MDS Clinical Trials at Einstein and Montefiore

www.mdstreatment.com
Low Platelets are a problem in MDS

Eltrombopag can stimulate platelet production in MDS and AML

- Incactive TPOR
- Membrane
- Cytoplasm
- Active TPOR

Signal transduction:

Inactivated TPOR

Eltrombopag

Activation of TPOR Signal

Increased PLT production
Eltrombopag in MDS and AML

Eltrombopag can have anti-leukemic activity:
Can induce differentiation

Eltrombopag can reverse Revlimid induced thrombocytopenia

Control

EP

Roth et al, Blood 2013

Tamari et al, Leuk Lymp 2014

PHASE II STUDY OF LENALIDOMIDE AND ELTROMBOPAG IN PATIENTS WITH SYMPTOMATIC ANEMIA IN LOW OR INTERMEDIATE I MYELODYSPLASTIC SYNDROME (MDS)
Results
27 patients accrued so far
15 Patients evaluable

Response Rate: 8/15 (55%)
6 patients achieved Red cell transfusion independence

2 Patients achieved Platelet transfusion independance
Response to Eltrombopag

Eltrombopag is effective in treating MDS patient with ASXL1 mutation.
STIMULATORY GROWTH FACTORS
Erythropoietin (EPO), GCSF, GMCSF, TPO, IL-3, SCF

HEMATOPOIESIS

STEM CELL

PROGENITORS

RED CELLS

W.B.Cs

PLATELETS

INHIBITORY CYTOKINES
TGF-beta

Phase II trial of TGF inhibitor in MDS
STAT3 INHIBITION IN MDS

STAT3 is overexpressed in MDS stem cells
High STAT3 levels are predictive of adverse prognosis

Pyrimethamine is a STAT3 inhibitor!

A Phase II Study of Pyrimethamine, a STAT3 Inhibitor, for the Treatment of Intermediate/High-risk MDS that has Relapsed or is Refractory to Azanucleosides
Trials for patients that have failed azacytidine

ALRN-6924: First Dual Inhibitor of MDM2 & MDMX
Activates p53 and kills tumor cells

Phase II trial of ALRN 6924 in patients with MDS and AML
Trials for patients that have failed azacytidine

Phase II trial of LSD1 inhibitor and Retinoic acid in MDS and AML
Causes leukemic blast cells to die
Open at Cornell and Montefiore

Combination of Aza with PD1 antibody
Stimulates the immune system to attack the cancer cells
Questions?