

**Supplemental Table 1.** Summarizes clinical features, treatment, and outcome of ATLL patients with CNS involvement at diagnosis, or after relapse (N=18).

Patient code	Age at diagnosis (yrs)	Gender	ATLL Subtype	CNS Site at Diagnosis	Initial Treatment	CNS relapse site	Subsequent Treatment and Outcome
ATLL2	37	Male	Acute	Not assessed initially	AZT-IFN x 6.5 yr (CR), had PD with nodal and lung disease, then oral etoposide x 4 wks (PD), AZT-vorinostat x 1 yr (objective response) followed by followed by oral AZT only > 4 yr (SD), after PD in nodal disease, BM, and perineal mass, had pralatrexate x 3 courses (PD), mogamulizumab x 2 courses (PD in CNS after seizures)	Leptomeningeal	Received alternating high dose MTX-AZT x 3 cycles with IT chemotherapy and EPOCH x 2 cycles (PR and CSF clearance), then became debilitated. Died from PD: OS= 13.4 yr
ATLL25	67	Male	Acute	Lymphomatous meningitis-presented with altered mentation	AZT-IFN x 8 days (PD), IT chemo, HD-MTX-AZT x 2 cycles, kinetic failure (PD)		Died from PD: OS= 2.7 mo
ATLL27	51	Female	Acute	Lymphomatous meningitis-presented with headaches and blurred vision	AZT-IFN with IT chemo x 1 (CR, then refused further IT chemo and AZT-IFN due to side effects), had PD after 2.8 yr, then VCAP-AP-VECP x 2 cycles (PR then PD), then oral etoposide (SD)		Died likely due to PD at outside center, OS= 4 yr
ATLL33	36	Female	Lymphomatous	Not assessed initially	EPOCH x 2 cycles (PR) followed by AZT-IFN x 2 weeks, progressed with mass extension into temporal lobe	Temporal lobe extension from zygomatic bone	Had IFRT followed by HD-MTX x 2 cycles (CR) and maintenance AZT-IFN; relapsed with soft tissue mass after 6.7 mo, had IFRT (CR); relapsed with severe refractory hypercalcemia. Died from PD: OS= 1.6 yr

ATLL46	43	Male	Lymphomatous	Lymphomatous meningitis-presented with blurred vision	HD-MTX x 2 cycles with IT chemotherapy		Alive at las follow up, went back to country of origin; OS= 4.3 weeks
ATLL49	55	Male	Acute	Lymphomatous meningitis-presented with cranial nerve deficits	HD-MTX x 1 cycle with IT chemotherapy while intubated		Died from infection (pneumonia, sepsis), multi-organ failure: OS= 11 days
ATLL53	58	Female	Acute	Lymphomatous meningitis-presented with altered mentation	IT chemotherapy with CSF clearance, then AZT-IFN (PD after 8 weeks); CHOP-ONTAK x 1 cycle		Lost follow after moving to another center. Died from PD: OS= 6 mo
ATLL80	43	Male	Acute	Positive CSF at diagnosis, unknown symptoms	IT chemotherapy, AZT-IFN started with normalization of lymphocyte count		Deceased outpatient from illicit drug overdose. OS= 2.6 wks
ATLL103	47	Female	Acute	Not assessed initially	AZT-IFN (PR, then PD after 4 weeks), followed by VCAP-AP-VECP x 7 cycles with IT chemotherapy prophylaxis (CR), followed by allogeneic SCT	Leptomeningeal	Received HD-MTX-AZT x 3 cycles with IT chemotherapy x 10 until CSF clearance. Completed craniospinal radiation. Deceased with sepsis after PD in bones. OS= 25 mo
ATLL114	55	Male	Lymphomatous	Lymphomatous meningitis with right eye orbit involvement-presented with diplopia	CODOX/IVAC with alternating HD-MTX-AZT x 5 cycles with IT chemotherapy with CSF clearance		PD with severe refractory hypercalcemia, renal failure, debilitation. Deceased; OS= 5.8 mo
ATLL115	77	Male	Lymphomatous	Negative CSF at diagnosis	EPOCH-bortezomib-raltegravir x 6 cycles (CR with PFS 28 mo); relapsed with nodal, and skin plaques, received brentuximab vedotin x 7 courses (CR, with PFS 28 months); progressed with nodal disease and skin disease, failed brentuximab, and progressed with CNS involvement	Leptomeningeal	Received HD-MTX (ongoing); OS= 5.6 yr

ATLL120	55	Female	Lymphomatous	Negative CSF at diagnosis	DA-EPOCH x 3 cycles switched to CHOEP x 3 cycles with oral AZT and IT chemotherapy as prophylaxis (CR with PFS 13 mo). Relapsed with leukemia, nodal disease, and CNS involvement	Leptomeningeal	Received alternating HD-MTX-Ara-C (x 2 cycles) and IVAC (x 1 cycle) with IT chemotherapy with CSF clearance, had PD, AZT-IFN (PD), then GVD (PD). Died after PD: OS= 1.6 yr
ATLL128	56	Female	Lymphomatous	Pituitary gland mass and positive CSF-presented with headache and diplopia	Partial pituitary tumor resection, high dose ARA-C/MTX, with IT chemotherapy followed by radiation, then MTX-AZT x 1 (PR), then PD, DHAP x 1 cycle (PD).		Deceased after PD (leukemia, persistent hypercalcemia); OS= 7.8 mo
ATLL148	65	Female	Acute	Positive CSF at diagnosis, no known symptoms	Hyper cVAD x 1 course (PR)		Was alive at last follow up, went back to country of origin; OS= 6 weeks
ATLL156	38	Female	Lymphomatous	Lymphomatous meningitis-presented with vision loss	Refused treatment		Hospice care, deceased: OS= 5.6 wks
ATLL195	47	Male	Lymphomatous	Sino-nasal mass with CNS extension	Refused treatment		Went to hospice care: OS= 2.1 wks
ATLL206	62	Female	Lymphomatous	Negative CSF at diagnosis	CHOP x 3 cycles with PR after cycle 2, refused further therapy, progressed with brain mass	Intracranial mass	Deceased: OS= 4.8 mo
ATLL222	56	Male	Acute	Diffuse patchy meningeal enhancement on brain MRI, proven positive by CSF	AZT-IFN x 17 days, IT chemotherapy (transient dramatic hematologic response, then PD)		Went to Hospice. Died of PD; OS= 4.3 weeks

**Ara-C:** Cytarabine; **AZT-IFN:** Zidovudine/Interferon alpha; **CHOEP:** etoposide, cyclophosphamide, vincristine, doxorubicin and prednisone; **CNS:** cerebrospinal fluid; **CODOX/IVAC:** cyclophosphamide, vincristine and doxorubicin/ifosfamide, etoposide and cytarabine; **CR:** Complete response; **CSF:** Cerebrospinal fluid; **DA-EPOCH:** dose-adjusted etoposide, cyclophosphamide, vincristine, doxorubicin and prednisone; **HDMTX:** High-dose methotrexate; **HyperCVAD:** cyclophosphamide, vincristine, doxorubicin and dexamethasone, alternated with high-dose cytarabine and methotrexate; **IFRT:** involved field radiation therapy; **IT:** Intrathecal; **OS:** overall survival; **PFS:** progression free survival; **PD:** Progressive disease; **SD:** stable disease; **UA:** Unable to assess; **VCAP-AP-VECP-->** **VCAP:** vincristine, cyclophosphamide, doxorubicin and prednisone; **AP:** doxorubicin, prednisone; **VECP:** vincristine, etoposide, carboplatin, and prednisone.

**Supplemental Figure 1.** PFS according to first-line chemotherapy regimen

