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For Immediate Release

Significant efficacy benefit of IMBRUVICA® (ibrutinib) plus venetoclax versus acalabrutinib plus venetoclax in frontline treatment of patients with chronic lymphocytic leukaemia suggested by indirect treatment comparison

Cross-study findings indicate significant clinical benefit of frontline fixed-duration ibrutinib plus venetoclax with improved likelihood of undetectable minimal residual disease and progression-free survival versus acalabrutinib plus venetoclax[1]

Phase 2 CAPTIVATE long-term follow-up data further supports sustained efficacy and safety profile of fixed-duration ibrutinib plus venetoclax treatment in patients receiving frontline treatment for chronic lymphocytic leukaemia[2]

BEERSE, BELGIUM (12 June 2025) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced new data from a matching-adjusted indirect comparison (MAIC) analysis assessing the efficacy of IMBRUVICA® (ibrutinib) in combination with venetoclax (I+V) vs acalabrutinib in combination with venetoclax (A+V) as fixed-duration (FD) treatments for adults with previously untreated chronic lymphocytic leukaemia (CLL).[1] The data were featured in a poster presentation at the 30th European Hematology Association (EHA) Congress (Poster presentation #PF587) and reported that the I+V regimen yielded significantly better efficacy when compared to the A+V regimen.[1] Patients treated with I+V were more likely to achieve disease clearance, as measured by undetectable minimal residual disease (uMRD) three months after the end of treatment (EOT+3), from both peripheral blood (PB) and bone marrow (BM).[1] In addition to this, progression-free survival (PFS) significantly favoured I+V compared to A+V.[1]

“In the absence of head-to-head trials, clinicians need reliable tools to effectively compare treatment options and make the best possible choices for their patients,” said Talha Munir, M.D., Consultant in Clinical Haematology at St James’s Hospital, Leeds, United Kingdom.* “The matching-adjusted indirect comparison data presented at EHA suggests that ibrutinib plus venetoclax may offer meaningful clinical advantages over acalabrutinib plus venetoclax with patients more likely to achieve higher rates of undetectable minimal residual disease, three months after treatment. This may translate into more time in remission and longer progression-free survival – outcomes that matter deeply to both patients and the healthcare professionals who treat them.”

Patients who met the AMPLIFY inclusion criteria from both the Phase 3 GLOW (NCT03462719) and Phase 2 CAPTIVATE (NCT02910583) studies were included in this analysis, and, after matching and balancing the treatment cohorts, comparative analyses between the trials suggested that I+V significantly reduced the risk of progression or death by 47 percent when compared to patients treated with A+V (hazard ratio [HR]: 0.53; 95 percent confidence interval [CI]: 0.33-0.85; p=0.0085).[1,3,4,5] The results also suggested that patients treated with I+V were almost twice (95 percent CI: 1.47-2.41; p<0.0001) and 2.4 times (95 percent CI: 1.78-3.12; p<0.0001) more likely to achieve uMRD than A+V at EOT+3, in PB and BM, respectively.[1] The GLOW and CAPTIVATE FD cohorts were based on individual patient-level data with a median follow-up of approximately 4.5 years, while the A+V cohort used aggregate level data from the AMPLIFY study with a median follow-up of approximately 3.4 years.[1]

Results from final analysis of CAPTIVATE

Long-term follow-up results from the Phase 2 CAPTIVATE study data were presented as a poster at the American Society of Clinical Oncology (ASCO) 2025 Annual Meeting (Poster presentation #219) and will also be presented as an encore oral presentation at EHA 2025 (Oral presentation #S156).[6] The data reinforced the durable clinical benefit of frontline I+V.[2] Phase 2 CAPTIVATE results demonstrated patients in the I+V FD cohort displayed a clinically meaningful PFS and overall survival (OS) vs the MRD-guided cohort.[2] After a median follow-up of 68.9 months, the 5.5-year PFS and OS rates for all treated

patients were 66 percent (95 percent CI: 58-72) and 97 percent (95 percent CI: 93-99), respectively.[2] Additionally, the 5.5 year PFS rate in patients who achieved uMRD in the PB at the EOT was 71 percent (95 percent CI: 60-80).[2] Furthermore, 1-year PFS and OS rates from the start of retreatment (with single-agent ibrutinib or FD I+V) were both 100 percent, whilst 2-year PFS and OS rates from the start of retreatment were 91 percent and 96 percent, respectively.[2] No new safety signals were observed during the CAPTIVATE study since the previous follow-up, with COVID-19, diarrhoea and hypertension being the most frequently reported adverse events (AEs).[2] In the total pooled CAPTIVATE population, 32 percent (n=64/202) of patients had progressive disease following 5.5 years of follow-up.[2] Of the 53 patients with available samples, none had acquired resistance-associated mutations in *BTK* or *PLCG2*.[2]

“The final analysis of CAPTIVATE highlights how ibrutinib continues to raise the bar in the treatment of chronic lymphocytic leukaemia, with durable minimal residual disease response, extended treatment-free intervals, and a tolerable safety profile,” said Ester in't Groen, EMEA Therapeutic Area Head Haematology, Johnson & Johnson Innovative Medicine. “With the longest follow-up of any oral fixed-dose regimen, ibrutinib is setting a new standard for what patients and clinicians can expect from targeted therapies. We remain committed to advancing science in complex blood cancers and improving outcomes across the cancer care landscape.”

“The updates presented at EHA add to the growing body of evidence in support of ibrutinib, the most extensively studied Bruton’s tyrosine kinase inhibitor, as the standard of care in the frontline treatment of chronic lymphocytic leukaemia,” said Jessica Vermeulen, Vice President, Lymphoma & Leukemia Disease Area Stronghold Leader, Johnson & Johnson Innovative Medicine. “Offering patients not only more time, but also the option for treatment-free remissions continues to be our goal and we are proud of the incredible contribution ibrutinib has made since its first European approval in 2014.”

About the MAIC analysis

The objective of this analysis was to compare the progression-free survival (PFS) and undetectable minimal residual disease (uMRD) data from the fixed-duration (FD) ibrutinib + venetoclax (I+V) cohorts from the Phase 3 GLOW (NCT03462719) and Phase 2 CAPTIVATE (NCT02910583) studies against the Phase 3 AMPLIFY (NCT03836261) data.[1] In absence of prospective head-to-head trials investigating different Bruton’s tyrosine kinase inhibitors (BTKis) plus B-cell lymphoma 2 (Bcl-2) strategies, this study utilised matching-adjusted indirect comparison (MAIC) to obtain useful insights on comparative efficacy.[1] Individual patient data from the FD I+V cohorts of the GLOW and CAPTIVATE studies were pooled and compared to aggregate published Intent-to-Treat (ITT) data of the acalabrutinib plus venetoclax (A+V) arm of the AMPLIFY study.[1,3,4,5] A MAIC was performed following method published by Signorovitch et al. and guidelines from the National Institute for Health and Care Excellence (NICE).[1,7] Patients who did not meet the inclusion criteria of AMPLIFY were excluded from the I+V pooled cohort to establish the I+V patient population for analysis.[1] The remaining I+V patients were then reweighted so that the average baseline characteristics of the pooled I+V cohort matched those of the A+V patients in AMPLIFY.[1] The reweighted outcomes from I+V were then compared to the reported outcomes for A+V using indirect treatment comparison.[1] Relative effects were quantified using relative risk (RR) and hazard ratios (HR) with 95 percent confidence intervals.[1] There are potential sources of bias that cannot be accounted for in MAIC, that should be considered when interpreting such data. Specifically, in this comparison, the measurement of progression was stricter in GLOW and CAPTIVATE, requiring computer or magnetic imaging regardless of suspected progression and the median follow-up was longer in I+V population.[1] Both may have biased the PFS results in favour of A+V.[1] Additionally, AMPLIFY reported multicolour flow cytometry use but with no details on the number of colours and comparability is assumed with the 8-colour assay used in I+V studies.[1] As in any non-randomised comparison there may be additional unreported clinically important prognostic patient baseline characteristics which cannot be accounted for.[1] For example, Cumulative Illness Rating Scale score data was not collected in CAPTIVATE and therefore could not be used in matching.[1]

About CAPTIVATE

The Phase 2 CAPTIVATE study (NCT02910583) evaluated previously untreated adult patients with chronic lymphocytic leukaemia (CLL), who were 70 years or younger, including patients with high-risk disease, in two cohorts with combined median age of 60 years: a minimal residual disease (MRD)-guided cohort (n=43) and an FD cohort (n=159; median age).[2,4,8] Patients in the FD cohort received three cycles of ibrutinib lead-in followed by 12 cycles of I+V (oral ibrutinib [420 mg/d]; oral venetoclax [five-week ramp-up to 400 mg/d]) and the primary endpoint was complete response rate.[4] In the MRD cohort, after completion of three cycles ibrutinib lead-in followed by 12 cycles I+V, patients with confirmed uMRD were randomly assigned to double-blind treatment with placebo, or continuous ibrutinib.[4] The primary endpoint was one-year disease-free survival.[4]

About the GLOW study

The GLOW study (NCT03462719) is a randomised, open-label, Phase 3 trial that evaluated the efficacy and safety of frontline, FD I+V versus chlorambucil plus obinutuzumab in adult patients with CLL who are (a) ≥65 years old, or (b) 18-64 years old with a Cumulative Illness Rating Scale score of greater than six or creatinine clearance less than 70 mL/min, who had active disease requiring treatment per the International Workshop on CLL criteria.[3]

About ibrutinib

Ibrutinib is a once-daily oral medication that is jointly developed and commercialised by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company.[9] Ibrutinib blocks the Bruton's tyrosine kinase (BTK) protein, which is needed by normal and abnormal B-cells, including specific cancer cells, to multiply and spread.[10] By blocking BTK, ibrutinib may help move abnormal B-cells out of their nourishing environments and inhibits their proliferation.[11]
Ibrutinib is approved in more than 100 countries and has been used to treat more than 325,000 patients worldwide.[12] There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of ibrutinib.[9,13] In October 2021, ibrutinib was added to the World Health Organization’s Model Lists of Essential Medicines (EML), which refers to medicines that address global health priorities and which should be available and affordable for all.[14]

Ibrutinib was first approved by the European Commission (EC) in 2014, and approved indications to date include:[9]

- As a single agent or in combination with rituximab or obinutuzumab or venetoclax for the treatment of adult patients with previously untreated CLL
- As a single agent or in combination with bendamustine and rituximab (BR) for the treatment of adult patients with CLL who have received at least one prior therapy
- As a single agent for the treatment of adult patients with relapsed or refractory (RR) mantle cell lymphoma (MCL)
- As a single agent for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy. In combination with rituximab for the treatment of adult patients with WM

For a full list of adverse events and information on dosage and administration, contraindications and other precautions when using ibrutinib please refer to the Summary of Product Characteristics.

About Chronic Lymphocytic Leukaemia

CLL is typically a slow-growing blood cancer of the white blood cells.[15] The overall incidence of CLL in Europe is approximately 4.92 cases per 100,000 persons per year and it is about 1.5 times more common in men than in women (based on individuals diagnosed 2000-2002).[16] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[17] While patient outcomes have dramatically improved in the last few decades, the disease is still characterised by consecutive episodes of disease progression and the need for therapy.[18] Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.[19]

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity.

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Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of daratumumab. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes in behaviour and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's most recent Annual Report on Form 10-K, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at http://www.sec.gov/, http://www.jnj.com/ or on request from Johnson & Johnson. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

**Talha Munir, M.D., Consultant in Clinical Haematology at St James's Hospital, Leeds, United Kingdom, has provided consulting, advisory, and speaking services to Janssen-Cilag International NV; he has not been paid for any media work.*

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