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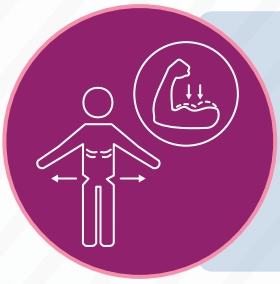
Clinical Management of Cancer Cachexia: A Multimodal Treatment Approach

Key components of multimodal approach and clinical trials on treatments of cancer cachexia

Cancer cachexia[1,2]



Multifactorial syndrome characterized by a persistent loss of skeletal muscle mass that cannot be fully reversed by nutritional support

Leads to progressive functional impairment, reduces the quality of life in patients with cancer, and is associated with poor survival

It is not typically seen in early stage, easily treatable patients with cancer

Standard treatment approaches[2,3,4]

Anti-neoplastic therapy

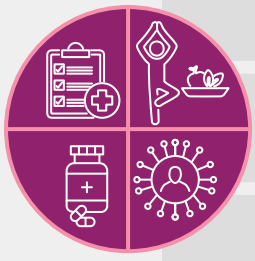
- Targets tumor progression and indirectly addresses cachexia-related mechanisms
- Can improve cachexia when combined with symptom management

Optimal palliation of symptoms

- Addressing pain, anorexia, nausea, diarrhea, and other nutritional impact symptoms like xerostomia (dry mouth) and dysgeusia (altered taste) improves treatment outcomes
- Tailoring nutritional care based on the patient's health condition and clinical trajectory is crucial

Owing to the extensive metabolic changes involved, including increased inflammatory responses, reversing cachexia by improving nutritional status and body composition poses significant challenges that require multimodal interventions to optimize treatment outcomes[3]

Need for multimodal treatment strategies[3,4,5]



Cachexia is not typically diagnosed in the early stage

Combination treatment strategies are recommended to address the diverse symptoms that arise due to cancer cachexia

Unimodal treatments, including pharmacologic management, exercise, and nutritional interventions, have had limited success in reversing cancer cachexia in clinical trials

Comprehensive and integrated treatment approach is vital for improving the quality of life of patients with cancer cachexia

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Management of cancer cachexia: Current landscape and clinical recommendations[5,8]

No FDA-approved medications currently exist for cachexia

ESMO and ESPEN Guidelines advocate a multimodal approach: nutrition, exercise, and pharmacotherapy[3,6,7]

ESMO: European Society For Medical Oncology; ESPEN: European Society for Clinical Nutrition and Metabolism

American Society of Clinical Oncology (ASCO) guidelines and recommendations to manage cachexia

Nutritional interventions

- Patients can be referred to registered dietitians for assessment and counseling
- Outside the context of a clinical trial, enteral tube feeding or parenteral nutrition should not be routinely offered

Pharmacological interventions

- There is limited evidence to strongly endorse the use of pharmacologic agents and clinicians may opt not to prescribe medications for cancer cachexia management
- Clinicians may consider low-dose olanzapine once nightly to improve weight gain and appetite
- The choice of agent and duration of treatment depends on the treatment goals and assessment of risks versus benefits

Other intervention: Exercise–evidence is insufficient for a recommendation

It is important that HCPs are aware of the guidelines to ensure best practice in varying clinical scenarios

Pharmacological agents in clinical trials for the treatment of cancer cachexia

Anamorelin: ghrelin receptor agonist

- Showed improvements in body weight and appetite in real-world settings and was recently approved in Japan
- However, it did not receive FDA approval due to a lack of improvement in hand grip strength

Ponsegromab[9]: a monoclonal anti-GDF-15 antibody

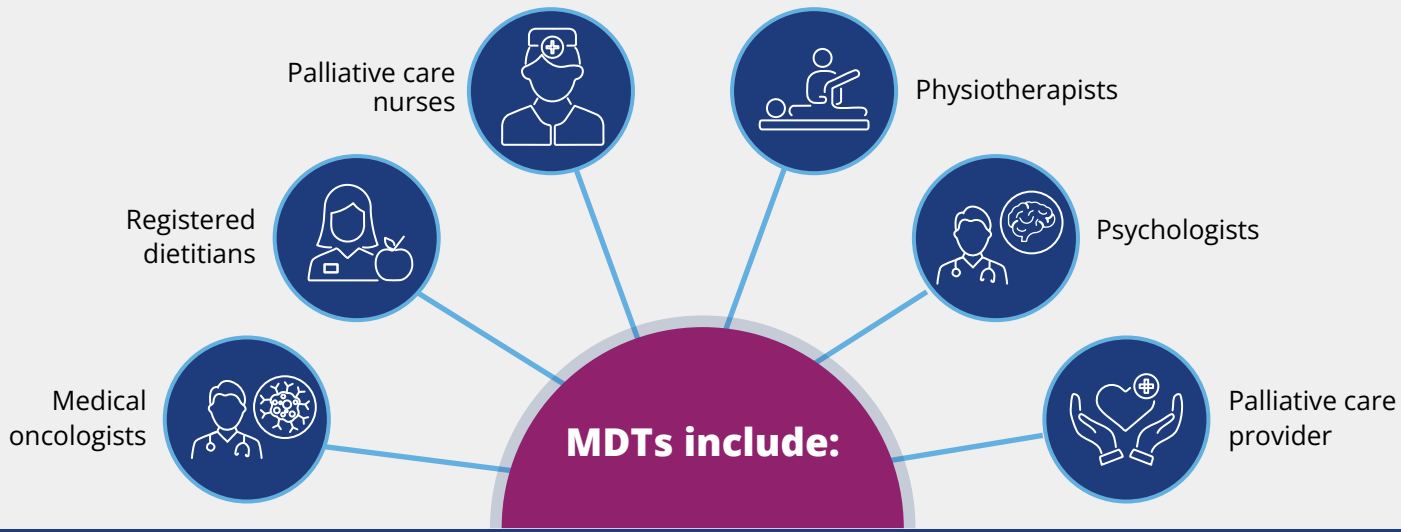
- It is a monoclonal antibody and is currently under investigation
- Positive outcomes and reduced cachexia symptoms noted in a phase 2b trial among patients

Several other pharmacologic agents are being explored in clinical trials

HCPs must stay updated on the results of these clinical trials and evolving guidelines to ensure they are equipped with the latest knowledge for improving patient outcomes in cancer cachexia management

Cachexia care model: multidisciplinary team (MDT)[4,10]

Cancer cachexia requires a team-based, multidisciplinary approach to ensure holistic management of the syndrome



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Clinical trials involving multimodal intervention care (MIC) models for cachexia

Multimodal exercise nutrition anti-inflammatory cachexia (MENAC) trial[11]

Objective

- To evaluate a multimodal intervention approach in patients with stage III or IV lung and pancreatic cancer undergoing systemic anti-cancer treatment

Results

- Stabilization of body weight in patients assigned to multimodal treatment compared to those receiving standard care
- No conclusive difference in muscle mass or in mean step counts between the groups

Multimodal cachexia intervention stabilized body weight compared to standard care after six weeks

Effect of MIC on cachexia in patients with advanced cancer compared to conventional management (MIRACLE study)[12]

Objective

- To investigate the efficacy and safety of a multimodal intervention comprising anti-inflammatory drugs, omega-3-fatty acids, nutritional supplements, counseling, physical exercise, psychiatric intervention, as well as Bojungikki-tang, in patients with advanced gastrointestinal cancer or lung cancer undergoing active palliative chemotherapy

Results

- Median changes in total lean body mass in the MIC group:
  - Increased without statistical significance compared to the conventional palliative care (CPC) group
- No difference in median handgrip strength between MIC and CPC groups

Multimodal intervention in the MIRACLE study did not improve cachexia-related outcomes and further studies are needed

Nutrition and Exercise Treatment for Advanced Cancer (NEXTAC)-ONE study[13]

Objective

- To evaluate the feasibility of early non-pharmacological, multimodal interventions for elderly patients with cancer with a high risk of cachexia

Results

- High attendance rate and satisfactory safety profile for the NEXTAC program
- Increased adherence rates with respect to supplement consumption, completing the diaries, and wearing pedometers/accelerometers
- First randomized trial to evaluate the efficacy and safety of a multimodal intervention

NEXTAC-TWO study[14]

Objective

- To determine the effectiveness of a 12-week NEXTAC program in improving disability-free survival in elderly patients (≥70 years) with advanced pancreatic or non-small cell lung cancer

Results

- Completion rate in the NEXTAC arm: 98.4%
- Median disability-free survival period
  - NEXTAC arm: 478 days
  - Observation/control arm: 499 days
  - No significant difference ($p = 0.884$)

NEXTAC-THREE study, an ongoing prospective study comprising a 12-week NEXTAC program combined with an appetite stimulant, ghrelin receptor agonist, may prevent disability while simultaneously improving skeletal muscle mass in patients with cancer cachexia

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Comprehensive educational strategies for increasing caloric intake and symptom management of cachexia[1,5,15,16]

Patient guidelines

Educate patients on the benefits of the frequent consumption of small meal portions every two to three hours

Provide practical advice on incorporating high-calorie and high-protein foods

Pharmacological agents to manage symptoms, such as dysgeusia, pain, nausea, and constipation and improve nutritional intake

Encourage moderate physical activity, which helps maintain muscle and increases hunger

Advice for limiting fluid intake during meals

Healthcare professional guidelines

Regularly evaluate patients' weight and nutritional status using tools like the Patient-Generated Subjective Global Assessment

Foster interdisciplinary collaboration among core MDT members

Retrain to counsel patients and caregivers effectively and set realistic goals

Design personalized dietary plans and recommend oral nutritional supplements when needed

Identify and address patient's emotional, social, and financial factors affecting nutritional intake

Conduct follow-ups to adapt treatment based on patient progress

Key messages

- **Effective palliation of symptoms, such as pain, anorexia, nausea, and diarrhea, is essential to improve nutritional intake and prevent further weight loss and muscle wasting**
- **A comprehensive multimodal approach utilizing both pharmacologic and non-pharmacologic interventions can effectively reverse or stabilize weight and muscle loss in cachexia**
- **MDTs comprising oncologists, palliative care specialists, dietitians, physical therapists, nurses, social workers, psychologists, and pharmacists play a crucial role in treating cachexia**
- **Patient and caregiver awareness is important for the management of the condition and education on increasing caloric intake should involve practical, stepwise approaches to minimize eating-related distress**

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Art. No.: CD010804

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