# Table of contents

## Chapter 1
### Introduction
1.1 Background 7  
1.2 Drugs used in this study 17  
1.3 Aim of the study 18

## Chapter 2
### Methods and materials 29
2.1 Reagents 29  
2.2 Cellular lines and primary cells cultures 29  
2.3 Cell proliferation test 31  
2.4 Agar clonogenic test (semisolid medium) 31  
2.5 Clonogenic test of human progenitors (semisolid medium) 32  
2.6 Cell cycle analysis 32  
2.7 Apoptosis evaluation 33  
2.8 Protein extraction and SDS page western blotting 33  
2.9 Mouse models 34  
2.9.1 SCID Ba/F3 JAK2 V617F –Luc+ mouse model 34  
2.9.2 C57Bl6/J JAK2 V617F KI mouse model 34  
2.10 Statistical methods 35

## Chapter 3
### Results
3.1 Impairment of cell viability 39  
3.2 Effect of the inhibitors on the clonogenic growth potential in agar 40  
3.3 Effect of the inhibitors on cell cycle in set2 cell line 40  
3.4 Effect of the inhibitors on apoptosis in set2 cell line 41  
3.5 Effect of the inhibitors on protein phosphorylation 41  
3.6 Effect of the inhibitors on the clonogenic potential of human primary cells 41  
3.7 Effect of the inhibitors on the clonogenic potential of primary cells from murine bone marrow 43  
3.8 Effect of drugs combinations on proliferation of cell lines 43  
3.9 Effect of drugs combinations on clonogenic growth 43  
3.10 Effect of drugs combinations on protein phosphorylation 43  
3.11 Effect of drugs combinations on erythroid endogenous colonies growth inhibition 44  
3.12 Combination of BEZ235 and Ruxolitinib synergistically inhibits cd34+-derived colonies from PMF patients 44
Study of intracellular signaling pathways in Chronic Myeloproliferative Neoplasms

3.13. Combination treatment of BEZ235 with Ruxolitinib improves survival in mice injected with Ba/F3 cells
3.14. Combination treatment of BEZ235 with Ruxolitinib improves survival in knock-in mice

Chapter 4
Discussion

References