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Undetectable Minimal Residual Disease Should be the Goal of Venetoclax Therapy in Relapsed and Refractory Chronic Lymphocytic Leukaemia

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Disclosures

Presenter:

Employee of the Walter and Eliza Hall Institute of Medical Research, which receives milestone and royalty payments related to venetoclax and travel assistance from AbbVie.

Co-authors:

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Aims

We aimed to assess:

- The timing of uMRD attainment
- The performance of peripheral blood MRD monitoring compared to bone marrow
- The longer-term outcomes associated with uMRD attainment
- The clinicopathological associations with uMRD attainment and subsequent MRD recrudescence

Methods

- Retrospective analysis of 62 patients with relapsed/refractory* CLL treated with **continuous** venetoclax with an objective response
- Patients treated between June 2011 and September 2018
- Patients were enrolled on one of three venetoclax trials:
  - Phase-1 study of venetoclax monotherapy n=36[1]
  - Phase-1b study of venetoclax plus rituximab therapy n= 14[2]
  - Phase-2 study of venetoclax monotherapy in del(17p) CLL n=12[3]
- Serial MRD monitoring in PB and BM using multiparameter flow cytometry (ERIC methodology[4])
- uMRD: <1 CLL cell per 10^4 leukocytes, minimum 200,000 leukocytes analysed

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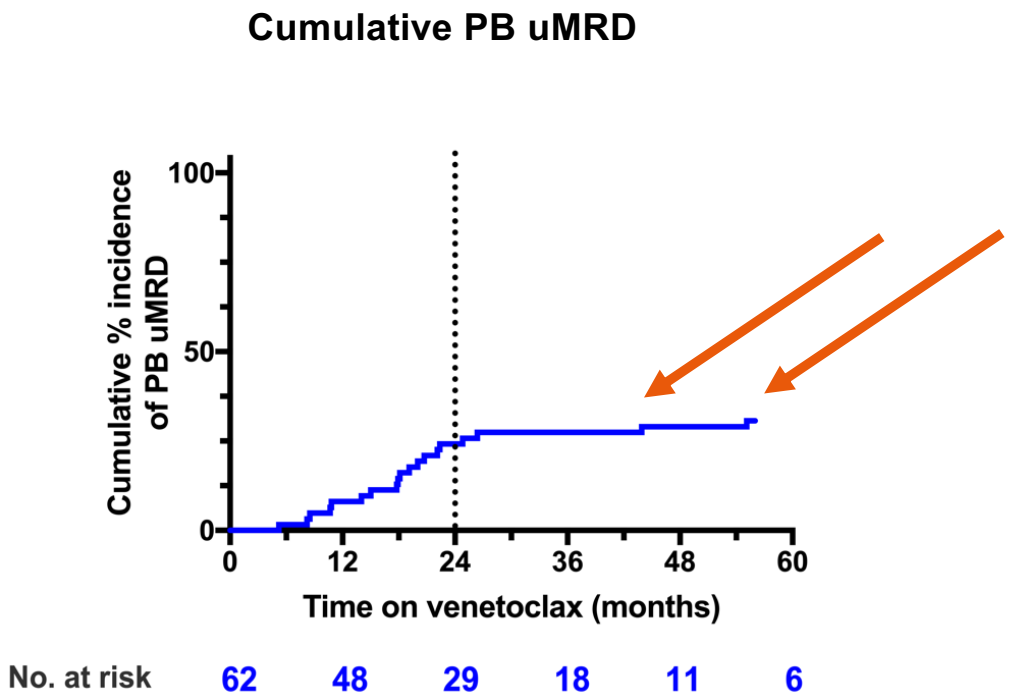
*2 previously untreated

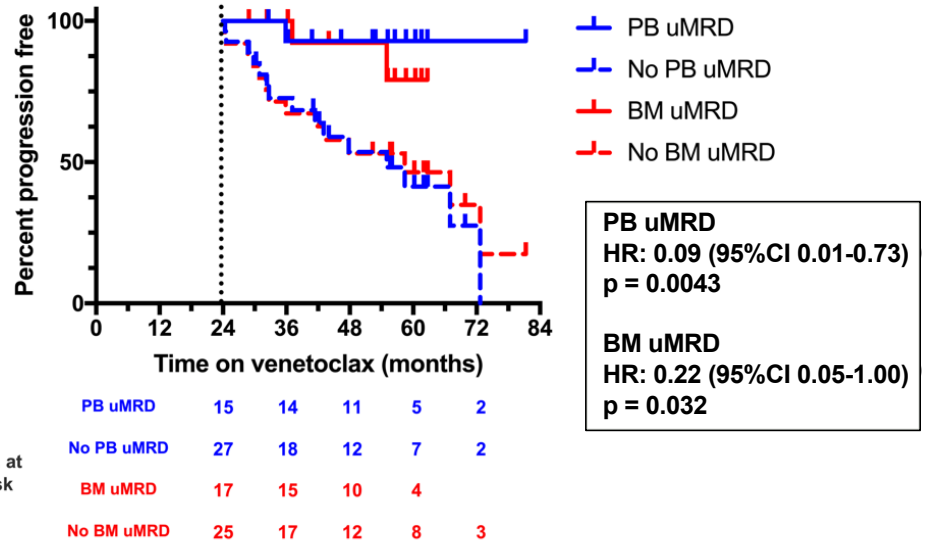
1. Roberts, *et al*. *NEJM* 2016;374:311-22.
2. Seymour, *et al*. *Lancet Oncol* 2017;18:230-40.
3. Stilgenbauer, *et al*. *Lancet Oncol* 2016;17:768-78
4. Rawstron, *et al*. *Leukemia* 2013;27:142-9

90% of uMRD attainment occurs within 24 months



PB and BM uMRD at 24 months has equivalent favourable prognostic impact

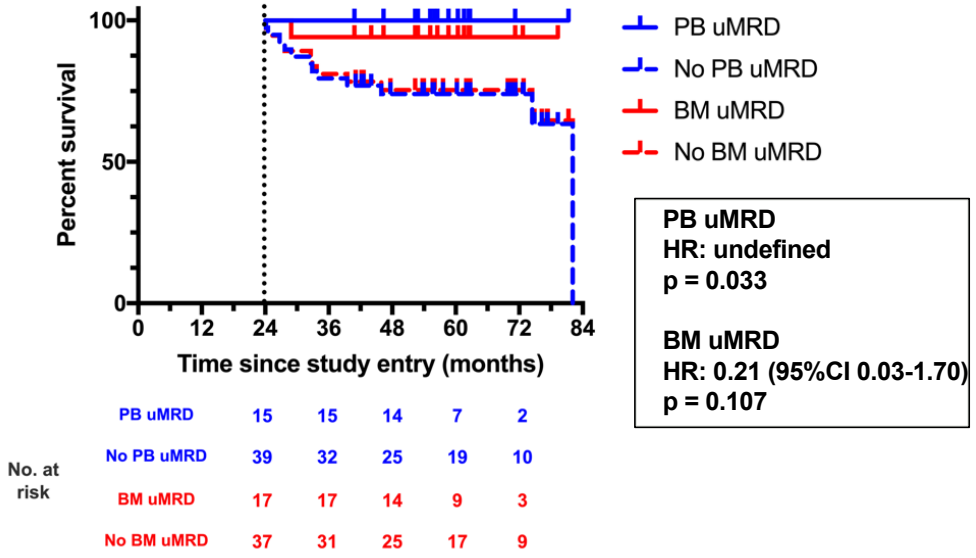
Time to progression



PB uMRD
HR: 0.09 (95%CI 0.01-0.73)
p = 0.0043

BM uMRD
HR: 0.22 (95%CI 0.05-1.00)
p = 0.032

Overall survival



PB uMRD
HR: undefined
p = 0.033

BM uMRD
HR: 0.21 (95%CI 0.03-1.70)
p = 0.107

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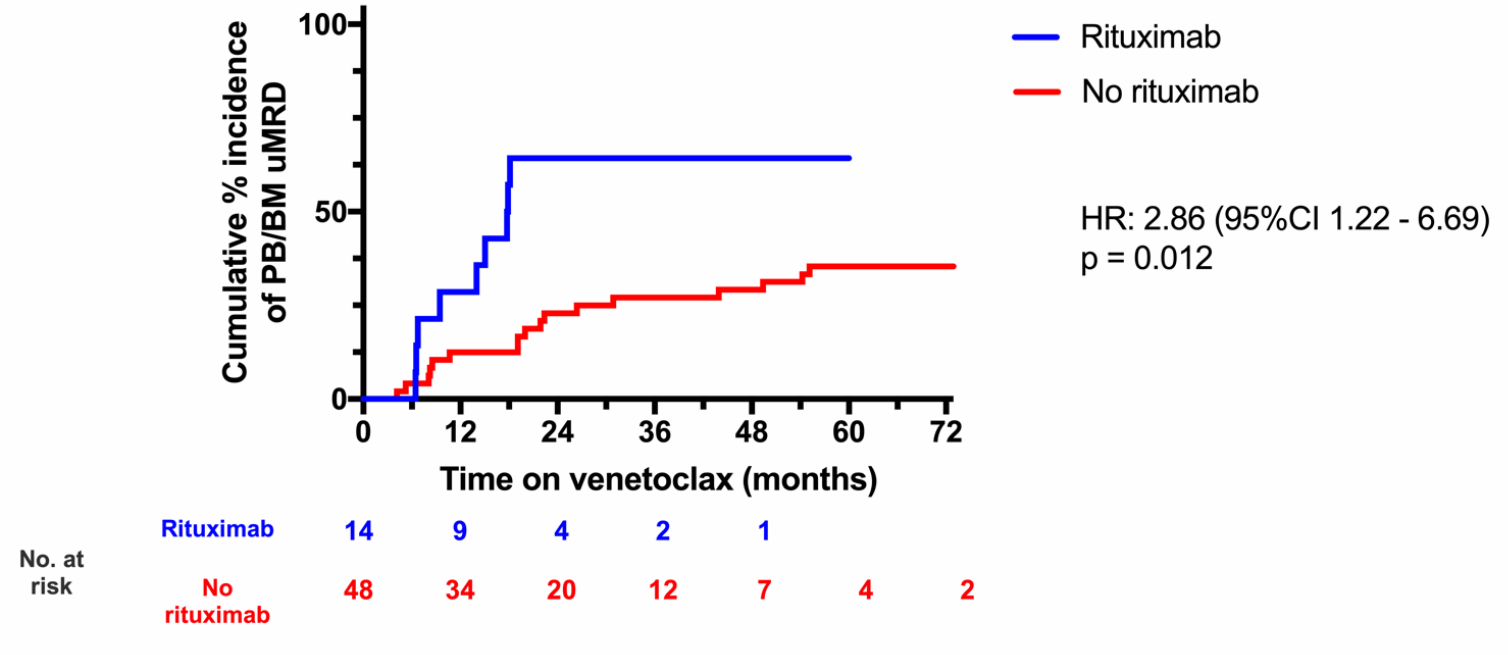
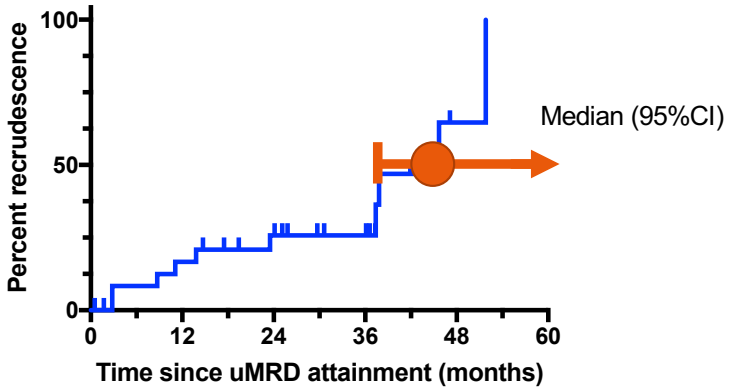
Concomitant rituximab is associated with uMRD attainment



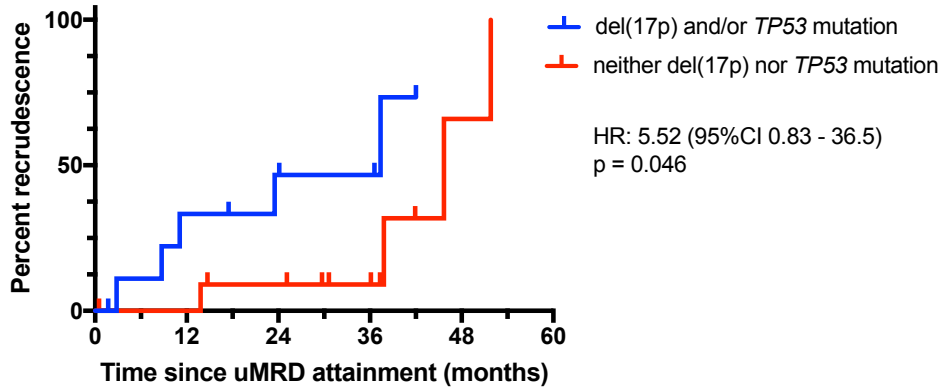
Confirmed recrudescence of MRD over time

Time to MRD recrudescence all patients



No. at risk					
	26	21	16	11	2

Time to MRD recrudescence by *TP53* status



No. at risk						
	p53 abnormal	10	7	5	4	
	p53 normal	12	12	10	7	2

Median time to iwCLL progression after PB MRD recrudescence was 17 (14-27) months

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Conclusions

In patients receiving continuous venetoclax for relapsed/refractory CLL:

- ~90% uMRD attainment occurs within 24 months of therapy
- uMRD attainment is associated with improved longer-term survival, and PB uMRD appears as informative as BM uMRD in this regard
- Concomitant rituximab is associated uMRD attainment
- MRD recrudescence is common and occurs at an estimated median > 3 years, but earlier in disease with *TP53* abnormalities

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