FAKULTNÍ NEMOCNICE BRNO

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XVIII IWCLL
International Workshop on CLL
20-23 SEPTEMBER 2019 EDINBURGH

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Minor-clone *TP53* mutations in CLL patients entering first-line treatment: clonal evolution and clinical impact

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Poster no. 2136

I have no disclosures

Aims

- To assess the risk of clonal expansion of minor-clone *TP53* mutations

- To evaluate the clinical impact of *TP53* mutations with different variant allele frequencies (VAFs)

…in patients entering first-line treatment

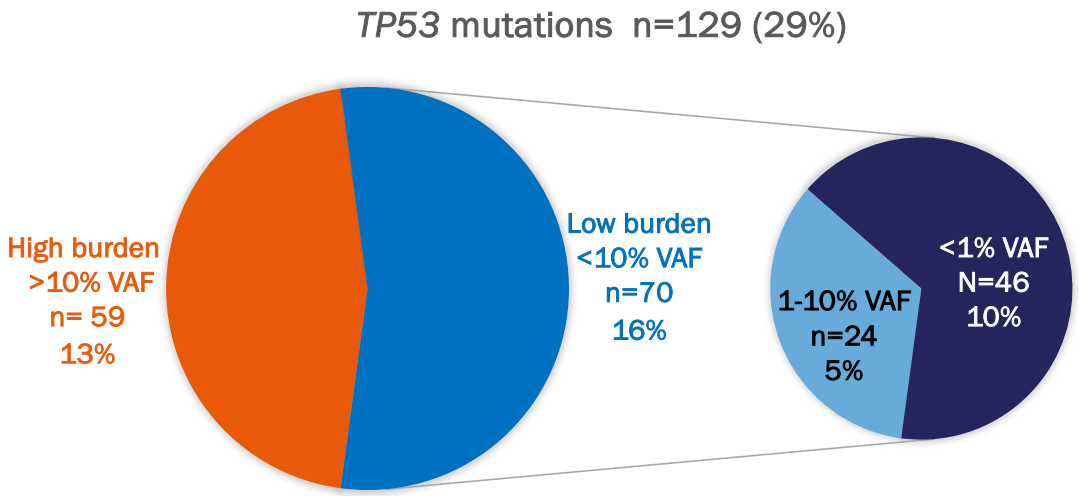
"TP53 gene assessment should always be performed prior to initiation of the first and every subsequent line of treatment"

iwCLL guidelines: Hallek et al., 2018

TP53 recommendations: Malcikova et al., 2019

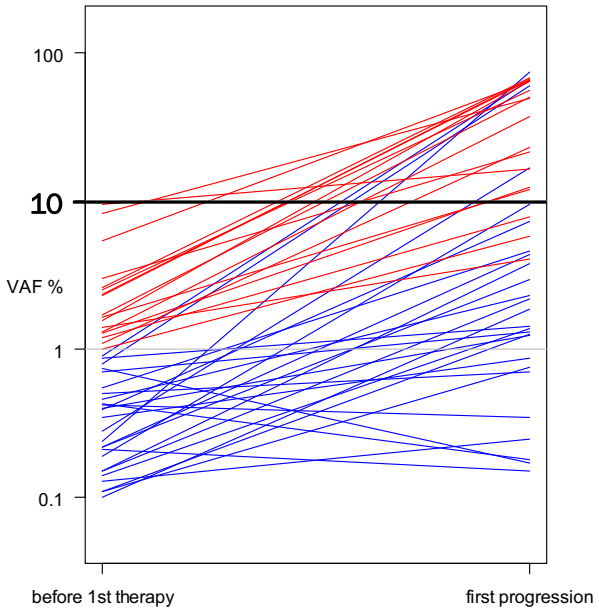
Patient cohort

- 450 patients
  - 72% unmutated IGHV
  - 84% received chemoimmunotherapy
- Amplicon NGS *TP53* analysis with detection limit 0.1-0.2% VAF

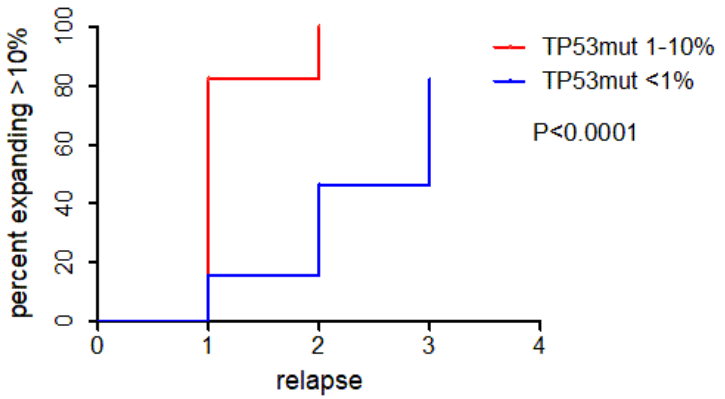


Clonal evolution of minor-clone *TP53* mutations

- Samples in first relapse available in 43 patients with detected low-burden *TP53* mutation



- 88% clonal expansion >1.5x
- Median fold change = 10x (0.2-309x)
- Increase in mutation VAF above 10%
  - Patients with mutation 1-10% VAF before treatment – 82% (14/17)
  - Patients with mutations <1% VAF before treatment – 15% (4/26)
    - Gradual expansion in subsequent relapses



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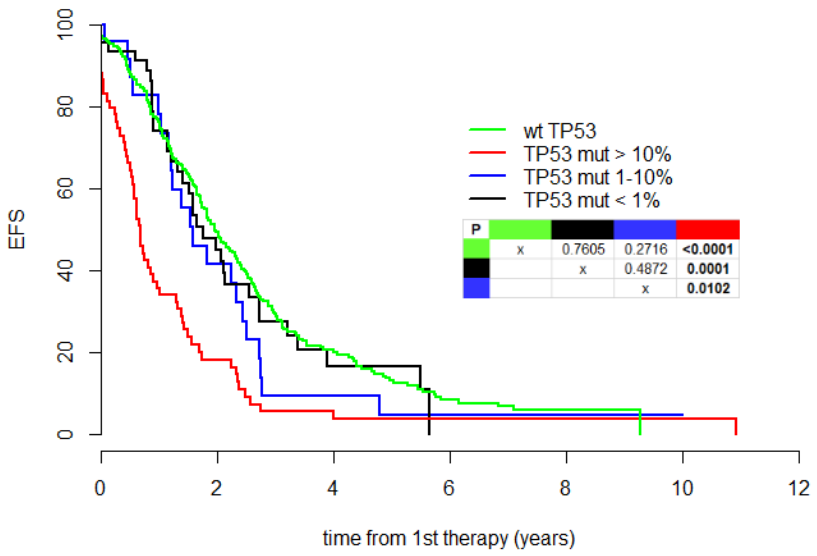
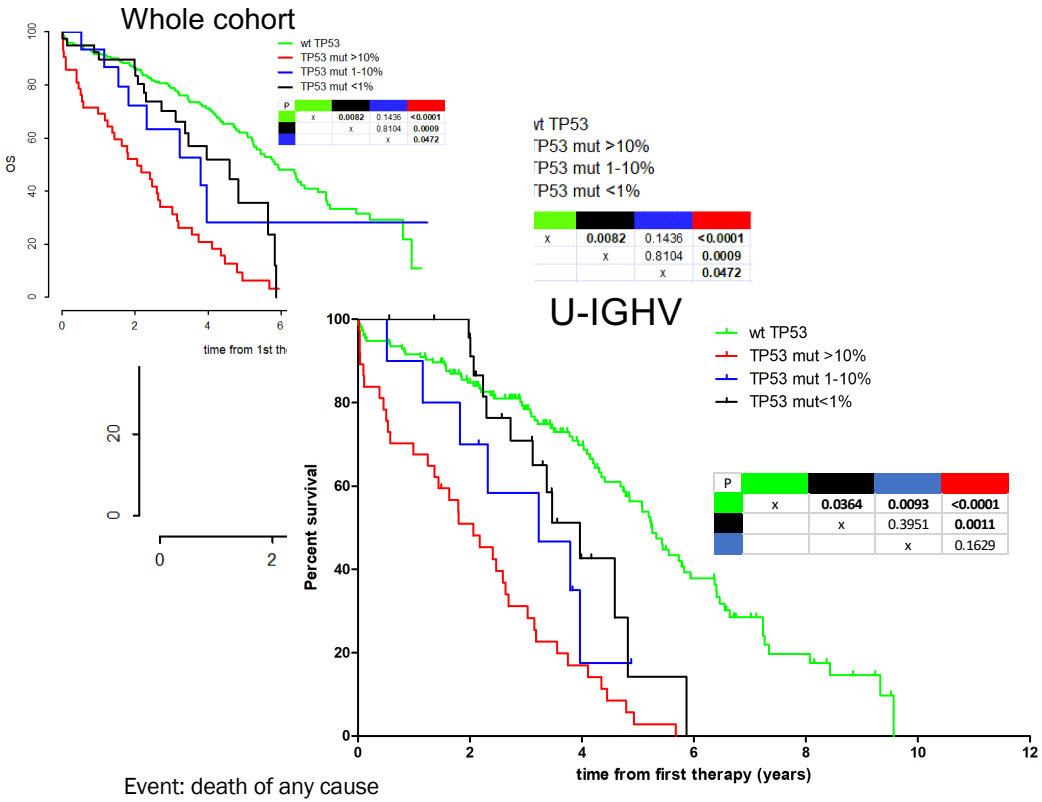
Clinical impact

Event-free survival



Event: progression, death of any cause, therapy change

Overall survival



Event: death of any cause
Excluded from OS analysis: switched to targeted therapy (88), allo-HSCT (14)

Conclusions

- Low-burden *TP53* mutations detected before first-line treatment
  - Increase in clonal proportion in first relapse in majority of patients with median fold change 10x
  - Did not significantly shorten response to first-line therapy
  - Affected OS at least in unmutated IGHV patients

- Unresolved issues remain → multicenter study is needed

Thank you for your attention

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