CareSearch Project Research Studies Register: Registration Proforma	0154

Study Title: Randomised, double blind control trial of megestrol acetate, dexamethasone and placebo in the management of anorexia in people with cancer

Brief description of the study: Background: Anorexia is a common and distressing problem in people with advanced cancer and other life-limiting illnesses. Dexamethasone is widely used in palliative care, including as an appetite stimulant, and is inexpensive. However, there is only low level evidence for its efficacy for this purpose in people with advanced cancer receiving palliative care, and there is a lack of clinical consensus on optimal dose/regimen/duration in this population. Megestrol acetate is the other established treatment for this indication and there is Level 1 evidence for its efficacy as an orexigenic agent in advanced cancer, including from an Australian study a decade ago. This study, found megestrol acetate 480 mg/day to have significantly greater appetite stimulation than 160 mg/d, which in turn did not show a statistically significant advantage over placebo. There have also been head-to-head studies of megestrol and dexamethasone in people with advanced cancer in the past, including a large, randomized US study which found that a non-significantly greater proportion of participants obtained appetite stimulation from high dose megestrol (800 mg /day) when compared with dexamethasone 3mg/day (46% vs. 38% at 4 weeks, respectively). There were similar rates of adverse events with the two agents, although the profiles were different. Despite the evidence, megestrol is not currently prescribed extensively as an appetite stimulant to Australian patients with advanced cancer, primarily due to its cost (only available on the PBS, by authority, for metastatic breast cancer). The results from the studies, or others, do not provide sufficient evidence of the net clinical benefit, relative efficacy, toxicity, or cost benefit of these two agents in people with advanced cancer receiving palliative care. Such people are likely to be sicker and have a shorter survival than those in the previous studies, and the principal aims of therapy (appetite stimulation and quality of life vs. weight gain and improved function) differ. Study design Double blind, placebo controlled, randomized Phase III trial of 3 arms: megestrol acetate 480 mg/day vs. Dexamethasone 4 mg/d vs. placebo. People with advanced cancer requiring palliative care and who have poor appetite will be eligible to participate. Those who provide consent will be randomised to receive either megestrol acetate 480 mg, dexamethasone 4mg or placebo, for up to 4 weeks if responding. Objectives The primary objective is to compare megestrol versus placebo and dexamethasone versus placebo for their ability to stimulate appetite. Secondary objectives are to compare relative consequences of therapy (efficacy, adverse events, quality of life and distress in participants and families, resource use and cost) and hence net clinical benefit and net benefit. Treatment schedule: 1. Megestrol acetate 480mg per day (3 capsules) 2. Dexamethasone 4mg per day (3 capsules) 3. Placebo (3 capsules per day) Primary Outcome Change in appetite score on a NRS for appetite at 1 week, with response defined as 25% increase in the baseline score. Secondary outcomes these include weight, QOL, functional status; adverse events; health outcomes and health services utilisation (relative costs of each treatment) assessed weekly over 4 weeks of follow-up. Assessments: Appetite will be assessed using an 11 point numeric rating scale and the

Memorial Symptom Assessment Scale. Quality of life will be assessed by the EORTC QLQ-C30 and the FACT-G. NCI Common Terminology Criteria for Adverse Events V3 will monitor safety. Analysis A total sample size of 159 participants (53 megestrol, 53 dexamethasone, 53 placebo) will provide 80% power, at a 2-tailed type I error of 0.05, to detect a significant difference in the proportion of those responding to megestrol or dexamethasone versus placebo, based on chi-squared tests. The analysis will be done on an intention-to-treat basis. No adjustment will be made for multiple comparisons. Economic analysis Within study relative net clinical benefit of megestrol, dexamethasone and placebo will be considered in comparing consequences including appetite scores (on NRS and FAACT), an assessment of family and carer distress, and adverse events over the 4 weeks of study follow-up. Resource use and costs will also be estimated over this period from Medicare data (PBS and MBS) in consenting participants, and hospital admissions data (number of admissions, DRG's, and bed days). Costs and consequences (appetite, adverse events, family and carer distress) data for each person in the study will be bootstrapped to estimate and present their joint distribution under uncertainty.

Study Methodology: (Please mark with an x which type of study methodology)

	Epidemiology
	Health Services / Health Economics / Quality Improvement
	Qualitative, Observational or Descriptive
	Mixed Method
	Systematic Review
X	Intervention: RCT
	Intervention: Comparative or cohort study
	Intervention: Case series

Project details:

Funding source (Optional): Australian Government Department of Health

Has the study received ethics approval?	**X**	Yes		No		Not applicable
Multi site:	**X**	Yes		No		Not applicable

Project starting date: January 2009

Project completion date: April 2015

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Associated publications / reports:
Topics (Admin only) Anorexia, Drug trial