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Onconova's oral rigosertib garners more excitement than IV version but not likely a game changer

Onconova Therapeutics' (NASDAQ:ONTX) oral formulation of rigosertib is more promising than the intravenous (IV) version in myelodysplastic syndromes (MDS), oncologists said. They all agreed the oral formulation would be more convenient than the IV version, but were hesitant to state that the agent would be a major breakthrough.

The oral formulation would certainly be more convenient for patients, said investigator Dr David Steensma, attending physician, hematologic oncology, Dana-Farber Cancer Institute, Boston. But, he cautioned, if the Phase III ONTIME trial of the IV version is not positive, the company may not have the funds to develop the oral version.

ONTIME has not garnered much excitement among investigators, who were unsure if it would reach its overall survival (OS) primary endpoint in relapsed/refractory higher risk MDS, this news service reported on 10 June 2013. Top-line data is expected this quarter.

The oral and IV versions have the same active pharmaceutical ingredient, so bringing the oral formulation to market would be easier if the IV version is approved, said Ramesh Kumar, president and CEO. Pending Phase III results, FDA and EMA filings for IV rigosertib are expected in 2H14, he noted.

The IV formulation, given via a 72-hour infusion, is a bit cumbersome, noted Dr Mahesh Seetharam, hematologist/oncologist, Arizona Oncology, and investigator Dr Azra Raza, director, MDS Center, Columbia University Medical Center, New York. Taking a pill twice a day is very nice for patients, added investigator Dr Joseph Jurcic, director, hematological malignancies section, Hematology/Oncology Division, New York-Presbyterian Hospital/Columbia University Medical Center. Jurcic noted he has been quite impressed with patients' responses to the oral version.

Onconova plans to initiate a Phase III trial of oral rigosertib in lower risk transfusion-dependent untreated MDS in 2014, this news service reported on 11 December 2013. Data from the Phase II ONTARGET trial of oral rigosertib in lower risk transfusion-dependent MDS was presented at the December 2013 American Society of Hematology (ASH) meeting.

The oral formulation is easier to take and can be given for a longer period of time, Kumar said. Since many cancer agents are now orally available, oral rigosertib can be easily combined with chemotherapies or targeted agents, he added.

The ONTARGET trial dosing schedule resulted in urinary toxicity, noted Raza and investigator Dr Gary Spitzer, hematologist/oncologist, Bon Secours St Francis Health System, Greenville, South Carolina. The dosing schedule was modified such that patients received the second daily dose in the afternoon, instead of at night, which helped reduce the occurrences significantly, Raza explained. The final dosing schedule was 580mg given in the morning and 260mg in the early afternoon, she said.

Oral rigosertib does not appear to cause myelosuppression, Kumar noted. No significant treatment-emergent myelosuppression was seen in the Phase II ONTARGET trial, according to the ASH presentation.

Giving an erythrocyte stimulating agent (ESA) such as **Janssen**'s Procrit (epoetin alfa) with oral rigosertib may help improve patients' anemia symptoms, Spitzer and Raza suggested. Many patients stop responding to ESAs, and some patients never respond to them, Steensma noted.

Of patients who responded to oral rigosertib in ONTARGET, 80% (12/15) were refractory to ESAs, according to the ASH presentation. Of these 12 ESA-refractory patients, 11 (92%) tolerated concomitant ESAs, suggesting

that oral rigosertib may have an effect on ESA resistance, the presentation stated. Oral rigosertib should be explored in ESA-refractory patients, Raza added.

Considering many patients in ONTARGET received ESAs alongside rigosertib, Steensma cautioned it is difficult to determine the independent contribution of each therapy.

by Juliana Wexler in New York