
Please Share the Following Information with Your Doctor

Use this document to facilitate a discussion with your doctor about participating in the SIERRA clinical trial.

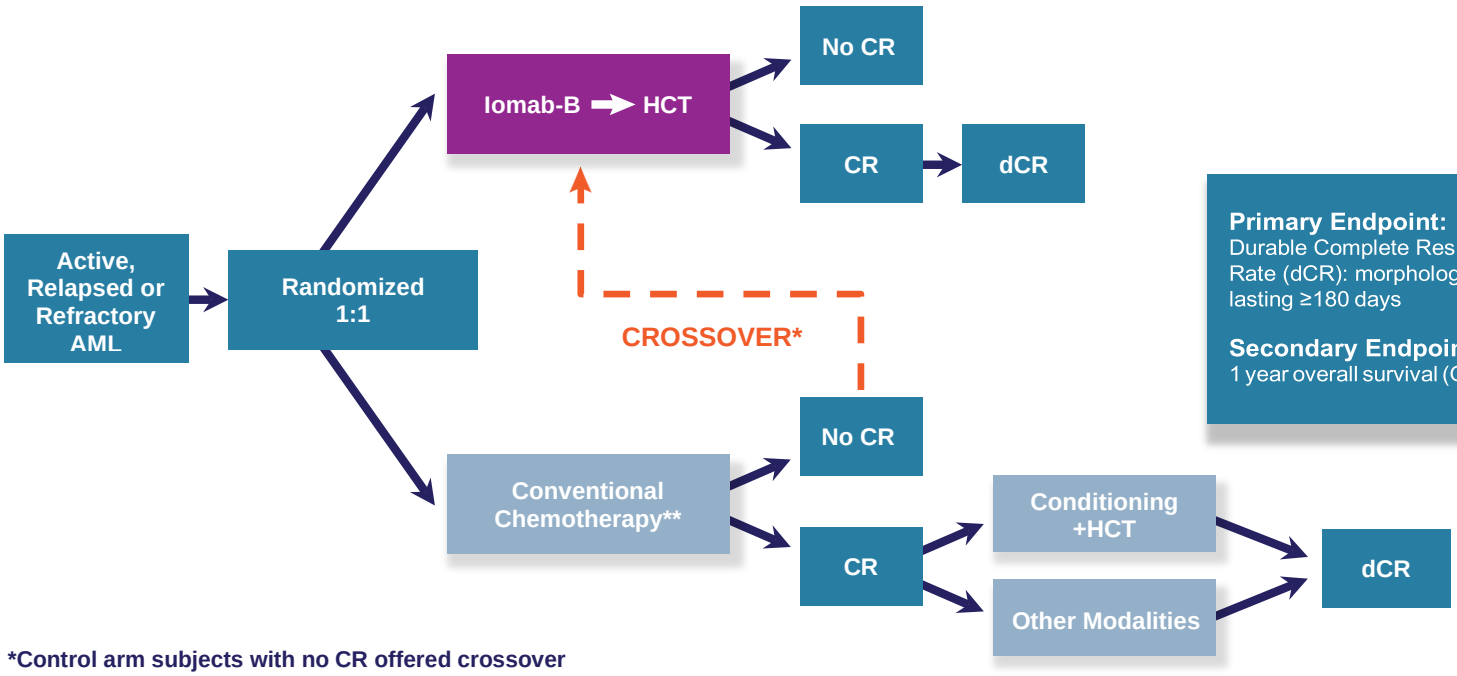
Transplant Can Be An Option for Patients with Active, Relapsed or Refractory Acute Myeloid Leukemia (AML)

SIERRA PHASE 3 Trial Now Enrolling
www.sierratrial.com

SIERRA (NCT02665065)

For patients ≥55 years with active, relapsed or refractory AML who might benefit from a transplant.
Allogeneic HCT now (^{131}I apamistamab; Iomab-B) or after further leukemic reduction (Conventional Care)

Study Design (N=150)



Primary Endpoint:
Durable Complete Response Rate (dCR): morphologic CR lasting ≥180 days

Secondary Endpoint:
1 year overall survival (OS)

*Control arm subjects with no CR offered crossover
**Wide range of flexible options at physician discretion

Key Eligibility Criteria

Inclusion

- 55 years and older with active, relapsed or refractory AML as defined by:
  - Refractory AML: primary induction failure
  - or Relapse after CR1 lasting <6 months
  - or Second or higher relapse
  - or Relapse refractory to salvage attempt
- Matched related/unrelated donor
- Karnofsky Performance Status ≥ 70

Exclusion

- Acute promyelocytic leukemia
- Active leukemic CNS involvement
- Have previously received hematopoietic cell transplant (HCT)
- Currently receiving any investigational agent

SIERRA
Study of Iomab-B in Elderly Relapsed/Refractory AML

The safety and efficacy of the investigational use of this product has not been determined. There is no guarantee that the investigational use listed will be filed with and/or approved for marketing by a regulatory agency.

For additional information, e-mail iomab@actiniumpharma.com or visit www.sierratrial.com.

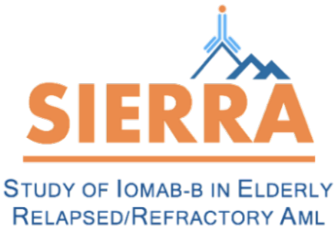
Actinium Pharmaceuticals, Inc.

SIERRA Clinical Trial Sites

Arizona	**Banner MD Anderson**	**Gilbert, AZ**	sierratrial.com/bannermda
Connecticut	**Yale Cancer Center**	**New Haven, CT**	sierratrial.com/yalecc
Florida	**Mayo Clinic**	**Jacksonville, FL**	sierratrial.com/mayoclfl
Illinois	**Loyola University**	**Maywood, IL**	sierratrial.com/loyolamed
Iowa	**University of Iowa**	**Iowa City, IA**	sierratrial.com/uihc
Kansas	**University of Kansas**	**Kansas City, KS**	sierratrial.com/kucc
Minnesota	**Mayo Clinic**	**Rochester, MN**	sierratrial.com/mayoclmn
Missouri	**Washington University**	**St. Louis, MO**	sierratrial.com/wustl
Nebraska	**University of Nebraska**	**Omaha, NE**	sierratrial.com/unmc
New York	**Memorial Sloan Kettering**	**New York, NY**	sierratrial.com/mskcc
	Stony Brook University	**Stony Brook, NY**	sierratrial.com/stonybrook
	Roswell Park	**Buffalo, NY**	sierratrial.com/roswellpark
	Weill Cornell Medicine	**New York, NY**	sierratrial.com/weillcornell
North Carolina	**University of North Carolina**	**Chapel Hill, NC**	sierratrial.com/unc
Ohio	**Ohio State University**	**Columbus, OH**	sierratrial.com/osucc
	University Hospitals	**Cleveland, OH**	sierratrial.com/uhseidman
Ontario	**The Ottawa Hospital**	**Ottawa, ON**	sierratrial.com/ottowahsp
	Princess Margaret Cancer Centre	**Toronto, ON**	sierratrial.com/pmtoronto
Texas	**Baylor University**	**Dallas, TX**	sierratrial.com/bayloru
	MD Anderson Cancer Center	**Houston, TX**	sierratrial.com/mdandersoncc
Washington	**Fred Hutch**	**Seattle, WA**	sierratrial.com/fredhutchcc
Wisconsin	**Medical College of Wisconsin**	**Milwaukee, WI**	sierratrial.com/medcollegewi

SIERRA Trial Site List as of Feb 202

Only Phase 3 Trial With Targeting Conditioning for Active, Relapsed/Refractory AML



This abstract is published online for the 2021 TCT Meeting.

Investigational Drug: Iodine (^{131}I) apamistamab [Iomab-B]

Oral Presentation February 10, 2021: 1:30 PM PT/4:30 PM ET

Myeloablative Targeted Conditioning with Anti-CD45 Iodine (^{131}I) Apamistamab [Iomab-B] Spares the GI Tract and Has Low Incidence of Severe Mucositis, Febrile Neutropenia and Sepsis in the Prospective, Randomized Phase 3 Sierra Trial for Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)

Rajneesh Nath, MD1, Boglarka Gyurkocza, MD2, Hannah Choe, MD3, Stuart E. Seropian, MD4, Patrick Stiff, MD5, Edward Agura, MD6, Sunil, Abhyankar, MD7, Mark R. Litzow, MD8, Benjamin Tomlinson, MD9, Camille Abboud, MD10, George L Chen, MD11, Parameswaran Hari, MD, MRCP12, Johnnie J. Orozco, MD, PhD13, Mitchell Sabloff, MD14, Zaid Al-Kadhimi, MD15, Koen Van Besien, MD, PhD16, Margarida Silverman, MD17, James Foran, MD18, Michael W Schuster, MD19, Partow Kebriaei, MD20, Moshe Yair Levy, MD6, Hillard M. Lazarus, MD21, Sergio A Giralt, MD22, Qing Liang, PhD23, Mark S. Berger, MD23, Vijay Reddy, MD, PhD23 and John M.Pagel, MD, PhD24

(1)Banner MD Anderson Cancer Center, Gilbert, AZ, (2)Memorial Sloan Kettering Cancer Center, New York, NY, (3)Ohio State University Wexner Medical Center, Columbus, OH, (4)Hematology, Yale University School of Medicine, New Haven, CT, (5)Loyola University Chicago Stritch School of Medicine, Maywood, IL, (6)Baylor University Medical Center, Dallas, TX, (7)Hematologic Malignancies and Cellular Therapeutics, University of Kansas Cancer Center, Westwood, KS, (8)Division of Hematology, Mayo Clinic, Rochester, MN, (9)Seidman Cancer Center, University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, OH, (10)Bone Marrow Transplantation & Leukemia Section, Division of Oncology, Washington University School of Medicine, St. Louis, MO, (11)Department of Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, NY, (12)Medical College of Wisconsin, Presenting on behalf of Plerixafor Mobilization Study Group of the CIBMTR, Milwaukee, WI, (13)Department of Medicine, University of Washington, Seattle, WA, (14)The Ottawa Hospital General Campus, BMT, Ottawa, ON, Canada, (15)Hematology/Oncology, University of Nebraska Medical Center, Omaha, NE, (16)Weill Cornell Medicine, New York, NY, (17)Internal Medicine, Division of Hematology, Oncology, and Blood and Marrow Transplantation, University of Iowa Hospitals and Clinics, Iowa City, IA, (18)Division of Hematology and Medical Oncology, Mayo Clinic, Jacksonville, FL, (19)Stony Brook University Hospital, Stony Brook, NY, (20)Stem Cell Transplantation & Cellular Therapy, University of Texas MD Anderson Cancer Center, Houston, TX, (21)Case Western Reserve University, Cleveland, OH, (22)Medicine, 1275 York Avenue, New York City/New York, NY, (23)Actinium Pharmaceuticals, New York, NY, (24))Swedish Cancer Institute, Seattle, WA

2021 TCT Meeting #59

Title: Myeloablative Targeted Conditioning with Anti-CD45 Iodine (131I) Apamistamab [Iomab-B] Spares the GI Tract and Has Low Incidence of Severe Mucositis, Febrile Neutropenia and Sepsis in the Prospective, Randomized Phase 3 Sierra Trial for Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)

Background: Older patients with active R/R AML are often unable to undergo HSCT due to the toxicity of myeloablative conditioning. We hypothesize that targeted conditioning with Iomab-B spares non-hematologic organs such as the GI tract, with a favorable toxicity profile of mucositis, febrile neutropenia (FN), and sepsis.

Methods: The SIERRA trial is a prospective trial for patients ≥55 years of age with R/R AML (≥5% blasts) and 8/8 HLA-MUD or related donors. Patients were randomized to Iomab-B or Conventional Care (CC) (Figure 1). Those in the Iomab-B group received a dosimetric infusion of Iomab-B followed by nuclear imaging to determine the personalized dose. Therapeutic dose calculations, utilizing the Olinda software (Version 2.1, Hermes Medical) to determine the delivery of a maximum of 24 Gy dose to the liver, were performed based on the imaging results. HSCT was performed 12-14 days following Iomab-B therapy, and Fludarabine (30 mg/m2 x 3) and total body irradiation of 2 Gy. CC patients received the investigator's choice of salvage therapy. AE variables of mucositis (Gr 3-4), FN (Gr 3-4) and sepsis were evaluated. An analysis was performed with both total activity of Iomab-B as well as with the radiation dose delivered to the bone marrow and the GI tract. For each of the 3 AEs, a multivariate analysis was performed, allowing each of the predictor variables to be included in the model.

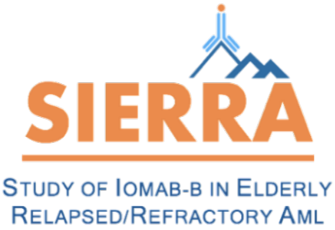
Results: A total of 113/150 (75%) patients were randomized at the time of analysis, with preliminary data available for 54 patients that received Iomab-B/HSCT and 56 for CC. The median dose of Iomab-B was 636 mCi (range 354-1027 mCi) and the median radiation dose delivered to the marrow in the Iomab-B group was 14.9 Gy (range 4.6 – 32 Gy) and 2.8 Gy to GI tract (Table 1). All patients (median age 64) treated with Iomab-B conditioning engrafted ANC at a median of 14.5 days (range 9-22), despite a median 27% marrow blasts prior to transplant. No correlation was found between rates of mucositis, FN, and sepsis and administered Iomab-B activity, nor with dose delivered to GI tract. Compared to standard of care transplant all AEs were lower in the Iomab-B group and sepsis was significantly reduced (p=0.026) (Table 1).

Conclusion: Targeted myeloablative conditioning with Iomab-B resulted in low rates of severe mucositis, FN, and sepsis, despite a high radiation dose (14.9 Gy) delivered to the bone marrow, likely due to the low dose of radiation (2.8 Gy) received by the GI tract. These results represent potentially significant improvements in the safe delivery of myeloablative therapy with high-dose targeted radioimmunotherapy prior to HSCT in older patients with R/R AML. This SIERRA trial is currently enrolling patients (www.sierratrial.com or clinicaltrials.gov **NCT02665065**).

Table 1

Adverse Event	Iomab-B till D100 N = 47	Crossover till D100 N = 27	Std HSCT till D100 N = 9	p-value: Iomab D100 vs. Std HSCT D100
Sepsis % (n)	4% (2)	22% (6)	33% (3)	**0.026**
FN Gr 3-4 % (n)	35% (16)	41% (11)	56% (5)	0.27
Mucositis Gr 3-4 % (n)	11% (5)	19% (5)	33% (3)	0.11
Radiation Dose to BM (Gy) Median (range)	14.9 (4.6-32)	15.4 (6.3-30)	NA	NA
Radiation Dose to GI Tract (Gy) Median (range)	2.8 (1.6-6.7)	3.2 (1.7-8.9)	NA	NA

Only Phase 3 Trial With Targeting Conditioning for Active, Relapsed/Refractory AML



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Investigational Drug: Iodine (^{131}I) apamistamab [Iomab-B]

Oral Presentation February 10, 2021: 1:45 PM PT/4:45 PM ET

Targeted Radioimmunotherapy with Anti-CD45 Iodine (131I) Apamistamab [Iomab-B] in Older Patients with Active, Relapsed or Refractory (R/R) Acute Myeloid Leukemia Results in Successful and Timely Engraftment Not Related to the Radiation Dose Delivered

Boglarka ***Gyurkocza, MD***[1], *Rajneesh Nath, MD*[2], *Hannah Choe, MD*[3], *Stuart E. Seropian, MD*[4], *Patrick Stiff, MD*[5], *Edward Agura, MD*[6], *Sunil Abhyankar, MD*[7], *Mark R. Litzow, MD*[8], *Benjamin Tomlinson, MD*[9], *Camille Abboud, MD*[10,11], *George L Chen, MD*[12], *Parameswaran Hari, MD, MRCP*[13], *Johnnie J. Orozco, MD, PhD*[14], *Mitchell Sabloff, MD*[15], *Zaid Al-Kadhimi, MD*[16], *Koen Van Besien, MD, PhD*[17], *Margarida Silverman, MD*[18], *James Foran, MD*[19], *Michael W Schuster, MD*[20], *Partow Kebriaei, MD*[21], *Moshe Yair Levy, MD*[6], *Hillard M. Lazarus, MD*[22], *Sergio A Giralt, MD*[23], *Qing Liang, PhD*[24], *Mark S. Berger, MD*[24], *Vijay Reddy, MD, PhD*[24] and *John M. Pagel, MD, PhD*[25],

[(1)]Memorial Sloan Kettering Cancer Center, New York, NY, [(2)]Banner MD Anderson Cancer Center, Gilbert, AZ, [(3)]Ohio State University Wexner Medical Center, Columbus, OH, [(4)]Hematology, Yale University School of Medicine, New Haven, CT, [(5)]Loyola University Chicago Stritch School of Medicine, Maywood, IL, [(6)]Baylor University Medical Center, Dallas, TX, [(7)]Hematologic Malignancies and Cellular Therapeutics, University of Kansas Cancer Center, Westwood, KS, [(8)]Division of Hematology, Mayo Clinic, Rochester, MN, [(9)]Seidman Cancer Center, University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, OH, [(10)]Bone Marrow Transplantation & Leukemia Section, Division of Oncology, Washington University School of Medicine, St Louis, MO, [(11)]Medicine, Oncology, Section Leukemia and BMT, 660 South Euclid Avenue , Campus Box 8056-29, St Louis, MO, [(12)]Department of Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, NY, [(13)]Medical College of Wisconsin, Presenting on behalf of Plerixafor Mobilization Study Group of the CIBMTR, Milwaukee, WI, [(14)]Department of Medicine, University of Washington, Seattle, WA, [(15)]The Ottawa Hospital General Campus, BMT, Ottawa, ON, Canada, [(16)]Hematology/Oncology, University of Nebraska Medical Center, Omaha, NE, [(17)]Weill Cornell Medicine, New York, NY, [(18)]Internal Medicine, Division of Hematology, Oncology, and Blood and Marrow Transplantation, University of Iowa Hospitals and Clinics, Iowa City, IA, [(19)]Division of Hematology and Medical Oncology, Mayo Clinic, Jacksonville, FL, [(20)]Stony Brook University Hospital, Stony Brook, NY, [(21)]Stem Cell Transplantation & Cellular Therapy, University of Texas MD Anderson Cancer Center, Houston, TX, [(22)]Case Western Reserve University, Cleveland, OH, [(23)]Medicine, 1275 York Avenue, New York City/New York, NY, [(24)]Actinium Pharmaceuticals, New York, NY, (25)Swedish Cancer Institute, Seattle, WA

2021 TCT Meeting #60

Title: Targeted Radioimmunotherapy with Anti-CD45 Iodine (131I) Apamistamab [Iomab-B] in Older Patients with Active, Relapsed or Refractory (R/R) Acute Myeloid Leukemia Results in Successful and Timely Engraftment Not Related to the Radiation Dose Delivered

Background: Older patients with active AML are not transplanted as they are unable to tolerate myeloablative conditioning, while reduced intensity has high rates of relapse. The SIERRA trial is a prospective, randomized, phase 3 trial for older patients with R/R AML to address this unmet need. We hypothesized that a targeted delivery of radiation to the marrow with Iomab-B, achieved with a limit of 24 Gy to the liver, enables successful engraftment despite active disease.

Methods: Eligible patients were ≥55 years with active R/R AML (≥5% blasts), with 8/8 HLA-matched donors. Patients were randomized to the Iomab-B or Conventional Care (CC) arm. Patients randomized to Iomab-B received a dosimetric dose and imaging to determine the therapeutic dose, followed by Fludarabine (30 mg/m2 x 3) and TBI 2 Gy with HSCT after 12-14 days. CC patients received investigator's choice of salvage therapy, and could proceed to standard HSCT if they achieved CR. If CC patients did not achieve CR, the study allowed them to crossover to Iomab-B/HSCT.

Results: A total of 113/150 (75%) patients were randomized with preliminary data available for 54 patients on Iomab-B and 56 on CC (Table 1). 84% (47/56) of CC patients failed salvage therapy, including 54% (30/56) who received targeted agents. Majority, 57% (27/47) crossed over to Iomab-B/HSCT. All Iomab-B/HSCT patients engrafted, despite a median of 27% marrow blasts at baseline. Median time to neutrophil and platelet engraftment were 14.5 days (9-22) and 17 days (4-39) respectively, with 89% of evaluable patients achieving full donor chimerism (>95%) by day 100. Patient age, donor type, marrow cellularity, blast %, stem cell dose, administered Iomab-B activity (mCi), and absorbed marrow radiation dose (Gy), were analyzed for time to engraftment. The radiation dose delivered to the marrow (median 14.9 Gy; range, 4.6-32 Gy) and the total administered activity (median 636 mCi; range, 354-1027 mCi) showed no correlation with the time to neutrophil (p value=0.525) or platelet engraftment (p value=0.952). Regression analyses, considering all the variables individually, did not indicate a statistically significant correlation ($p > 0.1$) between days to engraftment and radiation dose to the marrow. Furthermore, the radiation dose to the marrow did not show a significant correlation with % chimerism at day 28 in Iomab-B patients. These results were consistent for the Iomab-B cross-over patients as well.

Conclusion: Dosimetry to determine a patient-specific dose of Iomab-B provided marrow doses that allowed for reliable engraftment in older patients with R/R AML, despite a heavy leukemia burden of 27% median blasts prior to HSCT. There was no relationship between total administered activity or radiation dose delivered to the marrow with the speed of engraftment. The SIERRA trial is currently enrolling patients (www.sierratrial.com or clinicaltrials.gov **NCT02665065**).

Table1

Phase 3 SIERRA - Preliminary Results			
Baseline Characteristics	**Randomized to Iomab-B (N=54)**	**Randomized to Conventional Care (CC) (N=56)**	
Age (yrs., median, range)	64 (55-77)	65 (55-77)	
Molecular & Cytogenetic Risk[†]	Favorable: 2% Intermediate: 33% Adverse: 65%	Favorable: 6% Intermediate: 29% Adverse: 65%	
% Transplanted Intent-to-Treat Group	87%(47/54)	16% (9/56)	57% (27/47)[††]
Results	**Received Therapeutic Dose of Iomab-B & Transplanted (N=47)[††††]**	**Eligible To Receive Std. of Care Transplant Post-Salvage (N=9)**	**Evaluated for Crossover (N=47)[†††††]**
Cross-over Rate	n/a	n/a	Received Therapeutic Dose of Iomab-B (N=27) Transplanted (N=27) 57% (27/47)[††]
% Transplanted	**100% (47/47)**	**16% (9/56)**	**100% (27/27)**
BM Blast % @ baseline (median, range)	**27 (4-95)**	14 (5-97)	**25 (6-87)**
BM Blast % pre-transplant (median, range)	**27 (4-95)**	1 (0-3)[*]	30 (2-75)
Days to ANC Engraftment	**14.5 (9-22)[***]**	**17 (13-83)[#]**	**14 (10-37)[**]**
Days to Platelet Engraftment	**17 (4-39)[***]**	**22 (8-35)[#]**	**19 (1-38)[**]**
Days to HCT (Post Randomization)	**30 (23-60)**	**66 (51-86)**	**64 (36-100)[^^^^]**
Myeloablative Dose Delivered to Bone Marrow	**14.9 (4.6-32) Gy**	n/a	**15.4 (6.3-30) Gy**
Total Dose Administered	636 (354-1027) mCi	n/a	590 (313-1008) mCi
Chimerism >95% by D100	89% (40/45[^] Evaluable Pts)	67% (4/6[^^] Evaluable Pts)	88% (22/25[^^^] Evaluable Pts)
100-day non-Relapse Transplant-Related Mortality	**4.4% (2/45 Evaluable Pts)**	**22% (2/9 Evaluable Pts)**	**8% (2/25 Evaluable Pts)**

[†] Iomab pt data pending (1), CC pt data pending (2); [††] 3 additional patients confirmed crossover (2 had TI and 1 will have TI) & pending HCT

[††††] No Therapy Dose (7) due to: Declining KPS (4), Infusion Reaction (1), Unfavorable Biodistribution (1), Post Randomization Eligibility (1);
[†††††] Ineligible for Iomab B HCT after crossover evaluation - 13: due to Hospice Care/Progression (4), Declined/Ineligible for HCT (5), Died Pre Crossover (4). 4 Received Dosimetry but No Therapy Dose due to Declining KPS, 3 additional patients pending TI &HCT

[*] 1 pt with 8% BM blasts on D42 with CRp on D50,
[**] ANC engraftment data not available (N=4), platelet engraftment data not available (N=5);
[***] ANC engraftment data not available (N=3), platelet engraftment data not available (N=6);
[#] ANC and platelet engraftment data not available (N=2)

[^] Did not achieve ≥ 95% chimerism (5); Data pending (1); Died (1);
[^^] Did not achieve ≥ 95% chimerism (2) ; Data pending (1); Died (2)
[^^^] Did not achieve ≥ 95% chimerism (3); Data pending (4);
[^^^^] 1 patient at 161 days had delayed transplant due to infection & respiratory failure, received Iomab & transplant when stable, not included in range