# Predicting the Therapeutic Response of Venetoclax

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PROTEINA BUSINESS DEVELOPMENT UNIT

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OVERVIEW

# PPI PathFinder BCL2 Dx

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## Overview of BCL-2 Inhibitor Therapy

**Current Situation**

BCL-2 Inhibitors such as Venetoclax have shown to be an effective treatment for acute myeloid leukemia, achieving a 63% complete remission rate as presented at the 2023 European Hematology Association Annual Congress.

**Immediate Challenges**

1. Treatment Response Variability:
   About one in three patients show little to no response to BCL-2 inhibitor treatment*.
2. Adverse Side Effects:
   - Tumor lysis syndrome (TLS)
   - Low white blood cell counts (neutropenia)
   - Infections

**PROTEINA's Solution**

PPI PathFinder BCL2 Dx can optimize drug therapies on a per patient basis, aiding in patient stratification and risk mitigation. This methodology tackles drug response variability and assists with minimizing unwarranted side effects.

*Jonas, Brian A., et al.
"Timing of response with venetoclax combination treatment in patients with newly diagnosed acute myeloid leukemia." American journal of hematology 97.8 (2022): E299.

# PPI PathFinder BCL2 Dx

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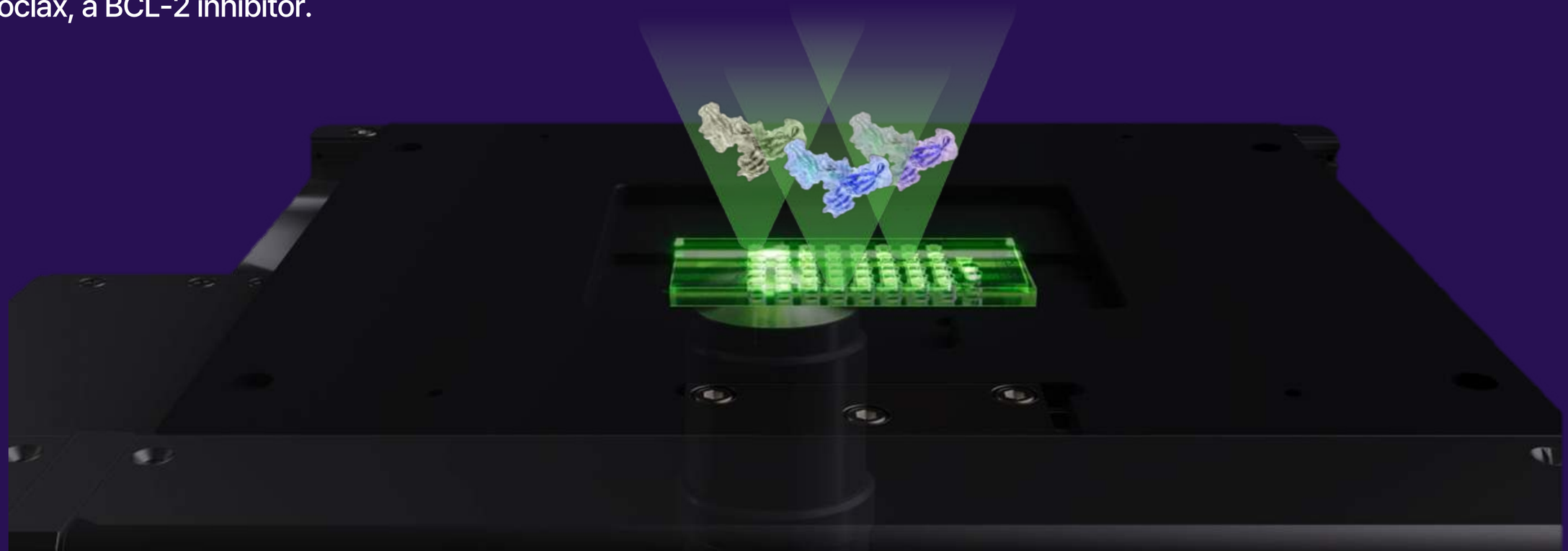
- Solution Overview

PPI PathFinder BCL2 Dx analyzes patterns in individual patient protein-protein interaction (PPI) networks, providing care providers with precision molecular diagnostics.

PROTEINA's solution focuses on analyzing the patterns of PPI networks affected by Venetoclax, a BCL-2 inhibitor.



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# PPI PathFinder BCL2 Dx

## Specifications

| PPI PathFinder BCL2 Dx | | | |
|---|---|---|---|
| | Probe Binding Assay (PBA) | Complex (CPX) | Level (Lv) |
| Targeted PPI Biomarker | BCL2-BIM<br>BCLxL-BIM<br>MCL1-BIM | BCL2-BAX<br>BCLxL-BAK<br>MCL1-BAK | BCL2<br>MCL1 |
| Sample Type Compatibility | • Bone marrow mononuclear cells (BMMCs)<br>• Peripheral blood mononuclear cells (PBMCs)<br>• Fresh frozen tissue | | |
| Minimum Input Amount of cells | • For BMMC > 500K cells | • For PMBC > 1,000K cells | |


### Personalized Therapy Prediction

PPI PathFinder BCL2 Dx predicts the effects of BCL-2 inhibitors in patient-specific cellular environments, ensuring tailored therapies for superior outcomes.

### Strategic Therapeutic Planning

By assessing the risk-benefit profile for Acute Myeloid Leukemia (AML), PPI PathFinder BCL2 Dx guides therapeutic choices and supports clinicians in designing tailored treatments for optimal patient care.

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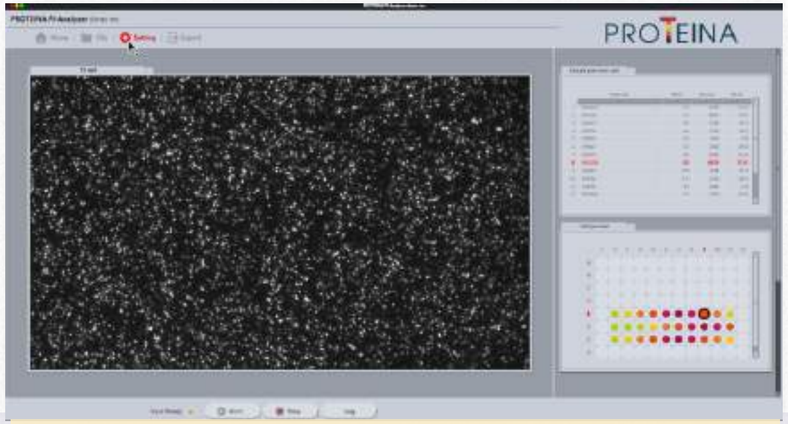
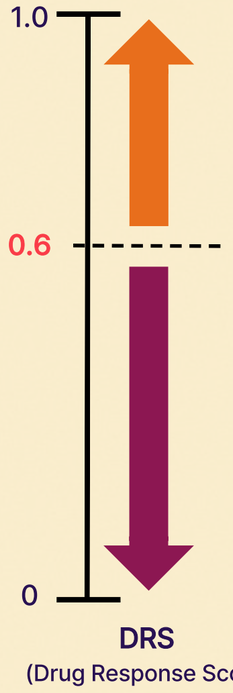
# PPI PathFinder BCL2 Dx

- Operation Procedure
  - PPI PathFinder BCL2 Dx is also available as a service.

| Quantification | Analysis | Decision |
| --- | --- | --- |
| Vital PPI biomarkers associated with BCL2 inhibitor response are quantified | PROTEINA Pi-Insight software converts proteomic bioinformation into actionable data | User decides course of treatment action using a clear "Go/No-Go" Indicator |




- **Above Threshold : Indicative of High Treatment Success**
  - → Proceed with treatment, anticipating a highly effective response
- **Below Threshold : Suggests Limited Efficacy**
  - → Hold off on treatment and consider alternative treatment options

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# PPI PathFinder BCL2 Dx

- Clinical Benefits

## 01

### Personalized Therapy Prediction

Implement precision molecular diagnostics by analyzing individual patient PPI network patterns to identify subgroups most likely to benefit from developing treatment strategies.

## 02

### Benefit-Risk Decision-Making Support

Facilitate informed decision-making on the administration of BCL-2 inhibitor therapy, reducing unnecessary risks for patients who are predicted to not respond effectively.

## 03

### Innovative Insight from PPI

Uncover new insights through comprehensive protein-protein interaction molecular diagnostics, surpassing traditional genetic and proteomic analysis.

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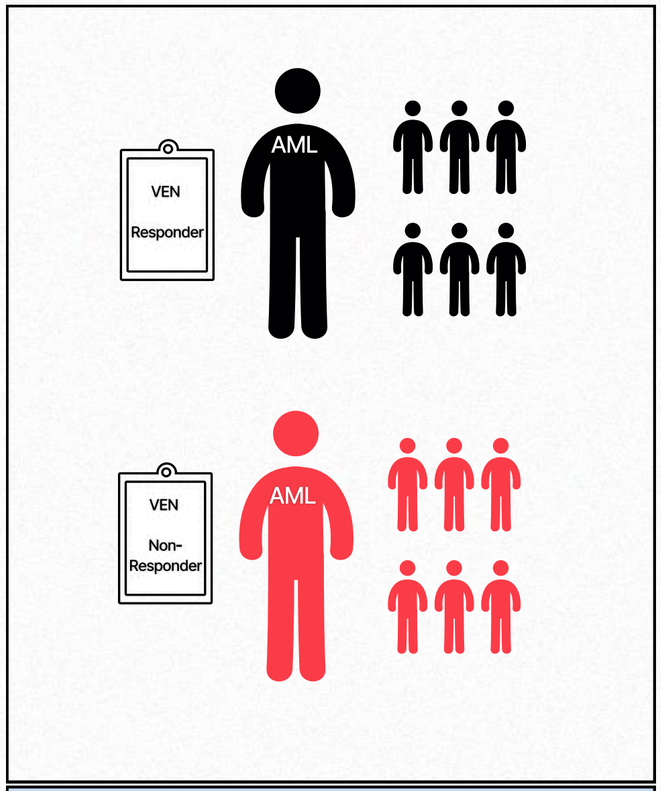
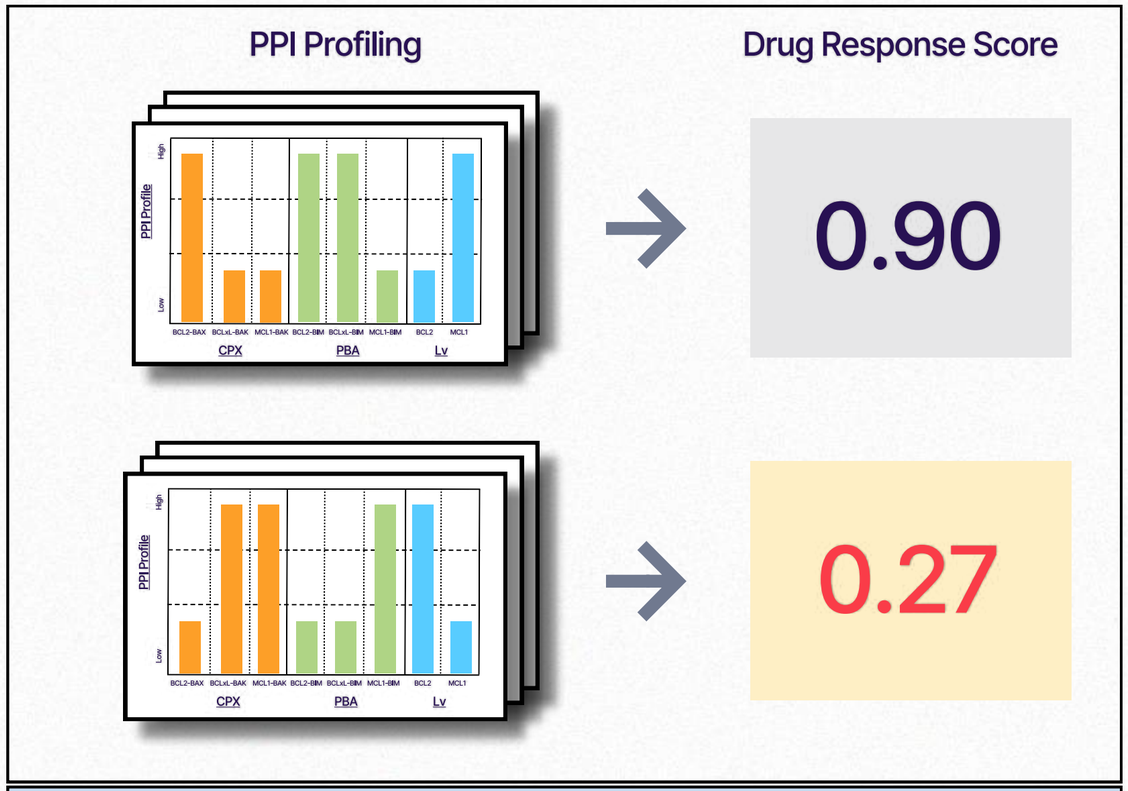
# PPI PathFinder BCL2 Dx

- Case 1: PPI profiling of samples with known Venetoclax response




Diagnostic samples from AML patients who responded or did not respond to Venetoclax.

Samples Sent to PROTEINA




Analysis of PPI Profiles in Venetoclax Responder and Non-Responder Groups

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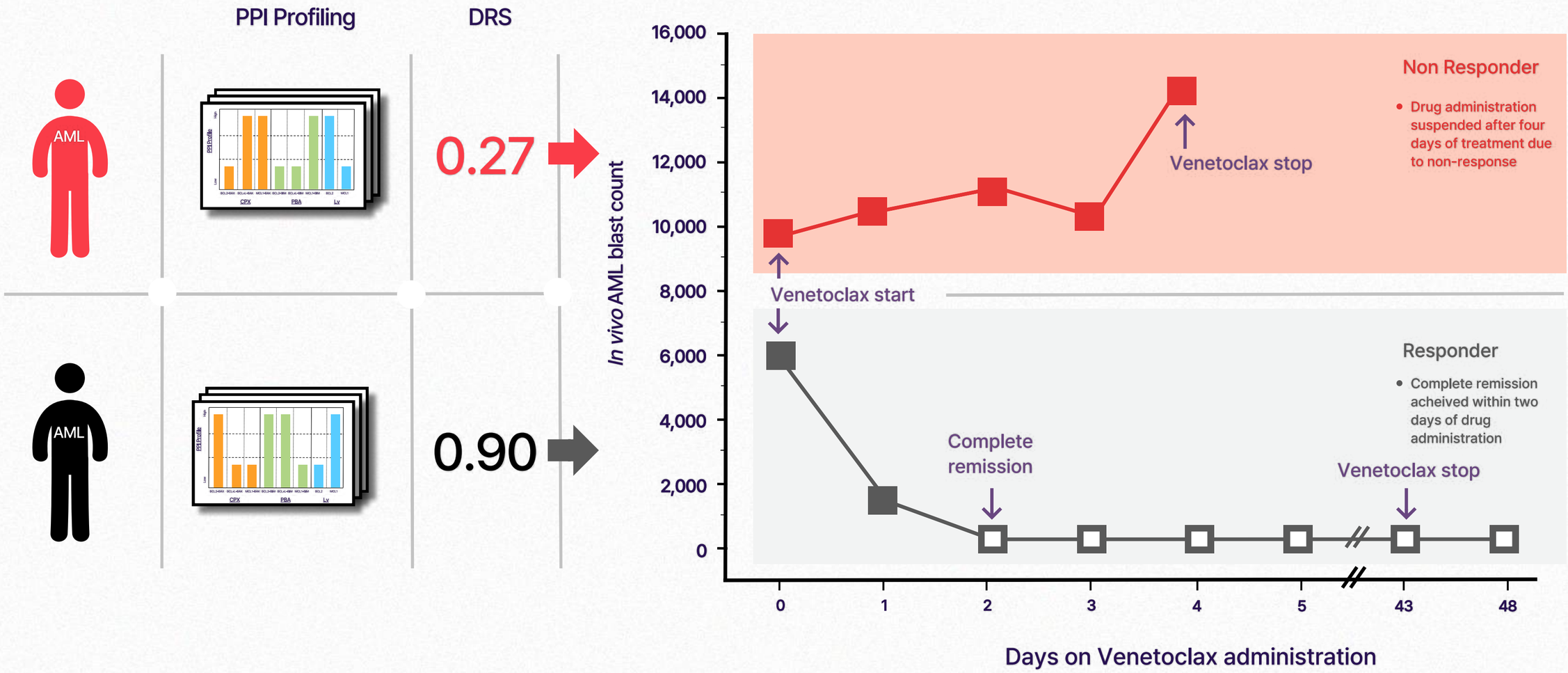
# PPI PathFinder BCL2 Dx

- Clinical Use ( Case #1 )



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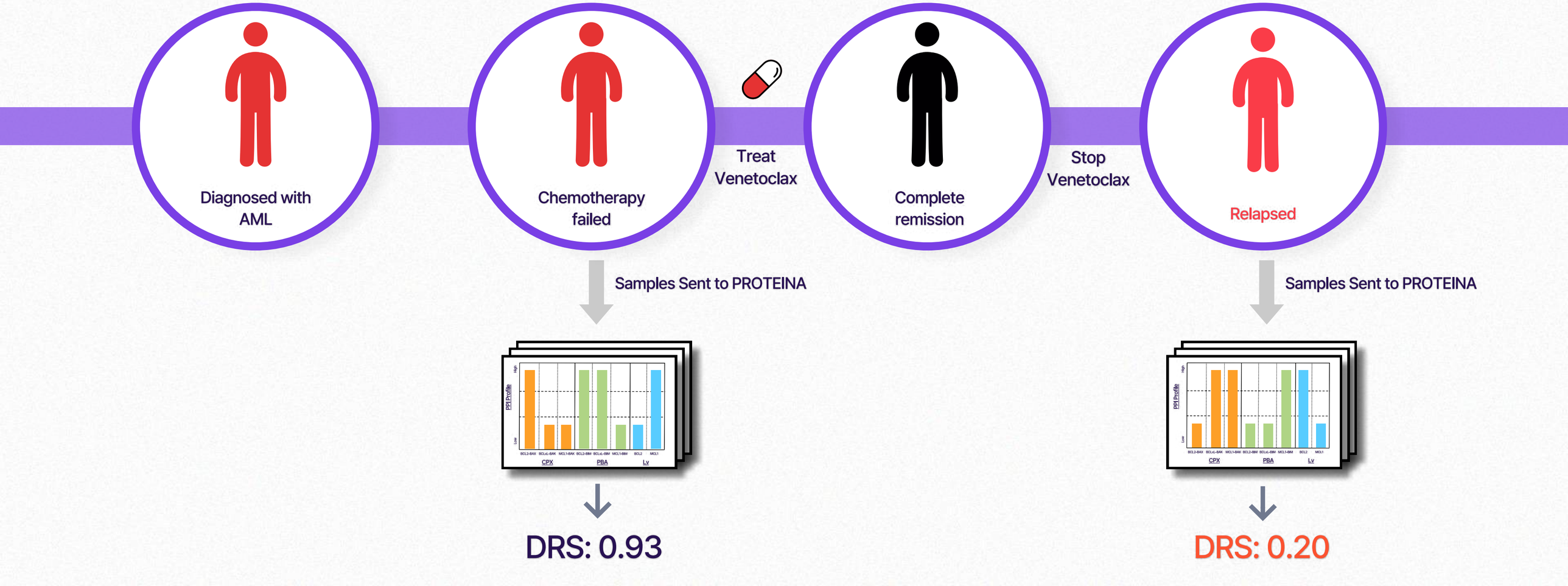
# PPI PathFinder BCL2 Dx

- Case 2: Tracking PPI Profile to study patient responses to Venetoclax



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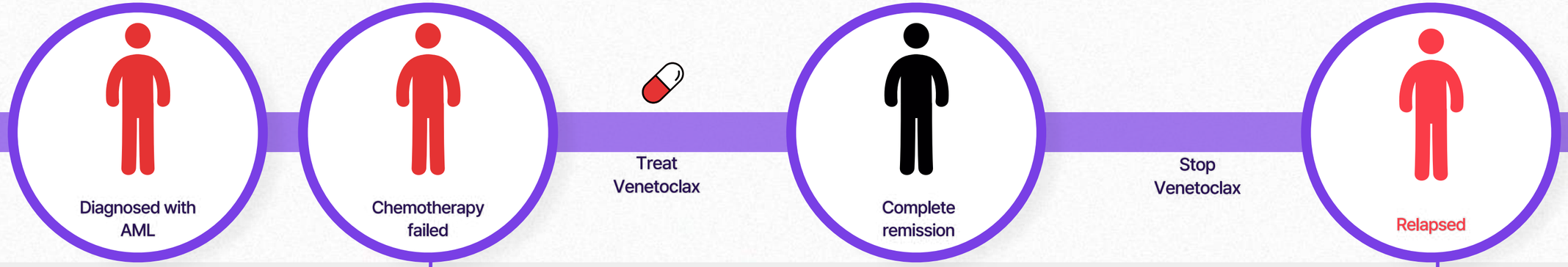
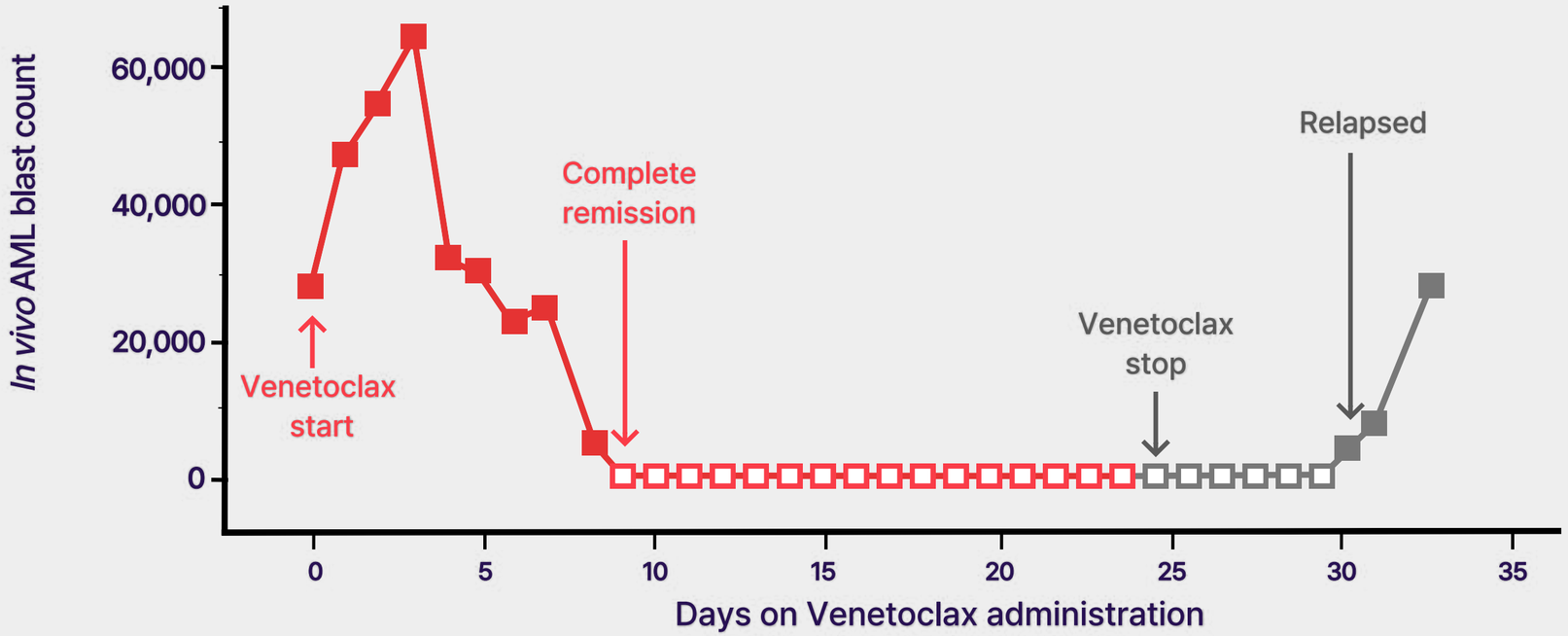
# PPI PathFinder BCL2 Dx

- Clinical Use ( Case #2 )




DRS : 0.93

DRS : 0.20



# 02.

# Collaboration

- Objectives
- Participation Process

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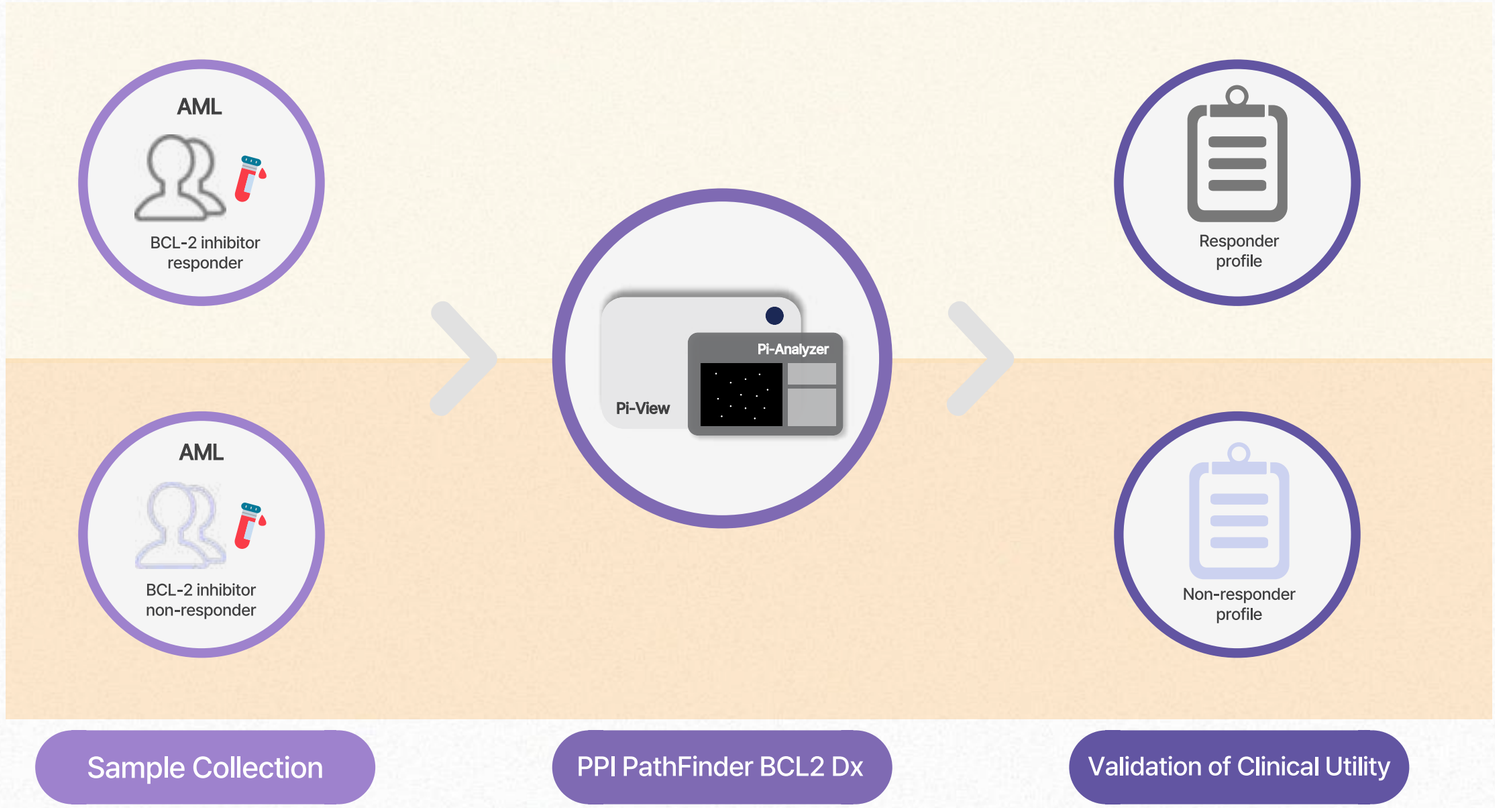
# Research Collaboration

- Objectives

1. The current lack of accurate methods to predict BCL2 inhibitor drug response highlights the critical need for our service.
2. A potential collaboration aims to clinically validate the prediction accuracy of PPI PathFinder BCL2 Dx, further establish our offering in the market, and build usage experience.



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# Research Collaboration

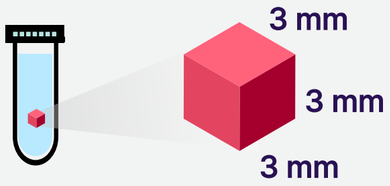
## 01. Sample Preparation

### Bone marrow mononuclear cells (BMMCs)

- Both preserved media and pellet forms are acceptable.
- Cell counts required > 5 x $10^5$

### Peripheral blood mononuclear cells (PBMCs)

- Both preserved media and pellet forms are acceptable.
- Cell counts required > 1 x $10^6$




### Fresh frozen tissue

- Recommended sample amount : 10-20mg
- Recommended tumor sample volume: ≥30%
- Minimum required tissue size: 27 $mm^3$ cube

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# Research Collaboration

## 02. Sample Packaging

▶ BMMCs, PBMCs, Fresh Frozen Tissue

- Pack the samples in a styrofoam box with dry ice for shipping.
- Please fill the box completely with dry ice to ensure temperature maintenance.

## 03. Sample shipping

▶ Shipping Address

- Suite 1301 Ace Techno Tower 8, 11 Digital-ro 33-gil, Guro-gu, Seoul, Korea

  Tel: +82 2 6959-9489

# THANK YOU.