Pattern of use of incretin-based medicines in a large sample of the Italian general population.

G. Roberto[1], F. Barone Adesi[2], F. Giorgianni[3], V. Pizzimenti[3], C. Bartolini[1], M. Maggini[4], R. Da Cas[4], S. Spila Alegiani[4], P. Francesconi[1], C. Ferraiolo[5], M. Tari[6], G. Trifirò[3], E. Poluzzi[7], F. Baccetti[8], R. Gini[1]

1)Agenzia regionale di sanità della Toscana, Epidemiology Unit, Florence, Italy; 2)University of Eastern Piedmont, Department of Pharmaceutical Sciences, Novara, Italy; 3)Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina, Italy; 4) National Institute of Health, National Centre for Drug Research and Evaluation, Rome, Italy; 5)Erasmus University Medical Center, Department of Medical Informatics, Rotterdam, Netherlands and Department of Experimental medicine, Regional Center of Pharmacovigilance and Pharmacoepidemiology of Campania, University of Campania, Naples, Italy; 6)Local Health Unit of Caserta, Caserta; Italy; 7)University of Bologna, Department of Medical and Surgical Science, Unit of Pharmacology, Bologna, Italy; 8)Local Health Authority of North-West Tuscany, Unit of Diabetology, Massa, Italy

Background

The incretin-based medicines GLP1 analogues (GLP1a) and dipeptidyl peptidase-4 inhibitors (DPP4i) are hypoglycaemic agents licensed for the treatment of type 2 diabetes mellitus (T2DM). Although these drugs posses comparable efficacy and low risk of hypoglycaemia, differences in terms of route of administration (subcutaneous *vs* oral), effect on body weight and gastrointestinal tollerability can impact their actual use in clinical practice.

Objectives

This study aimed to describe the real-world utilization of incretin-based medicines in the Italian clinical practice.

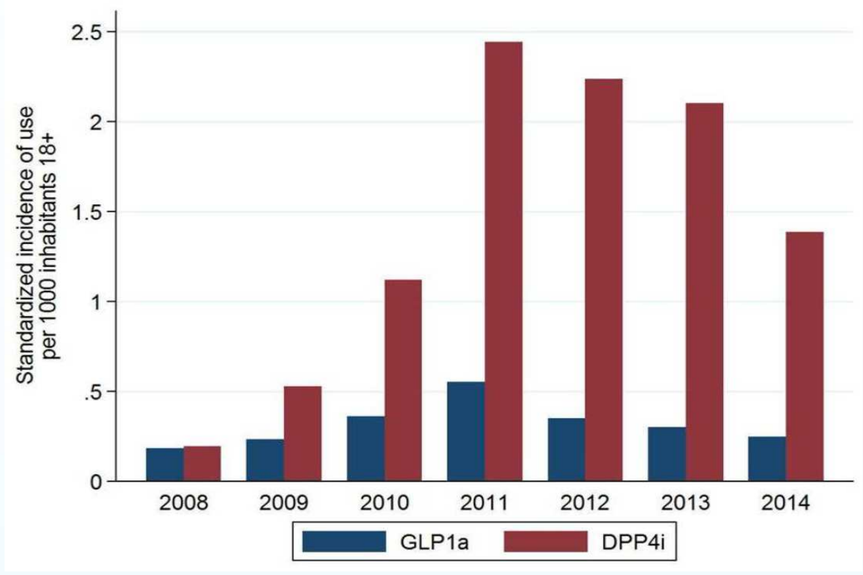
Materiali e metodi

Data source: Administrative data collected between 2008 and 2014 from three Italian geographic areas, 2 regions, Toscana and Umbria, and 1 Local Health Authority, Caserta, were used, The total source population corresponded to around 6 million subjects. The relevant data bases contains records of healthcere services reimbursed by the National Healthcare Service, including drug dispensings for otupatients.

Data extraction, management and analysis: A distributed database network approach was used. Raw data were extracted and tranformed in a common format at local level. The data management process was performed ina standardized, automatic fashion using the open source software *TheMatrix* (thematrix.isti.cnr.it). The resulting aggregated datasets were then shared and analyzed centrally at the Agenzia Regionale di Sanità della Toscana using Stata version 12.1.

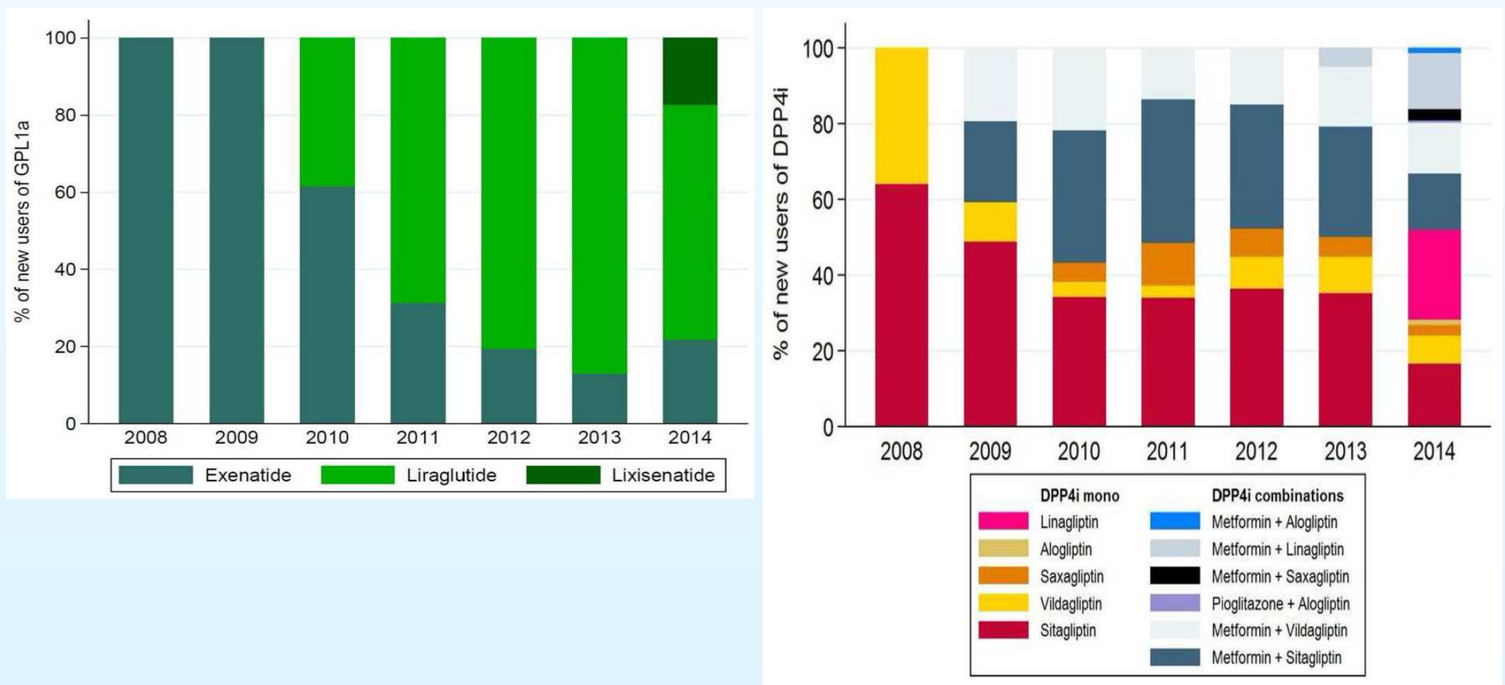
Study design and descriptive statistics: A multi-database, population-based, descriptive, cohort study was performed. At the 1st of january of each year of the observation period subjects aged ≥18 and with ≥ look-back were selected. New users were defined as those with ≥1 dispensing of GLP1a or DPP4i during the year of interest and none in the past. Trends of cumulative annual incidence of use in the general adult population were observed. New users of GLP1a or DPP4i were also described in terms of first active principle received, demographic characteristics and use of antidiabetic drugs during both 1 year before and after the first incretin-based medicine dispensing.

Figure 1. Cumulative annual incidence of use in the general adult population.



*standardized by age and sex.

Figure 2. New incretin-based medicines users by first active principles received.



Risultati

The overall study population included 4 943 952 subjects. A total of 7,357 new users of GLP1a and 41,907 of DPP4i were identified during the study period. The annual cumulative incidence of use (**Figure 1**) increased between 2008 (0.2‰ for both GLP1a and DPP4i) and 2011 (GLP1a=0.6‰; DPP4i=2.5‰) and started to decrease thereafter. In 2014, 61% of new GLP1a users received liraglutide (**Figure 2**) while 52% of new DPP4i users received metformin/DPP4i in fixed-dose. The percentage of new DPP4i users older than 65 years of age increased from 30.9 to 62.6% during the study period (**Table 1**). Around 12% of new users had not received any antidiabetic before starting an incretin-based therapy.

Table 1. Characterization of new users.

GLP1 analogues		2008	2009	2010	2011	2012	2013	2014	Total
N		587	753	1,158	2,035	1,160	950	714	7,357
Women, %		55.2	52.7	51.5	49.3	50.3	46.5	46.2	50.0
Mean age		57.9	58.2	58.7	58.0	57.6	58.6	57.2	58.1
Age bands, %	*18-44*	8.5	9.2	8.4	10.9	10.9	11.7	12.9	10.4
	45-64	65.6	63.7	63.5	62.4	63.9	57.2	61.1	62.4
	65-84	25.9	26.8	28.0	26.1	24.8	29.3	25.9	26.7
	85+		0.3	0.2	0.6	0.3	1.9	0.1	0.5
Prior antidiabetic treatments[1], %	*No antidiabetics*	3.7	4.8	6.6	16.5	11.6	18.6	16.9	12.3
	Insulin with/without non-insulin antidiabetics	23.0	25.4	22.3	20.6	25.7	23.5	19.0	22.6
	Non-insulin antidiabetic monotherapy	14.3	16.3	19.9	28.2	30.0	32.4	37.3	26.3
	≥1 non-insulin antidiabetic	58.9	53.5	51.2	34.7	32.7	25.5	26.8	38.9
Patients with 1 year follow-up (%)		99.8	99.7	99.9	99.7	99.3	98.9	0.0	89.9
Patients with 1 year follow-up, *N*		586	751	1,157	2,029	1,152	939	-	6,614
Following antidiabetic treatments[2], %	*≥1 additional dispensing of a DPP4i*	84.0	84.0	82.2	82.7	82.1	74.8	-	81.6
	Persistent use of incretins (any)	54.3	60.6	60.1	65.1	62.2	53.3	-	60.6
	Switcher to a GLP1a	3.4	3.7	6.2	5.7	8.1	4.7	-	5.6
	≥1 additional non-incretin antidiabetic dispensing	91.6	91.1	86.3	86.1	84.7	79.9	-	86.1
	≥1 additional dispensing of any antidiabetic	97.1	96.7	94.5	93.2	93.1	88.2	-	93.5
DPP4 inhibitors		**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**Total**
N		627	1,732	3,838	10,546	9,800	9,231	6,133	41,907
Women, %		46.1	45.6	46.8	46.6	45.4	47.0	44.1	46.0
Mean age		59.2	61.5	62.0	62.6	64.5	65.9	67.4	64.3
Age bands, %	*18-44*	8.3	5.6	6.3	5.7	4.5	5.1	3.3	5.0
	45-64	60.8	53.8	51.2	50.2	43.6	36.8	34.2	43.8
	65-84	30.6	39.8	41.7	42.8	49.6	53.8	57.5	48.5
	85+	0.3	0.8	0.9	1.3	2.4	4.2	5.1	2.7
Prior antidiabetic treatments[1], %	*No antidiabetics*	4.6	4.8	10.3	15.7	9.9	16.0	9.6	12.4
	Insulin with/without non-insulin antidiabetics	4.9	6.9	11.5	16.7	22.0	22.2	16.1	18.0
	Non-insulin antidiabetic monotherapy	34.9	30.9	26.1	27.4	29.9	28.6	36.1	29.7
	≥1 non-insulin antidiabetic	55.5	57.3	52.2	40.2	38.2	33.1	38.2	39.9
Patients with 1 year follow-up (%)		99.5	99.7	99.4	99.6	99.3	98.2	0.0	84.6
Patients with 1 year follow-up, *N*		624	1,727	3,815	10,504	9,731	9,067	-	35,468
Following antidiabetic treatments[2], %	*≥1 additional dispensing of a DPP4i*	87.3	89.8	84.8	86.6	88.4	80.6	-	85.5
	Persistent use of incretins (any)	57.2	65.5	59.1	66.7	65.3	55.4	-	62.4
	Switcher to a GLP1a	2.9	2.5	3.5	2.3	1.6	0.8	-	1.9
	≥1 additional non-incretin antidiabetic dispensing	92.5	81.5	74.8	76.7	76.0	72.6	-	75.8
	≥1 additional dispensing of any antidiabetic	97.0	97.3	93.0	93.4	95.3	89.9	-	93.2

[1]≥1 dispensing within 365 days preceding the start of the incretin-based medicines.

[2]Dugs dispensed during 365 days following the start of the incretin-based medicines.

Persistent use: no gaps ≥90 days between the end of the duration of a dispensing and the following one. The day of duration of each dispensing corresponded to the number of Defined Daily Doses dispensed.

Switchers: ≥1 dispensing of a different incretin-based medicines, i.e. DPP4i or GLP1a.

Conclusioni

During the study period, DPP4i rapidly became the most prescribed incretin-based medicine, particularly among older new user. The choice of the specific incretin-based medicine at first prescription appeared to be directed towards those with higher convenience of use, i.e. oral DPP4i rather than subcutaneous GLP1a, once-daily liraglutide rather than twice-daily exenatide (once-weekly exenatide was not available yet in Italy). The non-neglibile use of incretin-based medicines as first-line pharmacotherapy for T2DM was in contrast with national reimbursement criteria and warrants further effectiveness and safety evaluations to better define the place in therapy of these hypoglicemic agents.

Conflict of interest disclosure: No funding were received for the execution of this study

giuseppe.roberto@ars.toscana.it