

Palliative Care Journal Watch

A partnership between Pallium Canada and several Divisions of Palliative Care and Medicine across Canada and Internationally:

McMaster University, University of Calgary, University of Alberta, Queens University, University of Toronto, McGill University, University of Manitoba, Hadassah-Hebrew University Medical Center

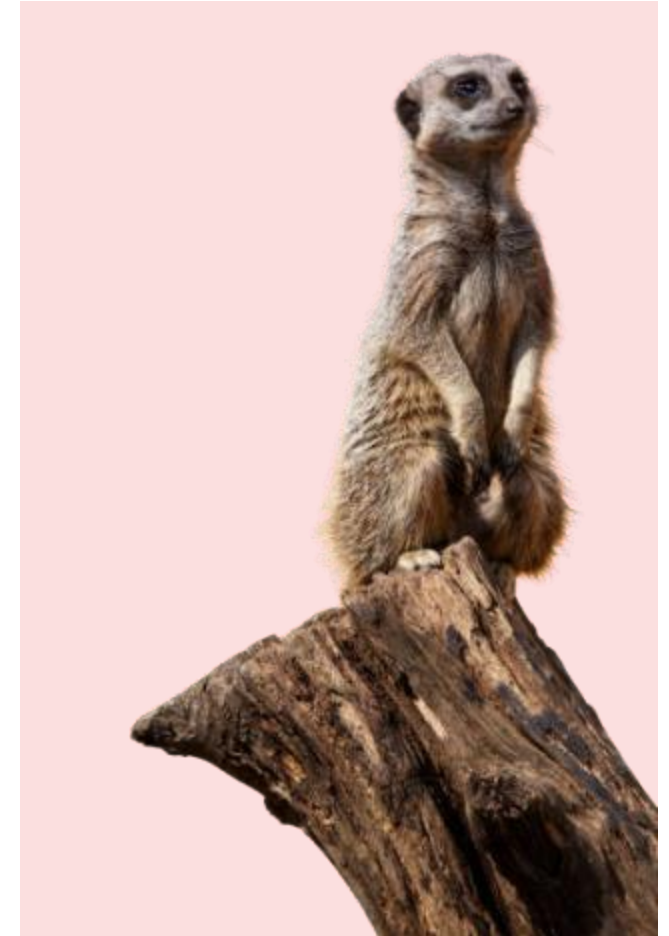


Hosts & Panelists: Dr. Leonie Herx, Dr. Sharon Watanabe, Dr. Vickie Baracos

Date: July 7th, 2025

Welcome to the Palliative Care Journal Watch!

- Keeps you up to date on the latest peer-reviewed palliative care literature.
- Led by palliative care experts from several divisions of palliative care/medicine across Canada and internationally.
 - McMaster University
 - Queen's University
 - McGill University
 - University of Toronto
 - University of Manitoba
 - University of Calgary
 - University of Alberta
 - Hadassah-Hebrew University Medical Center in Israel.
- We regularly monitor over 30 journals and highlight articles that challenge us to think differently about a topic or confirm our current practices.



The Palliative Care ECHO Project

The Palliative Care ECHO Project is a 5-year national initiative to cultivate communities of practice and establish continuous professional development among health care providers across Canada who care for patients with life-limiting illness.

The Palliative Care ECHO Project is supported by a financial contribution from Health Canada. The views expressed herein do not necessarily represent the views of Health Canada.



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What to expect from today's session

- We will present and discuss featured article selections and provide a list of honourable mentions at the end.
- This session is being recorded and will be shared with registrants within the next week.
- All articles featured today as well as those that were featured in past sessions can be accessed on our Journal Watch web page at www.echopalliative.com/palliative-care-journal-watch/

Introductions

Dr. Leonie Herx, MD, PhD, CCFP(PC), FCFP

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Disclosures

Pallium Canada

- National Registered Charitable organization
- Funded by:
 - Health Canada (through contribution agreements 2001-2007, 2013-2018), Patrick Gillin Family Trust (2013-2016), Li Ka Shing Foundation (2019 to current), CMA (2019 to 2022), Boehringer Ingelheim (dissemination of LEAP Lung courses 2019 to current).
 - Partnerships with some provincial bodies.
 - Revenues from LEAP course registration fees and licenses, sales of Pallium Palliative Pocketbook.

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- Health Canada in the form of a contribution program.

Disclosures of Hosts/Guest Panelists:

- Dr. Leonie Herx: No conflicts of interest to declare.
- Dr. Sharon Watanabe: No conflicts of interest to declare.
- Dr. Vickie Baracos: No conflicts of interest to declare.

Mitigating Potential Biases:

- The scientific planning committee had complete independent control over the development of course content.

Featured articles

- Bowers M, Petrasso C, McLuskie A, et al. **Multicomponent Interventions for Adults With Cancer Cachexia: A Systematic Review.** J Cachexia Sarcopenia Muscle. 2025;16(2):e13716. [doi:10.1002/jcsm.13716](https://doi.org/10.1002/jcsm.13716)
- Sandhya L, Devi Sreenivasan N, Goenka L, et al. **Randomized Double-Blind Placebo-Controlled Study of Olanzapine for Chemotherapy-Related Anorexia in Patients With Locally Advanced or Metastatic Gastric, Hepatopancreaticobiliary, and Lung Cancer.** J Clin Oncol. 2023;41(14):2617-2627. [doi:10.1200/JCO.22.01997](https://doi.org/10.1200/JCO.22.01997)
- Arrieta O, Cárdenas-Fernández D, Rodriguez-Mayoral O, Gutierrez-Torres S, Castañares D, Flores-Estrada D, Reyes E, López D, Barragán P, Soberanis Pina P, Cardona AF, Turcott JG. **Mirtazapine as Appetite Stimulant in Patients With Non-Small Cell Lung Cancer and Anorexia: A Randomized Clinical Trial.** JAMA Oncol. 2024 Mar 1;10(3):305-314. [doi: 10.1001/jamaoncol.2023.5232](https://doi.org/10.1001/jamaoncol.2023.5232). PMID: 38206631; PMCID: PMC10784994.
- Groarke JD, Crawford J, Collins SM, et al. **Ponsegromab for the Treatment of Cancer Cachexia.** N Engl J Med. 2024;391(24):2291-2303. [doi:10.1056/NEJMoa2409515](https://doi.org/10.1056/NEJMoa2409515)

Featured Articles

Multicomponent Interventions for Adults With Cancer Cachexia: A Systematic Review

Article Reference:

Bowers M, Petrasso C, McLuskie A, et al. Multicomponent Interventions for Adults With Cancer Cachexia: A Systematic Review. J Cachexia Sarcopenia Muscle. 2025;16(2):e13716. doi:10.1002/jcsm.13716

Presented by:
Sharon Watanabe

Background

- The complex pathophysiology of cancer cachexia suggests the need for a multitargeted intervention
- Many trials have embraced a multimodal approach, investigating combinations of pharmacological, nutritional, exercise and/or psychosocial intervention components
- It is not known how many of these multicomponent interventions (MCI) have targeted all the key features of cachexia or whether interventions that target more key features of cachexia are more effective at improving patient-centred outcomes including QoL
- The effect of tailoring interventions (targeted, individualized) has not been fully explored

Study Objective

- Synthesize studies of MCI for adults with cachexia to evaluate the extent to which they have targeted the key features of cachexia and been tailored to individuals, and whether these characteristics of MCI are associated with differential effects on QoL

Methods

- Systematic review
- Adults with diagnosis of cancer
- $\geq 75\%$ of participants at risk for cachexia (Stage 3/4 lung, upper GI, head & neck)
- Interventions with ≥ 2 components concurrently or sequentially
- Randomized or non-randomized
- Databases, clinical trial registers, grey literature
- Risk of bias tools
- Extracted intervention category, type, features of cachexia targeted, level of tailoring, QoL

Multicomponent Interventions for Adults With Cancer Cachexia: A Systematic Review

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Presented by:
Sharon Watanabe

Key Results

- 62 MCI studies: 39 randomized, 23 non-randomized
- Median age 64.2, weight loss 10%; lung 34%, GI 32%, H&N 12%; Stage 4 81%
- 232 individual components. Type: nutritional 43%, exercise/physical activity 27%, pharmacological 22%, psychosocial 9%. Targets: energy intake 44%, physical function 27%, weight/muscle loss 28%, metabolism 19%. Tailored: 54% tailored.
- 13 studies (10 randomized) had QoL data; all had high/critical risk of bias/concern.
- QoL scores declined in 2, improved in 11 studies. No indication that number of key features of cachexia targeted, or extent of tailoring, was associated with a greater improvement in QoL scores
- 4 studies compared MCI with usual care; QoL scores improved in 3; in 4th, QoL declined in both arms

Key Discussion Points

- First systematic review mapping out combinations of interventions, key features of cachexia targeted, tailoring
- While non-randomized studies provide valuable information, effectiveness of interventions cannot be adequately assessed; larger randomized trials are needed
- Future interventions should include a psychosocial component, use a tailored approach, measure QoL

Strengths and Limitations

- Risk of bias of QoL studies

Practice Impact

- Unclear if multicomponent interventions have significant impact on QoL in cachexia

Discussion

Randomized Double-Blind Placebo-Controlled Study of Olanzapine for Chemotherapy-Related Anorexia in Patients With Locally Advanced or Metastatic Gastric, Hepatopancreaticobiliary, and Lung Cancer

Article Reference:

Sandhya L, Devi Sreenivasan N, Goenka L, et al. Randomized Double-Blind Placebo-Controlled Study of Olanzapine for Chemotherapy-Related Anorexia in Patients With Locally Advanced or Metastatic Gastric, Hepatopancreaticobiliary, and Lung Cancer. J Clin Oncol. 2023;41(14):2617-2627. doi:10.1200/JCO.22.01997

Presented by:

Leonie Herx

Background

- Anorexia is common in advanced malignancies, worsened by chemotherapy
- Affects 40-60% of newly diagnosed cancers, GI and lung more prone
- Associated with insufficient oral intake, compromised nutritional status
- May indirectly worsen chemotherapy tolerance & compromise outcomes
- Current guidelines recommend dietary counselling but limited data to support pharmacological appetite stimulation
- Olanzapine (OLZ)– antipsychotic with DA and 5HT antagonism – stimulates appetite
 - augments appetite when added to megestrol in adv GI & lung ca
 - used routinely in cancer short duration for anti-emetic
 - appetite effects requires extended use

Study Objective

- Can continuous, low-dose olanzapine improve appetite and weight gain among newly diagnosed patients with advanced lung and upper GI cancer starting chemotherapy?

Methods

- Randomized double-blind, placebo-controlled study
- Adults with untreated, locally advanced or metastatic upper GI and lung cancers
- Received OLZ 2.5mg or placebo daily for 12 weeks
- Both groups received nutritional assessment and dietary advice
- **Primary outcomes:**
 - weight gain >5%, appetite (VAS & FAACT ACS score >37)
- **Secondary outcomes:**
 - nutritional status (SGA), QoL, chemotherapy toxicity

Randomized Double-Blind
Placebo-Controlled Study of
Olanzapine for Chemotherapy-
Related Anorexia in Patients
With Locally Advanced or
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Presented by:
Leonie Herx

Key Results

- 124 patients enrolled (OLZ 63, placebo 61), 112 eligible for final analysis (58 OLZ, 54 placebo)
- median age 55, majority (80%) had metastatic cancer (gastric 55%, lung 35%, HPB 10%)
- **Primary outcomes** - OLZ arm significant for:
 - Increased weight gain > 5% (60% OLZ vs 9% placebo)
 - Improved appetite by VAS (43% OLZ vs 13% placebo) & FAACT ACS (22% OLZ vs 4% placebo)
- **Secondary outcomes** – OLZ arm significant for:
 - Improved nutritional scores (43% OLZ vs 9% placebo)
 - Proportion of patients achieving >76% pf recommended daily calories (OLZ 52% vs 18% placebo)
 - Improved QOL from baseline (70% OLZ vs 50% placebo)
 - Reduced gd 3-4 chemo toxicity (12% OLZ vs 37% placebo)
 - Minimal side effects of OLZ (OLZ 23% vs 15% placebo); only 2 OLZ pts reported drowsiness which was mild & short lasting

Randomized Double-Blind Placebo-Controlled Study of Olanzapine for Chemotherapy-Related Anorexia in Patients With Locally Advanced or Metastatic Gastric, Hepatopancreaticobiliary, and Lung Cancer

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Sandhya L, Devi Sreenivasan N, Goenka L, et al. Randomized Double-Blind Placebo-Controlled Study of Olanzapine for Chemotherapy-Related Anorexia in Patients With Locally Advanced or Metastatic Gastric, Hepatopancreaticobiliary, and Lung Cancer. J Clin Oncol. 2023;41(14):2617-2627. doi:10.1200/JCO.22.01997

Presented by:
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Key Discussion Points

- Few studies addressing anorexia in context of newly dx cancer receiving chemotherapy
- Low dose daily OLZ is simple & well-tolerated intervention that significantly improves appetite & weight gain in newly diagnosed lung/upper GI cancers on chemo
- Concern that longer term use of OLZ needed for appetite stimulation & weight gain use might cause additional toxicities – AEs attributable to OLZ mild & manageable

Strengths and Limitations

- 12 week study period – no info on sustainability
- Heterogenous group of cancers & chemo regimens
- Anorexia measurement subjective – addressed through multiple direct and indirect measures (appetite using 2 scales, caloric intake, nutritional status, weight gain)
- Tertiary care centre with experienced dietician – may not be available in all centres
- Did not assess impact on survival

Practice Impact

- Consider adding low-dose OLZ, along with dietary advice, for patients newly diagnosed with advanced lung and upper GI cancers to improve appetite and weight gain

Discussion

Mirtazapine as Appetite Stimulant in Patients With Non-Small Cell Lung Cancer and Anorexia: A Randomized Clinical Trial

Article Reference:

Arrieta O, Cárdenas-Fernández D, Rodríguez-Mayoral O, Gutierrez-Torres S, Castañares D, Flores-Estrada D, Reyes E, López D, Barragán P, Soberanis Pina P, Cardona AF, Turcott JG. Mirtazapine as Appetite Stimulant in Patients With Non-Small Cell Lung Cancer and Anorexia: A Randomized Clinical Trial. JAMA Oncol. 2024 Mar 1;10(3):305-314. doi: 10.1001/jamaoncol.2023.5232. PMID:38206631; PMCID: PMC10784994.

Presented by:

Leonie Herx

Background

- Anorexia – abnormal appetite loss leading to insufficient oral intake, weight loss, decreased functionality, reduced tolerance to anti-cancer tx & poor survival
- Anorexia affects >half of patients with lung cancer
- No specific pharmacotherapy currently recommended to improve cancer-related anorexia
- Mirtazapine (MTZ) is a promising agent:
 - central 5HT antagonism with antidepressant, anti-emetic and analgesic effects
 - associated with appetite stimulation & increased body weight

Study Objective

- To assess the effect of mirtazapine on appetite and energy consumption in patients with advanced non small cell lung cancer (NSCLC)

Methods

- Randomized, double-blind, placebo-controlled trial
- Adults with advanced NSCLC receiving active oncologic treatment & with anorexia (Anorexia-Cachexia Score [ACS] >32)
- Received MTZ 15mg daily for 15 days then 30mg until 8 weeks or placebo. Cross overs allowed. All patients received personalized nutritional advice.
- Assessed anthropometric, body composition, appetite at baseline, 4wks & 8 wks after tx
- **Primary outcomes:**
 - appetite score, energy consumption, % of energy requirement achieved
- **Secondary outcomes:**
 - body composition/sarcopenia, health-related QoL, HADS-depression, HADS-anxiety scores & safety

Mirtazapine as Appetite Stimulant in Patients With Non-Small Cell Lung Cancer and Anorexia: A Randomized Clinical Trial

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Presented by:
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Key Results

- 114 patients assessed, 86 eligible - 43 MTZ & 43 placebo, 58 analyzed at 8 wk follow-up (31/43 MTZ, 27/43 placebo)
- Demographic & clinical characteristics balanced between MTZ & placebo
 - mean age 63.5 yrs, 57.7% women, ECOG 1 (90.2%), met disease (90.1%), received first line tx (70.4%: TKI 54.9%, chemo, 40.8%, immunotherapy 4.2%)
- Anthropometric & nutritional variables similar between MTZ & placebo:
 - 11% underweight (13.2% MTZ vs 9.1% placebo)
 - Median ACS 19.5 (18.6 MTZ vs 20.4 placebo)
 - 66.2% had sarcopenia (59.5% MTZ vs 75% placebo)
- **Primary outcomes:**
 - appetite scores significantly increased in both arms at 4 & 8 wks
 - at 4 wks MTZ arm significant for: incr energy intake incl protein, carbs & fats
 - at 8 wks, both groups had incr energy intake & significant incr in % of energy req't achieved, but only MTZ arm reached 100% of their requirements & had significant incr in fats >> protein consumption vs placebo
- **Secondary outcomes:**
 - MTZ arm - significant decr in proportion of pts with sarcopenia (57.1% MTZ vs 82.8% placebo)
 - HRQoL – incr in both but global health status significantly incr in MTZ
 - HADS-anxiety significantly improved in MTZ at 4wks vs placebo; HADS-depression improved in MTZ at 8 wks but not signif diff from placebo
 - Adverse effects – no diff in adverse events, GI and nonhematologic adverse effects between arms. Nightmares more freq in MTZ at 2wks (but not different at 4 & 8 wks) & MTZ group had less fatigue vs placebo at 8 wks.

Mirtazapine as Appetite Stimulant in Patients With Non-Small Cell Lung Cancer and Anorexia: A Randomized Clinical Trial

Article Reference:

Arrieta O, Cárdenas-Fernández D, Rodríguez-Mayoral O, Gutierrez-Torres S, Castañares D, Flores-Estrada D, Reyes E, López D, Barragán P, Soberanis Pina P, Cardona AF, Turcott JG. Mirtazapine as Appetite Stimulant in Patients With Non-Small Cell Lung Cancer and Anorexia: A Randomized Clinical Trial. JAMA Oncol. 2024 Mar 1;10(3):305-314. doi: 10.1001/jamaoncol.2023.5232. PMID:38206631; PMCID: PMC10784994.

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Key Discussion Points

- No diff in appetite scores MTZ vs placebo but MTZ group had a significant incr in energy consumption at 4wks, maintained at 8 wks largely through incr fat intake
- High fat intake assoc with significantly improved resp fctn markers in pts with lung ca (not assessed here)
- Incr energy intake is first step to stop unintentional wt loss & stabilize/incr body wt
- No difference in wt change for MTZ vs placebo but MTZ arm had significantly diminished proportion of patients with sarcopenia at 8 wks & stabilization of fat-free mass at 8 wks
- In previous reports, MTZ assoc with higher prevalence of somnolence & hallucinations. In this study, MTZ 30mg daily overall well tolerated (no cases of somnolence & nightmares not different at 4 & 8 wks)
- MTZ had positive effect on global health status and HADS score - ?related to positive effect of better energy intake vs sense of well being/improved mood.

Strengths and Limitations

- Strengths - first placebo-controlled RCT to test the effect on energy intake including carbs, protein and fat macronutrients and toxicity profile of mirtazapine in patients with advanced NSCLC with anorexia
- Limitations –single institution, small sample size with high drop out rate, different anti-cancer therapies, did not assess response to treatment, only 8 wks study period

Practice Impact

- Authors suggest to consider addition of MTZ in pts with advanced NSCLC & anorexia as a nutritional intervention to mprove energy consumption
- *Need further studies to look at role & longer term effect of MTZ in cancer-related AN*

Discussion

Ponsegromab for the Treatment of Cancer

Article Reference:

Groarke JD, Crawford J, Collins SM, et al. Ponsegromab for the Treatment of Cancer Cachexia. N Engl J Med. 2024;391(24):2291-2303. doi:10.1056/NEJMoa2409515

Presented by:
Sharon Watanabe

Background

- Growth differentiation factor 15 (GDF-15) is a stress-induced cytokine that binds to the glial cell–derived neurotrophic factor family receptor alpha-like protein (GFRAL) in the hindbrain
- The GDF-15–GFRAL pathway has emerged as a main modulator of anorexia and body-weight regulation and is implicated in the pathogenesis of cachexia
- The level of GDF-15 is elevated in cancer cachexia
- Ponsegromab is a humanized monoclonal antibody inhibiting GDF-15
- In a small, open-label, phase 1b study involving patients with cancer cachexia ponsegromab was associated with improved weight, appetite, and physical activity, along with suppressed serum GDF-15 levels.

Study Objective

- Assess the safety and efficacy of ponsegromab, as compared with placebo, in patients with cancer cachexia with elevated circulating GDF-15 levels, to test the hypothesis that GDF-15 is a main mechanistic driver of this condition

Methods

- Phase 2, randomized, double-blind, placebo-controlled multicentre trial,
- Patients with cancer cachexia (weight loss of > 5% within previous 6 months or > 2% with BMI < 20), elevated serum GDF-15 level, ECOG ≤ 3, life expectancy ≥ 4 months
- Ponsegromab 100 mg/200 mg/400 mg or placebo subcut every 4 weeks x 3 doses
- Primary end point: change from baseline in body weight at 12 weeks
- Key secondary end points: appetite, cachexia symptoms, physical activity, safety

Ponsegromab for the Treatment of Cancer

Article Reference:

Groarke JD, Crawford J, Collins SM, et al. Ponsegromab for the Treatment of Cancer Cachexia. N Engl J Med. 2024;391(24):2291-2303. doi:10.1056/NEJMoa2409515

Presented by:
Sharon Watanabe

Key Results

- 187 patients randomized
- Cancer types: non–small-cell lung 40%, pancreatic 32%, colorectal 29%
- 90% on systemic anticancer therapies
- At 12 weeks, ponsegromab groups had significantly greater weight gain than placebo group; median between-group difference 1.22 kg (95% credible interval, 0.37 to 2.25) in 100-mg group, 1.92 (95% credible interval, 0.92 to 2.97) in 200-mg group, and 2.81 (95% credible interval, 1.55 to 4.08) in 400-mg group
- Improvements across measures of appetite and cachexia symptoms, physical activity, CT lumbar skeletal muscle index in the 400-mg ponsegromab group relative to placebo
- Similar rates of adverse events in ponsegromab and placebo groups

Key Discussion Points

- First conclusive demonstration of GDF-15 as a common driver of cachexia across different solid tumours
- Ponsegromab has potential as a targeted therapy for cancer cachexia
- Possible implications for diseases other than cancer with elevated GDF-15

Strengths and Limitations

- Trial design
- Small sample size
- Pharmaceutical sponsor

Practice Impact

- Need larger confirmatory trials

Discussion

Honourable Mentions

- Pandey S, Bradley L, Del Fabbro E. **Updates in Cancer Cachexia: Clinical Management and Pharmacologic Interventions.** *Cancers (Basel)*. 2024;16(9):1696. [doi:10.3390/cancers16091696](https://doi.org/10.3390/cancers16091696)
- Blum D, Vagnildhaug OM, Stene GB, et al. **Top Ten Tips Palliative Care Clinicians Should Know About Cachexia.** *J Palliat Med*. 2023;26(8):1133-1138. [doi:10.1089/jpm.2022.0598](https://doi.org/10.1089/jpm.2022.0598)
- Yule MS, Brown LR, Waller R, Wigmore SJ. **Cancer cachexia.** *BMJ*. Published online October 23, 2024:e080040. doi:10.1136/bmj-2024-080040

Wrap-up

- Please fill out our feedback survey a link has been shared in the chat!
- A recording of this webinar and a copy of the slides will be e-mailed to registrants within the next week.
- Save the date for our next Journal Watch session on September 15th, 2025, from 12:00 pm to 1:00 pm ET
- To listen to this session and previous sessions, check out the **Palliative Care Journal Watch** podcast.



NOTE: recordings, slides and links to articles from all our sessions are available at www.echopalliative.com/palliative-care-journal-watch/.

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Thank You



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