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# UK CLL Forum 5 year update on 315 relapsed refractory CLL patients treated with ibrutinib in 66 UK and Ireland centres

UK CLL Forum

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## INTRODUCTION

UK and Ireland clinicians gained non-trial access to ibrutinib for relapsed CLL through a named patient scheme (NPS) for 7 months in 2014, and the UK CLL Forum has been following a cohort of NPS patients treated with ibrutinib at 66 UK and Ireland hospitals. We now update this dataset with up to 5 years follow-up.

## RESULTS 1

Of the original 315 patients, 213 have stopped ibrutinib and 159 patients have died, with all living patients having a survival update in 2019. With 55.6 months median follow-up, median DFS was 33.5 months (95% CI: 28.4–29.3) and median OS was 55.9 months (95% CI: 42.5–N/A). Four years after starting ibrutinib, 37.0% of patients were still taking ibrutinib and 52.4% were alive. Both Discontinuation Free Survival (DFS) and Overall Survival (OS) were inferior for older (age > median) and PS 2+ patients. Patients with 17p- have inferior DFS and OS compared to patients with other defined cytogenetic aberrations (13q-, 11q-, t(12)) and more patients with 17p- compared with non-17p- stopped ibrutinib for progressive CLL (PD) (26.4% vs 18.8%; p=0.01) and Richter's Syndrome (12.1% vs 8.3%; p=0.05).

## RESULTS

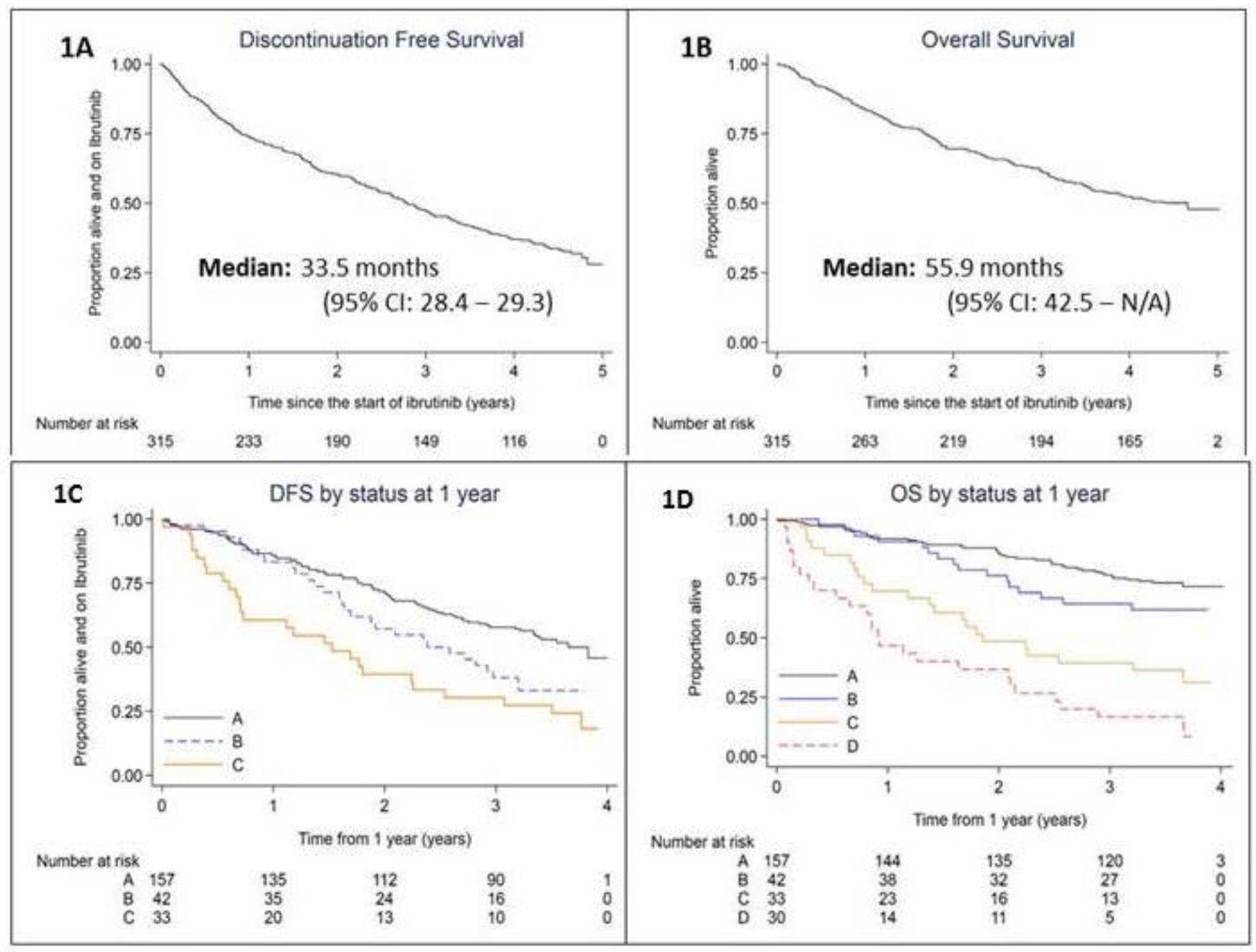


**Figure 1. A:** DFS and **B:** OS of entire cohort from initiation of ibrutinib treatment. **C:** DFS and **D:** OS from the end of year 1 ibrutinib therapy (**A:** No first year dose reductions or breaks, **B:** first year dose reductions but no breaks, **C:** Breaks>14 days but back on ibrutinib by the end of year 1, **D:** Permanently stopped ibrutinib by the end of year 1, but alive

## RESULTS 2

First relapse patients had more than a 3 fold lower rate of ibrutinib discontinuation due to CLL progression (7.1% versus 24.5%; two-tailed Fisher's exact test; p=0.001) compared with patients receiving ibrutinib at later lines of therapy, although DFS and OS for these groups were similar. With multivariable analysis of pre-treatment factors, older age, PS2+, 17p- and >1 prior line of therapy retained significance for earlier ibrutinib discontinuation and age, PS2+ and 17p- associated with inferior OS.

To analyze any potential impact of reduced ibrutinib dosing during the first year of therapy, we originally classified all patients alive at 12 months into 4 groups, depending on first-year ibrutinib treatment. *Group A*: No dose reductions or breaks >14 days; *Group B*: Dose reductions, but no breaks > 14 days; *Group C*: Breaks > 14 days but back on ibrutinib by 1 year; *Group D*: stopped ibrutinib permanently but still alive at 1 year. With extended follow-up, groups A and B retain similar DFS and OS initially, although beyond 2 years the curves separate (DFS HR: 1.62 (1.05–2.50), OS HR: 1.52 (0.86–2.70)). Interestingly, the dose-reduced group do not have a higher incidence of disease progression, (PD A:24.8%, PD B:23.8%), but have a higher chance of discontinuation for all non-PD causes (A:23.6%, B:42.9%). Patients from groups C and D had significantly impaired OS compared with group A, with 4 year OS 39.4% and 16.7% respectively compared with 76.4% for group A (p<0.001).

## RESULTS 3

Considering all patients who discontinued ibrutinib, stopping for AEs decreased over time (year 1: 57%, 2: 53%, 3: 30%, 4: 21%). The risk of stopping ibrutinib due to PD-CLL increases with time (year 1: 11%, 2: 18.6%, 3: 42.5%, 4: 57.6%). Of the PD-CLL patients, treatment with venetoclax had the best OS (n=43; 1 year OS: 77.5%) compared with the 7 treated with rituximab / idelalisib (1 year OS: 42.9%) and 14 treated with other palliative strategies (1 year OS: 10%).

## CONCLUSIONS

With approaching 5 years of follow-up, around one third of real-world UK / Ireland patients treated with ibrutinib for relapsed CLL remain on ibrutinib. Our data suggest that younger, better performance status patients who have had fewer prior lines of therapy and no evidence of 17p deletion seem most likely to remain on ibrutinib long-term. Treatment of PD-CLL with venetoclax post ibrutinib shows encouraging results.

## CONTACT INFORMATION

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