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For Immediate Release

Updated Phase 2 CAPTIVATE study results demonstrate sustained clinical benefit of fixed-duration IMBRUVICA® (ibrutinib) plus venetoclax as first-line treatment for patients with chronic lymphocytic leukaemia, including those with high-risk disease

At 5 years, 67 percent of patients were progression-free, with overall survival at 96 percent for all treated patients[1]

BEERSE, BELGIUM (14 June 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced updated findings from the Phase 2 CAPTIVATE study evaluating fixed-duration (FD) IMBRUVICA® (ibrutinib) in combination with venetoclax (I+V) in previously untreated patients with chronic lymphocytic leukaemia (CLL).[1] At 5.5-years of follow-up, the FD regimen continues to demonstrate a clinically meaningful progression-free survival (PFS), both in the overall population and in those with high-risk genomic features.[1] The data were featured in an oral presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #7009) in Chicago from 31 May - 4 June and as an encore presentation at the European Hematology Association (EHA) Congress (Poster #P675) in Madrid, Spain, from 13-16 June 2024.

“After more than five years, the CAPTIVATE study findings confirm the sustained benefit of the fixed duration combination of ibrutinib and venetoclax as a first-line treatment for patients living with CLL, including in those with higher risk genomic features,” said Paolo Ghia MD, Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milan, Italy, study investigator.‡ “This all-oral, chemotherapy-free, fixed-duration regimen offers eligible patients the advantage of an extended, treatment-free interval while effectively keeping their disease under control.”

Latest findings from the multicentre Phase 2 CAPTIVATE study showed that at a median follow-up of 61.2 months, 67 percent (95 percent confidence interval [CI]: 59-74) of the 159 patients treated with FD I+V, were progression-free and alive at 5-years.[1] Notably, median PFS was not reached even after up to 5.5 years of follow-up, indicating sustained disease control.[1] The 5-year overall survival (OS) rate was 96 percent for all treated patients, while those who had high-risk genomic features (del(17p)/ mutated *TP53*, or complex karyotype) exhibited an OS rate of 90 percent (95 percent CI: 77-96), compared to 100 percent for those without these features.[1] Moreover, for patients who achieved undetectable minimal residual disease (uMRD) status in the blood and bone marrow, this was associated with improved outcomes.[1] Patients with uMRD in the bone marrow at 3-months post end of treatment (EoT+3 months) had a 5-year PFS rate of 84 percent (95 percent CI: 73-90) compared to 50 percent (95 percent CI: 36-62) for those not achieving uMRD in the bone marrow at EoT+3 months.[1]

In the limited number of patients relapsing after FD I+V, subsequent treatment with ibrutinib-based regimens was shown to yield durable responses with an acceptable safety profile, even in patients with high-risk genomic features.[1] Of the 61 patients with progressive disease after completion of FD I+V, 32 initiated subsequent treatment with single-agent ibrutinib (n=25) or FD I+V (n=7).[1] With a median 21.9 months treatment on single-agent ibrutinib, 86 percent of patients achieved an overall response of partial response or better. With a median 13.8 months retreatment with FD I+V, the overall response rate (ORR) was 71 percent.[1]

At longer follow-up, 18 second malignancies occurred in 13 patients and overall, no new safety signals were observed for FD I+V since the previous analysis.[1] Adverse events (AEs) during subsequent treatment were consistent with the known safety profiles for single-agent ibrutinib and I+V.[1] The most common AEs during retreatment with ibrutinib-based regimens, occurring in ≥10 percent of patients with single-agent ibrutinib or ≥2 patients treated with I+V, included diarrhoea, hypertension, pyrexia, upper respiratory tract infection and nausea, with serious AEs reported in five patients.[1]

Results from six-year time to next treatment extrapolation curve for Phase 3 GLOW study

The most recently reported data on long-term evidence regarding the duration of therapeutic effect associated with FD I+V in patients with previously untreated CLL includes 57 months of follow up.[2] An extrapolation beyond the available time-to-next-treatment (TTNT) data was performed to estimate the number of patients who would be free from subsequent therapy after six years, with findings presented during a poster presentation at EHA (Poster #P699).[2] The extrapolation indicates that at six years, approximately 87 percent of patients treated with the FD I+V are unlikely to require a second line treatment.[2] These findings suggest the possibility of a long treatment-free period for patients with CLL, treated with the FD I+V regimen in the first-line setting.[2]

“Ibrutinib is the only Bruton’s tyrosine kinase inhibitor available as both a fixed duration and continuous treatment for chronic lymphocytic leukaemia and is the most comprehensively studied medicine in its class,” said Edmond Chan, MBChB, M.D. (Res), EMEA Therapeutic Area Lead Haematology, Johnson & Johnson Innovative Medicine. “The latest data presented at EHA reinforce our commitment to advancing patient care through innovative therapies, such as ibrutinib, that can be tailored to the evolving needs and preferences of patients.”

“At Johnson & Johnson, our ultimate goal is to eliminate blood cancer, and we are inspired by the transformative impact ibrutinib-based regimens continue to have on patient outcomes,” said Mark Wildgust, PhD, Vice President, Global Medical Affairs, Oncology, Johnson & Johnson Innovative Medicine. “Nearly 300,000 patients worldwide have been treated with ibrutinib, and latest findings demonstrate that patients with CLL experience deep and durable responses that translate into long treatment-free periods, with the fixed duration regimen.”

About CAPTIVATE

The Phase 2 CAPTIVATE study (NCT02910583) evaluated previously untreated adult patients with CLL, who were 71 years or younger, including patients with high-risk disease, in two cohorts: an MRD-guided cohort (n=43; median age, 58 years) and an FD cohort (n=159; median age, 60 years).[1,3,4] 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 remission rate.[3] In the MRD cohort, after completion of 3 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.[3] The primary endpoint was one-year disease-free survival.[3]

About the GLOW study

The GLOW study (NCT03462719) is a randomised, open-label, Phase 3 trial that evaluated the efficacy and safety of first-line, 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.[5]

About the 6-year TTNT extrapolation curve for the GLOW study

The six-year extrapolation was produced by applying survival distribution functions to the TTNT Kaplan-Meier data of I+V from GLOW (where TTNT was defined as time to subsequent treatment).[2] Survival distributions describe the probability of not experiencing an event (i.e., start of subsequent anti-cancer therapy) by time.[2] Exponential, Weibull, Gompertz, log-logistic, log-normal, Gamma and Generalized Gamma parametric models were applied for this analysis, in line with National Institute for Health and Care Excellence (NICE) Technical Decision Support Unit recommendation.[2] For each distribution, the fit to observed data was assessed by the Akaike Information Criterion (AIC) and Bayes Information Criterion (BIC).[2] When assessing which distribution best fits the data, AIC and BIC criteria were used as well as visual inspection.[2] Extrapolation was performed using data available at the time of analysis (46-month follow-up).[2]

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.[6] 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.[7] By blocking BTK, ibrutinib may help move abnormal B-cells out of their nourishing environments and inhibits their proliferation.[8]
Ibrutinib is approved in more than 100 countries and has been used to treat almost 300,000 patients worldwide.[9] There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of ibrutinib.[5,10] 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.[11]

Ibrutinib was first approved by the European Commission (EC) in 2014, and approved indications to date include[5]:

- 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.[12] 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.[13] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[14] 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.[15] Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.[16]

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.

Learn more at https://www.jnj.com/ or at www.janssen.com/johnson-johnson-innovative-medicine. Janssen Pharmaceutica NV, Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen-Cilag International NV, Janssen-Cilag Limited and Janssen Global Services, LLC are Johnson & Johnson companies.

‡Dr Ghia has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

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 ibrutinib. 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 materialize, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen-Cilag International NV, Janssen-Cilag Limited, Janssen Global Services, LLC and/or 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; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior 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 Annual Report on Form 10-K for the fiscal year ended December 31, 2023, 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 www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of Janssen Pharmaceutica NV, Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen-Cilag International NV, Janssen-Cilag Limited, Janssen Global Services, LLC nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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CP-459190
June 2024