

Topic Prognosis-Predictive factors of response to treatment

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Abstract title EX VIVO RESPONSE PROFILING OF RIGOSERTIB IDENTIFIES DISTINCT CLASSES OF RESPONDERS IN MYELODYSPLASTIC SYNDROME

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Abstract text Introduction:

Myelodysplastic syndrome (MDS) is a clonal myeloid neoplasm with limited treatment options. New treatments are needed, especially for patients that are refractory to HMA's. Rigosertib is a small molecule investigational agent, that disrupts the binding between RAS and RAS effector proteins, in late stage clinical development in patients with high risk MDS. Notable Labs' translational drug discovery platform was used to stratify responders to Rigosertib within the MDS patient population.

Methods:

Primary samples (either peripheral blood or bone marrow) were red blood cell lysed and mononuclear cells were screened in Notable Labs' translational drug discovery platform. Rigosertib was added to 384-well plates seeded with mononuclear cells, then incubated for 72 hours. Readouts were performed using high-throughput flow cytometry to generate a blast score, which quantifies the specific killing of malignant cells versus healthy cells.

Results:

51 primary samples from patients with myelodysplastic syndrome (MDS) were analyzed in Notable Labs' proprietary ex vivo drug sensitivity platform for response to a clinically achievable dose of Rigosertib. All 51 primary samples were screened at 70nM, representing the most comprehensive ex vivo analysis of Rigosertib sensitivity to date. The mean drug sensitivity-response of Rigosertib in the assay was 38.1% normalized blast viability with a 75th and 25th percentile response of 70% and 20% normalized blast viability, respectively.

Additionally, 8 samples were screened in 6-point dose response (2.6nM to 620nM). Responses in the assay were divided into two groups, a sensitive population and a population with reduced sensitivity. Blast killing in the reduced sensitivity group plateaued without reducing the blast population beyond 50% killing (n=4; Figure 1B) and added drug did not reduce this population further. However, Rigosertib reduced the sensitive population blast population below 20% (n=4; Figure 1A).