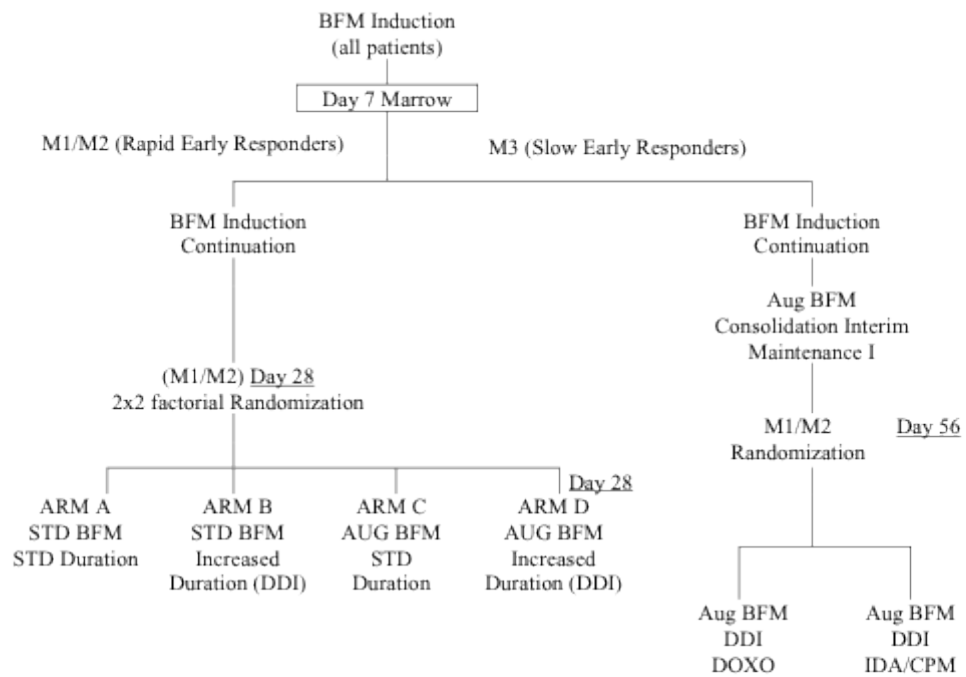


SUPPLEMENTAL DATA

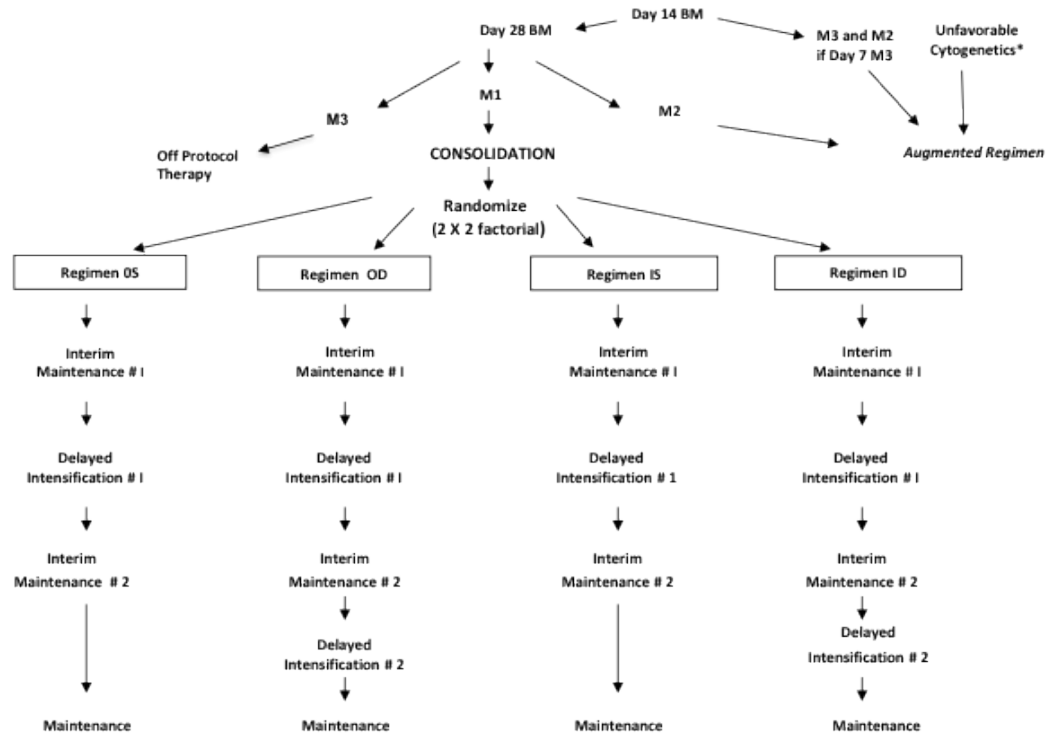
Supplemental Figure 1. Study Schema, CCG-1961



DDI = Double Delayed Intensification
STD = Standard
DOXO = Doxorubicin
IDA = Idarubicin
CPM = Cyclophosphamide

SUPPLEMENTAL DATA

Supplemental Figure 2. Study Schema, CCG-1991



* t(4;11)(q21;q23)(q34;q11), t(9;22), balanced t(1;19)(q23;p13), hypodiploidy with < 45 chromosomes.

SUPPLEMENTAL DATA

Supplemental Table I. Proportion of patients who experienced grade 3 or 4 toxicities, toxicity related delay in therapy, or significant Infections by sex, CCG-1961

Toxicity Site	Phase	Female %	Male %
Any grade 3 or 4 toxicities	Induction	51.1	45.6
Any grade 3 or 4 toxicities	Consolidation	40.8	34.3
Any grade 3 or 4 toxicities	IM 1	29.0	24.3
Any grade 3 or 4 toxicities	DI 1	35.9	26.4
Therapy delayed over a week due to toxicities	Induction	8.8	6.13
Therapy delayed over a week due to toxicities	Consolidation	50.07	46.62
Therapy delayed over a week due to toxicities	IM 1	19.18	15.23
Therapy delayed over a week due to toxicities	DI 1	53.79	52.69
Significant infection [†]	Induction	22.29	16.83
Significant infection [†]	Consolidation	16.73	16.81
Significant infection [†]	IM 1	8.3	6.59
Significant infection [†]	DI 1	20.17	16.03
Liver	Induction	16.75	16.50
Liver	Consolidation	17.65	14.77
Liver	IM 1	11.02	10.96
Liver	DI 1	9.87	8.70
Pancreas	Induction	23.13	16.42
Pancreas	Consolidation	3.27	2.58
Pancreas	IM 1	1.90	1.11
Pancreas	DI 1	4.15	3.81
Pancreas: glucose	Induction	21.69	15.44
Pancreas: glucose	Consolidation	2.35	1.96
Pancreas: glucose	IM 1	1.22	0.74
Pancreas: glucose	DI 1	3.72	3.13
Pancreas: other	Induction	2.17	1.31
Pancreas: other	Consolidation	1.44	0.98
Pancreas: other	IM 1	0.82	0.56
Pancreas: other	DI 1	0.57	0.68
Renal/Genitourinary	Induction	4.58	4.17
Renal/Genitourinary	Consolidation	0.39	0.89
Renal/Genitourinary	IM 1	0.68	0.28
Renal/Genitourinary	DI 1	1.57	0.98
Gastrointestinal	Induction	7.71	5.96
Gastrointestinal	Consolidation	10.07	6.58
Gastrointestinal	IM 1	13.20	9.29
Gastrointestinal	DI 1	8.87	5.18
Pulmonary	Induction	5.18	4.49
Pulmonary	Consolidation	1.57	1.16
Pulmonary	IM 1	1.09	0.56
Pulmonary	DI 1	1.43	0.98
Cardiac	Induction	4.34	3.92
Cardiac	Consolidation	0.92	1.42
Cardiac	IM 1	0.41	0.74
Cardiac	DI 1	1.43	0.98

Toxicity Site	Phase	Female %	Male %
Nervous system	Induction	4.58	3.27
Nervous system	Consolidation	8.10	5.78
Nervous system	IM 1	5.17	3.44
Nervous system	DI 1	7.01	4.59
Peripheral nervous system	Induction	2.41	1.72
Peripheral nervous system	Consolidation	5.10	3.63
Peripheral nervous system	IM 1	3.67	2.23
Peripheral nervous system	DI 1	5.15	2.35
Central nervous system	Induction	2.53	1.72
Central nervous system	Consolidation	4.84	2.76
Central nervous system	IM 1	2.04	1.49
Central nervous system	DI 1	2.52	2.54
Skin	Induction	0.60	0.98
Skin	Consolidation	2.35	2.31
Skin	IM 1	1.90	1.58
Skin	DI 1	1.14	1.37
Allergy	Induction	0.24	0.25
Allergy	Consolidation	1.18	1.69
Allergy	IM 1	1.36	1.02
Allergy	DI 1	0.57	0.29
Coagulation	Induction	10.60	11.60
Coagulation	Consolidation	1.96	1.42
Coagulation	IM 1	0.41	0.93
Coagulation	DI 1	2.43	3.03
Electrolytes	Induction	6.02	7.68
Electrolytes	Consolidation	1.31	1.33
Electrolytes	IM 1	0.54	0.56
Electrolytes	DI 1	1.72	0.59
Fever	Induction	1.33	0.25
Fever	Consolidation	0.26	0.44
Fever	IM 1	0.14	0.37
Fever	DI 1	0.86	0.59
Local	Induction	0.36	0.49
Local	Consolidation	0.39	0.18
Local	IM 1	0.54	0.28
Local	DI 1	0.57	0.10
Mood	Induction	1.20	0.98
Mood	Consolidation	1.31	0.62
Mood	IM 1	0.68	0.46
Mood	DI 1	1.57	0.39
Vision	Induction	0.12	0
Vision	Consolidation	0.13	0
Vision	IM 1	0	0
Vision	DI 1	0.14	0.10
Weight change	Induction	1.08	0.65
Weight change	Consolidation	0.78	0.80
Weight change	IM 1	0.82	0.19
Weight change	DI 1	0.14	0.10

Toxicity Site	Phase	Female %	Male %
Performance ²	Induction	1.33	1.06
Performance	Consolidation	1.05	0.80
Performance	IM 1	0.27	0.28
Performance	DI 1	0.57	0.59

Abbreviations: IM = Interim maintenance, DI = Delayed Intensification; ¹ Significant infections include pneumocystis, varicella/zoster, bacteremia/sepsis, central line related infection - bacteremia, meningitis, fungal infection and other infections that required hospitalization; ²Karnofsky/Lansky scores

SUPPLEMENTAL DATA

Supplemental Table II. Proportion of patients who received supportive care interventions by sex, CCG-1961

Supportive Care Interventions	Phase	Female %	Male %
Any Type	Induction	95.66	93.70
Any Type	Consolidation	93.73	90.84
Any Type	IM 1	46.26	39.65
Any Type	DI 1	83.40	77.13
IV antibiotics	Induction	75.42	69.42
IV antibiotics	Consolidation	62.22	60.14
IV antibiotics	IM 1	30.48	26.00
IV antibiotics	DI 1	57.65	51.03
Antifungals	Induction	13.73	8.83
Antifungals	Consolidation	11.37	8.01
Antifungals	IM 1	6.12	3.99
Antifungals	DI 1	11.02	7.43
Antivirals	Induction	6.27	4.17
Antivirals	Consolidation	5.62	3.83
Antivirals	IM 1	4.63	2.41
Antivirals	DI 1	5.58	4.40
Parenteral nutrition	Induction	10.24	6.62
Parenteral nutrition	Consolidation	12.81	8.19
Parenteral nutrition	IM 1	11.16	5.76
Parenteral nutrition	DI 1	9.44	6.35
Blood product	Induction	91.45	87.00
Blood product	Consolidation	90.85	85.50
Blood product	IM 1	25.03	17.18
Blood product	DI 1	70.82	59.73
Platelet transfusion	Induction	73.01	70.81
Platelet transfusion	Consolidation	50.00	37.63
Platelet transfusion	IM 1	8.71	4.92
Platelet transfusion	DI 1	43.49	34.02
Red blood cell transfusion	Induction	86.14	80.54
Red blood cell transfusion	Consolidation	88.60	84.52
Red blood cell transfusion	IM 1	23.95	15.69
Red blood cell transfusion	DI 1	67.53	54.35
Hematopoietic growth factor	Induction	4.82	2.53
Hematopoietic growth factor	Consolidation	8.25	6.05
Hematopoietic growth factor	IM 1	5.03	1.95
Hematopoietic growth factor	DI 1	10.59	6.55
IV analgesic	Induction	34.46	32.79
IV analgesic	Consolidation	21.20	17.44
IV analgesic	IM 1	15.26	11.79
IV analgesic	DI 1	15.88	14.08

Abbreviations: IM = Interim maintenance, DI = Delayed Intensification; IV = intravenous

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Supplemental Table III. Proportion of patients who experienced grade 3, 4 or 5 toxicities, CCG-1991

Toxicity Category	Phase	OS/OD/IS/ID		Augmented	
		Female %	Male %	Female %	Male %
Any Grade 3, 4, or 5 toxicities	Induction	42.87	37.00	68.91	61.74
Any Grade 3, 4, or 5 toxicities	Consolidation	24.55	26.53	49.52	44.93
Any Grade 3, 4, or 5 toxicities	IM-I	24.79	23.48	29.70	18.66
Any Grade 3, 4, or 5 toxicities	DI-I	38.00	31.77	45.54	35.94
Any Grade 3, 4, or 5 toxicities	IM-II	24.62	21.71	29.29	25.78
Any Grade 3, 4, or 5 toxicities	DI-II	39.52	34.78	45.45	43.09
Significant infections ¹	Induction	20.95	15.80	46.22	46.98
Significant infections ¹	Consolidation	13.74	13.91	30.48	24.64
Significant infections ¹	IM-I	9.98	8.42	13.86	7.46
Significant infections ¹	DI-I	21.23	17.21	20.79	26.56
Significant infections ¹	IM-II	8.93	8.37	12.12	14.06
Significant infections ¹	DI-II	21.60	21.20	26.26	16.26
Allergy/Immunology	Induction	0	0.07	0	0
Allergy/Immunology	Consolidation	0.10	0.08	0	3.62
Allergy/Immunology	3	0	0.25	0.99	1.49
Allergy/Immunology	4	0.21	0.60	0	0
Allergy/Immunology	5	0	0	0	0.78
Allergy/Immunology	6	0.22	0.72	0	0.81
Cardiovascular arrhythmias	Induction	0.08	0.20	0	2.01
Cardiovascular arrhythmias	Consolidation	0.10	0.08	0.95	0.72
Cardiovascular arrhythmias	IM-I	0.21	0	0	0
Cardiovascular arrhythmias	DI-I	0.42	0.09	0.99	0
Cardiovascular arrhythmias	IM-II	0	0	1.01	0
Cardiovascular arrhythmias	DI-II	0.22	0	0	0.81
Cardiovascular	Induction	5.05	5.60	12.61	8.72
Cardiovascular	Consolidation	1.21	1.14	2.86	1.45
Cardiovascular	IM-I	0.63	0.67	0	1.49
Cardiovascular	DI-I	1.06	0.77	0.99	0
Cardiovascular	IM-II	0	0	0	0
Cardiovascular	DI-II	0.86	1.27	2.02	3.25
Coagulation	Induction	6.68	5.66	6.72	7.38
Coagulation	Consolidation	0.51	0.57	0	2.17
Coagulation	IM-I	0.21	0.08	0.99	1.49
Coagulation	DI-I	2.02	1.36	0.99	3.91
Coagulation	IM-II	0	0	0	0.78
Coagulation	DI-II	1.94	1.45	3.03	1.63
Constitutional symptoms	Induction	1.22	1.25	1.68	0
Constitutional symptoms	Consolidation	0.61	1.14	0.95	0.72
Constitutional symptoms	IM-I	0.32	0.25	2.97	1.49
Constitutional symptoms	DI-I	0.53	0.26	0.99	0
Constitutional symptoms	IM-II	0.33	0.09	2.02	0.78
Constitutional symptoms	DI-II	0.86	0.91	0	0
Dermatology	Induction	2.28	1.97	2.52	4.03
Dermatology	Consolidation	0.81	1.22	2.86	2.17
Dermatology	IM-I	0.32	0.42	0.99	0
Dermatology	DI-I	1.06	1.02	0.99	0.78
Dermatology	IM-II	0.76	0.44	0	0.78

Toxicity Category	Phase	OS/OD/IS/ID		Augmented	
		Female %	Male %	Female %	Male %
Dermatology	DI-II	1.51	1.27	1.01	0.81
Endocrine	Induction	0	0.13	0.84	1.34
Endocrine	Consolidation	0	0.08	0	0
Endocrine	IM-I	0	0	0	0
Endocrine	DI-I	0	0	0	0
Endocrine	IM-II	0	0	0	0.78
Endocrine	DI-II	0	0	0	0
Gastrointestinal	Induction	6.19	6.58	11.76	15.44
Gastrointestinal	Consolidation	4.04	3.91	12.38	7.97
Gastrointestinal	IM-I	4.52	3.54	7.92	4.48
Gastrointestinal	DI-I	9.02	5.62	7.92	7.03
Gastrointestinal	IM-II	5.34	3.92	13.13	3.91
Gastrointestinal	DI-II	7.34	8.88	10.10	8.13
Hemorrhage	Induction	1.06	0.92	4.20	3.36
Hemorrhage	Consolidation	0.40	0.33	3.81	1.45
Hemorrhage	IM-I	0	0.08	0.99	0
Hemorrhage	DI-I	0	0.60	0	2.34
Hemorrhage	IM-II	0	0	0	0
Hemorrhage	DI-II	0.22	0.54	6.06	3.25
Hepatic	Induction	9.13	6.91	22.69	12.75
Hepatic	Consolidation	10.10	11.64	16.19	11.59
Hepatic	IM-I	12.29	13.64	11.88	4.48
Hepatic	DI-I	4.78	5.11	12.87	6.25
Hepatic	IM-II	11.87	11.60	14.14	10.16
Hepatic	DI-II	7.56	4.35	14.14	12.20
Metabolic	Induction	12.39	9.22	28.57	22.82
Metabolic	Consolidation	1.41	1.95	6.67	3.62
Metabolic	IM-I	0.95	0.51	1.98	2.99
Metabolic	DI-I	4.56	2.39	1.98	3.13
Metabolic	IM-II	1.53	0.61	4.04	3.91
Metabolic	DI-II	4.54	3.26	2.02	5.69
Musculoskeletal	Induction	0.90	0.79	0.84	0.67
Musculoskeletal	Consolidation	0.61	0.41	0.95	0.72
Musculoskeletal	IM-I	0.11	0.25	0	0
Musculoskeletal	DI-I	0.11	0.17	0	0
Musculoskeletal	IM-II	0.11	0	0	0
Musculoskeletal	DI-II	0	0	0	0
Neurology	Induction	0.90	0.46	0	0.67
Neurology	Consolidation	0.40	0.33	0.95	0
Neurology	IM-I	0	0.08	1.98	0
Neurology	DI-I	0.42	0.17	0	0
Neurology	IM-II	0.22	0.09	0	0
Neurology	DI-II	0.22	0.54	0	0
Ocular	Induction	0.16	0	0	0
Ocular	Consolidation	0.10	0	0	0
Ocular	IM-I	0.11	0.08	0	0
Ocular	DI-I	0.11	0.09	0	0.78
Ocular	IM-II	0	0.09	1.01	0.78
Ocular	DI-II	0	0	1.01	0
Pain	Induction	4.65	3.55	8.40	4.70
Pain	Consolidation	2.22	2.03	2.86	1.45
Pain	IM-I	0.21	0.59	1.98	2.24

Toxicity Category	Phase	OS/OD/IS/ID		Augmented	
		Female %	Male %	Female %	Male %
Pain	DI-I	3.29	1.70	0.99	3.13
Pain	IM-II	0.98	0.52	1.01	0.78
Pain	DI-II	4.10	2.72	5.05	0.81
Pulmonary	Induction	1.14	1.51	5.04	4.70
Pulmonary	Consolidation	0.51	0.98	0.95	1.45
Pulmonary	IM-I	0.63	0.51	0	0.75
Pulmonary	DI-I	1.27	0.43	0	1.56
Pulmonary	IM-II	0.54	0.17	0	0
Pulmonary	DI-II	1.08	0.36	5.05	1.63
Renal/Genitourinary	Induction	0.98	0.46	0	2.01
Renal/Genitourinary	Consolidation	0.51	0.24	0	0
Renal/Genitourinary	IM-I	0.11	0	0	0
Renal/Genitourinary	DI-I	0.21	0.09	0	0
Renal/Genitourinary	IM-II	0.11	0	0	0
Renal/Genitourinary	DI-II	0.22	0.18	0	0.81

Abbreviations: IM = Interim maintenance, DI = Delayed Intensification; ¹ Significant infections include pneumocystis, varicella/zoster, bacteremia, fungal infection and other infections that required hospitalization.