Vitamin D Summary

Most tissues and cells not only have a vitamin D receptor, but also have the ability to make 1,25-dihydroxyvitamin D.

Vitamin D deficiency has been associated with increased risk for many cancers, osteoporosis, cardiovascular disease, and diabetes mellitus.

Most benefit (in vivo and in vitro):

- Breast, prostate (w/ taxotere), melanoma, pancreatic, NSCLC (CYP 24 over expression), ALL and LL .
- Special groups- patients as risk for osteoporosis, w/ bone mets, on aromatase inhibitors, or bisphosphonates,

Mechanism of action (in vitro)-

Vitamin D3 has effects on cellular growth, differentiation, apoptosis, malignant cell invasion and metastasis

- **Inhibits cell growth and invasion**- inhibitory effect on the G1/S checkpoint of the cell cycle by upregulating the cyclin dependent kinase inhibitors p27 and p21, and by inhibiting cyclin D1)
- upregulation of transforming growth factor-beta and downregulation of the epidermal growth factor receptor
- **Induces apoptosis**- either through effects on the insulin-like growth receptor and tumour necrosis factor-alpha or via the Bcl-2 family system, the ceramide pathway, the death receptors (e.g. Fas) and the stress-activated protein kinase pathways (Jun N terminal kinase and p38)
- **Inhibits angiogenesis**- reduces the protein expression of both the regulated HIF-1alpha subunit and the vascular endothelial growth factor (VEGF).

Due to the results obtained in several studies, a more functional classification has recently been proposed:

Vitamin D levels (serum 25 (OH) D)	ng/ml	nmol/l
desirable	> 40	> 100
hypovitaminosis	20 - 40	50 -100
insufficient	10 - 20	25 - 50
deficient	<10	< 25

Note: The vitamin D3 supplementation necessary to achieve a 25(OH)D increment of 25 nmol/L may be at least 1500 IU/day.

Dose range: 2000 -10,000 + ? international units daily

Cautions: hypercalcemia (>60,000 IU vitamin D daily over a period of years)