ASH 2021 Comes to You!

February 2, 2022

11:30 AM PT, 12:30 PM MT, 1:30 PM CT, 2:30 PM ET
Speakers

Welcome
Robyn Brumble, MSN, RN
Director of Scientific Affairs and Research
CLL Society

Brian Koffman, MDCM (retired) MS Ed
Executive Vice President and Chief Medical Officer
CLL Society

Anthony Mato, MD, MSCE
Director, CLL Program
Memorial Sloan Kettering Cancer Center
ASH 2021
Update: CLL
Anthony Mato, MD MSCE
MSKCC
CLL Program
Leukemia Service
New York, NY
Front Line CLL
Long term results of A041202 show continued advantage of ibrutinib-based regimens compared with bendamustine plus rituximab chemoimmunotherapy

Jennifer A. Woyach, MD, Amy S. Ruppert, PhD, Nyla A. Heerema, PhD, Weiqiang Zhao, MD, PhD, Allison M Booth, Wei Ding, MD, PhD, Nancy L. Bartlett, MD, Danielle M. Brander, MD, Paul M. Barr, MD, Kerry Rogers, MD, Sameer A. Parikh, MD, Steven Coutre, MD, Gerard Lozanski, MD, Sreenivasa Nattam, MD, Richard A. Larson, MD, Harry P. Erba, MD, PhD, Mark R. Litzow, MD, James S. Blachly, MD, Carolyn Owen, MD, Charles Kuzma, Jeremy S. Abramson, MD, Jennifer R Brown, MD, PhD, Richard F. Little, MD, MPH, Scott E. Smith, MD, PhD, Richard M. Stone, MD, Sumithra J Mandrekar, PhD and John C. Byrd, MD
Untreated patients age ≥ 65 who meet IWCLL criteria for CLL treatment

Stratify*

Stratification
- High risk vs intermediate risk Rai Stage
- Presence vs absence of del(11q22.3) or del(17p13.1) on FISH performed locally
- < 20% vs ≥ 20% Zap-70 methylation of CpG 3 performed centrally

PRE-REGISTER

RANDOMIZE

Bendamustine 90mg/m² days 1&2 of each 28 day cycle + Rituximab 375 mg/m² day 0 cycle 1, then 500 mg/m² day 1 cycles 2-6

Crossover at progression

Ibrutinib 420mg daily until disease progression

Ibrutinib 420mg daily until disease progression + Rituximab 375 mg/m² weekly for 4 weeks starting cycle 2 day 1, then day 1 of cycles 3-6
### Pairwise Comparisons

**I vs BR:**
- Hazard Ratio: 0.36
- 95% CI: 0.26-0.52
- P <0.0001

**IR vs BR:**
- Hazard Ratio: 0.36
- 95% CI: 0.25-0.51
- P <0.0001

**IR vs I:**
- Hazard Ratio: 0.99
- 95% CI: 0.66-1.48
- P = 0.96

### Progression-free Survival

#### Patients-at-Risk

<table>
<thead>
<tr>
<th>Arm</th>
<th>Patients-at-Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm 1 (BR)</td>
<td>183 139 114 87 63 20 1 0</td>
</tr>
<tr>
<td>Arm 2 (I)</td>
<td>182 158 142 131 114 52 4 0</td>
</tr>
<tr>
<td>Arm 3 (IR)</td>
<td>182 156 142 130 117 44 2 0</td>
</tr>
</tbody>
</table>

### Median follow-up:
- 55 months
Interaction: Treatment Group and TP53 Abnormalities

### Treatment Effect

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>I/IR vs BR</td>
<td>0.39</td>
<td>0.27-0.55</td>
</tr>
<tr>
<td>No TP53 Abn</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TP53 Abn</td>
<td>0.07</td>
<td>0.03-0.18</td>
</tr>
</tbody>
</table>

Interaction P = 0.0006
Notable Adverse Events: Atrial Fibrillation/Flutter

All Grades

<table>
<thead>
<tr>
<th>Arm</th>
<th>Events/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR</td>
<td>6/176</td>
</tr>
<tr>
<td>IBR</td>
<td>69/361</td>
</tr>
</tbody>
</table>

Grades 3+

<table>
<thead>
<tr>
<th>Arm</th>
<th>Events/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR</td>
<td>5/176</td>
</tr>
<tr>
<td>IBR</td>
<td>30/361</td>
</tr>
</tbody>
</table>

Patients-at-Risk

| BR    | 176 155 149 146 131 123 115 111 104 |
| IBR   | 361 327 306 298 281 267 257 247 238 |

| BR    | 176 156 150 147 132 124 116 112 105 |
| IBR   | 361 337 320 313 302 289 283 276 269 |
Notable Adverse Events: Hypertension
New or Worsening

All Grades

Grades 3+

Patients - at-Risk

Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
     | Events/Total | IBR | 202  | 361  |     |     |     |    |    |    |    |

Censor

Arm  | Events/Total | BR  | 47   | 176  |
     | Events/Total | IBR | 220  |

Patients - at-Risk

Arm  | Events/Total | BR  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
     | Events/Total | IBR | 202  |

Censor

Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
     | Events/Total | IBR | 202  |

Censor

Arm  | Events/Total | BR  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
     | Events/Total | IBR | 202  |

Censor

Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
     | Events/Total | IBR | 202  |

Censor

Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
     | Events/Total | IBR | 202  |

Censor

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     | Events/Total | IBR | 202  |

Censor

Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
     | Events/Total | IBR | 202  |

Censor

Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
     | Events/Total | IBR | 202  |

Censor

Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
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Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
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Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
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Censor

Arm  | Events/Total | BR  | 176  | 119  | 113  | 111  | 101  | 97  | 90  | 86  | 77  |
     | Events/Total | IBR | 202  |

Censor
Ibrutinib Plus Rituximab Is Superior to FCR in Previously Untreated CLL: Results of the Phase III NCRI Flair Trial

Peter Hillmen, Alexandra Pitchford, Adrian Bloor, Angus Broom, Moya Young, Ben Kennedy, Renata Walewska, Michelle Furtado, Gavin Preston, Jeffrey R. Neilson, Nicholas Pemberton, Gamal Sidra, Nicholas Morley, Kate Cwynarski, Anna Schuh, Francesco Forconi, Nagah Elmusharaf, Shankara Paneesha, Christopher P. Fox, Dena Howard, Anna Hockaday, David Cairns, Sharon Jackson, Natasha Greateorex, Piers EM Patten, David Allsup and Talha Munir

Abstract No: 642, Oral Presentation, ASH Annual Meeting
Monday, December 13th 2021
Front-line trial for patients fit for FCR: NCRI Flair Trial

Front Line therapy in CLL: Assessment of Ibrutinib plus Rituximab

Patients with CLL requiring therapy by IWCLL Criteria (n=771)

F Oral Fludarabine (24mg/m²/day x 5 days; C1-6)
C Oral Cyclophosphamide (150mg/m²/days x 5 days; C1-6)
R Intravenous Rituximab (375mg/m² C1; 500mg/m²; C2-6)

6 monthly pb MRD until positive x3

Primary end-point:
To assess whether IR is superior to FCR in terms of PFS

Key secondary end-points:
Overall survival
Response including MRD
Safety and toxicity

Key Inclusion Criteria:
• Previously untreated CLL requiring therapy by IWCLL criteria
• Considered fit for FCR
• ≤75 years old

Key Exclusion Criteria:
Prior therapy for CLL; History of Richter’s transformation;
>20% TP53 deletion by FISH; Concomitant warfarin (or equivalent)
Symptomatic cardiac failure or angina

Hillmen et al., Abstract 642, ASH 2021
Primary end-point: Progression Free Survival

Median FU 52.7 months

Median PFS [95% CI]
- FCR: 66.53, [62.72, NR]
- IR: Median PFS NR

HR: 0.44 [0.32, 0.60], p-value: <0.001

Number at risk (number censored)

<table>
<thead>
<tr>
<th></th>
<th>Months from randomisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCR</td>
<td>386 (0) 363 (9) 324 (22) 254 (63) 171 (125) 76 (203) 6 (261)</td>
</tr>
<tr>
<td>IR</td>
<td>386 (0) 374 (5) 353 (11) 291 (58) 193 (145) 88 (244) 11 (316)</td>
</tr>
</tbody>
</table>

Data-lock: 24th May 2021

Hillmen et al., Abstract 642, ASH 2021
SEQUOIA: RESULTS OF A PHASE 3 RANDOMIZED STUDY OF ZANUBRUTINIB VERSUS BENDAMUSTINE + RITUXIMAB IN PATIENTS WITH TREATMENT-NAIVE CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA

Constantine S. Tam, MBBS, MD;1,2,3,4 Krzysztof Giannopoulos, MD, PhD;5,6 Wojciech Jurczak, MD, PhD;7 Martin Šimkovič, MD, PhD;8 Mazyar Shadman, MD, MPH;9,10,11 Anders Österborg, MD, PhD;12,13 Luca Laurenti, MD;14 Patricia Walker, MBBS, BMedSci, FRACP, FRCPA;15 Stephen Opat, MBBS (Hons), FRACP, FRCPA;16,17 Henry Chan, MBChB, FRACP, FRCPA;18 Hanna Ciepuch, MD, PhD;19 Richard Greil, MD;20,21,22 Monica Tani, MD;23 Marek Trněný, MD;24 Danielle M. Brander, MD;25 Ian W. Flinn, MD, PhD;26 Sebastian Grosicki, MD, PhD;27 Emma Verner, MBBS, BMedSci, FRACP, FRCPA;28,29 Jennifer R. Brown MD, PhD;30 Brad S. Kahl, MD;31 Paolo Ghia, MD, PhD;32 Jianyong Li, MD, PhD;33 Tian Tian, PhD;34 Lei Zhou, PhD;34 Carol Marimpietri34; Jason C. Paik, MD, PhD;34 Aileen Cohen, MD, PhD;34 Jane Huang, MD;34 Tadeusz Robak, MD, PhD;35 and Peter Hillmen, MBChB, PhD;36

1Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; 2University of Melbourne, Parkville, Victoria, Australia; 3St Vincent’s Hospital Melbourne, Fitzroy, Victoria, Australia; 4Royal Melbourne Hospital, Parkville, Victoria, Australia; 5Experimental Hematooncology Department, Medical University of Lublin, Lublin, Poland; 6Hematology Department, St. John’s Cancer Centre, Lublin, Poland; 7Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; 8Fourth Department of Internal Medicine - Haematology, University Hospital, Hradec Kralove, Czech Republic; 9Faculty of Medicine, Charles University, Prague, Czech Republic; 10Fred Hutchinson Cancer Research Center, Seattle, WA, USA; 11Department of Medicine, University of Washington, Seattle, WA, USA; 12Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden; 13Department of Hematology, Karolinska University Hospital, Stockholm, Sweden; 14 Fondazione Policlinico Universitario A Gemelli UCSC, Rome, Italy; 15Peninsula Private Hospital, Frankston, Victoria, Australia; 16Monash Health, Clayton, Victoria, Australia; 17Monash University, Clayton, Victoria, Australia; 18 North Shore Hospital, Auckland, New Zealand; 19Copernicus Regional Oncology Center, Gdańsk, Poland; 20Third Medical Department with Hematology, Medical Oncology, Rheumatology and Infectology, Paracelsus Medical University, Salzburg, Austria; 21Salzburg Cancer Research Institute (SCRI) Center for Clinical Cancer and Immunology Trials (CCCIT), Salzburg, Austria; 22Cancer Cluster Salzburg (CCS), Salzburg, Austria; 23Hematology Unit, Santa Maria delle Croci Hospital, Ravenna, Italy; 24First Department of Medicine, First Faculty of Medicine, Charles University, General Hospital, Prague, Czech Republic; 25Hematologic Malignancies and Cellular Therapy, Duke University School of Medicine, Durham, NC, USA; 26Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; 27Department of Hematology and Cancer Prevention, Health Sciences Faculty, Medical University of Silesia, Katowice, Poland; 28Concord Repatriation General Hospital, Concord, New South Wales, Australia; 29University of Sydney, Sydney, New South Wales, Australia; 30 Dana-Farber Cancer Institute, Boston, MA, USA; 31Washington University School of Medicine, St Louis, MO, USA; 32Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milano, Italy; 33Department of Hematology, The First Affiliated Hospital of Nanjing Medical University, Jiansu Province Hospital, Nanjing, China; 34BeiGene (Beijing) Co., Ltd., Beijing, China and BeiGene USA Inc., San Mateo, CA, USA; 35Medical University of Lodz, Lodz, Poland; and 36St James’s University Hospital, Leeds, United Kingdom

Sunday, December 12, 2021

642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological I
**SEQUOIA (BGB-3111-304)**

**Study Design**

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**Key Eligibility Criteria**

- Untreated CLL/SLL
- Met iwCLL criteria for treatment
- ≥65 y of age OR unsuitable for treatment with FCR<sup>a</sup>
- Anticoagulation and CYP3A inhibitors allowed

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**ClinicalTrials.gov: NCT03336333**

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**Stratification Factors**

- Age, Binet stage, IGHV status, geographic region

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**Arm A: Zanubrutinib**

160 mg bid until PD, intolerable toxicity, or end of study

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**Arm B:**

- **Bendamustine** (90 mg/m<sup>2</sup> D1 & D2)
- **+ Rituximab** (375 mg/m<sup>2</sup> C1, then 500 mg/m<sup>2</sup> C2-C6) x 6 cycles

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**Arm C: Zanubrutinib**

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**Arm D: Zanubrutinib + Venetoclax**

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Progression-Free Survival Per IRC Assessment

- BR, bendamustine + rituximab
- IRC, independent review committee
- PFS, progression-free survival

24-mo PFS
- Zanubrutinib: 85.5% (95% CI, 80.1–89.6)
- BR: 69.5% (95% CI, 62.4–75.5)

Hazard ratio: 0.42 (95% CI, 0.27–0.63); 2-sided P<0.0001

No. of patients at risk
- Zanubrutinib: 241, 237, 230, 224, 222, 214, 208, 195, 123, 79, 31, 17, 2, 1, 0
- BR: 238, 218, 210, 200, 187, 176, 164, 150, 89, 54, 20, 8, 1, 0

BR, bendamustine + rituximab; IRC, independent review committee; PFS, progression-free survival.
A RANDOMIZED PHASE III STUDY OF VENETOCLAX-BASED TIME-LIMITED COMBINATION TREATMENTS (RVE, GVE, GIVE) VS STANDARD CHEMOIMMUNOTHERAPY (CIT: FCR/BR) IN FRONTLINE CHRONIC LYMPHOCYTIC LEUKEMIA OF FIT PATIENTS: FIRST CO-PRIMARY ENDPOINT ANALYSIS OF THE INTERNATIONAL INTERGROUP GAIA (CLL13) TRIAL

GAIA/CLL13 Study: Design

Chemoimmunotherapy (FCR/BR) versus Rituximab + Venetoclax versus Obinutuzumab (G) + Ve versus G + Ibrutinib + Ve

Recruitment in 10 countries (DE, AU, CH, NL, BE, DK, SE, FL, IR, IL)

Fit patients with CLL: CIRS ≤ 6 & normal CrCl

No TP53 mutation or del(17p) in central screening

Stratification according to age, stage and region

Randomization

* ≤ 65 years: FCR
> 65 years: BR [50% FCR / 50% BR]

FCR/BR* 230

RVe 230

GVe 230

GIVe 230

920 pts

Coprimary endpoint (α 2.5%): uMRD at month 15

Coprimary endpoint (α 2.5%): PFS interim analysis postponed to Q1 2022 due to low number of events
Coprimary endpoint: uMRD ($< 10^{-4}$) at Mo15 in PB by 4-colour-flow

ITT analysis: 63 pts (34 CIT, 15 RVe, 10 GVe, 4 GIVe) with missing samples (6.8%) were counted as MRD positive

- GIVe vs CIT: 92.2% versus 52.0%: $p < 0.0001$
- GVe vs CIT: 86.5% versus 52.0%: $p < 0.0001$
- RVe vs CIT: 57.0% versus 52.0%: $p = 0.317$

<table>
<thead>
<tr>
<th></th>
<th>uMRD%</th>
<th>97.5% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>GIVe</td>
<td>92.2</td>
<td>87.3 – 95.7</td>
</tr>
<tr>
<td>GVe</td>
<td>86.5</td>
<td>80.6 – 91.1</td>
</tr>
<tr>
<td>RVe</td>
<td>57.0</td>
<td>49.5 – 64.2</td>
</tr>
<tr>
<td>SCIT</td>
<td>52.0</td>
<td>44.4 – 59.5</td>
</tr>
</tbody>
</table>
# Adverse Events ≥ CTC Grade 3 Overview

Severe AEs occurring in ≥5% of pts and AEs of interest independent from incidence

<table>
<thead>
<tr>
<th></th>
<th>CIT</th>
<th>RVe</th>
<th>GVe</th>
<th>GIVe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients [SP]</strong></td>
<td>216</td>
<td>237</td>
<td>228</td>
<td>231</td>
</tr>
<tr>
<td>Anemia</td>
<td>16 (7.4)</td>
<td>9 (3.8)</td>
<td>11 (4.8)</td>
<td>9 (3.9)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>113 (52.3)</td>
<td>109 (46.0)</td>
<td>127 (55.7)</td>
<td>112 (48.5)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>22 (10.2)</td>
<td>10 (4.2)</td>
<td>42 (18.4)</td>
<td>37 (16.0)</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>24 (11.1)</td>
<td>10 (4.2)</td>
<td>7 (3.1)</td>
<td>18 (7.8)</td>
</tr>
<tr>
<td>Infections</td>
<td>43 (19.9)</td>
<td>27 (11.4)</td>
<td>32 (14.0)</td>
<td>51 (22.1)</td>
</tr>
<tr>
<td>Tumor lysis syndrome*</td>
<td>9 (4.2)</td>
<td>24 (10.1)</td>
<td>20 (8.8)</td>
<td>15 (6.5)</td>
</tr>
<tr>
<td>Bleeding events</td>
<td>1 (0.5)</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
<td>4 (1.7)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1 (0.5)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>6 (2.6)</td>
</tr>
</tbody>
</table>

* Including clinical and laboratory TLS according to Cairo-Bishop
Relapsed/Refractory CLL
Pirtobrutinib, A Highly Selective, Non-covalent (Reversible) BTK Inhibitor In Previously Treated CLL/SLL: Updated Results From The Phase 1/2 BRUIN Study


1Memorial Sloan Kettering Cancer Center, New York, USA; 2Swedish Cancer Institute, Seattle, USA; 3University of North Carolina at Chapel Hill, Chapel Hill, USA; 4Medical College of Wisconsin, Milwaukee, USA; 5Herbert Irving Comprehensive Cancer Center, Columbia University, New York, USA; 6Department of Haematology, St. James’s University Hospital, Leeds, UK; 7Institute of Hematology and Transfusion Medicine, Warsaw, Poland; 8Oxford University Hospitals NHS Foundation Trust, Churchill Cancer Center, Oxford, UK; 9The Ohio State University Comprehensive Cancer Center, Columbus, USA; 10MD Anderson Cancer Center, Houston, USA; 11Linear Clinical Research and Sir Charles Gairdner Hospital, Perth, Australia; 12Wilmott Cancer Institute, Emory University, Atlanta, GA, USA; 13Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, USA; 14University of California San Francisco, San Francisco, USA; 15Mary Crowley Cancer Research, Dallas, USA; 16Peter MacCallum Cancer Center, Royal Melbourne Hospital, and University of Melbourne, Melbourne, Australia; 17Plymouth Hospitals NHS Trust - Derriford Hospital, Plymouth, UK; 18Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, USA; 19University of Miami Miller School of Medicine, Miami, USA; 20Fred Hutchinson Cancer Research Center, 21Sarah Cannon Research Institute, Nashville, USA; 22Department of Hematology and Medical Oncology, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY; 23Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL, USA; 24Cleveland Clinic, Cleveland, OH, USA; 25Northwell Health Cancer Institute, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, NY; 26Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milan, Italy; 27Loxo Oncology at Lilly, Stamford, CT, USA; 28Dana-Farber Cancer Institute and Harvard Medical School, Boston, USA; 29Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland
Pirtobrutinib Efficacy in BTK Pre-treated CLL/SLL Patients

Data cutoff date of 16 July 2021. *Patients with >100% increase in SPD. Data for 30 patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. **Efficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. **ORR includes patients with a best response of CR, PR, and PR-L. Response status per iwCLL 2018 according to investigator assessment. Total % may be different than the sum of the individual components due to rounding.

Efficacy evaluable BTK pre-treated CLL/SLL Patients

<table>
<thead>
<tr>
<th>Overall Response Rate, % (95% CI)</th>
<th>n = 252</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Best response</strong></td>
<td></td>
</tr>
<tr>
<td>CR, n (%)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>PR, n (%)</td>
<td>137 (54)</td>
</tr>
<tr>
<td>PR-L, n (%)</td>
<td>32 (13)</td>
</tr>
<tr>
<td>SD, n (%)</td>
<td>62 (25)</td>
</tr>
</tbody>
</table>

Data cutoff date of 16 July 2021. *Patients with >100% increase in SPD. Data for 30 patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. **Efficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. **ORR includes patients with a best response of CR, PR, and PR-L. Response status per iwCLL 2018 according to investigator assessment. Total % may be different than the sum of the individual components due to rounding.
BTK C481 Mutation Status is not Predictive of Pirtobrutinib Benefit

Progression-free survival by BTK C481 mutation status\textsuperscript{a} in CLL/SLL patients with progression on a prior BTK inhibitor

Data cutoff date of 16 July 2021. Response status per iwCLL 2018 according to investigator assessment. \textsuperscript{a}BTK C481 mutation status was centrally determined and based on pre-treatment samples.
Pirtobrutinib Safety Profile

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Treatment-emergent AEs, (≥15%), %</th>
<th>Treatment-related AEs, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1</td>
<td>Grade 2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>13%</td>
<td>8%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>15%</td>
<td>4%</td>
</tr>
<tr>
<td>Neutropenia(^a)</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Contusion</td>
<td>15%</td>
<td>2%</td>
</tr>
</tbody>
</table>

**AEs of special interest\(^b\)**

<table>
<thead>
<tr>
<th>AEs of special interest⁠</th>
<th>Treatment-emergent AEs, (≥15%), %</th>
<th>Treatment-related AEs, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1</td>
<td>Grade 2</td>
</tr>
<tr>
<td>Bruising(^c)</td>
<td>20%</td>
<td>2%</td>
</tr>
<tr>
<td>Rash(^d)</td>
<td>9%</td>
<td>2%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>Hemorrhage(^e)</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1%</td>
<td>4%</td>
</tr>
<tr>
<td>Atrial fibrillation/flighter(^f)</td>
<td>-</td>
<td>1%</td>
</tr>
</tbody>
</table>

No DLTs reported and MTD not reached

96% of patients received ≥1 pirtobrutinib dose at or above RP2D of 200 mg daily
1% (n=6) of patients permanently discontinued due to treatment-related AEs

Data cutoff date of 16 July 2021. Total % may be different than the sum of the individual components due to rounding. \(^a\)Aggregate of neutropenia and neutrophil count decreased. \(^b\)AEs of special interest are those that were previously associated with covalent BTK inhibitors. \(^c\)Aggregate of contusion, petechiae, ecchymosis, and increased tendency to bruise. \(^d\)Aggregate of all preferred terms including rash. \(^e\)Aggregate of all preferred terms including hematoma or hemorrhage. \(^f\)Aggregate of atrial fibrillation and atrial flutter. \(^g\)Represents 6 events (all grade 3), including 2 cases of post-operative bleeding, 1 case each of GI hemorrhage in the setting of sepsis, NSAID use, chronic peptic ulcer disease, and one case of subarachnoid hemorrhage in setting of traumatic bike accident. \(^h\)Of 10 total afib/aflutter TEAEs, 3 occurred in patients with a prior medical history of atrial fibrillation, 2 in patients presenting with concurrent systemic infection, and 2 in patients with both.
CLL and COVID-19
Humoral Response to mRNA Vaccines BNT162b2 and mRNA-1273 COVID-19 in Chronic Lymphocytic Leukemia Patients

Cristina Bagacean, Rémi Letestu, Chadi Al Nawakil, Ségolène Brichler, Vincent Lévy, Nanthara Sritharan, Alain Delmer, Caroline Dartigeas, Véronique Leblond, Damien Roos-Weil, Marie C Béné, Aline Clavert, Driss Chaoui, Philippe Genet, Romain Guieze, Kamel Laribi, Yamina Touileb, Bernard Drénou, Lise Willems, Cécile Tomowiak, Fatiha Merabet, Christian Puppink, Hugo Legendre, Xavier Troussard, Stéphanie Malartre, Florence Cymbalista and Anne-Sophie Michallet

Study of the French Innovative Leukemia Organization
Post-dose 2 response rate and treatment

- Treatment-naïve patients had the highest response rate as compared with previously treated patients \( (P=0.02) \) and with patients on therapy \( (P<0.001) \)

* \( P \leq 0.05 \); ** \( P \leq 0.01 \); *** \( P \leq 0.001 \); **** \( P \leq 0.0001 \)
Post-dose 3 response rate of patients seronegative after 2 doses

- Treatment-naïve patients and previously treated patients had a significantly higher response rate as compared with patients on therapy ($P=0.01$)

- The majority of patients on therapy were receiving BTKi (71%, 61/86) and had a response rate of 31% (19/61)

Response rate post-dose 3

(44/124)
Key Points: CLL

- Frontline BTK and BCL2 inhibitors are more effective than chemo-immunotherapy for high risk CLL patients
- Use of BTK inhibitors yields potential cardio-vascular risk, and novel and safer BTK inhibitors are being developed
- Novel and safer PI3K inhibitors could be used in the future to consolidate patients previously treated with a BTK inhibitor
- Novel and more potent BTK inhibitors are being developed for patients who develop BTK resistance
- COVID19 booster is recommended for CLL patients treated with biological therapy
- Clinica trials should continue to be the preferred option for RS patients
ASH 2021

Brian Koffman, MDCM (retired) MS Ed EVP and CMO CLL Society
ASH 2021 Abstracts
The Patient and Real-World Perspective
Awareness, Knowledge, and Preferences of United States (US) Patients with Chronic Lymphocytic Leukemia (CLL) and Their Caregivers Related to Finite Duration (FD) Therapy and Minimal (Measurable) Residual Disease (MRD)

B. Koffman\textsuperscript{1}, C. Stewart\textsuperscript{2}, L. Avruch\textsuperscript{1}, N. Bailey\textsuperscript{3}, R. Brumble\textsuperscript{1}, J. Byrd\textsuperscript{4}, A. Danilov\textsuperscript{5}, M. Davids\textsuperscript{6}, R. Furman\textsuperscript{7}, N. Jain\textsuperscript{8}, N. Kay\textsuperscript{9}, N. Lamanna\textsuperscript{10}, A. Mato\textsuperscript{11}, A. Skarbnik\textsuperscript{12}, C. Ujjani\textsuperscript{13}, J. Pagel\textsuperscript{3}

\textsuperscript{1}CLL Society, Chula Vista CA; \textsuperscript{2}Gallup Inc; \textsuperscript{3}Swedish Cancer Institute, Seattle, WA; \textsuperscript{4}University of Cincinnati College of Medicine, Cincinnati, OH; \textsuperscript{5}City of Hope National Medical Center, Duarte, CA; \textsuperscript{6}Dana Farber Cancer Institute, Boston, MA; \textsuperscript{7}Weill Cornell Medicine, New York, NY; \textsuperscript{8}University of Texas MD Anderson Cancer Center, Houston, TX; \textsuperscript{9}Mayo Clinic, Rochester, MN; \textsuperscript{10}Columbia University Medical Center, New York, NY; \textsuperscript{11}Memorial Sloan Kettering Cancer Center, New York, NY; \textsuperscript{12}Novant Health, Charlotte, NC; \textsuperscript{13}University of Washington/Fred Hutchinson Cancer Research Center, Seattle, WA
AWARENESS, KNOWLEDGE, AND PREFERENCES OF UNITED STATES (US) PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) AND THEIR CAREGIVERS RELATED TO FINITE DURATION (FD) THERAPY AND MINIMAL (MEASURABLE) RESIDUAL DISEASE (MRD)


BACKGROUND & INTRODUCTION
- Unique introduction of novel agents, such as Bruton’s tyrosine kinase inhibitors (BTKi), the management of CLL patients primarily involves duration-based chemotherapy (CDT). The use of CDT is significantly increased in patients with multiple comorbidities, continuous single-agent or dual therapy determined until disease progression or intolerance.

OBJECTIVES
- Understand patients’ self-assessed awareness, understanding, and preferences related to finite therapy and MRD testing in the present treatment.
- Analyze how these influences their decision-related therapy.
- Assess the influence of awareness and understanding that can be addressed through improved patient education and decision-making.

METHODS
- Study Design: CLL Society developed a survey instrument to assess patient and caregiver awareness, understanding, and preferences associated with the concepts of MRD and finite duration therapy. The survey was conducted via a web-based data collection platform.

Inclusion Criteria
- Respondents must be age 18 or older.
- Have a diagnosis of CLL/SLCL.
- Be a frequent or occasional patient with knowledge of the options.

Survey Recruitment
- Patients and caregivers were invited by CLL Society via e-mail newsletters, CLL Society website, emails, and multiple online communities. The survey was administered anonymously.

Statistical Analysis
- Data were analyzed using descriptive methods. Answers in individual surveys were checks for validity.

RESULTS

- 630 Respondents (64% Patients, 36% Caregivers)
- 5 Months Follow-up: SEP-2020 to FEB-2021
- 2 Formats: Options to respond via PC or mobile device

Patient Demographics
- Age, Median (range): 60 (30-90)
- Age: Male: 54%, Female: 46%
- Race: Caucasian: 52%
- Years with diagnosis: 27%
- Treatment Status: Worked on Hx and Rx: 38%
- Received complete 1st treatment: 38%

CLL Disease and Treatment Status and Awareness
- Home treatment: 58%
- Prognostic and Predictive Markers as Reported by Patients
- Importance of Factors in Therapy Choice

RESULTS (CONTINUED)

CONCLUSIONS
- Patient awareness, treatment options, and overall survival (OS) were the 1st and 3rd very or somewhat important factors in choosing a treatment. Ability to reach MRD was only more important than the OS after 3rd.
- Therapy to treat MRD included chemotherapy and bone marrow transplantation for some patients. MRD was treated with a trial for some patients.
- Despite high levels of self-reported confidence in understanding MRD, some patients had preferences for MRD testing when it was not considered. Self being considered for the treatment of some patients was demonstrated persistent for all. Regarding understanding of which treatments (BR, BMT), chemotherapy was important for about half of patients who were aware.

GIVEN THE OPPORTUNITIES TO REDUCE THE NUMBER OF PATIENTS AT RISK.

ABOUT CLL SOCIETY
- CLLs are on a U.S.-based 501(c)(3) non-profit with a global reach. It is focused on patient education and awareness efforts to improve the quality of life of those with CLL and other related disorders.

CHECKOUT
- CLL Society Website: https://www.cllsociety.org (contains patients guide, accurate and patient-friendly information for managing CLL, a discussion board, and resources, and more, as authors.)
- CLL Society offers free patient support and information services with members in 3 continents.
- Follow the Expert Access to CLL experts providing contact to patients who would otherwise have no access to CLL management.
- For more information, contact the CLL Society at info@cllsociety.org or 1-800-800-5287.
Awareness, Knowledge, and Preferences of United States (US) Patients with Chronic Lymphocytic Leukemia (CLL) and Their Caregivers Related to Finite Duration (FD)Therapy and Minimal (Measurable) Residual Disease (MRD)

BACKGROUND & INTRODUCTION
• Until the introduction of novel agents, such as Bruton tyrosine kinase inhibitors (BTKi), the management of CLL patients primarily utilized limited duration chemoimmunotherapy (CIT). The use of BTKi significantly changed the CLL treatment paradigm to include continuous single-agent oral therapy delivered until disease progression or intolerance.

• More recently, similar to past CIT protocols, new combinations of non-CIT agents are being used that can be given over a finite duration (AKA fixed or limited duration). In addition, measurable (minimal) residual disease (MRD) assessment is emerging as an important clinical tool. Understanding the patients’ perspective on these trends is critical to providing best care.

• CLL Society, a patient-facing, physician-curated nonprofit organization focused on the unmet needs of the CLL community, sought to understand patients’ self-assessed awareness, understanding and preferences related to this changing therapeutic landscape with the addition of finite duration non-CIT options and MRD testing, and to research how they influence patients’ decisions around treatment.
Awareness, Knowledge, and Preferences of United States (US) Patients with Chronic Lymphocytic Leukemia (CLL) and Their Caregivers Related to Finite Duration (FD)Therapy and Minimal (Measurable) Residual Disease (MRD)

OBJECTIVES

• Understand patients’ self-assessed awareness, understanding and preferences related to finite therapies and MRD testing in the present treatment era.

• Assess how these influence their decisions related to therapy.

• Identify gaps and misconceptions in awareness and understanding that can be addressed through improved patient education and shared decision making.
630 Responses
608 CLL patients
22 CLL Caregivers

5 Months
The survey was administered from SEP-2020 to FEB-2021

2 Formats
Options to respond via PC or mobile device

Patient Demographics

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Median (range)</td>
<td>63 (30-90)</td>
</tr>
<tr>
<td>Age, &gt;70</td>
<td>35%</td>
</tr>
<tr>
<td>Sex, Female</td>
<td>55%</td>
</tr>
<tr>
<td>Does not have caregiver</td>
<td>48%</td>
</tr>
<tr>
<td>Treatment Status</td>
<td></td>
</tr>
<tr>
<td>Watch and Wait</td>
<td>27%</td>
</tr>
<tr>
<td>Received or completed 1st treatment</td>
<td>38%</td>
</tr>
<tr>
<td>Received or completed 2nd or later treatment</td>
<td>34%</td>
</tr>
</tbody>
</table>

630 Respondents throughout every state in the USA
RESULTS: Limited Duration Therapy and Treatment Choice

Most Important Factors in Therapy When Forced to Rank Choice

- Overall Survival: 50%
- No Chemo: 30%
- Reach uMRD: 7%
- Limited Duration: 6%
- Good Future Options: 5%
- Minimal lab / office visits: 2%

Duration of Therapy Preference

- LD therapy that is stopped after reaching uMRD or preplanned period of time if uMRD is not reached: 63%
- LD therapy that is stopped after a preplanned period of time: 14%
- No preference for the duration of therapy: 10%
- A therapy that is taken indefinitely: 7%
- Don't know / Not sure: 6%
RESULTS: Limited Duration Therapy and Treatment Choice

**Perceived Benefits of Limited Duration Therapy**

- Chance for continued remission, while off treatment: 91% very important, 9% not important.
- Period of time without side effects: 75% very important, 22% not important.
- Treatment has a planned end vs. going on forever: 90% very important, 10% not important.
- Fewer daily reminders of my CLL: 39% very important, 27% somewhat important, 34% not important.
- Lower drug-related costs: 19% very important, 34% somewhat important, 47% not important.

**Importance of Factors in Therapy Choice**

- Good options if I relapse: 91% very important, 8% not important.
- Treatment does not contain chemotherapy: 71% very important, 22% somewhat important, 7% not important.
- Ability to reach uMRD: 66% very important, 30% somewhat important, 4% not important.
- Limited duration: 46% very important, 44% somewhat important, 10% not important.
- Minimal lab work and office visits: 33% very important, 48% somewhat important, 19% not important.
Association between the Leukemia Mortality-to-Incidence Ratio and State Geographic Healthcare Disparities in the United States

• **INTRODUCTION:** Leukemia ((AML, CML, ALL, CLL and others) is the seventh leading cause of cancer death in the United States (US) in 2021.

• The Mortality Incidence Rate Ratio, also known as Mortality-to-Incidence Ratio (MIR), is calculated by dividing the mortality rate by the incidence rate for selected cancers and population.

• The MIR provides a population-based indicator of cancer survival which has previously been used to assess healthcare disparities.

• **RESULTS:** The highest MIR (worst survival) was found in Mississippi (0.579), Wyoming (0.570), and Ohio (0.569) The lowest MIR (best survival) was found in Florida (0.374), New York (0.391), and New Jersey (0.412)
Association between the Leukemia Mortality-to-Incidence Ratio and State Geographic Healthcare Disparities in the United States

• **CONCLUSIONS:** There is a remarkable geographic difference in leukemia MIRs in the US between 2008-2017.

• Leukemia MIR was significantly associated with state health rankings.

• Quality of clinical care for leukemia patients remains to be an important predictor of mortality.

• Other determinants of health, including social, economic, and community and physical environment may also play a vital role in influencing leukemia survival. More in-depth analysis of these data focusing on specific leukemia subtypes as well as other factors (race, gender, age) may be helpful in identifying and addressing other non-medical issues negatively impacting on leukemia outcomes in different geographical regions in the US.
Uptake of Novel Agents (NAs) As First-Line Treatments for Black and White Patients with Chronic Lymphocytic Leukemia (CLL) in the Veterans Health Administration (VHA): A Retrospective Cohort Study

• **INTRODUCTION:** Since the introduction of NAs in 2013, the treatment paradigm for CLL has changed significantly with the increased uptake of NAs for first line (1L) and refractory CLL.

• Despite improvement in survival outcomes with CLL, black patients with CLL have demonstrated inferior overall survival.

There was a statistically significant difference in the use of NAs between Black and White patients with CLL in the VHA. However, when NA use was examined by year, the disparity was largest in the early study years.
Addressing a New Challenge in Chronic Lymphocytic Leukemia: Outcomes of Therapies after Exposure to Both a Covalent Bruton's Tyrosine Kinase Inhibitor and Venetoclax

<table>
<thead>
<tr>
<th>Subsequent therapy</th>
<th>Non-covalent BTKi</th>
<th>PI3Ki</th>
<th>Allogeneic stem cell transplant</th>
<th>CAR T-cell therapy</th>
<th>CIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of pts treated*</td>
<td>45</td>
<td>24</td>
<td>17</td>
<td>9</td>
<td>23</td>
</tr>
<tr>
<td>ORR (n=available responses)</td>
<td>75.0%</td>
<td>40.9%</td>
<td>76.5%</td>
<td>85.7%</td>
<td>31.8%</td>
</tr>
<tr>
<td>Median PFS (mos) (n=number with follow-up)</td>
<td>not reached</td>
<td>5</td>
<td>11</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Median follow-up (mos)</td>
<td>9</td>
<td>4</td>
<td>6.5</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Abbreviations: CLL: chronic lymphocytic leukemia, BTKi: Bruton’s Tyrosine Kinase inhibitor, PI3Ki: phosphatidylinositol 3-kinase inhibitor; CAR: chimeric antigen receptor; CIT: chemo +/- immunotherapy; mos: months; ORR: overall response rate; PFS: progression free survival.

*The 125 patients were treated with 211 cumulative lines of therapy following covalent BTKi and venetoclax. Of the 211 lines of therapy administered, 44 did not fit into one of the specified categories. Other therapies not listed in the table included: venetoclax re-treatment (n=6) and cBTKi (n=43).
Addressing a New Challenge in Chronic Lymphocytic Leukemia: Outcomes of Therapies after Exposure to Both a Covalent Bruton's Tyrosine Kinase Inhibitor and Venetoclax

Figure 1. Progression Free Survival for Selected Therapies for “Double Exposed” Patients

Abbreviations: PFS: progression free survival; BTKi: Bruton’s Tyrosine Kinase inhibitor; PI3Ki: phosphatidylinositol 3-kinase inhibitor; CIT: chemo+/-immunotherapy
ASH 2021 Abstracts
News We Can Use Now
Characterization of Bruton Tyrosine Kinase Inhibitor (BTKi)-Related Adverse Events in a Head-to-Head Trial of Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia (CLL)

• **BACKGROUND**: The prior phase 3 head-to-head trial of acalabrutinib (acala) vs. ibrutinib (ibr) (NCT02477696) demonstrated non-inferior efficacy and improved tolerability with acala in previously treated CLL.

• **CONCLUSIONS**: In this head-to-head trial of BTKis in CLL, event-based analyses demonstrated a higher BTKi-related toxicity burden with ibr, with a lower impact of CV-related toxicity with acala across subgroups.
Combined Ibrutinib and Venetoclax for First-Line Treatment of Patients with Chronic Lymphocytic Leukemia (CLL)- Focus on Long-Term MRD Results

• **BACKGROUND:** Ibrutinib (IBR) and venetoclax (VEN) combination is a highly effective therapy in first-line CLL.

• **CONCLUSIONS:** Remissions were durable with some pts having recurrence of blood MRD in follow-up, which may be an early indicator of relapse.

• In a small subset of the pts with bone marrow (BM) MRD+ disease at 24 cycles of combined therapy, additional VEN appears to lead to U-MRD remission in majority of pts.

• Whether this will lead to improved long-term progression free survival (PFS) remains to be determined.
ASH 2021 Abstracts

Promising Future Directions
Venetoclax, Obinutuzumab and Atezolizumab (PD-L1 Checkpoint Inhibitor) for Treatment for Patients with Richter Transformation

- **BACKGROUND:** Richter’s Transformation (RT) is a great unmet needs in CLL.
- Dysfunction of T cells, natural killer (N cells and other immune subsets is common in patients (pts) with CLL and RT.
- Venetoclax (VEN), a BCL-2 inhibitor and obinutuzumab (OBIN), a CD20 monoclonal antibody (mAb) have clinical activity in pts with DLBCL and RT.
- Atezolizumab, a PD-L1 checkpoint inhibitor (CPI), is approved for melanoma, lung cancer and other solid tumors.
- It takes the brakes of the T, NK and other immune cells to attack the RT.
- **RESULTS:** All 7/7 (100%) pts achieved a response (complete metabolic response, n=5; partial metabolic response, n=2).
Venetoclax, Obinutuzumab and Atezolizumab (PD-L1 Checkpoint Inhibitor) for Treatment for Patients with Richter Transformation

• Three pts proceeded to an allogeneic stem cell transplant (allo-SCT) in complete metabolic remission after 4.1, 4.2 and 6.6 months; these 3 pts also achieved bone marrow undetectable (U)-MRD remission.
Subcutaneous Epcoritamab in Patients with Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia: Preliminary Results

• **BACKGROUND:** Epcoritamab (CD3×CD20) is a bispecific antibody that can induce potent activation and cytotoxic activity of CD4+ and CD8+ T cells to specifically eliminate CD20-expressing cells.

![Diagram of cancer cell, cytotoxic granules, and immune cell with CD20, CD3, CD16A, and bispecific antibody connections.]
Subcutaneous Epcoritamab in Patients with Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia: Preliminary Results

- **RESULTS:** 7 pts with R/R CLL received epcoritamab. 5 pts were fully assessed.
- Pts had received a median of 4 lines of prior therapy. 6 of 7 pts had poor-risk features of del(17p), \(TP53\) mutations, or both. 3 of 7 pts had bulky disease.
- All pts experienced cytokine release syndrome (CRS) in the first cycle, but it was mild. No neurotoxicity or tumor lysis syndrome (TLS) was observed.
- Antileukemic activity has been observed at both dose levels, with partial responses in 3 of 5 pts.
1: Nx-5948, a Selective Degrader of BTK with Activity in Preclinical Models of Hematologic and Brain Malignancies

2: Targeting Venetoclax-Resistant CLL By Bcl-XL Degradation

- Resistance often develops to drugs that inhibit BTK such as ibrutinib or acalabrutinib or BCL-2 such as venetoclax when the targets mutate and the drugs can no longer bind to block them.
- Selective degraders uses the cells system to clear out unneeded proteins but are targeted at the overactive proteins such as BTK and BLC-2 to actually destroy them.
- Watch for trials with proteolysis targeting chimeras (PROTACs).
Investigating the Addition of Ianalumab (VAY736) to Ibrutinib in Patients with Chronic Lymphocytic Leukemia (CLL) on Ibrutinib Therapy: Results from a Phase Ib Study: Anti-BAFF-R antibody

Characterization of LP-118, a Novel Small Molecule Inhibitor of Bcl-2 and Bcl-Xl in Chronic Lymphocytic Leukemia Resistant to Venetoclax: Upregulation of Bcl-xL has been shown to drive resistance to venetoclax

A Phase 1 Study to Evaluate the Safety, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Lisaftoclax (APG-2575), a Novel BCL-2 Inhibitor (BCL-2i), in Patients (pts) with Certain Relapsed or Refractory (R/R) Hematologic Malignancies (HMs): First-in-human study suggested the feasibility of an abbreviated ramp-up

Efficacy and Safety of the BTK Inhibitor MK-1026 in Patients with Hematologic Malignancies: MK-1026 (formerly ARQ 531) is an orally available, reversible, noncovalent competitive inhibitor of wild-type and C481S-mutant BTK
Conclusions

• Patients’ voices are increasingly being heard, but there is more to do.
• Inequities remain that must be addressed.
• Unmet needs are being researched:
  – Double refractory disease
  – Richter’s Transformation
  – Medication intolerance
• The future includes improved versions of existing classes of drugs and entirely new drugs.
Audience Questions & Answers
Thank You for Attending!

Please take a moment to complete our post-event survey, your feedback is important to us.

If you’re question was not answered, please feel free to email asktheexpert@cllsociety.org

Save the Date! Friday, March 18th for our next Webinar on COVID-19

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