# LYMPHOMA SUBSETS

| CELL TYPE | PHENOTYPE | TYPICAL CYTOGENETIC ABNORMALITIES | MOLECULAR ABNORMALITY |
|---|---|---|---|
| Follicle center lymphoma | SIG+, CIG-, CD5, CD10+, CD23-/+, CD43-/+ | t(14;18) | BCL-2 rearrangement |
| Burkitt's lymphoma | SIG+,CD5+, CD23-, CD10+, CD5-, CD43 | t(8;14) (q24;q32); t(8;22) (q24;q11); t(2;8) (p12;q24) | MYC rearrangement or over-expression |
| B-cell CLL/SLL | SIG+, CD5+, CD10, CD23+, CD43+ | Trisomy 12 (30%) | |
| Immunocytoma | SIG+, CIG+, CD5-, CD10-, CD23-, CD43 -/+ | t(9;14) (p13;32q32) | ? |
| Mantel cell lymphoma | SIG+, CIG-, CD5+, CD10-, CD23- ,CD43+ | t(11;14) | BCL-1 (PRAD-1 or cyclin D1) rearrangement |
| Monocytoid B-cell | SIG+, CD5-, CD10-, CD23 | Trisomy 3, trisomy18, rearrangement of 1q21 or 1p34 | |
| Splenic marginal zone lymphoma | SIG+, CD5-, CD10-, CD23-/+, CD43-/+ | Chromosome 3 abnormalities | ? |
| Primary extranodal diffuse large cell lymphoma | B cell | 3q27 rearrangements with 14q23, 22q11, 2p12 | BCL-6 rearrangement |
| Ki-1 anaplastic large cell lymphoma (ALCL) | CD30+, CD15-, CD3+ T cell or Null cell | t(2;5) (p23;q35) | ALK fusion gene NPM-ALK1 |
| Malt Lymphoma | SIG=, CD5-, CD10-, CD23-/+, CD43-/+ | Trisomy 3 and 18; changes in 1q21 and 1p34; †(11;18) (q21q21) | ? |
| CLL= chronic lymphocytic leukemia; MALT= mucosa associated lymphoid tissue; SLL =small lymphocytic lymphoma. | | | |

<u>Reference</u>: UF Cytogenetics Laboratory.

# INTERNATIONAL PROGNOSTIC INDEX – DLBCL

| ACRONYM | PARAMETER | CRITERIA | SCORE* |
|---|---|---|---|
| A | Age | ≤ 60 years | 0 |
| | | > 60 years | 1 |
| P | Performance status | 0 – 1 | 0 |
| | | > 1 | 1 |
| L | Serum Lactate Dehydrogenase | Normal | 0 |
| | | High | 1 |
| E | Extranodal sites | 0 – 1 | 0 |
| | | > 1 | 1 |
| S | Ann Arbor stage | I – II | 0 |
| | | III – IV | 1 |

*SCORE:

Low risk: Total score of 0 or 1
Low – Intermediate risk: Total score 2
High-Intermediate risk: Total score 3
High risk: Total score 4 or 5

Reference: Shipp MA, et al. *N Engl J Med* 1993;329:987 – 94.

# INTERMEDIATE GRADE NON-HODGKIN'S LYMPHOMA – INTERNATIONAL PROGNOSTIC INDEX (IPI)

## INTERNATIONAL PROGNOSTIC INDEX (IPI) – OUTCOMES

| RISK GROUP | NO. OF RISK FACTORS | % OF PATIENTS | CR RATE (%) | 5YR RFS (%) | 5YR OS (%) |
|---|---|---|---|---|---|
| ALL PATIENTS (N=2031) | | | | | |
| Low | 0 or 1 | 35 | 87 | 70 | 73 |
| Low-Int | 2 | 27 | 67 | 50 | 51 |
| High-Int | 3 | 22 | 55 | 49 | 43 |
| High | 4 or 5 | 16 | 44 | 40 | 26 |
| AGE-ADJUSTED INDEX, AGE 60 YEARS OR LESS (N=1274) | | | | | |
| Low | 0 | 22 | 92 | 86 | 83 |
| Low-Int | 1 | 32 | 78 | 66 | 69 |
| High-Int | 2 | 32 | 57 | 53 | 46 |
| High | 3 | 14 | 46 | 58 | 32 |
| AGE-ADJUSTED INDEX, AGE GREATER THAN 60 (N=761) | | | | | |
| Low | 0 | 18 | 91 | 46 | 56 |
| Low-Int | 1 | 31 | 71 | 45 | 44 |
| High-Int | 2 | 35 | 56 | 41 | 37 |
| High | 3 | 16 | 36 | 37 | 21 |

Reference: Shipp MA, et al. *N Engl J Med* 1993;329:987 – 94.

# REVISED INTERNATIONAL PROGNOSTIC INDEX (R-IPI) FOR DLBCL IN ERA OF RITUXIMAB

Outcome according to International Prognostic Index factors in 365 patients treated with R-CHOP in British Columbia.

| RISK GROUP | NUMBER OF IPI FACTORS | % PATIENTS | 4-YR PFS (%) | 4-YR OS (%) |
|---|---|---|---|---|
| STANDARD IPI | | | | |
| Low | 0, 1 | 28 | 85 | 82 |
| Low-Int | 2 | 27 | 80 | 81 |
| High-Int | 3 | 21 | 57 | 49 |
| High | 4, 5 | 24 | 51 | 59 |
| REVISED IPI | | | | |
| Very Good | 0 | 10 | 94 | 94 |
| Good | 1, 2 | 45 | 80 | 79 |
| Poor | 3, 4, 5 | 45 | 53 | 55 |

Reference: Sehn LH, et al. *Blood.* 2006 Nov 14; [Epub ahead of print].

# FLIPI – FOLLICULAR LYMPHOMA INTERNATIONAL PROGNOSTIC INDEX

| ACRONYM | PARAMETER | CRITERIA | PROGNOSTIC FACTOR* | RELATIVE RISK OF DEATH |
|---|---|---|---|---|
| No | Number of nodal areas | ≤ 4 nodal areas | | |
| | | > 4 nodal areas | Poor | 1.39 |
| L | LDH | Below normal | | |
| | | Normal | | |
| | | Above normal | Poor | 1.5 |
| A | Age | ≤ 60 years | | |
| | | > 60 years | Poor | 2.38 |
| S | Stage (Ann Arbor) | I – II | | |
| | | III – IV | Poor | 2.00 |
| H | Hemoglobin | < 12 g/dL | Poor | 1.55 |
| | | ≥ 12 g/dL | | |

*RISK GROUPS:

Low Risk: 0 –1 adverse factor.
Intermediate Risk: 2 adverse factors.
High (Poor) Risk: ≥ 3 adverse factors.

# OUTCOME AND RELATIVE RISK OF DEATH ACCORDING TO RISK GROUP AS DEFINED BY THE FOLLICULAR LYMPHOMA INTERNATIONAL PROGNOSTIC INDEX (FLIPI)

| RISK GROUP | NUMBER OF FACTORS | DISTRIBUTION OF PATIENTS | 5-YEAR OS, % (SE) | 10-YEAR OS, % (SE) | RR | 95% CI |
|---|---|---|---|---|---|---|
| Low | 0 –1 | 36 | 90.6 (1.2) | 70.7 (2.7) | 1 | NA |
| Intermediate | 2 | 37 | 77.6 (1.6) | 50.9 (2.7) | 2.3 | 1.9 – 2.8 |
| High | ≥ 3 | 27 | 52.5 (2.3) | 35.5 (2.8) | 4.3 | 3.5 – 5.3 |

N = 1795
OS = overall survival; SE = standard error; CI = confidence interval; RR = relative risk (of death).

Reference for both tables: Solal-Celigny P, et al. *Blood* 2004;104:1258 – 65.

# PROGNOSTIC SYSTEM FOR HODGKIN'S DISEASE (HD)

## HODGKIN'S DISEASE

### EARLY STAGE (I–II) PROGNOSTIC INDEX

| RISK FACTORS |
| --- |
| Large Mediastinal Mass (>10cm in diameter)<br>Age ≥ 50years<br>Elevated ESR or B Symptoms<br>≥ 3 – 4 involved regions |
| |
| Early Stage **Favorable**:<br>Stage I–II supradiaphragmatic with no risk factor |
| Early Stage **Unfavorable**:<br>Stage I–II supradiaphragmatic with ≥ 1 risk factor |

Reference: Adapted from Diehl V. American Society of Hematology Education Book 2003.

# PROGNOSTIC SYSTEM FOR HODGKIN'S DISEASE (HD)

## ADVANCED STAGE (III–IV) PROGNOSTIC INDEX (HIPI)

### HIPIS ARE ENVIRONMENTALLY CONSCIOUS = ACRONYM GASLAAW

| ACRONYM | PARAMETER | LOG HAZARD RATIO | P VALUE | RELATIVE RISK | POINTS |
|---|---|---|---|---|---|
| G | Male sex | 0.30 ± 0.09 | 0.001 | 1.35 | 1 |
| A | Serum albumin, < 4 g/dL | 0.40 ± 0.10 | <0.001 | 1.49 | 1 |
| S | Stage IV disease | 0.23 ± 0.09 | 0.011 | 1.26 | 1 |
| L | Lymphocyte count, < 600/mm$^3$ or < 8% of white-cell count | 0.31 ± 0.10 | 0.002 | 1.38 | 1 |
| A | Age ≥ 45 yr | 0.33 ± 0.10 | 0.001 | 1.39 | 1 |
| A | Hemoglobin < 10.5 g/dL | 0.30 ± 0.11 | 0.006 | 1.35 | 1 |
| W | White cell count ≥ 15 x 10$^9$/L | 0.34 ± 0.11 | 0.001 | 1.41 | 1 |
| Hazard ratios and relative risks are for freedom from progression of disease in patients with the factors as compared with those without the factors. Plus-minus values are rate estimates ± SE (approximate 95 percent confidence intervals can be calculated as the rate estimates ± 2 SE). | | | | | |

Reference: Hasenclever D, et al. *N Eng J Med* 1998;339:1506 – 14.

## ADVANCED STAGE (III–IV) HIPI –OUTCOMES

| TOTAL POINTS | NO. OF PATIENTS (%) | RATES OF FREEDOM FROM DISEASE PROGRESSION (%) | 5 YEAR OS (%) |
|---|---|---|---|
| INDIVIDUAL | | | |
| 0 | 115 (7) | 84 ± 4 | 89 ± 2 |
| 1 | 360 (22) | 77 ± 3 | 90 ± 2 |
| 2 | 464 (29) | 67 ± 2 | 81 ± 2 |
| 3 | 378 (23) | 60 ± 3 | 78 ± 3 |
| 4 | 190 (12) | 51 ± 4 | 61 ± 4 |
| ≥ 5 | 111 (7) | 42 ± 5 | 56 ± 5 |
| GROUPED | | | |
| 0 OR 1 | 475 (29) | 79 ± 2 | 90 ± 2 |
| ≥ 2 | 1143 (71) | 60 ± 2 | 74 ± 2 |
| 0–2 | 939 (58) | 74 ± 2 | 86 ± 2 |
| ≥ 3 | 679 (42) | 55 ± 2 | 70 ± 2 |
| 0–3 | 1317 (81) | 70 ± 2 | 83 ± 1 |
| ≥ 4 | 301 (19) | 47 ± 2 | 59 ± 2 |
| Plus-minus values are rate estimates ± SE (approximate 95 percent confidence intervals can be calculated as the rate estimates ± 2 SE). | | | |

Reference: Hasenclever D, et al. *N Eng J Med* 1998;339:1506 – 14.