DOACs for Stroke Prevention in Patients with Atrial Fibrillation and Cancer

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Atrial fibrillation (AF) occurs at an increased frequency in patients with cancer, however the link between cancer and AF is not fully understood (1,2). Stroke prophylaxis in AF (SPAF) with oral anti-coagulation is beneficial even in the context of active cancer (3). However, this can prove challenging as cancer can predispose to an increased risk of haemorrhage as well as thrombosis (4). Traditionally warfarin has been used in this setting.

There remains limited evidence for direct oral anticoagulants (DOACs) in cancer patients for SPAF, nonetheless the existing retrospective data is encouraging. The ENGAGE AF-TIMI trial found preserved efficacy and safety of edoxaban compared to warfarin (5), and a subgroup analysis of the ARISTOTLE trial showed superior safety and efficacy of apixaban compared to warfarin (6). At the time of writing, a prospective non-interventional study has also been initiated (7). There have been no significant studies comparing DOACs to low molecular weight heparin (LMWH), which is occasionally used in the clinical setting for patients intolerant of oral anti-coagulation. With a lack of consensus regarding optimal anti-coagulation, there remains highly variable clinical practice, including the prescription of warfarin, LMWH and DOACs. Here we conduct a cross-sectional study on DOAC prescribing in AF and cancer at a single tertiary-care institution.

29 patients with cancer diagnoses receiving DOACs for SPAF were identified. The median age was 78 years (IQR 69-82years) and there was a male preponderance (83%). The mean duration of DOAC therapy was 10.9 months at the time of cross-sectional analysis. DOACs used included apixaban (52%), edoxaban (24%) and rivaroxaban (24%). The median CHA_2DS_2-VASc and HAS-BLED scores were 3 and 2, respectively. There were no embolic strokes/TIAs identified in any patient following commencement of DOAC (Fig 1), including in the 25 high-risk patients (CHA_2DS_2-VASc score$\geq$2). There were no major bleeding events,

as defined by the ISTH (8). 5 patients suffered from non-major bleeding, 4 of whom had gastrointestinal or genitourinary cancer. 9 patients were high-risk for bleeding (HAS-BLED score≥3), none of whom experienced bleeding events.

Our findings show that DOACs for SPAF in cancer can be effective, as evidenced by a lack of both thromboembolic events and major bleeding episodes, including in high-risk patients. Furthermore, non-major bleeding events occurred in patients predominantly with gastrointestinal/genitourinary cancers, which are both associated with a higher bleeding-risk. This was a small observational study from a single institution and the mean duration of DOAC treatment was relatively short. However, while we had limited numbers of patients with limited follow-up, it is likely our local data is reflective of wider UK practice in tertiary cardiology and cancer referral centres.

Cancer is a challenging setting in which to formulate anti-coagulation strategies. Multiple subgroup analyses have demonstrated a promising role for DOACs in SPAF and cancer, however these are difficult to interpret because of exclusion and heterogeneity across cancers. Data from registries and specialist cardio-oncology services like ourselves provide opportunities to fill data gaps, particularly given the heterogeneity of link between cancer and AF. The way forward will require a combination of big data epidemiology studies to look at comorbidity and interaction, and directed trials in particular patient subpopulations, although such trials would require large numbers of patients which may not be feasible.

Importantly, due to the many difficulties associated with active cancer, we believe anti-coagulation still needs to be individualised to provide optimal outcomes, taking into account cancer type, stroke and bleeding-risk, co-morbidities, and ongoing cancer-directed treatment.

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Nil relevant

Figure 1 Title: Distribution of cancer type and associated bleeding/thromboembolic complications in patients taking DOACs for SPAF