Imetelstat, A Potent Telomerase Inhibitor, Inhibits the Spontaneous Growth of CFU-Meg

In Vitro From Essential Thrombocytopenia Patients but Not From Healthy Individuals

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Background

Essential Thrombocythemia

Diagnostic Criteria (WHO):
- Thrombocytosis 2-100 G/L
- Bone marrow high number of large, mature megakaryocytes
- Episodes of thrombosis and hemorrhage
- Exclusion of other causes of thrombocytosis

Telomerase Inhibitor (Imetelstat Sodium GRN163L)

Cord Blood

Telomerase Inhibition by Imetelstat in CB Cells

Cord Blood

CFU-Mega (% in Patients with ET)

ET Patients and Healthy Individuals

CFU-Mega (% in Healthy Individuals)

Methods:

- Mononuclear cells (MNC) from 3 healthy individuals and from 11 ET patients (WHO 2009 criteria) were isolated from PB and suspended in IMDM or plated into collagen ± cytokines (TPO, IL3, IL6, SCF, EPO) and treated with 0, 0.1, 1 and 10 µM imetelstat or a mismatch control, and incubated for several hours (cell suspensions) or 10–12 days (collagen plus 5% CO2) at 37 °C.
- Megs were stained and the number of CFU-Meg was scored
- TA was measured in MNC by TRAP assay.

Summary and Conclusions

- Our data suggest a specificity of imetelstat for malignant megakaryocytic cells
- The impact of imetelstat’s clinical activity is being explored in an ongoing phase 2 study in ET patients who have failed at least one prior therapy or who refuse standard of care.

Conflicts of interest to disclose: Ning Go, Joi Ninomoto, Hooman Kashani, Monic J. Stuart: employees of Geron Corp.; Elisabeth Opliger Leibundgut, Gabriela M. Baerlocher: service contract and research funding by Geron Corp.