A PHASE II STUDY OF ALLOGENEIC TRANSPLANT FOR OLDER PATIENTS WITH AML IN FIRST MORPHOLOGIC COMPLETE REMISSION USING A NON-MYELOABLATIVE PREPARATIVE REGIMEN

SCHEMA PAGE 1 OF 2

Patient Eligibility (see Section 4.0)

Patients with acute myeloid leukemia (AML) (excluding FAB M3) who have achieved a first morphologic complete response and who meet all of the following criteria:

- Complete response (CR) as defined in Section 4.1.1;
- CR was achieved after no more than two cycles of induction chemotherapy with standard cytotoxic chemotherapy (e.g., cytarabine and an anthracycline) or after no more than four cycles of a hypomethylating agent containing regimen including either 5-azacytidine or decitabine;
- Patients may have received as many as but no more than two cycles of consolidation therapy prior to transplant. Any consolidation regimen that does not require transplant may be used. No more than six months can elapse from attainment of morphologically documented CR to transplant on this study.

≥ 4 weeks since prior chemotherapy, radiation or surgery.
Age ≥ 60 years and < 75 years.
Identification of Suitable Donor (see Section 5.0).
Performance Status 0-2
DLCO > 40% with no symptomatic pulmonary disease.
LVEF by ECHO or MUGA ≥ 30%
No uncontrolled diabetes mellitus or serious infection requiring antibiotics.
No known hypersensitivity to E.coli-derived products.
No HIV disease (see Section 4.10)

All therapy (including methotrexate and tacrolimus) and growth factor doses are to be based on corrected weight (see Section 9.4)

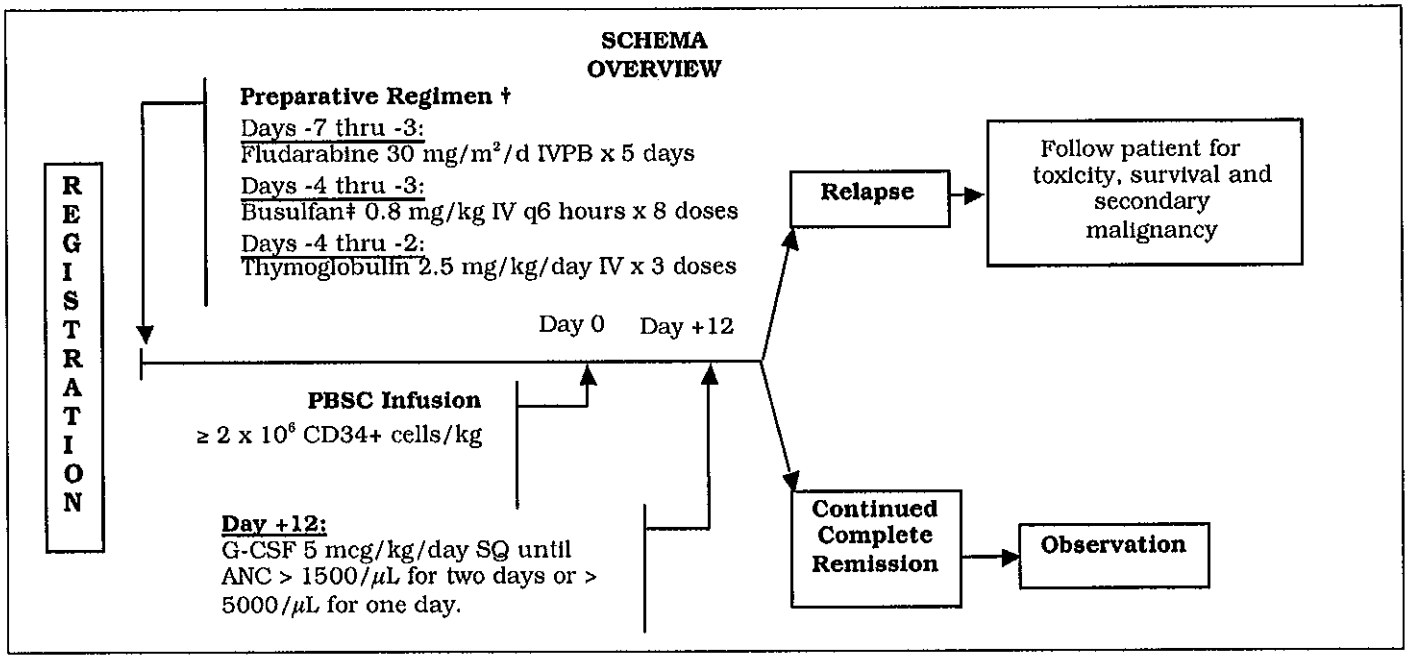
Initial Required Laboratory Values

Calculated Creatinine Clearance	≥ 40 cc/min
Bilirubin*	< 2 mg/dL
AST	< 3 x ULN

**If bilirubin is 2-3 mg/dL but direct bilirubin is normal patient is eligible.*

Donor Eligibility Criteria (see Sec. 5.0)

The donor may be an HLA-identical sibling (6/6) by serologic typing (A, B, DR) or low resolution molecular HLA tests or a 10/10 locus matched unrelated donor using high resolution DNA-based typing.
The donor must be healthy and must be an acceptable donor as per institutional standards for marrow or stem cell donation.
No significant cardiopulmonary, renal, endocrine, or hepatic disease.
There is no donor age restriction, if donor is a matched sibling.
Syngeneic donors will not be eligible.



† See Section 8.2 for supportive care guidelines.

A PHASE II STUDY OF ALLOGENEIC TRANSPLANT FOR OLDER PATIENTS WITH AML IN FIRST MORPHOLOGIC COMPLETE REMISSION USING A NON-MYELOABLATIVE PREPARATIVE REGIMEN

TREATMENT SCHEMA
Schema Page 2 of 2

Patient Preparative Regimen & Stem Cell Infusion (see Sections 8.1, 8.2, & 8.4)

Prior to initiating therapy, placement of a multi-lumen, indwelling Silastic catheter is required.

	F →																			
				B →																
				ATG →																
					Antiviral Prophylaxis— *in patients with a history of herpes simplex to Day +100* →																
						T — *begin taper between Day +90 - +120 to stop between Day +150 - +180* →														
								PBSCT												
									M		M			M					M	
						Antifungal Prophylaxis →									*through Day +100* →					
																				G-CSF
	PCP prophylaxis through Day +100 (see below).																			
Day	**-7**	**-6**	**-5**	**-4**	**-3**	**-2**	**-1**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**

F Fludarabine 30 mg/m^2/day IVPB over 30 minutes x 5 days on Days -7 through -3.

B Busulfan 0.8 mg/kg IV over 2 hours q 6 hours x 8 doses on Days -4 and -3.

ATG Rabbit antithymocyte globulin (thymoglobulin) 2.5 mg/kg/day IV over 6 hours x 3 doses on Days -4 through -2. After the first dose, thymoglobulin may be administered over 4 hours. See Section 8.2.1.3 for premedication instructions.

Antiviral Prophylaxis Antiviral prophylaxis will occur through Day +100 according to institutional guidelines for patients with a history of herpes simplex infection or seropositivity. Prophylaxis may be extended beyond Day +100 at the discretion of the treating physician. See Section 8.2.2.

PCP Prophylaxis PCP prophylaxis will occur through Day +100 according to institutional guidelines. See Section 8.2.4. In patients who develop chronic GVHD, PCP prophylaxis should be extended at the discretion of the physician.

T Tacrolimus target serum levels are 5-10 ng/mL. Serum levels are not to exceed 15 ng/mL. The suggested starting dose is 0.03 mg/kg PO BID beginning on Day -2. Begin tapering between Day +90 to +120 with a goal of stopping by Day +150 to +180 (see Section 8.2.1.1).

PBSCT Peripheral Blood Stem Cell Transplant. On Day 0 a minimum **total** CD34+ cell dose of 2 x 10^6/kg (actual weight - recipient) will be infused.

M Methotrexate 5 mg/m^2/day IV on Days +1, +3, +6 and +11. Hydrate intravenously and induce diuresis (see Section 8.2.1.2).

Antifungal Prophylaxis Antifungal prophylaxis will occur according to institutional guidelines through Day +100. See Section 8.2.3.

G-CSF Recipients will receive 5 mcg/kg G-CSF SQ daily beginning on Day +12 and continuing until ANC > 1500/μL for two consecutive days or > 5000/μL for one day. If ANC decreases to < 1000/μL then resume G-CSF at 5 mcg/kg/day.

HLA-Identical Sibling Donor Stem Cell Collection (see Section 8.3)

			G-CSF— *see below* →													
							Donor Pheresis									
Day	**-7**	**-6**	**-5**	**-4**	**-3**	**-2**	**-1**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**

G-CSF Donors will receive 10 mcg/kg SQ on Days -5 through-2 (and, if necessary -1).

Donor Pheresis On Days -1 (and 0) donors will undergo leukapheresis for 1-2 days to achieve a CD34+ cell dose of ≥ 2 x 10^6/kg (actual weight - recipient). If the yield of CD34+ cells is < 2 x 10^6/kg on Day -1, an additional pheresis will be performed on Day 0. If after two pheresis procedures the total CD34+ cell dose is at least 2.0 x 10^6/kg, no further pheresis is required. Target CD34+ cell doses will be based on institutional standards, as long as minimum of 2 x 10^6/kg is achieved. There is no maximum CD34+ cell dose.