

A photograph of the MD Anderson Cancer Center building, a tall, modern structure with a glass facade and a brick-like pattern, set against a blue sky with scattered white clouds.

# **CLL Clinical Care: Impact of Science**

A photograph of the MD Anderson Cancer Center building, showing a curved glass facade reflecting the surrounding cityscape and a brick building in the background.

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# **CLL Clinical Care: Impact of Science**

## **Developing Combination Strategy**

### **With Ibrutinib**

**MD Anderson**

**Nitin Jain**

**Bill Wierda**

**Michael Keating**



## **What is ibrutinib (Imbruvica)?**

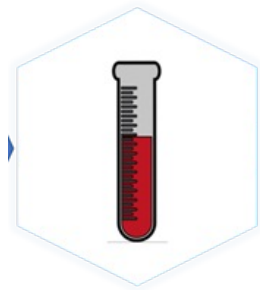
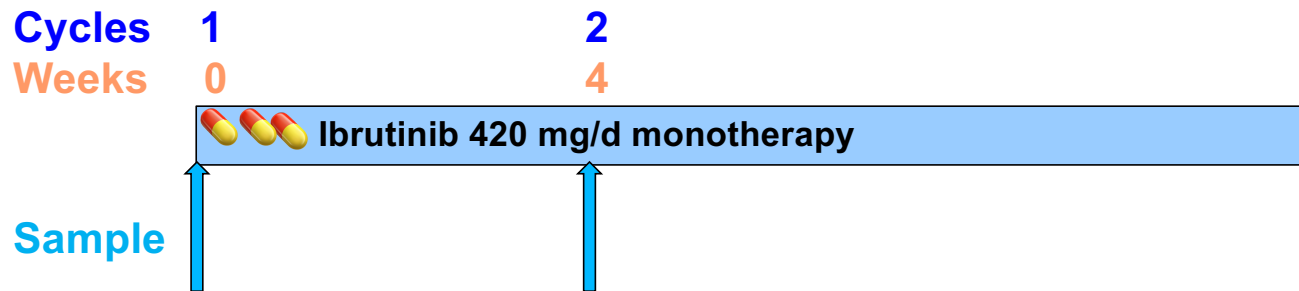
- First targeted therapy that was FDA approved for CLL
- Targets an enzyme/protein which is important for CLL
- Oral agent; very effective drug
- But need long-term use
- Low complete remission; no achievement of uMRD

**Unmet Need - Develop combination strategies!**



# Developing Ibrutinib Combinations

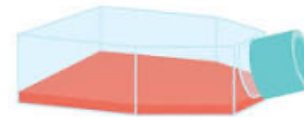
## Blood Sample Collection & Workflow



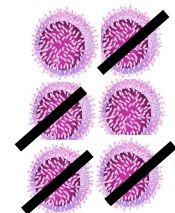
Blood samples  
from patient  
Before ibrutinib  
After 1 cycle



PBMCs  
isolated from  
blood, CLL  
cells enriched



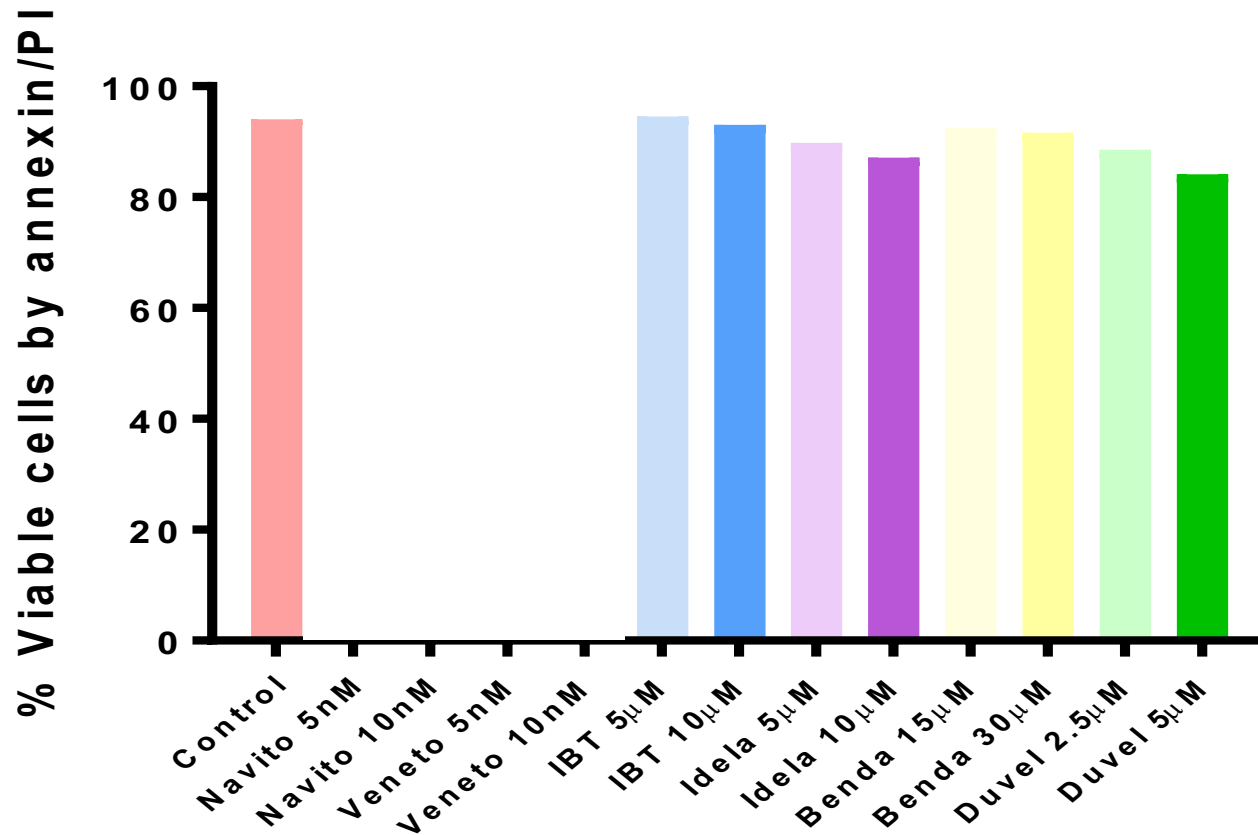
PBMCs incubate  
for 1 day with  
**A New Drug**



Check how many  
cells are alive



## Ex vivo pharmacological profiling of CLL cells after ibrutinib therapy



## Pharmacological rationale to combine ibrutinib with venetoclax

Cervantes-Gomez, F. et al. Clin Cancer Res 21:3705, 2015



## **What is venetoclax (Venclexta)?**

- **Another targeted therapy that is FDA approved for CLL**
- **Targets a protein (BCL-2) that helps CLL cells to survive**
- **Oral agent; very effective drug**
- **But need long-term use**
- **Low complete remission; low uMRD rate**

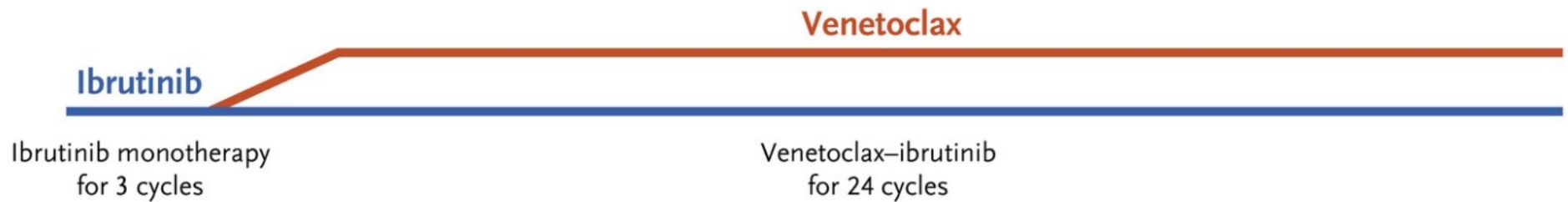
**We developed investigator initiated trial (IIT)**



# Design of Clinical Trial with Ibrutinib and Venetoclax For CLL Patients with Poor Prognosis

3 cycles only ibrutinib

24 cycles - combination



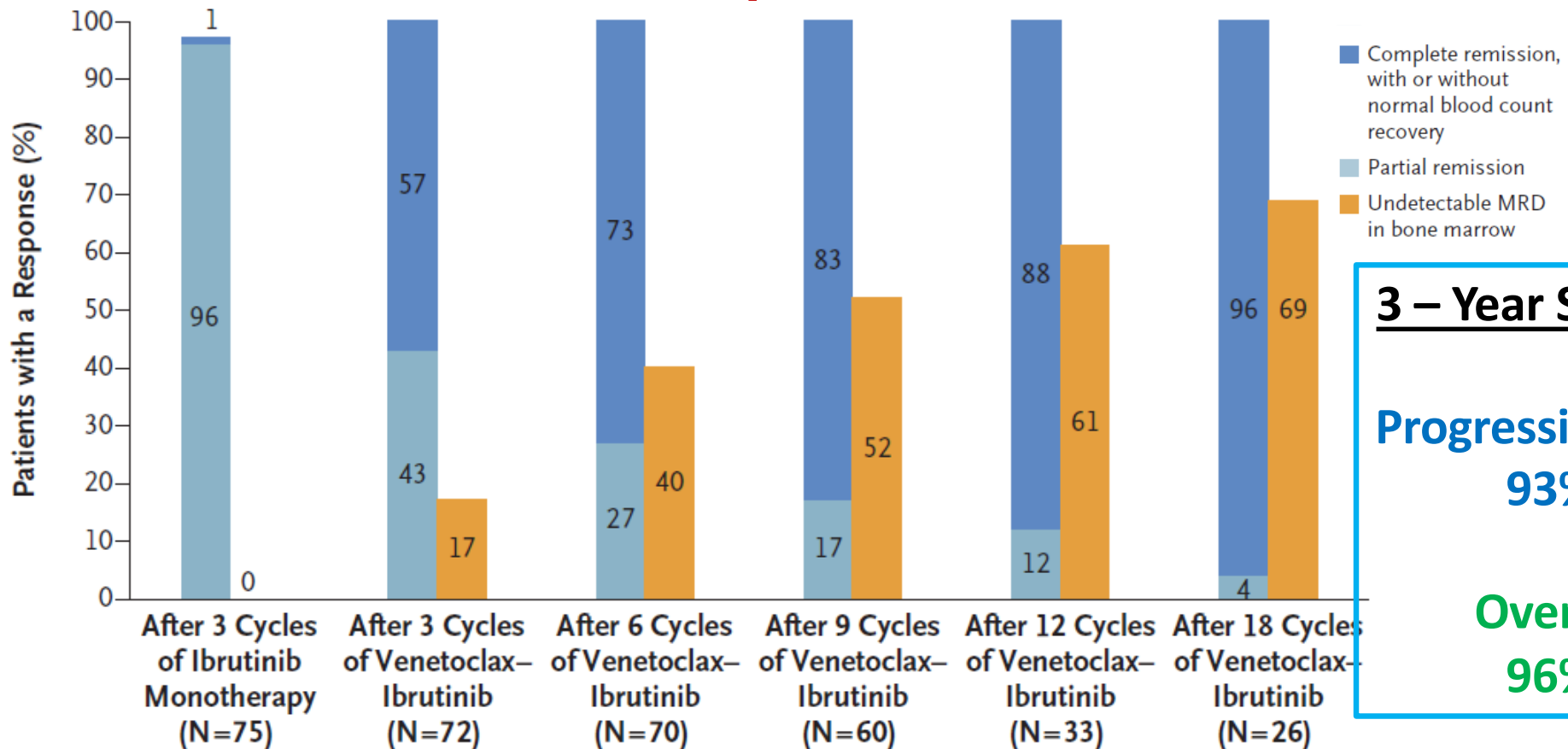
420mg daily

VEN duration 2 years, IBR until progression

Primary endpoint: CR/CRi



# Clinical Responses & MRD Status



## 3 – Year Survival

Progression-free  
93%

Overall  
96%

Median follow-up 14.8 months

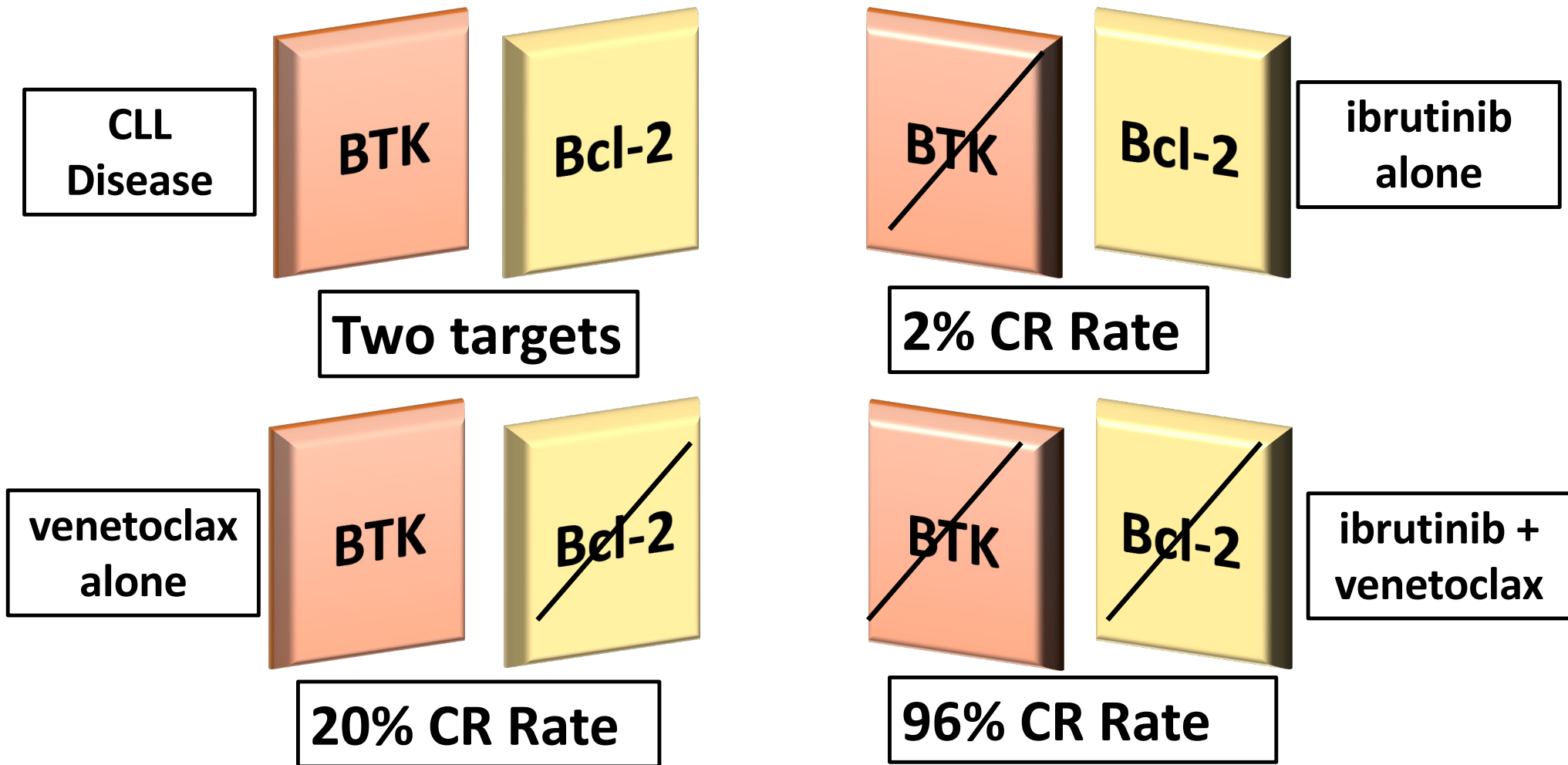
CR + CRi PR U-MRD

Jain N et al. ... Gandhi & Wierda NEJM. 2019

Jain N et al... Gandhi & Wierda JAMA Oncol 2021

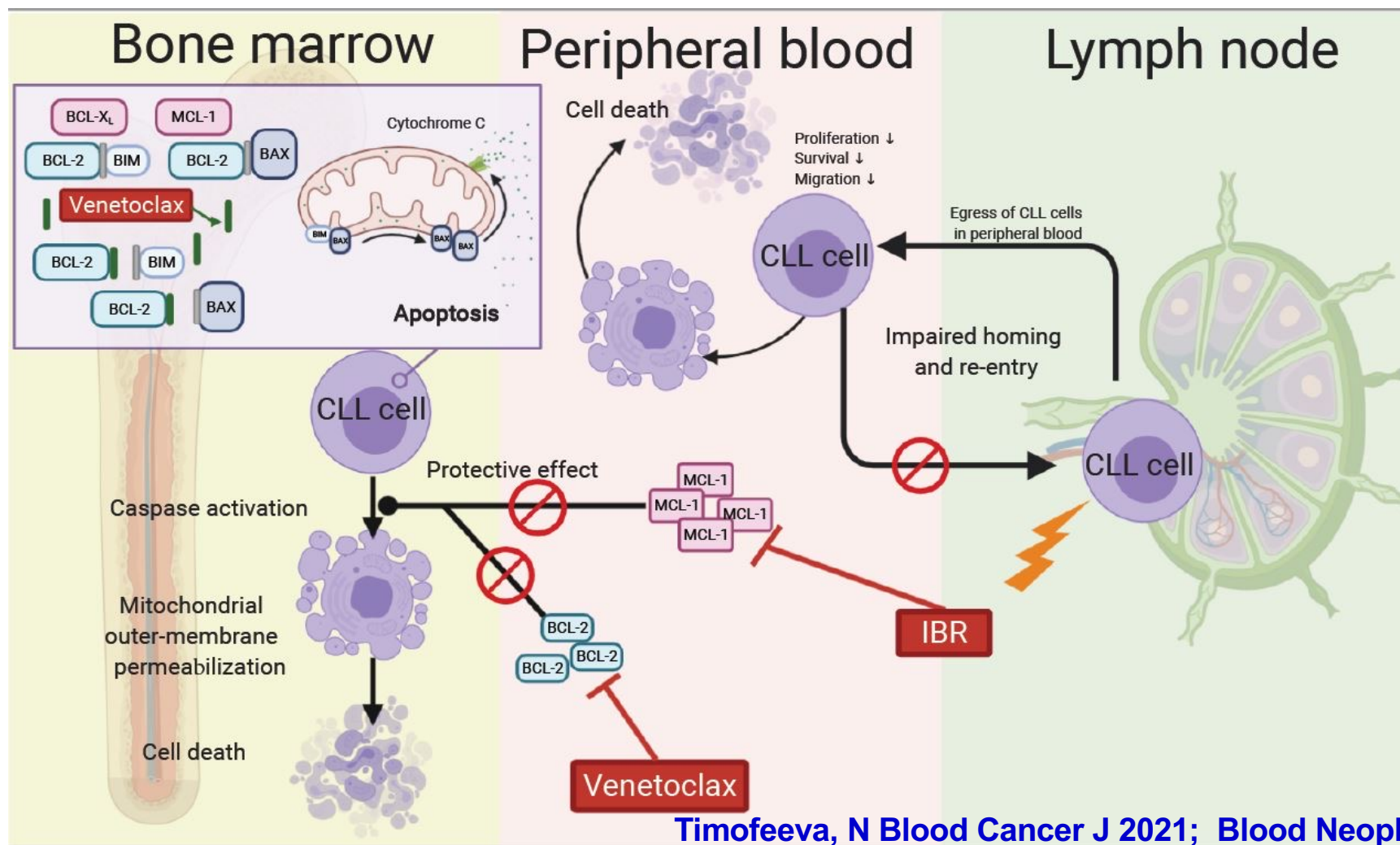


## Synergy/Synthetic Lethality of Ibrutinib and Venetoclax Combination to Cure CLL





## Ibrutinib and venetoclax interaction is more than 1 + 1





# Acknowledgements

## Lab Members

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## CLL Patients