



دانشگاه علوم پزشکی کرمان

Presented by :  
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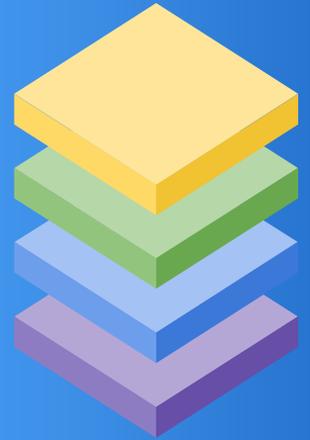
Advisor :  
Dr Roohollah Mirzaee

# Use of Deferasirox, an iron chelator, to overcome Imatinib resistance of Chronic Myeloid Leukemia Cells



# Korean Journal Intern Medicine

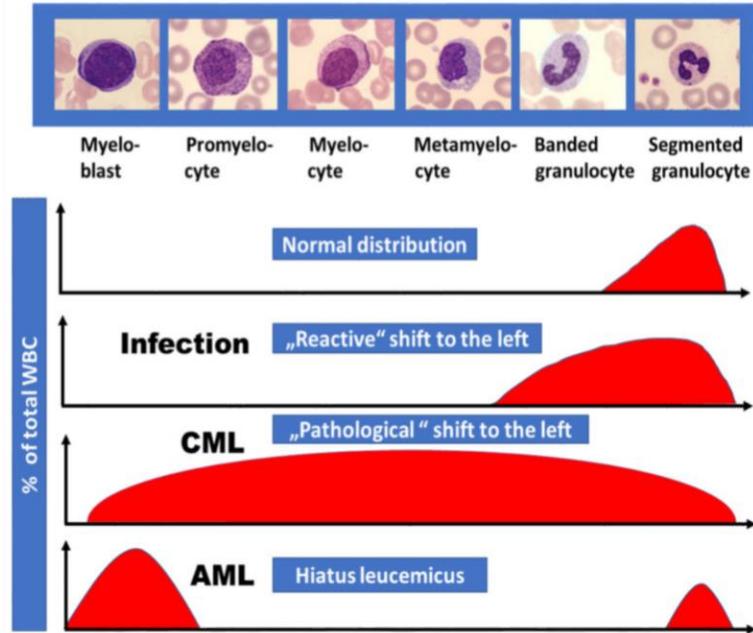
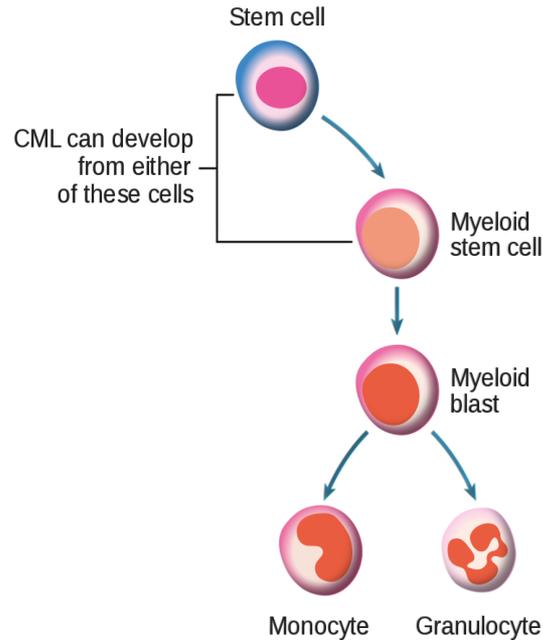
Medicine



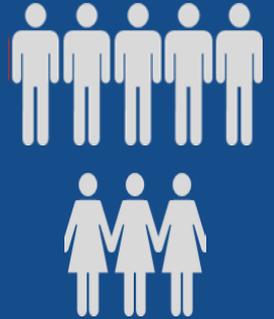
# INTRODUCTION

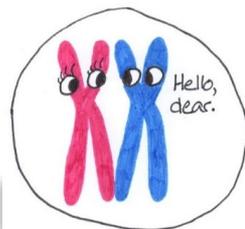


# Chronic Myeloid Leukemia :

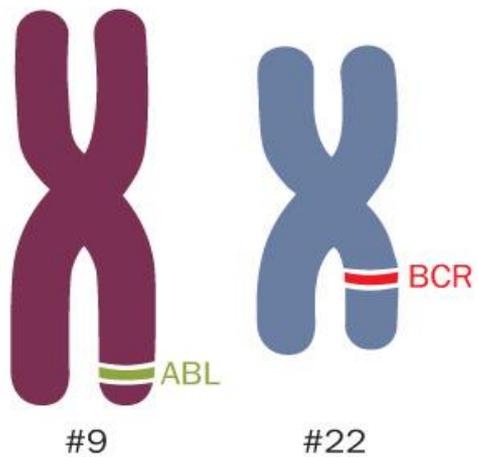


# Prevalence

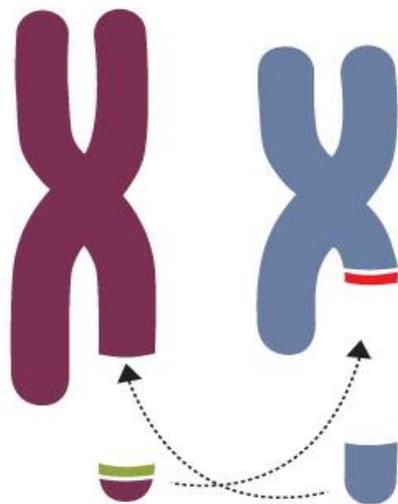




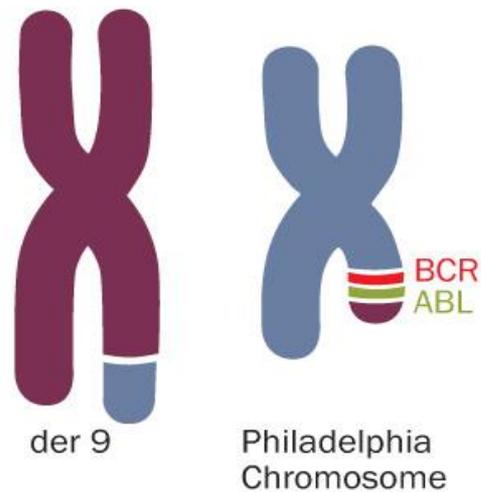
Before translocation

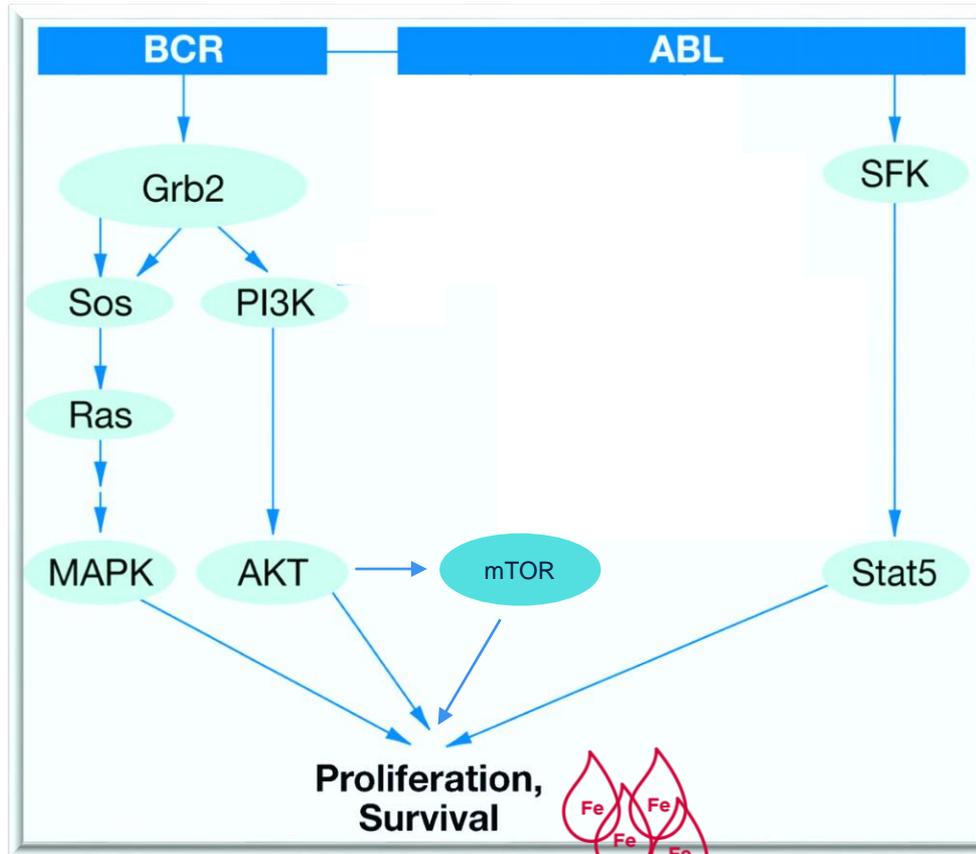


During translocation



After translocation





**TREATMENTS**





## Chemotherapy



- ✓ Busulfan
- ✓ Hydroxyurea



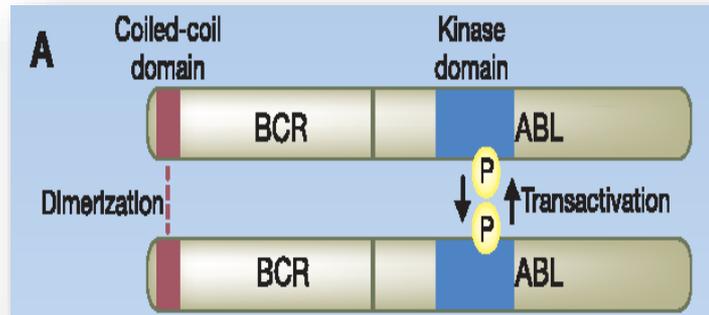
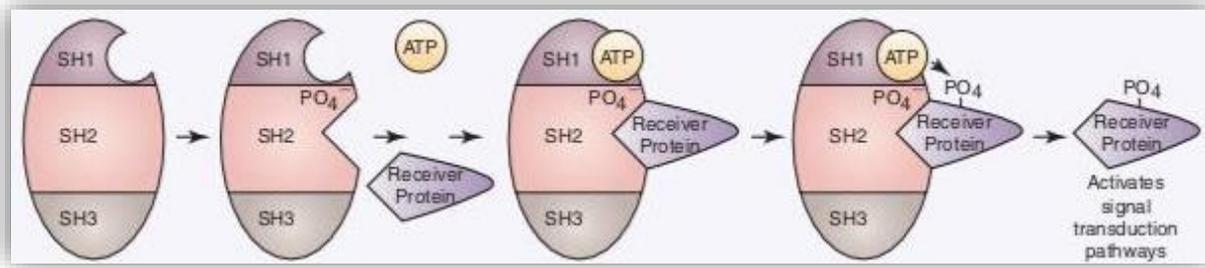
## HCST



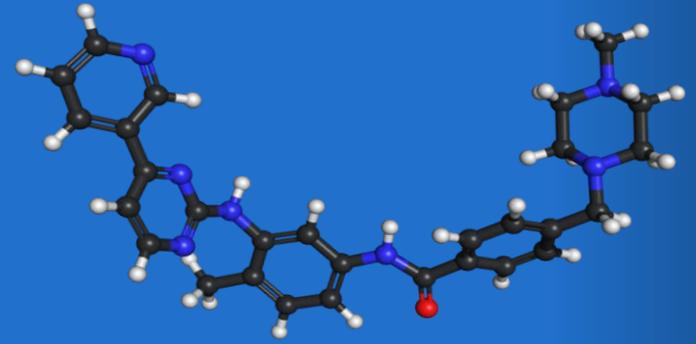
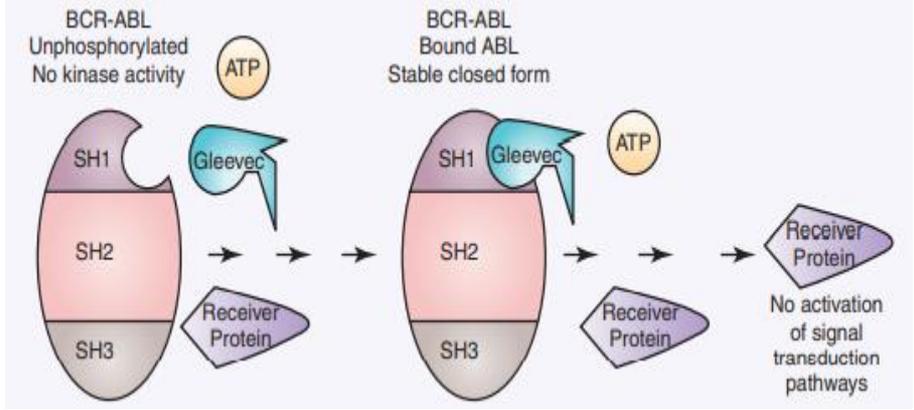
- ✓ Death caused by transplant
- ✓ Graft-versus-host disease



# ABL BCR-ABL



# Imatinib

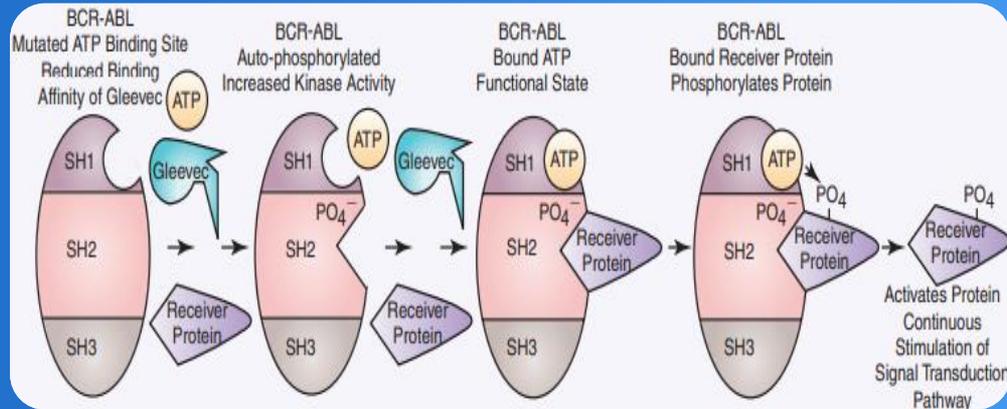




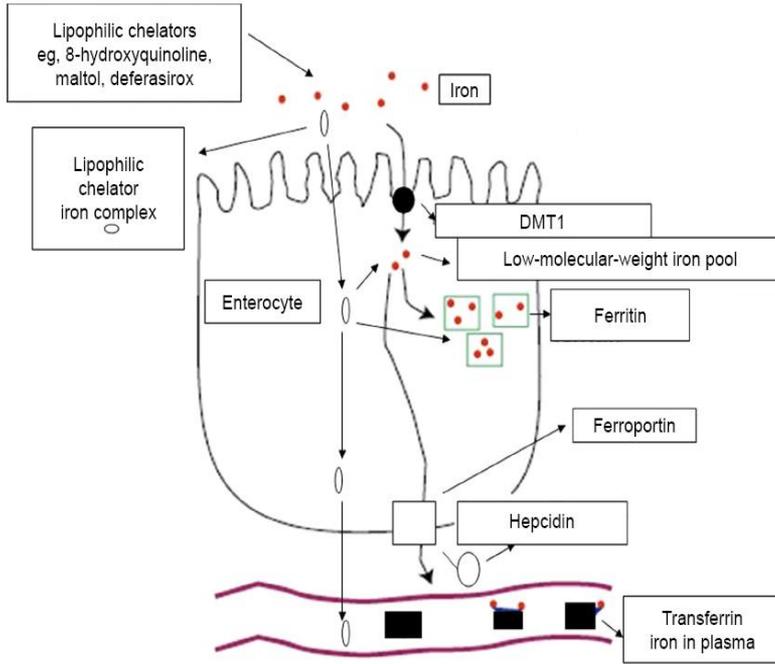
# Imatinib resistance:

Point mutations in the BCR-ABL kinase domain :

➤ **Mutation at the ATP binding site** ➔ **T315I**



# Deferasirox



# Deferasirox

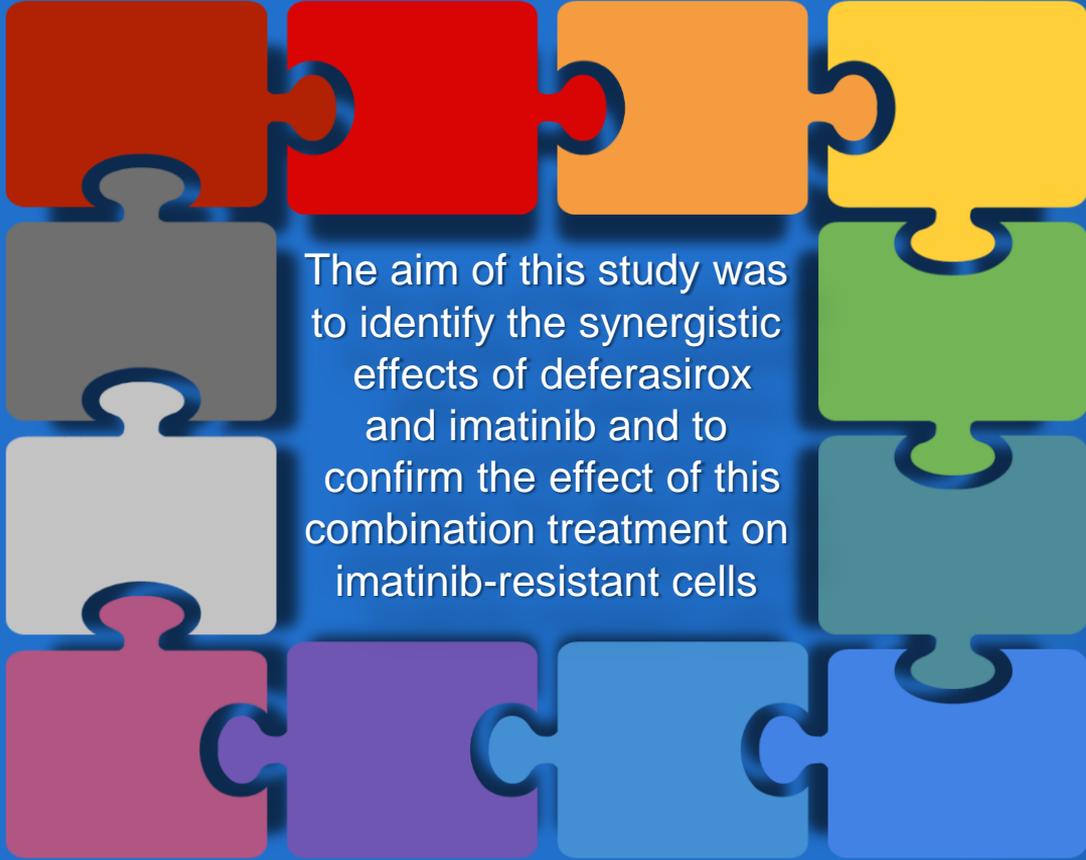


mTOR

WNT

NFKB

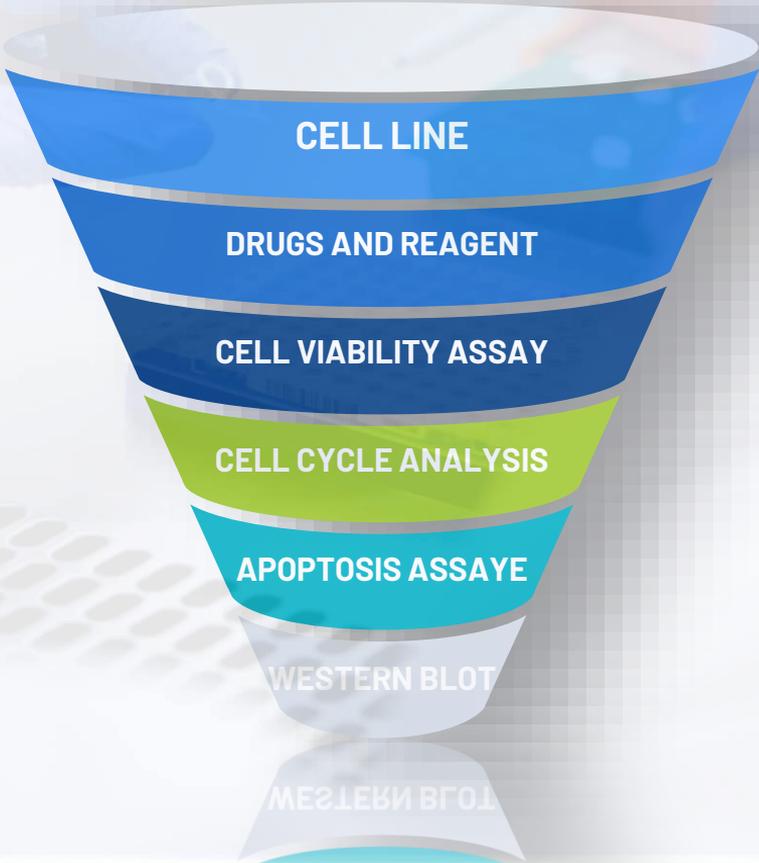




The aim of this study was to identify the synergistic effects of deferasirox and imatinib and to confirm the effect of this combination treatment on imatinib-resistant cells

# METHODS





CELL LINE

DRUGS AND REAGENT

CELL VIABILITY ASSAY

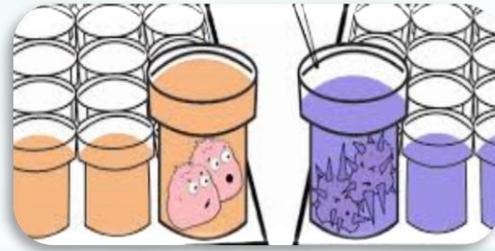
CELL CYCLE ANALYSIS

APOPTOSIS ASSAYE

WESTERN BLOT

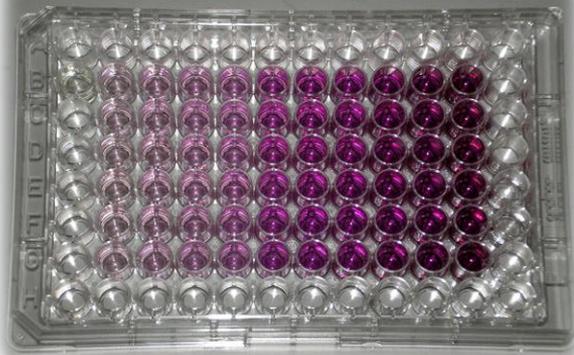
WESTERN BLOT

# XTT

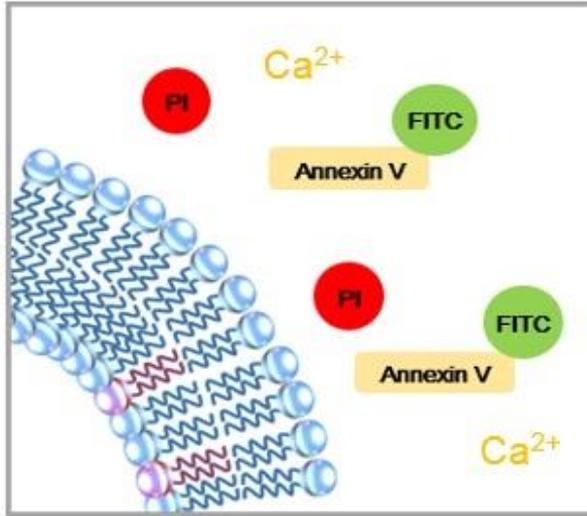


MTT

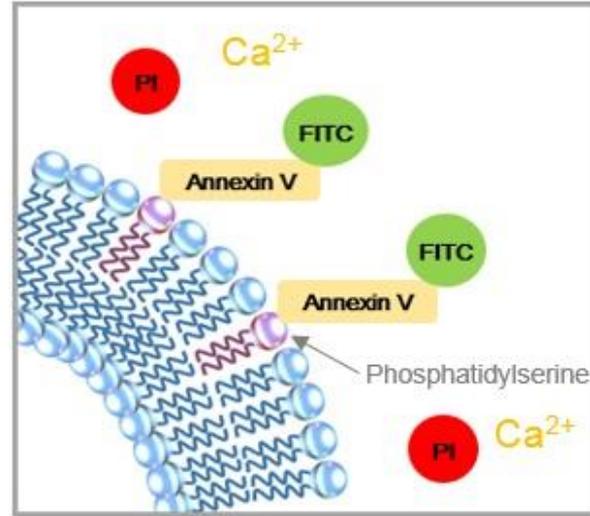
XTT



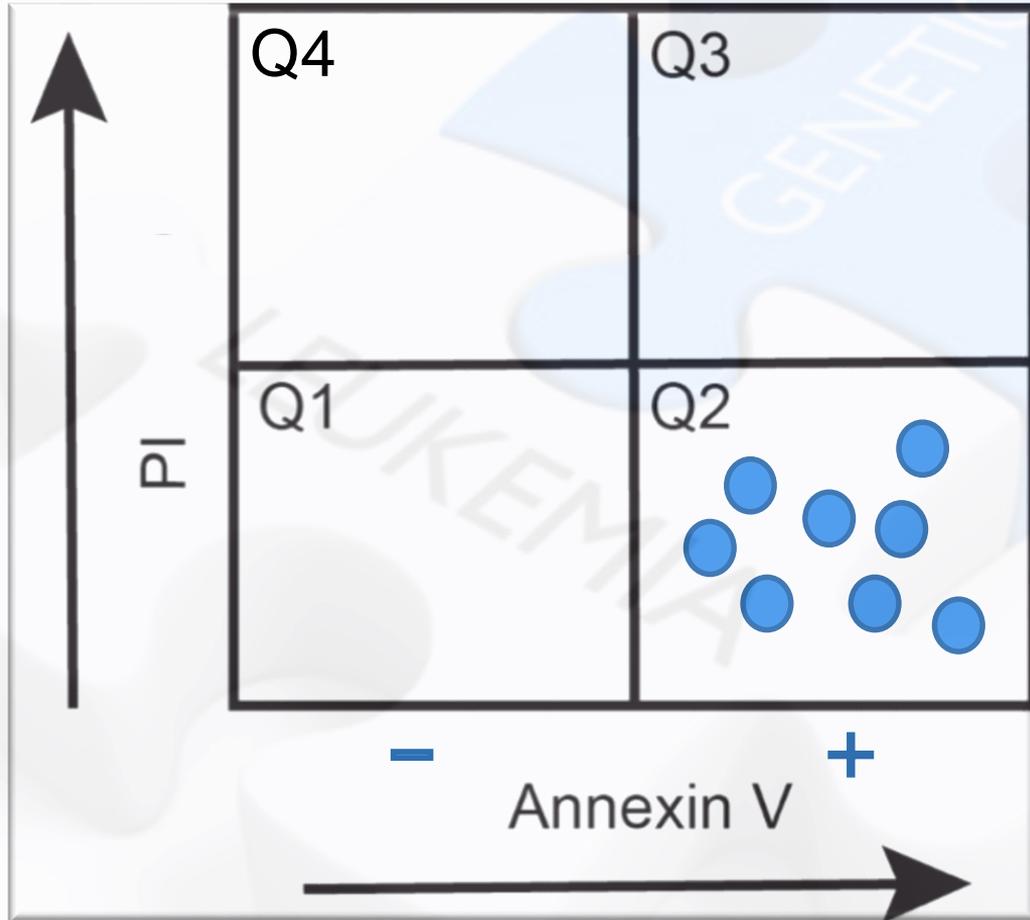
# APOPTOSIS ASSAYE



Normal cell



Apoptotic cell



**RESULT**



# Results

proliferation



Cell cycle analysis



P

C



Western blot

W

A

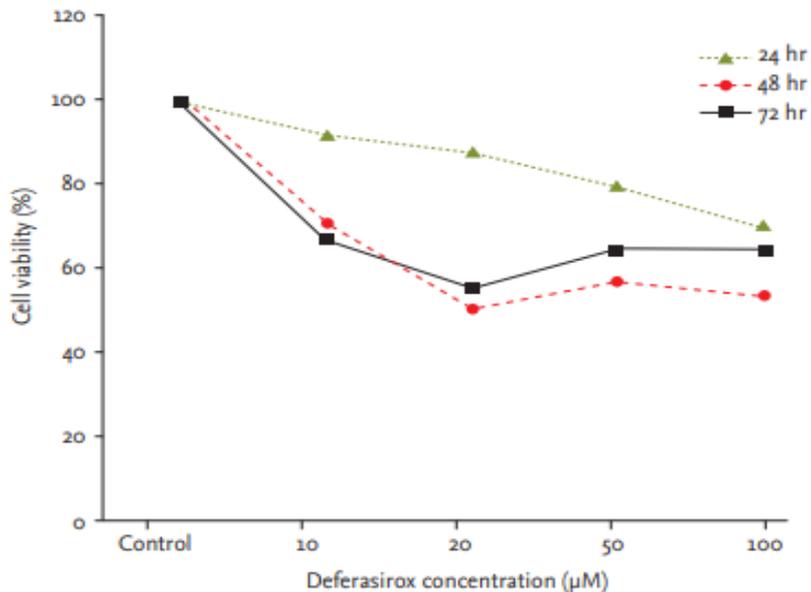


Apoptosis

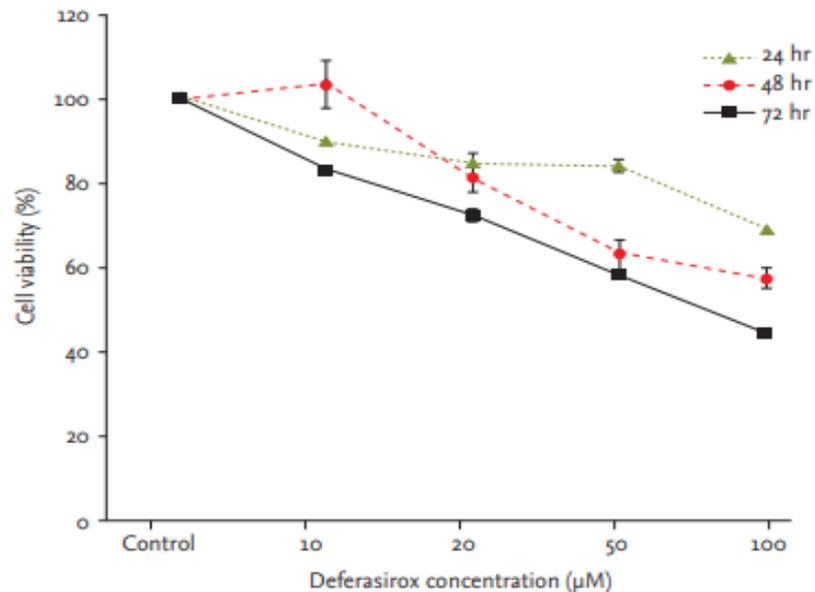


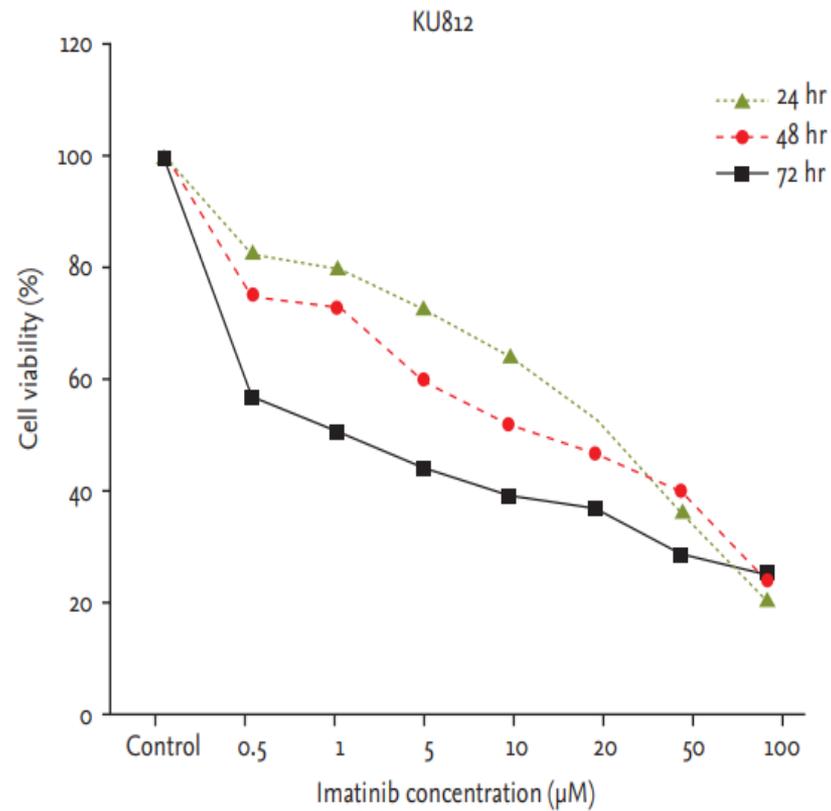
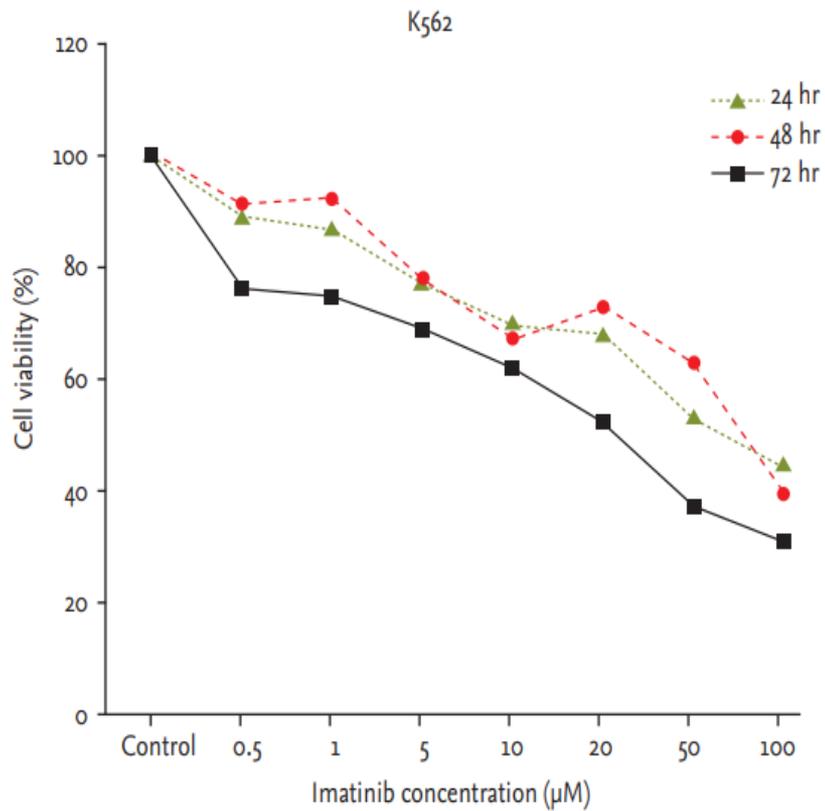
# Proliferation

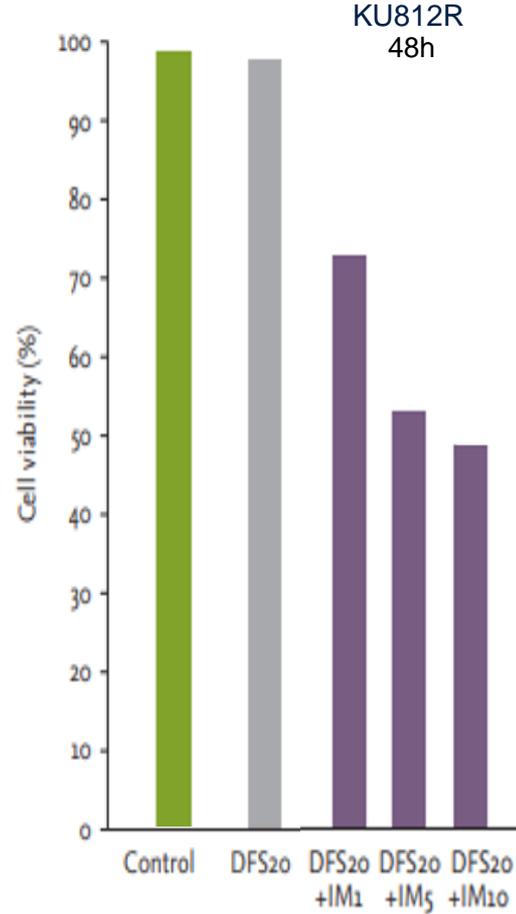
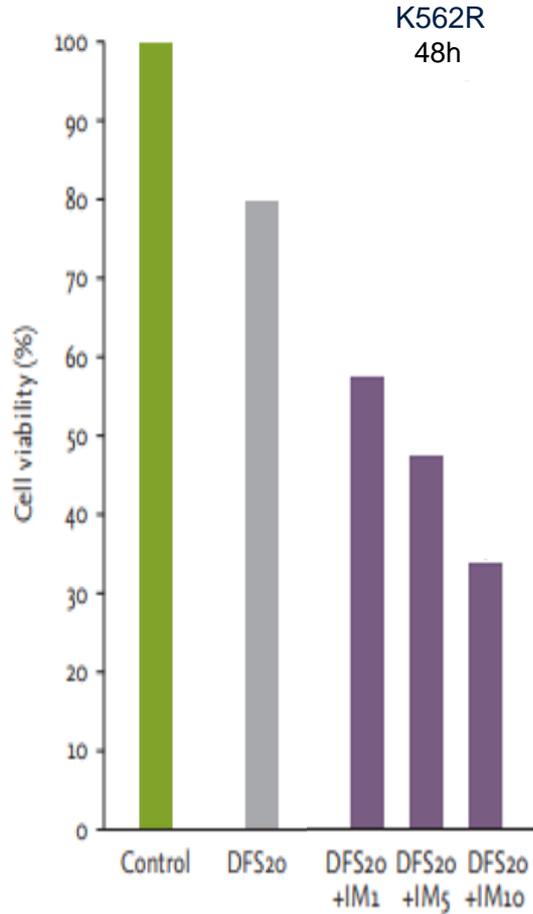
K562R



KU812R





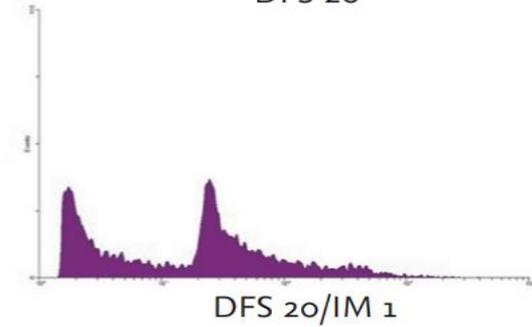
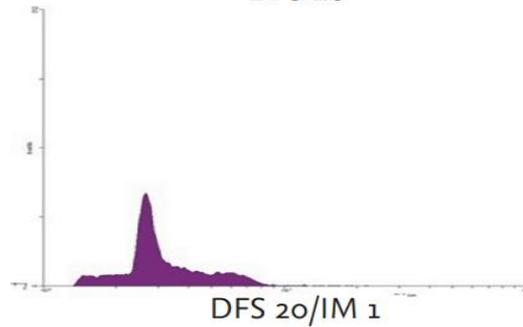
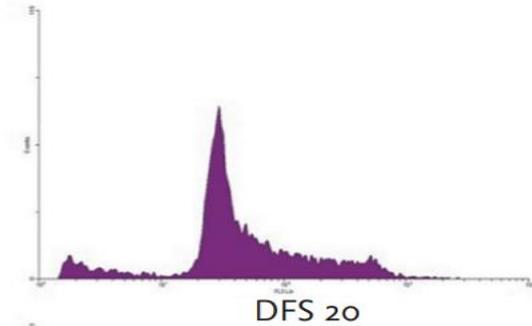
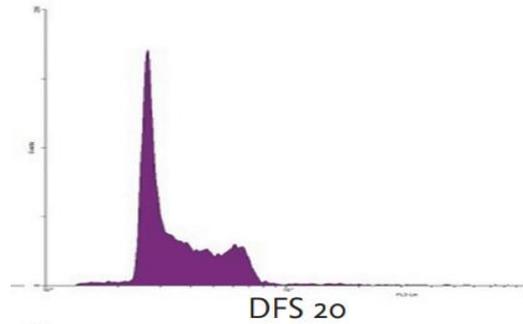
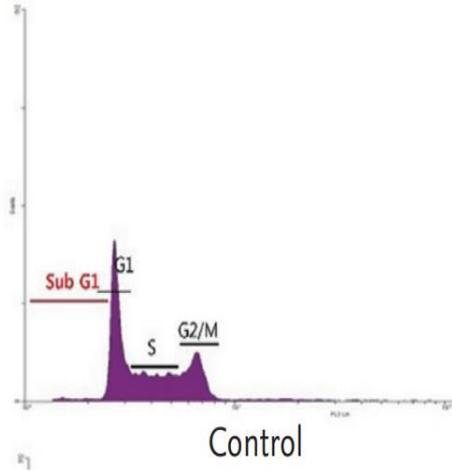


# CELL CYCLE ANALYSIS

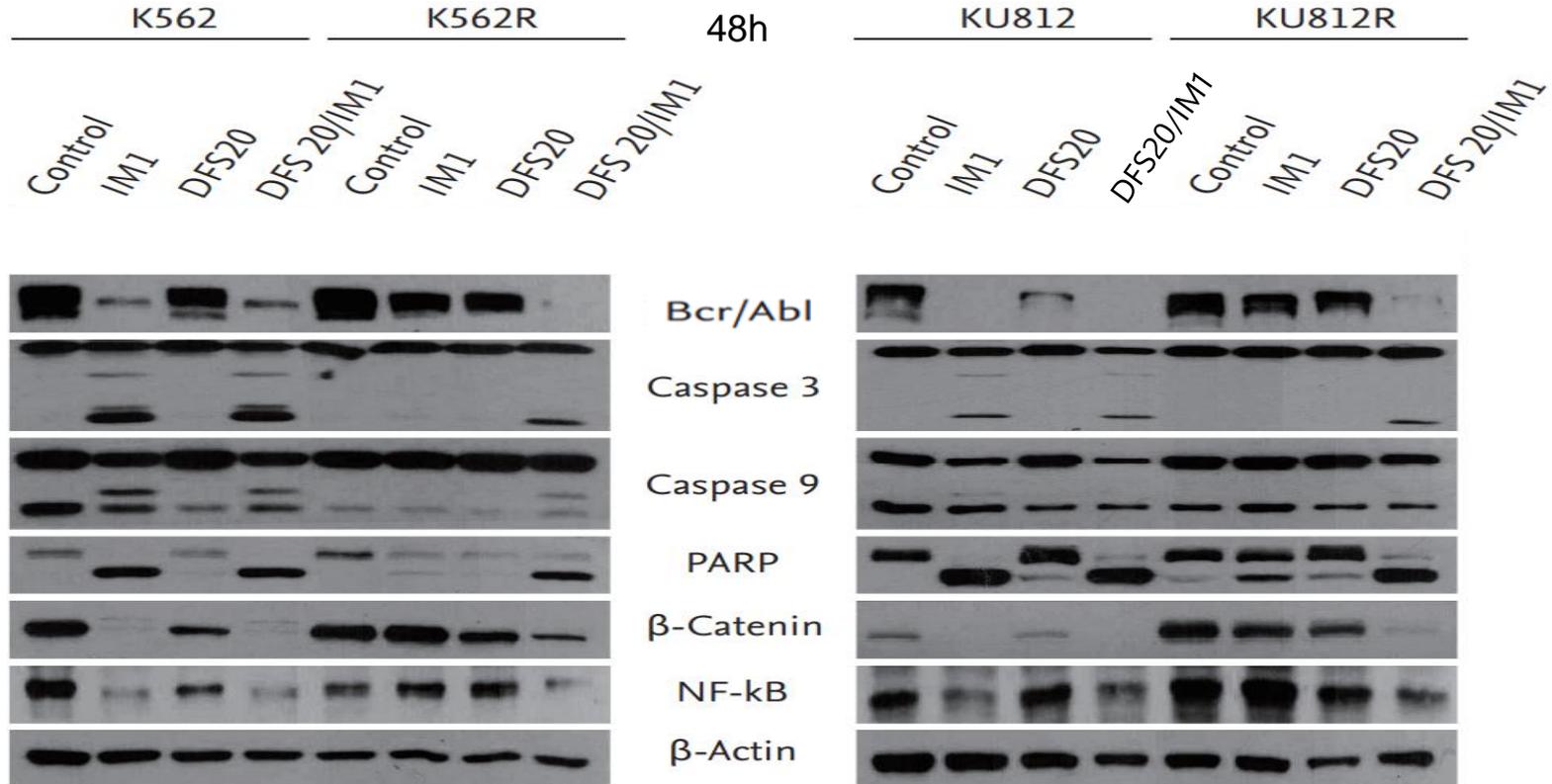


K562R  
48h

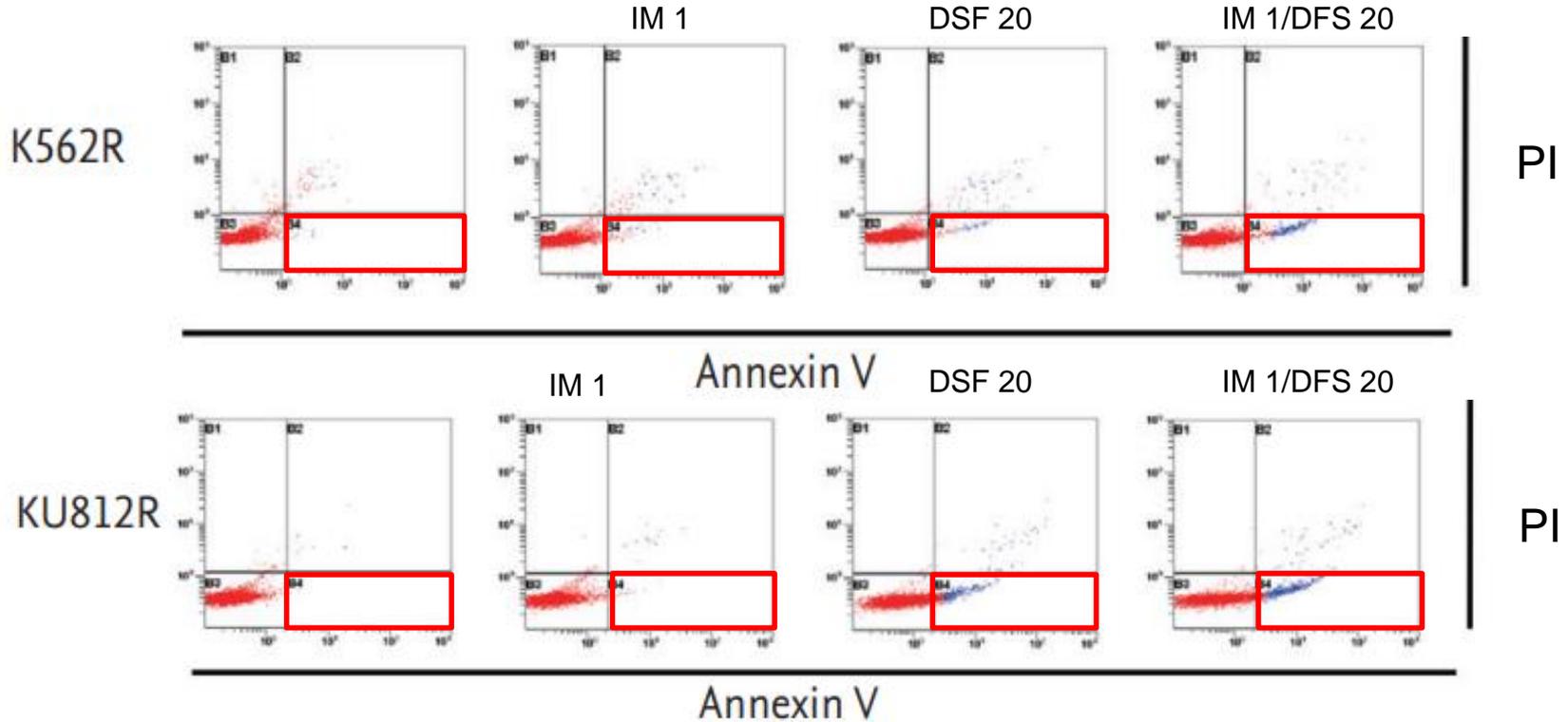
KU812R  
48h



# WESTERN BLOT

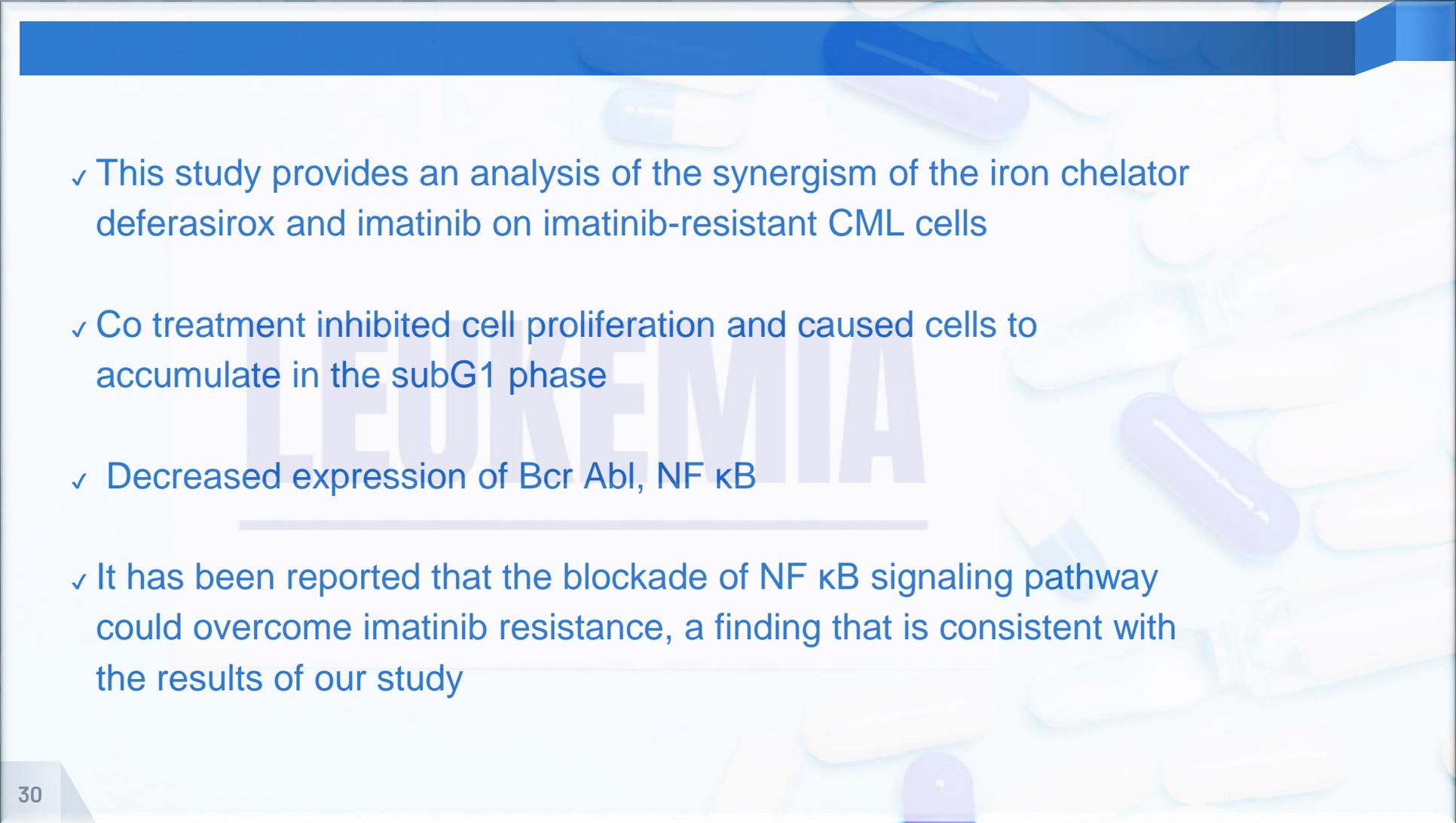


# APOPTOSIS



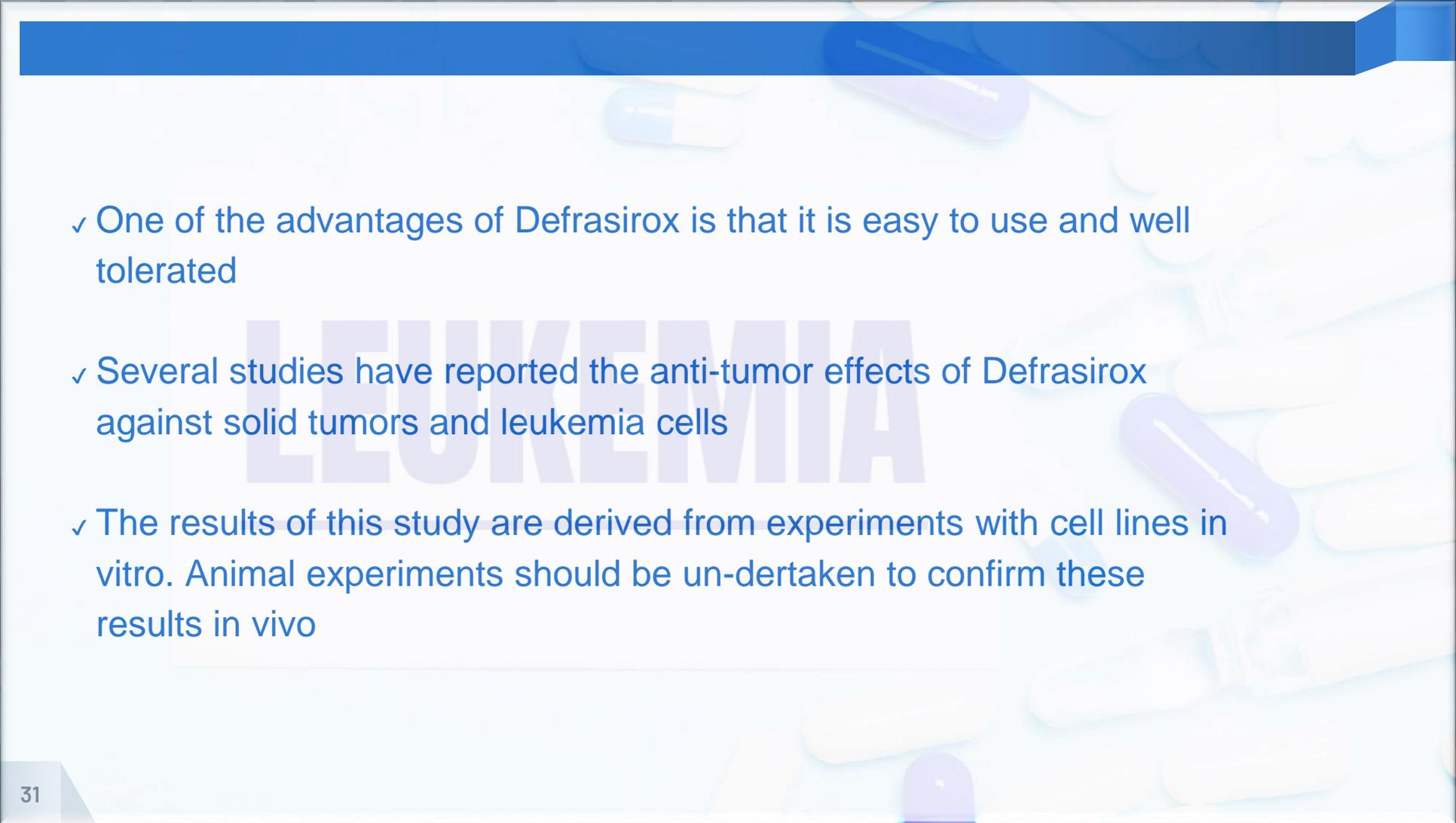
# DISCUSSION



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- ✓ This study provides an analysis of the synergism of the iron chelator deferasirox and imatinib on imatinib-resistant CML cells
  - ✓ Co treatment inhibited cell proliferation and caused cells to accumulate in the subG1 phase
  - ✓ Decreased expression of Bcr Abl, NF  $\kappa$ B

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  - ✓ It has been reported that the blockade of NF  $\kappa$ B signaling pathway could overcome imatinib resistance, a finding that is consistent with the results of our study

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- ✓ One of the advantages of Defrasirox is that it is easy to use and well tolerated
  - ✓ Several studies have reported the anti-tumor effects of Defrasirox against solid tumors and leukemia cells
  - ✓ The results of this study are derived from experiments with cell lines in vitro. Animal experiments should be undertaken to confirm these results in vivo



행운을 빕니다