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Novartis continues to innovate in CML

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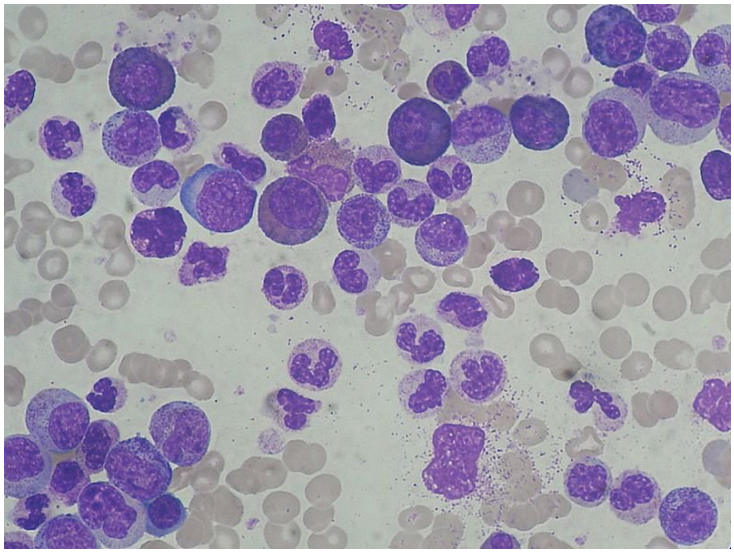
Novartis International AG / Novartis continues to innovate in CML with long-term treatment-free remission results following Tasigna use and promising combination data with investigational compound asciminib (ABL001).



Long-term follow-up data from the ongoing, pivotal open-label ENESTfreedom and ENESTop trials showed sustained treatment-free remission (TFR) after stopping frontline and second-line Tasigna (nilotinib) therapy in eligible adult patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in the chronic phase (CP). Separate data demonstrate promising results for asciminib (ABL001), an investigational allosteric BCR-ABL inhibitor, in combination with three different tyrosine kinase inhibitors (TKIs) in heavily pre-treated Ph+ CML-CP patients. The results will be presented at the 24th Congress of the European Hematology Association (EHA) in Amsterdam1-4.

"We are pleased to report many of our Tasigna clinical-trial patients continue to maintain treatment-free remission for nearly four years with a low adverse event burden," said John Tsai, MD, Head of Global Drug Development and Chief Medical Officer, Novartis. "Long-term trials like ENESTfreedom and ENESTop, as well as promising Phase I data from asciminib, are helping us to reimagine medicine and the way CML is treated."

Results from the ENESTfreedom study showed that about 44% of patients remained in TFR (84/190) for 192 weeks after stopping frontline Tasigna treatment. The treatment-free survival rate at 192 weeks was nearly 49%. About 99% (90/91) and 92% (84/91) of patients who resumed nilotinib due to loss of major molecular response (MMR) during the TFR phase regained MMR and molecular response4.5, respectively. Among 91 patients who resumed nilotinib, the most common adverse events (AEs) were nasopharyngitis (18.7%) as well as pruritus, fatigue and increased lipase (14.3% each). The majority of AEs were grade 1/21.

Consistent results were observed in the ENESTop trial: About 46% of patients remained in TFR (58/126) for 192 weeks after stopping second-line Tasigna treatment. The treatment-free survival rate at 192 weeks was over 50%. Among 59 patients who resumed nilotinib, the most common AEs were hypertension (20.3%) and arthralgia (13.6%). The majority of AEs were

grade 1/22.

Novartis will also present data from a Phase I trial of asciminib in combination with ATP-competitive TKI in heavily-pretreated patients with Ph+ CML-CP. Importantly, each combination was evaluated in a dose finding study assessing different asciminib dose levels, so results are not comparable across the three treatment arms. The preliminary results showed:

Among patients who at baseline did not achieve BCR-ABL1 International Scale [IS] <1%, by 48 weeks3,4:

60% (9/15) achieved molecular response <1% in the asciminib-plus-imatinib arm, and 43% (6/14) and 56% (5/9) patients achieved molecular response <1% in the asciminib-plus-nilotinib and asciminib-plus-dasatinib arms, respectively. In evaluable patients without MMR at baseline, by 48 weeks3,4: 42% (8/19) achieved MMR with asciminib plus imatinib with median treatment exposure of 54.6 weeks, and 31% (4/13) patients with asciminib plus nilotinib and 36% (5/14) patients with asciminib plus dasatinib, respectively, achieved MMR.

No patients with MMR at baseline lost MMR due to either of the three combination therapies. All combinations showed tolerable safety profile in heavily pretreated CML patients3,4:

- Among patients who received asciminib plus imatinib, the most common any-grade AEs were nausea (32%), increased lipase (20%), as well as abdominal pain, peripheral edema and vomiting (16% each).
- Among patients who received asciminib plus nilotinib, most common any-grade AEs were myalgia (35%), increased lipase (29%), and increased amylase, fatigue and pruritus (24% each).
- Among patients who received asciminib plus dasatinib, most common any-grade AEs were increased lipase (35%) and diarrhea, headache and nausea (18% each).

"While the introduction of TKIs has changed the CML treatment paradigm, there remains a subset of patients who are intolerant or resistant to TKI therapy," said Jorge Cortes, MD, Deputy Chair and Professor of Medicine in the Department of Leukemia at MD Anderson Cancer Center, Houston Texas. "These initial results from combination therapy with currently available TKIs and a BCR-ABL1 inhibitor like asciminib are encouraging - and give us the potential to increase molecular response and prevent development of mutations."