

Anamorelin for the Treatment of Cancer Anorexia-Cachexia in NSCLC: Results From the Phase 3 Studies ROMANA 1 and 2

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DISCLOSURES

- This study was supported by Helsinn Therapeutics, Inc. (USA)
- Dr Temel has no conflicts of interests to declare

Cancer Anorexia-Cachexia

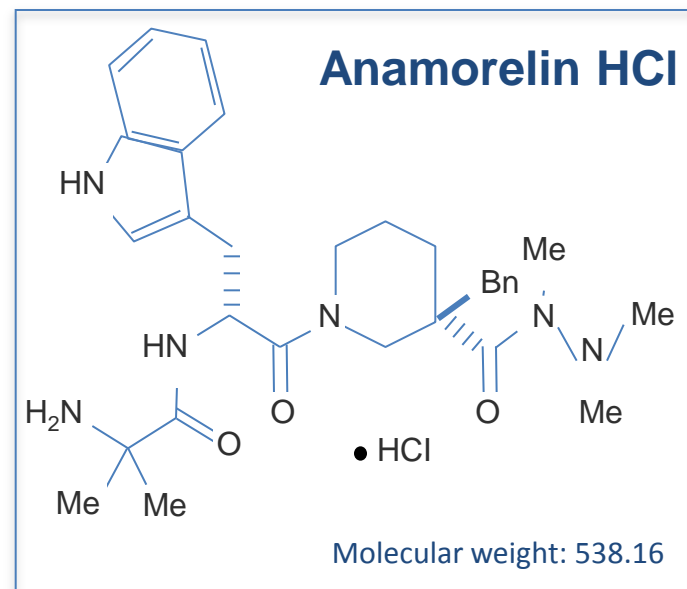
- Common and debilitating condition that can develop in up to 70% of patients with advanced cancer and often occurs in patients with advanced stage non-small cell lung cancer (NSCLC)¹
- Characterized by low appetite and decreased body weight, mainly through the loss of lean body mass (skeletal muscle)²
- Associated with a worse prognosis and poorer quality of life³
- Current treatment has very limited efficacy and potential risks, especially in patients with advanced cancers⁴

Ghrelin

- Released by the stomach and is the ligand of the ghrelin receptor that produces the release of growth hormone
- Stimulates multiple pathways which regulate body weight, lean body mass, appetite, and metabolism

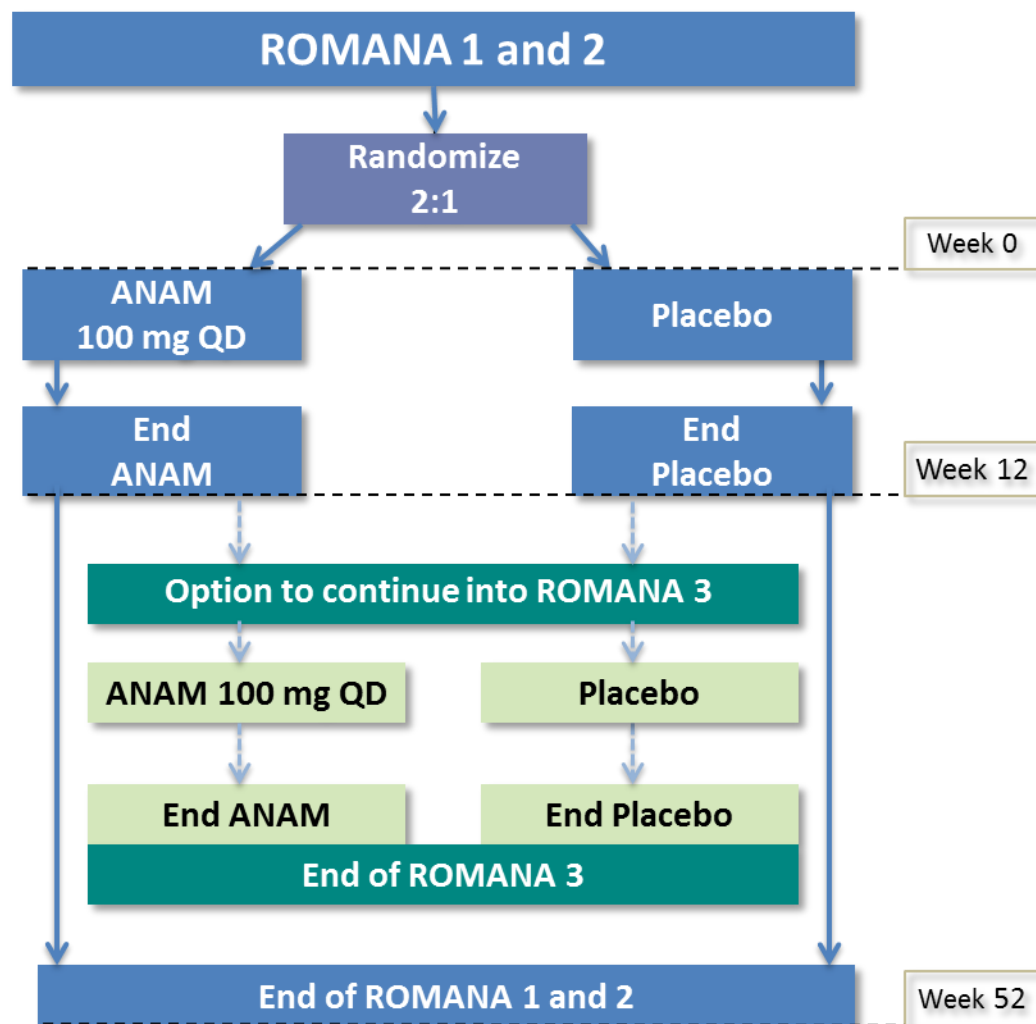
Anamorelin HCl (ANAM)

- Orally active, ghrelin mimetic/receptor agonist
- In a Phase 2 trial, patients with advanced NSCLC treated with ANAM experienced a significant increase in mean body weight at 12 weeks¹



Studies Design

- Two international, double-blind, Phase 3 trials
- Patients with unresectable stage III or IV NSCLC and cachexia ($\geq 5\%$ weight loss within prior 6 months or BMI $< 20 \text{ kg/m}^2$)
- Randomized (2:1) to receive either 100 mg ANAM or placebo, administered daily orally for 12 weeks
- Assess ANAM efficacy and safety



Inclusion Criteria

Key Inclusion Criteria

- Unresectable stage III or IV NSCLC
- Cancer anorexia-cachexia (weight loss of $\geq 5\%$ body weight < 6 months prior to screening or screening BMI < 20 kg/m²)
- Life expectancy of > 4 months
- ECOG performance status ≤ 2
- BMI ≤ 30 kg/m²

Inclusion Criteria

Concomitant Chemotherapy Inclusion Criteria

- Patients who began a new line of chemotherapy within ± 14 days of randomization
- Patients receiving maintenance chemotherapy
- Patients with no plan to initiate new chemotherapy within 12 weeks from randomization
 - Previous chemotherapy must have been completed >14 days prior to randomization

Concomitant Radiation Therapy Inclusion Criteria

- Patients who began radiation therapy within ± 14 days of randomization
- Patients with no plan to initiate new radiation therapy within 12 weeks from randomization
 - Previous radiation therapy must have been completed >14 days prior to randomization

Statistical Analysis

Co-Primary Endpoints

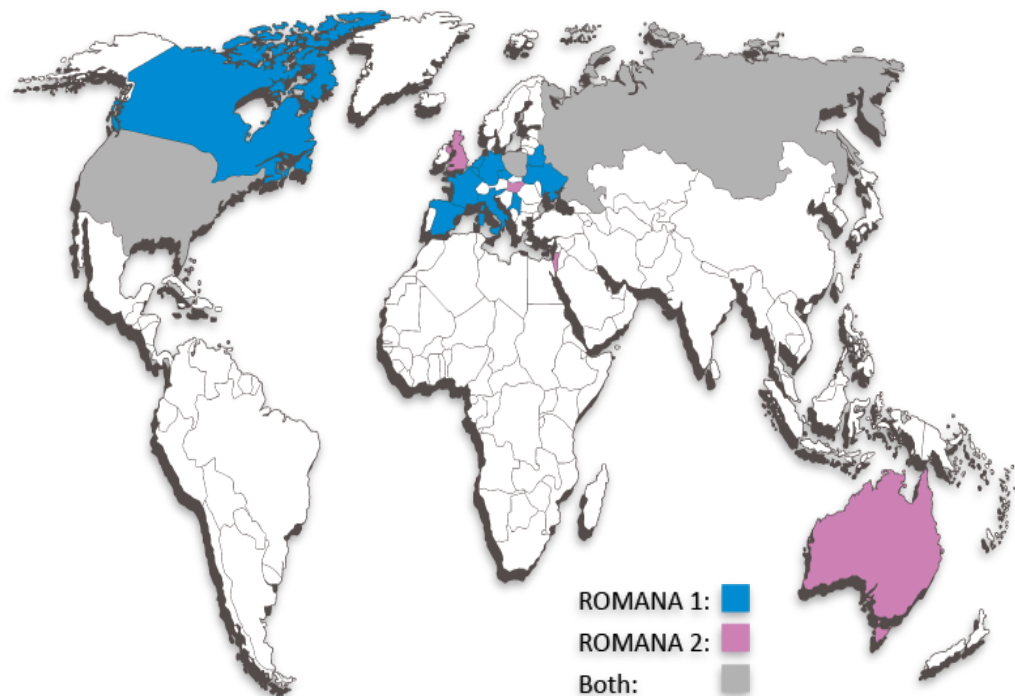
- Change from baseline over 12 weeks in:
 - Lean body mass (measured by dual-energy X-ray absorptiometry)
 - Hand grip strength of the non-dominant hand
 - 477 patients per study
 - 90% power to detect 2 kg difference in lean body mass and hand grip strength between treatment arms

Secondary Endpoints

- Change from baseline over time in:
 - Body weight
 - Quality of life as assessed by the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) and Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) questionnaires
- Overall survival

Studies Conduct

	ROMANA 1	ROMANA 2
First patient enrolled	Jul 8 2011	Jul 14 2011
Last patient completed	Jan 28 2014	Oct 31 2013
Database locked (excluding OS)	Mar 19 2014	Dec 6 2013



- Patients were treated for up to 12 weeks and followed for 1 year from randomization (every 3 months)

Patient Population

	ROMANA 1		ROMANA 2	
	Placebo (N = 161)	100 mg ANAM (N = 323)	Placebo (N = 165)	100 mg ANAM (N = 330)
Mean age (SD)	62.6 (8.52)	61.7 (9.65)	62.8 (9.26)	63.3 (8.25)
Male, n (%)	121 (75.2)	247 (76.5)	122 (73.9)	240 (72.7)
Race, n (%)				
Caucasian	159 (98.8)	319 (98.8)	162 (98.2)	326 (98.8)
Black/African American	0 (0)	1 (0.3)	1 (0.6)	2 (0.6)
Asian	0 (0)	1 (0.3)	1 (0.6)	0 (0)
Other/Unknown	2 (1.2)	2 (0.6)	1 (0.6)	2 (0.6)
Mean weight, kg (SD)	68.0 (13.3)	67.6 (13.0)	62.7 (12.9)	63.9 (13.3)
Mean BMI, kg/m² (SD)	23.3 (3.7)	23.2 (3.6)	22.1 (3.7)	22.5 (3.7)
ECOG PS, n (%)				
0	16 (9.9)	40 (12.4)	10 (6.1)	26 (7.9)
1	119 (73.9)	218 (67.5)	114 (69.1)	215 (65.2)
2	26 (16.1)	64 (19.8)	41 (24.8)	89 (27.0)
Unknown	0 (0)	1 (0.3)	0 (0)	0 (0)

Baseline Disease Characteristics

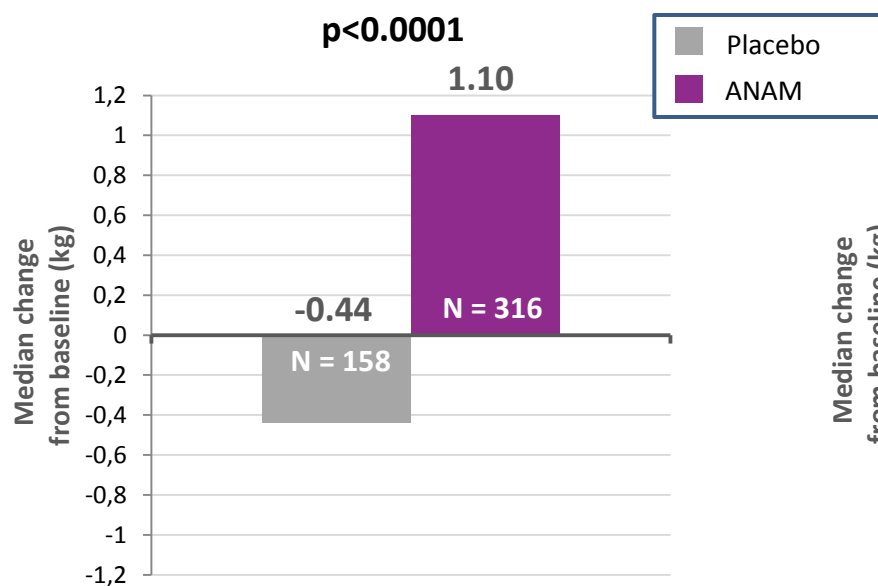
	ROMANA 1		ROMANA 2	
	Placebo (N = 161)	100 mg ANAM (N = 323)	Placebo (N = 165)	100 mg ANAM (N = 330)
Stage, n (%)				
Stage IIIA	16 (9.9)	19 (5.9)	16 (9.7)	29 (8.8)
Stage IIIB	30 (18.6)	48 (14.9)	36 (21.8)	62 (18.8)
Stage IV	114 (70.8)	256 (79.3)	113 (68.5)	238 (72.1)
Stage unknown	1 (0.6)	0 (0)	0 (0)	1 (0.3)

Concomitant Cancer Therapy

	ROMANA 1		ROMANA 2	
	Placebo (N = 161)	100 mg ANAM (N = 323)	Placebo (N = 165)	100 mg ANAM (N = 330)
Chemotherapy	139 (86.3)	288 (89.2)	125 (75.8)	256 (77.6)
Active therapy	134 (83.2)	275 (85.1)	101 (61.2)	225 (68.2)
Maintenance therapy	7 (4.3)	11 (3.4)	26 (15.8)	32 (9.7)
Adjuvant therapy	0 (0.0)	3 (0.9)	1 (0.6)	6 (1.8)
Radiation therapy	18 (11.2)	37 (11.5)	14 (8.5)	31 (9.4)
No cancer therapy	22 (13.7)	35 (10.8)	40 (24.2)	74 (22.4)

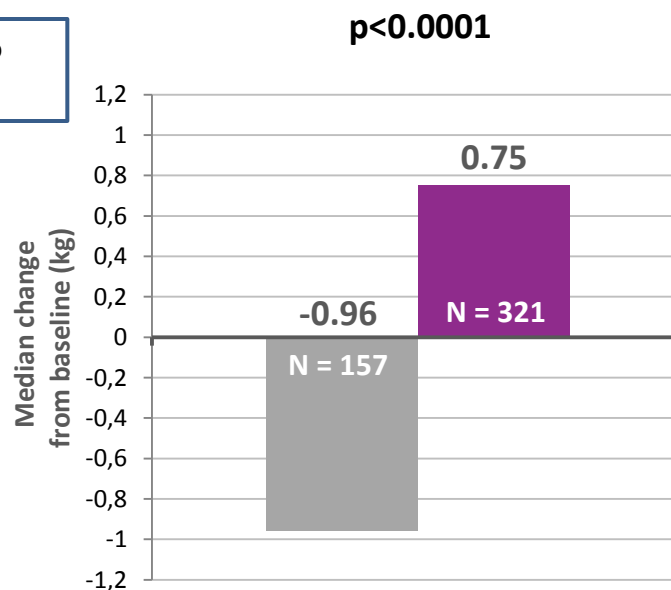
Lean Body Mass

ROMANA 1



Median change:
 ANAM: 1.10 kg (95% CI: 0.76, 1.42)
 Placebo: -0.44 kg (95% CI: -0.88, 0.20)

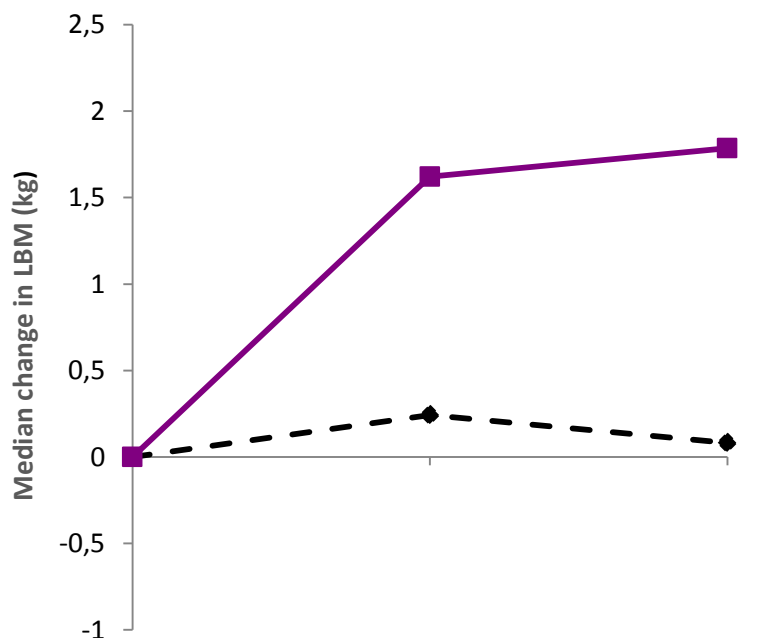
ROMANA 2



Median change:
 ANAM: 0.75 kg (95% CI: 0.51, 1.00)
 Placebo: -0.96 kg (95% CI: -1.27, -0.46)

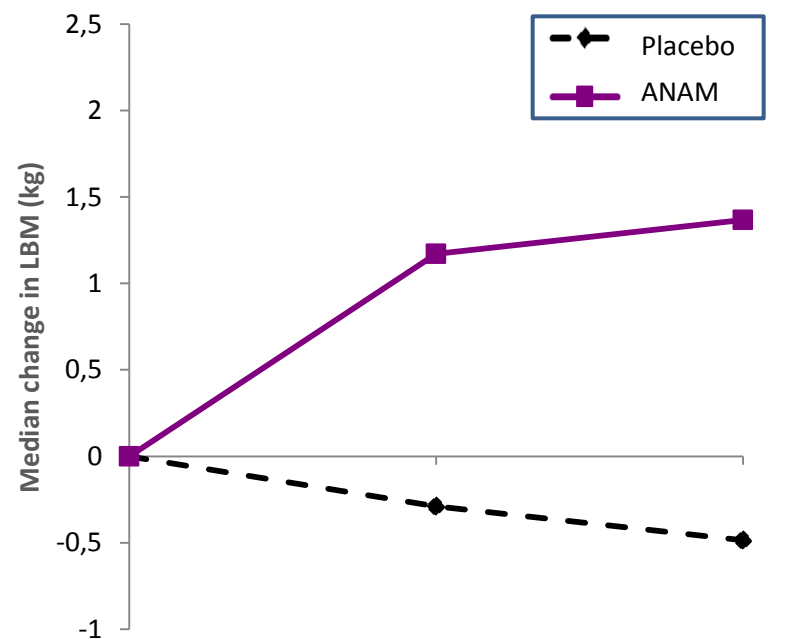
Observed Change in Lean Body Mass

ROMANA 1



	Baseline	Week 6	Week 12
Placebo :	156	127	101
ANAM :	319	257	199

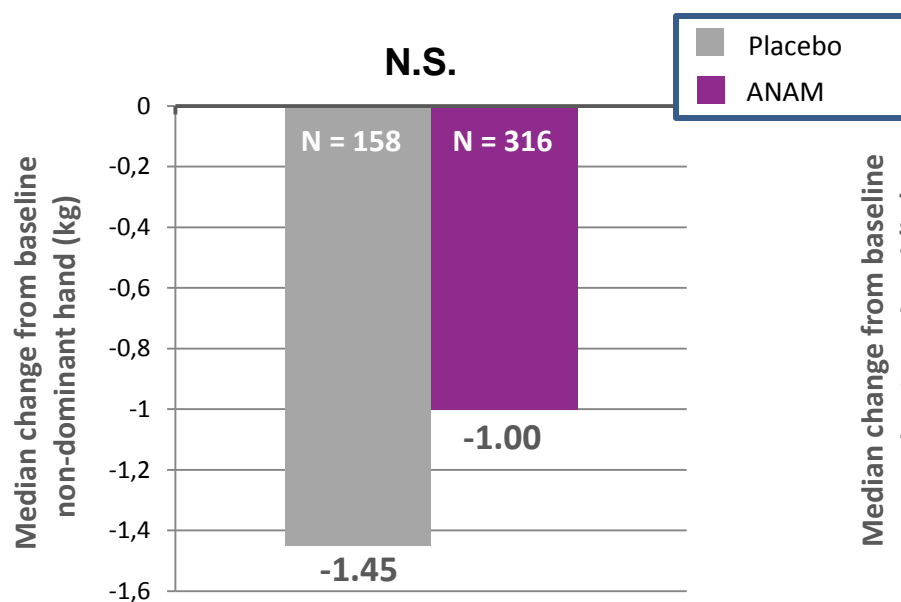
ROMANA 2



	Baseline	Week 6	Week 12
Placebo :	156	117	96
ANAM :	320	229	202

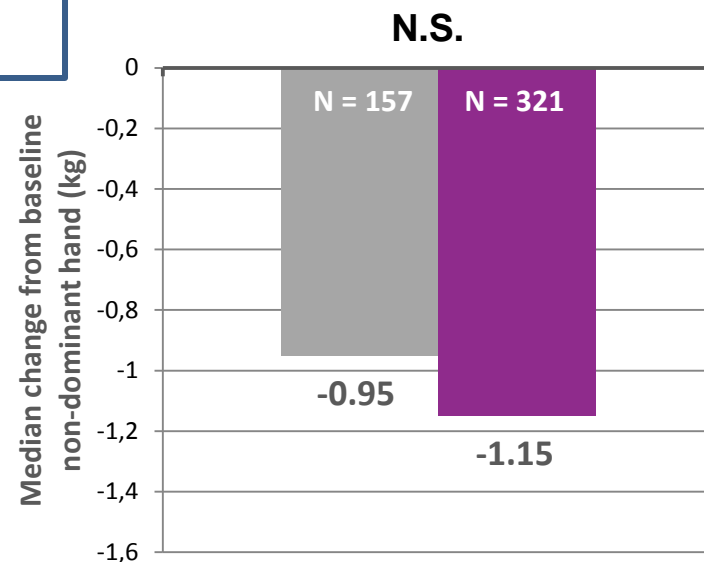
Hand Grip Strength

ROMANA 1



Median change:
 ANAM: -1.00 kg (95% CI: -1.60, -0.30)
 Placebo: -1.45 kg (95% CI: -2.69, -1.05)

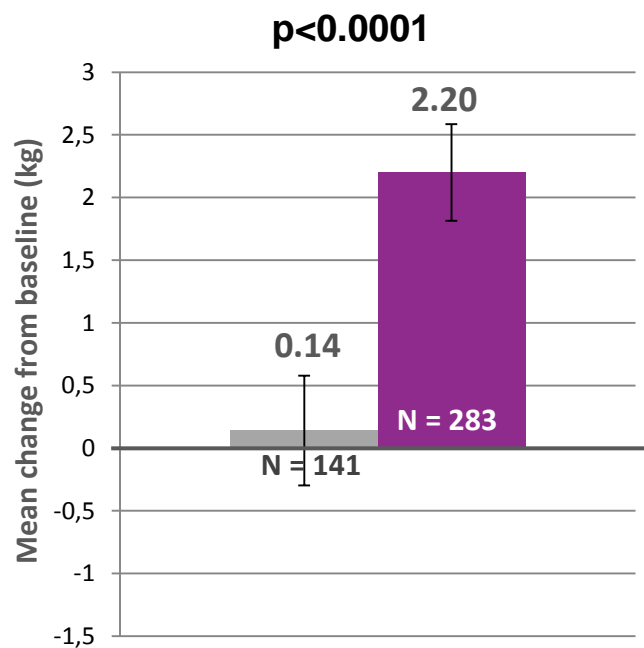
ROMANA 2



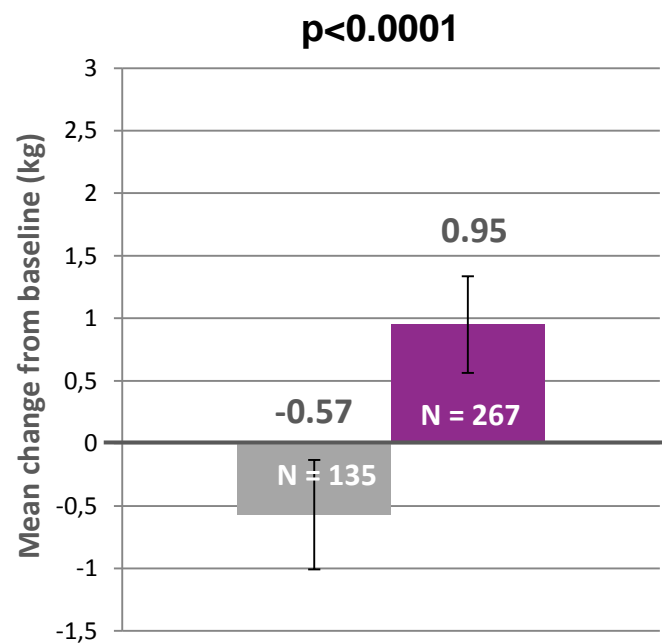
Median change:
 ANAM: -1.15 kg (95% CI: -2.05, -0.45)
 Placebo: -0.95 kg (95% CI: -1.60, 0.00)

Body Weight

ROMANA 1



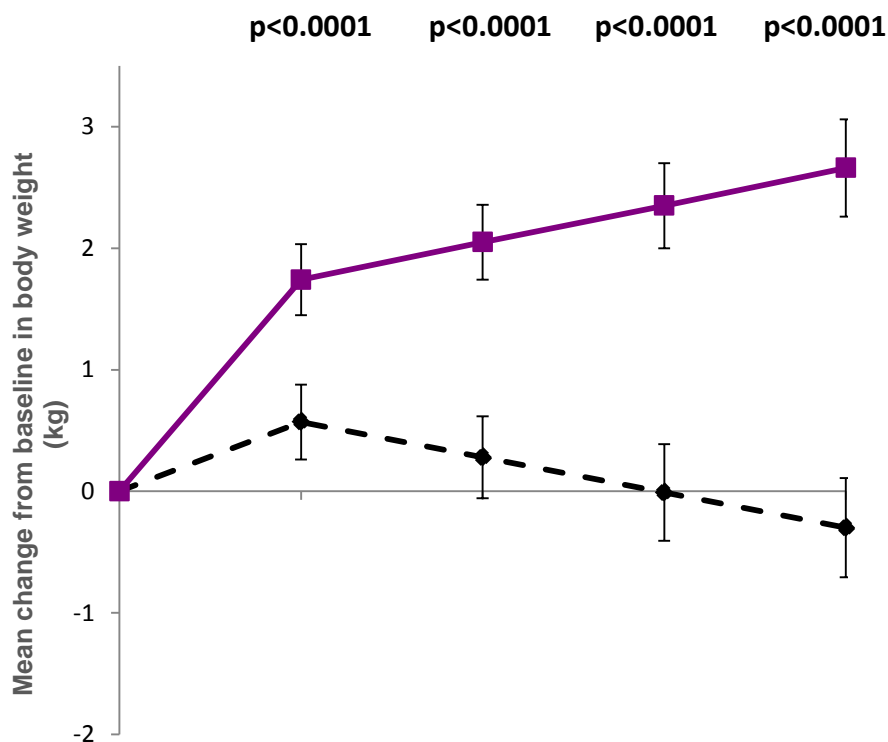
ROMANA 2



Placebo
ANAM

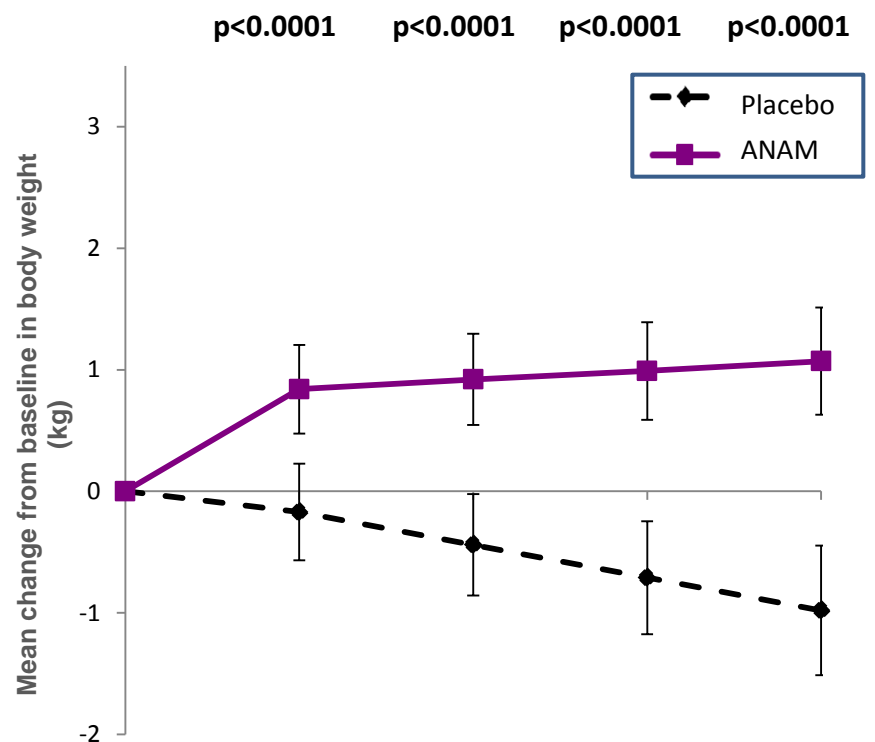
Observed Change in Body Weight

ROMANA 1



	Baseline	Week 3	Week 6	Week 9	Week 12
Placebo	141	140	139	126	120
ANAM	284	281	276	247	230

ROMANA 2



	Baseline	Week 3	Week 6	Week 9	Week 12
Placebo	136	135	133	121	117
ANAM	268	267	265	248	236

Anorexia/Cachexia Domain of FAACT

I have a good appetite

The amount I eat is sufficient to meet my needs

I am worried about weight

Most food tastes unpleasant to me

I am concerned about how thin I look

My interest in food drops as soon as I try to eat

I have difficulty eating rich or "heavy" foods

My family or friends are pressuring me to eat

I have been vomiting

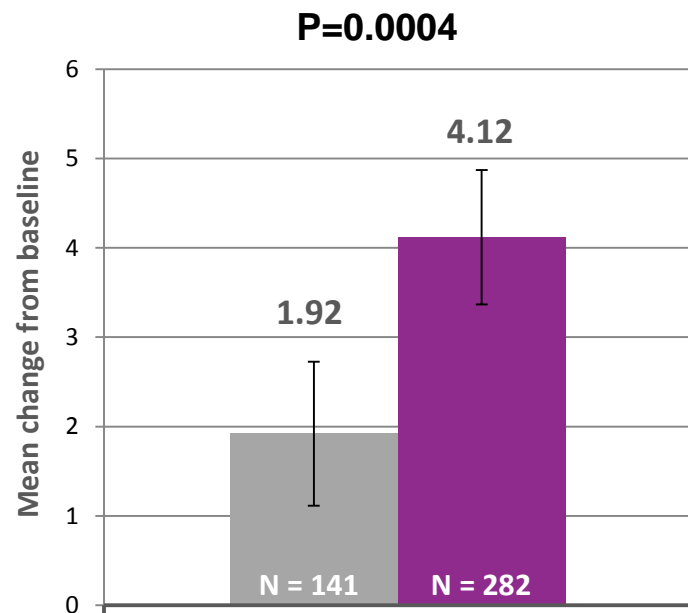
When I eat, I seem to get full quickly

I have pain in my stomach area

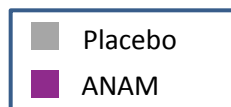
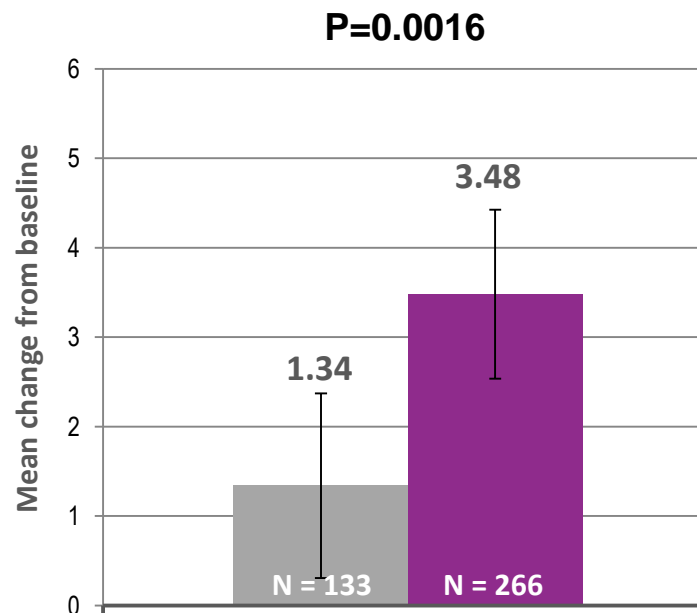
My general health is improving

FAACT Anorexia/Cachexia Domain

ROMANA 1



ROMANA 2

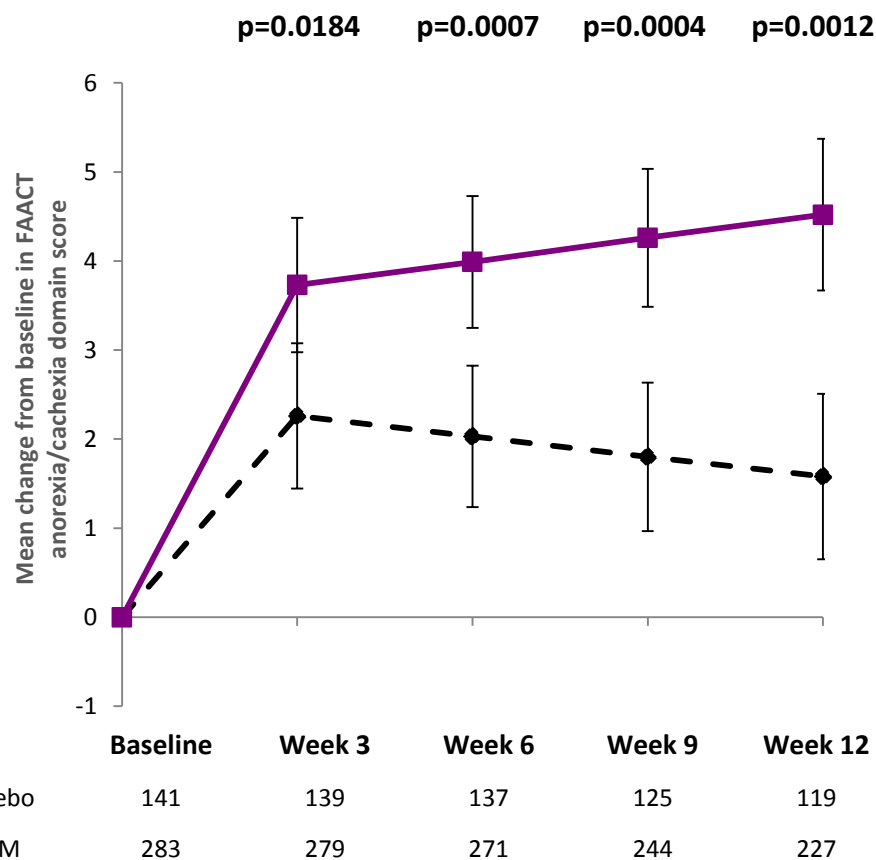


Improving

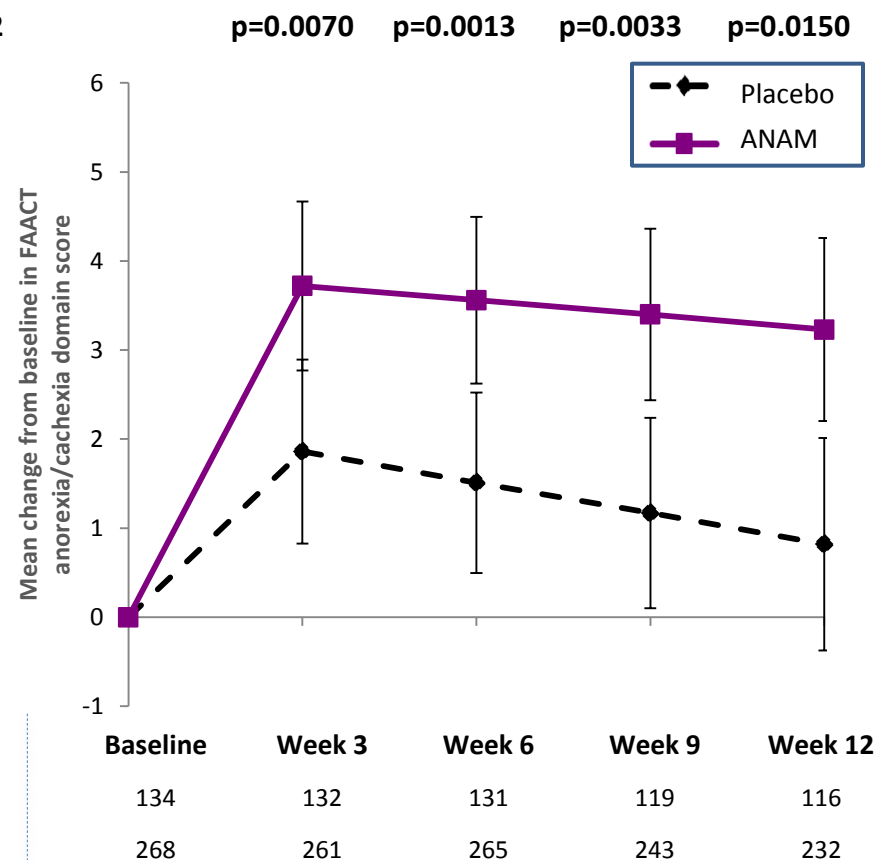


Observed Change in FAACT Anorexia/Cachexia Domain

ROMANA 1

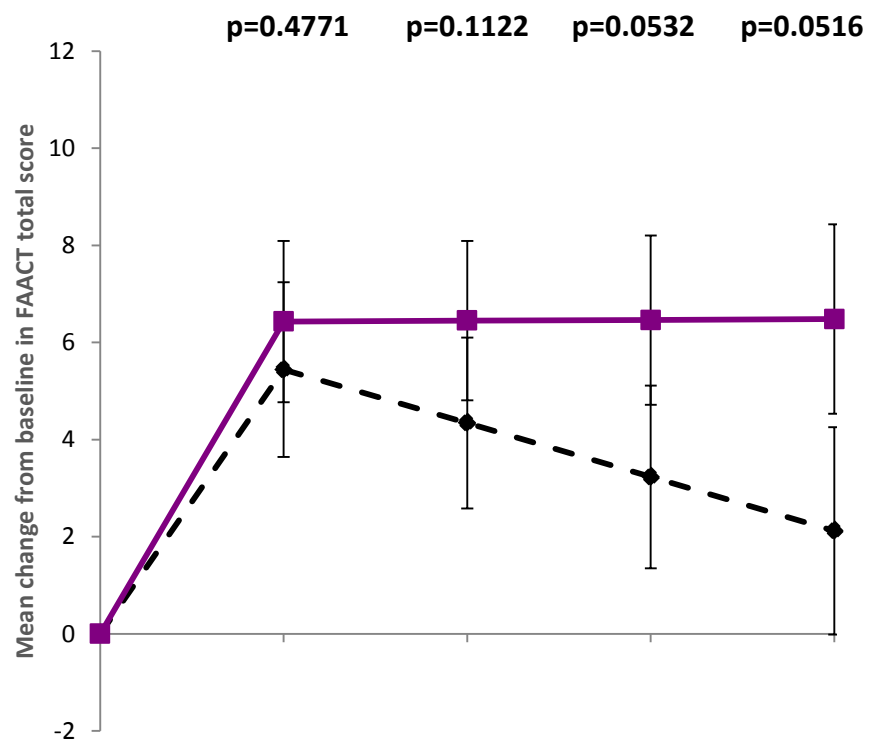


ROMANA 2



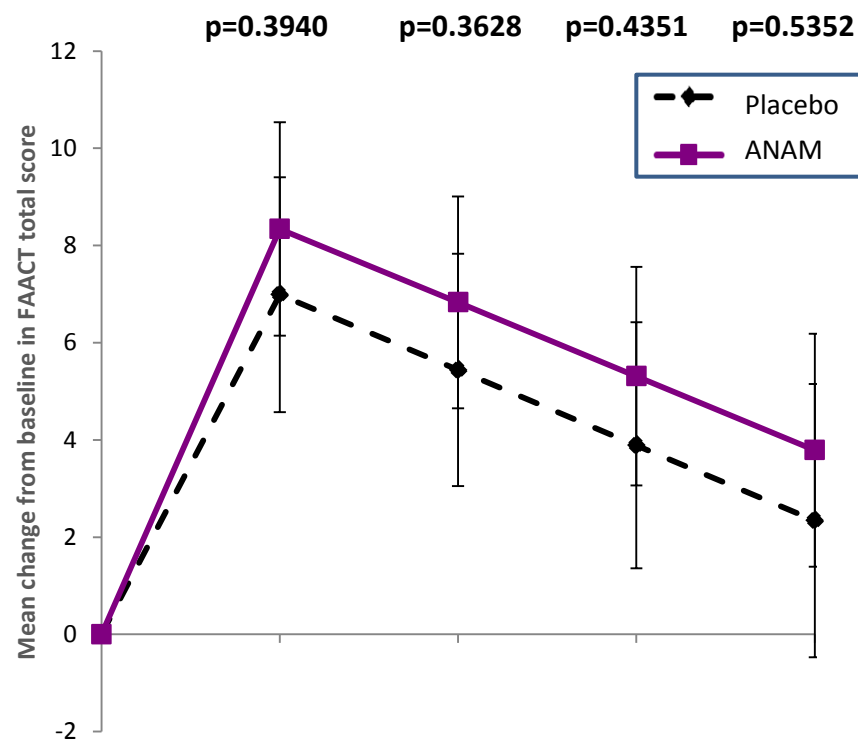
Observed Change in FAACT Total Score

ROMANA 1



	Baseline	Week 3	Week 6	Week 9	Week 12
Placebo	139	137	132	120	117
ANAM	278	273	264	238	223

ROMANA 2



	Baseline	Week 3	Week 6	Week 9	Week 12
Placebo	133	130	130	118	114
ANAM	266	260	262	242	230

Summary of Common (>2%) Drug-Related Adverse Events

	ROMANA 1		ROMANA 2	
	Placebo (N = 161)	100 mg ANAM (N = 320)	Placebo (N = 161)	100 mg ANAM (N = 330)
Patients with any drug-related TEAEs	15 (9.3)	46 (14.4)	12 (7.5)	32 (9.7)
Grade 1/2	13 (8.1)	43 (13.4)	8 (5.0)	22 (6.7)
Grade 3/4	2 (1.2)	3 (0.9)	4 (2.5)	9 (2.7)
Gastrointestinal disorders	3 (1.9)	20 (6.3)	6 (3.7)	6 (1.8)
Nausea	1 (0.6)	12 (3.8)	3 (1.9)	5 (1.5)
Metabolism and nutrition disorders	9 (5.6)	19 (5.9)	2 (1.2)	21 (6.4)
Diabetes mellitus, including inadequate control	4 (2.5)	3 (0.9)	0 (0.0)	7 (2.1)
Hyperglycemia	5 (3.1)	17 (5.3)	1 (0.6)	14 (4.2)

Conclusions

- ANAM significantly increased lean body mass and body weight in patients with advanced NSCLC
- ANAM did not improve hand grip strength
- Patients receiving ANAM also experienced an improvement in anorexia-cachexia symptoms and concerns
- ANAM was well tolerated when administered daily over 12 weeks
- Results on overall survival are pending

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