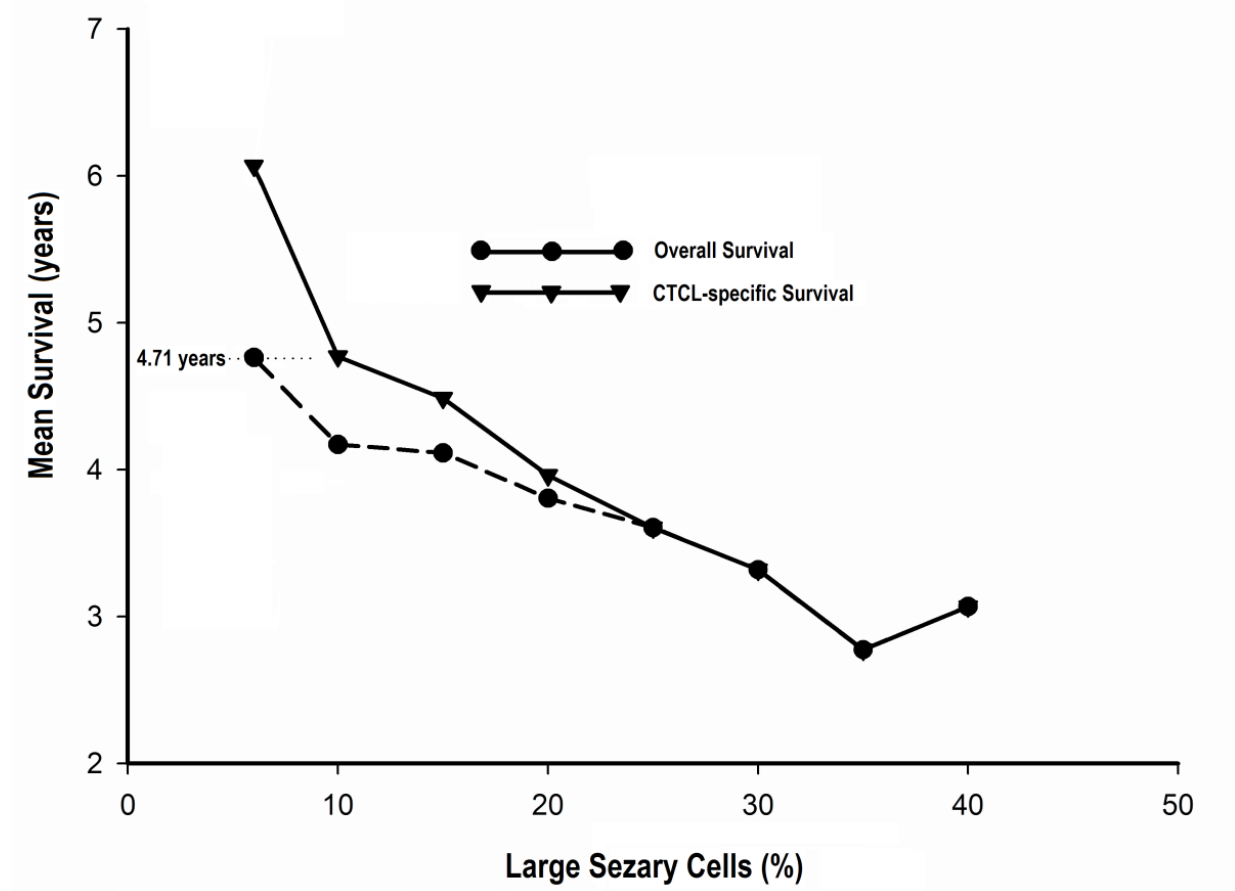
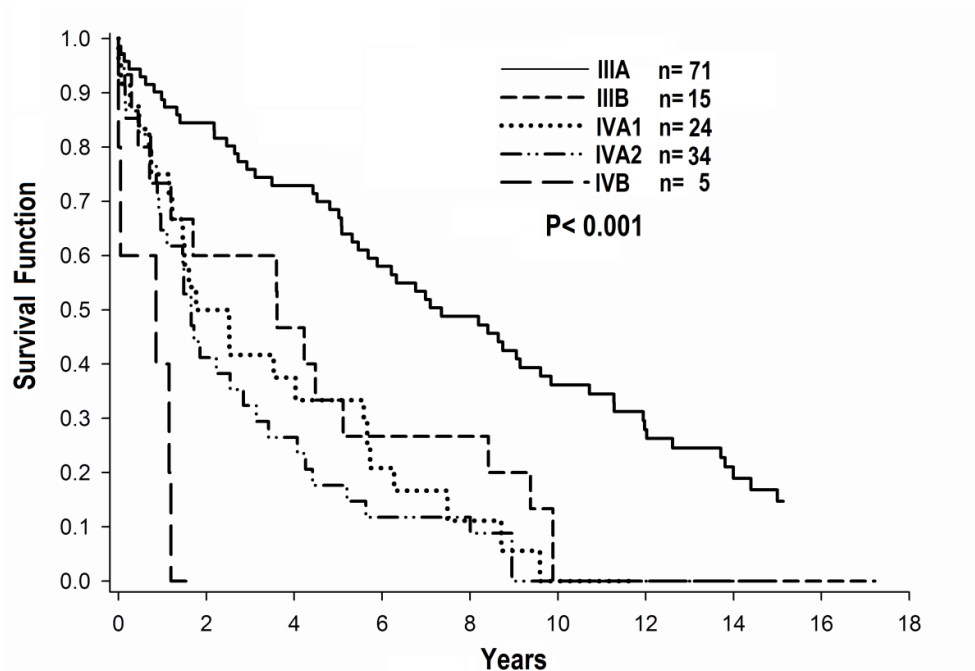


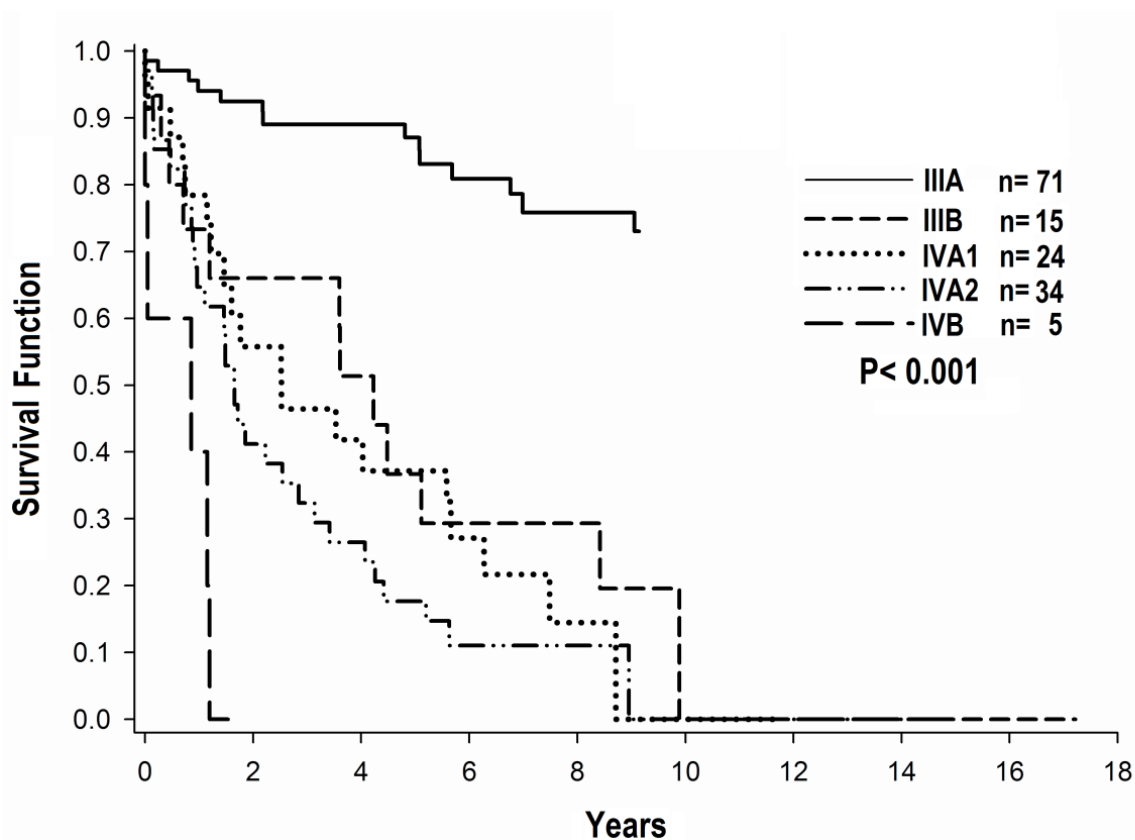
Supplemental Figures



Supplemental Figure 1: The estimated mean survival of patients with erythrodermic cutaneous T cell lymphoma decreases as the percentage of large Sézary cells with diameters $\geq 12 \mu\text{m}$ among lymphocytes increases. The dotted lines show the mean overall survival value for patients with a blood clone demonstrated by PCR.



Supplemental Figure 2: Overall survival curves of patients with erythrodermic cutaneous T cell lymphoma according to clinical stage with B1 and B2 thresholds defined as CD4/CD8 ratio ≥ 5 and ≥ 10 , respectively. See Supplemental Table 2 for mean and 5 year survival rates and comparison between curves.



Supplemental Figure 3: Disease-specific survival curves of patients with erythrodermic cutaneous T cell lymphoma according to clinical stage with B1 and B2 thresholds

defined as CD4/CD8 ratio ≥ 5 and ≥ 10 , respectively. See Supplemental Table 2 for mean and 5 year survival rates and comparison between curves.

Supplemental Tables

| Criteria | | | Overall Survival | | | CTCL-specific Survival | | |
|--|-------|-----|------------------|--------------------|----------|------------------------|--------------------|----------|
| ISCL-EORTC [†] | Stage | No. | Mean ± SEM | P-value | 5 yr (%) | Mean ± SEM | P-value | 5 yr (%) |
| <6% SzC or unconfirmed* | IIIA | 56 | 9.06 ± 1.05 | 0.236§ | 65 | 18.6 ± 21.27 | 0.005§ | 88 |
| ≥ 6% to <1.0 SzC/μL+confirmation | IIIB | 30 | 6.90 ± 0.93 | 0.151 [#] | 57 | 9.11 ± 1.31 | 0.012 [#] | 68 |
| ≥ 1.0 SzC/μL+confirmation | IVA1 | 27 | 4.88 ± 0.99 | 0.233 [¶] | 41 | 5.67 ± 1.22 | 0.145 [¶] | 43 |
| Any | IVA2 | 34 | 3.45 ± 0.71 | 0.034 [‡] | 21 | 3.60 ± 0.76 | 0.034 [‡] | 21 |
| Any | IVB | 5 | 0.98 ± 0.27 | | 0 | 0.98 ± 0.27 | | 0 |
| Alternative Model<20% SzC or unconfirmed | IIIA | 65 | 9.22 ± 0.94 | 0.019§ | 67 | 18.99 ± 1.10 | <0.001§ | 88 |
| ≥ 20% to <1.0 SzC/μL+confirmation | IIIB | 21 | 5.46 ± 0.93 | 0.611 [#] | 48 | 7.22 ± 1.35 | 0.279 [#] | 59 |
| ≥ 1.0 SzC/μL+confirmation | IVA1 | 27 | 4.88 ± 0.99 | 0.233 [¶] | 41 | 5.67 ± 1.22 | 0.145 [¶] | 43 |
| Any | IVA2 | 34 | 3.45 ± 0.71 | 0.034 [‡] | 21 | 3.60 ± 0.76 | 0.034 [‡] | 21 |
| Any | IVB | 5 | 0.98 ± 0.27 | | 0 | 0.98 ± 0.27 | | 0 |

[†]B ratings according to ISCL-EORTC recommendations. [19]

*Confirmation of neoplastic involvement in blood includes molecular genetic or cytogenetic evidence of a T cell clone, presence of very large Sézary cells (>14 μm diameter) or T cells with diminished expression of CD2, CD3, CD4 or CD5.

Difference in survival curves tested with log-rank test: IIIA and IIIB§, IIIB and IVA1[#], IVA1 and IVA2[¶], IVA2 and IVB[‡].

Supplemental Table 1: Mean overall and CTCL-specific survival for patients with erythrodermic cutaneous T cell lymphoma with B1 threshold defined as Sézary cells $\geq 6\%$ or $\geq 20\%$ plus confirmation that neoplastic cells are present.

| Criteria | | | Overall Survival | | | CTCL-specific Survival | | |
|-------------------------------------|-------|-----|------------------|----------------------|----------|------------------------|---------------------|----------|
| Gibson/Yale [†] | Stage | No. | Mean \pm SEM | P-value | 5 yr (%) | Mean \pm SEM | P-value | 5 yr (%) |
| CD4/CD8 <5 or unconfirmed* | IIIA | 71 | 9.53 \pm 0.90 | 0.022 [§] | 70 | 18.82 \pm 1.08 | <0.001 [§] | 89 |
| CD4/CD8 ≥ 5 to<10+confirmation | IIIB | 15 | 5.54 \pm 1.24 | 0.314 [#] | 40 | 6.21 \pm 1.42 | 0.476 [#] | 44 |

| | | | | | | | | |
|---|------|----|-------------|--------------------|----|--------------|---------------------|----|
| CD4/CD8 ≥ 10+confirmation | IVA1 | 24 | 3.92 ± 0.72 | 0.630 [¶] | 38 | 4.58 ± 0.85 | 0.336 [¶] | 42 |
| Any B | IVA2 | 34 | 3.45 ± 0.71 | 0.034 [‡] | 21 | 3.60 ± 0.76 | 0.034 [‡] | 21 |
| Any B | IVB | 5 | 0.98 ± 0.27 | | 0 | 0.98 ± 0.27 | | 0 |
| Alternative Model | | | | | | | | |
| CD4/CD8 < 4 or unconfirmed* | IIIA | 68 | 9.53 ± 0.90 | 0.011 [§] | 70 | 18.82 ± 1.08 | <0.001 [§] | 90 |
| CD4/CD8 ≥ 4 to <12+confirmation | IIIB | 22 | 5.56 ± 1.04 | 0.186 [#] | 50 | 6.69 ± 1.36 | 0.149 [#] | 53 |
| CD4/CD8 ≥ 12+confirmation | IVA1 | 20 | 3.59 ± 0.80 | 0.910 [¶] | 30 | 4.01 ± 0.86 | 0.709 [¶] | 35 |
| Any B | IVA2 | 34 | 3.45 ± 0.71 | 0.034 [‡] | 21 | 3.60 ± 0.76 | 0.034 [‡] | 21 |
| Any B | IVB | 5 | 0.98 ± 0.27 | | 0 | 0.98 ± 0.27 | | 0 |
| [‡] B ratings proposed by Gibson at Yale University [20]. *Confirmation of neoplastic involvement in blood includes molecular genetic or cytogenetic evidence of a T cell clone, presence of very large Sézary cells (>14 µm diameter) or T cells with diminished expression of CD2, CD3, CD4 or CD5 Difference in survival curves tested with log-rank test: IIIA and IIIB [§] , IIIB and IVA1 [#] , IVA1 and IVA2 [¶] , IVA2 and IVB [‡] . | | | | | | | | |

Supplemental Table 2. Mean overall and CTCL-specific survival for patients with erythrodermic cutaneous T cell lymphoma with B1 and B2 thresholds using CD4/CD8 ratios plus confirmation that neoplastic cells are present (4 patients excluded).

| Criteria | Stage | No. | Overall Survival | | | CTCL-specific Survival | | |
|---|-------|-----|------------------|---------------------|----------|------------------------|---------------------|----------|
| EORTC [†] | | | Mean ± SEM | P-value | 5 yr (%) | Mean ± SEM | P-value | 5 yr (%) |
| Max-CD4 ⁺ CD26 ⁻ /7 ⁻ <250/µL or unconfirmed* | IIIA | 9 | 7.85 ± 1.94 | 0.338 [§] | 65 | 9.85 ± 2.04 | 0.357 [§] | 78 |
| Max-CD4 ⁺ CD26 ⁻ /7 ⁻ ≥ 250 to <1,000/µL ⁺ confirmation | IIIB | 3 | 4.63 ± 3.36 | 0.937 [#] | 33 | 4.63 ± 2.74 | 0.803 [#] | 33 |
| Max-CD4 ⁺ CD26 ⁻ /7 ⁻ ≥ 1.0 K/µL ⁺ confirmation | IVA1 | 11 | 4.21 ± 1.60 | 0.784 [¶] | 36 | 5.02 ± 1.75 | 0.853 [¶] | 45 |
| Max-CD4 ⁺ CD26 ⁻ /7 ⁻ ≥ 1.0 K/µL ⁺ confirmation | IVA1 | 11 | 4.21 ± 1.60 | 0.784 [¶] | 36 | 5.02 ± 1.75 | 0.853 [¶] | 45 |
| Any B | IVA2 | 13 | 4.06 ± 1.34 | 0.047 | 23 | 4.54 ± 1.52 | 0.047 | 23 |
| Any B | IVB | 3 | 0.70 ± 0.34 | | 0 | 0.70 ± 0.34 | | 0 |
| | | | | | 5 yr | | | 5 yr |
| Max-CD4 ⁺ CD26 ⁻ /7 ⁻ <30% or unconfirmed* | IIIA | 9 | 7.85 ± 1.94 | 0.996 [§] | 65 | 9.87 ± 2.03 | 0.832 [§] | 78 |
| Max-CD4 ⁺ CD26 ⁻ /7 ⁻ ≥ 30% to < 60% ⁺ confirmation | IIIB | 4 | 8.12 ± 2.64 | 0.035 [#] | 60 | 9.12 ± 3.31 | 0.065 [#] | 60 |
| Max-CD4 ⁺ CD26 ⁻ /7 ⁻ ≥ | IVA1 | 10 | 1.95 ± | 0.122 [¶] | 22 | 2.50 ± | 0.225 [¶] | 33 |

| | | | | | | | | |
|-------------------------------|------|----|-------------|--------------------|----|-------------|--------------------|----|
| 60% [†] confirmation | | | 0.89 | | | 1.05 | | |
| Any B | IVA2 | 13 | 4.06 ± 1.34 | 0.047 [‡] | 23 | 4.54 ± 1.52 | 0.047 [‡] | 23 |
| Any B | IVB | 3 | 0.70 ± 0.34 | | 0 | 0.70 ± 0.34 | | |

[†]B ratings according to EORTC task force recommendations [21].
^{*}Confirmation of neoplastic involvement in blood includes molecular genetic or cytogenetic evidence of a T cell clone, presence of very large Sézary cells (>14 µm diameter) or T cells with diminished expression of CD2, CD3, CD4 or CD5.
Difference in survival curves tested with log-rank test: IIIA and IIIB§, IIIB and IVA1#, IVA1 and IVA2¶, IVA2 and IVB‡.

Supplemental Table 3. Mean overall and CTCL-specific survival for patients with erythrodermic cutaneous T cell lymphoma with B1 threshold defined using maximum percentage of CD4+CD26- or CD4+CD7- lymphocytes plus confirmation that neoplastic cells are present.

| B rating criteria | B1 threshold | B2 threshold | All deaths [*] | CTCL-specific deaths [*] |
|-----------------------------|--------------|--------------|------------------------------|-----------------------------------|
| EORTC criteria [†] | ≥ 250/µL | ≥ 1.0 K/µL | Δ 6.76; P=0.239 [‡] | Δ 6.77; P=0.238 [‡] |
| Alternative 1 | <20% | ≥ 50% | Δ 11.26; P=0.047 | Δ 12.79; P=0.025 |
| Alternative 2 | <20% | ≥ 60% | Δ 13.79; P=0.017 | Δ 14.69; P=0.012 |
| Alternative 3 | <30% | ≥ 50% | Δ 8.53; P=0.129 | Δ 8.43; P=0.134 |
| Alternative 4 | <30% | ≥ 60% | Δ 12.51; P=0.028 | Δ 11.52; P=0.042 |

[†]B ratings according to EORTC task force recommendations [21].
^{*}With age as covariate in Cox model.
[‡]Change (Δ) in -2 log likelihood statistic from baseline in Cox model. The larger the change is, the better the fit.

Supplemental Table 4: Maximum CD4+CD26- or CD4+CD7- values used to define B ratings for 39 patients with erythrodermic cutaneous T cell lymphoma.

| Max-CD4+CD26- /7- [*] (%) | No. | Max-CD4+CD26- /7- ≥ 1.0/µL (%) | SzC ≥ 1.0/µL or CD4/CD8 ≥ 10 (%) |
|------------------------------------|-----|-----------------------------------|-------------------------------------|
| ≥ 20% | 30 | 22 (73) | 22 (73) |
| ≥ 25% | 29 | 22 (76) | 21 (72) |
| ≥ 30% | 28 | 22 (79) | 21 (75) |
| ≥ 35% | 27 | 22 (81) | 21 (78) |
| ≥ 40% | 27 | 22 (81) | 21 (78) |
| ≥ 45% | 24 | 21 (88) | 21 (88) |
| ≥ 50% | 24 | 21 (88) | 21 (88) |

^{*}Maximum CD4⁺CD26⁻ or CD4⁺CD7⁻ lymphocyte percentage (whichever is larger).

Supplemental Table 5. Relationship between maximum CD4+CD26- or CD4+CD7- percentage and proposed criteria for B2 ratings (includes stages IVA2, IVB).