ONO PHARMACEUTICAL CO.,LTD.

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New Treatment Regimen Available for KYPROLIS® for Intravenous Injection, a Proteasome Inhibitor, in Combination with Darzalex® plus Dexamethasone for Treatment of Relapsed or Refractory Multiple Myeloma in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced today that an additional twice-weekly regimen has been available for KYPROLIS® (generic name: carfilzomib) for Intravenous Injection 10 mg and 40 mg ("KYPROLIS"), a proteasome inhibitor, in Japan, in combination with dexamethasone plus Darzalex® (generic name: daratumumab) Intravenous Infusion, a human anti-CD38 monoclonal antibody ("Darzalex") (DKd) for the approved indication of relapsed or refractory multiple myeloma.

This new combination therapy has been made available, based on the result of a global, multicenter, randomized, open-label Phase III study, CANDOR study (ONO-7057-07), evaluating a combination treatment with KYPROLIS, dexamethasone plus Darzalex (DKd: 312 patients), versus a combination treatment of KYPROLIS and dexamethasone (Kd: 154 patients) in patients with relapsed or refractory multiple myeloma (466 patients including 31 Japanese patients) who have received one to three previous lines of therapy.

In this study, the DKd group reduced the risk of disease progression or death by 37% as shown in the progression-free survival (PFS), a primary endpoint, versus the Kd group (HR=0.63; 95% Confidence Interval: 0.464 - 0.854; p=0.0014), demonstrating a statistically significant extension in PFS. The median PFS was 15.8 months in the Kd group, and not reached in the DKd group. The safety profile of the DKd group in this study was consistent with the one previously reported for each product. The most frequent treatment-related adverse events reported in ≥20% of patients in the DKd group were thrombocytopenia and hypertension.

In Japan, Janssen Pharmaceutical K.K., the manufacturer and distributor of Darzalex, today received a supplemental approval of Darzalex for DKd combination treatment based on the result from the above CANDOR study for a partial change in approved items. In association with its approval, ONO was granted to revise the ethical drug package insert of KYPROLIS regarding DKd treatment using the three drugs.

With this additional approval, KYPROLIS can be administered further in combination with dexamethasone plus darzalex in the twice-weekly regimen of KYPROLIS, and is expected to have a higher therapeutic effect.

In this revision of the package insert for KYPROLIS, the description in item 7.2 of Section 7 "Precautions concerning dosage and administration" was changed, and the description regarding the above global Phase III study (CANDOR study) was added to Section 17 "Clinical results", as an item 17.1.5.

About CANDOR study

CANDOR study is a global randomized, open-label Phase 3 study evaluating KYPROLIS, Darzalex and dexamethasone (DKd) compared to KYPROLIS and dexamethasone (Kd) in patients with relapsed or refractory multiple myeloma who have received one to three prior therapies. Patients were treated until disease progression or unacceptable toxicity. The primary endpoint of this study was progression-free survival (PFS), and the key secondary endpoints were overall response rate, minimal residual disease and overall survival.

About multiple myeloma

Multiple myeloma is a blood cancer caused by an abnormality of plasma cells in the bone marrow. It is reported that there are nearly 25,000 patients* in Japan. Several treatments for multiple myeloma are currently available to patients; however, the disease relapses and progresses and eventually becomes no longer responding to therapies, also known as refractory disease. Additionally, adverse drug reactions and complications have been reported following long-term treatment, making continued treatment a challenge. The development of new therapeutic options for multiple myeloma is expected.

*: Vital Statistics and Patients Survey, 2017 (Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare).

About KYPROLIS®

KYPROLIS is a highly selective proteasome inhibitor. Proteasome, an intra-cellular enzyme complex, functions to mediate degradation of polyubiquitinated proteins and control proliferation and differentiation of cells, as well as functional cell-death. KYPROLIS inhibits certain proteasome activity, thereby inducing functional cell-death of myeloma.

In September 2010, Ono Pharmaceutical Co., Ltd. (ONO) entered into an exclusive license agreement on a proteasome inhibitor, KYPROLIS (for injection) with U.S.-based Onyx Pharmaceuticals, Inc., now a wholly-owned subsidiary of Amgen, to develop and commercialize the product for all oncology indications in Japan.

ONO received the manufacturing and marketing approval of KYPROLIS in July 2016 and KYPROLIS was launched for the treatment of relapsed or refractory multiple myeloma in combination with lenalidomide and dexamethasone in August 2016 in Japan. In addition, ONO received a supplemental approval of KYPROLIS in May 2017 to expand a dosage and administration of KYPROLIS in combination with dexamethasone at a dosage of 20 mg/m^2 in Cycle 1 on Day 1 and 2, and escalate to 56 mg/m^2 thereafter. In September 2019, ONO also obtained a supplemental approval of KYPROLIS for additional dosage and administration in combination with dexamethasone at a dosage of 20 mg/m^2 only in Cycle 1 on Day 1, and escalate to 70 mg/m^2 once a week thereafter.

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