

2020). Furthermore, high expression of CYP1B1 has been implicated in the resistance of PC cells to docetaxel (Lin et al. 2022; McFadyen et al. 2001; Pastina et al. 2010). Multidrug resistance has also been reported in Docetaxel therapy in PC cells with high expression of ABCB1 (Linke et al. 2022; Seo et al. 2020). Thus, the potent molecular interaction of docetaxel with ABCB1 and CYP1B1 (Table 4.5 and Figures 4.7 and 4.8) may insinuate potential resistance of the cancer cells to docetaxel via increased expression of ABCB1 and CYP1B1. This correlates previous reports on increased expression of ABCB1 and CYP1B1 and cell proliferation following treatment with docetaxel (Martinez et al. 2008; Seo et al. 2020).

CHAPTER SIX: CONCLUSION

Taken together, these results indicate the susceptibility of the studied cancer patients drug resistance via increased expression of ABCB1 and CYP1B1 in tumour samples of the poor responders' category, and their associated molecular pathways. This is further depicted by the potent molecular interaction of both ABCB1 and CYP1B1 with the regimen drug, docetaxel. Although the study was initially planned to compare the three categories of patients; good responders, poor responders and those who exhibited excessive toxicity, the study was limited to only comparing the two groups of specimen (good and poor responders) due to the shortage of patients who exhibited excessive toxicity in the South African government database. The study was also limited to expression studies without investigation of the identified pathways and predicted enzymes activities (obtained from proteomics studies). We therefore propose further investigation of these pathways and enzyme activities in both pre-treated and post-treated patients with PC. This will give a clear understanding on the interaction of the drug and the expressed proteins in order to cognize how genetic factors affect drug transport and metabolism cause individual responses to chemotherapy vary, as well as give a clearer picture of the potential molecular mechanism of the drug effect in patients. This pilot study served as an initial exploration, focusing on delivering a proof of concept and establishing a methodology. However, it is imperative to underscore that a more extensive study is indispensable for comprehensive insights. Subsequent investigations must employ freshly obtained patient biopsies, as opposed to archived specimens, to ensure an ample supply of RNA and proteins for precise expression level analyses.

APPENDIX

Epithelial tumours		Acute myeloid leukaemia	9861/3
<i>Glandular neoplasms</i>		B lymphoblastic leukaemia/lymphoma	9811/3
Acinar adenocarcinoma	8140/3		
Atrophic		Miscellaneous tumours	
Pseudohyperplastic		Cystadenoma	8440/0
Microcystic		Nephroblastoma	8960/3
Foamy gland		Rhabdoid tumour	8963/3
Mucinous (colloid)	8480/3	Germ cell tumours	
Signet ring-like cell	8490/3	Clear cell adenocarcinoma	8310/3
Pleomorphic giant cell		Melanoma	8720/3
Sarcomatoid	8572/3	Paraganglioma	8693/1
Prostatic intraepithelial neoplasia,		Neuroblastoma	9500/3
high-grade	8148/2		
Intraductal carcinoma	8500/2	Metastatic tumours	
Ductal adenocarcinoma	8500/3		
Cribriform	8201/3	<i>Tumours of the seminal vesicles</i>	
Papillary	8260/3	Epithelial tumours	
Solid	8230/3	Adenocarcinoma	8140/3
Urothelial carcinoma	8120/3	Squamous cell carcinoma	8070/3
<i>Squamous neoplasms</i>			
Adenosquamous carcinoma	8560/3	Mixed epithelial and stromal tumours	
Squamous cell carcinoma	8070/3	Cystadenoma	8440/0
Basal cell carcinoma	8147/3		
		Mesenchymal tumours	
Neuroendocrine tumours		Leiomyoma	8890/0
Adenocarcinoma with neuroendocrine		Schwannoma	9560/0
differentiation	8574/3	Mammary-type myofibroblastoma	8825/0
Well-differentiated neuroendocrine tumour	8240/3	Gastrointestinal stromal tumour, NOS	8936/1
Small cell neuroendocrine carcinoma	8041/3	Leiomyosarcoma	8890/3
Large cell neuroendocrine carcinoma	8013/3	Angiosarcoma	9120/3
		Liposarcoma	8850/3
Mesenchymal tumours		Solitary fibrous tumour	8815/1
Stromal tumour of uncertain malignant potential	8935/1	Haemangiopericytoma	9150/1
Stromal sarcoma	8935/3		
Leiomyosarcoma	8890/3	Miscellaneous tumours	
Rhabdomyosarcoma	8900/3	Choriocarcinoma	9100/3
Leiomyoma	8890/0	Seminoma	9061/3
Angiosarcoma	9120/3	Well-differentiated neuroendocrine tumour /	
Synovial sarcoma	9040/3	carcinoid tumour	8240/3
Inflammatory myofibroblastic tumour	8825/1	Lymphomas	
Osteosarcoma	9180/3	Ewing sarcoma	9364/3
Undifferentiated pleomorphic sarcoma	8802/3		
Solitary fibrous tumour	8815/1	Metastatic tumours	
Solitary fibrous tumour, malignant	8815/3		
Haemangioma	9120/0		
Granular cell tumour	9580/0		
Haematolymphoid tumours			
Diffuse large B-cell lymphoma	9680/3		
Chronic lymphocytic leukaemia /			
small lymphocytic lymphoma	9823/3		
Follicular lymphoma	9690/3		
Mantle cell lymphoma	9673/3		

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) (917A). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours. The classification is modified from the previous WHO classification (756A), taking into account changes in our understanding of these lesions.

Appendix 1. Prostate tumours' histological classification by the World Health Organization in 2016 Adapted without permission (Humphrey, 2016).

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