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Original Article

Persistence and adherence to overactive bladder medications in Japan: A large nationwide real-world analysis

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Abbreviations & Acronyms
CI = confidence interval
fMPR = fixed medication possession ratio
IQR = interquartile range
MPR = medication possession ratio
OAB = overactive bladder
SD = standard deviation
UK = United Kingdom
US = United States
vMPR = variable medication possession ratio

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Objectives: To evaluate persistence and adherence to mirabegron and antimuscarinics in Japan using data from two administrative databases.

Methods: The present retrospective study evaluated insurance claims for employees and dependents aged ≤75 years, and pharmacy claims for outpatients. From October 2012 to September 2014, new users of mirabegron or five individual antimuscarinics indicated for overactive bladder in Japan (fesoterodine, imidafenacin, propiverine, solifenacin and tolterodine) were identified and followed for 1 year. Persistence with mirabegron and antimuscarinics were evaluated using Kaplan–Meier methods. Any associations between baseline characteristics (age, sex and previous medication use) and persistence were explored. Adherence was assessed using the medication possession ratio.

Results: In total, 3970 and 16 648 patients were included from the insurance and pharmacy claims databases, respectively. Mirabegron treatment was associated with longer median persistence compared with antimuscarinics (insurance claims: 44 [95% confidence intervals 37–56] *vs* 21 [14–28] to 30 [30–33] days, pharmacy claims: 105 [96–113] *vs* 62 [56–77] to 84 [77–86] days). The results were consistent when patients were stratified by age, sex and previous medication. Persistence rate at 1 year was higher for mirabegron (insurance claims: 14.0% [11.5–16.8%] *vs* 5.4% [4.1–7.0%] to 9.1% [5.3–14.2%], pharmacy claims: 25.9% [24.6–27.3%] *vs* 16.3% [14.0–18.6%] to 21.3% [20.2–22.4%]). Compared with each antimuscarinic, a higher proportion of mirabegron-treated patients had medication possession ratios ≥0.8.

Conclusions: This large nationwide Japanese study shows that persistence and adherence are greater with mirabegron compared with five antimuscarinics.

Key words: antimuscarinics, compliance, Japan, mirabegron, overactive bladder.

Introduction

Epidemiological studies carried out in Japan have estimated that the prevalence of OAB is between 11.2% and 12.4%.[1,2] These investigations also showed that prevalence increased with age, and the presence of OAB had a negative effect on quality of life.

Antimuscarinics are the principal therapeutic approaches for managing patients with OAB.[3] However, they are associated with several side effects, including dry mouth and constipation,[4] which might limit persistence (the overall duration of time from initiation to discontinuation of therapy) and adherence (the intensity of drug use during the period of therapy).[5,6] In fact, 1-year initial treatment discontinuation and non-adherence rates of 65–86% and 80–85% have been respectively noted in UK and US studies after antimuscarinic treatment.[7,8] Consequently, there exists a need for alternative therapeutic options with an improved safety profile, which might lead to improvements in patient persistence.

Mirabegron is a β3-adrenoceptor agonist that is clinically approved for the treatment of OAB symptoms.[9] Three 12-week, international, phase III studies showed that mirabegron use can lead to significant improvements in incontinence episodes and micturitions compared with placebo, and that mirabegron and placebo have similar overall safety profiles.[10] The efficacy of mirabegron has also been shown in the Japanese patient population, with several studies indicating that mirabegron use is associated with reductions in both urinary frequency and urgency.[11,12] Furthermore, the favorable safety profile of mirabegron

compared with antimuscarinics might lead to the increasing use of mirabegron as a first-line therapy in Japan.[13,14]

Previous studies, each from a single healthcare site, have investigated persistence with OAB medications in the Japanese patient population, and recent investigations have shown that 12-month persistence rates with mirabegron vary between 12% and 29%.[15–18] Building on these results, the present study is the first large-scale, nationwide survey in Japan to explore persistence and adherence to mirabegron and antimuscarinics using data from two databases.

Methods

Objectives

The primary objective of the present retrospective study was to descriptively compare persistence and adherence to mirabegron and each antimuscarinic. Any association between baseline characteristics (age [insurance claims: ≤55 and >55 years, pharmacy claims: <75, 75–80 and >80 years], sex, meteorological season at index [winter: January–March, spring: April–June, summer: July–September, autumn: October–December] and previous OAB medication use) and persistence was also explored. The secondary objective was to descriptively compare persistence with any OAB medication in the same patient population; that is, after starting the index medication, switching to other OAB medication(s) was allowed.

Study design

The present study involved the use of two Japanese administrative databases. As of October 2016, the Japan Medical Data Center database (https://www.jmdc.co.jp/en/) included information on insurance claims from approximately 3.8 million employees and their dependents (approximately 3% of the Japanese population). The majority of the patients were ≤65 years old, and the maximum age was 75 years. The Medi-Trend® (Tokyo, Japan) pharmacy claims database provided by Kyowa Kikaku contained data from 3.4 million outpatients (approximately 2% of out-of-hospital dispensations annually), and did not have any age restrictions.

New users of mirabegron or each of five antimuscarinics (fesoterodine, imidafenacin, propiverine, solifenacin and tolterodine) between 1 October 2012 and 30 September 2014 were identified from the databases and followed for a maximum of 1 year. New users were defined as patients who had not been dispensed their index medication (mirabegron or the five antimuscarinics) for ≥1 year. The date of the initial use of the medication was defined as the index date. Use of other target medication(s) during the 1-year pre-index period was allowed, and those patients were designated as treatment-experienced users. Patients who had not received any target medication during this period were defined as treatment-naïve. Patient identification number, birth year, sex, dispensing date, index medication code and days of supply were extracted from each database.

This study was approved by the Astellas Medical Affairs Japan Regional Protocol Committee (meeting: MAJ-PRC 03102016).

Eligibility criteria

For the insurance claims database, eligibility was confirmed using enrollment/disenrollment records, whereas for the pharmacy claims database, patients were eligible if the pharmacy continued to provide data during the entire pre-index period.

Patients aged ≥18 years at the index date were eligible. During the pre-index period, patients had to remain a beneficiary of the same insurance program (insurance claims) or have ≥1 dispensing claim for any medication every 3 months (pharmacy claims). Patients were ineligible if they had received ≥2 target medications on their index date.

Statistical analysis

Patient persistence with mirabegron and each antimuscarinic was compared descriptively. The Kaplan–Meier method was used to estimate the distribution for days to discontinuation. Median persistence was calculated as the 50th percentile of the Kaplan–Meier estimates, and two-sided 95% CIs were provided. For the primary objective, patients were considered to have discontinued treatment if the grace period exceeded 30 days (defined as the day after the last day of the prior supply to the next dispensing date) or they switched to another OAB treatment, whichever came first. Patients were censored 365 days from the index date or at the end of the eligibility period, at the last date of the disenrollment month (insurance claims), or at the last date of the month that the pharmacy stopped providing data (pharmacy claims). Sensitivity analyses were carried out using grace periods of 15, 60 and 90 days. Switching to other OAB target treatments was permitted for the secondary objective analyses.

Adherence was defined according to MPR[19,20] (both fMPR and vMPR) during the follow-up period. fMPR provides data on adherence over the 1-year follow-up period and was calculated by dividing the total days of supply by 365; that is, fMPR = all days of supply (≤365) / 365. Patients were excluded from this analysis if <1 year of data were available. vMPR provides information on adherence over the days of supply in patients with ≥2 dispensing records, and was calculated by subtracting the last dispensing date from the first dispensing date to obtain the denominator. The total days of supply, not counting the days of supply from the last dispensing date, was subsequently divided by the denominator to calculate the parameter; that is, vMPR = all days of supply / elapsed days (exclusive of last dispensation). The patients were grouped according to whether they were adherent <50% (<0.5), between 50% and 80% (0.5–0.8), or ≥80% (≥0.8) of the time.

The number of dispensations during the follow-up period was categorized as 1, 2–3 or ≥4 dispensations. The days of supply for each dispensation were grouped by specific timeframes (1–6, 7–13, 14–27, 28–59, 60–89, 90–179 and ≥180 days).

Results

Demographics

In total, 3970 and 16 648 patients were identified from the insurance and pharmacy claims databases, respectively.

Patient demographics are shown in Table 1. Insurance claims database patients were younger than those from the pharmacy claims database (mean age 52.6 and 75.9 years, respectively). In both databases, patients who received mirabegron were generally older, and more likely to be male and treatment-experienced compared with the patients who received antimuscarinics.

Persistence

In terms of the primary objective, median persistence was notably longer with mirabegron than with any antimuscarinic (44 [95% CI 37–56] *vs* 21 [95% CI 14–28] to 30 [95% CI 30–33] days for the insurance claims database, and 105 [95% CI 96–113] *vs* 62 [95% CI 56–77] to 84 [95% CI 77–86] days for the pharmacy claims database). Although the estimate of persistence rate at 1 year was low for mirabegron (insurance claims 14.0% [95% CI 11.5–16.8%]; pharmacy claims 25.9% [95% CI 24.6–27.3%]), the results obtained were higher than for each antimuscarinic (insurance claims 5.4% [95% CI 4.1–7.0%] to 9.1% [95% CI 5.3–14.2%], pharmacy claims 16.3% [95% CI 14.0–18.6%] to 21.3% [95% CI 20.2–22.4%]; Fig. 1 and Table S1). Several factors were associated with longer persistence, including increased age, male sex and prior OAB medication use during the pre-index period (Figs 2,3). Meteorological season at index was not associated with persistence (data not shown). For each of the baseline characteristics studied, mirabegron treatment was generally associated with longer median persistence compared with each antimuscarinic. The grace period sensitivity analyses consistently showed that persistence was longer with mirabegron regardless of the grace period evaluated (Fig. S1).

The results of the secondary objective analyses, where switching OAB medication was allowed, also showed that persistence rate at 1 year was higher when mirabegron was used as the initial medication (insurance claims 17.4% [95% CI 14.7–20.4%], pharmacy claims 32.4% [95% CI 30.9–33.8%]) compared with starting with any antimuscarinic (insurance claims 8.7% [95% CI 6.4–11.4%] to 14.6% [95% CI 9.7–20.5%], pharmacy claims 24.4% [95% CI 22.6–26.3%] to 31.3% [95% CI 28.4–34.2%]; Fig. S2 and Table S2).

Adherence

Compared with each antimuscarinic, a slightly higher proportion of patients who received mirabegron had fMPR and vMPR results of ≥0.8. This finding was observed for both the insurance and pharmacy claims databases (Table 2). For example, the results from the pharmacy claims database showed that 32.9% of the patients who received mirabegron had an fMPR of ≥0.8 compared with 20.9–26.6% of patients who received an antimuscarinic. The differences in fMPR results between mirabegron and each antimuscarinic were more substantial than the differences in vMPR data.

Dispensing

The dispensing data showed that 52.6% and 37.3% of patients from the insurance and pharmacy claims databases, respectively, received only one dispensation of index medication (Table 3). A slightly greater proportion of patients received mirabegron treatment more than once (insurance claims 57.5%, pharmacy claims 66.1%) compared with any antimuscarinic (insurance claims 41.1–50.6%, pharmacy claims 59.0–63.5%). Overall, the days of supply was <28 days in 43.8% and 36.6% of the dispensations from the insurance and pharmacy claims databases, respectively.

Discussion

The present study is the most extensive investigation carried out to date in Japan to explore persistence and adherence to mirabegron and antimuscarinics. The results showed that persistence was greater with mirabegron compared with any antimuscarinic, both in terms of median persistence and persistence rate at 1 year. In support of this finding, a range of clinical studies that compared persistence with mirabegron and antimuscarinics have shown similar results.[21–24] In contrast, a Japanese urology outpatient study found no significant difference in persistence rate between mirabegron and solifenacin, although the study involved just 148 women with OAB.[18] The increased persistence that has been typically observed with mirabegron might be due to the relative absence of anticholinergic side effects that are believed to contribute to treatment discontinuation with antimuscarinics.[5,18,25]

As baseline factors, increased age, male sex and previous OAB medication use were consistently associated with longer persistence irrespective of the medication dispensed. As mirabegron use was typically associated with higher age, a male dominant distribution and a higher proportion of prior OAB medication use, the longer persistence with mirabegron compared with antimuscarinics might be confounded by these baseline characteristics. However, the results were consistent in both high- and low-age groups, males and females, and treatment-naïve and treatment-experienced patients. Therefore, we believe that persistence with mirabegron was longer than with antimuscarinics, regardless of the different baseline characteristics.

Principally because of the older patient population enrolled, the pharmacy claims database showed considerably longer persistence than the insurance claims database. Furthermore, the requirement that patients from the pharmacy claims database had to have ≥1 dispensing claim for any medication every 3 months might have also contributed to the longer persistence observed. This eligibility criterion could have led to the inclusion of patients who were loyal to the pharmacy and more likely to persist with OAB medication than the patients from the insurance claims database.

The association between increased age and persistence shown in the present study is supported by the results of several earlier investigations carried out both in Japan and elsewhere.[23,24,26] Contrasting results were observed in a UK-based study, although this might have been due to the short-term nature of the study and the relatively small population of 197 patients enrolled.[27] Improved persistence with increasing age has been observed with several other chronic

Table 1 Patient demographics and baseline characteristics

Parameter	All	Mirabegron	Fesoterodine	Imidafenacin	Propiverine	Solifenacin	Tolterodine
Insurance claims database							
Patients (*n*)	3970	731	174	1039	504	1336	186
Age (years)							
Mean (SD)	52.6 (12.9)	56.1 (11.2)	52.4 (12.5)	51.3 (13.3)	50.8 (13.7)	52.7 (12.8)	51.6 (13.6)
Median (IQR)	54.0 (45.0–62.0)	57.0 (49.0–64.0)	53.0 (46.0–61.0)	52.0 (43.0–61.0)	52.0 (42.0–61.0)	54.0 (44.5–62.0)	53.0 (43.0–62.0)
Range	18.0–75.0	18.0–75.0	18.0–75.0	18.0–75.0	18.0–75.0	18.0–75.0	18.0–74.0
Age group							
≤55 years	2181 (54.9)	321 (43.9)	104 (59.8)	603 (58.0)	308 (61.1)	740 (55.4)	105 (56.5)
>55 years	1789 (45.1)	410 (56.1)	70 (40.2)	436 (42.0)	196 (38.9)	596 (44.6)	81 (43.5)
Sex							
Female	2213 (55.7)	334 (45.7)	105 (60.3)	586 (56.4)	268 (53.2)	812 (60.8)	108 (58.1)
Male	1757 (44.3)	397 (54.3)	69 (39.7)	453 (43.6)	236 (46.8)	524 (39.2)	78 (41.9)
Previous OAB medication use							
Treatment-experienced	326 (8.2)	121 (16.6)	39 (22.4)	55 (5.3)	29 (5.8)	60 (4.5)	22 (11.8)
Treatment-naïve	3644 (91.8)	610 (83.4)	135 (77.6)	984 (94.7)	475 (94.2)	1276 (95.5)	164 (88.2)
Season at initial treatment							
Winter	1154 (29.1)	207 (28.3)	25 (14.4)	342 (32.9)	138 (27.4)	384 (28.7)	58 (31.2)
Spring	885 (22.3)	146 (20.0)	86 (49.4)	221 (21.3)	113 (22.4)	285 (21.3)	34 (18.3)
Summer	698 (17.6)	153 (20.9)	43 (24.7)	154 (14.8)	89 (17.7)	239 (17.9)	20 (10.8)
Autumn	1233 (31.1)	225 (30.8)	20 (11.5)	322 (31.0)	164 (32.5)	428 (32.0)	74 (39.8)
Pharmacy claims database							
Patients (*n*)	16 648	4138	991	3365	2130	5014	1010
Age (years)							
Mean (SD)	75.9 (10.4)	76.5 (9.3)	75.9 (10.6)	75.6 (10.5)	75.7 (11.5)	75.8 (10.8)	76.0 (10.3)
Median (IQR)	77.0 (71.0–83.0)	77.0 (71.0–83.0)	77.0 (71.0–83.0)	77.0 (70.0–83.0)	77.0 (70.0–83.0)	77.0 (70.0–83.0)	77.0 (71.0–83.0)
Range	18.0–105	21.0–105	18.0–98.0	18.0–102	18.0–105	18.0–102	22.0–103
Age group							
<75 years	6425 (38.6)	1534 (37.1)	379 (38.2)	1351 (40.1)	816 (38.3)	1960 (39.1)	385 (38.1)
75–80 years	4346 (26.1)	1145 (27.7)	275 (27.7)	863 (25.6)	535 (25.1)	1262 (25.2)	266 (26.3)
>80 years	5877 (35.3)	1459 (35.3)	337 (34.0)	1151 (34.2)	779 (36.6)	1792 (35.7)	359 (35.5)
Sex							
Female	8779 (52.7)	1759 (42.5)	588 (59.3)	1733 (51.5)	1169 (54.9)	2965 (59.1)	565 (55.9)
Male	7869 (47.3)	2379 (57.5)	403 (40.7)	1632 (48.5)	961 (45.1)	2049 (40.9)	445 (44.1)
Previous OAB medication use							
Treatment-experienced	3520 (21.1)	1383 (33.4)	451 (45.5)	519 (15.4)	305 (14.3)	616 (12.3)	246 (24.4)
Treatment-naïve	13 128 (78.9)	2755 (66.6)	540 (54.5)	2846 (84.6)	1825 (85.7)	4398 (87.7)	764 (75.6)
Season at initial treatment							
Winter	4760 (28.6)	1101 (26.6)	222 (22.4)	967 (28.7)	653 (30.7)	1499 (29.9)	318 (31.5)
Spring	3847 (23.1)	916 (22.1)	407 (41.1)	746 (22.2)	482 (22.6)	1110 (22.1)	186 (18.4)
Summer	3029 (18.2)	775 (18.7)	273 (27.5)	601 (17.9)	341 (16.0)	885 (17.7)	154 (15.2)
Autumn	5012 (30.1)	1346 (32.5)	89 (9.0)	1051 (31.2)	654 (30.7)	1520 (30.3)	352 (34.9)

All data shown are in terms of *n* (%), unless otherwise stated.

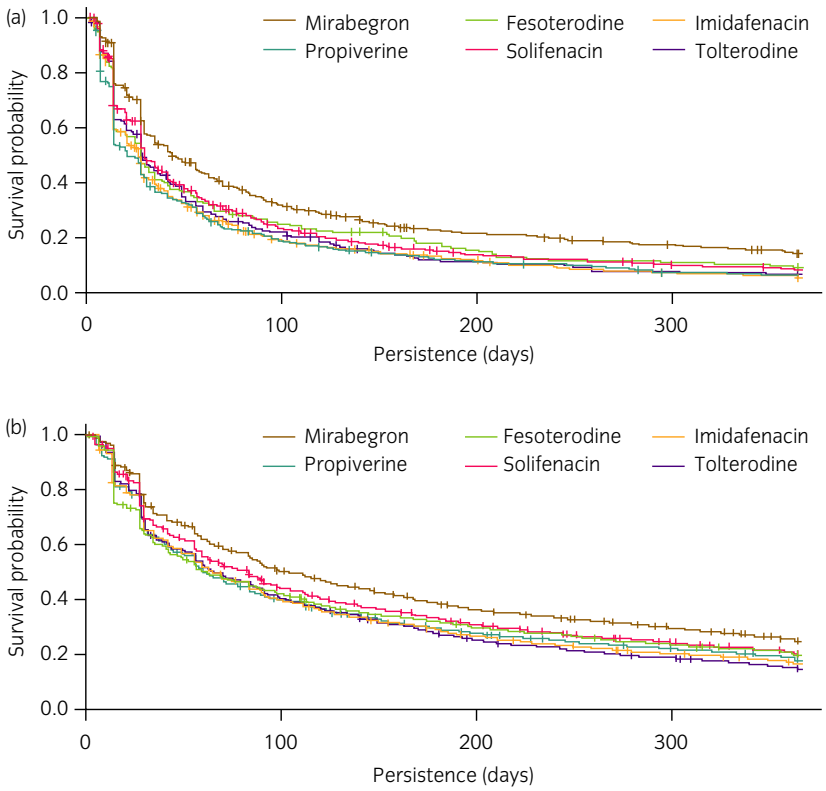

Fig. 1 Kaplan–Meier curves showing patient persistence with each of the target medications using data from (a) the insurance claims or (b) the pharmacy claims databases.

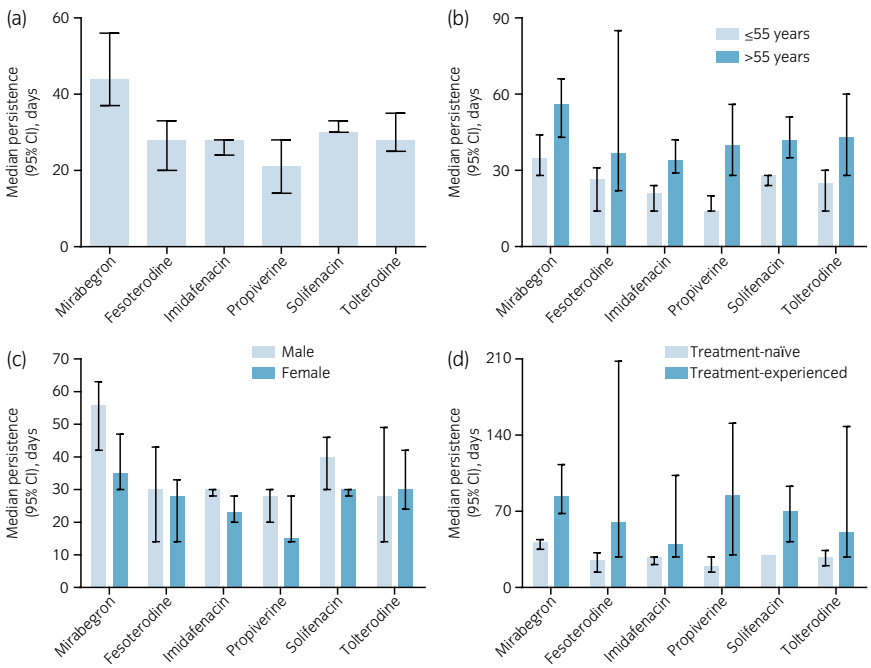

Fig. 2 Median persistence with each of the target medications using data from the insurance claims database. Results are presented in terms of (a) overall data or stratified according to (b) age, (c) sex or (d) OAB medication use during the pre-index period.

medications including angiotensin II receptor blockers, prostaglandin analogs, statins, bisphosphonates and oral antidiabetics.[28]

Mixed results have been reported in previous studies that have investigated the effect of sex on mirabegron persistence. In contrast to the findings reported herein, studies carried out in Canada and the Czech Republic showed that persistence rates were higher in women than they were in men.[23,29] However, in agreement with the results of the present study, a previous investigation that stratified according to sex showed that increased persistence was associated with mirabegron treatment compared with antimuscarinics.[24]

Persistence with mirabegron is consistently higher in treatment-experienced compared with treatment-naïve patients.[23,24] Unfamiliarity with the side effects associated with OAB therapy might lead to treatment-naïve patients

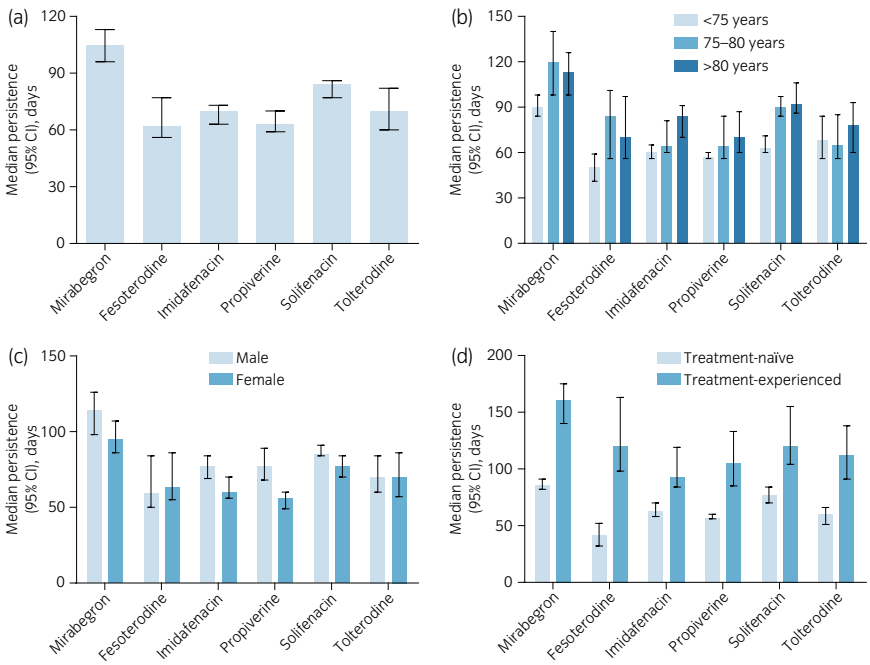

Fig. 3 Median persistence with each of the target medications using data from the pharmacy claims database. Results are presented in terms of (a) overall data or stratified according to (b) age, (c) sex or (d) OAB medication use during the pre-index period.

Table 2 fMPR and vMPR adherence results for each of the target medications using data from the insurance claims and pharmacy claims databases

Parameter	All	Mirabegron	Fesoterodine	Imidafenacin	Propiverine	Solifenacin	Tolterodine
Insurance claims database							
fMPR, *n* (%)	*n* = 3175	*n* = 571	*n* = 152	*n* = 829	*n* = 414	*n* = 1076	*n* = 133
<0.5	2612 (82.3)	421 (73.7)	127 (83.6)	707 (85.3)	353 (85.3)	890 (82.7)	114 (85.7)
0.5–0.8	220 (6.9)	47 (8.2)	8 (5.3)	61 (7.4)	28 (6.8)	68 (6.3)	8 (6.0)
≥0.8	343 (10.8)	103 (18.0)	17 (11.2)	61 (7.4)	33 (8.0)	118 (11.0)	11 (8.3)
vMPR, *n* (%)	*n* = 2096	*n* = 463	*n* = 98	*n* = 499	*n* = 236	*n* = 707	*n* = 93
<0.5	326 (15.6)	62 (13.4)	26 (26.5)	78 (15.6)	46 (19.5)	103 (14.6)	11 (11.8)
0.5–0.8	329 (15.7)	68 (14.7)	15 (15.3)	82 (16.4)	41 (17.4)	106 (15.0)	17 (18.3)
≥0.8	1441 (68.8)	333 (71.9)	57 (58.2)	339 (67.9)	149 (63.1)	498 (70.4)	65 (69.9)
Pharmacy claims database							
fMPR, *n* (%)	*n* = 16 115	*n* = 4005	*n* = 955	*n* = 3293	*n* = 2025	*n* = 4872	*n* = 965
<0.5	10 132 (62.9)	2225 (55.6)	627 (65.7)	2202 (66.9)	1347 (66.5)	3071 (63.0)	660 (68.4)
0.5–0.8	1691 (10.5)	461 (11.5)	105 (11.0)	342 (10.4)	176 (8.7)	504 (10.3)	103 (10.7)
≥0.8	4292 (26.6)	1319 (32.9)	223 (23.4)	749 (22.7)	502 (24.8)	1297 (26.6)	202 (20.9)
vMPR, *n* (%)	*n* = 11 500	*n* = 3012	*n* = 673	*n* = 2240	*n* = 1412	*n* = 3505	*n* = 658
<0.5	1249 (10.9)	302 (10.0)	109 (16.2)	233 (10.4)	176 (12.5)	363 (10.4)	66 (10.0)
0.5–0.8	1500 (13.0)	335 (11.1)	127 (18.9)	298 (13.3)	183 (13.0)	475 (13.6)	82 (12.5)
≥0.8	8751 (76.1)	2375 (78.9)	437 (64.9)	1709 (76.3)	1053 (74.6)	2667 (76.1)	510 (77.5)

discontinuing medication more rapidly than treatment-experienced patients. The comparatively high proportion of mirabegron patients that were treatment-experienced could partially explain the increased persistence that was observed with the β3-adrenoceptor. In support of the present study, other investigations have found that both treatment-naïve and treatment-experienced patients typically persist with mirabegron for a longer median period of time compared with antimuscarinics.[23,24]

Overall, observed persistence was low in the present study, which is consistent with previous reports that showed that lower persistence is apparent with OAB medication compared with other chronic medication classes.[28] A variety of factors might be responsible for this finding, including the unmet expectations of OAB medication, the occurrence of specific adverse events and recognition by patients of the chronic nature of their OAB symptoms.[23] Owing to the different study setting and data sources used, shorter persistence was generally observed in this study compared with previous Japanese studies that investigated persistence with OAB medication.[15–18] For the secondary objective, patients were allowed to switch to another OAB medication. Accordingly, persistence rate was higher than that observed for the index medication only, but was still limited. Despite the potential to switch medication, persistence with initial mirabegron treatment was still higher compared with each antimuscarinic, a finding that supports the primary objective results.

Table 3 Dispensing data for each of the target medications using data from the insurance claims and pharmacy claims databases

Parameter	All	Mirabegron	Fesoterodine	Imidafenacin	Propiverine	Solifenacin	Tolterodine
Insurance claims database							
Patients (*n*)	3970	731	174	1039	504	1336	186
No. dispensations, *n* (%)							
1	2088 (52.6)	311 (42.5)	86 (49.4)	592 (57.0)	297 (58.9)	700 (52.4)	102 (54.8)
2–3	1091 (27.5)	230 (31.5)	47 (27.0)	271 (26.1)	118 (23.4)	375 (28.1)	50 (26.9)
≥4	791 (19.9)	190 (26.0)	41 (23.6)	176 (16.9)	89 (17.7)	261 (19.5)	34 (18.3)
Dispensations (*n*)	10 908	2314	579	2625	1271	3660	459
Days of supply, *n* (%)							
<7	232 (2.1)	13 (0.6)	21 (3.6)	60 (2.3)	60 (4.7)	69 (1.9)	9 (2.0)
7–13	1183 (10.8)	164 (7.1)	44 (7.6)	364 (13.9)	162 (12.7)	409 (11.2)	40 (8.7)
14–27	3358 (30.8)	610 (26.4)	297 (51.3)	897 (34.2)	411 (32.3)	1026 (28.0)	117 (25.5)
28–59	5324 (48.8)	1248 (53.9)	193 (33.3)	1165 (44.4)	567 (44.6)	1881 (51.4)	270 (58.8)
60–89	535 (4.9)	174 (7.5)	10 (1.7)	89 (3.4)	51 (4.0)	192 (5.2)	19 (4.1)
90–179	276 (2.5)	105 (4.5)	14 (2.4)	50 (1.9)	20 (1.6)	83 (2.3)	4 (0.9)
Pharmacy claims database							
Patients (*n*)	16 648	4138	991	3365	2130	5014	1010
No. dispensations, *n* (%)							
1	6211 (37.3)	1403 (33.9)	392 (39.6)	1307 (38.8)	873 (41.0)	1830 (36.5)	406 (40.2)
2–3	3699 (22.2)	919 (22.2)	184 (18.6)	787 (23.4)	452 (21.2)	1114 (22.2)	243 (24.1)
≥4	6738 (40.5)	1816 (43.9)	415 (41.9)	1271 (37.8)	805 (37.8)	2070 (41.3)	361 (35.7)
Dispensations (*n*)	77 502	18 900	5319	15 339	9505	24 280	4159
Days of supply, *n* (%)							
<7	495 (0.6)	86 (0.5)	31 (0.6)	93 (0.6)	113 (1.2)	137 (0.6)	35 (0.8)
7–13	3660 (4.7)	606 (3.2)	361 (6.8)	900 (5.9)	480 (5.0)	1065 (4.4)	248 (6.0)
14–27	24 179 (31.2)	4429 (23.4)	2849 (53.6)	5160 (33.6)	2822 (29.7)	7815 (32.2)	1104 (26.5)
28–59	40 948 (52.8)	10 592 (56.0)	1697 (31.9)	7925 (51.7)	5311 (55.9)	13 127 (54.1)	2296 (55.2)
60–89	5281 (6.8)	1960 (10.4)	244 (4.6)	851 (5.5)	543 (5.7)	1372 (5.7)	311 (7.5)
90–179	2937 (3.8)	1227 (6.5)	137 (2.6)	408 (2.7)	236 (2.5)	764 (3.1)	165 (4.0)
≥180	2 (0.0)	0	0	2 (0.0)	0	0	0

The present study showed that adherence to mirabegron was slightly higher than adherence to any antimuscarinic, particularly in terms of fMPR. Compared with antimuscarinic therapy, greater adherence has been previously reported with mirabegron when MPR and median proportion of days covered by index drug were used to measure patient adherence.[23,24] The present study also showed that the vMPR results were considerably higher than the fMPR results, which indicates that patients returned for a repeat dispensation almost immediately after they had completed their previous supply of medication.

Despite the wealth of data obtained, the present study has some limitations. First, both databases had selection bias. The insurance claims database was limited to employees and dependents, and therefore the age distribution was skewed towards the younger population. The pharmacy claims database did not include data from in-hospital dispensing, and the data were acquired from just 2% of pharmacies available in Japan, so patients might have received other OAB medications from alternative pharmacies. Data from two different Japanese databases were utilized in this study to try and circumvent the aforementioned bias associated with each database. A further limitation was that no information was available on whether the patient actually took the medication. Therefore, patients who were not exposed to their index drug might also have been included. There was also a lack of data on the reasons for discontinuation. Patients might have intentionally taken the medication intermittently or their symptoms might have resolved; in both scenarios, the patients would have been identified as being non-compliant. Finally, the attending physicians' specialty (i.e. urologist or primary physician) could not be analyzed in the present study because these data were largely missing from the databases. It was therefore possible that drug utilization patterns and/or persistence/adherence might differ between urologists and other specialties.

In conclusion, this nationwide retrospective Japanese study showed that persistence and adherence were greater with mirabegron in comparison with five antimuscarinic medications. This finding was consistently observed when the results were stratified according to age, sex and previous OAB medication use. The possibility of prolonged persistence and adherence with mirabegron could bring distinct benefits to the patients. However, overall persistence was short in this study, because a significant proportion of patients received the medication only once, when a 30-day grace period was applied. In addition, we could not obtain efficacy or safety findings, information on the reasons for switching or discontinuation, or data about the prescribers' specialty (urologist or primary physician). These missing variables could be important confounders for the persistence data obtained, and further comprehensive investigations are therefore required to examine persistence and adherence to OAB medications in Japan.

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Conflict of interest

All authors are employees of Astellas Pharma.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Figure S1. Median persistence with each of the target medications with respect to different grace periods using data from (a) the insurance claims or (b) the pharmacy claims databases.

Figure S2. Kaplan–Meier curves showing patient persistence with each of the target medications when switching was allowed using data from (a) the insurance claims or (b) the pharmacy claims databases.

Table S1. Kaplan–Meier estimates of patient persistence with each of the target medications using data from (a) the insurance claims or (b) the pharmacy claims databases.

Table S2. Kaplan–Meier estimates of patient persistence with each of the target medications when switching was allowed using data from (a) the insurance claims or (b) the pharmacy claims databases.