THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Protocol Page

A Preliminary Study of Dexamethasone for Dyspnea in Cancer Patients
2012-0001

Core Protocol Information

Short Title	Dexamethasone Dyspnea Study
Study Chair:	David Hui
Additional Contact:	Julio A. Allo Susan Frisbee-Hume Vera J. DeLaCruz
Additional Memo Recipients:	**Recipients List** **OPR Recipients** (for OPR use only) OPR DSMB **Study Staff Recipients** None
Department:	Palliative Care and Rehabilitation Medicine
Phone:	713-792-6258
Unit:	1414
Full Title:	A Preliminary Study of Dexamethasone for Dyspnea in Cancer Patients
Protocol Type:	Standard Protocol
Protocol Phase:	Phase II
Version Status:	Activated 12/02/2013
Version:	14
Document Status:	Saved as "Final"
Submitted by:	Vera J. DeLaCruz--11/5/2013 3:28:10 PM
OPR Action:	Accepted by: Virginia M Gonzales -- 11/14/2013 2:18:01 PM

Which Committee will review this protocol?

(•) The Clinical Research Committee - (CRC)

Protocol Body

1.0 Objectives

A. Objectives

A.1. Primary Objective. To determine the feasibility of conducting a randomized controlled trial (blinded phase) on dexamethasone in cancer patients with dyspnea. Our working hypothesis is that at least 50% of patients will complete the dyspnea numeric rating scale (NRS) on day 7+/-2.

A.2. Objective #2. To compare the intensity of dyspnea (NRS), forced expiratory volume (FEV1) and quality of life in cancer patients between baseline and after 4 days of dexamethasone use. Our *working hypothesis* is that 4 days of dexamethasone will improve dyspnea, respiratory function and quality of life for cancer patients.

A.3. Objective #3. To compare the intensity of dyspnea (NRS, cancer dyspnea scale), FEV1, and quality of life in cancer patients between baseline and after 7 days of dexamethasone use. Our *working hypothesis* is that 7 days of dexamethasone will improve dyspnea, respiratory function and quality of life for cancer patients.

A.4. Objective #4. To compare the intensity of dyspnea (NRS, cancer dyspnea scale), FEV1, in cancer patients between the dexamethasone arm and the placebo arm at 4 and 7 days. Our *working hypothesis* is that dexamethasone will improve dyspnea, and respiratory function for cancer patients compared to placebo.

A.5. Objective #5. To compare the intensity of dyspnea (NRS, cancer dyspnea scale), FEV1, and quality of life in cancer patients after 7 days of dexamethasone between the dexamethasone arm (8mg BID for 4 days followed by 4mg BID for 3 days) and the placebo arm (4mg BID for 7 days during the open label phase). Our *working hypothesis* is that a higher dose of dexamethasone will improve dyspnea, respiratory function and quality of life for cancer patients compared the lower dose.

2.0 Background and Significance

B. Background and Significance

B.1. Significance of Dyspnea. Dyspnea is a subjective awareness of difficulty breathing, which may be associated with the distressing sensation of suffocation. It is one of the most common and most feared symptoms among cancer patients, occurring in approximately 20-40% of patients at the time of diagnosis of advanced disease (Ripamonti *et al.* 1998, Tishelman *et al.* 2007) and in up to 70% of patients in the last 6 weeks of life (Ben-Aharon *et al.* 2008). Dyspnea is associated with fatigue, anxiety, decreased function and lower quality of life. Furthermore, dyspnea has been shown to be an important prognostic factor in patients with advanced cancer (Hauser *et al.* 2006, Maltoni *et al.* 2005).

B.2. The Pathophysiology of Dyspnea is shown in Figure 1. The sensory cortex receives afferent input from mechanoreceptors in airways and the chest wall, stretch and irritant receptors in the lungs, chemoreceptors in the brainstem, and other signals from the motor cortex, generating the sensation of breathlessness (Mahler 2011, Manning and Schwartzstein 1995). Causes of dyspnea can be classified as cancer-related, treatment-related and/or psychological factors. Progressive disease may result in parenchymal metastasis, lymphangitic carcinomatosis, airway obstruction, atelectasis, and/or pleural effusion, all of which may cause difficulty breathing.

B.3. The Current Management of Dyspnea involves treatment of any reversible causes and supportive measures to minimize the sensation of dyspnea. Relief of dyspnea can be achieved through a number of pharmacologic and non-pharmacologic measures. Common medications for dyspnea include opioids, bronchodilators, corticosteroids and benzodiazepines (Ben-Aharon *et al.* 2008, Cranston *et al.* 2008, Jennings *et al.* 2002). A systemic review suggested that oral and parenteral, but not nebulized, opioids are effective in managing dyspnea (Jennings *et al.* 2002). However, the potential benefit of opioids is limited by their adverse effects, including sedation and opioid-induced neurotoxicity at higher doses. Supplemental oxygen has been shown to be efficacious only in patients with hypoxemia (Abernethy *et al.* 2010, Cranston *et al.* 2008). For patients with chronic obstructive pulmonary diseases, systemic corticosteroids have been clearly shown to reduce respiratory symptoms, improve FEV1 and shorten hospitalization in acute exacerbations (Falk *et al.* 2008, Walters *et al.* 2009, Wood-Baker *et al.* 2007). Furthermore, inhaled steroids have been demonstrated to improve various clinical outcomes in COPD patients including the number of physician visits and airway hyperreactivity (Calverley *et al.* 2007, Lung Health Study Research 2000, Yang *et al.* 2007). However, the efficacy of corticosteroids for dyspnea has not been clearly elucidated in cancer patients.

B.4. Corticosteroids for Dyspnea in Cancer Patients. No study to date has specifically examined the relationship between inflammation and dyspnea in cancer patients. However, cancer is known to induce host inflammatory response and often produces a number of cytokines with both systemic and peripheral effects (Wang *et al.* 2010). Thus, cancer is similar to COPD which is also a disease characterized by a significantly inflammatory component, including airway wall infiltration of T lymphocytes and macrophages, increased lung TNFa and IL8, increased lung IL6 during exacerbations, and elevated serum leptin, IL6, TNFa, CRP, fibrinogen, peripheral neutrophil activation, and activation of apoptosis of peripheral lymphocytes (Falk *et al.* 2008). The severity of dyspnea of COPD as determined by the FEV1 correlated with concentrations of IL-1b, MIP-1b, CD83, IL-1 receptor 2, and IL-1 receptor antagonist as measured by gene microarray (Oudijk *et al.* 2005). Steroids have been shown to modulate the inflammatory response and improve dyspnea (Calverley *et al.* 2003, Lapperre *et al.* 2009). More recently, a randomized controlled trial on an IL8 monoclonal antibody also found significant improvement in the sensation of dyspnea (Mahler *et al.* 2004). The available evidence suggests that modulation of the inflammatory response may improve the sensation of dyspnea. Given that inflammation is a significant mediator of dyspnea in cancer patients, we hypothesize that corticosteroids could have a therapeutic benefit for cancer patients.

Few clinical studies have addressed the role of corticosteroids for dyspnea in cancer patients. In a case series, Elsayem et al. reported significant improvement in dyspnea after administration of high dose steroids among patients with upper airway obstruction (Elsayem and Bruera 2007). In a prospective series, Hardy et al. found that 5/13 advanced cancer patients experienced some improvement with dexamethasone, 6/13 had no change and 2/13 did worse (Hardy *et al.* 2001). Matso et al. surveyed 120 Japanese palliative care physicians about their use of steroids. 37% of physicians perceived the positive effect of steroids on dyspnea to take place within 24 hours, 38% within 1-2 days, and 24% within 3-7 days (Matsuo *et al.* 2011). The main perceived predictors of steroid efficacy were lymphangitic carcinomatosis, airway obstruction, multiple lung metastases. The main side effects after 1 week of use were hyperglycemia, insomnia, delirium and oral candidiasis. A recent systematic review on dyspnea interventions found no study on corticosteroids, and concluded that high quality randomized controlled trials are needed to examine the effectiveness of corticosteroids for dyspnea (Viola *et al.* 2008). A study examined the effect of prednisone in healthy men on induced dyspnea using inspiratory resistors and breathholding, and concluded that prednisone intake was associated with significant increase in minute ventilation during breathing compared to placebo (Kallas De Carvalho *et al.* 2002).

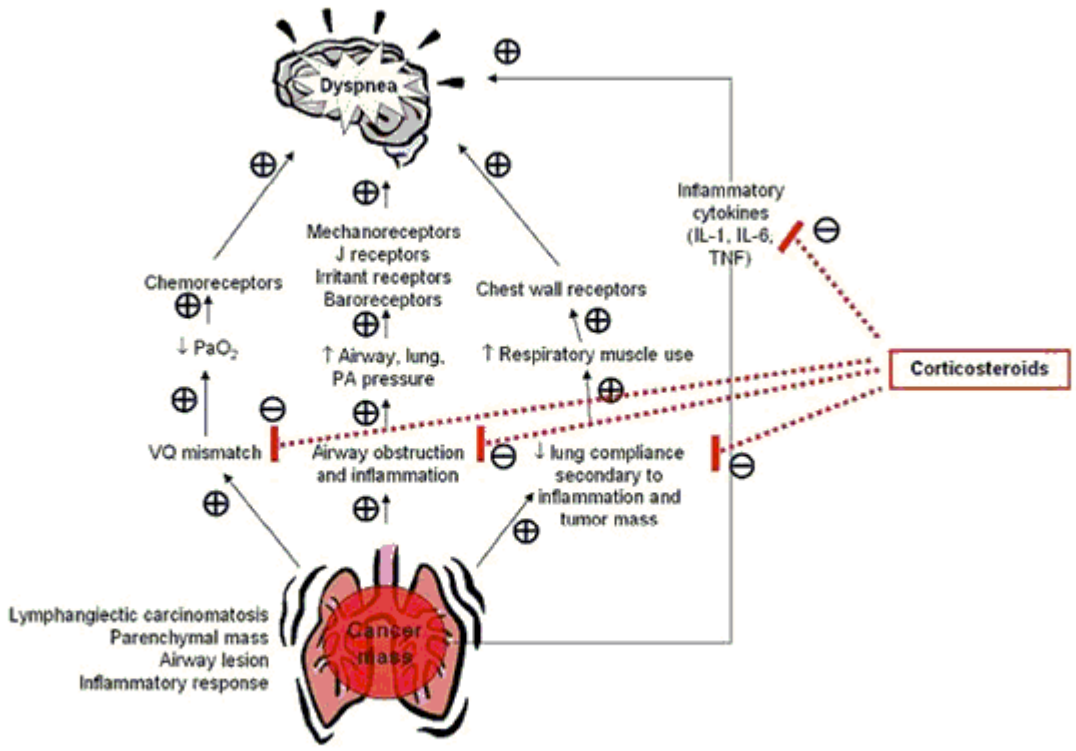

Figure 1. Conceptual Framework for Dyspnea and Potential Mechanisms of Action of Corticosteroids.

B.5. Preliminary data. One of our co-investigators, Dr. Yennu, recently completed a randomized controlled trial comparing dexamethasone 4mg twice a day versus placebo for cancer related fatigue, with dyspnea as a secondary endpoint. Use of dexamethasone was associated with significant improvement in dyspnea compared to placebo.

	Dexamethasone Arm		Placebo Arm		
	N	Change	N	Change	P-value
Day 4 - baseline	49	-2 (-4 to 0)	44	-1 (-3 to 0)	0.31
Day 8 - baseline	43	-1 (-3 to 1)	38	0 (-2.25 to 0)	0.59
Day 15 - baseline	36	-2 (-4.75 to 0)	32	0 (-2.75 to 0)	0.04
Day 22 - baseline	35	-2 (-4 to 0)	26	0 (-3 to 1)	0.04

3.0 Experimental Approach

C.1. Overall Study design. This is a 2-arm, double blind, parallel randomized controlled trial of dexamethasone and placebo for cancer patients with dyspnea (Figure 1). The main goal of this study is to determine the effect size for both dexamethasone and placebo arm to inform a larger, adequately powered confirmatory randomized controlled trial. For this preliminary study, we plan to enroll 20 patients per arm, with a total of 40 patients for the entire study (see statistical considerations for more details). Patients will randomized to either dexamethasone or placebo for 7 days in a blinded fashion; this will be followed by an open label phase in which patients in both arms would take dexamethasone for 7 days. The rationale for the open label phase is to give all patients an opportunity to try the study medication, and to examine the use of dexamethasone at a different dose as an exploratory endpoint (objective #5). Based on our experience conducting symptom control trials, we believe this study design is feasible and would not add undue burden for patients. To reimburse patients for their time and effort, we will provide a gift card for $20 per visit (day 7+/-2 and day 14+/-2).

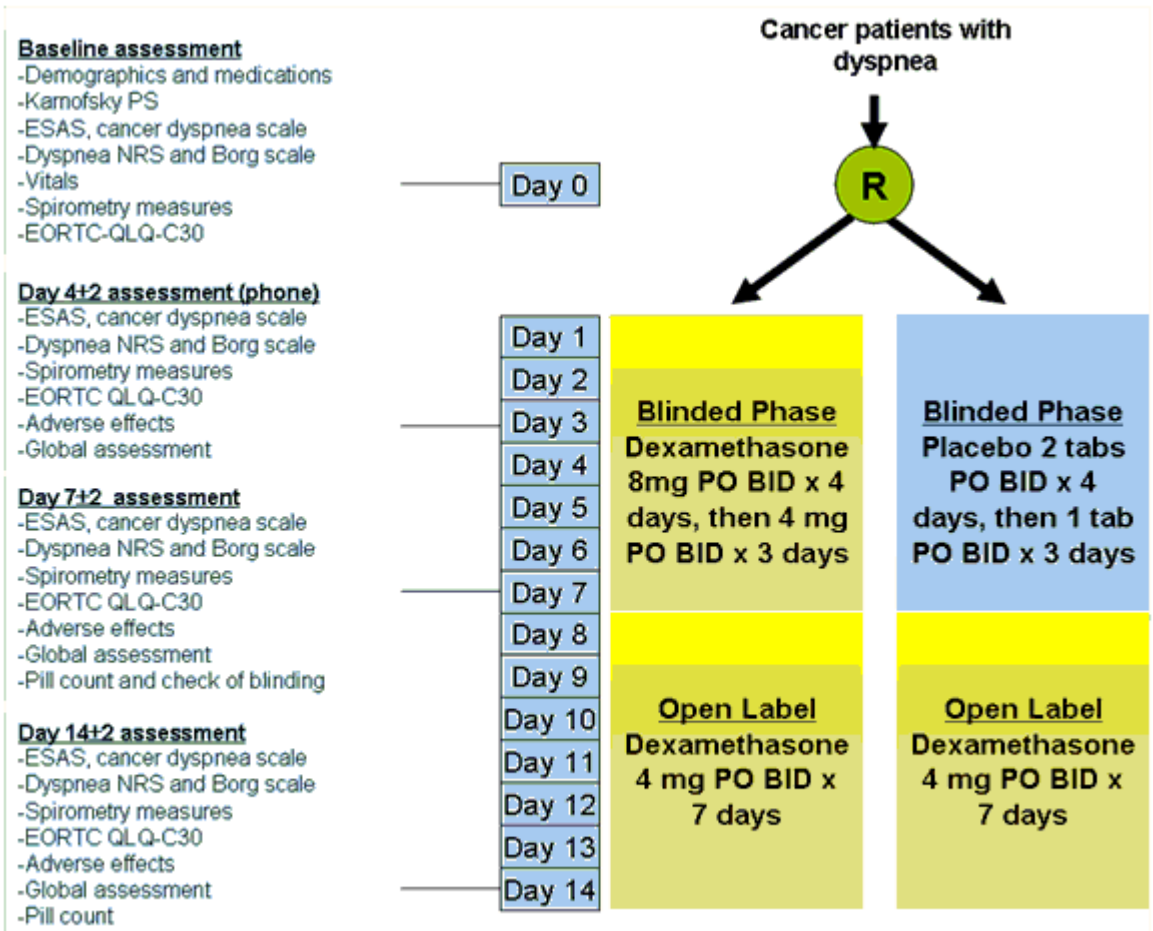

Figure 1. Study Flow Chart. BID=twice a day; NRS=numeric rating scale

C.2. Eligibility Criteria. The eligibility criteria are shown in Table 2.

Table 2. Study Eligibility Criteria
Inclusion Criteria
Diagnosis of cancer
Dyspnea with an average intensity level >3/10 on the numeric rating scale over the past week
Clinical or radiologic history of lung/pleural involvement (primary or metastatic), lymphangitic carcinomatosis or airway involvement secondary to tumor infiltration
Outpatients at MD Anderson Cancer Center seen by the Supportive Care, Rehabilitation Service, Thoracic Oncology or Pulmonary Medicine
Able to communicate in English
Karnofsky performance status >=40%
Age 18 or older
Permission from the attending medical oncologist if the patient is currently on an interventional cancer therapy trial.
Exclusion Criteria
Delirium (i.e. Memorial delirium rating scale >13)
Oxygen saturation <90% despite supplemental oxygen >6L/min
Previous allergic reactions to dexamethasone
Uncontrolled hyperglycemia as defined by any blood glucose of >300 mg/dl in the past two weeks
Severe anemia (Hb <7g/L) not corrected prior to study enrollment (bloodwork is not required if patient did not have recent chemotherapy within last 2 weeks)
Post-surgical open wound that has not been healed at the time of enrollment
Any infection requiring antibiotics within the past 2 weeks
Major surgery within the past 2 weeks
Megestrol use at the time of study enrollment
Neutropenia (absolute neutrophil count < 1.0) (bloodwork is not required if patient did not have recent chemotherapy within last 2 weeks)
Currently on or expected to start cytotoxic chemotherapy within 1 week of study enrollment
Chronic obstructive pulmonary disease (COPD) exacerbation at the time of study enrollment
Heart failure exacerbation at the time of study enrollment
Chronic systemic corticosteroid use (>14 days) at the time of study enrollment
Unwilling to provide informed consent

C.3. Study screening. A 2 step consent process will be used. A verbal script is provided in the Appendix P. First, a verbal consent will be obtained by the study staff to proceed with screening of potential participants for eligibility and to characterize their dyspnea using the dyspnea survey and the cancer dyspnea scale. Eligible patients will then be formally enrolled onto the study after they have signed the informed consent indicating a willingness to participate in the trial. The number of patients screened, approached, eligible and enrolled will be documented. Reasons for refusal for eligible patients will also be captured.

C.4. Randomization. A computer generated sequence in permuted blocks will be used to assign patients to either dexamethasone or placebo via CORe, a secured website. We will stratify by FEV1/FVC ratio (<0.8 vs. >/= 0.8). CORe will set up a Randomization website and Investigational Pharmacy personnel will perform the randomization assignment. Susan Frisbee-Hume, our research manager, will provide the necessary CORe training for the research team.

C.5. Blinding. Both patients and the research staff conducting the assessment will be blinded to the treatment assignment. Placebo capsules identical to dexamethasone 4mg capsules in appearance and taste will be compounded by Green Park Compounding Pharmacy, and both will be dispensed by Investigational Pharmacy at MD Anderson. At the end of the blinded phase, we will assess blinding by asking patients which study arm they believe they have been randomized to.

C.6. Research staff. An orientation will be held with research staff involved in this study to introduce them with the study design, and standardize the provision of each intervention.

C.7. Study Interventions. The intervention arm will receive dexamethasone 8 mg (2 capsules of 4 mg) given orally twice a day for 4 days, then 4 mg given orally twice a day for 3 days. This dose was chosen partly based on our feasibility data demonstrating that dexamethasone improved dyspnea.

Dexamethasone is a commonly used medication in cancer patients. It is approved by the US Food and Drug Administration for treatment of multiple indications, including allergic disorder (including asthma), cerebral edema associated with primary or metastatic brain tumor, craniotomy, or head injury, collagen disease, disorder of ear, disorder of endocrine system, disorder of eye, disorder of gastrointestinal tract, disorder of hematopoietic structure, disorder of respiratory system (treatment of berylliosis, fulminating or disseminated pulmonary tuberculosis (when used concurrently with appropriate antituberbulosis therapy), idiopathic eosinophilic pneumonias and symptomatic sarcoidosis, Loeffler's syndrome not manageable by other means and aspiration pneumonitis), disorder of skin, exacerbation of multiple sclerosis, hypercalcemia of malignancy, idiopathic thrombocytopenic purpura, inflammatory disorder of musculoskeletal system, macular retinal edema, mycosis fungoides, neoplastic disease, palliative management of leukemias and

lymphomas, nephrotic syndrome, Idiopathic or due to lupus erythematosus without uremia, non-infectious posterior uveitis, trichinosis with neurologic or myocardial involvement, tuberculosis of meninges with subarachnoid block or impending block when used concurrently with antituberculosis therapy (http://www.thomsonhc.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/7CB60A/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/0CC381/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DisplayDrugdexDocument?docId=0221&contentSetId=31&title=Dexamethasone&servicesTitle=Dexamethasone&topicId=clinicalApplicationsSection&subtopicId=therapeuticUsesSection#4.5.A.74). However, it has not been specifically approved for management of dyspnea.

Dexamethasone is commonly used in oncology practice for management of cerebral edema, spinal cord compression, chemotherapy induced nausea and vomiting, bowel obstruction, pain, anorexia, dyspnea and fatigue. For patients with chronic obstructive pulmonary diseases, systemic corticosteroids have been clearly shown to reduce respiratory symptoms, improve FEV1 and shorten hospitalization in acute exacerbations (Falk et al. 2008, Walters et al. 2009, Wood-Baker et al. 2007). Furthermore, inhaled steroids have been demonstrated to improve various clinical outcomes in COPD patients including the number of physician visits and airway hyperreactivity (Calverley et al. 2007, Lung Health Study Research 2000, Yang et al. 2007). However, the efficacy of corticosteroids for dyspnea has not been clearly elucidated in cancer patients.

Our study proposes to use oral dexamethasone for the management of dyspnea. The dose of dexamethasone we plan to use is 8mg PO BID for 4 days, then 4 mg PO BID x10 more days. This is similar to doses we use for CINV prophylaxis (8-20mg IV/PO prior to chemotherapy, then 4-8mg q12h for up to 4 days after chemotherapy) (Mullin and Beckwith, www.ifvrh.com/policies_quick_ref/Treatment_of_CINV.html). This is study is purely exploratory in nature, and we do not plan to seek FDA approval for the new indication of dyspnea.

The control arm will receive placebo capsules prepared by a compounding pharmacy (Green Park Compounding Pharmacy) identical in appearance to dexamethasone 4 mg capsules, and will be instructed to take two capsules twice a day for 4 days, followed by one capsule twice a day for 3 days.

In the open label phase, patients assigned to either arm will be asked to take dexamethasone 4 mg orally twice a day for 7 days. Both dexamethasone and placebo capsules used throughout this study will be compounded by Green Park Compounding Pharmacy and dispensed by Investigational Pharmacy at MD Anderson. Dexamethasone/placebo capsules will be provided free of charge to patients during the 14 day study period.

C.8. Medication use during study. We will ask patients to record the use of study medications using a medication diary. We will also keep track of their adherence by asking them to bring their medication boxes for a pill count. Phone call reminders will be provided daily. To document the co-intervention effect on dyspnea, patient use of regular and breakthrough opioids (for any reason) and bronchodilators at enrollment and during the study. Patients will receive daily phone calls for reminders and assessments. They can take it as soon as possible if they forget a dose.

C.9. Feasibility endpoints. Our primary objective is to test the feasibility of a protocol that uses dexamethasone and placebo for dyspnea, and to determine the feasibility of these two interventions for advanced cancer patients with persistent dyspnea. We will document the following:

- Rates of recruitment and retention (see section D1).
- Reasons for refusal and dropout
- Outcome measure—we will compare the sensitivity of Numeric rating scale and Borg scale to change, and identify key measure for future study
- Participant satisfaction—participants will provide an opinion regarding their satisfaction with study overall

C.10. Study assessments. See Table 4 for a detailed description of all study assessments.

Table 4. Summary of Study Assessments

Assessments	Baseline **(In person)**	**Day 4+/-2 (by phone)**	**Day 7+/-2 (In person/by phone)**	**Day 14+/-2 (In person/by phone)**
Demographics and Cancer Diagnosis[1]	X			
Medication History[2]	X			
Karnofsky Performance Status[3]	X			
Dyspnea Survey[4]	X			
O2 saturation and Respiratory Rate	X			
Cancer Dyspnea Scale[5]	X	X	X	X
Edmonton Symptom Assessment Scale[6]	X	X	X	X
Dyspnea Numeric Rating Scale[7]		Daily	Assessment	
Dyspnea Borg scale[8]	X	X	X	X
Spirometry Measures[9]	X	X	X	X
EORTC QLQ-C30[10]	X	X	X	X
Adverse effects[11]		X	X	X
Global assessment[12]		X	X	X
Pill count			X	X
Check of blinding			X	

1 patient initials, medical record number, date of birth, sex, race, education, marital status, cancer diagnosis, co-morbidities, cause(s) of dyspnea.

2 medications that could be used to treat dyspnea, including scheduled and as needed opioids, bronchodilators, and steroids will be documented.

3 an 11-point assessment scale that rates patients' functional status between 0% (death) and 100% (completely asymptomatic) based on their ambulation, activity level, and disease severity (Schag *et al.* 1984).

4 characterization of patients dyspnea including the following: presence of dyspnea at rest, average dyspnea in last 24 hours, worse dyspnea in last 24 hours, best dyspnea in last 24 hours, number of episodes of exacerbation per day, triggers of breakthrough dyspnea, average duration of each episode, current treatment for breakthrough dyspnea. It also adopted 3 questions from EORTC Lung module about dyspnea.

5 validated 12-item questionnaire specifically designed to assess the quality of dyspnea in cancer patients during the past few days (Tanaka *et al.* 2000). Each item has a score between 1 and 5, for a maximum of 60. There are sub-scores for sense of effort, anxiety, and discomfort.

6 validated questionnaire that measures 10 common symptoms in the past 4 hours (pain, fatigue, nausea, depression, anxiety, drowsiness, shortness of breath, appetite, sleep, and feeling of well being) using numeric rating scales (Bruera *et al.* 1991).

7 a 0 (no dyspnea) to 10 (worst dyspnea) categorical scale validated for rating the severity of dyspnea (Dorman *et al.* 2007, Gift and Narsavage 1998, Powers and Bennett 1999).

8 a 0 to 10 categorical scale for rating the severity of dyspnea. It is a ratio scale with descriptive anchors throughout the range in which a rating of 8 signifies breathlessness twice as severe as 4, which in turn is twice as severe as 2 (Dorman *et al.* 2007, Gift and Narsavage 1998, Kendrick *et al.* 2000, Powers and Bennett 1999).

9 the MicroLoop Spirometer (Micro Direct Inc, Lewiston, ME) will be used at baseline, day 7 and day 14. It is approved by the American Thoracic Society and US Food and Drug Administration. Various spirometry parameters will be obtained, such as vital capacity (VC), forced expiratory volume in 1 second (FEV1), forced vital capacity

(FVC), FEV1/FVC, peak inspiratory flow, and peak expiratory flow. As an exploratory measure, patients will also be asked to use the portable Microlife PF 100 Peak Flow Meter (Microlife, Clearwater, FL) to measure peak flow and FEV1 on a daily basis.
10 a well-validated quality of life instrument for cancer patients, consisting of 30 items that encompasses 3 symptom scales (pain, fatigue, nausea/vomiting), 6 single-item symptom items, 5 functional scales (physical, cognitive, role, emotional, and social), and one scale assessing global health status/quality of life. Each scale consists of 2-5 items. All items have four response categories (not at all, a little, quite a bit, very much), except for 2 items assessing overall health status/quality of life, which use a seven-point scale.
11 adverse effects related to the use of dexamethasone, such as edema, fever, infections, insomnia, anxiety, personality change, dyspepsia will be rated using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
12 patients will be asked about their dyspnea (worse, about the same, or better) comparing the level of dyspnea before and after the study (Guyatt *et al.* 1993, Redelmeier *et al.* 1996).
13 patients will be asked be record their study medication use, as well as any use of opioids and bronchodilators for relief of dyspnea.

C.11. Patient Safety, Monitoring, and Confidentiality. Prior to study initiation, all research staff participating in this study will receive an orientation to the devices and forms in this study to ensure consistent assessments. During the study, trained research staff will be performing study assessments and monitoring the patient carefully throughout the study period. In addition to daily phone calls, patients will be given the contact information of the research nurse in case they develop any significant adverse effects, and will be treated as they arise as per clinical practice. The study may be discontinued at the discretion of the treating physician or study principal investigator. Regulatory monitoring will be provided by the principal investigator, the Institutional Review Board, and the Data Safety and Monitoring Board. Patient confidentiality will be ensured by use of patient initials, secure storage of clinical data, and anonymous reporting.

4.0 Statistical Analysis

D.1. Sample Size Calculation. This pilot study is based on a convenience sample of 20 subjects per arm.

D.2. Data Analysis

Primary Objective: Our primary objective is to determine the completion rate for patients enrolling in this study. Patients who complete the dyspnea NRS on day 72 will be counted as successes. Dropouts are defined as subjects who do not complete the dyspnea NRS on day 7 +/- 2, and will be counted as failures toward the feasibility outcome. We will declare the study as feasible if we observe at least 20 successes, based on a recent review of Supportive Oncology studies in our department in which we found that approximately 50% patients completed their interventional clinical trial.

Objective #2. We will test our hypothesis that 4 days of dexamethasone will improve dyspnea, respiratory function and quality of life for cancer patients using paired t-tests.

Objective #3. We will test our hypothesis that 7 days of dexamethasone will improve dyspnea, respiratory function and quality of life for cancer patients using paired t-tests. A sample size of 20 per arm will allow us to detect an effect size of 0.9 in the change of dyspnea NRS between baseline and day 7 with an 80% power and an alpha of 5%, assuming a standard deviation of 2.

Objective #4. We will test our hypothesis that dexamethasone will improve dyspnea, respiratory function and quality of life for cancer patients compared to placebo using two-sample t-tests on the differences between baseline and 4 and 7 days for each outcome measure.

Objective #5. We will test our hypothesis that increased dose results in better outcomes by comparing the first 7 days of treatment arm to the last seven days of the placebo arm. We will use two-sample t-tests on the differences between baseline (day 0 for treatment arm, day 7 for placebo arm) and 7 days later (day 7 for treatment arm, day 14 for placebo arm).

5.0 Data Confidentiality Procedures

Health information will be protected and we will maintain the confidentiality of the data obtained from the patient's chart.

Collection of identifiers: We will collect and securely store patients' identifiers (including name, medical record number and demographic specifications). Each patient will be assigned a study number that will be the only identifier to figure in the analytical file and personal data will not be disclosed in any form. The key linking these numbers will be retained in a securely locked file by the investigator.

Data Storage: Protection of electronic and paper records will be guaranteed. All electronic records will be stored on password-protected institution computers behind the institution firewall. Any paper records will be classified and stored in locked files inside a locked office.

Training of personnel: Only MDACC personnel trained in maintaining confidentiality, the principle investigators and co-investigators, will have access to study records.

Data sharing: Study data will not be shared with any individuals or entities. The data will be kept by the principle investigator in a locked file cabinet.

Final disposition of study records: These data will be used only for this research study data files will be destroyed 5 years after publication of the findings.

6.0 References

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