



La **DIAGNOSTICA** **EMATOPATOLOGICA** nell'ERA della **MEDICINA** di **PRECISIONE**

Clinical case

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Disclosures of Valentina Tabanelli

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
None	None	None	None	None	None	None	None

M, 61 yo



**CLL / SLL
diagnosis**

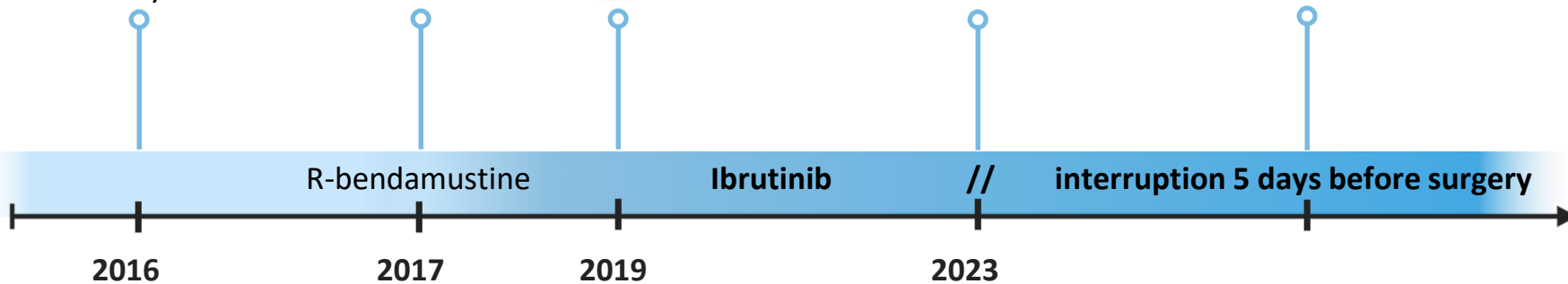
Unmutated IGHV
TP53 wt
Trisomy 12

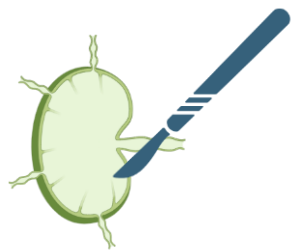


Planned surgery
for invasive lung
adenocarcinoma



Generalized
lymph node
enlargement

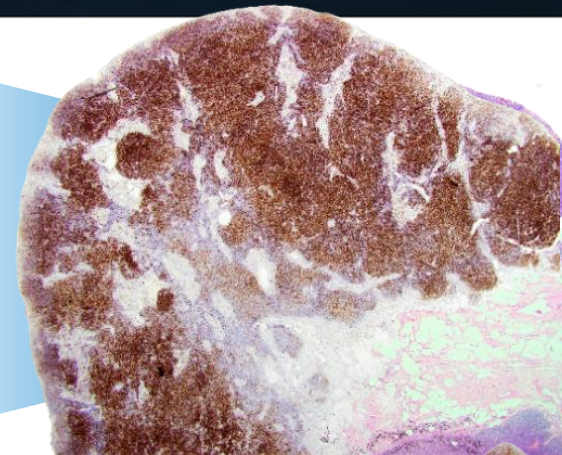
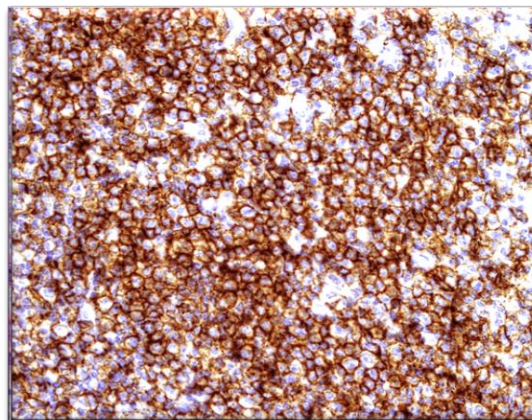




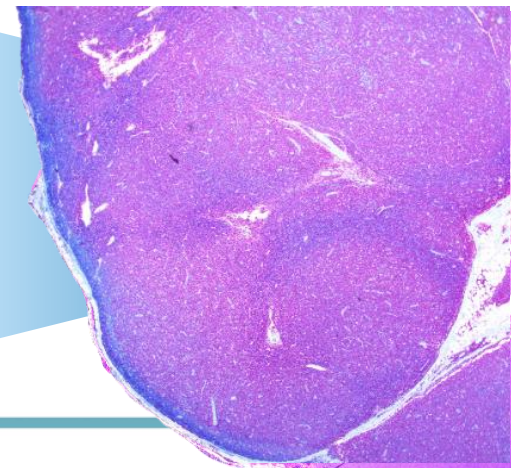
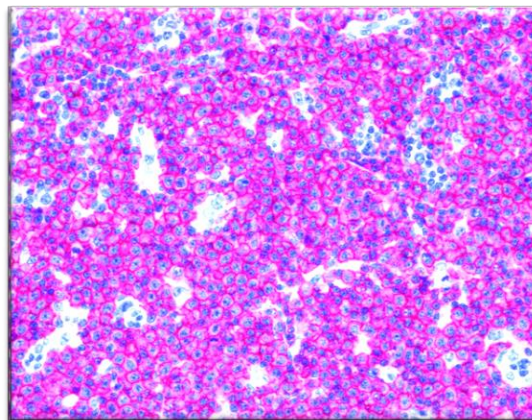
Atypical segmental
resection of the left
upper lung lobe

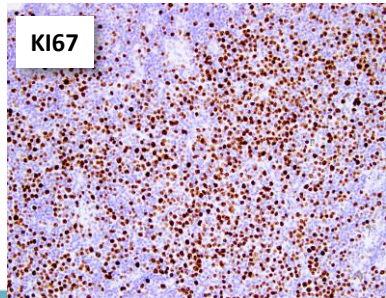
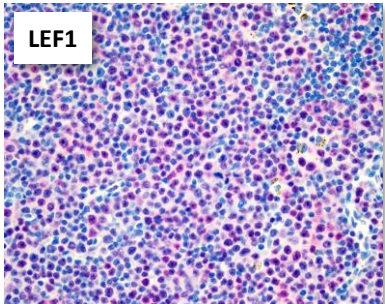
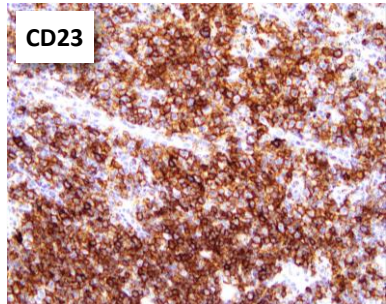
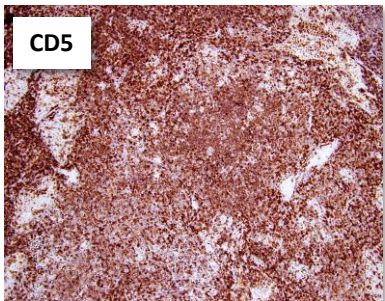
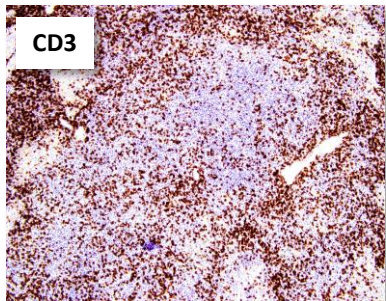
Enlarged lymph nodes
were sampled during
surgery

Ibrutinib hold



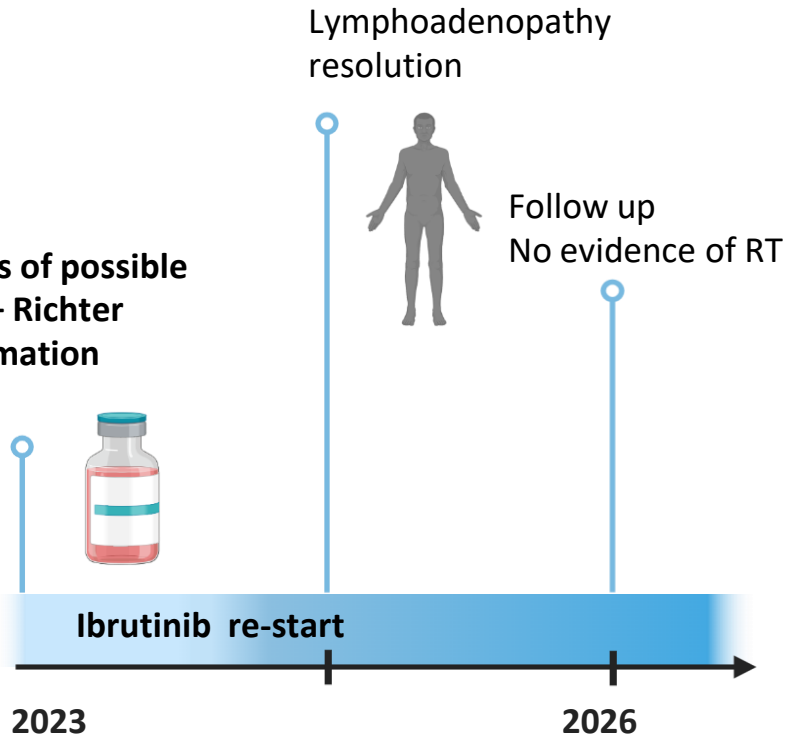
CD20





- CD5+, CD23+, LEF1+, high Ki67
- Others IHC: cyclin D1-, SOX11-, CD10-, Bcl6-, IRF4+, Bcl2+, c-myc < 40%
- MYC and BCL2 not rearranged
- EBV negative, TP53 wt

**Diagnosis of possible
Pseudo – Richter
transformation**

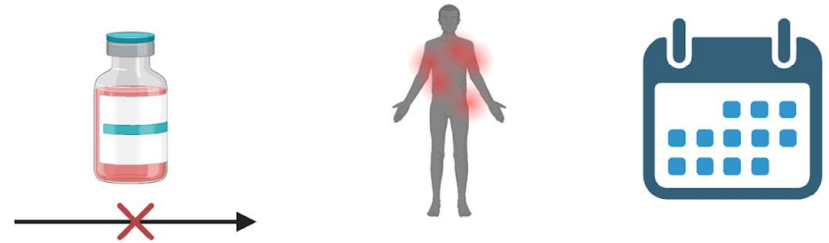


Pseudo-Richter Transformation (pseudo-RT)

Rare but clinically significant phenomenon

- Transient large B-cell proliferation after BTKi interruption
- Mimics true RT, but **reversible**

- Temporary BTKi interruptions occur in >40% of patients
- Common causes: surgery, adverse events, infections



Clinical features

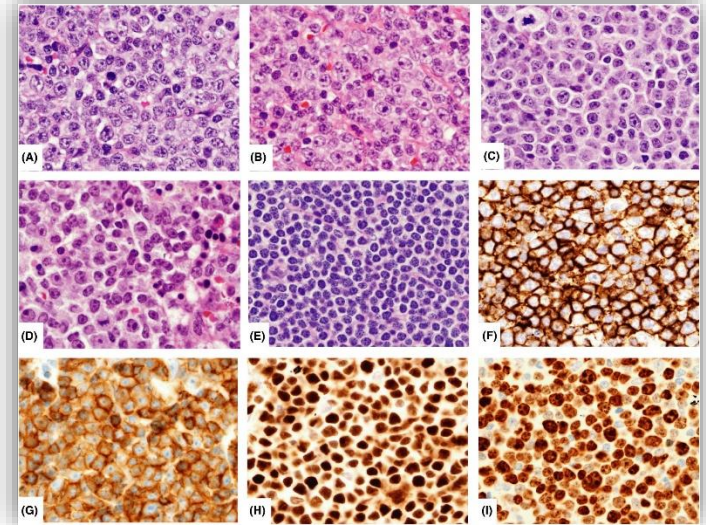
- Median BTKi duration before hold: 20 months (range, 10-48)
- Onset: 1 - 2 weeks (as early as 2 days)
- B symptoms, lymphadenopathy
- Lab: lymphocytosis, ↑LDH

Biological Features

- Vaguely nodular or diffuse infiltrate
- Centroblastoid or immunoblastic large B cells
- High Ki-67 (50 - 90%)
- Non-GCB phenotype, EBV negative
- Retains CLL profile: CD5+, CD23+, LEF1+

Genetics

- Unmutated IGHV
 - Trisomy 12 (~78%)
 - NOTCH1, TP53 alterations
- } Shared RT risk features



Barnea Slonim et al. *Br J Haematol.* 2020; 191(1):e22-e25
Hampel et al. *Blood Adv.* 2020; 4(18):4508-4511
Anagnostopoulos et al. *Virchows Archiv* 487,2 (2025): 287-307

Clinical course

- Reversible with BTKi restart
- Resolution \leq 4 weeks
- No progression to true RT reported

Mechanism

- BCR reactivation after BTKi withdrawal
- Transient proliferative surge

Differential diagnosis

BTKi “disease flare”

- Both after BTKi interruption (\leq 4 weeks) and reversible
- Disease flare: clinical, laboratory and radiologic worsening
- Flare: no histologic transformation

Accelerated / histologically aggressive CLL

- Not transient and not linked to BTKi interruption

