


REVIEW

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Risk of atrial fibrillation in patients with multiple myeloma: what is known and directions for future study

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Abstract

Background Multiple myeloma (MM) is a prevalent hematological tumor, and recent clinical data have highlighted the significance of atrial fibrillation (AF) as a crucial complication affecting the prognosis of MM. This review aims to consolidate findings from published clinical studies, focusing on the epidemiological characteristics of AF in MM patients and the associated risks arising from MM treatments such as autologous hematopoietic stem cell transplantation, proteasome inhibitors, and immunomodulatory agents.

Main body While existing data partially demonstrate a strong correlation between MM and AF, further clinical studies are necessary to comprehensively investigate their association. These studies should encompass various aspects, including the risk of AF resulting from MM treatment, the impact of AF-induced embolic events and heart failure on MM prognosis, as well as the influence of AF management methods like catheter ablation or left atrial appendage closure on MM prognosis.

Conclusions The supplementation of future data will provide more precise guidance for managing MM patients. By incorporating information regarding AF risk associated with MM treatment and examining the effects of AF management strategies on MM prognosis, healthcare professionals can enhance their decision-making process when caring for individuals with MM.

Keywords Multiple myeloma, Atrial fibrillation

Background

Multiple myeloma (MM) is one of the most common hematological malignancies, accounting for 0.9% of all cancers worldwide in 2020, with 176,404 new cases and 117,077 deaths [1]. The survival of MM has significantly improved with the development of new therapies

such as immunomodulatory drugs (IMiDs), proteasome inhibitors (PIs), and autologous hematopoietic stem cell transplantation (ASCT) [2]. Prior to 2000, relapsed MM patients had a reported median survival of 12 months, which increased to 24 months after 2000 [3]. Another study observed an increase in the 5-year relative survival rate of MM patients from 34% in 1989–1992 to 56% in 2001–2005 [4].

However, despite the encouraging progress in treating the primary disease, more than half of real-world MM patients have comorbidities that directly influence clinical decision-making and significantly increase the risk of death [5]. Among these comorbidities, cardiovascular complications are particularly noteworthy [6]. Previous clinical practice has recognized that MM patients are at a higher risk of developing heart failure due to various

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Table 1 Details of the literature with epidemiology

References	Type	Area	Population	Sample size	Conclusion
Yun et al. [9]	Cohort study based on health insurance database	Korea	Patients who were diagnosed with cancer between 2009 and 2016 were enrolled Non-cancer subjects were selected as control group	816,811 patients with cancer and 1,633,663 non-cancer controls were enrolled	During a median follow-up of 4.5 years, cancer was an independent risk factor for incident atrial fibrillation (AF) (adjusted subdistribution hazard ratio [aHR]: 1.63; 95% confidence interval [CI]: 1.61 to 1.66). The impact on AF development varied by cancer type, and multiple myeloma (MM) showed a higher association with incident AF (aHR: 3.34; 95% CI: 2.98 to 3.75)
Khan et al. [10]	Cross-sectional study based on national inpatient database	United States	All adult patients (≥ 18 years) who were hospitalizations and diagnosed with cancer between 2005 to 2015	40,030,380 patients with cancer were included, and the prevalence of AF in these cancer patients was 14.6%	In patients age < 80 years, AF has significant association with MM and lung cancer, where as in patients age > 80 years, it has significant association with non-Hodgkin lymphoma and prostate cancer
Li et al. [11]	Single-center retrospective cohort study	Xi'an, China	Patients with MM between January 2015 to April 2020	A total of 319 patients with MM were included, with 6% combined AF	During a median follow-up of 18.3 months, the all-cause mortality rate of MM patients with AF and without arrhythmias were 73.7% (14/19) and 50.6% (84/166)

treatments or secondary cardiac amyloidosis [7]. With advancements in treatment methods and deeper clinical understanding, another common cardiac complication receiving increasing attention is atrial fibrillation (AF). Studies have shown that MM patients with AF face a significantly increased risk of death and medical costs [8]. Furthermore, a recent study published in the *Journal of the American College of Cardiology* reported that MM patients have the highest risk of developing AF compared to other cancer patients [9].

In summary, AF is a comorbidity that cannot be ignored in MM patients. Currently, there is a lack of comprehensive summaries and reviews regarding clinical data on the co-occurrence of MM and AF. The purpose of this review is to summarize existing research, systematically explore the connection between MM and AF, and provide a reference for assessing the risk of AF in MM management.

Main text

Epidemiology

Some studies have reported the epidemiological correlation between MM and AF (Table 1). A study utilizing the National Inpatient Sample (NIS) database, the largest inpatient database in the United States, discovered that among 40,030,380 adult cancer patients diagnosed between 2005 and 2015, the prevalence of AF was 14.6% [10]. When observing MM patients, the prevalence of AF in three age groups was as follows: group 1 (<65 years old)—22,646/345,247 (6.6%), group 2 (65–80 years old)—84,372/457,525 (18.4%), and group 3 (>80 years old)—52,551/186,174 (28.2%). Multiple regression analysis demonstrated a significant increase in the risk of AF associated with MM. The odds ratio (OR) values with their corresponding 95% confidence interval (CI) for groups 1, 2, and 3 were as follows: group 1—OR=1.59 [1.57–1.61], $P<0.0001$; group 2—OR=1.21 [1.20–1.22], $P<0.0001$; group 3—OR=1.01 [1.00–1.02], $P=0.006$. Importantly, combined AF significantly elevated mortality rates in MM patients: group 1—(4.3% vs. 2.5%, $P<0.0001$); group 2—(3.7% vs. 3.3%, $P<0.0001$).

Another study conducted using the Korean National Health Insurance Service (NHIS) database, a government-administered insurance plan covering nearly the entire population, included all newly diagnosed cancer patients from January 1st, 2009 to December 31st, 2016. Follow-up was conducted until December 13th, 2017 to observe the risk of AF in cancer patients [9]. The data revealed the following probabilities and incidence rates of new-onset AF within specific time frames of MM diagnosis: within 90 days—probability: 282/4,034 (7.0%), incidence rate: 19.95 per 1000 person-years; within 1 year—probability: 277/3,843 (7.2%), incidence

rate: 20.36 per 1000 person-years; within 5 years—probability: 34/1,087 (3.1%), incidence rate: 20.14 per 1000 person-years.

Additionally, a survey conducted at a single center in China reported a prevalence rate of AF in MM patients as 19/319 (6.0%) [11].

Atrial fibrillation risk during multiple myeloma treatment *Autologous hematopoietic stem cell transplantation*

ASCT has become one of the preferred treatment options for newly diagnosed MM patients after induction therapy [12]. However, existing evidence indicates that cardiotoxicity is a significant complication that cannot be ignored following ASCT [13]. ASCT survivors have a 2–4 times higher risk of cardiovascular death compared to general population [14, 15]. AF is the most common cardiac arrhythmia observed after ASCT [16]. The incidence of AF in MM patients after ASCT has been reported to be as high as 27%, occurring at a mean duration of 14.8 days following the procedure [17].

Multiple regression analysis revealed several factors significantly associated with AF after ASCT: baseline renal dysfunction (OR 15.2 [5.08–45.6]), left ventricular systolic dysfunction (OR 9.55 [2.78–32.79]), dilated left atrium on echocardiogram (OR 4.97 [1.8–13.78]), and hypertension (OR 3.6 [1.36–9.52]) [17]. Moreover, a study conducted at Mayo Clinic identified baseline diastolic dysfunction and weight gain greater than 7% as significant risk factors for AF in MM patients undergoing ASCT [18]. Within this study, researchers found that out of 395 MM patients undergoing ASCT, there were 39 cases of new-onset AF (9.9%) during a median follow-up period of 2.6 years, with approximately 72% occurring within 21 days after the transplantation.

Melphalan

ASCT with high-dose melphalan conditioning was once considered the standard therapy for MM [19, 20]. The recommended dosage for melphalan conditioning in patients with normal renal function is 200 mg/m² [21]. In a clinical trial reported in 1999, investigating melphalan induction at a dose of 220 mg/m² combined with ASCT, 2 out of 27 subjects (7.4%) developed paroxysmal AF following melphalan treatment and were successfully treated with amiodarone [22]. Similarly, when investigating a dose of 280 mg/m² of melphalan, 3 out of 36 subjects (8.3%) developed AF [23].

Palifermin is a recombinant human keratinocyte growth factor approved for the prevention of oral mucositis in chemoradiotherapy for hematological malignancies [24, 25]. In a phase I dose-escalation trial of palifermin plus melphalan, among 18 subjects with normal renal function who received up to 280 mg/m² of

melphalan, one subject developed AF [26]. Considering that renal failure is associated with increased melphalan toxicity [27], studies recommend reducing the melphalan dose to 140 mg/m² in patients with renal insufficiency [28, 29]. Another study involving MM patients with a creatinine clearance of 60 mL/min/1.73m² or lower found that melphalan at a dose of 180 mg/m² was safe when used in combination with palifermin [30]. Among the 15 subjects, AF was not observed except in one patient who had a history of AF and developed it during dose escalation to 160 mg/m².

Additionally, Mileschkin et al. found in their study that patients aged 60 years or older had an increased risk of cardiotoxicity (particularly AF) compared to younger adults during high-dose chemotherapy and ASCT. However, these complications were manageable and similar to the long-term prognosis of younger adults [31].

Lenalidomide

Lenalidomide is an immunomodulatory agent that significantly improves the survival rate of patients with MM and plays a crucial role in both induction therapy and maintenance therapy for MM [12, 32]. While myelosuppression and infection are common adverse effects, it is important to address the increased risk of AF associated with lenalidomide use [33]. In a clinical trial investigating the combination of lenalidomide and dexamethasone for MM treatment, the incidence of AF was 2.9% (10/346) in the “lenalidomide + dexamethasone” group compared to 0.9% (3/345) in the “placebo + dexamethasone” group [34].

Proteasome inhibitor

Proteasome inhibitors, such as bortezomib, have been shown to significantly improve the prognosis of patients with MM. A study utilizing the United States Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) database assessed the risk of AF associated with various anticancer drugs [35]. The findings indicated that bortezomib (1.5%) and carfilzomib (1.5%) ranked second in terms of AF risk, following ibrutinib (5.3%) and venetoclax (1.6%).

Daratumumab

Between 2015 and 2020, the United States FDA approved six new drugs for treating the MM: elotuzumab, which activates natural killer cells [36]; ixazomib, a proteasome inhibitor [37]; daratumumab, which targets CD38 [38]; panobinostat, an inhibitor of histone deacetylase (HDACs) [39]; belantamab, an antibody drug conjugate that targets B cell maturation antigen [40]; and selinexor, a selective inhibitor of XPO1 [41]. Daratumumab has been incorporated into first-line regimens for MM

treatment in clinical practice [12]. Analysis based on the FAERS database revealed a high incidence of AF in MM patients treated with daratumumab, reaching 6.5% [42]. Additionally, MM patients treated with ixazomib had a 3.5% risk of AF.

Histone deacetylase inhibitor

HDACs are expressed at increased levels in various malignant tumors and are considered one of the prominent targets for anticancer therapy [43]. Panobinostat (mentioned earlier) is the first FDA-approved HDAC inhibitor for MM treatment and has shown a 1.3% incidence of AF in MM patients based on data from the FAERS database [42]. Quisinostat, a highly potent second-generation selective HDAC inhibitor with orally activity, has demonstrated promising therapeutic effects against MM in rodent models and human samples tested in vitro [44–46]. Considering the synergistic effect observed between quisinostat and bortezomib in mice, their combined regimen is currently under further investigation [47]. In a phase Ib dose study involving 12 mg of quisinostat, AF was reported in 1 out of 6 subjects (16.7%) [48].

Conclusions

MM is a prevalent hematological malignancy that has witnessed significant advancements in treatment methods leading to improved prognosis. Consequently, managing complications has emerged as a critical approach for optimizing MM treatment further. This review aims to provide a comprehensive analysis by aggregating relevant data from clinical trials and observational studies to elucidate the association between MM and AF. Existing evidence suggests that MM may have the strongest correlation with AF among all cancers. The prevalence of AF in patients with MM is notably high and increases with age, reaching nearly 30% [10]. Moreover, combined treatments for MM often elevate the risk of AF. We have discussed the risks of AF associated with ASCT, melphalan, lenalidomide, daratumumab, and other therapeutic modalities. However, several commonly used treatments lack sufficient observational data regarding their impact of AF risk.

Cancer is characterized by changes in inflammation levels [49–51], which also serve as a significant risk factor for AF [52–54]. This theory partially explains the association between MM and AF. Notably, research has demonstrated an association between AF and almost all cancer subtypes, suggesting an independent link between cancer and AF [55]. The emerging field of onco-cardiology emphasizes the importance of managing cardiovascular complications to improve cancer prognosis. In cancers requiring systemic therapy such as chemotherapy

or immunotherapy, cardiovascular complications exert a more substantial influence on prognosis. Given MM patients' heightened risk of AF, it is crucial to explore further how these two conditions interact and impact individual prognoses.

The current clinical data on the relationship between MM and AF are overall very limited. Many newly introduced drugs in clinical practice still lack comprehensive observational data regarding their impact on MM and AF, including immunomodulatory agents, proteasome inhibitors, and HDAC inhibitors. However, studies conducted by Al-Yafeai et al. and Ahmad et al. partially address this knowledge gap [35, 42]. Despite the available data, the risk of AF is often incidentally reported and underappreciated by researchers. It is important to note that although "cardiovascular disease" is a general term used in complication reports of clinical research articles, it encompasses various conditions such as coronary heart disease, heart failure, arrhythmia, and cardiomyopathy that differ significantly in management and prognosis. Therefore, more detailed classification and reporting, similar to high-quality research reports, are necessary.

The risk of AF at each stage of MM management necessitates careful consideration by clinicians regarding its advantages and disadvantages. However, there is a scarcity of evidence available for reference. Despite limited observational studies reporting on the likelihood of developing AF with specific treatment modalities, clinicians often struggle to effectively compare the risks associated with AF against potential clinical benefits, leading to challenges in making rational decisions. The primary risks associated with AF are embolic events and heart failure, both potentially fatal. However, in MM patients, there is lack of in-depth clinical data to elucidate the correlations between AF and these risks. Therefore, dedicated clinical investigations are required to comprehensively analyze the risk and prognosis of AF in MM-specific drug treatments. Moreover, it remains unclear whether aggressive treatment for AF improves outcomes in MM patients who also have AF. While management approaches like catheter ablation and left atrial appendage occlusion have proven effective in enhancing the prognosis of typical AF patients [56], the perioperative risks of embolic events and bleeding, as well as treatment benefits, need to be evaluated specifically in future clinical trials involving MM patients.

Recent studies have attempted to answer the benefits of AF ablation in cancer patients. Analysis based on the United States National Readmissions Database identified the association between active cancer and higher odds of periprocedural complications and all-cause and bleeding-related readmissions in patients undergoing AF ablation [57]. A META analysis showed that cancer survivors

have an increased risk of bleeding after ablation for AF to patients without cancer, with significant difference in the efficacy of ablation for maintenance of sinus rhythm [58]. The impact of cancer activity on ablation timing, and the impact of ablation of long-term prognosis need to be further demonstrated in future large-scale trials.

Abbreviations

MM	Multiple myeloma
IMiDs	Immunomodulatory drugs
PIs	Proteasome inhibitors
ASCT	Autologous hematopoietic stem cell transplantation
AF	Atrial fibrillation
NIS	National Inpatient Sample
OR	Odds ratio
CI	Confidence interval
NHIS	National Health Insurance Service
FDA	Food and Drug Administration
FAERS	Food and Drug Administration Adverse Event Reporting System
HDACs	Histone deacetylase

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Author contributions

TF, YXC and LL were responsible for the writing of the major parts of this review. ZHL and WS took responsibility for retrieving and collecting the related articles. XZ and JY provided ideas for the writing and were responsible for reviewing the quality of the manuscript.

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

All authors have reviewed the manuscript and agreed for publication.

Competing interests

The authors declare that they have no competing interests.

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References

- Sung H, Ferlay J, Siegel RL et al (2021) Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 71(3):209–249
- Kazandjian D (2016) Multiple myeloma epidemiology and survival: a unique malignancy. *Semin Oncol* 43(6):676–681
- Kumar SK, Rajkumar SV, Dispenzieri A et al (2008) Improved survival in multiple myeloma and the impact of novel therapies. *Blood* 111(5):2516–2520
- Schaapveld M, Visser O, Siesling S et al (2010) Improved survival among younger but not among older patients with Multiple Myeloma in

- the Netherlands, a population-based study since 1989. *Eur J Cancer* 46(1):160–169
5. Sverrisdóttir IS, Rögnvaldsson S, Thorsteinsdóttir S et al (2021) Comorbidities in multiple myeloma and implications on survival: a population-based study. *Eur J Haematol* 106(6):774–782
 6. Okwuosa TM, Anzevino S, Rao R (2017) Cardiovascular disease in cancer survivors. *Postgrad Med J* 93(1096):82–90
 7. Plummer C, Driessen C, Szabo Z et al (2019) Management of cardiovascular risk in patients with multiple myeloma. *Blood Cancer J* 9(3):26
 8. Jackson I, Etuk AS, Jackson N (2022) Impact of atrial fibrillation on inpatient outcomes among hospitalized patients with multiple myeloma. *Cureus* 14(5):e25252
 9. Yun JP, Choi EK, Han KD et al (2021) Risk of atrial fibrillation according to cancer type: a nationwide population-based study. *JACC CardioOncol* 3(2):221–232
 10. Khan MZ, Gupta A, Patel K et al (2021) Association of atrial fibrillation and various cancer subtypes. *J Arrhythm* 37(5):1205–1214
 11. Li Y, Tang M, Zhong L et al (2021) Incidence of arrhythmias and their prognostic value in patients with multiple myeloma. *Front Cardiovasc Med* 8:753918
 12. Chinese Hematology Association, Chinese Society of Hematology (2022) Guidelines for the diagnosis and management of multiple myeloma in China (2022 revision). *Zhonghua Nei Ke Za Zhi* 61(5):480–487
 13. Armenian SH, Chow EJ (2014) Cardiovascular disease in survivors of hematopoietic cell transplantation. *Cancer* 120(4):469–479
 14. Bhatia S, Francisco L, Carter A et al (2007) Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: report from the Bone Marrow Transplant Survivor Study. *Blood* 110(10):3784–3792
 15. Majhail NS, Ness KK, Burns LJ et al (2007) Late effects in survivors of Hodgkin and non-Hodgkin lymphoma treated with autologous hematopoietic cell transplantation: a report from the bone marrow transplant survivor study. *Biol Blood Marrow Transplant* 13(10):1153–1159
 16. Tonorezos ES, Stillwell EE, Calloway JJ et al (2015) Arrhythmias in the setting of hematopoietic cell transplants. *Bone Marrow Transplant* 50(9):1212–1216
 17. Sureddi RK, Amani F, Hebbar P et al (2012) Atrial fibrillation following autologous stem cell transplantation in patients with multiple myeloma: incidence and risk factors. *Ther Adv Cardiovasc Dis* 6(6):229–236
 18. Fatema K, Gertz MA, Barnes ME et al (2009) Acute weight gain and diastolic dysfunction as a potent risk complex for post stem cell transplant atrial fibrillation. *Am J Hematol* 84(8):499–503
 19. Child JA, Morgan GJ, Davies FE et al (2003) High-dose chemotherapy with hematopoietic stem-cell rescue for multiple myeloma. *N Engl J Med* 348(19):1875–1883
 20. Bladé J, Rosiñol L, Cibeira MT et al (2010) Hematopoietic stem cell transplantation for multiple myeloma beyond. *Blood* 115(18):3655–3663
 21. Moreau P, Facon T, Attal M et al (2002) Comparison of 200 mg/m² melphalan and 8 Gy total body irradiation plus 140 mg/m² melphalan as conditioning regimens for peripheral blood stem cell transplantation in patients with newly diagnosed multiple myeloma: final analysis of the Intergroupe Francophone du Myélome 9502 randomized trial. *Blood* 99(3):731–735
 22. Moreau P, Milpied N, Mahé VB et al (1999) Melphalan 220 mg/m² followed by peripheral blood stem cell transplantation in 27 patients with advanced multiple myeloma. *Bone Marrow Transplant* 23(10):1003–1006
 23. Spencer A, Horvath N, Gibson J et al (2005) Prospective randomised trial of amifostine cytoprotection in myeloma patients undergoing high-dose melphalan conditioned autologous stem cell transplantation. *Bone Marrow Transplant* 35(10):971–977
 24. Blijlevens N, Sonis S (2007) Palifermin (recombinant keratinocyte growth factor-1): a pleiotropic growth factor with multiple biological activities in preventing chemotherapy- and radiotherapy- induced mucositis. *Ann Oncol* 18(5):817–826
 25. Spielberger R, Stiff P, Bensinger W et al (2004) Palifermin for oral mucositis after intensive therapy for hematologic cancers. *N Engl J Med* 351(25):2590–2598
 26. Abidi MH, Agarwal R, Tajeja N et al (2013) A phase I dose-escalation trial of high-dose melphalan with palifermin for cytoprotection followed by autologous stem cell transplantation for patients with multiple myeloma with normal renal function. *Biol Blood Marrow Transplant* 19(1):56–61
 27. Sirohi B, Powles R, Kulkarni S et al (2001) Glomerular filtration rate prior to high-dose melphalan 200 mg/m² as a surrogate marker of outcome in patients with myeloma. *Br J Cancer* 85(3):325–332
 28. Knudsen LM, Nielsen B, Gimsing P et al (2005) Autologous stem cell transplantation in multiple myeloma: outcome in patients with renal failure. *Eur J Haematol* 75(1):27–33
 29. Badros A, Barlogie B, Siegel E et al (2001) Results of autologous stem cell transplant in multiple myeloma patients with renal failure. *Br J Haematol* 114(4):822–829
 30. Abidi MH, Agarwal R, Ayash L et al (2012) Melphalan 180 mg/m² can be safely administered as conditioning regimen before an autologous stem cell transplantation (ASCT) in multiple myeloma patients with creatinine clearance 60 mL/min/1.73 m² or lower with use of palifermin for cytoprotection: results of a phase I trial. *Biol Blood Marrow Transplant* 18(9):1455–1461
 31. Mileskin LR, Seymour JF, Wolf MM et al (2005) Cardiovascular toxicity is increased, but manageable, during high-dose chemotherapy and autologous peripheral blood stem cell transplantation for patients aged 60 years and older. *Leuk Lymphoma* 46(11):1575–1579
 32. Kumar SK, Rajkumar SV, Dispenzieri A et al (2008) Improved survival in multiple myeloma and the impact of novel therapies. *Blood* 11(5):2516–2520
 33. Rodriguez APG (2011) Management of the adverse effects of lenalidomide in multiple myeloma. *Adv Ther* 28:1–10
 34. Hazarika M, Rock E, Williams G et al (2008) Lenalidomide in combination with dexamethasone for the treatment of multiple myeloma after one prior therapy. *Oncologist* 13(10):1120–1127
 35. Ahmad J, Thurlapati A, Thotamgari S et al (2022) Anti-cancer drugs associated atrial fibrillation—an analysis of real-world pharmacovigilance data. *Front Cardiovasc Med* 9:739044
 36. Magen H, Muchtar E (2016) Elotuzumab: the first approved monoclonal antibody for multiple myeloma treatment. *Ther Adv Hematol* 7(4):187–195
 37. Raedler LA (2016) Ninlaro (Ixazomib): first oral proteasome inhibitor approved for the treatment of patients with relapsed or refractory multiple myeloma. *Am Health Drug Benefits* 9(Spec Feature):102–105
 38. Sanchez L, Wang Y, Siegel DS et al (2016) Daratumumab: a first-in-class CD38 monoclonal antibody for the treatment of multiple myeloma. *J Hematol Oncol* 9(1):51
 39. Laubach JP, Moreau P, San-Miguel JF et al (2015) Panobinostat for the treatment of multiple myeloma. *Clin Cancer Res* 21(21):4767–4773
 40. Offidani M, Corvatta L, Morè S et al (2021) Belantamab mafodotin for the treatment of multiple myeloma: an overview of the clinical efficacy and safety. *Drug Des Devel Ther* 15:2401–2415
 41. Joseph NS, Tai YT, Anderson KC et al (2021) Novel approaches to treating relapsed and refractory multiple myeloma with a focus on recent approvals of belantamab mafodotin and selinexor. *Clin Pharmacol* 13:169–180
 42. Al-Yafeai Z, Ghoweba M, Ananthaneni A et al (2022) Cardiovascular complications of modern multiple myeloma therapy: a pharmacovigilance study. *Br J Clin Pharmacol*. <https://doi.org/10.1111/bcp.15499>
 43. Shah RR (2019) Safety and tolerability of histone deacetylase (HDAC) inhibitors in oncology. *Drug Saf* 42(2):235–245
 44. Arts J, King P, Mariën A et al (2009) JNJ-26481585, a novel “second-generation” oral histone deacetylase inhibitor, shows broad-spectrum preclinical antitumoral activity. *Clin Cancer Res* 15(22):6841–6851
 45. Deleu S, Lemaire M, Arts J et al (2009) The effects of JNJ-26481585, a novel hydroxamate-based histone deacetylase inhibitor, on the development of multiple myeloma in the 5T2MM and 5T33MM murine models. *Leukemia* 23(10):1894–1903
 46. Stühmer T, Arts J, Chatterjee M et al (2010) Preclinical anti-myeloma activity of the novel HDAC-inhibitor JNJ-26481585. *Br J Haematol* 149(4):529–536
 47. Deleu S, Lemaire M, Arts J et al (2009) Bortezomib alone or in combination with the histone deacetylase inhibitor JNJ-26481585: effect on myeloma bone disease in the 5T2MM murine model of myeloma. *Cancer Res* 69(13):5307–5311
 48. Moreau P, Facon T, Touzeau C et al (2016) Quisinstat, bortezomib, and dexamethasone combination therapy for relapsed multiple myeloma. *Leuk Lymphoma* 57(7):1546–1559
 49. Coussens LM, Werb Z (2002) Inflammation and cancer. *Nature* 420(6917):860–867

50. Singh N, Baby D, Rajguru JP et al (2019) Inflammation and cancer. *Ann Afr Med* 18(3):121–126
51. Greten FR, Grivennikov SI (2019) Inflammation and cancer: triggers, mechanisms, and consequences. *Immunity* 51(1):27–41
52. Allan V, Honarbakhsh S, Casas JP et al (2017) Are cardiovascular risk factors also associated with the incidence of atrial fibrillation? A systematic review and field synopsis of 23 factors in 32 population-based cohorts of 20 million participants. *Thromb Haemost* 117(5):837–850
53. Issac TT, Dokainish H, Lakkis NM (2007) Role of inflammation in initiation and perpetuation of atrial fibrillation: a systematic review of the published data. *J Am Coll Cardiol* 50(21):2021–2028
54. Engelman MDM, Svendsen JH (2005) Inflammation in the genesis and perpetuation of atrial fibrillation. *Eur Heart J* 26(20):2083–2092
55. Jakobsen CB, Lamberts M, Carlson N et al (2019) Incidence of atrial fibrillation in different major cancer subtypes: a nationwide population-based 12 year follow up study. *BMC Cancer* 19(1):1105
56. Hindricks G, Potpara T, Dagres N et al (2021) 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): the task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 42(5):373–498
57. Agarwal S, Munir MB, Krishan S et al (2023) Outcomes and readmissions in patients with cancer undergoing catheter ablation for atrial fibrillation. *Europace* 25(9):euad263
58. Costa TA, Felix N, Clemente M et al (2023) Safety and efficacy of catheter ablation for atrial fibrillation in cancer survivors: a systematic review and meta-analysis. *J Interv Card Electrophysiol*. <https://doi.org/10.1007/s10840-023-01677-8>

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