

Effects of Initiating or Switching to a Six-Monthly Triptorelin Formulation on Prostate Cancer Patient–Healthcare Interactions and Hospital Resource Use: a Real-World, Retrospective, Non-Interventional Study

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ABSTRACT

Introduction: Luteinising hormone-releasing hormone agonist (LHRHa) injections are currently used in the treatment of advanced prostate cancer, but the frequency of injections may represent a burden to patients and healthcare services. The aim of this study was to collect real-world evidence about clinical and practical outcomes for patients with prostate cancer initiating six-monthly triptorelin, or switching from shorter-acting formulations to six-monthly triptorelin, in hospitals in the DECapeptyl SERvice Evaluation project.

Methods: Up to 2 years of data were collected retrospectively by physicians from records of 88 patients receiving six-monthly triptorelin at

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three centres. The primary outcome measure was the change in the number of patient–healthcare interactions (patient reviews, prostate-specific antigen (PSA) tests, and LHRHa injections) over a 24-month treatment period.

Results: This analysis included 47 patients newly initiated on six-monthly triptorelin and 41 who received 12 months of a one- or three-monthly LHRHa before switching to six-monthly triptorelin. After switching to six-monthly triptorelin, there was a statistically significant reduction in patient reviews (46.8%), injections (46.8%), and PSA tests (26.6%; all $P < 0.0001$). The total number of patient–healthcare interactions was significantly reduced (41.5%; $P < 0.0001$). Based upon cost of these interactions only, the cost reduction of switching to six-monthly triptorelin was £10,214.85 (£249.14 per patient) over 12 months. At 12 months, median PSA was 1.30 ng/mL (23.50 ng/mL at diagnosis) for newly treated patients and 0.24 ng/mL (0.35 ng/mL at switch) for patients who had switched treatment. No safety issues were identified.

Conclusion: Switching from one- or three-monthly LHRHa to six-monthly triptorelin significantly reduced patient–healthcare interactions and associated costs while maintaining PSA control over a 12-month treatment period. This not only translates into healthcare savings but may release men from the restriction of

repeated healthcare interactions and thus improve the overall patient experience as the population of long-term prostate cancer survivors continues to increase.

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Keywords: Luteinising hormone-releasing hormone agonist; Prostate cancer; Prostate-specific antigen; Real-world evidence; Resource utilisation; Six-monthly triptorelin

INTRODUCTION

Prostate cancer (PCa) is the most common cancer in men in Europe and the UK [1, 2]. PCa incidence has increased markedly in many countries, increasing by 147% between 1979 and 2012 in the UK; however, this is partly attributable to improved early detection by prostate-specific antigen (PSA) testing [1]. Consequently, the proportion of long-term survivors (> 10 years) has increased from 25% in the 1970s to over 80% in recent years [3]. However, with an expanding elderly population and a peak PCa incidence at ages 75–79 years, the number of new cases and associated economic burden are still predicted to increase [1, 3–5].

Total annual European healthcare costs of diagnosing and treating PCa were estimated at €8.43 billion [£7.51 billion; (28 September 2018; €1 = £0.890513; <https://www.xe.com/>)] in 2009, ranging between €106.7 million (£95.0 million) and €179.0 million (£159.4 million) in the UK, Germany, France, Italy, Spain, and the Netherlands [4–6]. The total annual economic cost, taking into account premature deaths, time off work, and unpaid carers, in addition to treatment costs, was estimated at £800 million in the UK [7]. The first year after diagnosis incurs a high proportion of direct PCa costs, estimated at £97 million for the NHS in 2007 [4].

Since the introduction of the first synthetic analogue in the 1970s [8], luteinising hormone-releasing hormone agonist (LHRHa) therapy has evolved from formulations requiring daily subcutaneous injections to longer-acting (i.e. one-, three-, and six-monthly) formulations offering

similar efficacy (castrate testosterone levels) and tolerability (mostly mild adverse events, AEs) [8–10]. In a pivotal trial, using six-monthly triptorelin, 97.5% of patients with locally advanced and metastatic PCa achieved castrate testosterone levels (≤ 0.5 ng/mL) 29 days after the first injection, which was maintained at 12 months (98.3%) [9, 10].

Patients prefer long-acting formulations involving fewer injections and associated injection site reactions, pain, and compliance issues [8]. Furthermore, patients often prefer six-monthly LHRHa formulations over one- or three-monthly formulations for placing less restriction on their daily activities, improving their quality of life, and reminding them less of their disease [11–13].

As the incidence and treatment costs of PCa continue to grow, six-monthly LHRHa formulations may alleviate the strain on healthcare practitioners' time, reduce costs, and improve patient outcomes compared with one- or three-monthly formulations. However, with a current lack of real-world evidence to support this, we present the findings of a real-world, retrospective, non-interventional DEscapeptyl SERVICE Evaluation (DESERVE). DESERVE assessed LHRHa therapy in patients with metastatic PCa or as a neoadjuvant or adjuvant treatment to evaluate the real-world impact of prescribing six-monthly triptorelin by comparison with a one- or three-monthly LHRHa regimen in terms of healthcare burden (resource utilisation and cost) and outcomes (PSA control).

METHODS

Study Design

The real-world, retrospective, non-interventional DESERVE project evaluated LHRHa therapy in adult patients with PCa regardless of age (range 53–99 years), treated in metastatic, neoadjuvant, or adjuvant settings. Up to 2 years of retrospective data were collected from the records of PCa patients who received LHRHa therapy at University Hospitals Coventry and Warwickshire NHS Trust, Medical Specialist Group, Guernsey, or The Royal Liverpool and

Broadgreen University Hospitals NHS Trust. The project aimed to assess the change in number and cost of patient–healthcare interactions after switching from one- or three- to a six-monthly LHRHa formulation and was not designed to assess drug acquisition costs.

Data Collection

Physicians entered up to 2 years of retrospective data from the records of PCa patients into a web-based data collection programme. Information recorded within the patient notes was inconsistent across the centres and data gaps were identified. To overcome centre differences, the following key assumptions were agreed before data collection, allowing for standardised data.

For inclusion in the analysis, patient records for those who had switched treatment (switch group) must have included details of at least three reviews or 12 months of treatment prior to switching to six-monthly triptorelin, and details of two reviews in the 12-month period after switching. A review at baseline (i.e. at time of switching) counted as a pre-switch review. Switch group records had to include all relevant resource utilisation data (i.e. patient–healthcare interactions) required to calculate the primary outcome measure and associated cost impact of switching to six-monthly triptorelin, as described below.

Records for patients receiving six-monthly triptorelin as their first LHRHa regimen (newly initiated group) had to include details of a new initiation review at baseline, and two further reviews in the 12-month period after initiating six-monthly triptorelin.

Anonymised baseline demographics and patient characteristics data were collected for all patients.

Data entry into the real-world treatment evaluator for eligible patients took place between December 2014 and February 2015. Data collected for the switch group covered a 12-month pre-switch and 12-month post-switch period for each patient receiving treatment from August 2011 to April 2015. The LHRHa-naïve (newly initiated) group was

studied from baseline (i.e. time of initiation) to 12 months post-LHRHa initiation between March 2011 to April 2015.

All data entered were checked for sense and any anomalies were re-checked by the data entry operative by cross-referencing with the original patient notes and records.

Primary Outcome Measures

The primary outcome was evaluated for the switch group, defined as the change in the total number of patient–healthcare interactions (sum of the number of patient reviews, serum PSA, and LHRHa injections) in the post-switch versus pre-switch period.

Secondary Outcome Measures

Efficacy in the switch and newly initiated groups was assessed by comparison of PSA levels at 6 and 12 months with those at baseline or switch. The cost impact of switching from a one- or three-monthly LHRHa to six-monthly triptorelin was determined by calculating the cost of the total number of patient–healthcare interactions, as specified for the primary outcome above, using the costings listed in Table 1.

Investigators at each participating centre were responsible for recording AEs reported within this study.

Statistical Analysis

The Microsoft Excel Descriptive Statistics Toolpak was utilised to calculate descriptive statistics and conduct the Student's *t* test to assess statistical significance ($P < 0.05$) for the primary outcome measure. Changes (%) were evaluated with 95% confidence intervals.

Serum PSA levels were expressed as median values including interquartile ranges (Q_1 , Q_3). Patient records missing serum PSA data (at baseline, and 6 or 12 months post-switch or post-initiation) were excluded from the efficacy analysis.

Table 1 Typical primary and secondary care costs for each single patient–healthcare interaction at the time of the analysis, utilised to calculate the cost impact of switching to six-monthly triptorelin

Patient–healthcare interaction	Cost (GBP) ^a
Primary care	
One review	11.00
One injection	11.00
One PSA test	4.65
Secondary care	
One review	70.00
One injection	70.00
One PSA test	4.65

GBP pound sterling, PSA prostate-specific antigen

^a Costs per treatment defined by Ipsen Ltd data on file: DEC034/DEC15 (unpublished data). Secondary care costs based upon a 30-min appointment, adjusted for 20 min

Ethics

This observational study was a retrospective, non-interventional service evaluation of an aspect of routine practice and, as such, did not require ethics committee approval although approval of the medical director was granted.

The study was not registered on a clinical trials database as it was a non-interventional and retrospective evaluation of patient records from routine clinical practice.

RESULTS

Patient Disposition

Six of the 121 patient records entered into the real-world treatment evaluator were excluded due to incomplete data entry. The remaining 115 records of patients with PCa who had received six-monthly triptorelin therapy between March 2011 and April 2015 were included in the baseline demographics and patient characteristics analysis (Fig. 1).

Complete patient records meeting all inclusion criteria for the subsequent data analysis were available for 88 of 115 patients i.e. 41 switch patients and 47 newly initiated patients (Fig. 1).

All of the 41 switch patients changed from a three-monthly formulation: 28 (68.3%) from three-monthly triptorelin and 13 (31.7%) from three-monthly goserelin. Thirty (73.2%) patients were changed as part of clinical practice, while 10 (24.4%) were switched due to patient choice, and one patient (2.4%) had been switched due to poor tolerability of the prescribed three-monthly LHRHa regimen.

In the newly initiated group, 47 records of patients receiving an LHRHa were included in the final data analysis. Details of the patients included at each participating centre are provided in Table 2.

Baseline Characteristics

Baseline demographics and patient characteristics were collated and summarised from the records of all 115 eligible patients i.e. the 63 records of patients in the switch group and the 52 records of patients in the newly initiated group (Table 3).

All Patients at Initiation of LHRHa Therapy

Overall, the 115 eligible patients were elderly with a mean age of 73 years at LHRHa therapy initiation and a mean duration of PCa of 220 days (Table 3). Most patients had serum PSA levels > 20 ng/mL (64.4%), and/or a Gleason score of 8–10 (57.4%) at initiation of LHRHa therapy. Almost a third of all patients (32.2%) had metastatic disease and 38.3% had comorbidities, including ischaemic heart disease (27.0%) and diabetes (16.5%). A third of patients (33.9%) had received prior neoadjuvant LHRHa treatment, either radiotherapy (40.9%) or an undisclosed treatment (26.1%). Nine patients had received prior adjuvant LHRHa treatment (7.8%) and either radiotherapy (0.9%) or surgery (1.7%).

Of all 115 patients, 30.4% had previously received three-monthly triptorelin 3 mg injections, 19.1% had received three-monthly

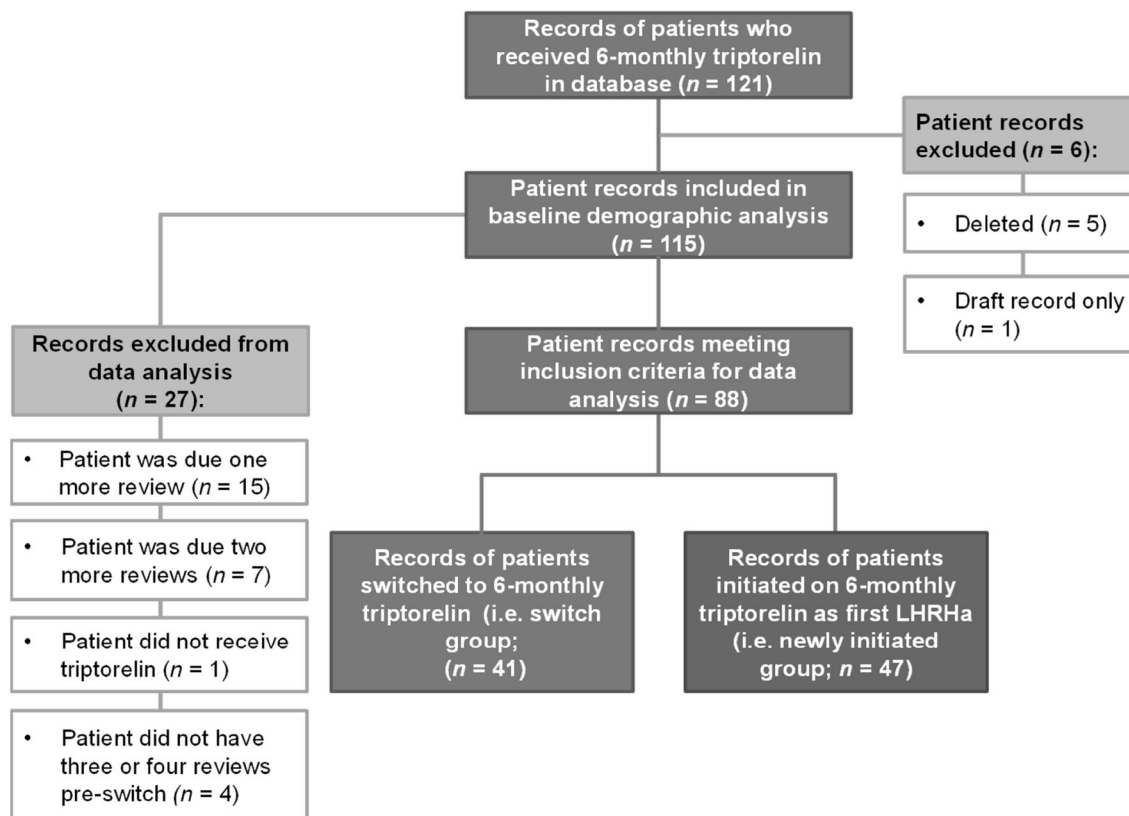


Fig. 1 Patient disposition flow diagram

Table 2 Distribution of the 88 patients included in the data analysis by centre

Centre	Switch group n (%)	Newly initiated group n (%)
University Hospitals Coventry and Warwickshire NHS Trust	0 (0.0)	30 (63.8)
Medical Specialist Group, Guernsey	9 (22.0)	17 (36.2)
The Royal Liverpool and Broadgreen University Hospitals NHS Trust	32 (78.0)	0 (0.0)
Total patients per group	41 (100)	47 (100)

NHS National Health Service

goserelin acetate 10.8 mg injections, 1.7% started on 3.75 mg, and 11.25 mg leuprorelin acetate injections, and 0.9% started on ‘other’. All others (non-switch; 45.2%) were started on six-monthly triptorelin (Table 3).

Comparisons Between the Switch and Newly Initiated Groups

Baseline demographics were generally similar between the switch and newly initiated groups (Table 3). Patients in the switch group had a higher mean duration of PCa (260 days versus 172 days respectively) but a lower proportion had metastatic disease (27.0% versus 38.5%) at

Table 3 Baseline demographics and patient characteristics for all patients and for those who received six-monthly triptorelin in the switch and newly initiated groups

Baseline variable	All patients		Switch group		Newly initiated group	
	<i>n</i> = 115	%	<i>n</i> = 63	%	<i>n</i> = 52	%
Mean age (SD) at initiation of LHRHa therapy (years)	73.3	9.4	73.7	9.0	72.9	9.9
Age range at initiation of LHRHa therapy [<i>n</i> (%)]						
50–59 years	5	4.4	2	3.2	3	5.8
60–69 years	35	30.4	20	31.8	15	28.9
70–79 years	44	38.3	23	36.5	21	40.4
80–89 years	27	23.5	16	25.4	11	21.2
90–99 years	4	3.0	2	3.2	2	3.9
Family history of prostate cancer [<i>n</i> (%)]	10	8.7	8	3.2	2	3.9
Mean age at time of data entry (SD) (years)	76	9.6	77	9.4	74.7	143.7
Age range at time of data entry [<i>n</i> (%)]						
50–59 years	3	2.6	0	0.0	3	5.8
60–69 years	30	26.1	18	28.6	12	23.1
70–79 years	42	36.5	19	30.2	23	44.2
80–89 years	33	28.7	22	34.9	11	21.2
90–99 years	7	6.1	4	6.4	3	5.8
Serum PSA [<i>n</i> (%)]						
< 10 ng/mL	16	13.9	7	11.1	9	17.3
10–20 ng/mL	23	20.0	12	19.1	11	21.2
> 20 ng/mL	74	64.4	43	68.3	31	59.6
Missing data	2	1.7	1	1.6	1	1.9
Gleason score [<i>n</i> (%)]						
≤ 6	3	2.6	3	4.8	0	0.0
7	18	15.7	10	15.9	8	15.4
8–10	66	57.4	37	58.7	29	55.8
Missing data	28	24.4	13	20.6	15	28.9
Clinical stage [<i>n</i> (%)]						
T1a	2	1.8	1	1.6	1	1.9
T1b	0	0.0	0	0.0	0	0.0
T1c	5	4.4	3	4.8	2	3.9
T2	5	4.4	2	3.2	3	5.8

Table 3 continued

Baseline variable	All patients		Switch group		Newly initiated group	
	<i>n</i> = 115	%	<i>n</i> = 63	%	<i>n</i> = 52	%
T2a	1	0.9	1	1.6	0	0.0
T2b	6	5.2	4	6.4	2	3.9
T2c	8	7.0	4	6.4	4	7.7
T3	19	16.5	9	14.3	10	19.2
T3a	4	3.5	4	6.4	0	0.0
T3b	14	12.2	9	14.3	5	9.6
T4	17	14.8	8	12.7	9	17.3
TX	1	0.9	0	0.0	1	1.9
M1	7	6.1	3	4.8	4	7.7
M1a	1	0.9	0	0.0	1	1.9
M1b	12	10.4	8	12.7	4	7.7
M1c	1	0.9	0	0.0	1	1.9
N1	6	5.2	5	7.9	1	1.9
Not entered	6	5.2	2	3.2	4	7.7
Risk [<i>n</i> (%)]						
Localised (T1a–T2c)	27	23.5	15	23.8	12	23.1
Locally advanced	54	47.0	30	47.6	24	46.2
Mets (M1–N1)	27	23.5	11	17.5	16	30.8
Missing data/not entered	7	6.1	2	3.2	5	9.6
Neoadjuvant treatment [<i>n</i> (%)]						
External beam radiotherapy	31	27.0	14	22.2	17	32.7
Others	30	26.1	28	44.4	2	3.9
Adjuvant treatment [<i>n</i> (%)]						
Surgery	2	1.7	1	1.6	1	1.9
Surgery; no radiotherapy	1	0.9	1	1.6	0	0.0
Surgery; EBRT	1	0.9	0	0.0	1	1.9
No surgery	7	6.1	3	4.8	4	7.7
No surgery; EBRT	4	3.5	3	4.8	1	1.9
No surgery; low-dose rate brachytherapy	1	0.9	0	0.0	1	1.9
No surgery; no radiotherapy	2	1.7	0	0.0	2	3.9

Table 3 continued

Baseline variable	All patients		Switch group		Newly initiated group	
	<i>n</i> = 115	%	<i>n</i> = 63	%	<i>n</i> = 52	%
Mean duration (SD) of disease at initiation of LHRHa therapy, days	220	672.0	260	720.0	172	611.0
Comorbidities [<i>n</i> (%)] ^a						
Any comorbidity	44	38.3	24	38.1	20	38.5
0	71	61.7	39	61.9	32	61.6
1	30	26.1	15	23.8	15	28.9
2	12	10.4	8	12.7	4	7.7
Ischaemic heart disease	31	27.0	18	28.6	13	25.0
Diabetes	19	16.5	10	15.9	9	17.3
Osteopenia	2	1.7	2	3.2	0	0.0
Osteoporosis	2	1.7	2	3.2	0	0.0
Metastatic disease [<i>n</i> (%)]	37	32.2	17	27.0	20	38.5
Neoadjuvant treatment [<i>n</i> (%)] ^b	39	33.9	15	23.8	24	46.2
Adjuvant treatment [<i>n</i> (%)]	9	7.8	4	6.4	5	9.6
Other	29	25.2	27	42.9	2	3.9
Other treatment [<i>n</i> (%)]	30	26.1	27	42.9	3	5.8
Prior therapy [<i>n</i> (%)]						
Surgery ^c	3	2.6	1	1.6	2	3.9
Radiotherapy ^d	47	40.9	27	42.9	20	38.5
Goserelin acetate 10.8 mg 3-monthly	22	19.1	22	34.9	–	–
Leuprorelin acetate 11.25 mg 3-monthly	2	1.7	2	3.2	–	–
Leuprorelin acetate 3.75 mg monthly 3-monthly	2	1.7	2	3.2	–	–
Triptorelin 3 mg monthly	35	30.4	35	55.6	–	–
Other	1	0.9	1	1.6	–	–

EBRT external beam radiotherapy, *LHRHa* luteinising hormone-releasing hormone agonist, *PSA* prostate-specific antigen, *SD* standard deviation

^a Comorbidities were ischaemic heart disease, diabetes, osteopenia, and osteoporosis

^b This refers to triptorelin injections only (i.e. post-switch for the switch group)

^c Radical prostatectomy

^d External beam radiotherapy (*n* = 46) or low-dose brachytherapy (*n* = 1). No prior LHRHa (–)

the time of initiation of LHRHa therapy (Table 3).

Primary Outcome: Patient–Healthcare Interactions in the Switch Group

Switching of a one- or three-monthly LHRHa regimen to six-monthly triptorelin injections was associated with a statistically significant 41.5% reduction in patient–healthcare interactions ($P < 0.0001$; Table 4). Switching was associated with a statistically significant decrease in the number of reviews (46.8%), PSA blood tests (26.6%), and injections (46.8%; all $P < 0.0001$; Table 4) compared to one- or three-monthly LHRHa regimens.

Secondary Outcomes

Cost Impact of Switching to 6-Monthly Formulation

DESERVE was not set up to account for drug acquisition cost, instead focussing on the cost saving associated with the change in patient–healthcare interactions pre- and post-switch. Compared with 12 months of treatment with a one- or three-monthly LHRHa regimen

(the pre-switch period), switching to six-monthly formulation for a 12-month period was associated with a 46.8% reduction in these costs (Table 5). The costs due to injections, PSA tests, and reviews reduced by 47.3%, 26.6% and 47.3%, respectively, upon switching (all $P < 0.0001$ for post-switch versus pre-switch period; Table 5).

The calculated annual cost reduction associated with patient–healthcare interactions of switching from three- to six-monthly formulation was £10,214.85, or a saving per patient switching from the three- to six-monthly formulation of £249.14 over a 12-month period (Table 5). Reductions in reviews and number of injections were the main contributors to the cost reduction of switching (each represented a £5040—or £122.93 per patient—cost saving). The estimated annual saving for every 10,000 patients switching from three- to six-monthly formulation is £2,491,427, or £11,211,420.73 for the remaining lifetime duration of every 10,000 switched patients (based on an average survival of 4.5 years; Table 5).

Time-Saving Impact for Switching

Compared with 12 months of treatment with a one- or three-monthly LHRHa regimen,

Table 4 Summary of results for primary outcome measure in patients who were switched to six-monthly triptorelin

Efficacy	Number of patient–healthcare interactions in 12-month pre-switch period	Number of patient–healthcare interactions in 12-month post-switch period	Percentage decrease in patient–healthcare interactions post-switch versus pre-switch (%)	P value
Individual components of primary outcome measure				
Injections	154	82	46.8	< 0.0001
PSA blood tests	109	80	26.6	< 0.0001
Reviews	154	82	46.8	< 0.0001
Primary outcome measure ^a	417	244	41.5	< 0.0001

^a The primary outcome measure was defined as the total change in patient–healthcare interactions (i.e. post-switch versus pre-switch period)

Table 5 Cost impact of switching from a one- or three-monthly LHRH agonist regimen to six-monthly triptorelin

	Costs pre-switch	Costs post-switch	Saving	Reduction in cost (%)	Annual saving per patient switching from three- to six-monthly injections	Annual saving per 10,000 patients switching from three- to six-monthly injections	Saving per average patient lifetime (4.5 years) per 10,000 patients switched from three- to six-monthly injections
Review ^a	£10,662.00	£5,622.00	£5040.00	47.3	£122.93	£1,229,268.00	£5,531,707.32
Injections	£10,662.00	£5622.00	£5040.00	47.3	£122.93	£1,229,268.00	£5,531,707.32
PSA test	£506.85	£372.00	£134.85	26.6	£3.29	£32,890.00	£148,006.10
Total	£21,830.85	£11,616.00	£10,214.85	46.8	£249.14	£2,491,427.00	£11,211,420.73

PSA prostate-specific antigen

^a Secondary care costs based upon a 30-min appointment, adjusted for 20 min

switching to six-monthly formulation for a 12-month period was associated with a 45.3% reduction in total treatment time across the switch group (Table 6). Amongst switch patients, the reduced number of patient–healthcare interactions owing to secondary care reviews/injections and PSA tests meant time savings of 47.4% and 26.6%, respectively, with no change in the total number of primary reviews/injections (all $P < 0.0001$ for post-switch versus pre-switch period; Table 6).

The overall annual capacity impact saving of switching from three- to six-monthly formulation was 50.4 h, or 1.2 h per patient. The estimated annual saving for every 10,000 patients switching from three- to six-monthly triptorelin is 12,296.7 h (Table 6), equivalent to 512.4 days. This is 55,335.4 h (or 2305.6 days) for the remaining lifetime duration of every 10,000 switched patients (based on an average survival of 4.5 years; Table 6).

Efficacy: Maintaining Stable PSA Levels

In the switch group, the records of five patients did not have serum PSA test data available for each of the three time points evaluated and were therefore excluded from the PSA analysis ($n = 36$ analysed). Median serum PSA levels were stabilised and remained low following the

switch from one- or three-monthly LHRHa regimens to six-monthly triptorelin (0.18 ng/mL at 6-months and 0.24 ng/mL at 12-months post-switch versus 0.35 ng/mL at baseline; Fig. 2).

Serum PSA data were available for all three time points from 45 of the 47 patient records in the newly initiated group ($n = 45$ analysed). In the newly initiated group, six-monthly triptorelin was associated with a pronounced reduction in median serum PSA levels from baseline (23.5 ng/mL at diagnosis) that was maintained below the 4.0 ng/mL threshold for 6 and 12 months (0.84 and 1.30 ng/mL, respectively; Fig. 2).

Adverse Events/Tolerability

Adverse events were consistent with those previously reported for triptorelin and other LHRHa formulations. The incidences of reported fatigue (26.3% versus 12.3%), frequent urination (31.6% versus 8.8%), and bone pain (14.0% versus 7.0%) were higher in the pre-switch versus the post-switch period (Table 7).

Four patients had given the reason for changing medication as ‘tolerability’; three were previously on three-monthly goserelin, and the other patient was incorrectly marked as medication change (data entry error). One patient, previously on three-monthly goserelin,

Table 6 Time-saving impact of switching from a one- or three-monthly LHRH agonist regimen to six-monthly triptorelin

	Care time (min)	Pre-switch time total in DESERVE study (min)	Post-switch time total in DESERVE study (min)	Reduction in treatment time in DESERVE study (min, %)	Time saving per patient in 12 months (min)	Annual saving per 10,000 patients switching from three- to six-monthly injections (h)	Saving per average patient lifetime (4.5 years) per 10,000 patients switched from three- to six-monthly injections (days)
Primary care review	15	30.0	30.0	0.0 (0.0)	0.0	0.0	0.0
Primary care injection	15	30.0	30.0	0.0 (0.0)	0.0	0.0	0.0
Secondary care review	20	3040.0	1600.0	1440.0 (47.4)	35.1	5853.7	1097.6
Secondary care injection	20	3040.0	1600.0	1440.0 (47.4)	35.1	5853.7	1097.6
PSA test	5 ^a	545.0	400.0	145.0 (26.6)	3.5	589.4	110.5
Total	–	6685.0	3660.0	3025.0 (45.3)	73.8	12,296.7	2305.6

PSA prostate-specific antigen

^a PSA test time is made on the assumption of a 5-min blood sample. Care time calculated by Ipsen Ltd data on file: DEC041/NOV16 (unpublished data)

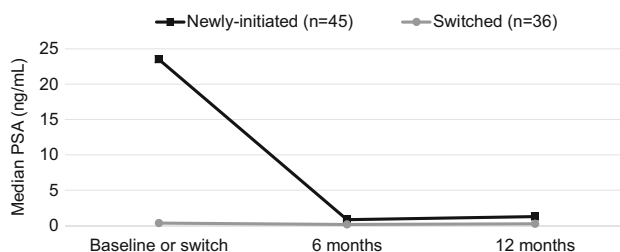


Fig. 2 Median prostate-specific antigen (PSA) values for 36 evaluable patients in the switch group and 45 evaluable patients in the newly initiated group. Five patients in the switch group and two patients in the newly initiated group

did not have PSA test data available for each of the three time points on six-monthly triptorelin and were therefore excluded from this analysis

changed medication due to ‘side effects’. Three patients in the switch group discontinued six-monthly triptorelin; at time of discontinuation, their PSA levels were 0.00, 0.00, and 5.70 ng/mL.

In the newly initiated group, six-monthly triptorelin injections were associated with a higher incidence of fatigue (11.5% versus 3.8%) and bone pain (3.8% versus 1.9%) and a lower frequency of urination (5.8% versus 30.8%) and

Table 7 Summary of adverse events of any grade reported by patients in the switch or newly initiated groups

Adverse event of any grade	Patients experiencing at least one adverse event in the switch group, <i>n</i> (%) of 47 patients		Patients experiencing at least one adverse event in the newly initiated group, <i>n</i> (%) of 41 patients	
	Pre-switch period	Post-switch period	Baseline	Post-initiation period
Fatigue	15 (26.3)	7 (12.3)	2 (3.8)	6 (11.5)
Bone pain	8 (14.0)	4 (7.0)	1 (1.9)	2 (3.8)
Frequent urination	18 (31.6)	5 (8.8)	16 (30.8)	3 (5.8)
Sleeping	8 (14.0)	0 (0.0)	1 (1.9)	1 (1.9)
Loss of appetite	1 (1.8)	1 (1.8)	4 (7.7)	2 (3.8)
Other	23 (40.4)	4 (7.0)	3 (5.8)	2 (3.8)

loss of appetite (3.8% versus 7.7%) compared with baseline values (Table 7). Three patients in the newly initiated group discontinued six-monthly triptorelin. PSA levels at time of discontinuation were all below the 4 ng/mL threshold (3.90, 3.40, and 0.14 ng/mL).

DISCUSSION

In this study in the real-world setting, switching PCa patients to six-monthly triptorelin 22.5 mg injections for 12 months significantly reduced patient–healthcare interactions and associated costs, while maintaining serum PSA control, compared with one- or three-monthly LHRHa therapy for the 12 months pre-switch. Furthermore, initiation of triptorelin six-monthly in newly diagnosed LHRHa-naïve patients (newly initiated group) provided significant and sustained PSA control over 12 months. In both groups, six-monthly triptorelin was well tolerated with reported AEs consistent with previous trials [10, 14–18].

Switching was associated with a statistically significant 41.5% reduction ($P < 0.0001$) in overall patient–healthcare interactions. Although the study did not assess overall costs, the cost saving of switching based on the reduction in clinician reviews, injections, and PSA testing was calculated to be £10,214.85, or a saving per patient of £249.14 over 12 months. This translates into significant annual cost savings of £2,491,427.00 per 10,000 patients who

switch to six-monthly triptorelin. Assuming an average life duration for PCa patients of 4.5 years, the lifetime cost-saving of switching 10,000 patients from shorter-acting regimens to six-monthly triptorelin would be £11,211,420.73. In this group of switch patients with stable and controlled serum PSA levels, six-monthly PSA testing is considered as appropriate and effective for disease monitoring as three-monthly testing [19]. Switching also enables the reallocation of scarce nursing resource to other patients in need.

Consistent with our findings, a published analysis across nine European countries demonstrated that another six-monthly LHRHa regimen (leuprolide) retained similar levels of PSA control and tolerability, yet the costs of three-monthly and one-monthly leuprolide were 2.5–37.6% higher and 15.5–151.6% higher, respectively [20].

Patients and physicians alike prefer six-monthly LHRHa injections to one- or three-monthly injections [13, 21]. In one study, 68% of PCa patients preferred fewer LHRHa injections and, while believing efficacy was the most important treatment benefit, 84% also considered maintaining lifestyle during therapy as important [13]. In a second study, the number of patients preferring less frequent (≥ 6 months) and more frequent (≤ 3 months) dosing were comparable (32.4% and 38.1%, respectively), while 29.6% had no particular preference [11]. Since patients preferring more

frequent injections in this study tended to have progressive disease, patients preferring less frequent injections may have had more stable/controlled disease [11]. In a French study, physicians and patients perceived six-monthly rather than three-monthly LHRHa formulations to be simpler regimens and associated with fewer unnecessary visits [21]. In this study, 170 patients switched from three- to six-monthly LHRHa injections for similar reasons [21].

Patients receiving short-acting formulations reported greater physical discomfort, more cancer-related worries, and more frequently considered themselves to be in ‘fair’ or ‘poor’ health than those receiving orchidectomy [12, 13]. However, as three-monthly formulations appear to be preferred by patients with progressive disease [11], physicians should take this into account and include the patient in the choice of LHRHa formulation [12].

It should be noted that some men with prostate cancer may prefer shorter follow-up intervals, for psychological support, closer patient management, monitoring, and reviewing other interventions [21].

Six-monthly triptorelin achieved and/or sustained effective PSA control. Additionally, there were significant reductions in patient–healthcare interactions and associated cost savings in this real-world setting reflecting the range of elderly patients treated in daily clinical practice.

The limitations of this study include its retrospective and non-randomised design. The study was not designed to capture AEs, which are difficult to measure and interpret retrospectively. Data on the effects of treatment on sexual function are not reported as these were not available, and any such data are difficult to recover retrospectively. Other limitations include the relatively small number of patients evaluated; the mix of those receiving neoadjuvant, adjuvant, and metastatic treatments; and the ad hoc rather than formal cost analysis of the healthcare resource utilisation data. The primary and secondary care cost assumptions were from data provided by the study funder, and while we believe these to have been accurate at the time of the study, we acknowledge that these costs can vary significantly and that

other assumptions may have provided different cost estimates to those reported here. Furthermore, the present analysis is limited in its geographical spread, since it does not include data from Wales, Scotland, or Northern Ireland. Testosterone levels were also not assessed in this study; patients presented with early and/or stable disease, whereas testosterone measurements are usually made once patients exhibit progressive disease.

CONCLUSIONS

Switching to six-monthly triptorelin 22.5 mg significantly reduces patient–healthcare interactions, while maintaining serum PSA control, which translates into a significant healthcare saving associated with these interactions [11, 13, 21]. Use of six-monthly triptorelin may therefore offer advantages over one- or three-monthly LHRHa formulations for patients, prescribers, and payers alike. Further cost analyses comparing different six-monthly and three-monthly LHRHa formulations are warranted in defined treatment settings. Increased use of six-monthly LHRHa formulations could help release valuable funds and healthcare resources as the prevalence of PCa continues to rise and the life expectancy of the growing population of men being treated with LHRHa increases.

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Compliance with Ethics Guidelines. This observational study was a retrospective, non-interventional service evaluation of an aspect of routine practice and, as such, did not require ethics committee approval although approval of the medical director was granted.

Data Availability. The datasets generated during and/or analysed during the current study are not publicly available because the data have not been de-identified.

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