Diagnostic to Determine which Low-Risk MDS Patients to Treat with Lenalidomide to Restore Sensitivity to Erythropoietin

Myelodysplastic syndromes (MDS) are characterized by progressive bone marrow failure manifesting as blood cytopenia and a variable risk of progression into acute myeloid leukemia. Due to the complexity of somatic mutations and gene hypermethylation, only a subset of patients respond to current treatment modalities and most responders eventually lose their response. Once the first line treatment fails, management becomes more challenging. To help solve this difficulty, this companion diagnostic uses a CD45 isoform profile to predict the efficacy of combination lenalidomide and erythropoietin treatment in patients with a Epo-refractory, lower-risk non-del(5q) MDS. Lenalidomide restores sensitivity to erythropoietin in these MDS patients without added toxicity.

COMMERCIAL OPPORTUNITY

- In the United States, approximately 13,000 new cases of MDS are diagnosed each year. MDS patients possess a risk of progression to acute myeloid leukemia. The patients are generally categorized into lower-risk (IPSS low or intermediate-1) and higher-risk (IPSS high or intermediate-2) groups that are subject to different treatments.
- In lower-risk MDS, the risk of AML progression is less and survival is longer. The main priority is the treatment of cytopenias and the improvement of quality in life. Erythropoiesis stimulating agents such as Epo are the first choice for treatment of anemia. Nevertheless, the response rate is only around 50%. Then there is a possibility of using lenalidomide, hypomethylating agents, or other drugs as a second line treatment. However, it is difficult for doctors to determine which agent to use making disease management more challenging.
- Lenalidomide has Epo-promoting activity in non-del(5q) MDS. Clinical trial results show that 26% of patients achieved durable transfusion independence and cytogenetic responses up to about 10 months. This invention uses a CD45 isoform profile to predict efficacy of combination lenalidomide and erythropoietin treatment in patients with an Epo-refractory, lower-risk non-del(5q) MDS.
- A potential market for this diagnostic could be estimated with the assumption that about two thirds of new cases of MDS are lower-risk. The percent that are Epo refractory could be assumed to be approximately equivalent to the two thirds number in steady state if Epo plus G-CSF treatment gives a 38% to 80% erythroid response rate with a median response duration of around 2 years. All of these patients might then be tested using this diagnostic, and with an estimated cost of $3,000, this leads to a potential market size of 13,000*0.66*$3,000=$26M.

TECHNOLOGY

The invention utilizes a CD45 isoforms profile as a predictor of lenalidomide and erythropoietin combination therapy response. In a clinical trial using 195 patients, response to combined treatment was found associated with baseline CD45 isoform distribution in CD71+ erythroid precursors. Patients achieving major erythroid response had a significantly lower CD45 RA+RB: RO isoform ratio (median:1.51) compared to non-responder (median: 4.21, p=0.04).

PUBLICATION/PATENT

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