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REVIEW ARTICLE

Management of anticoagulation in patients with metastatic castration–resistant prostate cancer receiving abiraterone + prednisone

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Abstract

Purpose Abiraterone has been proven to be an effective agent used in the management of metastatic castration–resistant prostate cancer, significantly improving overall and progression-free survival. Due to the pharmacodynamic and pharmacokinetic properties of abiraterone, concurrent use with anticoagulation may pose a challenge for clinicians. Thrombosis within the cancer setting continues to increase patient mortality; therefore, appropriate anticoagulation through the use of a management algorithm can reduce adverse events and increase quality of life.

Methods A review of the literature was preformed by a medical oncologist, haematologist and pharmacists to identify relevant randomized controlled trials, meta-analyses and retrospective studies. Major society guidelines were reviewed to further aid in developing the anticoagulation protocol for non-valvular atrial fibrillation and venous thromboembolism within this patient population. After reviewing the literature, a clinical framework was designed to aid clinicians in the management of those patients receiving abiraterone concurrently with an anticoagulant.

Results In this review, we describe the potential interactions between abiraterone and various anticoagulants and provide management strategies based on the most recent literature for atrial fibrillation, venous thromboembolism and mechanical heart valves to avoid potential drug–drug interactions.

Conclusion Abiraterone therapy has become a mainstay of the management of advanced prostate cancer and is often used over prolonged years. In this review, we have summarized a framework of how to use abiraterone in men with prostate cancer on anticoagulants. Evidence available to date suggests that patients with an indication for anticoagulation such as atrial fibrillation, venous thromboembolism and mechanical heart valves can be treated safely with abiraterone in the appropriate setting, with appropriate monitoring.

Keywords Anticoagulation · Abiraterone · Pharmacokinetics · Supportive care · Prostate cancer

Introduction

Prostate cancer (PC) is the most frequently diagnosed cancer among men and has become the third leading cause of cancer related male deaths in developed nations [1, 2]. The incidence of PC tends to increase with age and may present within a population with an increased risk of comorbidities requiring anticoagulation [3–6]. A similar age trend is seen in the diagnosis of atrial fibrillation, a common indication for anticoagulant use, as the incidence rate increases from 0.13 per 1000-patient years in men < 55 years of age to 7.65 per 1000-patient years in men ≥ 85 years of age [7]. Comparably, it has been widely documented that increasing age correlates with increasing incidence rates of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) [8, 9].

Abiraterone acetate is an oral irreversible inhibitor of CYP17A1, a rate-limiting enzyme in the androgen biosynthesis cascade [10]. The primary sites of action of androgen synthesis inhibition include testes, adrenal glands and the prostate [11]. CYP17 is expressed in 17-fold higher concentrations in castration-resistant prostate cancer than primary prostate tumours [12]. Abiraterone has been proven to be an effective agent in the

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management of metastatic castration–resistant prostate cancer (mCRPC). In the Phase III COU-AA-302 trial, men with mCRPC who received abiraterone with prednisone had significantly improved primary outcomes including radiographic progression-free survival and overall survival [13]. At the time of the interim analysis, more deaths were observed in the prednisone-alone group vs. the abiraterone + prednisone group (34% vs. 27%.) [13]. Abiraterone has also been shown to increase overall and progression-free survival in metastatic castration–sensitive prostate cancer based on the results of the LATITUDE and STAMPEDE trials [14, 15].

Due to pharmacodynamic and pharmacokinetic interference, abiraterone can pose a challenge for patients receiving concurrent anticoagulation. It has been shown to impair various enzymatic pathways, creating the possibility for interactions with several anticoagulants. Specifically, abiraterone is a strong inhibitor of CYP2D6, CYP2C8 and CYP1A2 and in vitro data suggests moderate inhibition of CYP3A4, CYP2C9 and CYP2C19 [16, 17]. Additionally, in vitro data suggests abiraterone has little inhibitory effect on P-glycoprotein (P-gp); therefore, no clinical drug–drug interactions are expected [17]. Typically, prednisone is co-administered with abiraterone to reduce the risk of mineralocorticoid excess [18]. However, long-term steroid use even at modest doses may increase the risk of bleeding when coupled with other medications such as acetylsalicylic acid, other non-steroidal antiinflammatory drugs and anticoagulants [18–20]. Altogether, the administration of abiraterone + prednisone may potentially lead to sub- or supratherapeutic anticoagulant levels and thus may result in thromboembolic events and/or significant bleeding.

There is insufficient literature surrounding the incidence of anticoagulation complications in patients receiving abiraterone + prednisone as increased rates of thromboembolism or bleeding were not reported in all major abiraterone trials. The rate of study patients with concurrent anticoagulation was not reported, and outcomes related to patients receiving anticoagulation were not specific study endpoints. Thus, it is possible such adverse events may not have been published [13].

After reviewing the available literature, it appears there is minimal clinical guidance for anticoagulation management in PC patients receiving abiraterone and prednisone therapy [21]. Accounting for the lack of a guided anticoagulation management strategy for clinicians treating mCRPC patients receiving abiraterone +prednisone, the following article will provide rationale and guidance on the safe use of anticoagulants in combination with abiraterone + prednisone in men with PC.

Main indications for anticoagulant use in men with prostate cancer

Currently, guidelines recommend consideration of anticoagulation therapy for embolic stroke prophylaxis in patients with atrial fibrillation [22]. The embolic stroke risk can be determined by the $CHADS_2$ scoring algorithm, based on congestive heart failure, hypertension, age (> 65), diabetes (1 point each) and prior stroke history (2 points) [22]. The Canadian Cardiovascular Society currently recommends no anticoagulation for patients < 65, a $CHADS_2 = 0$ and no evidence of arterial vascular disease and therapeutic anticoagulation for patients ≥ 65 and/or a $CHADS_2 \geq 1$ [22]. It is important to note stroke prediction tools have not been validated in patients with cancer and atrial fibrillation [22, 23]. Current evidence suggests that patients with active malignancy and preexisting atrial fibrillation with a higher $CHADS_2$ score are at an increased risk of ischemic stroke [23]. Due to the substantial increase in progression-free and overall survival seen in men with metastatic PC undergoing abiraterone therapy initiating stroke prophylaxis is reasonable.

Cancer-associated VTE is the second leading cause of death in ambulatory cancer patients, second only to progression of disease [24]. VTE in this population can occur as a result of cancer treatment or secondary to the hypercoagulable state associated with malignancy, with a significantly increased risk of development within the metastatic setting [25, 26]. Data shows that cancer patients with VTE have a 2-fold or greater increase in mortality compared to those without VTE [21]. Although the association of VTE with prostate cancer is lower when compared to other solid tumours, active prostate malignancy is an increased risk factor for VTE development, especially when patients are undergoing androgen deprivation therapy [20, 25, 26]. A recent analysis at our institution revealed that 39% of men undergoing abiraterone + prednisone therapy use anticoagulants and/or antiplatelet medications [27].

The hypercoagulable state in cancer involves several complex mechanisms, increasing the risk of thromboembolism in these patients [28]. Anticoagulation management within these patients is complicated by the fact that they are also at an increased risk of bleeding episodes [28]. As a result, it is important for clinicians to provide anticoagulation options that minimizing the risk of bleeding complications [28]. With this analysis, we hope to provide a guided tool for clinicians to follow when using anticoagulation concurrently with abiraterone.

Potential effects of abiraterone + prednisone on various classes of anticoagulants

Direct oral anticoagulants

Current guidelines propose the use of direct oral anticoagulants (DOACs) for the treatment of VTE and stroke prophylaxis in the setting of non-valvular atrial fibrillation [22, 29]. These recommendations are based on non-inferiority data, improved safety profiles and increased adherence due to predictable pharmacokinetics without the need for routine monitoring [22, 29,

30]. DOACs are subjected to potential drug–drug interactions due to cytochrome P450 and P-gp-mediated processes [22, 29, 30]. As a result, co-administration of DOACs with abiraterone + prednisone has the potential for both pharmacokinetic and pharmacodynamic interactions. All pharmacological data for available DOACs in comparison with warfarin and low molecular weight heparins (LMWH) are listed in Table 1.

Rivaroxaban

Rivaroxaban has been shown to be non-inferior to warfarin for the prevention of stroke or systemic embolism in patients with non-valvular atrial fibrillation (1.7% vs. 2.2%) [35]. As per the ROCKET AF trial, major and non-major clinically relevant bleeding events were similar between arms. However, rivaroxaban was associated with significantly less intracranial haemorrhages (0.5% vs. 0.7%) and bleeding fatalities (0.2% vs. 0.5%) [35]. With respect to VTE, rivaroxaban was shown to be non-inferior to warfarin for the treatment of acute DVT (2.1% vs. 3.0%) and pulmonary embolism (2.1% vs. 1.8%) [36, 37]. Recent evidence from the SELECT-D pilot trial compared rivaroxaban vs. dalteparin for the extended treatment and prevention of VTE recurrence in the cancer setting [38]. Of the 406 patients recruited for the pilot trial, 59% had metastatic disease and 4% had prostate cancer. The VTE recurrence rate at 6 months for dalteparin was 11% (95% CI, 7–16%) and 4% for rivaroxaban (95% CI, 2–9%). With respect to safety, the rates of major bleeding episodes were similar across the two arms (3% on dalteparin vs. 4% on rivaroxaban (95% CI, 0.68–4.96); however, there was an increase in clinically relevant non-major bleeding (CRNMB), driven by higher rates of upper GI bleeds within the rivaroxaban arm [38]. The cumulative rate of CRNMB at 6 months was 4% for dalteparin and 13% for rivaroxaban (HR, 3.76; 95% CI, 1.63–8.69) [38]. While these results are the first comparing rivaroxaban to LMWH for VTE treatment in cancer patients, confirmation in a large phase III trial is needed [38].

Due to the fact that rivaroxaban is metabolized by CYP3A4 and is a substrate of the P-gp transporter, inducers or inhibitors of these processes may affect rivaroxaban kinetics. Moderate inhibitors of CYP3A4 when used in conjunction with rivaroxaban have been shown to increase the mean AUC by 1.4-fold; however, this did not clinically translate to an increased risk of bleeding as shown in the ROCKET AF trial in patients taking amiodarone (moderate CYP3A4 inhibitor) [35, 39]. Because abiraterone is a moderate inhibitor of CYP3A4 and features minimal P-gp inhibition in vitro, no dose adjustments of rivaroxaban are recommended [39]. Our recommendations for rivaroxaban use in atrial fibrillation and VTE are seen in Figs. 1 and 2 respectively.

Edoxaban

High dose (60 mg) edoxaban was shown to be non-inferior to warfarin in patients with non-valvular atrial fibrillation for the prevention of stroke and systemic embolism (1.18% vs.

Table 1 Pharmacokinetics of anticoagulants [31–34]

Agent	Target(s)	Prodrug	Bioavailability (%)	Food Effect	Peak effect	Half life	Renal elimination (%)	Metabolic pathway(s)	Drug interactions
Warfarin	II, VII, IX, X	No	100	Vitamin K containing foods reduce effect	4–5 days	40 h	0	CYP 2C9 (s-warfarin) CYP 3A4, 1A2, 2C19 (r-warfarin)	Many
Dabigatran	IIa	Yes	7	Delays plasma peak concentration by 2 h	1–3 h	14-17 h	80	Liver conjugation	P-gp
Rivaroxaban	Xa	No	80	Yes (food increases bioavailability at doses of 15 and 20 mg)	2–4 h	7-11 h	33	CYP 3A4, 2J2	3A4, P-gp
Apixaban	Xa	No	60	No	1–2 h	8–14 h	27	Major: CYP 3A4/5 Minor: CYP 1A2, 2C8, 2C9, 2C19, 2 J2	3A4, P-gp
Edoxaban	Xa	No	62	No	1–2 h	5–11 h	50	Glucuronidation, CES1, CYP 3A4	P-gp
LMWH	Xa/IIa	No	90	No	3–4 h	3–5 h	40	Desulphation and depolymerization	Pharmacodynamic

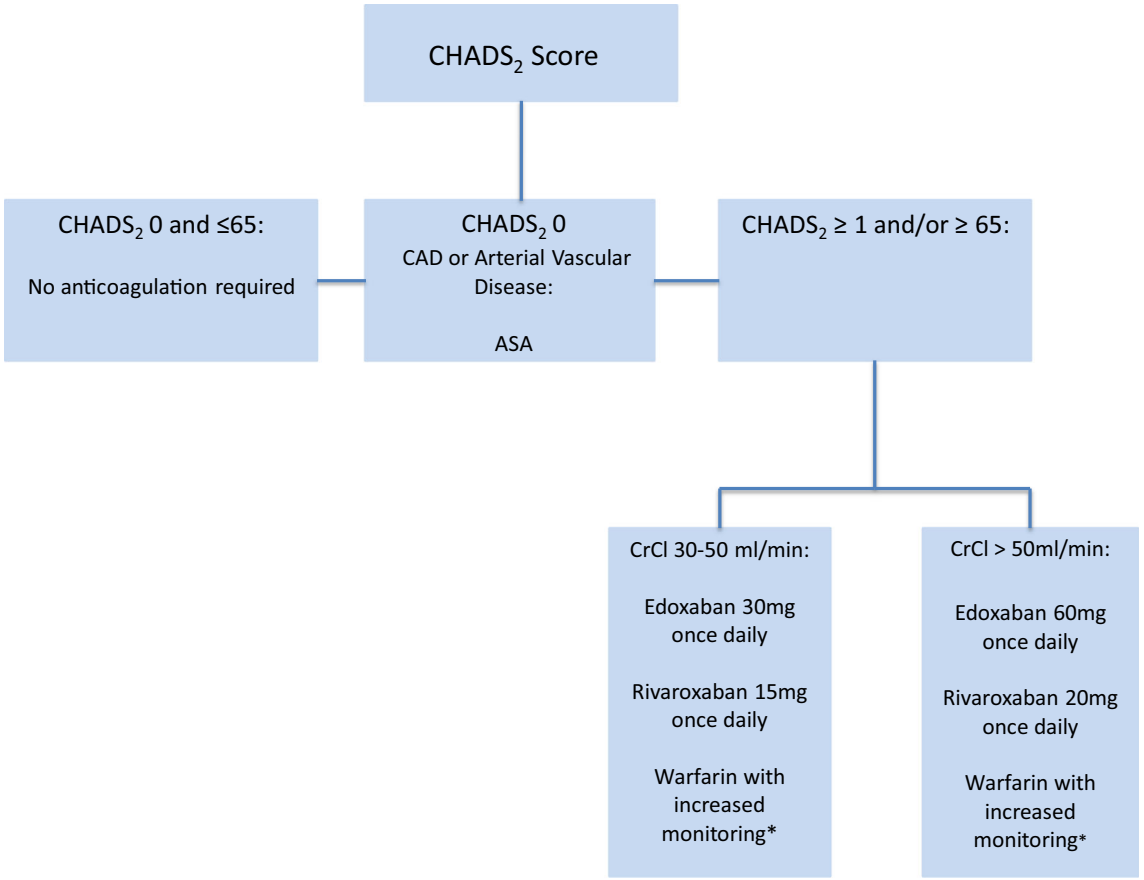

Fig. 1 Anticoagulation management for non-valvular atrial fibrillation in a patient receiving abiraterone + prednisone [22, 35, 38, 40, 43]. CAD coronary artery disease, ASA acetylsalicylic acid, CHADS2 congestive heart failure, hypertension, age > 65, diabetes, prior stroke or transient attack, CrCl creatinine clearance, INR international normalized ratio. Asterisk—monitor INR 3 days after initiation and then once weekly for 4 weeks, as INR becomes stable the interval may be increased slowly. Due to increased amount of evidence supporting DOAC use within the oncology setting, warfarin should be reserved for those patients in whom DOACs are not indicated

1.50%) [40]. The ENGAGE AF-TIMI 48 trial also concluded that reduced dose (30 mg) edoxaban was non-inferior to warfarin for the primary outcome of stroke prevention (1.61% vs. 1.50%). A dose reduction was conducted for patients with high bleeding risk as defined by low body weight (< 60 kg), moderate-to-severe renal dysfunction (CrCl 30–50 mL/min) and concomitant use of a strong P-gp inhibitor [40, 41]. The annualized rate of major bleeding events was 3.43% with warfarin, 2.75% with high dose edoxaban and 1.61% with low dose edoxaban ($p < 0.001$).

In terms of VTE management, edoxaban was shown to be non-inferior to warfarin in the prevention of recurrent VTE (3.2% vs. 3.5%) [42]. Recent evidence from the Hokusai trial has demonstrated that edoxaban is non-inferior to LMWH (dalteparin) for the treatment of cancer-associated VTE [43]. A primary outcome event occurred in 12.8% in the edoxaban group vs. 13.5% in the dalteparin group ($p = 0.006$ for non-inferiority, $p = 0.87$ for superiority) [43]. The rates of major bleeding were 6.9% in the edoxaban group vs. 4.0% in the dalteparin group (HR, 1.77; $p = 0.04$), which was driven by the higher rate of upper GI bleeds in the edoxaban study arm [43]. Gastrointestinal tumour types resulted in the majority of major bleeding episodes in the edoxaban arm, as they accounted for 13.2% of all major bleeds [43]. Of the study population, genitourinary cancers contributed to 12.5% of the edoxaban study arm and 52.5% had metastatic disease. As for the anticancer therapies used in the edoxaban study arm, 7.9% of the 522 patients were on hormonal therapies, further demonstrating the applicability of the results to patients receiving abiraterone. The results of this trial were the first involving a DOAC where outcomes in active malignancy were specially examined as a primary objective.

Edoxaban is a substrate for the P-gp transport system undergoing metabolism mainly through glucuronidation with minimal metabolism via CYP3A4 (< 10%) [44]. As a result, edoxaban is subjected to P-gp-mediated drug interactions. Since pharmacokinetic studies have shown abiraterone to have minimal P-gp inhibitory effects in vitro, no dose adjustments are necessary when edoxaban is administered concurrently with abiraterone [17]. Our recommendations for edoxaban use in atrial fibrillation and VTE are found in Figs. 1 and 2 respectively.

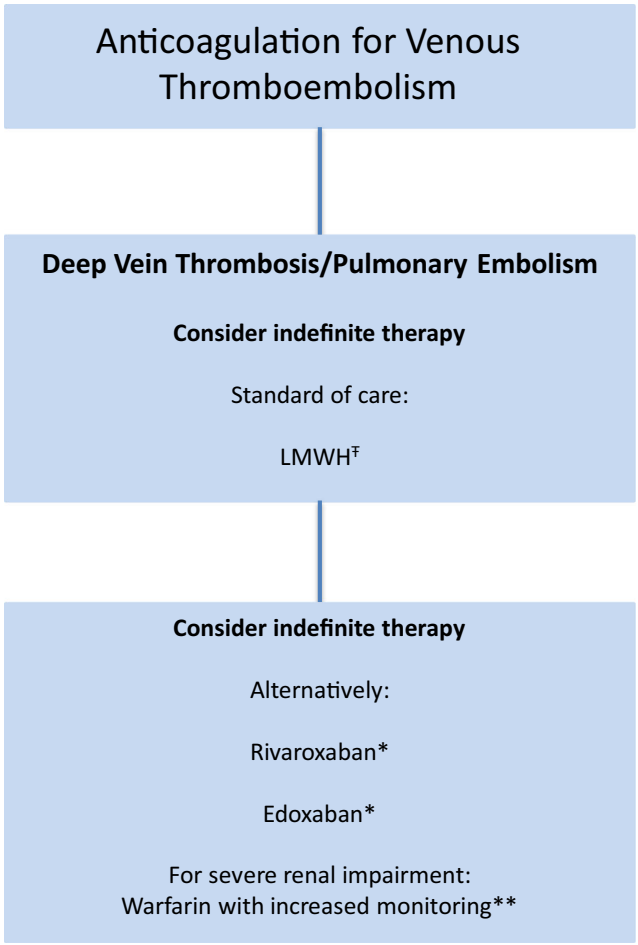

Fig. 2 Anticoagulation management for venous thromboembolism in a patient receiving abiraterone + prednisone [38, 43, 56]. LMWH low molecular weight heparin. Letter T with stroke—dose adjust for renal function and body weight; asterisk—dose adjust for renal function; not recommended CrCl < 30 mL/min; double asterisks—monitor INR 3 days after initiation and then once weekly for 4 weeks, as INR becomes stable the interval may be increased slowly

Apixaban

Apixaban has been shown to be superior to warfarin for the prevention of stroke or systemic embolism in patients with non-valvular atrial fibrillation (1.27% vs. 1.60% $p = 0.01$ for superiority) [45]. For the treatment of acute VTE, apixaban is non-inferior to warfarin (2.3% vs. 2.7%) but safer as defined by the composite outcomes of major bleeding and clinically relevant non-major bleeding (4.3% vs. 9.7%) [46]. A subgroup analysis of cancer patients in the AMPLIFY trial suggested that apixaban is at least as effective as LMWH/warfarin in this patient population and is associated with less bleeding events [47]. This analysis had many limitations as only 3.7% of the study population had active cancer and those with a life expectancy < 6 months were excluded from the trial [46]. The comparative arm of LMWH/warfarin is not the standard of care for prevention of VTE recurrence in cancer patients; therefore, the efficacy and safety of apixaban vs. long term LMWH still remain in question [47–49].

Apixaban carries a similar pharmacokinetic profile to rivaroxaban, undergoing metabolism via CYP3A4 and is a P-gp substrate [31, 45, 46]. Moderate inhibitors of both CYP3A4 and P-gp have been shown to increase the AUC of apixaban by 1.4-fold [50]. The manufacturer does not suggest any dose adjustments however recommends to use apixaban cautiously with moderate inhibitors of CYP3A4 and P-gp [50]. As previously mentioned, there is no in vivo data confirming abiraterone to be a moderate inhibitor of CYP3A4 and P-gp. Therefore, the concurrent use with apixaban does not require dose adjustments but warrants careful monitoring [17, 50].

Dabigatran

In patients with non-valvular atrial fibrillation, dabigatran administered at a dose of 110 mg daily was comparable to warfarin for the prevention of stroke or systemic embolism (1.53% vs. 1.69%). However, dabigatran administered at the 150 mg dose was shown to be superior to warfarin (1.11% vs. 1.69% $p < 0.001$ for superiority) for the primary outcome [51]. For the treatment of acute VTE, dabigatran was found to be non-inferior to warfarin for recurrent VTE (2.4% vs. 2.1%) [52]. Recently, the evidence surrounding the safety profile of dabigatran has been conflicting [51, 52]. A systematic review and meta-analysis found dabigatran was associated with a moderate but statistically significant higher risk of gastrointestinal bleeds compared to warfarin [53]. A more recent retrospective analysis of patients using dabigatran for atrial fibrillation or for non-atrial fibrillation indications found the bleeding risk to be comparable to warfarin in patients under the age of 65; however, bleeding risk was increased significantly in those over the age of 75 [54].

Dabigatran is not metabolized through the hepatic cytochrome P450 enzymatic process; therefore, no dose adjustments are required with cytochrome inhibitors or inducers [51]. Dabigatran is a P-gp substrate, and therefore, drugs affecting this pathway may necessitate dabigatran dose adjustments [55]. No dabigatran dose adjustments are indicated with the concurrent use of the weak P-gp inhibitor abiraterone; however, patient-specific demographics such as age, renal function and bleeding history should be taken into consideration if dabigatran therapy is initiated [17, 53–55].

Low molecular weight heparins

Dalteparin has been described as the standard of care in numerous guidelines for the prevention of recurrent VTE in cancer patients based on the CLOT (Comparison of Low-Molecular-Weight Heparin versus Oral Anticoagulant Therapy for the Prevention of Recurrent Venous Thromboembolism in Patients

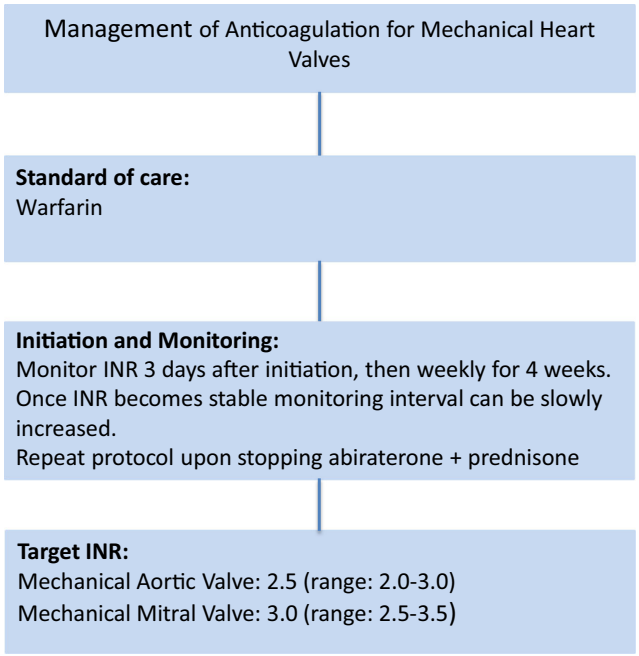

Fig. 3 Initiation and monitoring of anticoagulation for mechanical heart valves in patients receiving abiraterone + prednisone [64, 65, 67]. INR international normalized ratio

with Cancer) trial demonstrating the superiority of dalteparin to the vitamin K antagonists warfarin and acenocoumarol [48, 49, 56]. The primary outcome occurred in 8.0% in the dalteparin arm vs. 15.7% in the oral anticoagulant arm (HR, 0.48; $p = 0.002$). It is important to highlight that the VTE rates in the CLOT trial were much higher than events seen in recent studies investigating oral anticoagulation for cancer-associated thrombosis [38, 43, 56]. Patients receiving abiraterone can be safely treated for cancer-associated thrombosis with LMWH dosed according to body weight and accounting for renal function [29]. Concurrent use of abiraterone + prednisone does not pose a significant drug interaction risk with LMWH, but continuous clinical monitoring is necessary based on the increased risk of upper gastrointestinal bleeds with prednisone use [18, 33, 34]. Until the recent evidence of edoxaban and rivaroxaban compared to LMWH, the use of DOACs in the setting of cancer-associated VTE was based on sub-group and meta-analyses [43, 56, 57]. A systematic review of DOAC use in the prevention of recurrent VTE within the oncology setting demonstrated DOACs to be at least as effective and as safe as LMWH [57]. When comparing the safety profile of LMWH and DOACs for cancer-associated thrombosis, Sobieraj et.al. published a meta-analysis in 2018 investigating anticoagulation options in the oncology patient population [58]. The results of this analysis showed that the risk of major bleeding was higher with DOACs vs. LMWH (RR: 1.14; 95% CI, 0.64–2.03); however, statistical significance was not reached [58].

There has been an increase in the body of evidence for the use of LMWH in the setting of atrial fibrillation. This evidence consists mainly in the setting of cardioversion as an alternative to unfractionated heparin for acute treatment of atrial fibrillation; however, at this time, LMWH has not been validated as a long-term anticoagulant in patients with atrial fibrillation and should not routinely be used in place of other agents with established stroke prophylaxis evidence such as warfarin and DOACs [59].

Drug interactions with LMWH are mainly of the pharmacodynamic nature; therefore, no further dose adjustments of LMWH are necessary when co-administered with abiraterone. Our recommendations for LMWH use in VTE are found in Fig. 2.

Vitamin K antagonist

Vitamin K antagonists (VKAs) were the mainstay of oral anticoagulation for decades as they were the first of their kind. They continue to be excellent therapeutic options for patients with good adherence, contraindications to other anticoagulants, and those with mechanical heart valves. The use of VKAs such as warfarin is associated with a variety of drug interactions that can pose challenges when initiating new therapies [25]. In vitro pharmacokinetic studies have shown abiraterone to be a moderate inhibitor of CYP2C9, the metabolizing enzyme of s-warfarin [17]. Currently, no in vivo data suggests the CYP2C9 inhibition of abiraterone to be clinically significant [17]. However, abiraterone and warfarin share similarly high albumin binding capacity (~ 99%) [17, 59]. Initiating or stopping abiraterone in patients on warfarin

Table 2 Recommended management strategies for anticoagulation in patients receiving abiraterone + prednisone

Atrial fibrillation:	Therapy:
CHADS2 score 0 and age ≤ 65	No anticoagulation
CHADS2 score 0 and CAD	ASA
CHADS2 score ≥ 1 and/or age ≥ 65	Anticoagulation with edoxaban, rivaroxaban or warfarin*
Deep vein thrombosis/pulmonary embolism	LMWH is standard of care
	Rivaroxaban or edoxaban as alternative
Mechanical heart valve	Warfarin* is the only acceptable anticoagulant

CAD coronary artery disease, *CHADS2* congestive heart failure, hypertension, age diabetes, prior stroke or transient attack, *LMWH* low-molecular weight heparin

*Close monitoring of INR

therapy may cause an increase in the fraction of unbound warfarin, necessitating intensified INR monitoring [60–62].

As previously mentioned, corticosteroid use has been shown to increase the risk of gastrointestinal bleeding due to injury of the gastrointestinal mucosa, thus increasing the bleeding risk with warfarin co-administration [19, 62]. As a result, patients in whom warfarin therapy is indicated will require close monitoring directed by INR results (notably at the beginning and end of abiraterone therapy) and/or clinical signs of bleeding [62].

Vitamin K antagonists are currently the only acceptable anticoagulant used in patients with a mechanical heart valve within the ambulatory setting [63, 64]. Current guidelines recommend a target INR of 2.5 (range 2.0–3.0) for patients with mechanical aortic valves and a target INR of 3.0 (range 2.5–3.5) for those patients with a mechanical mitral valve [64, 65]. The only clinical trial comparing DOACs with warfarin for patients with mechanical heart valves resulted in early termination due to an interim analysis showing increased adverse events in the DOAC study arm [64–66]. As a result, DOACs are not a standard treatment within this patient population [65, 66]. Concurrent use of warfarin with abiraterone is not contraindicated but does require close monitoring [62, 63]. Adverse effects with warfarin therapy can be minimized by assessing the risk of harm due to drug interactions, increasing the frequency of INR monitoring and making warfarin dose adjustments when necessary [63]. Our approach is to monitor INR 3 days after initiation, as abiraterone will reach steady state in approximately 3 days ($t½ = 12–15$ h) [67]. Thereafter, we recommend monitoring INR once weekly for 4 weeks, as INR becomes stable the length of time between monitoring can be slowly increased. This process must be repeated once abiraterone has been discontinued to prevent any labile INR values. Our recommendations are found in Fig. 3. A summary of our recommended anticoagulation algorithms for patients receiving abiraterone + prednisone is found in Table 2.

Conclusion

Abiraterone + prednisone therapy has become a mainstay of the management of advanced prostate cancer, and is often used over prolonged periods of time counted in years. This treatment results in possible pharmacokinetic and pharmacodynamic interactions with most anticoagulants available, a group of commonly utilized co-medications in typically elderly men with prostate cancer. Given the narrow therapeutic index of anticoagulants, the drug interaction risk can pose challenges for clinicians prescribing these medications concurrently [8]. While awaiting a more complete understanding of these drug interactions, we have summarized herein a framework of how to use abiraterone + prednisone in men with prostate cancer on anticoagulants, applying best current knowledge. Recent Canadian guidelines on cancer-associated thrombosis management advise clinicians to apply a pharmacokinetic assessment to determine any significant drug–drug interactions on each patient prior to initiating therapy [68]. We believe this framework that was developed for anticoagulation use in patients receiving abiraterone + prednisone coincides with the recently published guidelines. Evidence available to date suggests that patients with an indication for anticoagulation such as atrial fibrillation, VTE and mechanical heart valves can be treated safely with abiraterone + prednisone in the appropriate setting with appropriate monitoring.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest. Dr. Urban Emmenegger has received clinical research support (personal and institutional) from Janssen Inc., Canada, and has attended advisory board meetings.

Disclaimer The authors of this manuscript have full control of the data presented. We agree to let the Journal of Supportive Care in Cancer review the data if requested.

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