

## **Ibrutinib for relapsed/refractory chronic lymphocytic leukemia: a UK and Ireland analysis of outcomes in 315 patients**

**UK CLL Forum**

©2016 Ferrata Storti Foundation. This is an open-access paper. doi:10.3324/haematol.2016.147900

Received: April 15, 2016.

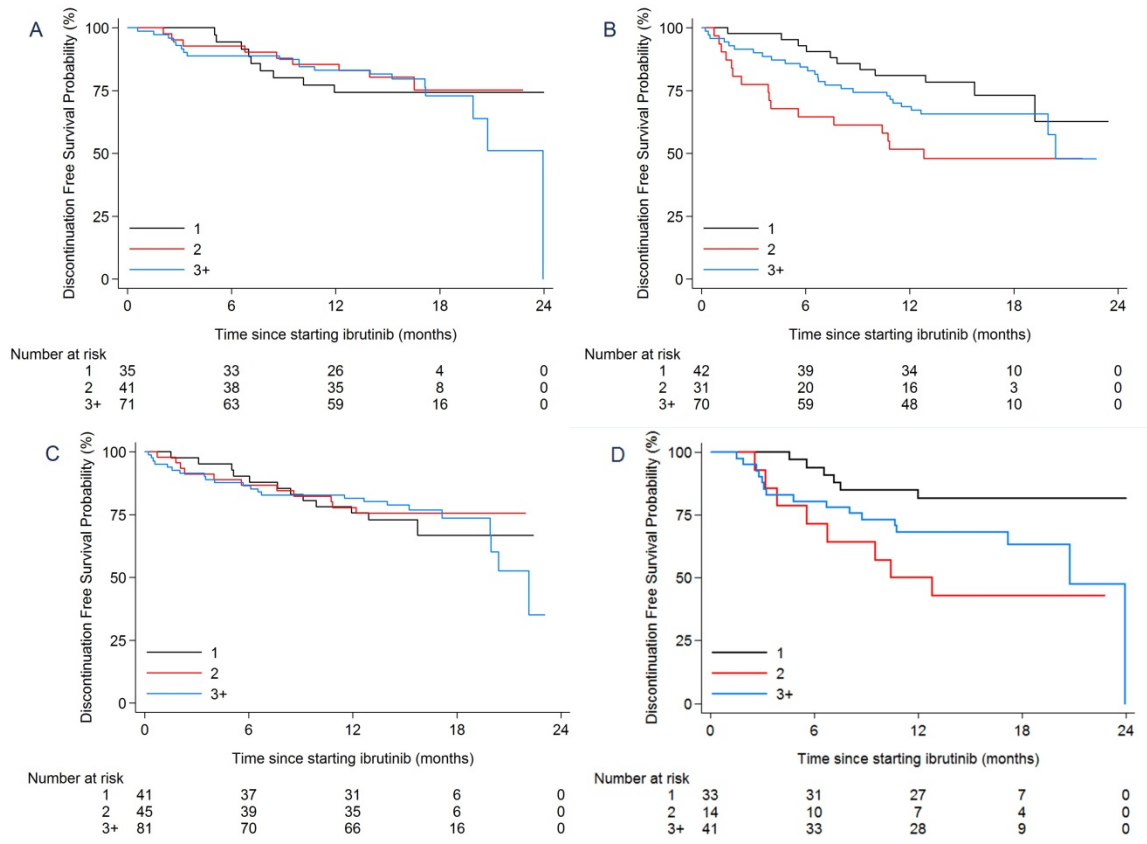
Accepted: October 10, 2016.

Pre-published: October 18, 2016.

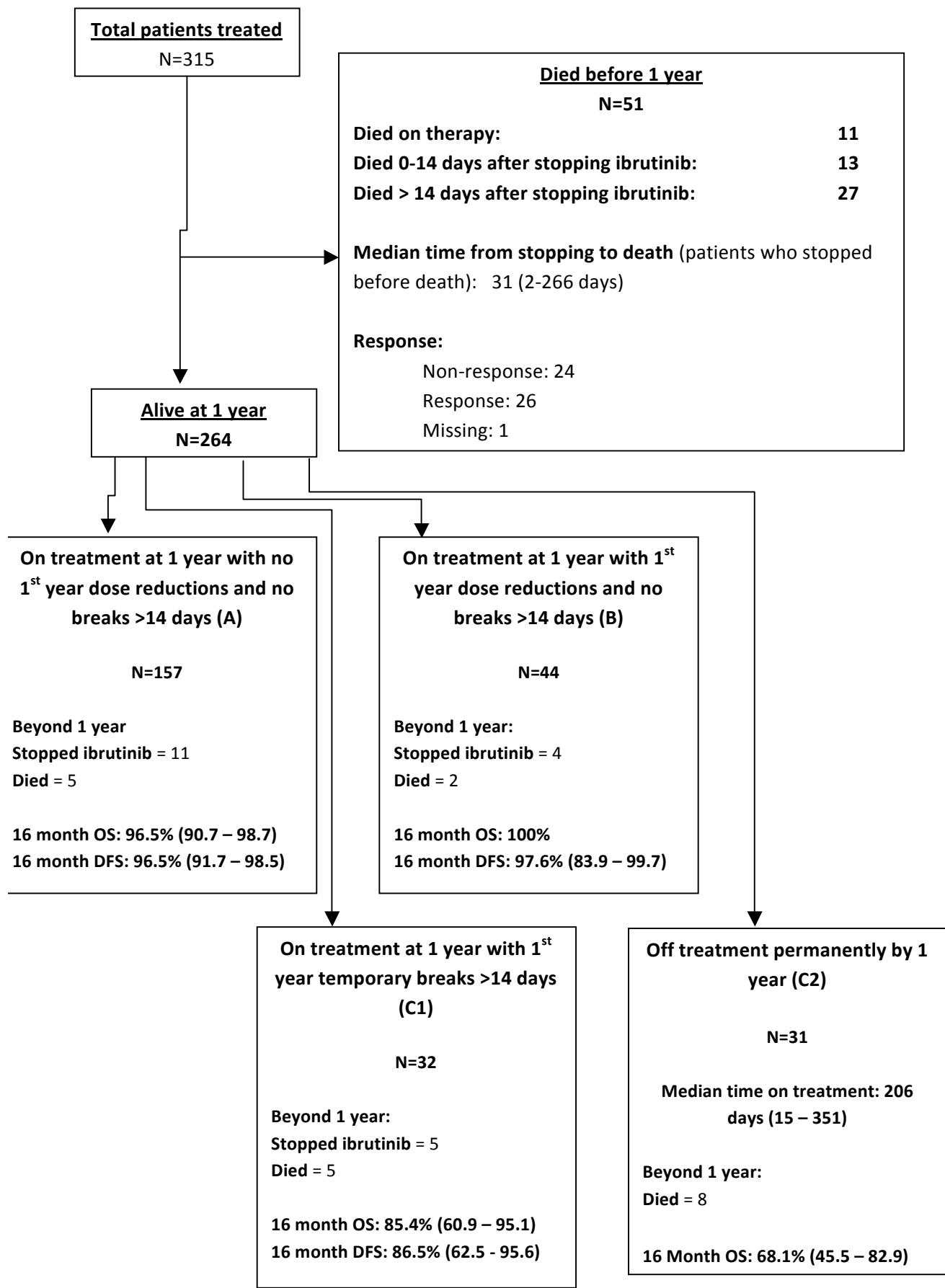
Correspondence: [george.follows@addenbrookes.nhs.uk](mailto:george.follows@addenbrookes.nhs.uk)

---

## Supplementary Figures



**Supplementary Figure 1:** Kaplan-meier plots of DFS for (A) patients equal to or younger than the median age and (B) patients older than the median age and (C) patients without 17p deletion and (D) patients with 17p deletion stratified by the number of prior lines of therapy



**Supplementary Figure 2.** Flow chart detailing the patient numbers in groups A through C2 up to 1 year and beyond to 16 months median follow-up

## **Supplementary Tables**

Question theme	Specific Questions
<b>Demographics</b>	Hospital / Sex / age or DoB / number in this series
<b>Patient characteristics</b>	Number of prior lines / performance status pre-ibrutinib
<b>CLL Characteristics</b>	Known FISH profile
<b>Ibrutinib dates</b>	Start date for ibrutinib / Still on ibrutinib at one year? / Stop date for ibrutinib  Is your patient still on ibrutinib at most recent review?
<b>Ibrutinib dosing</b>	Any dose reductions or stopping in first year?  Reasons for dose reductions / stopping  Maximal duration of ibrutinib withdrawal  Maximal dose reduction  Was ibrutinib stopped permanently because of an adverse event (AE)?
<b>Adverse events</b>	Any clinically significant AE possibly related to ibrutinib
<b>Response assessments</b>	Best clinical response  Overall, did / does your patient feel their QoL was / is better since ibrutinib therapy?
<b>Transformation</b>	Any clinical suspicion for Richter's transformation?  Any biopsy evidence of Richter's transformation?
<b>On-going assessments</b>	Date of most recent review / confirmation of status / Date of death

**Supplementary Table 1.** Ibrutinib service evaluation questionnaire

Hospital	Number of patients contributed	Clinician (s)
Southampton	22	F Forconi, AS Duncombe
Cambridge	20	GA Follows, I Ringshausen
Oxford	20	A Schuh, TA Eyre
Royal Marsden	19	S Iyengar, C Dearden
Nottingham	14	CP Fox, H Knight
James Paget, Gt Yarmouth	12	S Sadullah
UCLH, London	11	K Cwynarski, B von Barsewisch
Truro RCHT	10	R Noble, J Blundell
Edinburgh	10	F Scott
Norwich	10	KM Bowles
Leicester	9	DBJ Kennedy, S Wagner, MJS Dyer, C Balotis
Leeds	9	P Hillmen, T Munir
Birmingham Heartlands	8	S Paneesha
Taunton	7	M Ewings
Christie, Manchester	7	A Bloor
Newcastle	7	J Wallis
Dublin SJH	6	E Vandenberghe
Colchester	6	M Hamblin, G Campbell
KCH, London	6	PEM Patton, S Devereux
Wexham Park	6	N Bienz
Derriford, Plymouth	6	C Hutchinson, S Rule, D Tucker
Ipswich	5	A Hodson, I Whalley
Barts, London	5	SG Agrawal, J Gribben
Worthing	5	S Narat
The London Clinic	4	J Gribben, R Marcus
West Wales	4	P Cumber
GSTT, London	4	PEM Patten
Altnagelvin	4	F McNichol
University Hospital, Birmingham	3	H Parry, G Pratt, P Moss
Southend	3	M Badat, P Cervi
Sheffield RHS	3	N Morley
Beaumont, Dublin	3	P Thornton
Cardiff	3	C Fegan
RFH	3	E Kumar
West Sussex SRH	3	S Janes, S Narat
RHCH	3	J Arnold
Cork	3	S Glavey
Sandwell and BMH	2	RJA Murrin

<b>Russell Hall</b>	1	J Neilson
<b>Basildon</b>	2	P Jasani
<b>Ayr</b>	2	P Micallef-Eynaud
<b>North Tyneside</b>	2	C Williams, J Allen
<b>Princess Royal University Hosp</b>	2	C De Lord, S Bowcock
<b>Forth Valley</b>	2	R Boulton-Jones
<b>Doncaster</b>	2	S Kaul, S Sorour
<b>Wolverhampton</b>	2	A Jacob
<b>Drogheda</b>	1	S Glavey
<b>Worcester</b>	1	E Maughan
<b>Basingstoke</b>	1	AE Milne
<b>Mater, Dublin</b>	1	S Glavey
<b>Kent and Canterbury</b>	1	C Pocock
<b>West Suffolk Hospital</b>	1	M Karanth
<b>Limerick</b>	1	S Glavey
<b>North Bristol</b>	1	AJ Whiteway
<b>Nevill Hall</b>	1	N Parry-Jones
<b>Beatson, Glasgow</b>	1	N Leach
<b>Sunderland</b>	1	S Marshall
<b>Withybush Hospital, Wales</b>	1	S Kundu
<b>Hexham</b>	1	C Williams, J Allen
<b>East Surrey/Crawley</b>	1	P Kaczmarek
<b>Lewisham</b>	1	S Updyke, N Mir

**Supplementary Table 2.** Contributing Hospitals with Lead Clinicians and patient numbers

				HR(95% CI)	P-value
<b>Discontinuation Free Survival</b>					
<b>Older age</b>					
	1 prior line			0.75 (0.30 – 1.86)	0.53
	2 prior lines			4.50 (1.90 – 10.63)	0.001
	3+ prior lines			1.71 (0.60 – 2.64)	0.26
<b>17p</b>					
	1 prior line			0.48 (0.15 – 1.54)	0.22
	2 prior lines			4.00 (1.48 – 10.84)	0.006
	3+ prior lines			1.71 (0.88 – 3.33)	0.12
<b>Prior lines</b>					
	2 prior lines	Younger age	No 17p	0.34 (0.10 – 1.13)	0.08
	2 prior lines	Younger age	17p	2.84 (0.72 – 11.24)	0.14
	2 prior lines	Older age	No 17p	2.03 (0.78 – 5.32)	0.15
	2 prior lines	Older age	17p	17.04 (4.16 – 69.79)	<0.001
	3+ prior lines	Younger age	No 17p	0.64 (0.24 – 1.72)	0.38
	3+ prior lines	Younger age	17p	2.29 (0.67 – 7.75)	0.19
	3+ prior lines	Older age	No 17p	1.21 (0.50 – 2.91)	0.67
	3+ prior lines	Older age	17p	4.34 (1.27 – 14.83)	0.019
<b>PS 2+</b>				2.40 (1.51 – 3.82)	<0.0001
<b>Overall survival</b>					
<b>Older age</b>					
	1 prior line			0.68 (0.25 – 1.90)	0.47
	2 prior lines			2.00 (0.74 – 5.41)	0.17
	3+ prior lines			1.76 (0.85 – 3.64)	0.13
<b>17p</b>					
	1 prior line			0.48 (0.13 – 1.81)	0.28
	2 prior lines			2.69 (0.75 – 9.72)	0.13
	3+ prior lines			1.82 (0.84 – 3.92)	0.13
<b>Prior lines</b>					
	2 prior lines	Younger age	No 17p	0.40 (0.10 – 1.49)	0.17
	2 prior lines	Younger age	17p	2.22 (0.43 – 11.31)	0.34
	2 prior lines	Older age	No 17p	1.15 (0.36 – 3.68)	0.81
	2 prior lines	Older age	17p	6.47 (1.17 – 35.81)	0.033
	3+ prior lines	Younger age	No 17p	0.45 (0.14 – 1.43)	0.18
	3+ prior lines	Younger age	17p	1.71 (0.41 – 7.23)	0.46
	3+ prior lines	Older age	No 17p	1.16 (0.43 – 3.14)	0.77
	3+ prior lines	Older age	17p	4.39 (1.10 – 17.49)	0.036
<b>PS 2+</b>				2.58 (1.52 – 4.38)	<0.001

**Supplementary Table 3.** All HRs taken from a model which included Age, 17p, prior lines, PS and interaction terms for age and prior lines and 17p and prior lines. 17p was included with 3 categories; no 17p deletion, 17p deletion and unknown. Unknown had been omitted from the table as we are unable to draw any conclusions from this group.