Novartis drug Revolade® shows long-term disease control for chronic/persistent immune thrombocytopenia (ITP)

- Nearly 70% of patients maintained platelet counts of $\geq 30 \times 10^9$/L without rescue therapy for prolonged periods, reducing the overall risk of bleeding
- More than one-third of patients permanently stopped one or more concomitant ITP medications (including corticosteroids, danazol, azathioprine)
- Study establishes long-term safety profile for and demonstrates treatment benefit with Revolade

Basel, October 18, 2017 – Novartis today announced long-term study results supporting the positive safety and efficacy of Revolade (eltrombopag) in adults with chronic/persistent (enrolling patients that were 6 or more months from diagnosis) immune (idiopathic) thrombocytopenia (ITP) were published online in Blood. The EXTEND study found that a majority of patients maintained a substantial clinical response and many no longer needed concomitant ITP medications. The research evaluated patients for up to 8 years of continuous treatment (median exposure of 2.4 years)\(^1,2\).

ITP is a rare and potentially serious blood disorder where the blood doesn’t clot as it should due to a low number of platelets. As a result, patients with ITP experience bruising, bleeding and, in rare cases, serious hemorrhaging that can be fatal\(^3\). The goal of treatment in chronic/persistent ITP is to maintain a safe platelet count that reduces the risk of bleeding\(^1,3\).

“The EXTEND data published in Blood validate Revolade as an important oral treatment option that, by often increasing platelet counts, significantly decreased bleeding rates and reduced the need for concurrent therapies in certain patients with chronic/persistent immune thrombocytopenia,” said lead author James Bussel, M.D., professor emeritus of pediatrics at Weill Cornell Medicine. “With this information, physicians can better optimize long-term disease management for appropriate patients living with this chronic disease.”

The efficacy results of EXTEND demonstrated that median platelet counts were elevated to $\geq 50 \times 10^9$/L within two weeks of Revolade treatment, with median platelet counts $>50 \times 10^9$/L maintained for more than four years. Post-baseline, overall bleeding rates declined and the majority of bleeding that occurred during the study was Grade 1 or 2 according to the World Health Organization bleeding scale. Some patients (39%) were capable of reducing or permanently stopping one or more concomitant ITP medications without the need for rescue therapy, many of which sustained reduction for at least 24 weeks\(^1,2,4\).

“We conducted this trial, the largest of its kind in adult patients, to ensure that clinicians have comprehensive data on hand as they work with their ITP patients to make treatment decisions,” said Vas Narasimhan, M.D., Global Head Drug Development and Chief Medical Officer, Novartis. “The EXTEND results reinforce Revolade as a trusted treatment option that can be used over the long-term for those living with this chronic and rare disease.”
Overall, the safety profile of Revolade was consistent with previous studies. The most common adverse events were headache (28%), nasopharyngitis (25%) and upper respiratory tract infection (23%). During treatment on EXTEND, 6% of patients experienced thromboembolic events.1,2,4

About the EXTEND Clinical Trial
EXTEND, an open-label extension study of four trials (TRA100773A, TRA100773B, TRA102537/RAISE and TRA108057/REPEAT) of Revolade, enrolled 302 adults with chronic/persistent ITP (6 or more months from diagnosis) who had received prior therapy for their ITP, and is the largest study of its kind. To qualify for the prior trials, patients must have had thrombocytopenia for at least 6 months (chronic ITP was previously defined as thrombocytopenia for 6 or more months). The objectives were to assess the safety and efficacy of long-term treatment with Revolade, including the proportion of patients achieving stable platelet counts during treatment with Revolade; maximum duration of platelet count elevation ≥50×10^9/L or ≥30×10^9/L during treatment with Revolade, and the effect of Revolade on reducing and/or sparing concomitant ITP therapies, while maintaining a platelet count ≥50×10^9/L.1,2

The study allowed each patient to achieve an individualized dose and schedule of eltrombopag based upon their platelet counts in the desired range between 50 to 200 Gi/L. Therefore, patients who were enrolled in EXTEND must have completed the treatment and follow-up periods as defined in previous protocol and must have not experienced eltrombopag-related toxicity or other drug intolerance on prior eltrombopag study even if resolved. In addition, patients who discontinued from a previous study due to toxicity were not eligible unless they received placebo1,2.

Revolade was started at a dose of 50 mg/day and titrated to 25-75 mg/day or less often based on platelet counts. Maintenance dosing continued after minimization of concomitant ITP medication and optimization of Revolade dosing. The overall median duration of exposure was 2.37 years (range, 2 days to 8.76 years) and mean average daily dose was 50.2 (range, 1–75) mg/day.1,2 One hundred thirty five adult patients (45%) completed the study and 75 adult patients (25%) were treated for four or more years. Most patients were aged <65 years, female, and had platelet counts <30×10^9/L at baseline. About one-third were using concomitant medications at baseline, and 53% had received three or more prior ITP therapies.1,2 In addition, 91% (276/302) of patients achieved platelet counts ≥30×10^9/L without rescue treatment, and 86% (259/302) achieved platelet counts ≥50×10^9/L without rescue treatment1,2,4.

Grade 3 and 4 adverse events (AEs) occurred in 26% and 6% of patients, respectively. Grade 3 cataracts occurred in four (1%) patients and Grade 3 pain in extremity in six (2%) patients. Grade 3 AEs occurring in three (<1%) patients each included diarrhea, headache, migraine, dyspnea, decreased platelet count, and menorrhagia; those occurring in five (2%) patients each included pneumonia, fatigue, back pain, increased alanine aminotransferase, increased aspartate aminotransferase, anemia, and hypertension. Grade 4 anemia and thrombocytopenia occurred in three (<1%) and four (1%) patients, respectively. All other Grade 4 events occurred in one patient each1,2.

About Chronic/Persistent ITP
Chronic/persistent ITP is a rare and potentially serious blood disorder that is characterized by the improper functioning or destruction of platelets, which are blood cells that allow the blood to clot properly. People who have ITP often have purple bruises or tiny red or purple dots on the skin. They also display symptoms such as nosebleeds, bleeding from the gums during dental work, or other bleeding that is hard to stop. The potential for drops in platelet counts may also cause emotional distress and may result in a hindered ability to do work or embarrassment due to visible symptoms.
ITP is classified by duration from diagnosis into: acute (0-3 months), persistent (3-12 months duration) and chronic (>12 months duration). Chronic/persistent ITP is more likely to occur in adults, and women are affected two to three times more often than men.

The goal of treatment in chronic/persistent ITP is to maintain a safe platelet count that reduces the risk of bleeding. Treatment is determined by the severity of the symptoms. In most cases, drugs that alter the immune system's attack on the platelets are prescribed to help manage bleeding and bruising in adults.

About Eltrombopag
Eltrombopag, marketed as Promacta® in the United States and Revolade® in countries outside the US, is approved in more than 100 countries worldwide for the treatment of thrombocytopenia in adult patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an inadequate response or are intolerant to other treatments, approved in over 45 countries worldwide for the treatment of patients with severe aplastic anemia (SAA) who are refractory to other treatments, and also approved in more than 50 countries for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow them to initiate and maintain interferon-based therapy. Eltrombopag is approved in the US and in the European Union for the treatment of thrombocytopenia in pediatric patients 1 year and older with chronic immune (idiopathic) thrombocytopenia (iTP) who have had an insufficient response to corticosteroids and immunoglobulins.

Important Safety Information for Revolade® (eltrombopag)
Revolade may cause serious side effects, such as liver problems, high platelet counts and a higher chance for blood clots, bleeding after stopping treatment, and bone marrow problems. Revolade may damage the liver and cause serious, even life threatening, illness. Blood tests to check the liver are needed before taking Revolade and during treatment. When certain antiviral treatments are given together with Revolade for the treatment of thrombocytopenia due to hepatitis C virus (HCV) infections, some liver problems can get worse.

A doctor will order the blood tests and any other tests required. In some cases, Revolade treatment may need to be stopped. Patients should tell a doctor right away if they have any of these signs and symptoms of liver problems: yellowing of the skin or the whites of the eyes (jaundice), unusual darkening of the urine, unusual tiredness, or right upper stomach area pain.

Patients have a higher chance of getting a blood clot if their platelet count is too high during treatment with Revolade; but blood clots can occur with normal or even low platelet counts. Patients who have cirrhosis of the liver are at risk of a blood clot in a blood vessel that feeds the liver. Patients may have severe complications from some forms of blood clots, such as clots that travel to the lungs or that cause heart attacks or strokes. A doctor will check the patient's blood platelet counts, and change the dose or stop Revolade if platelet counts get too high. Patients should tell their doctor right away if they have signs and symptoms of a blood clot in the leg, such as swelling or pain/tenderness of one leg.

When patients with chronic ITP stop taking Revolade, their blood platelet count will drop back down to what it was before they started taking Revolade. These effects are most likely to happen within 4 weeks after patients stop taking Revolade. The lower platelet counts may increase risk of bleeding. A doctor will check platelet counts for at least 4 weeks after patients stop taking Revolade. Patients should tell their doctor or pharmacist if they have any bruising or bleeding after they stop taking Revolade.

Patients being treated for the disease may have problems with their bone marrow. Medicines like Revolade could make this problem worse. Signs of bone marrow changes may show up as abnormal results in blood tests. A doctor may also carry out tests to directly check the bone marrow during treatment with Revolade.
The most common side effects of Revolade when used to treat adult patients with chronic ITP include headache, anemia, decreased appetite, insomnia, cough, nausea, diarrhea, alopecia, pruritus, myalgia, pyrexia, fatigue, influenza-like illness, asthenia, chills and peripheral edema.

The most common side effects of Revolade when used to treat pediatric patients with chronic ITP include upper respiratory tract infection, nasopharyngitis, cough, diarrhea, pyrexia, rhinitis, abdominal pain, oropharyngeal pain, toothache, rash, increased AST and rhinorrhea.

The most common side effects of Revolade when used to treat patients with chronic HCV and antiviral agents include headache, anemia, decreased appetite, insomnia, cough, nausea, diarrhea, alopecia, pruritus, myalgia, pyrexia, fatigue, influenza-like illness, asthenia, chills and peripheral edema.

The most common side effects of Revolade when used to treat patients with severe aplastic anemia (SAA) include headache, dizziness, insomnia, cough, dyspnea, oropharyngeal pain, rhinorrhea, anemia, diarrhea, abdominal pain, transaminases increased, ecchymosis, arthralgia, muscle spasms, pain in extremities, fatigue, febrile neutropenia, and pyrexia. Common side effects that may show up in blood tests include increase in some liver enzymes and laboratory tests that may show abnormal changes to the cells in the bone marrow.

Please see full EU Summary of Product Characteristics for Revolade (eltrombopag).

Disclaimer
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pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 119,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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References