Supplementary Table S2. Therapy-Related Childhood APL Case Studies

A) Therapy-Related APL Cases Diagnosed by Cytogenetics

Primary Tumor/Disease	Sex	Age at t-APL diagnosis (yrs)	Treatment for Primary Disease	Latency (mo)	Karyotype/Diagnostic Method	FAB	Treatment for APL	Outcome	Reference
Acute lymphoblastic leukemia	M	10	RT, VP-16, Cy, VM-26	72	46,XY,t(11;17)(q32;q21)	M2	N/A	CR, 8 months	Pui et. al (1989,1991) [206, 207]
Brain astrocytoma	M	12	RT	26	46,XX,t(15;17)	M3	DNR, ARA-C	CR, 6+ months	Beaumont et. al (2003) [208] Detourmignies et al (1992) [36]
Germ cell tumor (choriocarcinoma)	M	15	Epipodophyllotoxin	21.6	47,XXYc,t(15;17)(q22;q21)	M3	N/A	N/A	Smith et. al (1999) [209]
Glioblastoma	M	20	RT (40 Gy)	31	t(15;17)	N/A	N/A	Died	Attili et. al (2006) [210]
Familial hemophagocytic lymphohistioctosis	F	2	VP-16	24	t(15;17)	M3	N/A	CR, 4+ months	Rudd et. al (2006) [211]
EBV-associated hemophagocytic lymphohistiocytosis	M	3	VP-16, dexamethasone, cyclosporine, intrathecal MTX	18	t(15;17)(q22;q12)	N/A	ATRA, DNR, Ara-C	CR	Sathiyamoorthy et. al (2011) [212]
Hodgkin Lymphoma	F	18	ABVD, mantle field RT (36 Gy), paraaortic field (30 Gy)	23	t(15;17)	M3	ATRA, Dox	CR	Elezovic et. al (2000) [213]
Hodgkin Lymphoma	F	19	ABVD, RT	33 [a]	PML-RARA by RT-PCR	N/A	N/A	N/A	Hasan et. al (2010) [214]
Hodgkin Lympohma CS IIIB	F	19	ABVD, RT	23	46, XX,t(15;17)(q22;q11-21)	M3	N/A	N/A	Antonijevic et. al (2011) [215]
Hodgkin Lymphoma	F	19	ABVD, RT	33	PML-RARA by RT-PCR	N/A	N/A	N/A	Ottone et. al (2012) [216]
T-cell Non-Hodgkin Lymphoma	M	20	ACVBP, high dose MTX, VP-16, Ara-C, IFM	N/A	46,XX,t(15;17)	N/A	ATRA, DNR, Ara-C	CR, 83+ months	Beaumont et. al (2003) [208]
Non-Hodgkin Lymphoma	M	10	VP-16	30	46 XY t(11q-; 17q+)	M5	N/A	N/A	Sugita et. al (1993) [217]
Non-Hodgkin Lymphoma	F	8	Dox, Cy, VCR, MTX, L-asparaginase, 6-mercaptopurine	37	46,XX,inv(1)(p11;q12),t(15;17)(q22;q21), add(17)p13	M3	Pirarubicin, Ara-C, ATRA, BMT, MTX	CR	Ogami et. al (2004) [228]
Langerhans cell histiocytosis	F	6	VBL, PSL, MTX, VP-16	23	46,XX,t(15;17)(q22;q21)	M3	VP-16, Ara-C, MX	CR	Horibe et. al (1993) [222]
Langerhans cell histiocytosis	F	3	VCR, MTX, PSL, Cy, VP-16	36	46,XX,t(15;17)(q22;q12)	M3	BFM-83 Protocol	Died, 13 months	Horibe et. al (1993) [222]
Langerhans cell histiocytosis	F	7	VP-16, PSL	56	46,XX,11p-,14q+,t(15;17)	M3	DNR, Ara-C, VCR, 6-mercaptopurine, MX	CR, 5+ months	Matsuzaki et. al (1994) [227]
Langerhans cell histiocytosis	M	5	VP-16, PDN	40	46 XY t(15;17)	M3	N/A	N/A	Haupt et. al (1997) [221]
Langerhans cell histiocytosis	F	7.4	VBL, PDN, VP-16	61.2	46,XX,t(15;17)	M3v	N/A	N/A	Haupt et. al (1997) [221]
Langerhans cell histiocytosis	M	9	VBL, PSL, vindesine	102 [a]	t(15;17)	N/A	BMT	CR	Kudo et. al (1998) [37]
Langerhans cell histiocytosis	F	10.75	VP-16, MP, VBL	60	t(15;17)	M3	Ara-C, idarubicin, ATRA, MTX, VP-16, thioguanine	CR, 3+ yrs	Dufour et. al (2001) [219]
Liver transplant (ornithine transcarbamylase deficiency)	F	13.75	Immunosupressive therapy: tacrolimus, azathiprine	21	46,XX,t(15;17)(q22;q12), PML-RARA by PCR	M3	Ara-C, DNR, ATRA, MP, MTX	CR, 14+ months	Sato et. al (2005) [231]
Liver transplant (congenital biliary atresia)	F	7	Immunosupressive therapy: tacrolimus	46	46,XX,t(15;17)(q22;q12)	M3	Ara-C, DNR, ATRA, PSL	CR, 3 months	Sato et. al (2005) [231]
Multiple sclerosis	F	21	MX	52	46, XX,t(15;17)(q22;q12)	M3	ATRA, idarubicin, HCST	CR	Ledda et. al (2006) [223]
Neuroblastoma	F	5.8	VP-16, Carboplatin	3 [b]	t(15;17)	M3	N/A	Died	Schiavetti et. al (2001) [232]
Psoriasis	M	17	Bimolane	36	46,XY/46,XY, lp+, t(15;17) (q22;q12)	M3	ATRA	CR, 57+ months	Xue et. al (1992) [233]
Psoriasis	F	21	Bimolane	24	46,XX/46, XX, t(15;17) (q22;q12)	M3	ATRA	CR, 21 months	Xue et. al (1992) [233]
Rhabdomyosarcoma	M	8	Cy, IFM, CDDP, Act-D, anthracycline, VP-16, RT	45	44,XY, -5,-17,del(7)(q22;q35), dic(?;11;?;21)(?::11q22->11p15::?::21p13->21qter, +der(5)t(5;17)(q11;q11) [c]	M2	N/A	N/A	Rubin et. al (1991) [230]
Wilms' Tumor	M	2	IFM, Act-D,VP-16, RT	21	46,XY,-8,dir dup(3)(p21-> p25)t(5;17)(q31;p11),+der8, t(8;13)(p21;q12) [d]	M2	N/A	N/A	Rubin et. al (1991) [230]

B) Therapy-Related APL Cases Diagnosed by Morphology

Ewings sarcoma	M	10	CDDP, VM 26, VP-16, VCR, Cy, Act-D, Dox, IFM	32	N/A, cytogenetic analysis was unsucessful due to technical difficulties	M3	ATRA	CR, 8+ months	Lopez-Andrew et. al (1994) [226]
Hodgkin Lymphoma	M	7	splenectomy, chemotherapy (alternating MOPP and ABVD for six cycles,) mantle field RT (2500 rad), inverted Y irradiation (25 Gy)	4	46,XY,t(8;21)(q22;q22),t(9;22)(q34;q11) [e]	M3	DNR + Ara-C; high-dose Ara-C; ablative therapy, ABMT	Died, 6 months	Dallorso et. al (1990) [218]
Langerhans cell histiocytosis	F	7	VP-16, VBL, steroids	46.8	46,XX,del(2)(q11;q13) at relapse [e]	M3	N/A	N/A	Haupt et. al (1997) [221]
Langerhans cell histiocytosis	F	0.8	VP-16	30	46,XX,+ ring,-6,-10, +marker [e]	M3v	Ara-C, idarubicin, TBRT, melphalan, ABMT	N/A	Haupt et. al (1997) [221]
Langerhans cell histiocytosis	F	8	VP-16, Cy, ADR, VBL, steroids	105.6	N/A	M3	N/A		Haupt et. al (1997) [221]
Langerhans cell histiocytosis	M	7	VBL, PDN, VP-16	18 [f]	46, XY t(1;3)(p36;q21); del(17), del 18p, iso 16q [e]	M3	ATRA, thioguanine, Dox, Ara-C	N/A	Lopes et. al (1999) [225]
Langerhans cell histiocytosis	F	11	VP-16	47	46, XX,del(20)(q11;q13) [e]	M3	Chemotherapy	Died	Ogami et. al (2004) [228]
Malignant ependymoma	M	12	RT	20	N/A	M3	N/A	Died	Pai et. al (1985) [229]
Multiple sclerosis	F	21	MX	18	N/A	N/A	N/A	CR	Ellis and Bogglid (2009) [220]
Psoriasis	F	19	Bimolane	21.6	N/A	M3	N/A	N/A	Li et. al (1989) [224]

[a] Latency defined as interval between primary diseae and development of t-APL.

[b] Latency defined as time from interruption of treatment for primary disease to development of t-APL.

[c] karyotype for 55% of 20 metaphse cells examined. Karotype for remaining cells: 46 XY (15%), 45 XY,-5,-17, del(7),(q22q35),+der(5)t(5;17)(q11;q11) (10%); 46 XY,-5-7, +21, del(7)(q22q35), +der(5)t(5;17)(q11;q11) (10%)

[d] karyotype for 38% of 24 metaphase cells examined. Karoytype for remaining cells: 46,XY,dir dup(3),(p21-> p25), t(5;17)(q31;p11) (29%); 46,XY,-2,dir dup(3),(p21-> p25),t(3;?)(q27;?), t(5;17)(q31;p11),t(21;?)(q11;?),+der(2),t(2;13)(q31;q12) (33%)

[e] cytogenetics inconsistent with APL

[f] treatment for LCH was irregular due to social-economic family problem. Time between treatment for LCH and APL was unclear.

ABMT, autologous bone marrow therapy; ABVD, adriamycin (doxorubicin), bleomycin, vinblastine, dacarbazine; Act-D, actinomycin D; ACVBP, doxorubicin, cyclophosphamide, vindesine, bleomycin, prednisone; Ara-C, cytosine arabinoside (cytarabine); AN, anthracyclines; ATRA, all trans retinoic acid; AVBD, adriamycin, bleomycin, vinblastine & dacarbazine; BI, bleomycin; CDDP, cisplatinum; CR, complete remission; Cy, Cyclophosphamide; D, dacarbazine; DNR, daunorubicin; Dox, Doxorubicin (adriamycin); HDMP, high dose methylprednisolone; IFM, iphoshamide; LCH, Langerhans Cell Histiocytosis; MOPP, mechlorethamine, vincristine, procarbazine, prednisone; MP, methylprednisolone; MTX, methotrexate; MX, mitoxantrone; N, nitrogen mustard; PDN, predinisone; P, procarbazine; PSL,prednisolone; RT, radiotherapy; TBRT, tumor bed radiotherapy; VBL, vinblastine; VCR, vincristine; VM-26, teniposide; VP-16, etoposide.