATITIS, HYPOGLYCEMIA, & DIABETIC KETOACIDOSIS ADD TO SUSPICIONS OF CLASS-WIDE SIDE EFFECT ISSUES - ESPECIALLY FOR DPP-4 DRUGS.
- POST-MARKETING AE REPORTS FROM TYPE 2 DRUGS CAN BE ASSIGNED DIRECT MEDICAL COSTS IN ORDER TO ESTIMATE A DRUG'S DOWNSTREAM FINANCIAL IMPACT.
- THE 3 HIGHEST PER PRESCRIPTION COST BURDENS WERE FROM BYETTA (GLP-1), FARXIGA (SGLT2), AND NESINA (DPP-4).

### LIMITATIONS

A NUMBER OF LIMITATIONS MUST BE CONSIDERED WHEN USING AND INTERPRETING THIS SYSTEM, INCLUDING REPORTING RATES AND POTENTIAL BIASES CONTAINED IN FAERS. THE "PRIMARY SUSPECT" DESIGNATION IN FAERS IS SUBJECTIVE AND THE INFLUENCE OF OTHER DRUGS OR FACTORS CANNOT BE RULED OUT FROM A GIVEN CASE REPORT. WHILE WE EXCLUDED OBVIOUS CASES WHERE A DISEASE-RELATED SYMPTOM WAS MISTAKENLY DENOTED AS AN AE, WE ASSUME THAT WE DID NOT CATCH ALL SUCH MISTAKES. OUR COST ESTIMATES COME FROM MAPPING AHRQ HCUP COST SURVEY DATA TO MEDDRA TERMS FOUND IN FAERS. WHILE WE BELIEVE THIS IS APPROPRIATE, WE COULD NOT DETERMINE IF VARIATIONS BETWEEN FAERS PATIENT POPULATIONS AND THOSE USED FOR HCUP SURVEYS COULD INFLUENCE THE RESULTS PRESENTED HERE. FINALLY, LIMITATIONS IN BOTH THE ACCURACY OF MEPS DATA AND PATIENT EXPOSURE ESTIMATES USED HEREIN MAY CAUSE ARTIFICIAL INCREASES, OR DECREASES, IN CALCULATED DIRECT MEDICAL COSTS. WE VIGOROUSLY RECOMMEND THAT PATIENTS MUST HAVE A CONSULTATION WITH THEIR PRESCRIBING PHYSICIAN BEFORE TAKING ANY ACTION THAT RELATES TO FAERS OR THE DATA PRESENTED HERE. **DISCLOSURE:** KBH, AG, AND MD OWN STOCK OPTIONS IN, AND ARE EMPLOYEES OF, ADVERA HEALTH ANALYTICS, INC.