Drug Development:

Nilotinib

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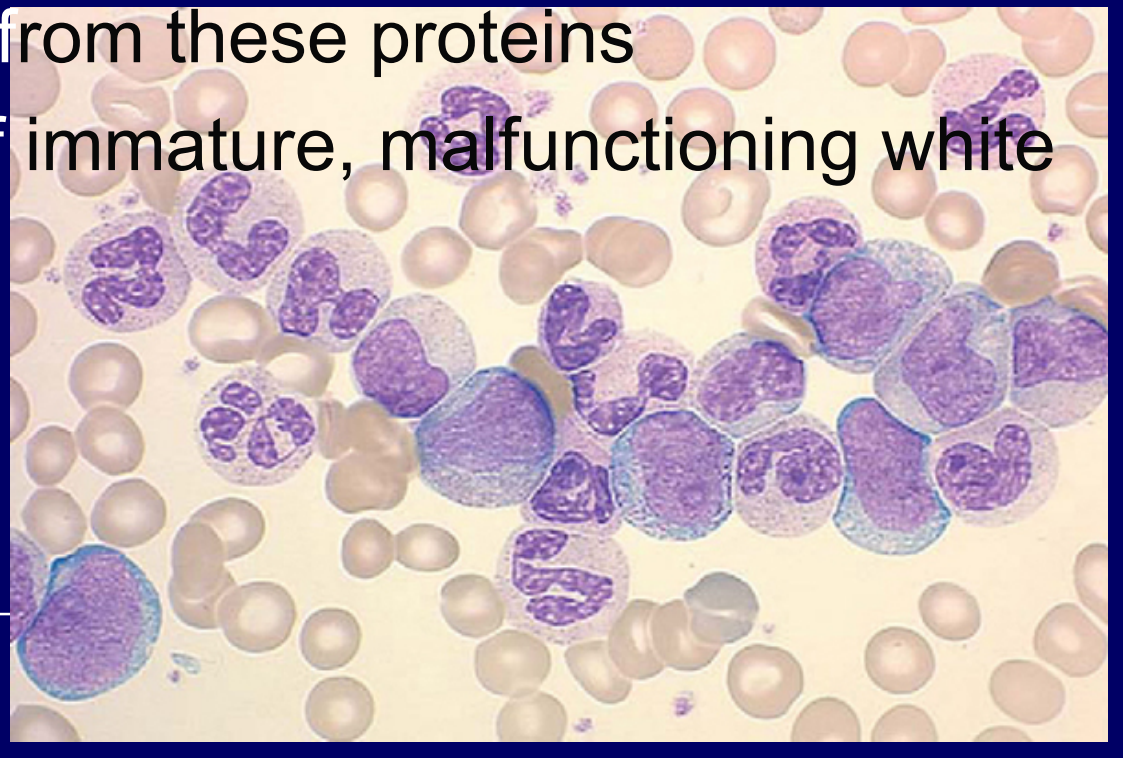
Introduction

- a tyrosine kinase inhibitor used targeted therapy for blood cancer , Chronic myelocytic leukemia (CML)
- Bcr-Abl protein
- Blocks the signals from these proteins
- Stop overgrowth of immature, malfunctioning white blood cells

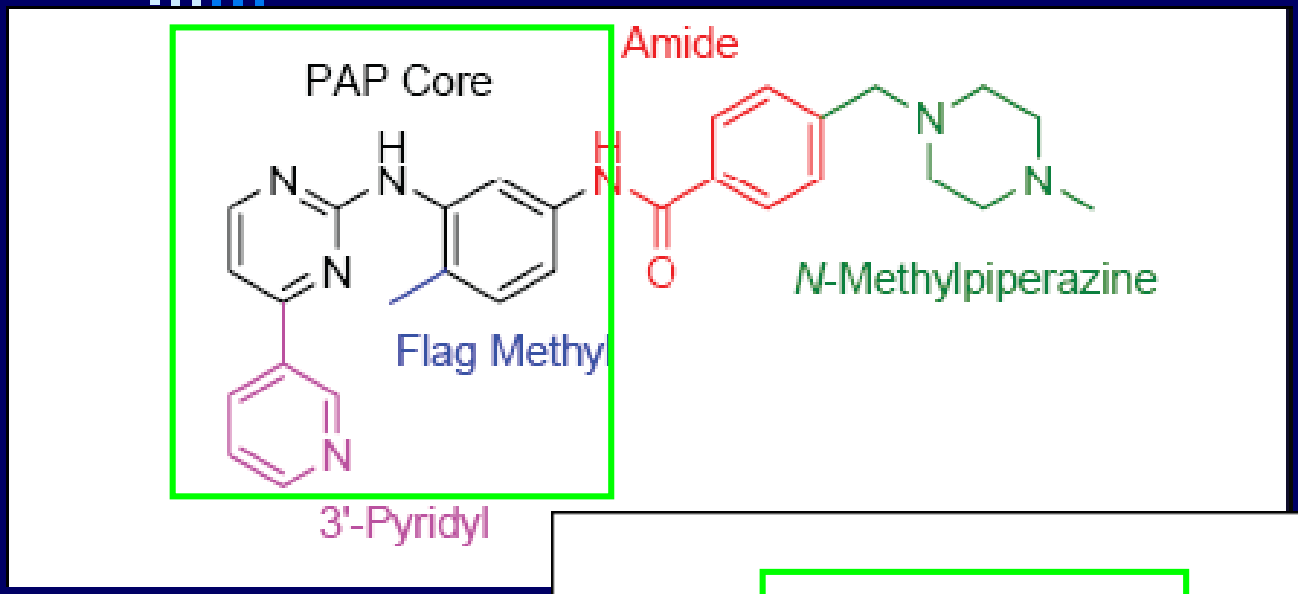


Lead Compound Discovery

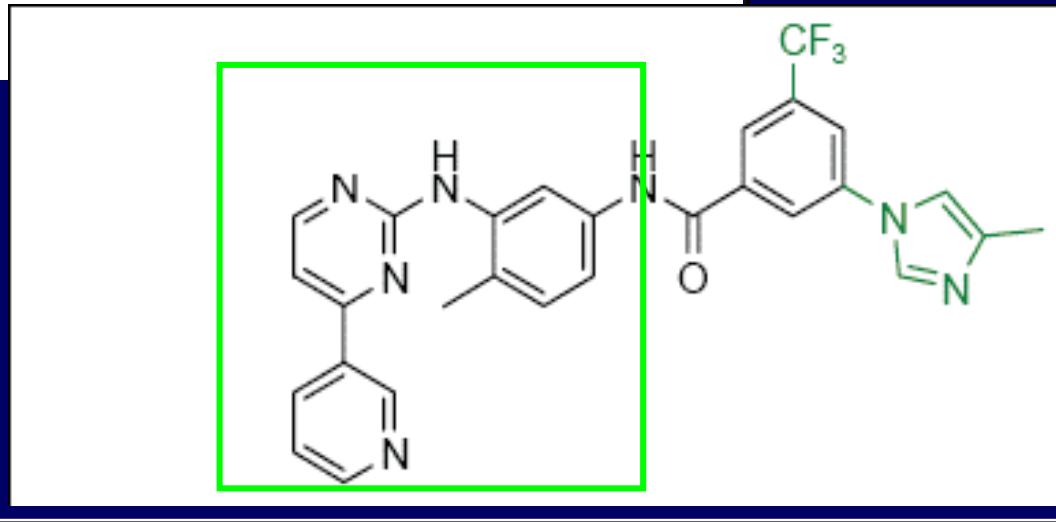
Imatinib

- first-generation drug
- inhibit the Bcr-Abl protein to avoid excess white blood cells formation
- more and more people had resistant
- improving the target specificity of Imatinib

Molecular Modification

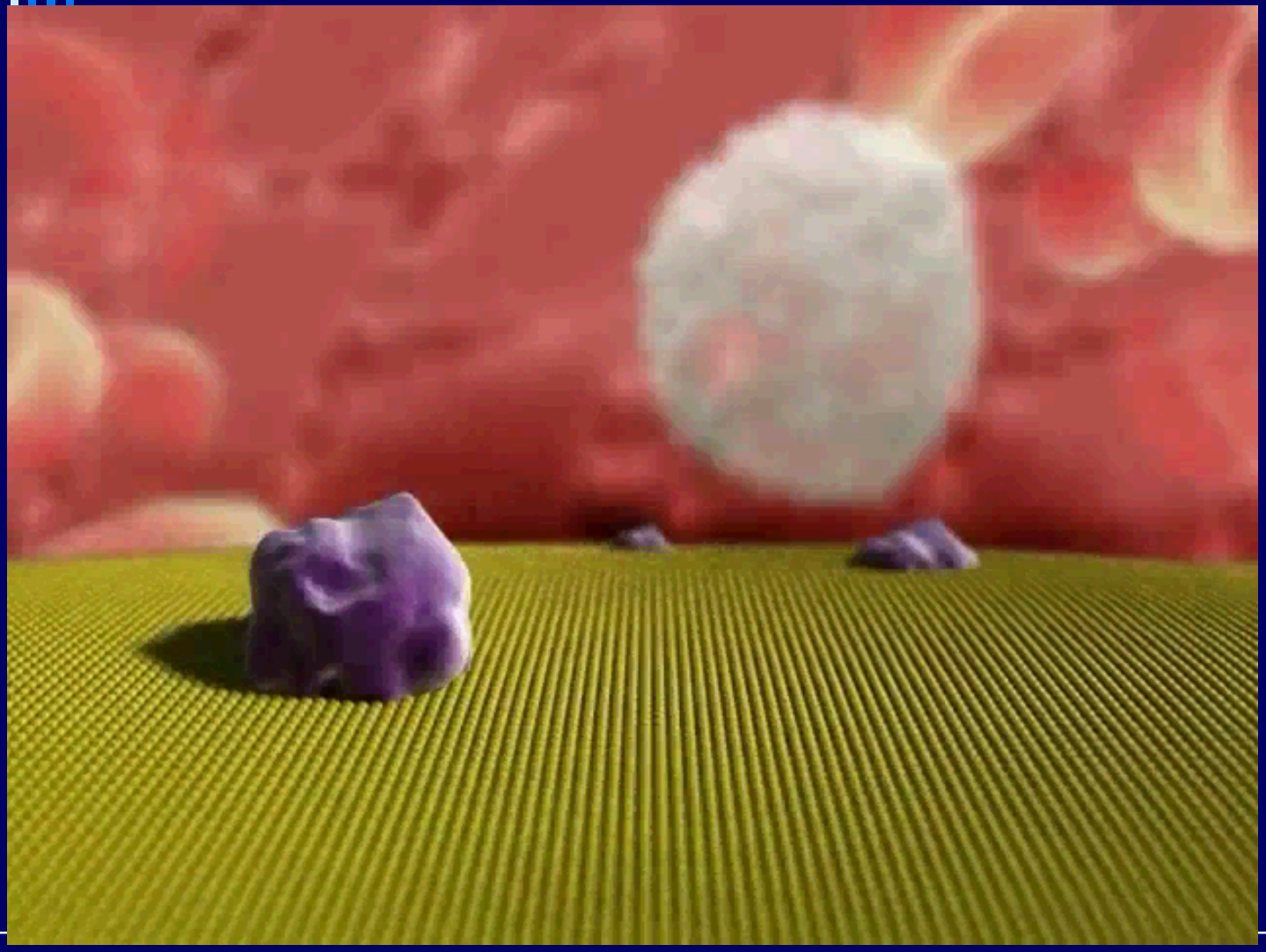


Imatinib



Nilotinib

Working Principle



- http://www.youtube.com/watch?v=7ZMVQ1Vbb7Y&NR=1

Safety Tests and Human Trials

	Phase I	Phase II
Period	from May 25, 2004 to May 4,2005	After the study of Phase **I**
Number of people	119 patients (with resistant to imatinib)	316 chronic-phase patients
Conclusion (what the study can show?)	1. The posterior probability of dose-limiting toxicity was 0.30.	1.an acceptable tolerability profile with a low incidence of vents related to fluid retention 2. no non-hematologic cross-intolerance between imatinib and nilotinib.

Formulation Development

- white/slightly yellowish powder
- Tasigna (nilotinib) capsules
- for oral use
- contain 150 mg or 200 mg nilotinib base
- FDA recommend that 400 mg orally and twice daily (12 hours apart)

Approval for Marketing

- Food and Drug Administration (FDA) approved
- In USA:

  June 2010
- In Hong Kong:

  Hospital Authority still considering