



IOR
Un istituto
affiliato all'USI

Biomarkers Predittivi

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

Hematology

IOSI - Oncology Institute of Southern Switzerland

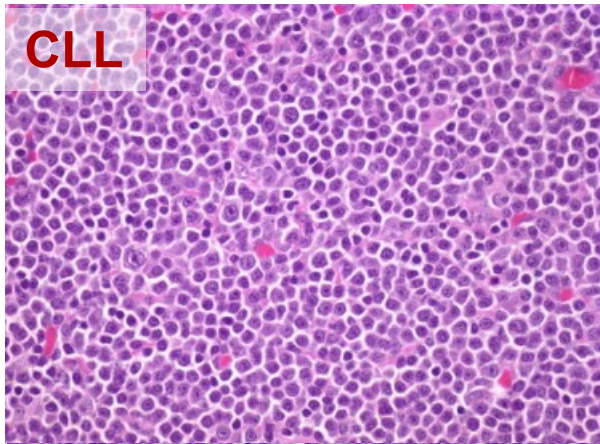
IOR - Institute of Oncology Research

USI – Università' della Svizzera Italiana

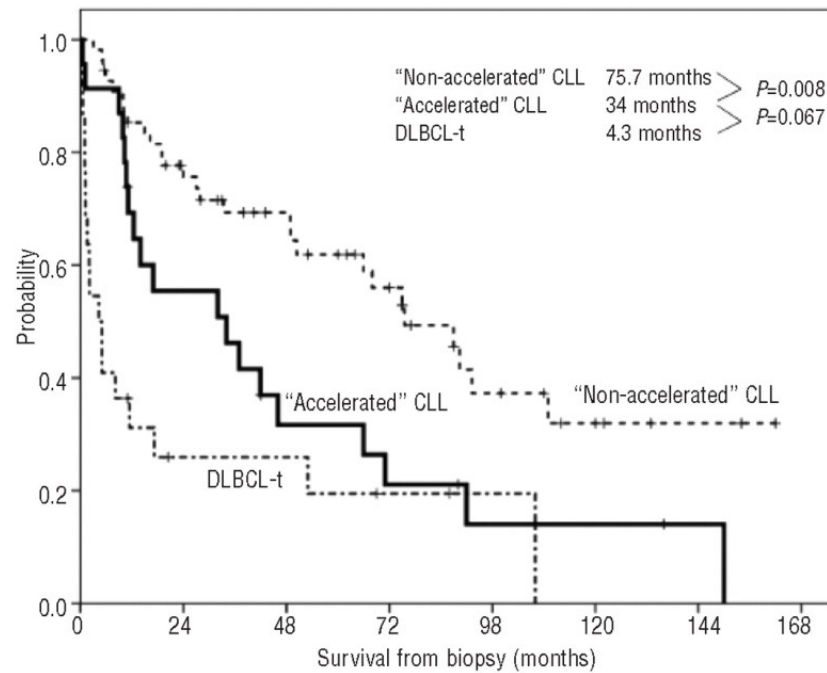
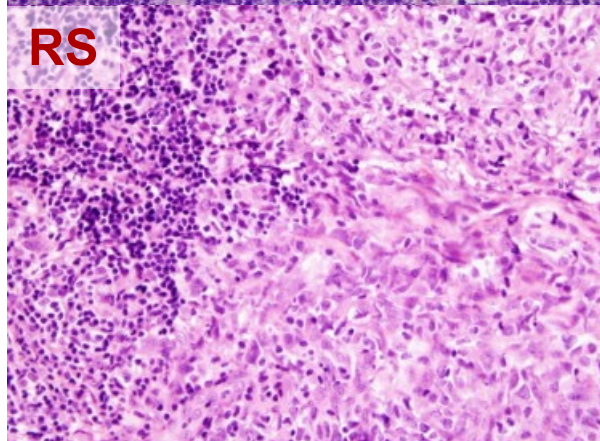
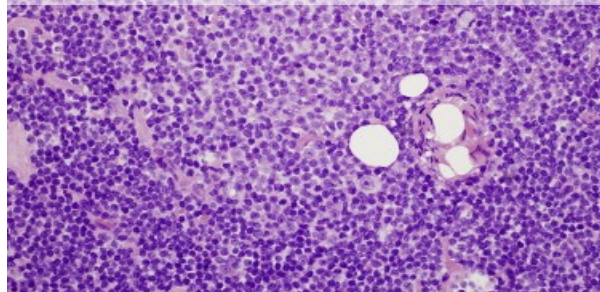
Bellinzona - Switzerland

Histology

The different histologies of CLL



Histologically aggressive CLL

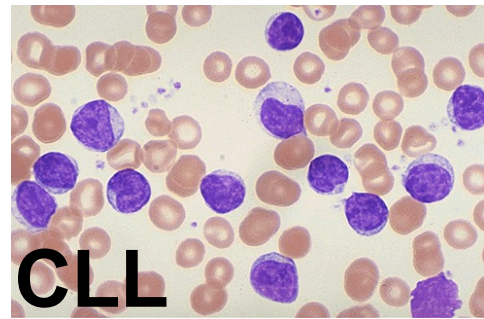


Ginè et al, Haematologica 2010

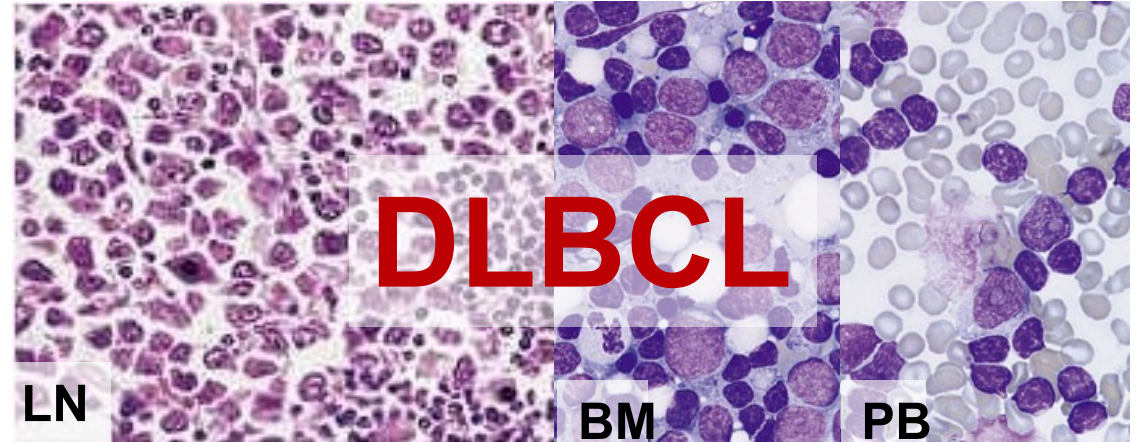
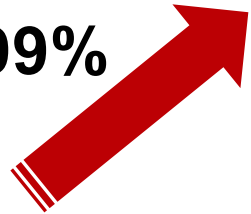
After pathology revision, ~20% of 'RS' are downgraded to histologically aggressive CLL

Soilleux et al, Histopathology 2016

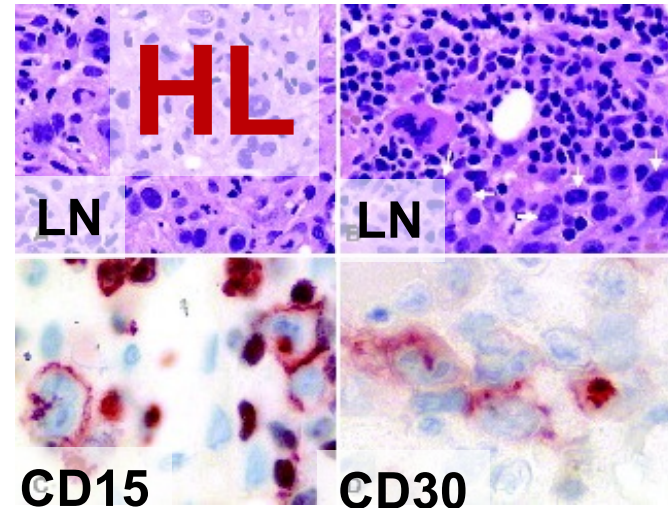
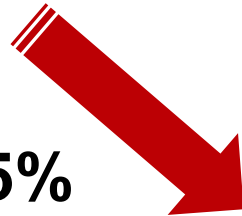
The different histologies of Richter syndrome



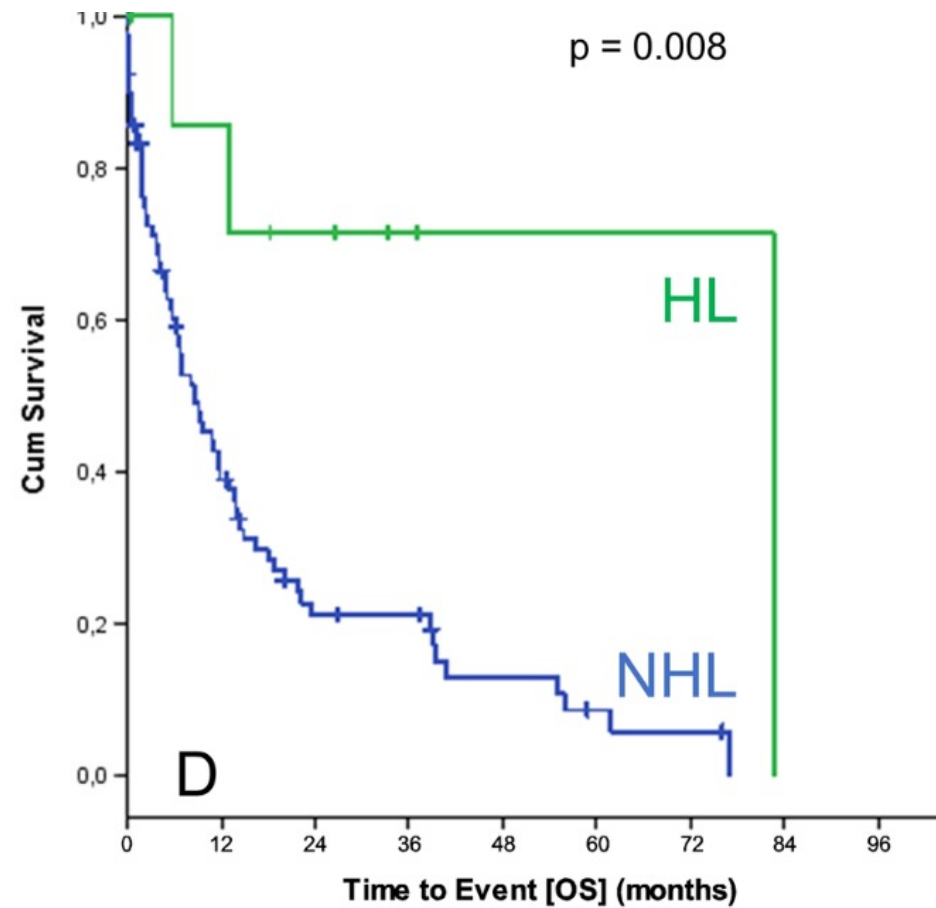
95-99%



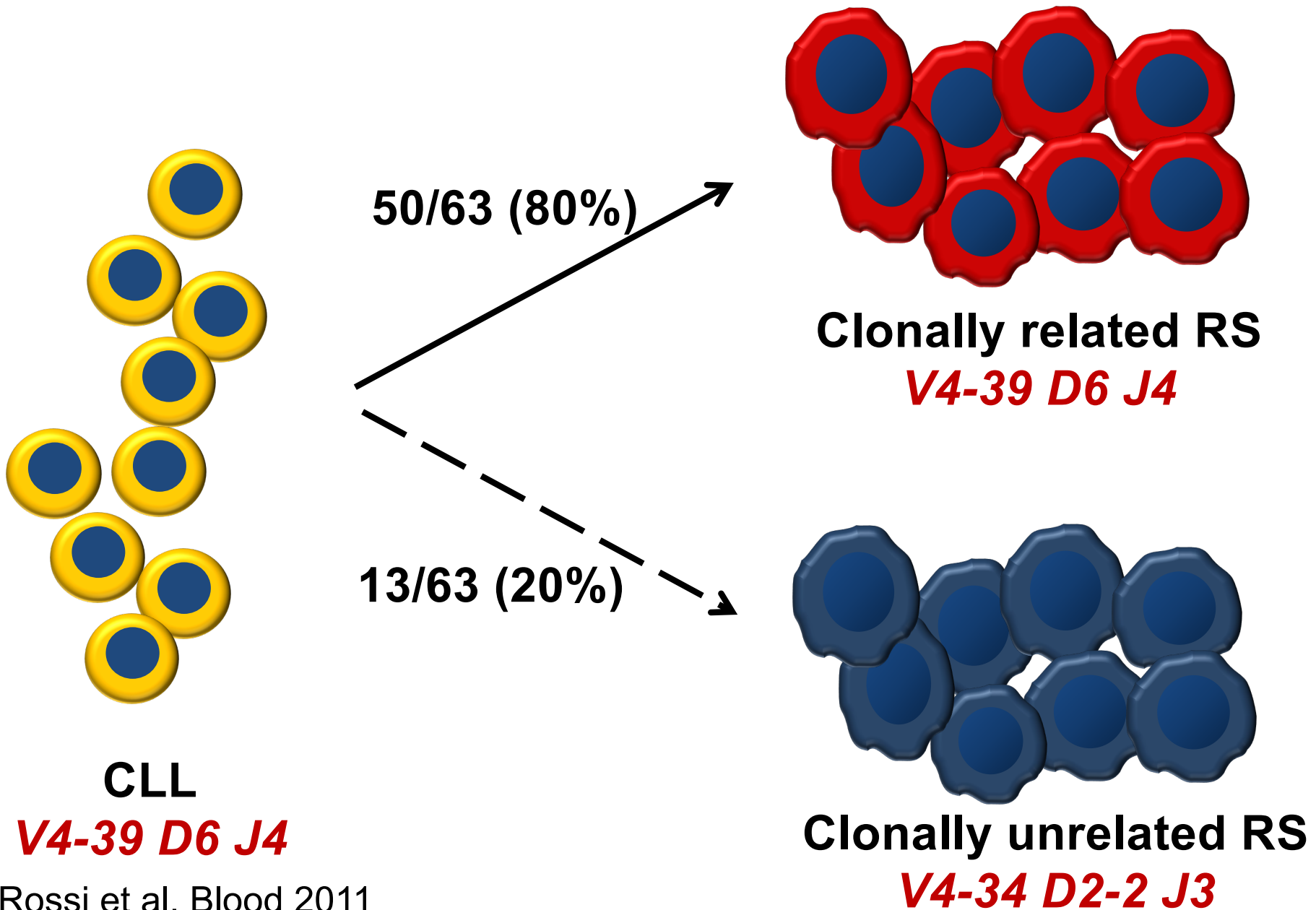
1-5%



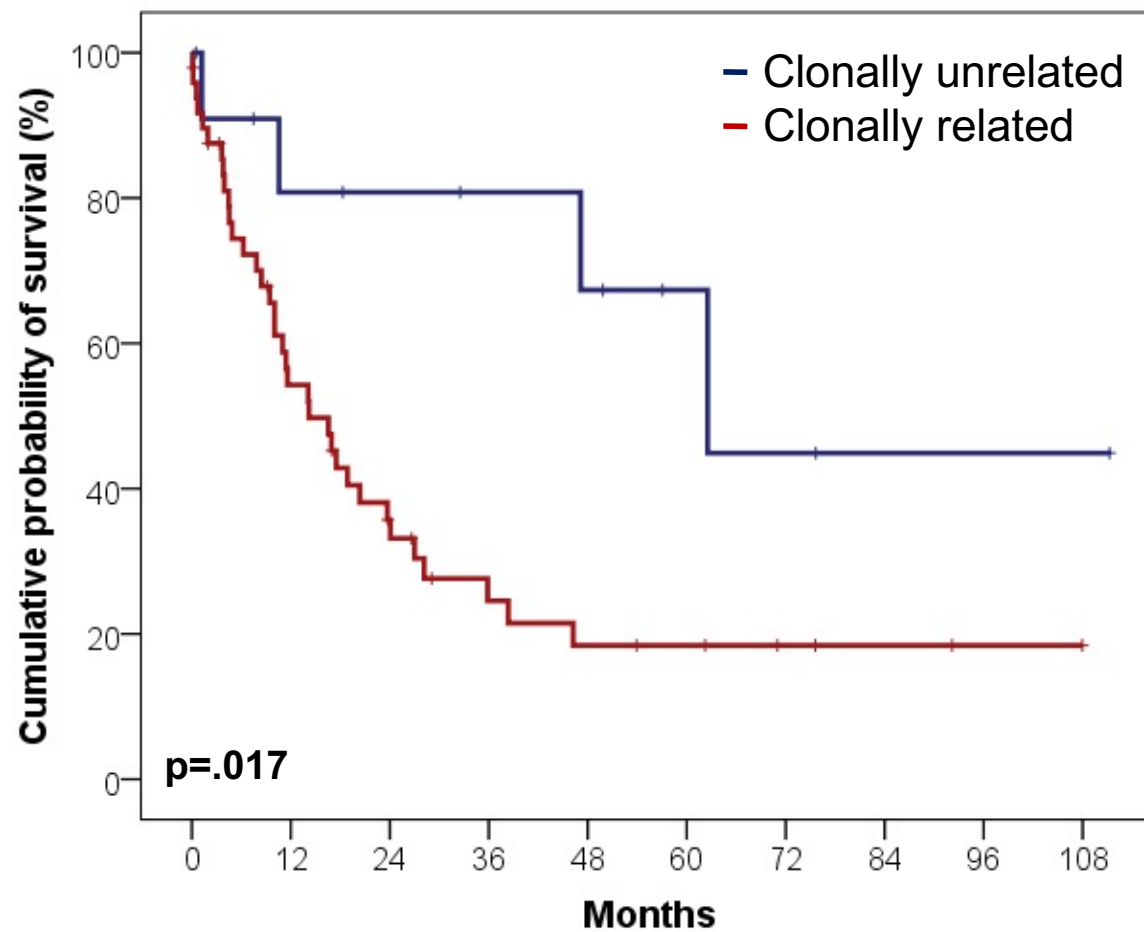
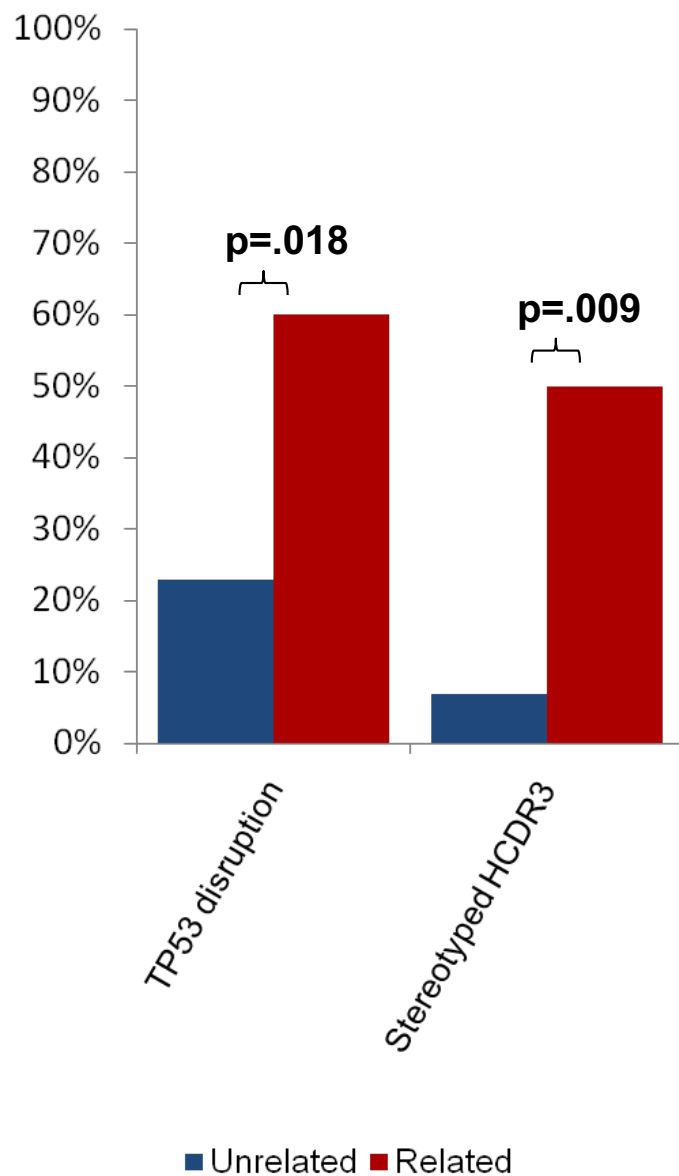
Post-transformation survival according to histology



Clonally related vs unrelated variant of Richter syndrome

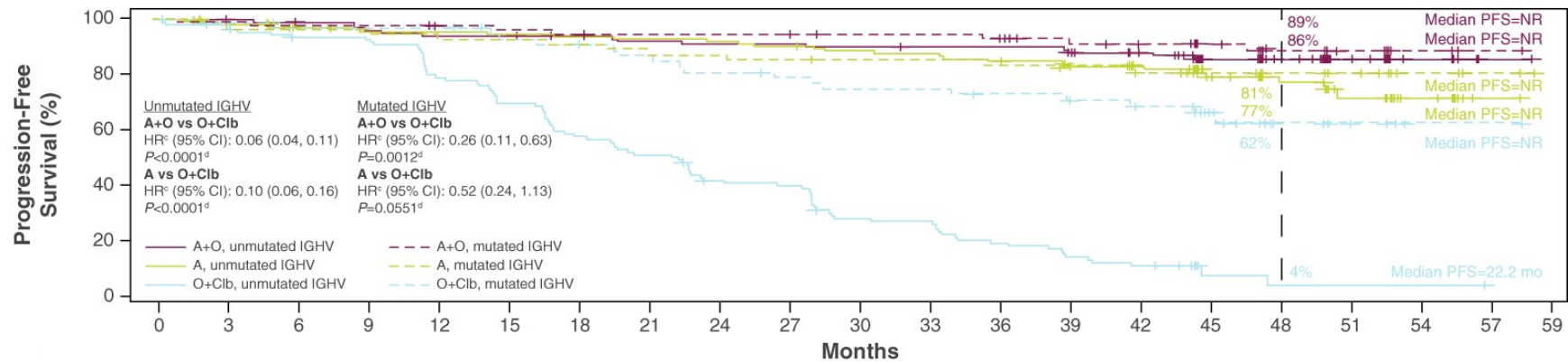
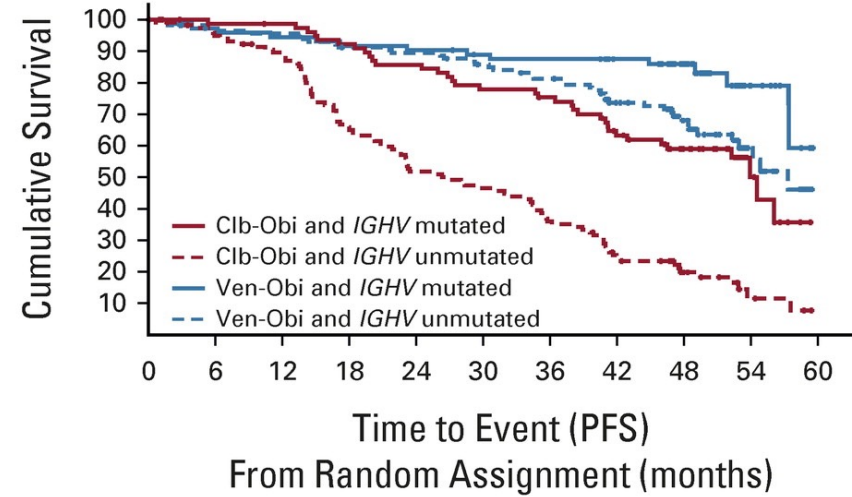
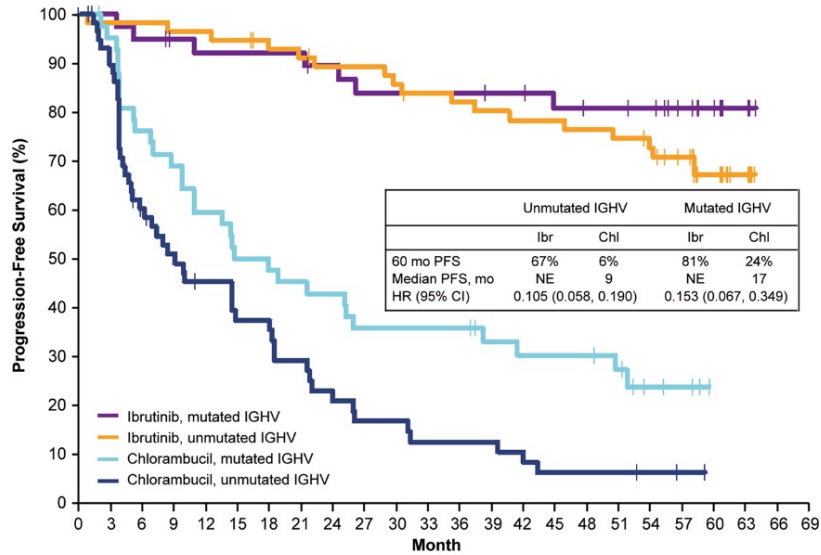


The molecular profile of clonally unrelated RS differs from that of clonally related RS



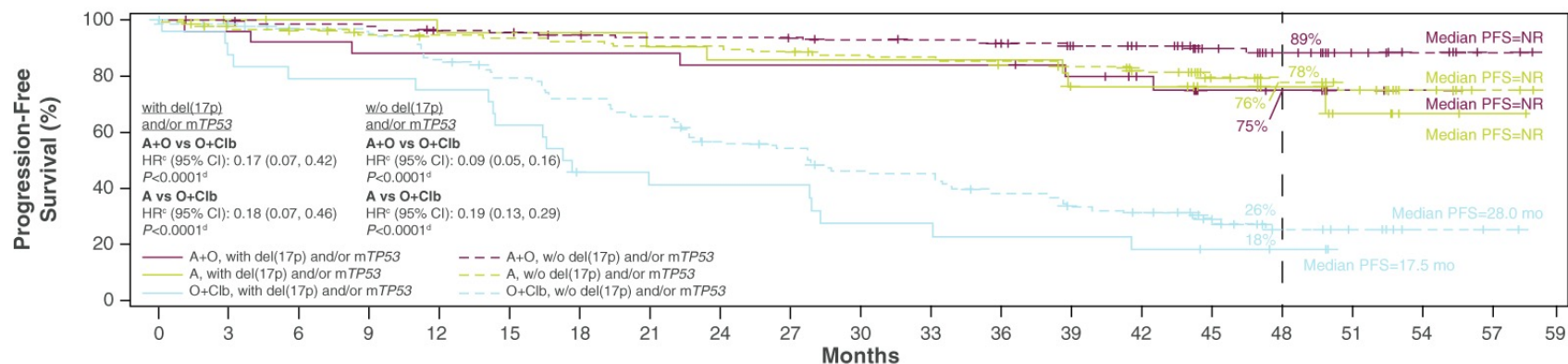
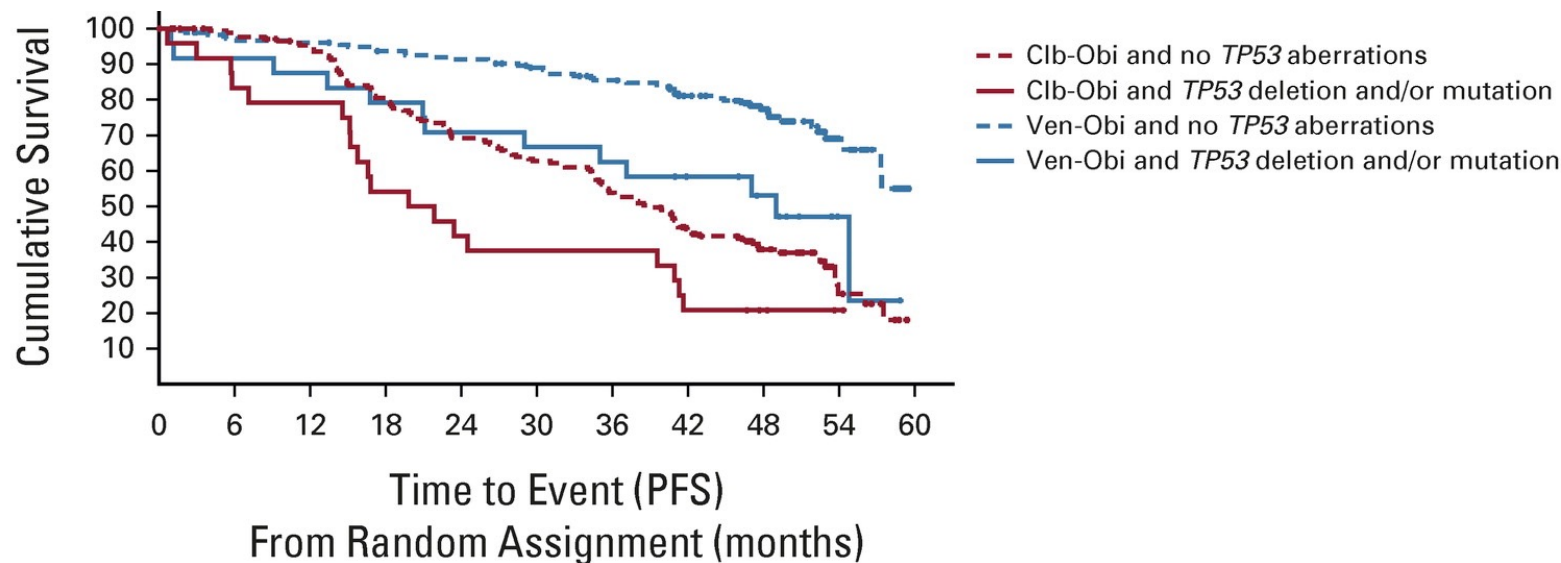
Genetics

IGHV mutation status

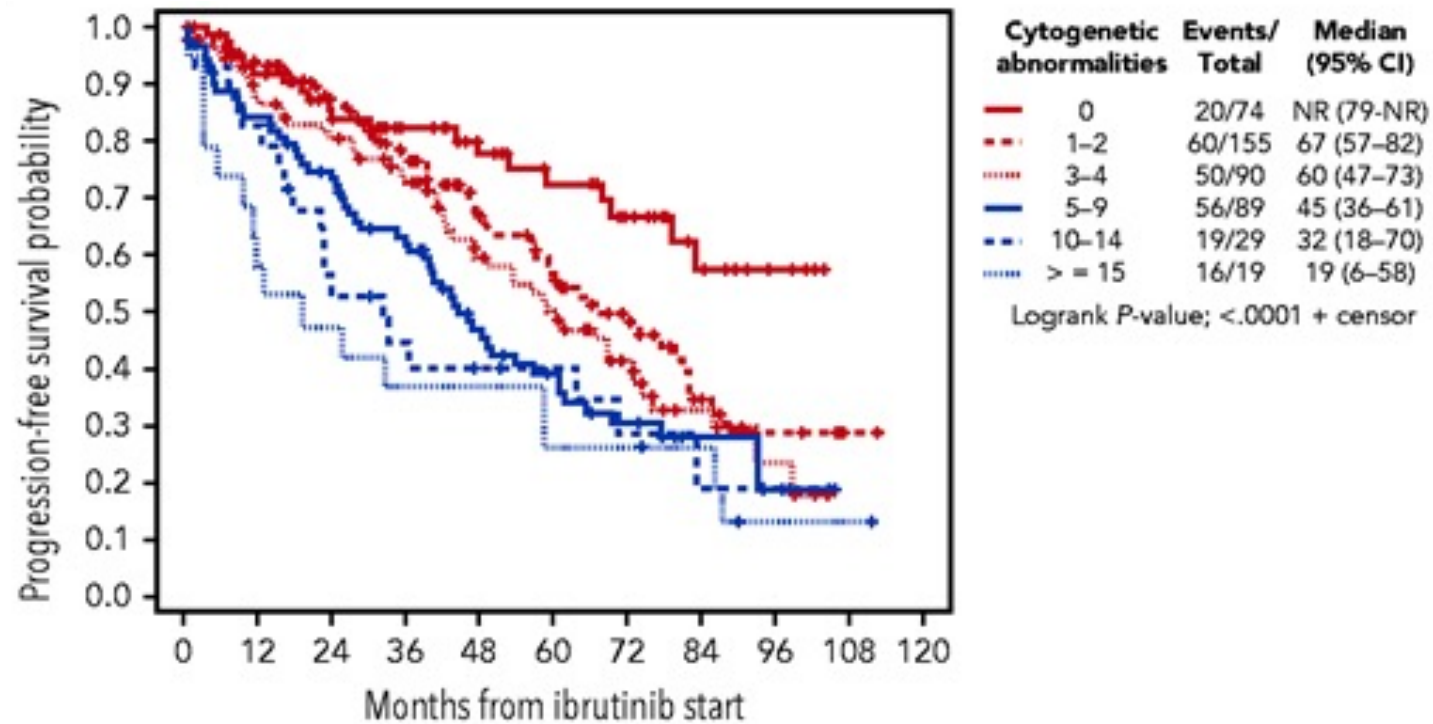


Sharman JP, et al. Leukemia. 2022
 Burger JA, et al. Leukemia. 2020
 Al-Sawaf O, et al. J Clin Oncol. 2021

TP53 status



Karyotype status



Kittai AS, et al. Blood. 2021

Resistance mutations to BTKi and BCL2i

Ibrutinib

BTK mutation
70% of cases

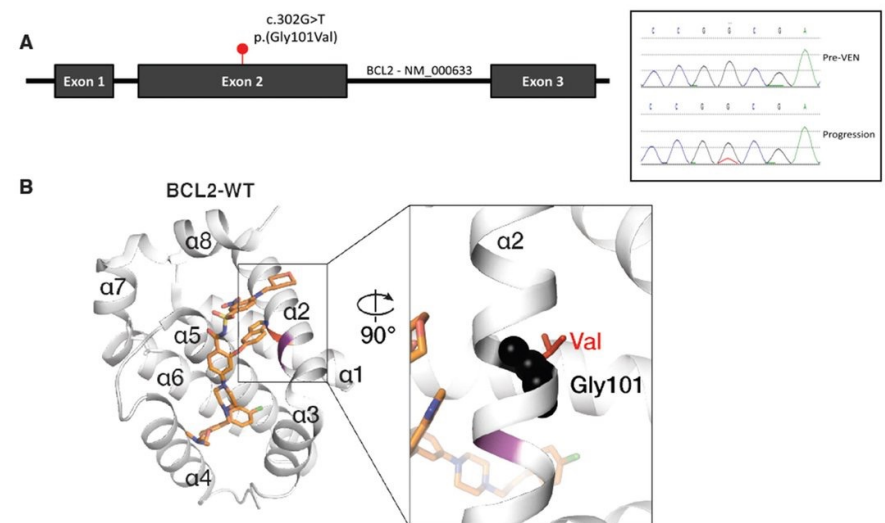
C481S BTK



Furman RR et al. N Engl J Med 2014;370:2352-2354.

Venetoclax

BCL2 mutation
50% of cases

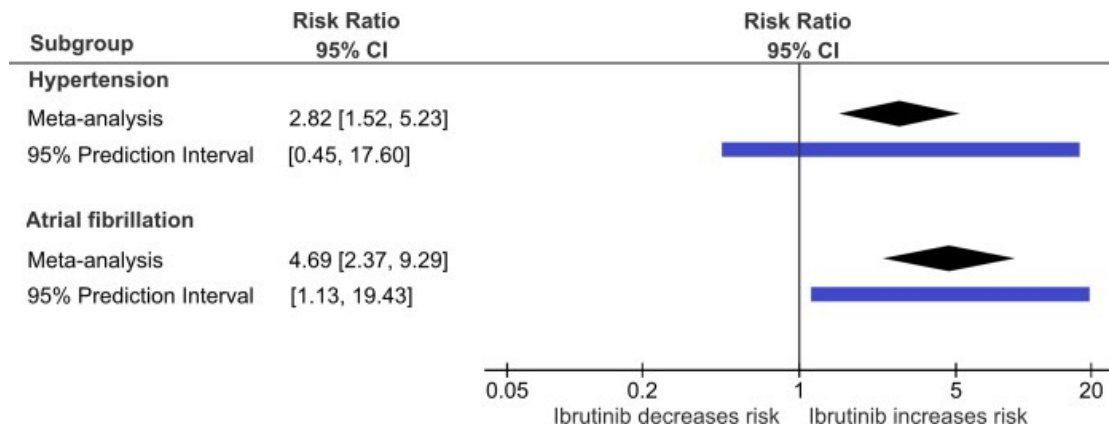


Blombery et al, Cancer Discovery 2019

Patient's comorbidities

Cardiac risk factors

Meta-analysis of 8 RCTs



Risk factors for Afib

- heart failure
- left atrial abnormality on electrocardiogram
- past history of AF
- left atrial diameter by echocardiography
- atrial fibrillation risk score

Caldeira D, et al. PLoS One. 2019

Lentz R, et al Leuk Lymphoma. 2019
Archibald WJ, et al. Ann Hematol. 2020
Reda G, et al. J Hematol Oncol. 2018
Mato AR, et al. Cancer Biol Ther. 2018

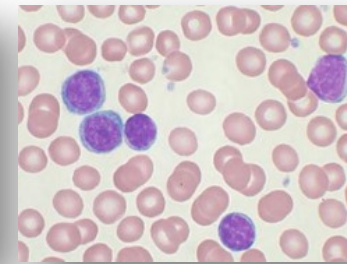
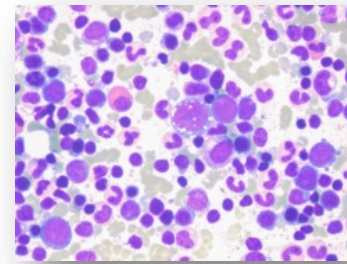
Cardiac risk factors

Bleeding incidence before and after prohibiting concomitant use of DOCs in CLL12

| Estimated marginal means for the incidence of bleeding events per month | | Mean | Std. Error | 95% Wald Confidence Interval | |
|---|----------------------------------|------|------------|------------------------------|-------|
| | | | | Lower | Upper |
| Ibrutinib-Group | before amendment (2015/07/20) | 7.9% | 2.1% | 4.8% | 13.2% |
| | after amendment (2015/07/20) | 1.7% | 0.4% | 1.1% | 2.6% |

Conclusions

- Histology: differentiate “histologically aggressive” CLL vs Richter syndrome
- Richter syndrome: differentiate clonally related LBCL vs clonally unrelated LBCL vs cHL
- First line: test for *TP53* status
- Relapsed disease: test for *BTK* and *BCL2* mutations
- Patient assessment for comorbidities and con-med



• Lymphoma

• Leukemia



Laboratory of experimental Hematology IOR

- | | |
|--|--|
| <p>Post Doc</p> <p>Lab Technician</p> <p>Research Fellow</p> <p>Bioinformatician</p> | <p>Alessio Bruscaffin PhD Deborah Piffaretti PhD Simone Bocchetta PhD Gabriela Forestieri BSc Katia Pini BSc Marco Marangon BSc Adalgisa Conduluci MD, PhD student Cristina Piroso MD, PhD student Joyce Marques De Almeida MD, PhD student Lodovico Terzi Di Bergamo MSc, PhD student Matin Salehi MSc, PhD student</p> |
|--|--|



krebsforschung schweiz
recherche suisse contre le cancer
ricerca svizzera contro il cancro
swiss cancer research

