- **Increased HLA-E Expression Correlates with Early Relapse in Multiple Myeloma**
  *Alessandro Lagana, PhD, Institute for Next Generation Healthcare, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 8:30 a.m. on Saturday, December 1; Grand Ballroom 7 (Marriott Marquis San Diego Marina)

  Conclusion: Researchers demonstrated that HLA-E expression correlates with worse PFS in newly diagnosed MM patients. Our data suggests that HLA-E-mediated inhibition of NKG2A-expressing NK cells and T cells is a significant factor in host immune responses and clinical outcome in MM. We are currently analyzing a larger cohort of patient samples by mass cytometry to look more closely at phenotypes and functions of T cells, NK cells and myeloid cells.

- **Infusion of a Cryopreservable Human Megakaryocyte-Biased Cell Product Results in Sustained Platelet Reconstitution In Vivo**
  *Ami Patel, Tisch Cancer Institute, Department of Hematology and Medical Oncology, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 10 a.m. on Saturday, December 1; Grand Hall A (Manchester Grand Hyatt San Diego)

  Conclusion: Researchers created a potent transfusable MK cell product that provides robust and sustained PTL and hematopoietic engraftment in vivo and maintains this capability after cryopreservation. Clinical development of such product is now being pursued for the treatment of thrombocytopenia in acute leukemia patients undergoing chemotherapy.

- **Myeloproliferative Neoplasm (MPN) Blastic Transformation Occurs at the Level of Hematopoietic Stem Cells**
  *Xiaoli Wang, PhD, The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 10:30 a.m. on Saturday, December 1; Room 7B (San Diego Convention Center)

  Conclusion: Researchers' ability to serially transplant the LIC from these patients has allowed us to create the first MPN-BP PDX model that will not only extend our understanding of MPN-BP stem cell biology but might also prove useful for screening drugs to treat MPN-BP.

- **Phase 2 Expansion Study of Oral Rigosertib Combined with Azacitidine (AZA) in Patients (Pts) with Higher-Risk (HR) Myelodysplastic Syndromes (MDS): Efficacy and Safety Results in HMA Treatment Naïve & Relapsed (Rel)/Refractory (Ref) Patients**
  *Shyamala C. Navada, MD, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 4:15 p.m. on Saturday, December 1; Grand Hall A (Manchester Grand Hyatt San Diego)

  Conclusion: The combination of oral rigosertib and AZA in HMA naïve patients with HR-MDS is encouraging compared to single agent AZA. The combination also has activity and reverses the HMA clinical resistance in a substantial number of patients after Rel/Ref, a finding with potentially significant clinical implications. Dose exploration with a higher dose of oral rigosertib (1120mg) administered in different dosing schemes in combination with standard dose AZA continues to be studied to optimize safety and efficacy. By employing risk mitigation strategies, the incidence of GU AEs, including hematuria, has been substantially reduced. We will update the safety and efficacy data at the time of presentation. Based on this data a pivotal trial is planned.

- **Serial Biomarker Monitoring Early after HCT Identifies Different Risks for Relapse and Graft-Vs-Host Disease**
  *Mina D. Aziz, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 9:45 a.m. on Sunday, December 2; Grand Hall A (Manchester Grand Hyatt San Diego)

  Conclusion: Researchers found that a serial monitoring strategy using GVHD biomarkers for one month after HCT is able to identify two groups of patients with very different risks of lethal GVHD and relapse. For these patients, the intensity of immunosuppression after day 28 could be tailored according to the probabilities of developing lethal GVHD and relapse in the context of clinical trials.

- **Results of the Myeloproliferative Neoplasms - Research Consortium (MPN-RC) 112 Randomized Trial of Pegylated Interferon Alfa-2a (PEG) Versus Hydroxyurea (HU) Therapy for the Treatment of High Risk Polycythemia Vera (PV) and High Risk Essential Thrombocythemia (ET)**
  *John Mascarenhas, MD, The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai*
  Oral Presentation: 7 a.m. on Monday, December 3; Grand Hall D (Manchester Grand Hyatt San Diego)

Conclusion: The final analysis of MPN-RC 112 revealed that the CR rates in pts with high risk ET/PV treated with PEG and HU at 12 and 24 months were similar. PEG was associated with a higher rate of grade 3/4 toxicity. Each drug appeared equally capable of modifying the natural history of high risk ET/PV based upon their effects on spleen size, karyotypic abnormalities, histopathological parameters and the low incidence of thrombotic complications and disease evolution in both arms.

- **Results of the Pivotal STORM Study (Part 2) in Penta-Refractory Multiple Myeloma (MM): Deep and Durable Responses with Oral Selinexor Plus Low Dose Dexamethasone in Patients with Penta-Refractory MM**
  *Ajai Chari, MD, The Tisch Cancer Institute, Icahn School of Medicine*
  Oral Presentation; 7:45 a.m. on Monday, December 3; Room 6F (San Diego Convention Center)

  Conclusion: Results of the pivotal STORM Part 2 in penta (PI, IMiD, dara)-refractory MM demonstrated that oral selinexor plus low-dose dexamethasone (Sd) was highly active with an ORR of 26.2%. Importantly, responses were rapid and deep with 2 patients achieving sCRs (both MRD negative) in these heavily pre-treated penta-refractory MM pts (median 7 prior regimens, 53% high risk). AEs are a function of dose/schedule/disease severity and can be managed with dose modifications and supportive care. No major organ toxicity was observed and AEs were typically transient and reversible. Sd is an all-oral, first in class mechanism with novel MOA and represents a potential therapeutic option to the growing number of pts with penta-refractory MM who have exhausted approved therapies.

- **Imetelstat Is Effective Treatment for Patients with Intermediate-2 or High-Risk Myelofibrosis Who Have Relapsed on or Are Refractory to Janus Kinase Inhibitor Therapy: Results of a Phase 2 Randomized Study of Two Dose Levels**
  *John Mascarenhas, MD, The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 10:30 a.m. on Monday, December 3; Grand Hall A (Manchester Grand Hyatt San Diego)

  Conclusion: Imetelstat at 9.4 mg/kg IV every 3 weeks has demonstrated clinical activity in int-2 or high-risk MF patients who are relapsed/refractory to JAKi, notably in observed OS. Though no formal study has reported survival for patients who are truly relapsed/refractory to JAKi, median OS of patients who were previously treated with JAKi has been reported to be 12-14 mo (Kuykendall Ann Hematol 2018; Newberry Blood 2017). The safety profile for imetelstat was considered acceptable for this poor-

prognosis population. Imetelstat at 9.4 mg/kg IV every 3 weeks is a promising agent for JAKi-pretreated MF patients and warrants further testing in clinical trials.

- **A Novel iPSC Model Reveals a Role for RUNX1 in the Maintenance of AML Leukemia Stem Cells**
  *Josephine Wesely, PhD, MSc; Tisch Cancer Institute, Department of Oncological Sciences, Icahn School of Medicine at Mount Sinai*
  Oral Presentation: 3:30 p.m. on Monday, December 3; Grand Hall B (Manchester Grand Hyatt San Diego)

  Conclusion: In summary, we developed a new model that enables us to prospectively isolate large numbers of genetically clonal human AML LSCs and perform genome-wide integrative molecular studies, with which we obtained new insights into the biology of AML LSCs.

- **A "De Novo Leukemogenesis" iPSC Model Charts the Clonal Evolution of Acute Myeloid Leukemia**
  *Tiansu Wang, PhD, Tisch Cancer Institute, Department of Oncological Sciences, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 3:45 p.m. on Monday, December 3; Grand Hall B (Manchester Grand Hyatt San Diego)

  Conclusion: Researchers successfully employed CRISPR/Cas to introduce driver mutations into iPSCs in a stepwise manner to “de novo” reconstruct the development of AML. These panels of iPSCs capture the distinct mutational steps along the evolution of AML in a clonal state and isogenic conditions. They should enable mechanistic studies into the processes of leukemogenesis and the effects of specific mutations acting at distinct stages of this progression, their cooperation and the order by which they are acquired. They should also prove a powerful tool to investigate the minimal genetic requirements for leukemia development, the potential need for cooperating epigenetic insults and the effects of the cellular context in myeloid transformation.

- **Additive Effects of Decreased TfR1 and Ablated Erfe Improve Both Ineffective Erythropoiesis and Iron Overload in β-Thalassemic Mice**
  *Marc Ruiz Martinez, PhD, The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 4:30 p.m. on Monday, December 3; Pacific Ballroom 24 (Marriott Marquis San Diego Marina)

Conclusion: Taken together, these experiments provide evidence of the differential and additive effects of TfR1 and ERFE loss in th3/+ mice, with a predominantly erythropoietic benefit of TfR1 loss, a predominantly iron-homeostatic benefit of ERFE loss, and synergy of both in optimizing Epo responsiveness.

- **Mitochondrial Regulation Is Essential for Erythroid Nuclear Clearance**
  *Raymond Liang, PhD, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 5 p.m. on Monday, December 3; Grand Hall C (Manchester Grand Hyatt San Diego)

  Conclusion: Researchers provide evidence for the first time of a link between erythroid enucleation and mitochondrial metabolism. The process described establishes a model of mitochondrial compartmentalization within the cell for providing essential metabolites in a precise spatial and temporal manner. These findings are likely to improve the in vitro production of RBC and might be relevant to anemias of congenital mitochondrial disorders and aging.

- **Atezolizumab in Combination with Daratumumab with or without Lenalidomide or Pomalidomide: A Phase Ib Study in Patients with Multiple Myeloma**
  *Hearn Jay Cho, MD, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai*
  Oral Presentation; 7:30 a.m. on Monday, December 3; Room 6F (San Diego Convention Center)

  Conclusion: Atezo plus dara and in combination with len or pom demonstrated acceptable tolerability; no new safety signals were identified. Some pts treated with either atezo plus dara or atezo plus dara and IMiD appeared to have deep and durable responses. The benefit-risk profile of atezo in combination with dara with/without pom in R/R MM pts is promising. These early data support continuation of the study.