Vit D and Cancer

Introduction

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Clinical status in Cancer

- Known activity against breast cancer cell lines, clinical studies led to the development of analogues by Leo pharma.

- Not recognised as an important issue by most oncologists.

Vit D Scientific status

- First MRC Nobel prize to Sir Frederick Hopkins 1929 for essential nutrients especially Milk!

- Vit D essentially discovered post first world war and its importance to bone disease and Rickets became established.

Vit D and Rickets

- Correction of Vit D deficiency in infancy can correct (cure) Rickets.
- Major Implications for other conditions clearly associated with vit D deficiency.
- Existence of vit D resistant Rickets.

Vit D complexity

- Absorbtion (lactulose intolerance)
- Skin and UV light
- Liver
- Kidney
- Acts through receptors (polymorphisms)
- Can be sequestered in fat tissues
- It is a cholesterol based substance

- So many (?weak) links to break!

Mechanisms of Action

- Cell culture and experimental models show that Calcitrol – Vit D3

- Promotes cell differentiation.
- Inhibits cancer proliferation.
- Is anti-inflammatory, anti-angiogenic and proapoptotic.
- Apart from known effects on bone, many other systems are affected such as the immune system, blood vessels, muscle, neurological tissues etc.

Vit D and Cancer

- Literature is confusing-NEJM review 3/11
- Observational studies link low Vit D3 levels to increased cancer risk and mortality . Randomised studies are generally null especially Breast and Prostate cancer and the “rarer” cancers.
- Colorectal more convincing data but negative supplementation data.
- New trials accessing higher doses under way.

Vit D links and Cancer

- Vitamin D Receptor polymorphisms

- Vit D gene contains numerous variants

- Some are associated with complex conditions including osteoporosis, short stature, diabetes and cancer

VDR polymorphisms

- 470 Single Nucleotide Polymorphisms (SNPs)

- Only a few have functional consequences
- Associated with ;

- Breast, Ovarian, Gastro-Intestinal,
- Melanoma and Prostate cancer

VDR pms

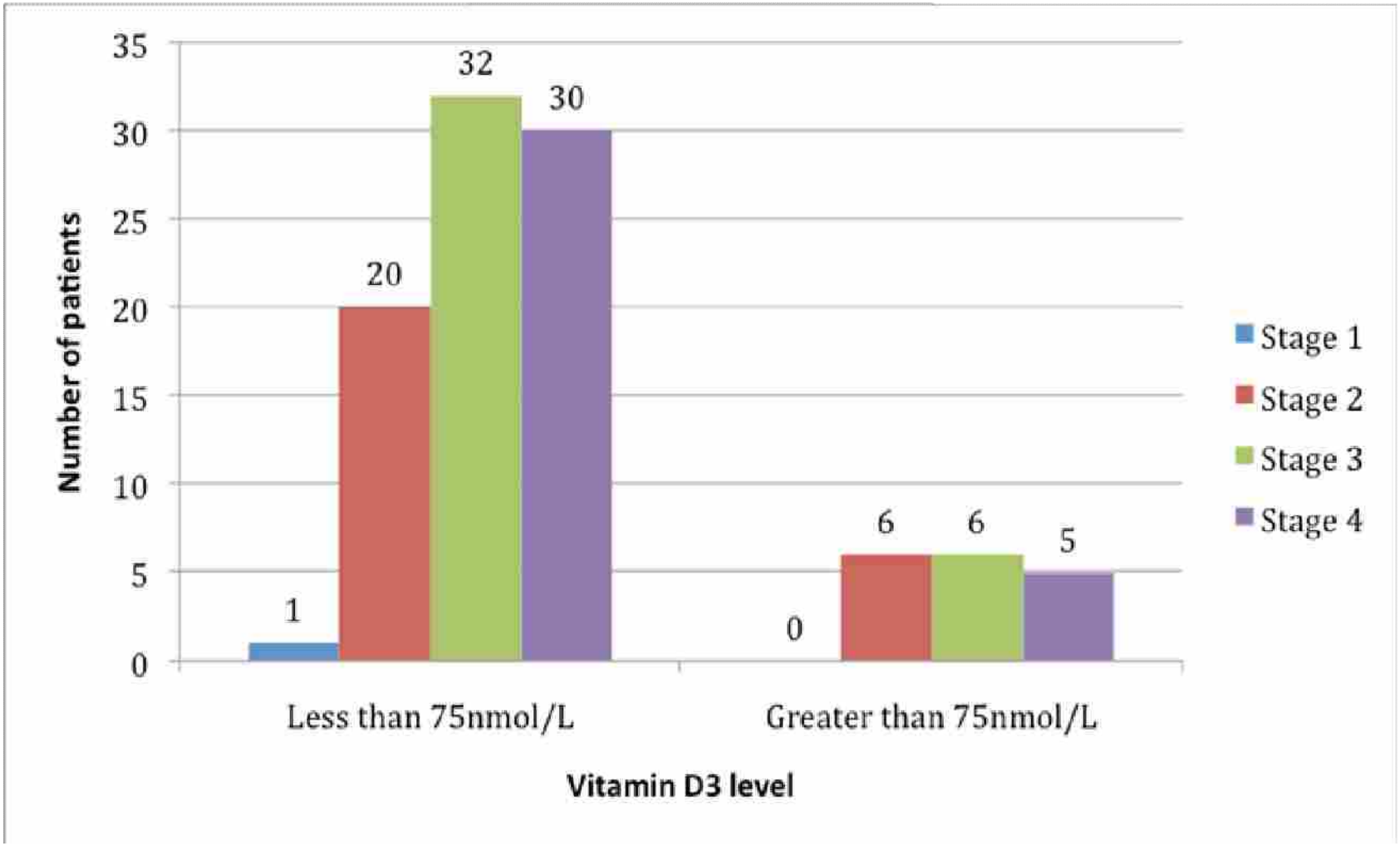
- Associated with low colon cancer risk with low sugar high fibre diets (Ff/ff FokI,) and with high risk, red meat consumption in Rectal Cancer (FF)

- Associated with D3 anti-proliferative activies in resistant cell lines

Melanoma

- Newton-Bishop et al JCO 2009, reported that D3 levels are associated with Breslow thickness at presentation and survival from melanoma which is independent of Breslow thickness.

vitD3 levels and stage



SGH patients

- Over a third had very low levels< 20
- Only one above normal range but was on 10,000 i.u.s!
- Several very low patients reported excellent diet and sun exposure through exercise. Only one used excessive sun block at all times.

Speculation

- Is Vit D absorbtion/metabolism the Factor X in the risk factors for melanoma?

Purpose

- Review all available data.
- ?Role in prevention and what dose recommendations.
- ? Role in co-treatments eg with surgery, immunotherapy, chemotherapy, radiotherapy.
- ? High dose as treatment.
- ?VDR SNPs as guide to management.