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International survey of androgen deprivation therapy (ADT) for non-metastatic prostate cancer in 19 countries

Alexander Liede,[1] David C Hallett,[2] Kirsty Hope,[3] Alex Graham,[3] Jorge Arellano,[4] Vahakn B Shahinian[5]

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For numbered affiliations see end of article.

Correspondence to
Dr Alexander Liede;
aliede@amgen.com

ABSTRACT

Background: Continuous androgen deprivation therapy (CADT) is commonly used for patients with non-metastatic prostate cancer as primary therapy for high-risk disease, adjuvant therapy together with radiation or for recurrence after initial local therapy. Intermittent ADT (IADT), a recently developed alternative strategy for providing ADT, is thought to potentially reduce adverse effects, but little is known about practice patterns relating to it. We aimed to describe factors related to physicians' ADT use and modality for patients with non-metastatic prostate cancer.

Methods: A 45 min online survey was completed by urologists and oncologists responsible for treatment decisions for non-metastatic prostate cancer from 19 countries with high or increasing prevalence of non-metastatic prostate cancer.

Results: There were 441 treating physicians who completed the survey which represented 99 177 patients with prostate cancer under their care, of which 76 386 (77%) had non-metastatic prostate cancer. Of patients with non-metastatic prostate cancer, 38% received ADT (37% gonadotropin-releasing hormone (GnRH), 2% orchiectomy); among patients on GnRH, 54% received CADT (≥6 without >3 months interruption), 23% IADT and 23% <6 months. Highest rates of ADT were reported among oncologists (62%) and in Eastern Europe (Czech Republic, Hungary and Poland). Prostate-specific antigen (PSA) levels (65%), Gleason score (52%) and treatment guidelines (48%) were the most common reasons for CADT whereas PSA levels (54%), patient request (48%), desire to maintain sexual function (40%), patient age and comorbidities (38%) were cited most frequently as reasons for IADT.

Conclusions: This international survey with 441 treating physicians from 19 countries showed that ADT is commonly used in treating patients with non-metastatic prostate cancer, and type of ADT is influenced by high-risk criteria (PSA and Gleason), treatment guidelines and patient preferences. IADT use was primarily driven by PSA levels, patient request and patient age/comorbidities, likely reflecting an attempt to minimise adverse effects of ADT in patients with lower risk tumours.

Key questions

What is already known about this subject?

Androgen deprivation therapy (ADT) is often administered to patients with prostate cancer as primary therapy of non-metastatic disease; however, there still exists a lack of evidence of efficacy and the profile of patients most likely to benefit from intermittent versus continuous therapy. Little is known about practice patterns and determinants of intermittent ADT use in the USA and other countries.

What does this study add?

Urologists and oncologists from several countries frequently administer ADT in treating their patients with non-metastatic prostate cancer. The most common reasons for these participating physicians choosing the type of ADT in managing their patients were high-risk criteria, treatment guidelines and patient preferences.

How might this impact on clinical practice?

The study provides real-world data on the treatment patterns and determinants of intermittent versus continuous use of ADT among practitioners from 19 countries, which provides acknowledgement of practice patterns when clinical guidelines are reviewed in the treatment of non-metastatic prostate cancer.

INTRODUCTION

Prostate cancer is the most commonly diagnosed malignancy and the second leading cause of cancer death in men in the USA.[1] Prostate cancer incidence varies more than 25-fold worldwide and represents the second most common cancer among men worldwide with an estimated 1.1 million men diagnosed in 2012 with almost 70% of the cases occurring in more developed regions.[2–5] Prostate cancer is androgen-dependent,[6 7] which forms the basis for androgen deprivation therapy (ADT), usually achieved medically with gonadotropin-releasing hormone (GnRH) agonists or antagonists or, to a

much less frequent extent, surgically via bilateral orchiectomy (approximately 1–3% of ADT).[8] The benefits of ADT are well established when used for palliation of symptomatic metastatic disease or as an adjuvant to radiation therapy for high-risk disease, but it is also very commonly used in other settings without clear evidence of efficacy such as for primary therapy of non-metastatic disease or for biochemical recurrence following initial local therapy.[9 10]

With its common use, there has been increasing recognition of harmful effects from continuous androgen deprivation.[11] The most common side effects of continuous ADT include anaemia, hot flashes, sexual dysfunction, cognitive dysfunction, bone loss, bone complications (eg, fractures), metabolic and cardiovascular consequences, fatigue, depression and anxiety.[11 12] This appreciation of the detrimental effects of ADT has led to much interest in reducing ADT exposure during the course of treatment.[13] One such alternative therapeutic strategy, initially described in 1986, is intermittent use of GnRH agonist therapies.[14] Typically, treatment is discontinued after 6–9 months of ADT or when the prostate-specific antigen (PSA) reaches its nadir; ADT is resumed when PSA rises back to a predetermined higher level. The hormonal recovery that occurs during off-treatment cycles[15 16] potentially facilitates responsiveness of tumour cells to treatment and theoretically limits toxicity.[13]

Recent reviews comparing efficacy, side effects, time to castration resistance, overall and cancer-specific survival between intermittent and continuous ADT have been summarised; however, the evidence regarding the trade-offs between the benefits and risks of intermittent ADT remains inconclusive.[17–23] Generally the consensus is that overall survival is equivalent between intermittent and continuous ADT in most settings. However, concerns remain with high-risk disease, as one of the larger trials did not meet criteria for non-inferiority of an intermittent regimen in men with metastatic cancer.[24] Although intermittent ADT appears to have a modestly beneficial impact on sexual function and hot flashes, event rates in studies to date for serious effects such as fractures and cardiovascular outcomes have been too low to draw definitive conclusions.

Despite the ongoing uncertainty, little is known about practice patterns and determinants of intermittent ADT use in the USA and other countries. The objective of this study was to describe factors related to physicians' ADT use and choice of intermittent ADT regimens for patients with non-metastatic prostate cancer from a detailed international survey of treating urologists and oncologists.

METHODS

Development of survey instrument

An instrument was developed for this study based on expert opinion, clinical consensus and a review of the literature. The initial qualitative development phase ensured data stability, survey feasibility, and optimisation, before developing the quantitative online questionnaire. Eighteen 1 hour in-depth interviews (IDIs) were distributed evenly across Spain, France and Germany, incorporating physician feedback in real time. The IDIs confirmed appropriateness and accuracy of definitions used within the survey for the patient population with prostate cancer. A pilot phase with nine physicians from six countries was rolled out after being proof-read by native speakers, ensuring survey question accuracy.

The final survey instrument included 35 questions, answered in various forms. Demographic questions included were year of qualification, specialty type, practice size, setting, region and number of patients with total prostate cancer currently under care. The online survey was designed to be completed in approximately 45 min.

Study population and eligibility criteria

The 19 countries selected for this study represent those with high or increasing incidence of non-metastatic prostate cancer, prevalent use of ADT among treating urologists and oncologists, and widespread PSA screening. Eligible respondents included physicians who were responsible for treatment decisions in patients with non-metastatic prostate cancer, with at least 10 non-metastatic patients seen per month (and at least 10 treated with ADT at the time of the survey), representing more than 25% of their patient-related time (>15% in Nordics, Czech Republic, the Netherlands and the USA), and year of qualification in their medical specialty between 1971 and 2009. Physicians also estimated how many patients they treated at each stage in the treatment.

Numerous recruitment approaches were employed based on country knowledge, specialist recruitment agencies, panel of physicians and other contacts which facilitated a large sample to be achieved within a short timeframe. For example, email invitations to panel physicians (USA), telephone recruitment (France) and face-to-face recruitment (Poland) were carried out. The online survey was completed online by all recruited physicians over a 1-month period (September 2012).

Urologist versus oncologist distribution in the sampling for each country was consistent with practice patterns as determined by research partners at the country level and literature.[25] For example, radiation oncologists were included in Australia as they also prescribe drug therapies such as ADT for patients with prostate cancer.

ADT was defined in the online survey for respondents as treatment using GnRH agonists/antagonists or bilateral orchiectomy (excluding antiandrogenic agents). Continuous ADT was specifically defined as GnRH treatment for at least 6 months without having a break for more than 3 months at any point since initial GnRH administration, or bilateral orchiectomy. The difference in the delineation between intermittent and continuous ADT was the stipulation of an off-treatment period of more than 3 months.[13 19] Locally advanced disease was

considered non-metastatic for the purposes of the survey, which may include limited local lymph node involvement. Relapsing or recurring tumours following surgery were also considered to be non-metastatic if the disease had not spread to other organs or bones.

All respondents provided informed consent and were incentivised for their time (eg, using vouchers and money). All national laws protecting personal data and guidelines from bodies such as British Healthcare Business Intelligence Association (BHBIA), World Association for Market, Social and Opinion Research (ESOMAR), European Pharmaceutical Market Research Association (EphMRA), and other national codes of market research practice were followed.

Statistical analysis

All descriptive statistics were reported as unweighted frequencies and percentages. SAS software for Windows V.9.4 (SAS institute Inc, Cary, North Carolina, USA) was used to perform all analyses.

RESULTS

Respondents

For this physician survey, response rates ranged from 1% to 86% (averaging 5% overall) using email, fax (Australia), and telephone invitations. Response rates represent survey completion among invitations sent out, which differed by specialty where higher completion rates were observed for oncologists. Response also differed by country or region with lower rates observed for the USA, the Netherlands and Norway. Highest completion rates were achievable using telephone recruitment, such as for participants practicing in EU5 (range 14% (France) to 76% (UK)), or via face-to-face invitations (an approach used exclusively in Poland (86%)). Potentially eligible participants were identified from validated country-specific physician panels. Overall, 7.8% of potential participants were excluded after applying the eligibility criteria. Main reasons for exclusion among potentially eligible physicians were not spending more than 25% of their time treating patients with non-metastatic prostate cancer or not treating at least 10 non-metastatic patients with GnRH agents per month.

A total of 441 physicians completed the survey from 19 countries (table 1). Most respondents were urologists (88%), and physicians from 10 countries were strictly urologists. The highest proportion of medical oncologist respondents were from Finland, Switzerland and Sweden; radiation oncologists were recruited in Australia consistent with ADT prescribing patterns.

Overall, 76% of respondents received their specialty qualification between 1991 and 2009. Forty-seven per cent of treating physicians indicated that they work in a general non-academic setting, nearly identical to the number in teaching/university academic settings (46%). Fifty-four per cent of respondents indicated that they saw at least 40 men diagnosed with non-metastatic prostate cancer per month.

Use of ADT for the treatment of non-metastatic patients

Survey respondents estimated that 99 177 patients with prostate cancer were under their care, 77% (76 386) classified as having non-metastatic disease (figure 1).

Table 1 Physician characteristics by use of continuous or intermittent androgen deprivation therapy (ADT) among patients with non-metastatic prostate cancer

Characteristic	Number of physicians (%)	Continuous ADT ≥6 months (%)	Intermittent ADT (%)
Specialty			
Urology	385 (87.3)	63.6	31.2
Medical oncology	47 (10.7)	72.2	23.6
Radiation oncology	7 (1.6)	64.2	35.8
Internal medicine	2 (0.5)	43.8	50.0
Year of qualification			
1971–1980	27 (6.1)	57.7	39.7
1981–1990	81 (18.4)	69.2	26.9
1991–2000	169 (38.3)	61.5	32.8
2001–2009	164 (37.2)	66.1	28.7
Practice type			
Academic/specialist	202 (45.8)	67.6	26.8
General/non-academic	206 (46.7)	64.0	31.9
Other/missing	33 (7.5)	47.6	45.8
Practice setting			
Urban	392 (88.9)	64.7	30.4
Rural	49 (11.1)	62.2	32.3
Patients with non-metastatic prostate cancer seen/month			
10–28	141 (32.0)	68.7	26.4
29–50	155 (35.1)	63.3	31.0
>50	145 (32.9)	61.3	34.3

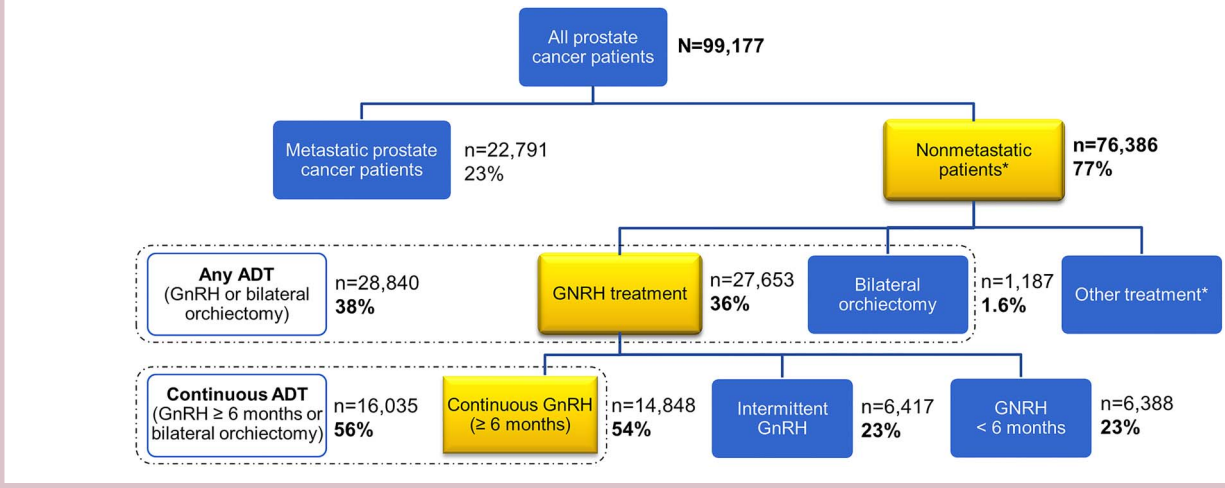
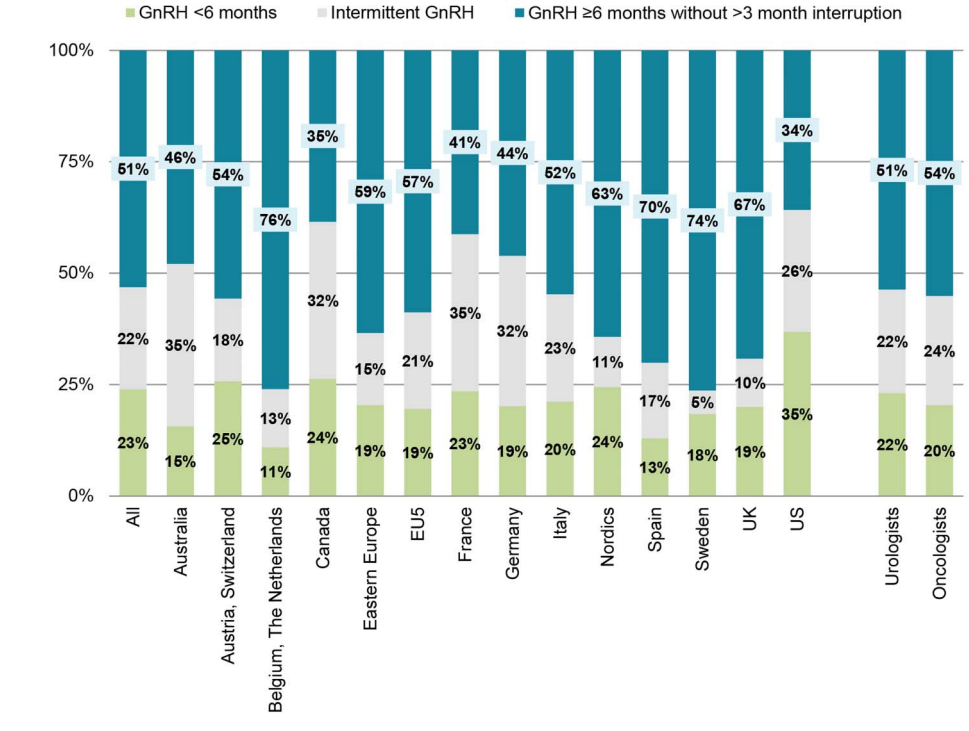


Figure 1 Patients represented by 441 physicians surveyed from 19 countries, depicted in the patient journey from diagnosis to ensuing treatment with ADT. ADT, androgen deprivation therapy; GnRH, gonadotropin-releasing hormone.

Among patients with non-metastatic prostate cancer under treatment, physicians reported that 38% (28 840) received ADT: 36% (27 653) received GnRH agents, and 1.6% (1187) underwent bilateral orchiectomy. Among their GnRH-treated patients, 54% were treated continuously (≥6 months without >3-month interruption), 23% for less than 6 months, and 23% were managed with intermittent ADT (figure 2).

Table 2 provides the percentages of any ADT and treatment of at least 6 months duration in the non-metastatic setting by region. The highest proportion of ADT use was reported by physicians in Eastern Europe



Physicians	441	30	19	38	30	45	171	30	50	30	43	30	19	31	65		387	54
Patients	28840	1689	571	3469	2783	1660	9868	1304	2492	971	1966	1867	1060	3234	6834		26498	2342

Figure 2 Proportion of continuous, intermittent, and limited (<6 months) use of ADT among patients with non-metastatic prostate cancer treated with gonadotropin-releasing hormone (GnRH) by region and physician type.

Table 2 ADT use among men with non-metastatic prostate cancer according to treating physicians by country or region (n=441)

	n	Non-metastatic patients	Any ADT (%)	GnRH treated (%)	GnRH ≥6 months (%)	Intermittent ADT (%)	Continuous ADT (%)	Bilateral orchiectomy (%)
All	441	76 386	38.4	36.8	27.1	9.3	28.8	1.6
Australia	30	6752	25.0	24.2	20.5	8.9	21.3	0.8
Austria	10	955	35.9	34.7	23.9	4.2	25.1	1.3
Austria, Switzerland	19	1725	32.0	30.7	23.7	6.4	24.9	1.3
Belgium	25	5615	50.2	49.7	45.4	7.3	46.0	0.6
Belgium, The Netherlands	38	8895	35.7	35.1	31.3	4.2	31.9	0.6
Canada	30	9530	29.2	26.4	19.5	9.3	22.3	2.8
Czech Republic	10	810	44.1	34.2	29.0	16.4	38.9	9.9
Denmark	14	9405	35.6	34.7	23.8	3.5	24.7	0.9
Eastern Europe	45	2448	68.4	64.5	51.3	10.5	55.2	3.9
EU5	171	22 700	42.9	41.5	33.0	10.6	34.5	1.5
Finland	6	3643	43.6	43.2	29.0	13.9	29.3	0.4
France	30	4996	26.1	25.8	19.8	9.1	20.0	0.3
Germany	50	5641	44.2	42.4	33.8	14.3	35.6	1.8
Hungary	10	414	82.4	80.9	63.3	5.6	64.7	1.4
Italy	30	1587	61.2	57.8	45.6	13.9	49.0	3.4
The Netherlands	13	3280	19.8	19.1	15.7	0.9	16.4	0.7
Nordics	43	4310	45.6	44.4	33.6	4.9	34.9	1.2
Norway	4	562	99.3	96.6	74.9	1.8	77.6	2.7
Poland	25	1224	78.6	77.4	60.8	8.3	62.0	1.2
Spain	30	4551	41.0	40.7	35.4	6.9	35.7	0.3
Sweden	19	4856	49.3	47.6	38.9	2.5	40.5	1.7
Switzerland	9	770	29.6	28.3	23.5	7.8	24.8	1.3
UK	31	5925	54.6	52.6	42.0	5.5	44.0	2.0
USA	65	20 026	34.1	32.5	20.7	9.0	22.3	1.7

Any ADT: GnRH agonist/antagonist (includes both continuous and intermittent use (figure 1)) or bilateral orchiectomy procedure.
Continuous ADT: GnRH treatment for ≥6 months or bilateral orchiectomy.
Nordics: Denmark, Finland, Norway, Sweden; EU5: France, Germany, Italy, Spain, UK; Eastern Europe: Czech Republic, Hungary, Poland.
ADT, androgen deprivation therapy; GnRH, gonadotropin-releasing hormone.

(68%), driven by higher rates in Hungary (82%) and Poland (79%). Treating physicians reported administering ADT to 43% of their patients in 5-country Europe (EU5: France, Germany, Italy, Spain and the UK); however, respondents varied noticeably between France (26%), the UK (55%) and Italy (61%). US physicians reported any ADT use in 34% of their patients, somewhat higher than responses from treating physicians in Canada (29%).

In general, treatment rates of ADT were higher among oncologists (62%) versus urologists (38%), although the proportion of ADT given as intermittent therapy was similar (figure 2). Intermittent ADT appeared to be most common among Australian, Canadian, French and German practitioners, representing approximately 35% of their GnRH use. In the USA, intermittent regimens represented 28% of ADT prescribed, and physicians from remaining countries prescribed intermittent ADT between 5% (Sweden) and 24% (Italy).

Reasons for administering ADT

Table 3 presents drivers of the decision to initiate ADT based on PSA levels, PSA doubling time and Gleason score. In choosing to initiate GnRH therapy for their patients with non-metastatic prostate cancer, 64% of physicians identified absolute PSA levels as one of the main reasons. Among respondents who relied on PSA values, 81% were inclined to use a GnRH agent if PSA was ≥10 ng/mL, while 45% indicated initiation of GnRH when PSA reached ≥20 ng/mL. More than half (58%) of treating physicians identified PSA doubling time as the reason to assess GnRH use, and 78% of these respondents cited using a doubling time of ≤6 months. Sixty-six per cent of treating physicians identified the use of Gleason score as a reason to assess GnRH treatment; of these, 91% specified using a GnRH agent if Gleason score was 7 or higher.

With respect to reasons for prescribing continuous versus intermittent ADT, physicians indicated (more

Table 3 Physician behaviour and motivations for continuous or intermittent ADT among patients with non-metastatic prostate cancer

Behaviour and GnRH reason for use	Number of physicians (%)	Continuous ADT ≥6 months (%)	Intermittent ADT (%)
PSA testing frequency (n=441)			
≥1/month	2 (0.5)	40.7	59.3
Every 1–3 months	151 (34.2)	66.6	27.5
Every 4–6 months	208 (47.1)	63.4	32.3
Every 7–12 months	72 (16.3)	63.1	31.2
<1/year	8 (1.8)	67.9	27.9
PSA level used for decision to initiate GnRH (n=441)			
Yes	282 (63.9)	64.6	30.2
No	159 (36.1)	63.9	31.4
PSA level, yes (n=282)			
0–9	53 (18.8)	64.8	29.0
10–20	172 (61.0)	64.5	31.5
>20	57 (20.2)	64.8	27.2
PSA doubling time used for decision to initiate GnRH (n=441)			
Yes	254 (57.6)	63.2	31.2
No	187 (42.4)	66.1	29.8
PSA doubling time, yes (n=254) (months)			
0–3	74 (29.1)	67.2	29.1
>3–6	123 (48.3)	60.1	34.1
>6–12	52 (20.5)	62.5	29.3
>12	5 (2.0)	85.5	11.1
Gleason score used for decision to initiate GnRH (n=441)			
Yes	290 (65.8)	65.7	30.2
No	151 (34.2)	62.4	31.6
Gleason score, yes (n=290)			
3–5	7 (2.4)	65.1	25.1
6	20 (6.9)	66.4	30.6
7–8	250 (86.2)	65.2	31.1
9–10	13 (4.5)	73.4	16.9
Testosterone testing frequency			
≤3 months	43 (9.8)	62.7	30.9
4–6 months	61 (13.8)	67.5	29.2
7–12+ months	36 (8.2)	54.7	40.4
<1 per year	44 (10.0)	62.4	34.4
Do not test	257 (58.3)	65.7	28.8

ADT, androgen deprivation therapy; GnRH, gonadotropin-releasing hormone; PSA, prostate-specific antigen.

than one reason could be selected) PSA levels (65%), Gleason score (52%) and treatment guidelines (48%) as the most common reasons for choosing continuous ADT (figure 3). PSA levels (54%), patient request (48%), desire to maintain sexual function (40%), comorbidities (38%) and patient age (38%) were cited most frequently as the reasons for managing patients with non-metastatic prostate cancer with intermittent ADT. Despite reasons cited for prescribing continuous versus intermittent ADT, there were no differences observed with respect to physician characteristics or behaviours such as frequency of PSA testing.

DISCUSSION

This international survey provides a detailed understanding of how ADT is prescribed among patients with non-metastatic prostate cancer under the care of 441 treating physicians from 19 countries. Respondents indicated that ADT was prescribed for 38% (range 25–68%) of their patients with non-metastatic prostate cancer, and mainly related to prognostic indicators (Gleason score, PSA and PSA doubling time) or on signs of disease progression or recurrence manifested by rising PSA values after initial or primary therapy. Physicians from the USA reported that 34% of their patients were treated with ADT; a treatment rate lower than previously reported in the literature, but may suggest that the decreasing trend in ADT following Medicare reimbursement policy changes in 2004 and 2005 continues, resulting in overall lower use by 2012.[8]

The use of ADT differed by region, with highest rates reported in Eastern Europe. We also found that among patients receiving GnRH agonists, roughly a quarter were prescribed intermittent ADT, suggesting that the use of this strategy is relatively common, although rates

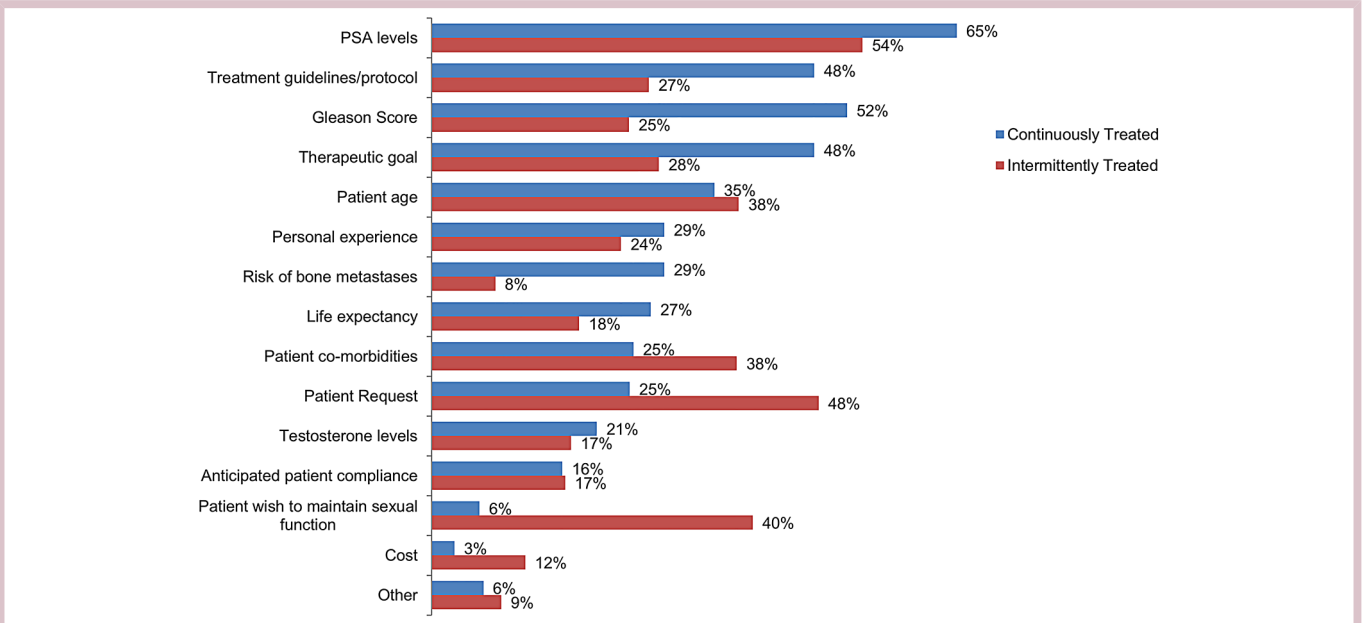


Figure 3 Reasons for prescribing GnRH agents continuously versus intermittently. GnRH, gonadotropin-releasing hormone; PSA, prostate-specific antigen.

of intermittent GnRH varied substantially by region. Guidelines for the treatment of prostate cancer also differ by region. In the USA, the American Urological Association (AUA) guidelines do not address intermittent use of ADT (http://www.auanet.org/education/guidelines/). The updated National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines (Prostate Cancer) (http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf) recommend intermittent ADT for patients with biochemical failure and without metastases based on a clinical trial showing that overall survival was non-inferior versus continuous ADT (NCIC PR-7 trial), and intermittent use is not recommended for metastatic patients.[26] The European Association of Urology (EAU) guidelines recommend intermittent ADT for asymptomatic metastatic patients citing a different set of clinical trials[24 27–30] that did not show significant differences in overall survival between continuous and intermittent ADT, also citing patient acceptability, quality of life and fewer toxicities such as effects on cardiovascular or bone health.[24 31] Surveyed physicians noted that intermittent use was primarily driven by PSA levels, patient request and patient age/comorbidities, likely reflecting an attempt to minimise adverse effects of ADT in patients with lower risk tumours. In general, ADT use differed by physician specialty, with higher use among oncologists who may see men with higher risk disease.

ADT is often administered for 6 months or longer, on a continuous basis. The decision to prescribe continuous ADT was based on PSA level, Gleason score and treatment guidelines—likely related to less favourable prognostic markers, or imminent or diagnosed castration resistance. Not surprisingly, bilateral orchiectomy was not a common treatment for patients with non-metastatic prostate cancer (<2%) with highest rates reported in Eastern Europe (Hungary and Poland). ADT was generally used for a total duration of 6 months or longer as either continuous or intermittent ADT (>75% of patients)—only US practitioners reported using ADT for this duration in less than 70% of their patients, possibly another consequence of the reimbursement rulings on GnRH described elsewhere.[8]

Although several therapies and improved management strategies exist for side effect management, the most effective form of prevention involves avoiding ADT administration when it is not necessary (ie, neo-adjuvant therapy before prostatectomy and short-term ADT in addition to radiation therapy for low-risk disease).[32] Intermittent ADT has been associated with fewer side effects and increased health-related quality of life indicators in a number of clinical trials;[24 26–30] however, some of the evidence can be inconsistent, and further work is needed to determine the patient populations who will benefit most in the reduction and prevention of the long-term harmful effects compared with continuous ADT.[20–21 24]

EAU guidelines recommend monitoring testosterone and reinitiating ADT based on clinical progression or prespecified PSA levels.[31] In our study, physicians reiterated the importance of PSA as the key measurement taken during the treatment course of their patients with non-metastatic prostate cancer; however, testosterone is reserved for those who may be at high risk of developing bone metastases. There are intermittent ADT protocols derived using mathematical models[33] to determine the on-treatment and off-treatment periods; nonetheless, the evidence to date is not sufficient to accurately predict

the effectiveness, likelihood of response and adverse effects of these protocols in the real world.[34] There is growing evidence to support intermittent ADT as effective as continuous ADT in specific cohorts of patients; nonetheless, clinicians face the challenge of prescribing appropriate evidence-based and guideline-endorsed GnRH treatment regimens for their patients while attempting to minimise the exposure and toxicity when possible. Accordingly, clinicians devise individualised treatment courses of optimal length based on patient characteristics while accounting for associated risks and benefits of ADT.[35] This individualised clinical approach is represented in the variation of survey responses as it can become difficult to compartmentalise patients when deciding on treatment strategies. The observations from this cross-sectional survey therefore provide useful insights into how clinicians are treating men with non-metastatic prostate cancer with ADT.

Several limitations must be acknowledged related to this study and survey research in general. Although we ascertained the total number of patients treated in the disease pathway, findings are qualitative in nature and limited to physician-reported data with no confirmation from patient charts. In the qualitative development interviews, it was noted that physicians did not easily identify the differences between continuous and intermittent treatment. Spontaneous definitions of continuous ADT included 'lifelong', 2–6 years and 'long-term' treatment. We therefore presented the definitions of intermittent and continuous ADT and overall treatment duration to ensure physicians could answer the online survey questions consistently. Most physicians used individualised treatment plans and therefore could not predict whether patients, in general, would be treated continuously or not in the long term. Questions related to treatment duration are dependent on the physicians' current workloads at the time of the research, and treatment is likely to change over time. Although we achieved an adequate (for physician-level research) response rate of 12%, we acknowledge that treating physicians who completed the survey may differ from non-respondents. Since this was a self-reported questionnaire, there is a potential bias in respondents giving answers based on perception or guidelines. Finally, given the small number of respondents in some countries, the results must be interpreted with caution.

CONCLUSION

This international survey of 441 treating physicians from 19 countries furthers our understanding of how men with non-metastatic prostate cancer are treated with ADT. Urologists and oncologists indicated that their decisions to treat patients with prostate cancer continuously with ADT was based on PSA levels, Gleason score and treatment guidelines, likely related to less favourable prognostic markers, or imminent or diagnosed castration resistance. Despite limited number of studies supporting the use of intermittent ADT relative to continuous ADT, clinicians estimated that among their GnRH-treated non-metastatic patients, a quarter were prescribed intermittent ADT. These data suggest that the use of intermittent ADT is quite common but varies substantially by region. Intermittent use was driven by PSA levels, patient request, patient age and comorbidities, possibly reflecting attempts to minimise adverse effects of ADT in patients with lower risk tumours. Further clinical research is warranted to confirm that intermittent ADT can reduce major long-term complications of androgen deprivation, and to determine the selected patient groups that would benefit the most.

Author affiliations
[1]Center for Observational Research, Amgen Inc., South San Francisco, California, USA
[2]Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada
[3]Adelphi Research, Macclesfield, UK
[4]Global Health Economics, Amgen Inc., Thousand Oaks, California, USA
[5]Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA

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