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Contemporary Real-world Treatment Patterns of Chronic Lymphocytic Leukaemia (CLL) in England

B. T. Blak [1], S. Hori [1*], K. Lock [1], C. Livings [1], C. Chen [2] and A. SM. Yong [1]*

*Joint first-authors

1 AstraZeneca, Luton, United Kingdom

2 Health Data Insight CIC, Cambridge, United Kingdom

AstraZeneca

simulacrum

INTRODUCTION

- CLL is the most common type of adult Leukaemia in the Western world, with a male predominance and a median age at diagnosis of 70 years[1]
- Presentation and clinical course of CLL is highly variable, ranging from asymptomatic, indolent disease that may never require therapy to active disease with B-symptoms, fatigue, recurrent infections, autoimmune complications and progressive lymphocytosis[2]
- Novel targeted inhibitors of B-cell receptor signalling (such as Bruton's tyrosine kinase and isoform-selective phosphatidylinositol 3-kinase inhibitors) and anti-apoptotic molecule BCL-2 (BCL2 antagonists) have emerged as important therapeutic options for treatment of patients with CLL over the last decade[3]
- With expanding choice of therapies, the understanding of real-world treatment patterns of CLL would be of considerable interest

AIM

- To investigate the patient characteristics and treatment patterns of CLL in England using Public Health England's (PHE) national cancer registration and analysis service (NCRAS)

METHOD

- Patients in England with a diagnosis of CLL (International Classification of Diseases 10: C911) and first recorded systemic treatment between 1st July 2014 and 31st March 2018 were included from NCRAS
- The earliest recorded date of CLL diagnosis allowed in this study was 2001, which had to occur on or prior to the first recorded systemic treatment
- Combination therapies were identified by overlapping cycle dates of individual drugs
- Study feasibility and methodology were supported by The Simulacrum[4] (a synthetic version of NCRAS) which was then applied by PHE to NCRAS data
- Statistical analysis was performed using R (v3) and only full anonymous aggregate results were released
- A potential limitation of our methodology is that the Systemic Anti-Cancer Therapy (SACT) dataset collection commenced in 2012, therefore patients' first recorded treatment may not necessarily be their first ever treatment received. The majority of the study patients however had their CLL diagnosed from 2011 onwards

RESULTS

- In total, 4095 patients were included with around 3/4 having their diagnosis recorded in 2011 onwards
- The median time from CLL diagnosis to first recorded systemic treatment was 2.5 years (IQR: 0.6-5.4) (table), which is likely to be reflective of the initial 'watch and wait' period in this group of patients
- FCR and BR were the two most frequently used treatment modalities for CLL patients with a mean age at the start of treatment of 62 and 71 years, respectively
- 12% of patients received Ibrutinib with a median time from diagnosis to treatment of 5.2 years (IQR: 2.4-8.0). This may, in part, be influenced by the restricted reimbursement conditions of Ibrutinib in England
- Chlorambucil-based combinations were found to be preferentially used in older patient groups with worse performance scores

First recorded treatment*	Number (%)	Mean age at first treatment, years (SD)	Number of males (%)	Performance Status (PS) at first treatment, number (%)	Median time from diagnosis to first treatment, years (IQR)
All	4095 (100)	71.0 (10.4)	2752 (67)	PS 0-1: 2532 (61) PS ≥ 2: 301 (8) Missing: 1262 (31)	2.5 (0.6; 5.4)
Fludarabine/ Cyclophosphamide/ Rituximab (FCR)	740 (18)	62.3 (8.5)	522 (71)	PS 0-1: 503 (68) PS ≥ 2: 11 (1) Missing: 226 (31)	1.6 (0.3; 4.1)
Bendamustine/ Rituximab (BR)	725 (18)	71.2 (7.1)	508 (70)	PS 0-1: 467 (64) PS ≥ 2: 40 (6) Missing: 218 (30)	2.3 (0.5; 5.3)
Trial	516 (13)	65.9 (10.1)	373 (72)	PS 0-1: 381 (74) PS ≥ 2: 7 (1) Missing: 128 (25)	2.0 (0.5; 4.6)
Ibrutinib	506 (12)	71.4 (9.4)	327 (65)	PS 0-1: 310 (61) PS ≥ 2: 48 (9) Missing: 148 (29)	5.2 (2.4; 8.0)
Chlorambucil/ Obinutuzumab	329 (8)	76.5 (6.5)	211 (64)	PS 0-1: 222 (67) PS ≥ 2: 36 (11) Missing: 71 (22)	2.3 (0.6; 4.4)
Chlorambucil/ Rituximab	308 (8)	79.7 (6.5)	179 (58)	PS 0-1:166 (54) PS ≥ 2: 34 (11) Missing: 108 (35)	2.5 (0.5; 6.4)
Chlorambucil	270 (7)	82.4 (6.6)	154 (57)	PS 0-1: 101 (37) PS ≥ 2: 70 (26) Missing: 99 (37)	2.6 (0.7; 5.5)
Other**	230 (6)	71.1 (9.8)	156 (68)	PS 0-1: 122 (53) PS ≥ 2: 16 (7) Missing: 92 (40)	2.2 (0.3; 5.2)
Rituximab	198 (5)	72.8 (12.0)	139 (70)	PS 0-1: 102 (52) PS ≥ 2: 17 (9) Missing: 79 (40)	2.6 (0.7; 5.3)
Chlorambucil/ Ofatumumab	84 (2)	77.5 (7.0)	49 (58)	PS 0-1: 47 (56) PS ≥ 2: 10 (12) Missing: 27 (32)	2.2 (0.5; 4.3)
Idelalisib/ Rituximab	83 (2)	73.7 (9.1)	57 (69)	PS 0-1: 55 (67) PS ≥ 2: 7 (8) Missing: 21 (25)	4.2 (1.2; 6.8)

Table. First recorded systemic treatments and characteristics of CLL patients in England (n ≥50) between 2014-2018

*Following treatments had less than 50 patients: Alemtuzumab monotherapy, Bendamustine monotherapy, Idelalisib monotherapy, Obinutuzumab monotherapy, Ofatumumab monotherapy, Venetoclax monotherapy use not supported by the Cancer Drugs Fund (CDF), Fludarabine + Cyclophosphamide, Ibrutinib + Rituximab. Compounds supported by the CDF were excluded. ** Includes rare treatments. SD: Standard Deviation. IQR: Inter-quartile range

CONCLUSION

- Despite the emergence of novel targeted agents, chemo-immunotherapies (FCR / BR) continues to be the most commonly used treatment modality of choice
- The relative low usage of ibrutinib in England may, in part, be due to the restricted reimbursement conditions of this agent to high-risk CLL patients in first-line setting

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CONTACT INFORMATION

Corresponding author: **Satoshi Hori**

Satoshi.Hori@astrazeneca.com