Incidence of cardiac-related deaths (CRDs) among patients (pts) aged ≥65 years with B-cell malignancies (BCMs) treated with ibrutinib (ibr)

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Background

Ibr is associated with increased risk of fatal cardiac failure in clinical trials; however, real-world (RW) ibr cardiovascular safety data are limited. We assessed RW incidence of CRD in Medicare beneficiaries with BCM receiving ibr.

Methods

This retrospective study used the deidentified Medicare Fee-for-Service (FFS) database. Pts were included if they initiated ibr between 2017-2021 (National Death Index [NDI] data cutoff), had ≥2 nondrug claims ≥1 day apart for the same qualifying BCM and had ≥12 mo of continuous Medicare enrollment prior to index date of ibr initiation. Pts were followed until earliest of ibr discontinuation, death, end of enrollment/study. Baseline characteristics were summarized using descriptive statistics overall and by BCM group (CLL/SLL, single non-CLL BCM, multiple BCMs). CRD was defined as diagnosis codes for cardiac arrest/sudden cardiac death (CA), atrial fibrillation/flutter (AF), heart failure (HF), myocardial infarction, ventricular fibrillation/flutter, ventricular tachycardia, sudden death, or ischemic stroke listed as cause of death in NDI. Number and proportion of events were summarized. Incidence rate (IR) was estimated as number of events per 1000 person-years (pys) on ibr. Cumulative incidence was estimated at key times, with death from other causes as a competing risk. Age- and sex-adjusted CRD IR was also estimated among general FFS beneficiaries in 2021.

Results

Of 13,241 pts, 10,499 had CLL/SLL, 2,622 had non-CLL BCM, 170 had multiple BCMs. Median age at index was 77.2 years (IQR, 72.2-82.8). Most were male (57.7%) and non-Hispanic White (90.7%). Median baseline NCI comorbidity index was 0.29 (IQR, 0-0.74); most common comorbidities were hypertension (73.6%) and hyperlipidemia (69.2%).

A total of 568 (4.3%) CRDs were identified with an overall IR of 35.2 per 1000 pys (**Table**). Most CRDs were CA (n=243), HF (n=190), or AF (n=148). Median ibr treatment duration was 268 days (IQR, 119-659). In pts with CLL/SLL, median follow-up was 298 days (IQR, 120-718) with most CRDs of CA (n=189; 1.8%), HF (n=147; 1.4%), AF (n=112; 1.1%). Among >16 million general Medicare beneficiaries in 2021, adjusted CRD incidence was 2.1% with an IR of 19.1 per 1000 pys.

Conclusion

In this large RW cohort of pts aged ≥65 years with BCM treated with ibr, the incidence of 35.2 CRDs per 1000 pys on ibr was higher than that observed in the general Medicare population of similar age and sex distribution. Most events occurred in first 6 mo of treatment, with cumulative incidence increasing over the duration of ibr exposure.

During Ibr treatment	Overall	CLL/SLL	Non-CLL BCM
CRD events, n (%)	568 (4.3)	438 (4.2)	>120 (>4.5)
CRD IR per 1000 pys (95% CI)	35.2 (32.4-38.2)	32.3 (29.3-35.5)	50.6 (42-60.4)
Time to event in pts with CRD, median (IQR), days	146.5 (60.5-423.5)	153 (65-456)	135 (47-300)
Cumulative CRD probability, % **Day 180** **Day 365**	 2.7 3.8	 2.6 3.5	 3.3 4.9