ProSure[®] Strength to Fight and Get Back to Life

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ProSure. Strength to Fight and Get Back to Life 5004 1112 166 D1 Cancer care is evolving at an incredibly fast pace, and the prognosis for a person with cancer in 2012 is better than ever before. Both length of life and quality of life are now recognized as important goals of therapy.

Today's presentation will focus on recent advances in the area of therapeutic nutrition for people with cancer. The program highlights the rationale and clinical support for use of ProSure, an Abbott Nutrition product.







International experts in cancer cachexia research developed a definition to help improve recognition and management of this condition.

The consensus definition focuses on the complex interplay between reduced food intake and abnormal metabolism and identifies loss of skeletal muscle as key in patients' functional impairment. Such emphasis supports the concept that skeletal muscle mass can be both a marker for the syndrome and an important therapeutic target.



Cachexia is a serious condition. It's associated with reduced physical function, reduced ability to tolerate anticancer therapy, and reduced survival.



1 in 5 patients die from cachexia not from cancer.



Cachexia is a reducible risk.

16 clinical studies prove that ProSure may help reduce the adverse effects of cachexia.



With ProSure, cachexia doesn't have to interrupt patients' lives.





Tumors promote cancer cachexia by 2 different pathways (represented in purple and green):

- 1. The presence of cancer cells initiates the inflammatory response which causes cells of the immune system to release regulatory proteins called proinflammatory cytokines such as:
 - tumor necrosis factor-alpha (TNF-α)
 - interleukin-1 (IL-1)
 - interleukin-6 (IL-6)

Proinflammatory cytokines set off a chain of events that lead to weight loss by:

- (a) Causing Anorexia or appetite depression, leading to decreased food/calorie intake, with consequent weight loss.
- (b) Initiation of the acute phase response (APR), the body's normal response to stress, trauma, infection, inflammation, and cancer. Usually the inflammatory response is limited and stops when healing occurs. But sometimes the inflammatory response does not shut itself off, such as in the presence of a tumor. A persistent APR is associated with an increased resting energy expenditure and depletion of lean body mass. C-reactive protein is often used as a marker for APR.
- (c) Altered metabolism of the macronutrients (fat, protein, and carbohydrate), i.e. decreased protein synthesis and increased fat and protein breakdown causing loss of lean body mass and weight.
- 2. Tumors release cytokines that produce local inflammatory effects, as well as proteolysis-inducing factor (PIF). PIF interacts with skeletal muscle and causes loss of lean body mass by increasing protein breakdown and decreasing protein synthesis. PIF has been found in the urine and serum of people with a variety of different tumors, but only in patients who are experiencing cancer-associated weight loss. Since PIF is not present in weight-losing people without cancer, it appears to be a specific marker for cancer-induced weight loss.

If these metabolic problems are not addressed, eating more food or using standard nutritional supplements is rarely enough to prevent or reverse the weight and muscle loss.

Altogether, these pathways lead to cancer cachexia with weight loss, muscle wasting, inflammation, fat depletion, poor clinical outcomes, decreased quality of life and physical activity.



Fearon and colleagues identified 3 stages of cancer cachexia that represent a continuum of clinical relevance.

In the precachexia stage, patients may first notice weight loss, sometimes even before the cancer diagnosis has been made.

The cachexia syndrome is characterized by weight loss in combination with evidence of systemic inflammation and reduced food intake.

People with advanced cachexia have depletion of fat reserves, severe muscle wasting, and immunocompromise, and they are likely to die primarily as a result of these issues.

Not all patients will progress through each stage of the spectrum.

Risk of progression depends on tumor type and stage, presence of systemic inflammation, reduced food intake, and lack of response to anticancer treatment.

	PRECACHEXIA	CACHEXIA	REFRACTORY CACHEXIA
	Weight loss ≤5% Anorexia and metabolic change	Weight loss >5% or BMI <20 and weight loss >2% or Sarcopenia and weight loss >2% Often reduced food intake/systemic inflammation	Variable degree of cachexia Cancer disease both procatabolic and not responsive to anticancer treatment Low performance score
an	nted from The Lancet Oncology, 12, Fearon K. Strasse	inflammation	<3 months expected survival an international consensus, 489-495, Cappinght (2017), with permission from Elsevier.

In a study of patients with advanced pancreatic cancer, Fearon et al sought to identify clinical features of cachexia that impact patients' function and survival. They identified 3 key features, listed on this slide.

- Weight loss (> 10%)
- Systemic inflammation (C-reactive protein > 10 mg/L)
- Reduced food intake (< 1500 kcal/day)

Patients who displayed all 3 of these factors had reduced lean body mass and poorer scores on subjective and objective indices of functional health than did those who were identified by weight loss alone. Defined in this multi-dimensional way, fewer patients meet the criteria for cachexia syndrome. But those who did meet these criteria were likely to experience devastating consequences.

Appendicular refers to the arms and legs.



This slide details adverse outcomes associated with the development of cancer cachexia.

- Body weight, tolerance to treatment, quality of life, and survival time are *decreased* by cancer cachexia.
- With cancer cachexia, weakness, infections, and other complications are *increasingly likely to occur*.



Body mass index does not distinguish between muscle and fat and therefore does not identify signs of muscle wasting.

Body composition can be measured by anthropometry, bioelectrical impedance analysis, dual energy x-ray absorptiometry, magnetic resonance imaging, or computed tomography (CT) scans. As with total weight loss, loss of lean body mass is directly correlated with poor tolerance to treatment, decreased quality of life, and decreased survival.



CT imaging can distinguish between different adipose deposits (visceral, subcutaneous, and intermuscular).

CT images are routinely available for most cancer patients for diagnosis and monitoring of treatment and disease progression. Image analysis software is available to analyze CT scans for body composition. Diagnostic images used to identify muscle wasting. Can evaluate both muscle and fat

Red color indicates skeletal muscles: *rectus abdominus*, oblique and lateral abdominal muscles, psoas, paraspinal muscles. Patient at left shows sarcopenia (severe muscle depletion); both patients have identical BMI (28 kg/m²) and body surface area.

Computed tomography (CT) images of skeletal muscle at defined vertebral landmarks: the 3rd lumbar vertebra and the 4th thoracic vertebra Because these images are readily available for most cancer patients, they can provide a way for clinicians to monitor nutritional status over time based on:

- · skeletal muscle wasting
- altered distribution of body fat
- · accumulation of visceral adipose tissue
- pathological accumulation of lipids in tissues (i.e., hepatosteatosis, myosteatosis)

Computed Tomography (CT) Images of Skeletal Muscle

- A way to monitor nutritional status over time based on:
- skeletal muscle wasting altered distribution of body fat
- accumulation of visceral adipose tissue
- · pathological accumulation of lipids in tissues (i.e., hepatosteatosis, myosteatosis)



When patients with cancer lose lean body mass, there can be significant effects on clinical and functional status.

Research has shown reduced functional status in cancer patients who have lost lean body mass. In patients with stage 3 and 4 head and neck cancer who lost lean body mass there was a significant decline in physical performance, a significant increase in functional dependence with ADLs, and a significant decrease in total physical activity level for household, leisure-time, and sports activities.

In addition, research has also shown that a loss of lean body mass is associated with reduced tolerance to treatment as demonstrated by dose reduction, treatment interruption or discontinuation as well as decreased survival. A small study of lung cancer patients who received radiation showed that in patients with decreased body protein, there was earlier recurrence of disease and a decreased survival. Also, a large retrospective study of over 1500 patients treated over a 6 year period showed that patients with weight loss received less treatment, had decreased survival, and decreased treatment response, quality of life and performance status.



2115 patients with solid tumours of the respiratory or gastrointestinal tract from a cancer treatment centre serving northern Alberta, Canada

 Prado CM, Lieffers JR, McCargar LJ, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *Lancet Oncol.* Jul 2008;9(7):629-635.

This study provides evidence of the great variability of body composition in patients with cancer and links body composition, especially sarcopenic obesity, to clinical implications such as functional status, survival, and potentially, chemotherapy toxicity.

- Tan BH, Birdsell LA, Martin L, Baracos VE, Fearon KC. Sarcopenia in an overweight or obese patient is an adverse prognostic factor in pancreatic cancer. *Clin Cancer Res.* 2009;15:6973–79.
- Prado CM, Birdsell LA, Baracos VE. The emerging role of computerized tomography in assessing cancer cachexia. *Curr Opin Support Palliat Care*. 2009;3:269–75.
- Prado CM, Baracos VE, McCargar LJ, et al. Body composition as an independent determinant of 5-fl uorouracil-based chemotherapy toxicity. *Clin Cancer Res.* 2007;13:3264–68.
- Prado CM, Baracos VE, McCargar L, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. *Clin Cancer Res.* 2009;15:2920–26.

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In a study of 55 women with metastatic breast cancer who were receiving capecitabine, sarcopenia was found to be a factor in dose-limiting toxicity and treatment interruptions (dose reductions or delays). Twenty-five percent of the women in the study were classified as sarcopenic, which occurred in normal weight, overweight, and obese individuals. Toxicity developed in 50% of sarcopenic patients compared with only 20% of nonsarcopenic patients (P = 0.03). Patients with sarcopenia also experienced shorter time to tumor progression (101.4 days; confidence interval, 59.8-142.9) compared to nonsarcopenic patients (173.3 days; confidence interval, 126.1-220.5; P = 0.05).

 Prado CM, Baracos VE, McCargar LJ, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. *Clin Cancer Res.* Apr 15 2009;15(8):2920-2926.

Lean Body Mass and Cancer Treatment

- Patients with metastatic breast cancer receiving capecitabine (n = 55)
 - 25% identified as sarcopenic
 - Low LBM is a determinant of chemotherapy toxicity and time to progression
 - Toxicity present in 50% of sarcopenic patients compared with only 20% of nonsarcopenic patients (P = 0.03)
 - Time to tumor progression shorter in sarcopenic patients than in nonsarcopenic patients (101.4 vs 173.3 days, P = 0.05)



N=55 patients

Sorafenib accelerates LBM wasting

Dose-limiting toxicity (DLT) was most common (41%) in sarcopenic patients whose body mass index (BMI) was <25 kg/m².

This difference was especially prominent in males, of which those with DLT were on average 3.3 units of BMI lighter than those without (P < 0.02). Males with DLT had significantly less skeletal muscle than those without DLT.

Antoun S, Baracos VE, Birdsell L, Escudier B, Sawyer MB. Low body mass index and sarcopenia associated with dose-limiting toxicity of sorafenib in patients with renal cell carcinoma. *Ann Oncol.* Aug 2010;21(8):1594-1598.

Lean Body Mass and Cancer Treatment

Patients with renal cell carcinoma receiving sorafenib (n = 55) • BMI < 25 kg/m² with decreased skeletal muscle mass is a significant predictor of dose-limiting toxicity

		Variable, average (SD)	Patients with dose-limiting	Patients who received the entire planned dose	Statistical values, P
		Male	n = 8	<i>n</i> = 29	
		Weight (kg)	75.1 (9.9)	84.8 (12.9)	NS
		BMI (kg/m ²)	24.3 (2.7)	27.6 (3.5)	0.02
		Skeletal muscle L3 index ^a	48.6 (4.4)	54.1 (6.0)	0.02
		Adipose tissue L3 index ^a	92.3 (56.7)	118.4 (51.0)	NS
				Antoun S, e	et al. Ann Oncol. Aug 2
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Since weight loss is common among cancer patients, a number of nutritional and pharmacological strategies have been tried. In patients with cancer cachexia, the conventional strategies listed on this slide have supported weight stabilization, and sometimes weight gain. However, they provide little or no help for increasing lean body mass. The main reason these strategies have been met with little success is that they do not address the physiological mechanisms underlying cachexia.

Nutritional counseling – including the encouragement of standard oral supplements.

A systematic review and meta-analysis of thirteen studies that included 1414 cancer patients evaluated the effect of oral nutritional interventions (defined as dietary advice, oral nutritional supplements, or both) in malnourished patients with cancer. Nutritional intervention was found to result in statistically significant improvements in weight and energy intake. Some aspects of quality of life (emotional functioning, dyspnea, loss of appetite, and global QOL) also showed improvement, but there was no effect on mortality. (Baldwin C, Spiro A, Ahern R, Emery PW. Oral nutritional interventions in malnourished patients with cancer: a systematic review and meta-analysis. *J Natl Cancer Inst.* Mar 7 2012;104(5):371-385.)

Standard oral nutritional supplements – a 1999 review showed that of 11 RCT's (in patients with cancer), 9 investigated weight change; however, only one showed a significant increase in weight in supplemented vs. control patients. (Stratton, RJ and Elia, *M.Clinical Nutrition.* 1999;18, S2:29-84).

Tube feeding (enteral nutrition)

Should be reserved for patients with a functioning GI tract and whose nutritional status cannot be maintained with oral nutrition. Few randomized controlled trials have been conducted in people with cancer receiving enteral nutrition; larger, prospective studies are needed.

Total parenteral nutrition (TPN) – Requires invasive procedures, is expensive, and is associated with potentially serious complications. TPN should be reserved for patients with non-functional GI tracts. A number of randomized trials have evaluated the effect of TPN in people receiving chemotherapy for a variety of tumor types. These studies found that people who received TPN in conjunction with chemotherapy had a lower survival rate than people receiving chemotherapy alone. As a result of this meta-analysis, The American College of Physicians published a position paper discouraging the use of TPN in people with cancer undergoing chemotherapy and recommended further trials to determine which subgroups might benefit from nutrition support

Appetite stimulants may help weight gain, but this weight is mostly as water and fat rather than lean body mass.

Conventional Nutrition Interventions Have Limited Success for Cachexia

- Dietary counselling^{1, 2}
- Standard oral nutritional products^{1, 2}

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- Enteral nutrition²⁻⁴
- Total parenteral nutrition²⁻⁶
- Appetite stimulants⁵⁻⁷

Conventional interventions do not address the mechanisms underlying cachexia

Baldwin C, et al. J Natl Cancer Inst. Mar. 220(2):104(5):377-188.
 van Bokhovie van der Schwarten MA. Eur J Control Inst. 2005; 80uppl 2:574-83.
 Domotor CL, et al. Gastroentero Res. Pract. 2017; 2017:501434.
 Domotor L et al. Mar Market Control Version 2012; 6.
 Gallet NP, et al. Mar Market Controlware: Dia. J and 30:012.
 Gallet NP, et al. Carr Pred/ Cancer. Market 2017;55(2):58-00.
 Berrotterin ES. Ortiz Z. Controme J Database System Res. 2005(2):C0004310.

ProSure. Strength to Fight and Get Back to Life This classic study demonstrates how simply increasing food intake does not overcome the adverse metabolic changes and weight loss attributed to cachexia. The 1993 study by Ovesen and colleagues examined the effects of nutritional counseling on patients undergoing chemotherapy. This study enrolled 105 patients with small-cell lung, ovarian, or breast cancer. Each patient was randomized to receive either no counseling or counseling with the aim of increasing caloric intake to 1.5 to 1.7 x resting energy expenditure. Although patients who received counseling had significantly increased appetites and dietary intakes and increases in triceps skinfold measurement, there was no significant benefit in terms of weight gain, response rate, and overall survival.



A number of treatment strategies have been employed to help build and preserve muscle. I will discuss protein and omega-3 fatty acids, specifically eicosapentaenoic acid, ingredients found in ProSure.



In this presentation, I will review some clinical study results about ProSure, cancer-specific therapeutic nutrition from Abbott.

A key message from today's presentation is that ProSure has been clinically shown to help delay and/or reverse symptoms of cachexia-weight loss, muscle loss and weakness, and decreased physical activity. Use of ProSure as an oral dietary supplement is also recognized to help maintain guality of life, as reported by patients. Used early in the course of disease. ProSure is expected to help prevent and/or delay development of the harmful symptoms of cachexia.

Cancer-Specific Nutrition May Help Delay or Reverse Cachexia-Related Weight and Lean Body Mass Loss 0 3 3 prosure prosure Cancer-specific nutrition may also help maintain or restore quality of life by relieving symptoms, enhancing strength, and supporting physical activity. ProSure. Strength to Fight and Get Back to Life Abbott

Dietary eicosapentaenoic acid (EPA) benefits people with cancer by attenuating cachectic mechanisms. EPA is a long-chain polyunsaturated omega-3 fatty acid, which is synthesized by marine algae. EPA occurs naturally in deep-sea oily fish such as salmon, mackerel, herring, and sardines. In turn, when humans eat fish, they build up EPA reservoirs, which vary according to eating habits of populations and individuals.

Long-chain PUFAs such as EPA are the main components of phospholipids in cell membranes, thus playing a structural role in cells. Cell membrane PUFAs also serve as a reservoir of lipid precursor molecules needed for synthesis of regulatory molecules, e.g., prostaglandins and leukotrienes. These molecules variously control cellular inflammatory processes in the human body.

Sourced from the diet, PUFAs such as arachidonic acid produce prostaglandins and leukotrienes that are highly inflammatory; EPA is a precursor to mediators that are similar but with lessinflammatory properties. Dietary intake of EPA may help avert excessive and harmful inflammatory responses to tumors.

Eicosapentaenoic Acid (EPA), a Novel Nutritional Approach

- Long-chain omega-3 fatty acid (20:5n-3) found naturally in deep-sea oily fish
- Component of cell membranes
- Decreases proinflammatory cytokine production^{1, 2, 3, 4} .
- Down-regulates the inflammatory response^{1, 2, 3, 5}

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Down-regulates level/activity of proteolysis-inducing factor (PIF)^{3, 6}

Eicosapentaenoic acid (EPA)

.0



In animal and human studies, dietary EPA (fish oil or pure EPA), has been linked with a wide range of beneficial effects in conditions of excessive inflammation, namely

Decreases proinflammatory cytokine production^{1, 2, 3, 4}

Down-regulates the inflammatory response^{1, 2, 3, 5}

Down-regulates level/activity of proteolysis-inducing factor (PIF)^{3, 6}

1. Wigmore SJ, et al. Nutrition. Jan 1996;12(1 Suppl):S27-30.

- 2. Wigmore SJ, et al. Clin Sci (Lond). Feb 1997;92(2):215-221.
- 3. Barber MD, et al. *Nutr Cancer.* 2001;40:118-124.

4. Endres S, et al. N Engl J Med. Feb 2 1989;320(5):265-271.

5. Jho D, et al. Am Surg. Jan 2003;69(1):32-36.

6. Lorite MJ, et al. Br J Cancer. 1997;76(8):1035-1040.

Based on these actions, dietary EPA is expected to lessen symptoms of cancer cachexia. Does it work? Let's move to the next slide.

Dietary EPA Blunts Inflammation



Intake of EPA has been specifically shown to stabilize weight in weight-losing patients with tumors. This slide summarizes designs and results of 2 oral EPA nutrition studies conducted by Wigmore and colleagues.

Wigmore 1996—Study done with fish oil (max EPA) capsules. Weight-losing patients with unresectable pancreatic tumors (n=18) were instructed to take up to 16 one-gram fish oil capsules (2 g EPA) each day over a median interval of 3 months. Median weight change +0.3 kg/month.

Wigmore 2000—Dose response study. 26 patients with unresectable pancreatic cancer. Patients instructed to take up to 12 capsules each day (6 g EPA) (high-purity EPA capsules—not available on the market). Saw no advantage with 6 g over 2 g/day in previous study.

During the study weight stabilized. Such results contrast with the usual weight-losing profile of patients with pancreatic cancer. 2 g EPA per day appears to be the optimum dose for weight stabilization. With fish oil capsules, patient generally had difficulty consuming the recommended amount (up to 16 capsules/day). Some patients complained of a fishy aftertaste, fishy odor on their skin, or transient diarrhea.

Dietary EPA Studies

Study	Design	Results	
Wigmore SJ, et al. Nutrition. 1996;12:S27.	 18 patients with pancreatic cancer Weight loss of 2.9 kg/month before EPA 2.0 g EPA/day for 12 wks 	Weight stabilization	
Wigmore SJ, et al. Nutr Cancer. 2000;36:177.	 26 patients with pancreatic cancer Weight loss of 2.0 kg/month before EPA 6 g EPA/day for 12 weeks 	Weight stabilization	

<2 g EPA/day MAY NOT BE EFFECTIVE
 2 g EPA/day = recommended dose
 6 g EPA/day MAY NOT BE BETTER than 2 g



I will now review results of several studies using ProSure in a number of different cancer types.



Hypothesis - If fish oil and EPA stabilize weight by attenuating harmful metabolic and inflammatory changes associated with cancer cachexia, EPA in combination with energy, protein and micronutrients will support new tissue synthesis and will result in weight gain. To test this hypothesis, a specialized EPA containing nutritional formulation, now known as ProSure, was developed.



ProSure[®], a therapeutic nutritional product, is scientifically formulated to help manage cancer cachexia and weight loss.

- ProSure[®] is enriched with eicosapentaenoic acid (EPA), an omega-3 fatty acid that helps decrease the harmful inflammatory and metabolic changes caused by the presence of cancer cells.
- ProSure[®] contains a high amount of high quality protein to help build lean body mass (16 g protein per serving)
- ProSure[®] is calorically dense (300 calories per serving)

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The Fearon et al. 2003 study was designed as a prospective, double-blind, randomized, multi-center trial enrolling 200 patients with unresectable pancreatic cancer who were experiencing weight loss. This study was conducted in 12 sites in 7 countries (England, Scotland, Netherlands, Italy, Belgium, Australia, Canada).

Patients were randomly assigned to receive either ProSure or an isocaloric, isonitrogenous control supplement without EPA. The therapeutic goal was for each patient to consume 2 servings per day for 8 weeks. Median weight loss was 3.3 kg/month before enrollment. 95 patients were randomized to the experimental group that received ProSure; 105 patients were randomized to the control group that received an isocaloric, isonitrogenous nutritional product. The difference between nutrition supplements was that ProSure contained EPA, and the control product did not (a specifically designed control, not a marketed formula).



Results illustrated on this slide show gains in weight and lean body mass in patients who consumed ProSure. The effects of ProSure are dose-related, and results suggest that patients need to consume 1.5 to 2 servings/day of ProSure nutrition supplement for optimal benefit.



Moses and colleagues studied the effect of ProSure on physical activity level (PAL) in 19 weight-losing patients with pancreatic cancer. Study participants were asked to consume 2 servings/ day of nutritional supplement (control, n=12; ProSure, n=7) over an interval of 8 weeks. The control supplement was identical to ProSure, but it lacked EPA.

Total energy expenditure (TEE) was measured at baseline (within the first 14 days of the study) and again between 6 and 8 weeks using the doubly-labeled water technique. Resting energy expenditure (REE) was measured by indirect calorimetry, and PAL was calculated by the formula PAL=TEE/REE.



There was a statistically significant (P = 0.005) increase from baseline PAL in the ProSure group. There was no significant PAL change in the control group; most patients remained confined to bed. This significant increase in PAL parallels the significantly increased Karnofsky Performance Status previously reported for pancreatic cancer patients who received ProSure nutrition. (Barber, et al. *Br J Cancer.* 1999).

The values for the chart on the slide are from: *Moses AG, Slater C, Barber MD, Fearon KC, Preston T. An experimental nutrition supplement enriched with n-3 fatty acids and antioxidants is associated with an increased physical activity level in patients with pancreatic cancer cachexia. *Clin Nutr.* 2001;20 (Suppl 3):21.



A study by Guarcello and colleagues evaluated weight losing patients with lung cancer who were scheduled to undergo chemotherapy. Patients (n=46) were randomized to supplement their usual oral diet with either 2 servings per day of ProSure (high-protein, energy-dense, low-fat, EPA-containing nutrition supplement) or an isocaloric, isonitrogenous nutrition supplement without EPA. The study length was 60 days, with assessments at baseline, 30 days, and 60 days.



Over the 2-month study interval when chemotherapy was administered, only patients who received ProSure showed significant increases in body weight and quality of life, as shown in this table.

ProSure-consuming patients also had significant increases in energy and protein intakes, as well as improved appetite. In patients who consumed ProSure, negative acute phase proteins increased (prealbumin, transferrin levels), while C-reactive protein, an inflammatory marker, decreased. Study Findings: Significant Increase in Body Weight and Functional Quality of Life (QOL) with ProSure

	ProSure (n=26)			Co	ntrol (n=20)	
	Baseline	30 days	60 days	Baseline	30 days	60 days
Body weight, kg	57.7	58.6*	58.6*	59.1	57.0	59.1
QOL EORTC QLQ-C30 FS†	64.4	82.2*	77.7*	62.2	72.4	72.2

*P< 0.05 vs baseline (Wilcoxon Test) †EORTC-QLQ-C30 FS, self-administered 30-item questionnaire measuring physical functioning

	Guarcello M, et al. Nutr Ther & Metab. 2007;25(1):25-30.
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This slide summarizes some of the most recent clinical studies of ProSure. As will be summarized in the following series of slides, intake of ProSure nutrition provided benefits to patients with many other types of cancer, including those who were undergoing active cancer treatment.

ProSure Clinical Trials Show Efficacy in Other Cancer Types Bayram 2009 Children with leukemia and solid tumors Read 2007 Adults undergoing chemotherapy for advanced colorectal cancer Van der Meij 2010, 2012 Adults receiving chemo-radiotherapy for lung cancer Ryan 2009 Adults requiring surgery for esophageal cancer

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ProSure. Strength to Figh and Get Back to Life Bayram et al conducted a study of children with cancer who were receiving chemotherapy. Children were advised to drink two 8-oz servings per day (morning and evening) of ProSure in addition to their usual food. Weight and body mass index were evaluated at 3 months.



After 3 months, only 6.1% of children in the ProSure group lost weight, compared to 47.4% of children in the control group. Similarly, 12.1% of the children in the ProSure group had a lowered body mass index (BMI), compared to 52.6% of children in the control group. These differences were associated with a higher rate of cancer remission in the ProSure group compared to the control group (87.9% vs 63.2%, P=0.036).

Pediatric applications are advised at the discretion of the treating physician.



In a prospective, open-label study by Read and colleagues, patients with advanced colorectal cancer were given ProSure 3 weeks before chemotherapy began and for 9 weeks during chemotherapy. n=23 patients enrolled, n=20 patients completed 3 weeks; and n=15 completed 9 weeks. Study measures included weight, body composition, C-reactive protein, and cytokine levels.



Results of the Read study showed that drinking ProSure (average daily intake 408 mL) during chemotherapy produced:

- significant increase in weight
- preservation of lean body mass (and although the improvement in LBM was not statistically significant, an approximate increase of 1.4 kg LBM may be clinically relevant and contribute to the improvement in QOL)
- significant decrease in C-reactive protein, an inflammatory marker, by end of trial (during or after chemotherapy)
- maintained quality of life (QOL)

Study Findings: ProSure Increases Weight, Preserves LBM, and Maintains QOL During Chemotherapy

Nutritional and inflammatory markers and functional status for patients requiring chemotherapy for advanced colorectal cancer, Mean values (SD)

Marker	Baseline	Pre-chemo End week 3	During or post-chemo End week 9	P value*
Weight, kg	75.9 (17.0)	78.4 (17.5)	78.4 (17.4)	0.03
Lean body mass, kg	50.3 (10.7)	51.4 (10.2)	51.7 (10.6)	NS
C-reactive protein, mg/L	18.2 (13.9)	33.1 (32.6)	19.4 (17.7)	0.004 (wk3) 0.02 (wk 9)
QOL-overall well-being	7 (2.2)	7 (1.7)	8 (1.7)	0.05

*P values are for baseline vs timepoint value; NS, not significant

		Read J, et al. Support Care Cancer. 2007;15:301-307.
ProSure. Strength to Fight and Get Back to Life	40	Abbott A Promise for Life

van der Meij and colleagues conducted a double-blind, randomized, controlled trial of patients with stage III non-small cell lung carcinoma (n=40). Patients were asked to consume two servings a day of either ProSure nutrition supplement or an isocaloric control supplement during 5 weeks of chemo-radiotherapy.

Outcome measures: included body weight, physical activity (by physical activity monitor), and quality of life (by EORTC QLQ-C30).



Findings of the van der Meij study underscore the beneficial effects of high-protein, calorically-dense, low-fat nutrition with EPA (ProSure) on nutritional status and physical activity in patients with lung cancer undergoing chemo-radiotherapy.

Physical activity was measured by a sophisticated physical activity monitor. This device was more than a pedometer because it was able to measure a greater range of physical activity.

Compared to the control group, the ProSure group had higher physical activity levels at weeks 3 and 5 (P < 0.05). In addition, there was better weight maintenance than controls during weeks 2 and 4 (P < 0.05) and better maintenance of fat-free mass after 3 and 5 weeks (P < 0.05).



Esophageal cancer is particularly challenging to patients because of severity of both the cancer and its treatment. Ryan and Reynolds also showed benefits with the use of ProSure by patients undergoing surgery for esophageal cancer (esophageal resection or esophagectomy).

For this study, patients were randomly assigned to receive either ProSure (2 servings, with a total of 2.2 g EPA per day; n=28) or an isocaloric, standard nutritional formula (n=25) for 5 days before and for 21 days after surgery. Measures included lean body mass (measured by bioelectrical impedence analysis [BIA]) and serum cytokine levels.

Ryan 2009



In the hospital, 39% of patients fed the standard formula experienced severe weight loss (defined as > 5% total body weight), but only 8% of patients fed ProSure showed such loss, a difference that was statistically significant (P =0.03).



Patients fed ProSure had no significant loss in lean body mass throughout the study, while patients fed control (standard enteral nutrition without EPA) lost significant amounts of muscle from the arm (0.2 kg; P = 0.0.01), trunk (1.4 kg; P = 0.03), and leg (0.3 kg; P = 0.05)—a total loss of 1.9 kg lean body mass.





While early studies demonstrating ProSure efficacy were conducted in severe weight-losing patients with pancreatic cancer, more recent study results have confirmed benefits of ProSure in patients with a wide range of cancer types, as summarized on this slide.



Further, the well-recognized benefit of ProSure nutrition therapy to promote weight gain in cancer patients has now been confirmed and extended to include a wide range of other important benefits. ProSure also:

- · Helps build or maintain lean body mass
- Improves appetite and dietary intake
- Attenuates the proinflammatory response
- Increases strength
- Improves physical activity
- · Improves quality of life
- Reduces treatment interruptions/toxicities

Clinic Studies c	cally-Supported Benefits of ProSure®
• P	romote weight gain ¹⁻¹⁴
• B	uild or maintain muscle ^{1, 3-5, 8, 10, 12, 15, 16}
• In	nprove appetite and dietary intake ^{1, 4, 5, 8, 9, 16-18}
• A	ttenuate the proinflammatory response ^{2, 9, 10, 14-16, 19, 20}
ProSure i	is also associated with:
• Inc	creased strength in those who gained weight ²¹
• Im	proved physical activity ^{1, 18, 22} Clinically Demonstrated Results
• Im	proved quality of life ^{4, 5, 9, 10, 16, 17, 21-23}
• Re	educed treatment interruptions/toxicities ^{13, 16, 23, 24}
1. Barber M, et a 2003;52:1479-1 Ann Nutr Metab 10. Read J, et a Head Neck, Jul 15. Ryan AM, et 2004;23:239-24 (2):140. • 21. y	al die / Gene 1998/81 40.86, - 3 Bahren Mit ein / Mon Genero 2019/21 (1974) 3 Barben Mit ein (Gri 66, 2009).8389/84, - 4 Fannes K ein G. 6, 46, - 4 Eause 26, 000 - 5 Guard Conference / 2007/21 (- 1, all.a), - 4 - 2 (- 2016).000 - 2019/21 (- 2018), - 2018, -

- When prescribing ProSure, the recommended intake is 2 servings per day for at least 3 weeks—in addition to normal food.
- ProSure can be started early to help manage and/or delay onset of cancer cachexia.
- To help improve tolerance of cancer treatments (chemotherapy, radiation therapy, or surgery), ProSure intake can be started for a week or more before treatment or surgery.
- A person should continue to take ProSure for as long as he or she is at risk for ongoing weight loss and inflammation.



This slide summarizes the impact of cancer cachexia; describes the rationale for energy-dense, high-protein, EPA-containing ProSure as therapeutic nutrition for people with cancer; and reviews clinically-proven benefits of ProSure nutrition.

Abbreviations: EPA, eicosapentaenoic acid

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Abbott

ProSure. Strength to Figh and Get Back to Life This slide summarizes take-home messages about ProSure based on the presentation today. ProSure is:

- Clinically-proven to provide a range of health benefits for people with cancer
- A high-protein, energy-dense formulation that contains an efficacious amount of EPA
- EPA attenuates harmful metabolic changes underlying cancer cachexia and weight loss
- Provides measurable results in some patients in as few as 3 weeks with 2 servings per day

ProSure Conclusions	
 ProSure is a clinically-proven¹⁻¹⁴ nutritional product that may help people with cachexia and weight loss or risk for these conditions 	
ProSure is a high-protein, energy-dense formulation that contains an efficacious amount of EPA, which has been shown to attenuate certain metabolic changes underlying cancer cachexia and weight loss ¹⁻¹⁸	1
Results in some patients can be seen in as few as 3 weeks ¹⁻³ with as little as 2 servings daily	
1. Bunch M, et al. Bri J, Can. 1998;11:0:48 2. Bunch MD, et al. Nucl Cancers 2011;40:111-314 3. Banch MD, et al. Clin Sei 2000;93:30:30:4 F. 2005;21:1171-1164 6. Bunch JD, Cancer S, Sopper Clan Cancers Apr 2005;11(4):270:4 1, Junky, et al. / Con Crest. 2005;21(2):2469;271 1, 3. Sub Anal Mark Apr 2005;45(2):56:4 8. una der MBB, et al. J Alar, Cot 2001;14(9):1774-1780 8. Gauersisk M, et al. Nucl Free & Messa 2007;24 3. Sub Anal Mark Apr 2005;45(2):56:4 8. una der MBB, et al. J Alar, Cot 2001;14(9):1774-1780 8. Gauersisk M, et al. Nucl Free & Messa 2007;25 4. Sub Anal Mark Apr 2005;45(2):57:4 8. Una der MBB, et al. J Alar, Cot 2001;14(9):1774-1780 8. Gauersisk M, et al. Nucl Free & Messa 2007;25 4. Sub Anal M, and 2007;27(13): - 11. Tatal M, et al. Alar (Anal Cot 2010;25(2)):71:74-11 14. Vasa A, et al. (PRIJ) Aprente Chemology Anal April A	aron K, et al. Gut. s Luis DA, et al. Ann 1):25:30. + 10. sed HG, et al. Head s. 15. Wigmore SJ, Med. Feb 2
ProSure. Strength to Fight and Get Back to Life Strength to Fight Strengt Strengt Strength To Fight St	Abbott A Promise for Life



This case is intended to support discussion with clinicians based on the preceding presentation of background information. The following are points to emphasize:

- Lung cancer and its treatment by surgery are both likely to increase inflammatory processes in the patient's body.
- Caloric deficits and weight loss are therefore likely in a patient such
 - as Clive.
- Consider the following points in your discussion about cancer nutrition:
 - ProSure therapy is clinically proven to promote weight gain, help build lean body mass, enhance physical activity, increase strength, and improve appetite and dietary intake.
 - ProSure also attenuates inflammatory responses that can occur with surgery.
- A recent clinical study showed health benefits of ProSure nutrition therapy (significantly better weight maintenance and physical activity- van der Meij 2010, 2012)
- ProSure is recommended at a dose of 2 servings per day, usually taken in addition to usual food between meals.
- The goal for nutritional therapy for Clive is to maintain or improve his nutritional status and quality of life during cancer therapy, and to improve tolerance to treatment.



In addition to her small stature and recent weight loss, this patient is at nutritional risk due to the tumor and its treatments (surgery and chemotherapy).

Consider the following points in your discussion about cancer nutrition:

- ProSure therapy is clinically proven to promote weight gain, help build lean body mass, enhance physical activity, increase strength, and improve appetite and dietary intake.
- ProSure also attenuates inflammatory responses that can occur with surgery.

Dosing and regimen for ProSure therapy:

- In addition to usual food, ProSure is recommended as 2 servings per day.
- In a study by Read et al, ProSure was started 3 weeks before chemotherapy began and continued during chemotherapy.
- ProSure nutrition should be considered as long as chemotherapy is ongoing.



To summarize, cachexia is a serious but reducible risk.



With ProSure, cachexia doesn't have to interrupt cancer patients' lives.



