New development of prognostic scoring systems

Davide Rossi, M.D., Ph.D.

Hematology
IOSI - Oncology Institute of Southern Switzerland
IOR - Institute of Oncology Research
USI – Universita' della Svizzera Italiana
Bellinzona - Switzerland

Time to first treatment

Prognostication of time-to-first therapy: IPS-E

Condoluci A, Blood. 2020

Variable	Points
IGHV unmutated	1
Lymphocytes >15x10^9/L	1
Nodal involvement	1

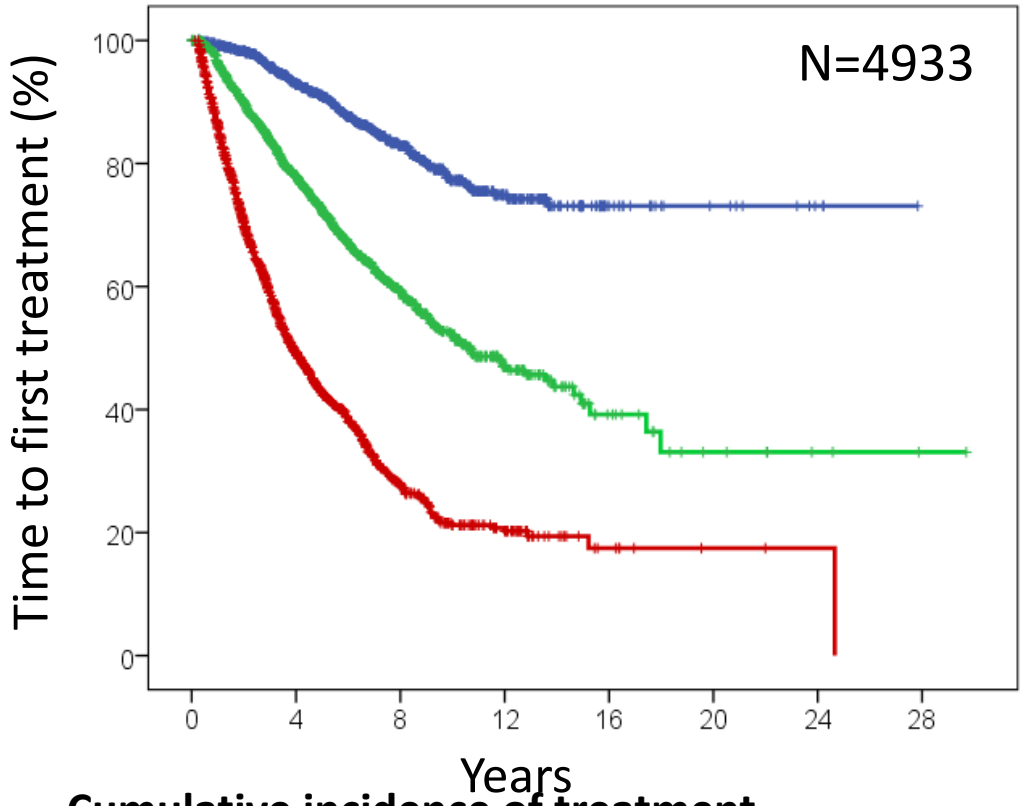
Risk group	Score
Low risk	0
Intermediate risk	1
High risk	2-3

Validation

Smolej L, Br J Haematol. 2020

Morabito F, et al. Eur J Haematol. 2021

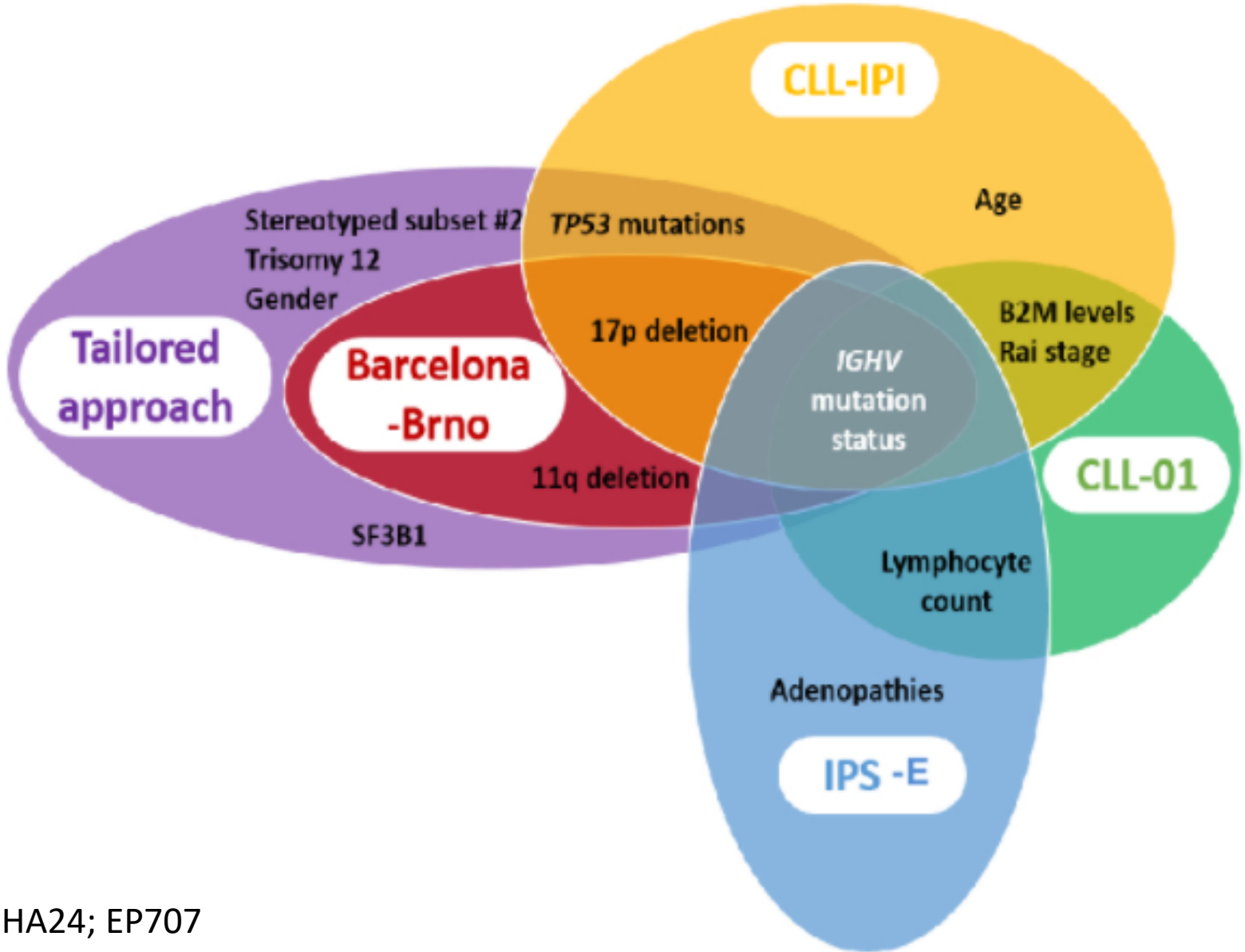
González-Gascón, EHA24; EP707



Cumulative incidence of treatment

	1 year	5 years
Low risk	<1%	8%
Intermediate risk	3%	28%
High risk	14%	61%

What is the most robust biomarker for early stage CLL prognostication?



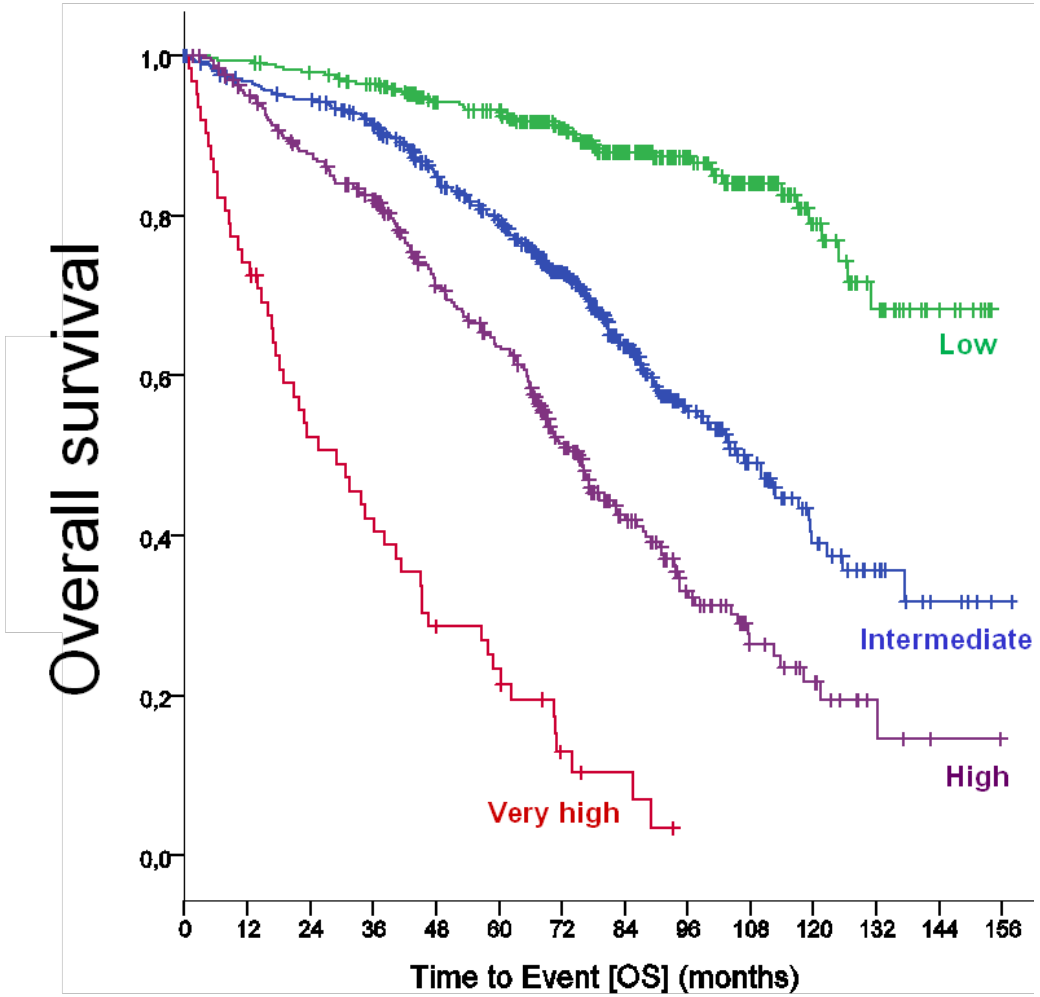
González-Gascón, EHA24; EP707

Overall survival

Prognostication of overall survival: CLL-IPI

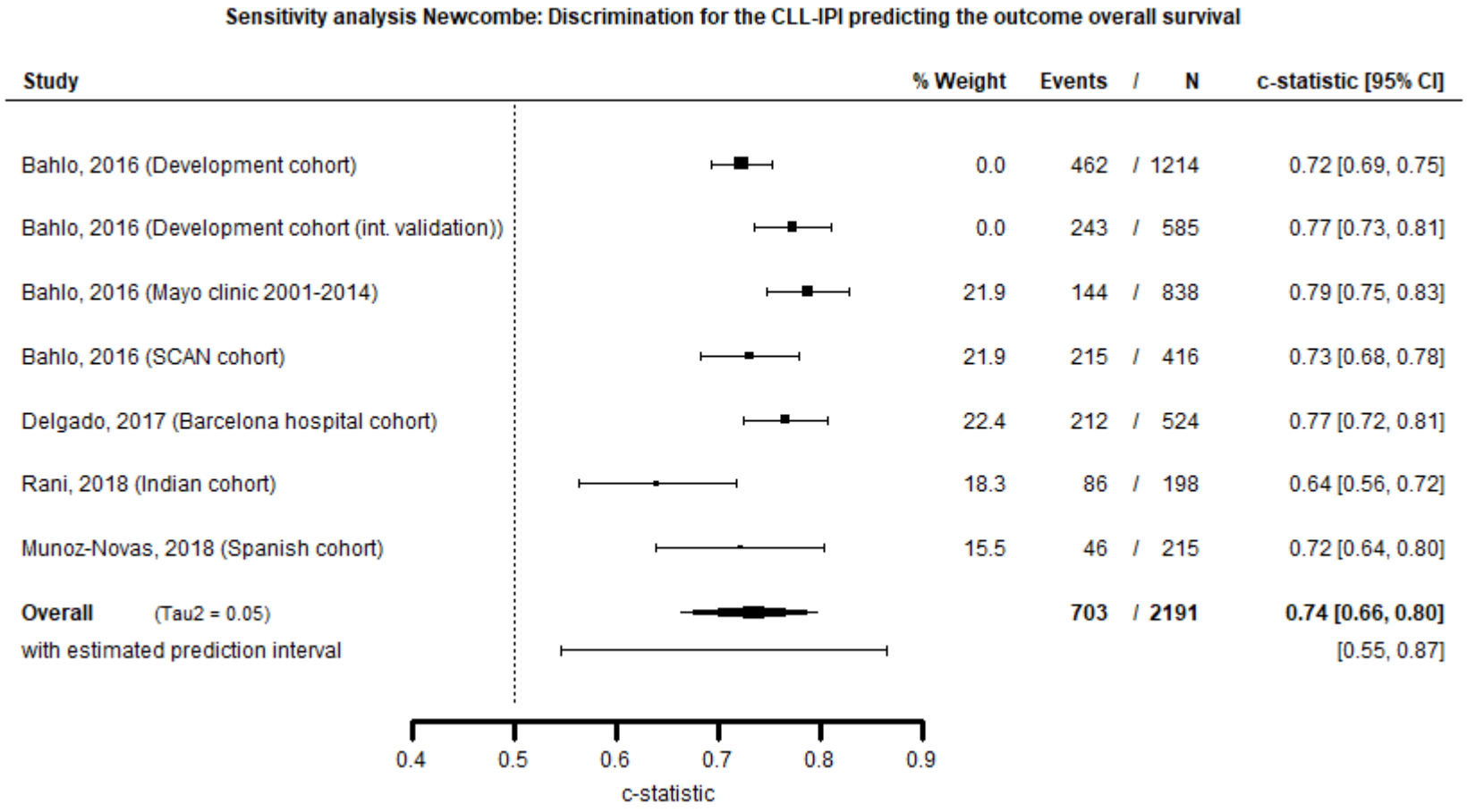
Variable	Adverse factor	Coeff.	HR	Grading
TP53 (17p)	deleted and/or mutated	1.442	4.2	4
IGHV status	Unmutated	0.941	2.6	2
B2M, mg/L	> 3.5	0.665	2.0	2
Clinical stage	Binet B/C or Rai I-IV	0.499	1.6	1
Age	> 65 years	0.555	1.7	1
Prognostic Score				0 – 10

Risk group	Score	Patients N (%)	5-year OS, %
Low	0 – 1	340 (29)	93.2
Intermediate	2 – 3	464 (39)	79.4
High	4 – 6	326 (27)	63.6
Very High	7 – 10	62 (5)	23.3



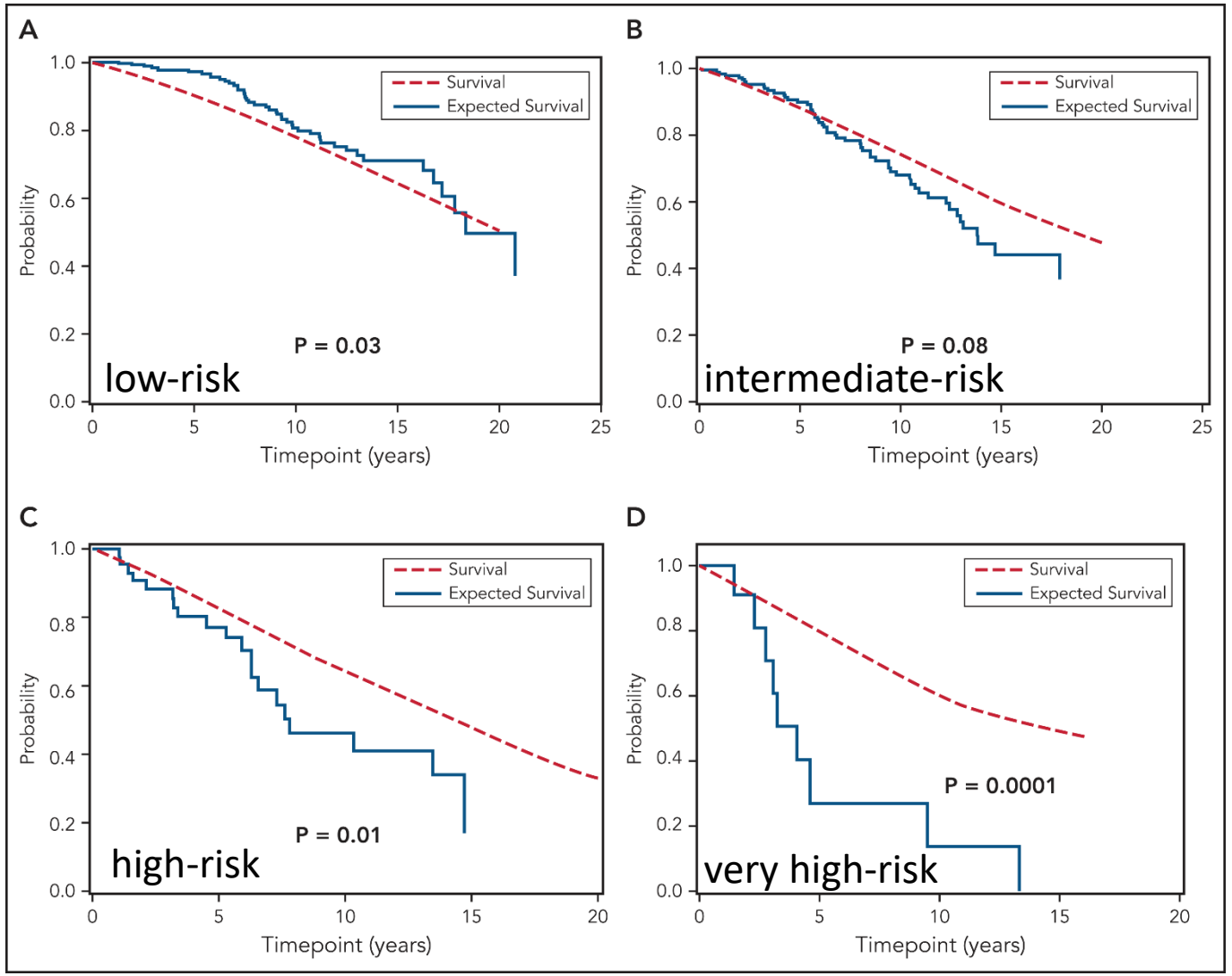
International CLL-IPI working group. Lancet Oncol 2016

CLL-IPI is strongly validated at a ca. 70% accuracy



Kreuzberger N, Cochrane Database Syst Rev. 20200%

Survival of early stage CLL according to the CLL-IPI



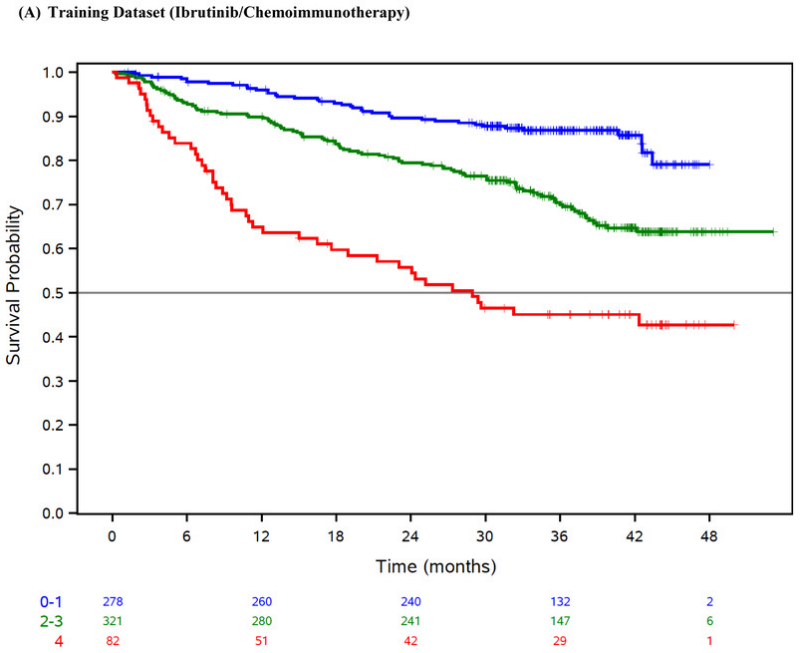
Parikh SA, Blood. 2021

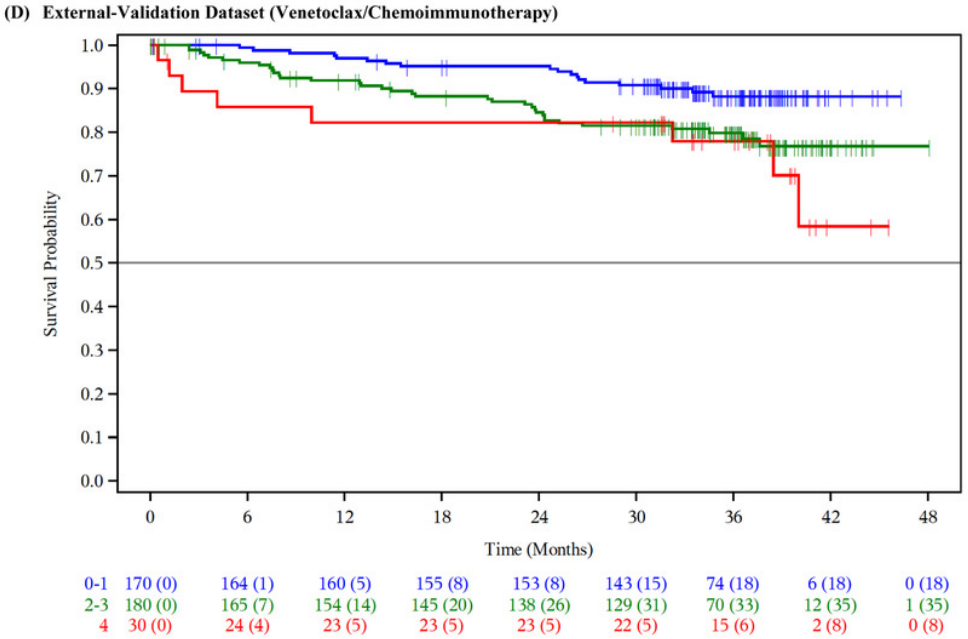
Outcome after therapy

Prognostication of survival after ibrutinib or venetoclax treatment: BALL score

Variable	Points
Time from last Tx ≥24mo	1
Hb <normal (120 M; 110 F)	1
B2M ≥5 mg/l	1
LDH ≥250 U/l	1

Risk group	Score
Low risk	0-1
Intermediate risk	2-3
High risk	4





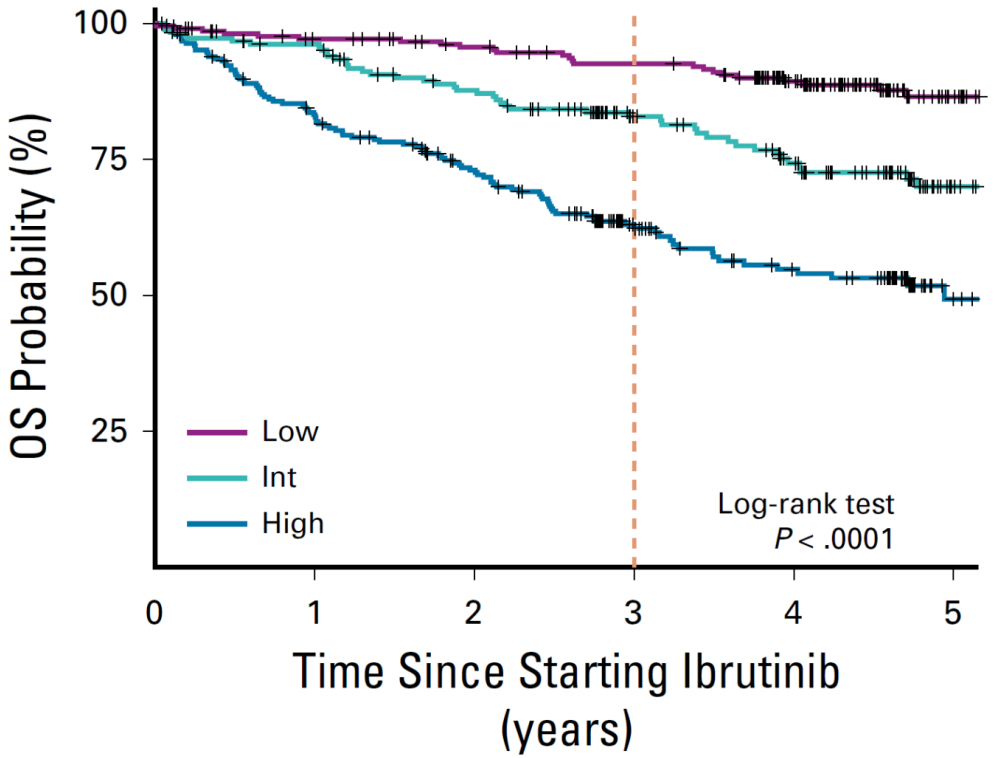
Complex karyotype not included in the analysis
IGHV status and TP53 status not selected in the final model

Soumerai JD, Lancet Haematol 2019

Prognostication of survival after ibrutinib treatment: 4F score

Variable	Points
TP53 aberration	1
Prior treatment	1
B2M ≥5 mg/l	1
LDH ≥250 U/l	1

Risk group	Score
Low risk	0-1
Intermediate risk	2
High risk	3-4



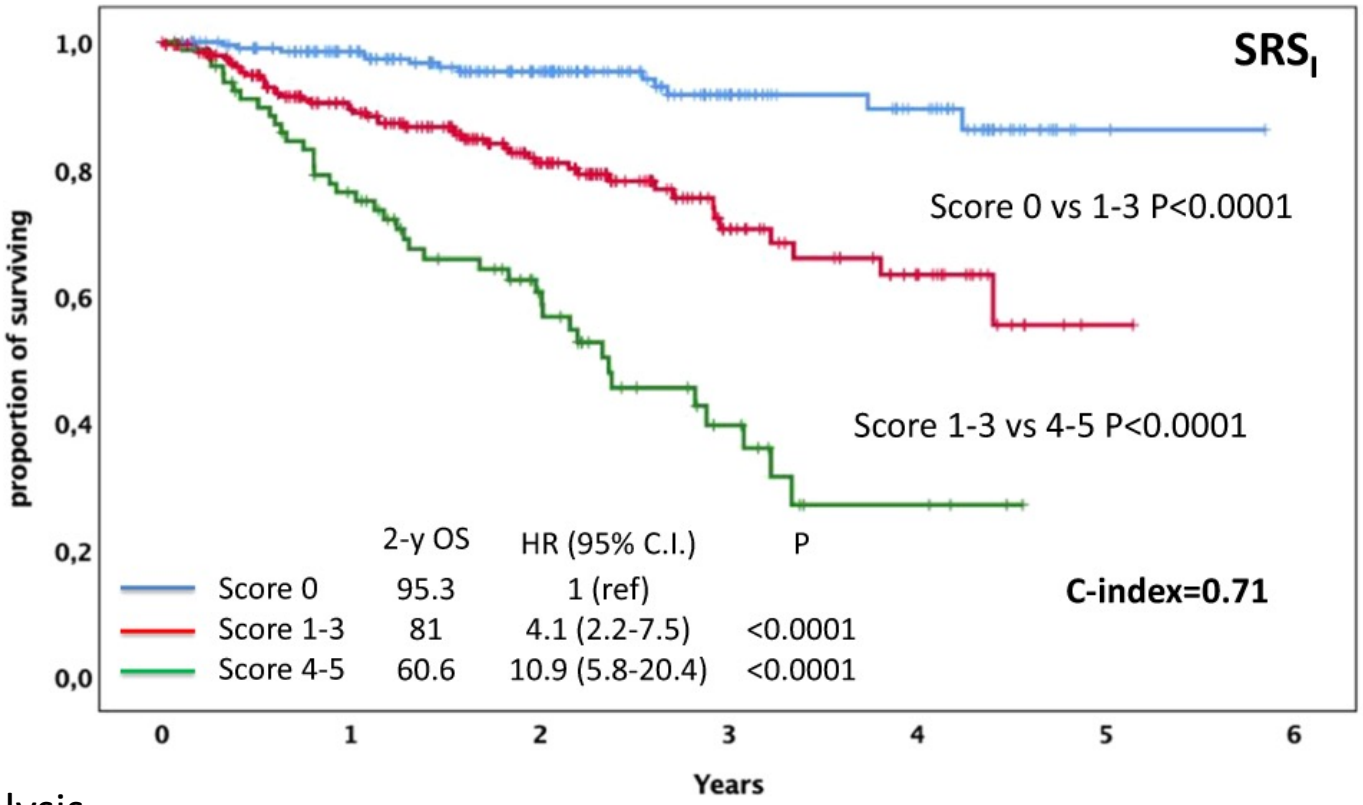
Complex karyotype not included in the analysis
IGHV status not selected in the final model

Ahn IE, J Clin Oncol. 2021

Prognostication of survival after ibrutinib treatment: SRS score

Variable	Points
B2M ≥5 mg/l	1
Hb <normal (120 M; 110 F)	2
LDH ≥250 U/l	2

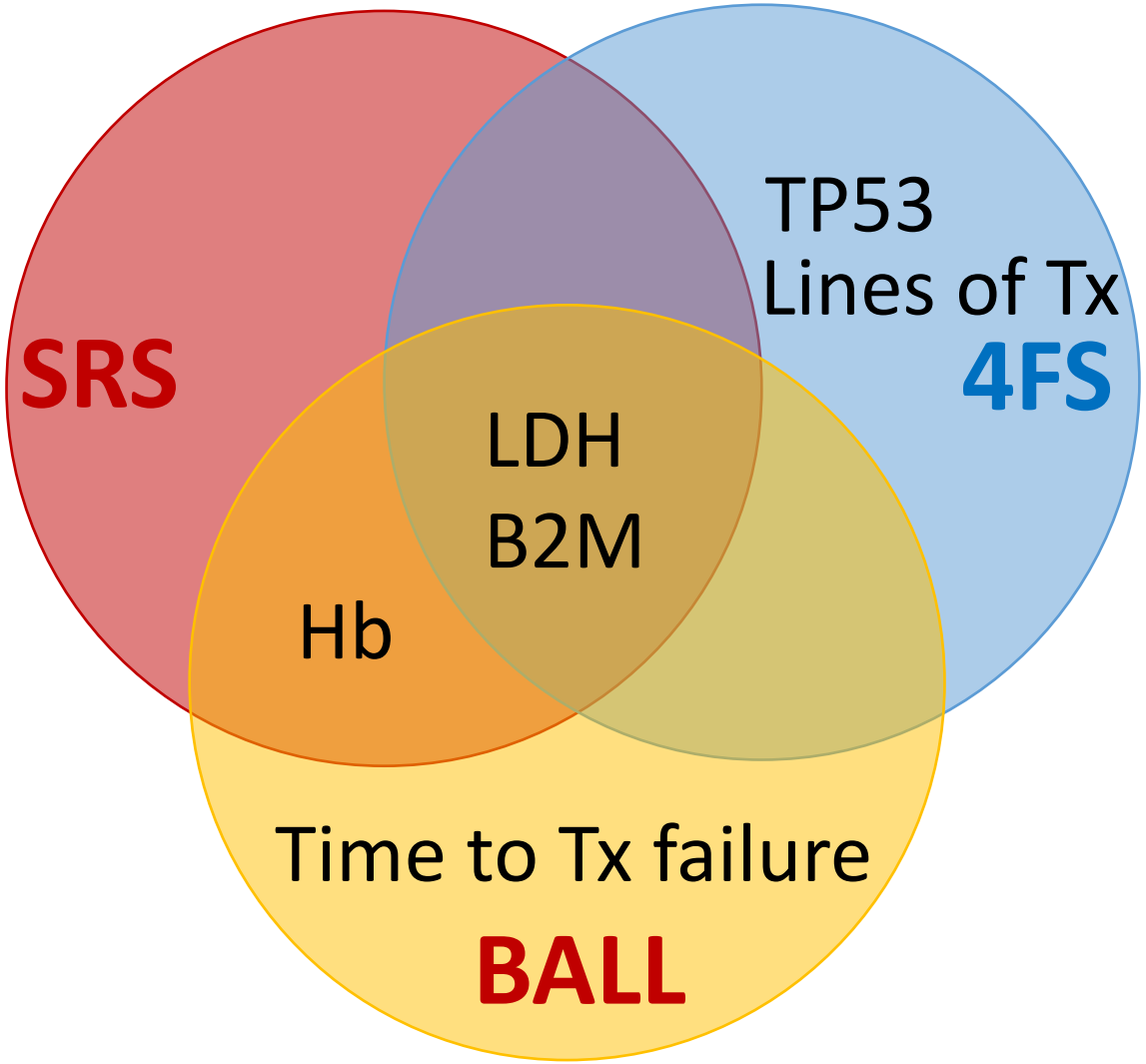
Risk group	Score
Low risk	0
Intermediate risk	1-3
High risk	4-5



Complex karyotype not included in the analysis
IGHV status and TP53 status not selected in the final model

Gentile M, Leukemia. 2021

What is the most robust biomarker?



IGHV mutation status: not selected as independent variable
Complex karyotype: not analyzed

Summary

- IPS-E for TTFT prognostication in early stage CLL
- CLL-IPI for OS prognostication in early stage CLL
- IGHV and *TP53* are no longer strong biomarkers in patients treated with BTKi
- Biomarkers in patients treated with time limited venetoclax-based tx are unknown
- Is CKT an independent prognostic factor?