PRC

The preMENAC Study

Barry Laird and Tora Solheim


XJ6

The preMENAC Team

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The challenge in treating lung cancer and pancreatic cancer is to optimise quality of life care taking into consideration the modest survival benefits of anti-cancer therapy

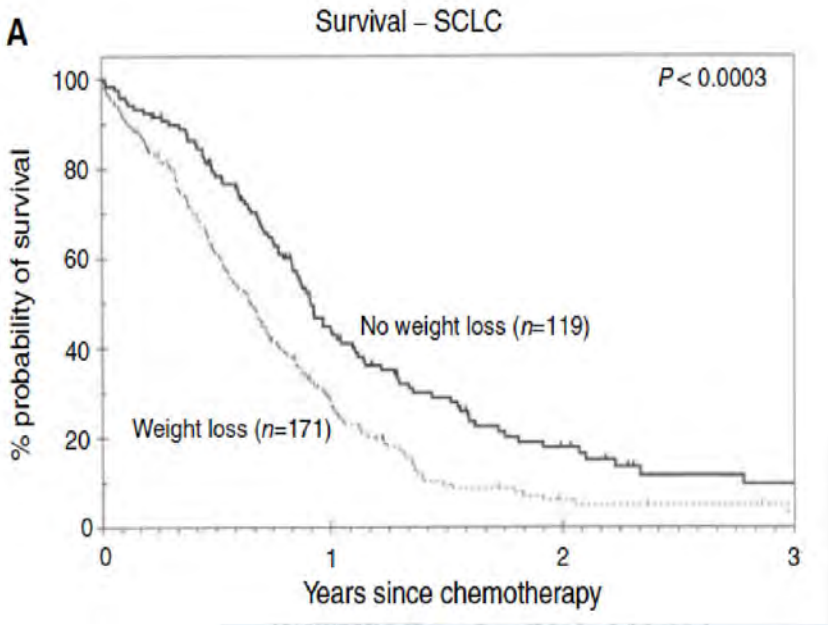
Do patients with weight loss have a worse outcome when undergoing chemotherapy for lung cancers?

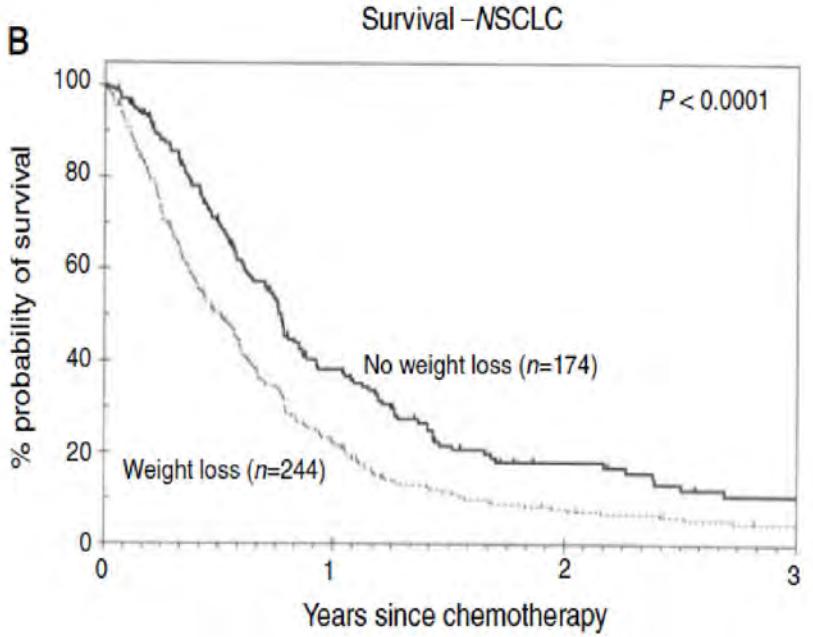
PJ Ross[1], S Ashley[1], A Norton[1], K Priest[1], JS Waters[1], T Eisen[1], IE Smith[1] and MER O'Brien*[,1]
[1]Lung Unit, Royal Marsden Hospital, Downs Road, Sutton SM2 5PT, UK

British Journal of Cancer (2004) 90, 1905–1911

NSCLC

- weight loss associated with delivery of fewer cycles of chemotherapy ($p<0.003$)
- more treatment delays ($p=0.04$),
- more anaemia ($p=0.003$),
- more symptoms at presentation($p<0.0001$)
- less symptomatic benefit from chemotherapy ($p=0.004$).





"A well designed study to evaluate the benefit of nutritional support in patients with weight loss receiving chemotherapy is needed" PJ Ross et al 2004

Why has research in cachexia been slow?

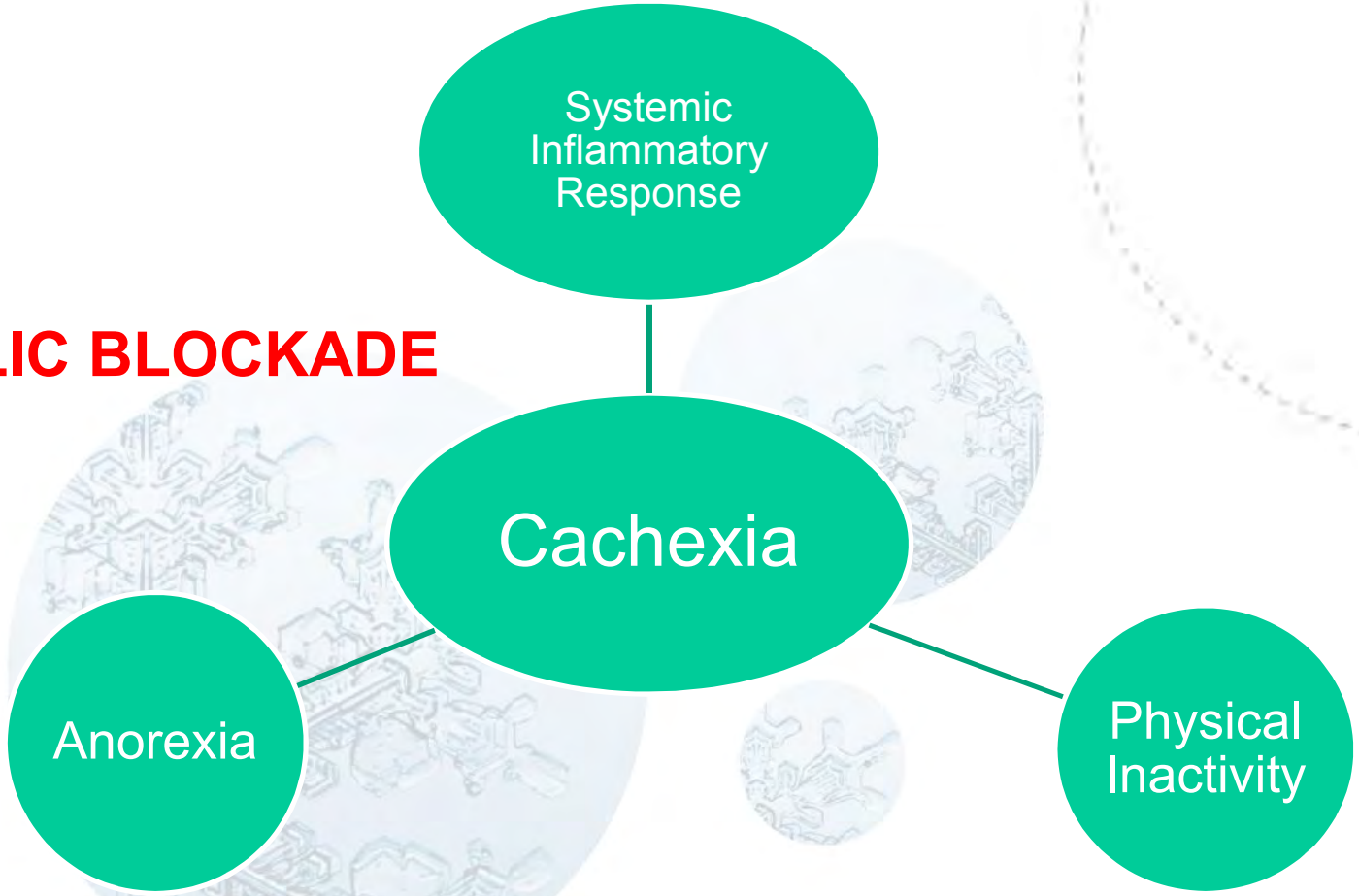
- Unimodal therapy trials
- Prerequisite of oncology trials

You are not eligible if you are taking part in another trial “fastidious vs pragmatic trials”

- Limited pharmaceutical funding

- Cachexia is a very complex syndrome.....

ANABOLIC BLOCKADE



Interventions should be multimodal tackling all of these issues simultaneously

EJC
EUROPEAN JOURNAL OF CANCER

Cancer cachexia: Developing multimodal therapy for a multidimensional problem

44 (2008) 1124–1132

K.C.H. Fearon*

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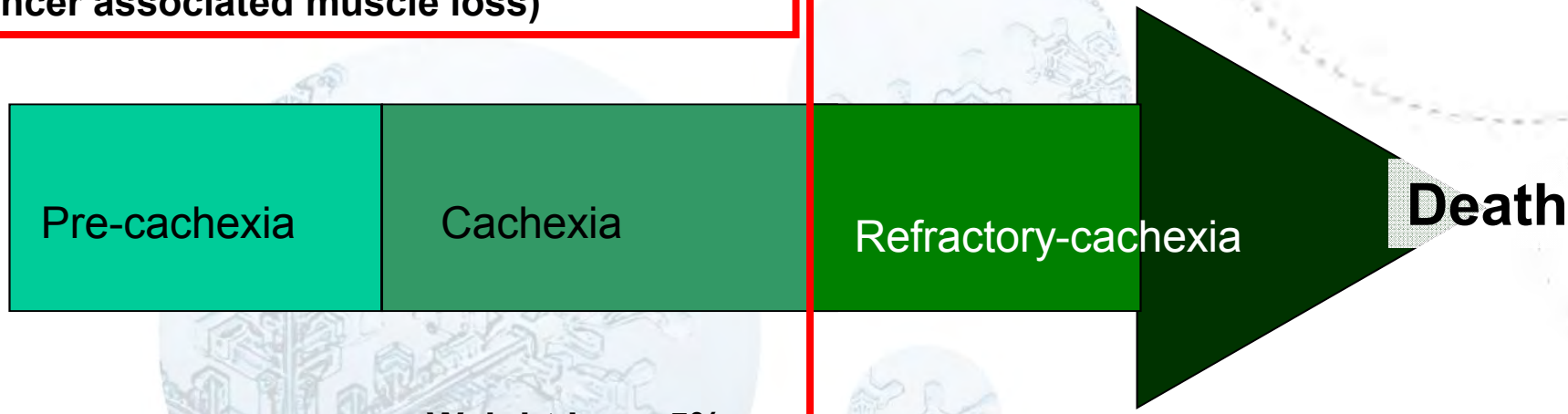
Multimodal Therapy:

- High protein nutrition
- Anti-inflammatory agents to down regulate the APPR
- Routine mobilisation programmes to prevent deconditioning and encourage physical activity-induced stimulation of post prandial anabolism.

Nutritional Rehabilitation (pre-habilitation) in Oncology

(cancer associated muscle loss)

The Refractory Patient



Weight loss <5%

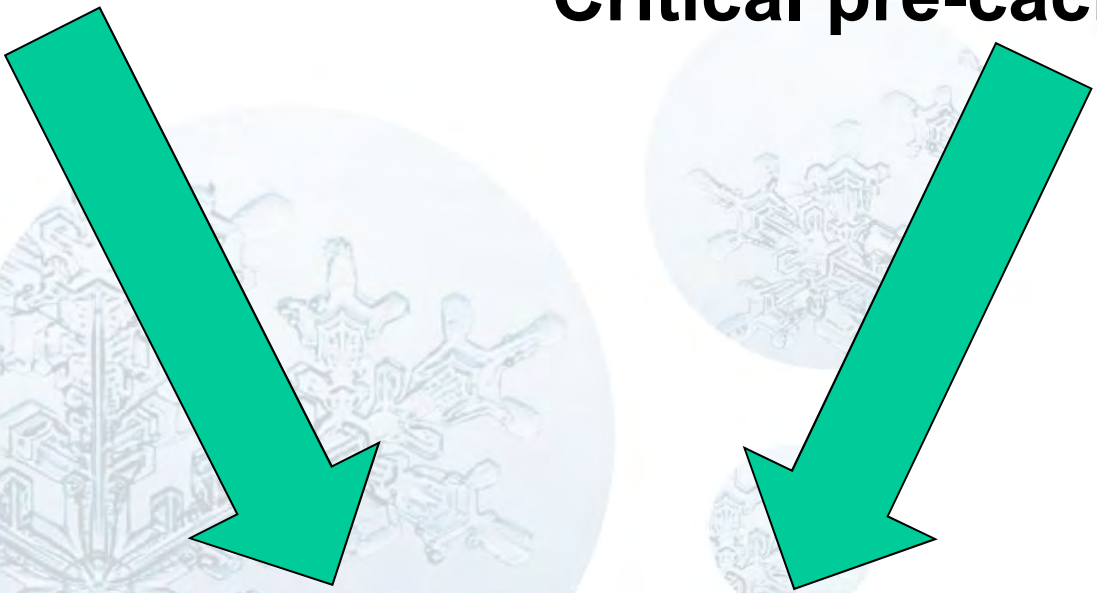
Anorexia & metabolic change

Weight loss>5% or BMI<20 and weight loss >2% or sarcopenia and weight loss >2%

Variable degree of cachexia. Cancer disease both procatabolic and not responsive to anti-cancer treatment. Low PS, survival <3 months

Multimodal Intervention

Critical pre-cachexic phase



In combination with anti-cancer therapy

preMENAC Study

A multicentre, open, randomized phase II study comparing a multimodal intervention (oral nutritional supplements, celecoxib and physical exercise) for cachexia versus standard cancer care.

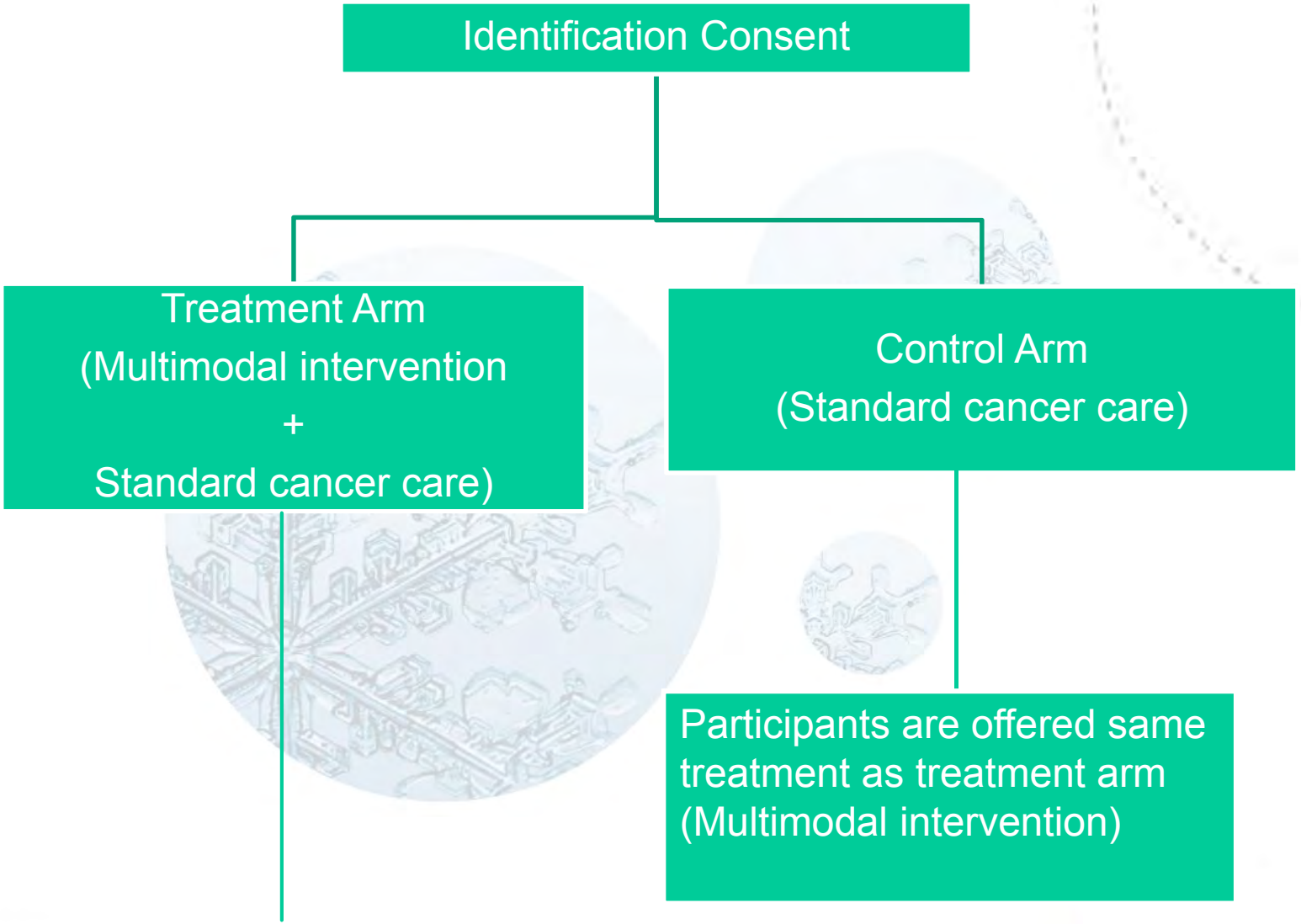
(EudraCT number: 2010-022897-14)

Funding EU FP6 framework

EAPC

PRC European Palliative Care Research Centre

HYPOTHESIS: Early intervention to treat or minimise weight loss may improve symptoms and allow anti-cancer therapy to be given more efficiently with the ultimate aim of improving survival.


Identification Consent
Treatment Arm
(Multimodal intervention
+
Standard cancer care)
Control Arm
(Standard cancer care)
Participants are offered same treatment as treatment arm (Multimodal intervention)
Week 0
Week 6
Week 12

Multimodal Intervention (1) - Nutrition

Aim: promote energy balance & ensure optimal protein intake

Dietician led interview – targets set.
Information on dietary intake assessed.
Advice given to modify diet to achieve targets

Oral nutritional supplements
2 cartons (2x 220mls) per day of ProSURE.
Contains 1.1g of EPA per carton. Energy and protein dense.

Multimodal Intervention (2) - Exercise

Aim: to stabilize muscle mass, strength and improve physical performance

Physiotherapist – initial instruction and assessment

Aerobic – minimum 2 x 30 minute sessions per week (Borg scale 12-14)

Resistance – tailored 0.5-5kg weights. 3x20 minute sessions per week. Increasing weight over period of study

Multimodal Intervention (3) - COXII

Aim: to target overproduction of inflammatory cytokines

Celecoxib –most studied, may have beneficial effects in cachexia

Dose 300mg per day.

Multimodal Intervention delivered on a background of palliative care

Eligibility Criteria

- Diagnosis of non operable non-small cell lung cancer (NSCLC) (stage III-IV) or pancreatic cancer
- Due to commence chemotherapy or chemoradiotherapy
- NOT receiving parenteral nutrition or enteral nutrition via feeding tube
- NO Weight loss >20% over the previous 6 months
- NO BMI >30 kg/m^2
- NO Severe anorexia (less than 50% pre-illness food intake and unable to take oral supplements)

Aims

Primary

- Feasibility of recruitment
- Compliance with intervention, procedures, data collection
- Contamination rate
- Inform sample size

Secondary

- Effect on muscle mass
- Effect on weight
- Effect on activity


Iceland
Atlantic Ocean
Faroe Islands
UK
Norway
Sweden
Finland
Denmark

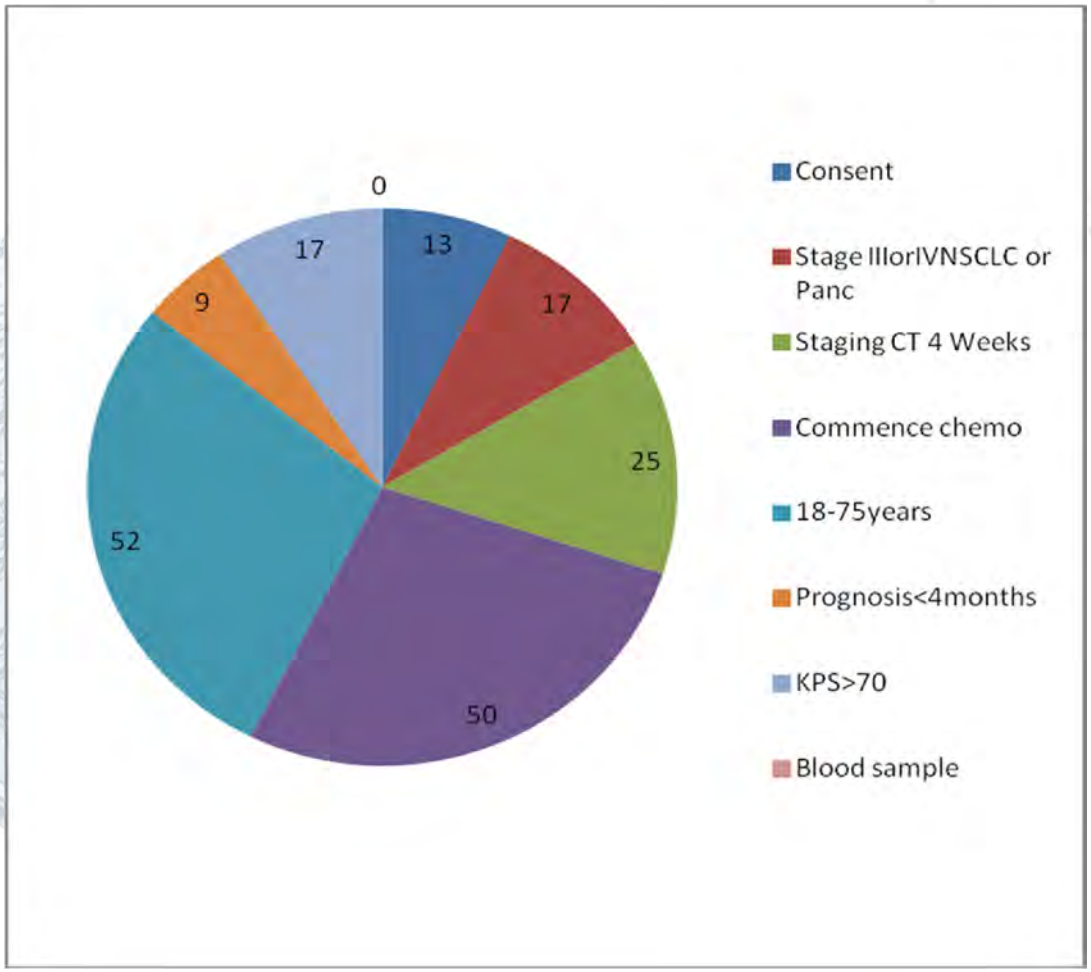
Preliminary findings……

Screening

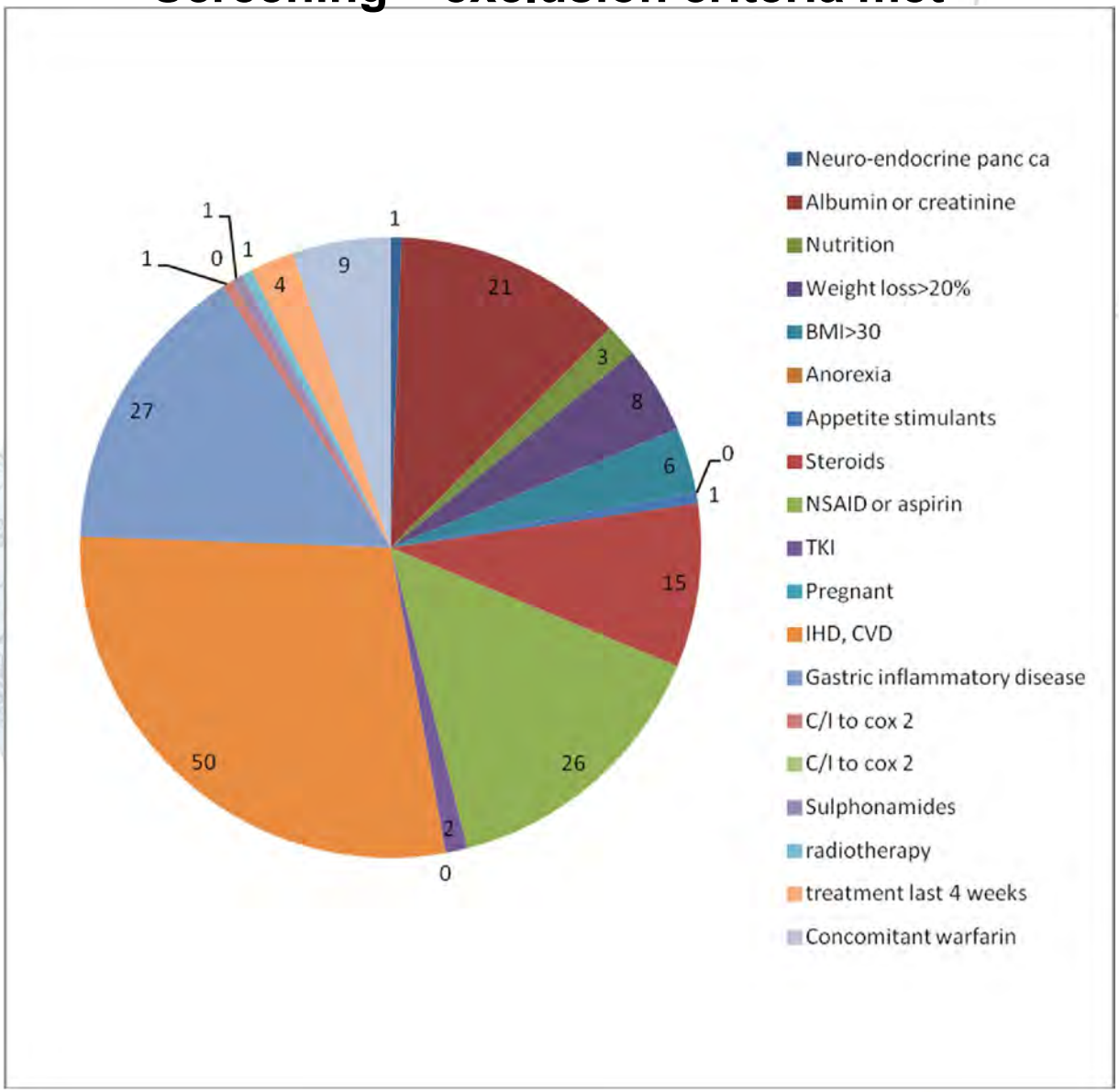
- 399 patients screened
- 41 patients recruited

- Formalisation of screening logs necessary

Screening – inclusion criteria not met



Screening – exclusion criteria met

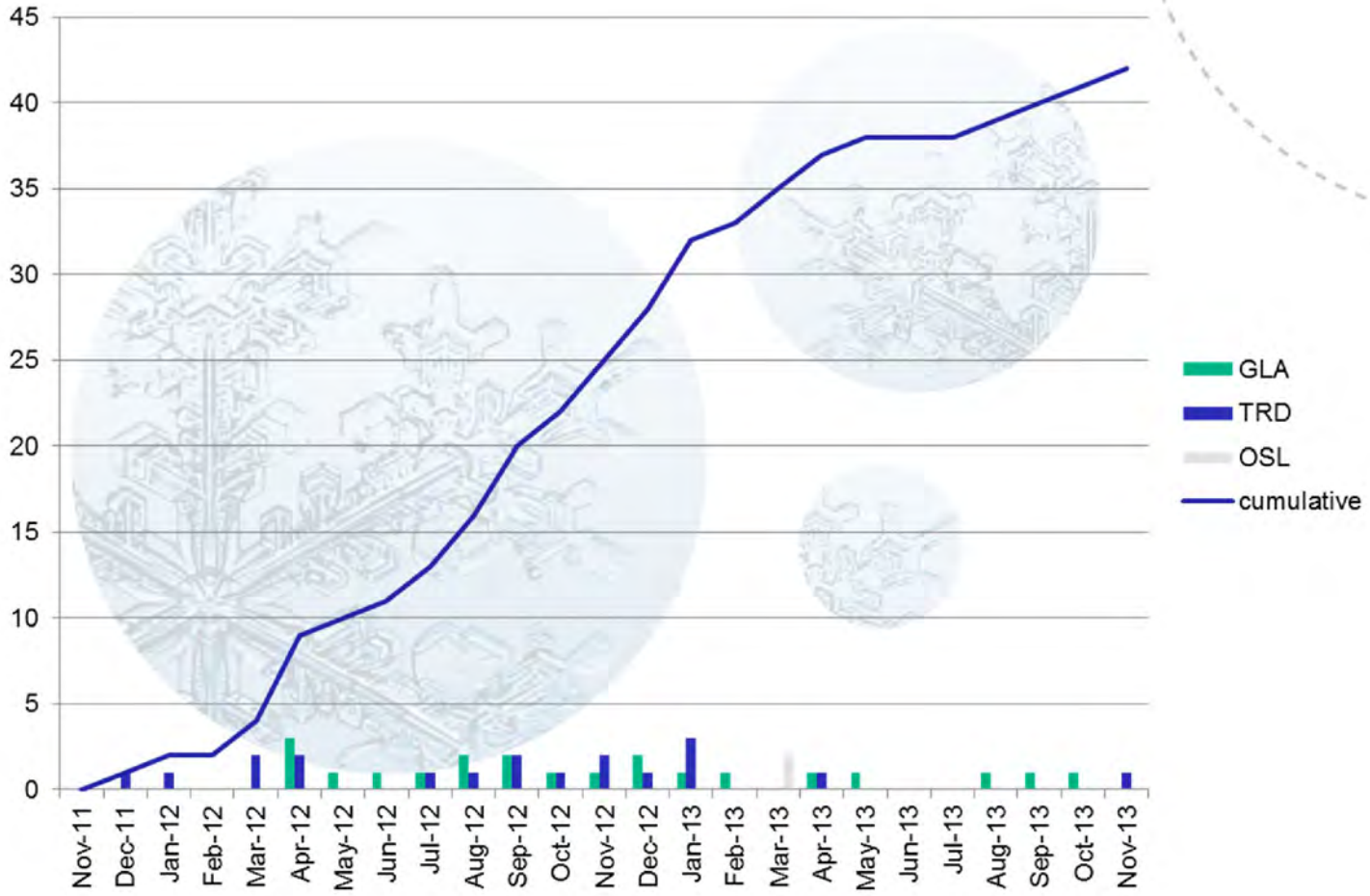


Key challenges with recruitment

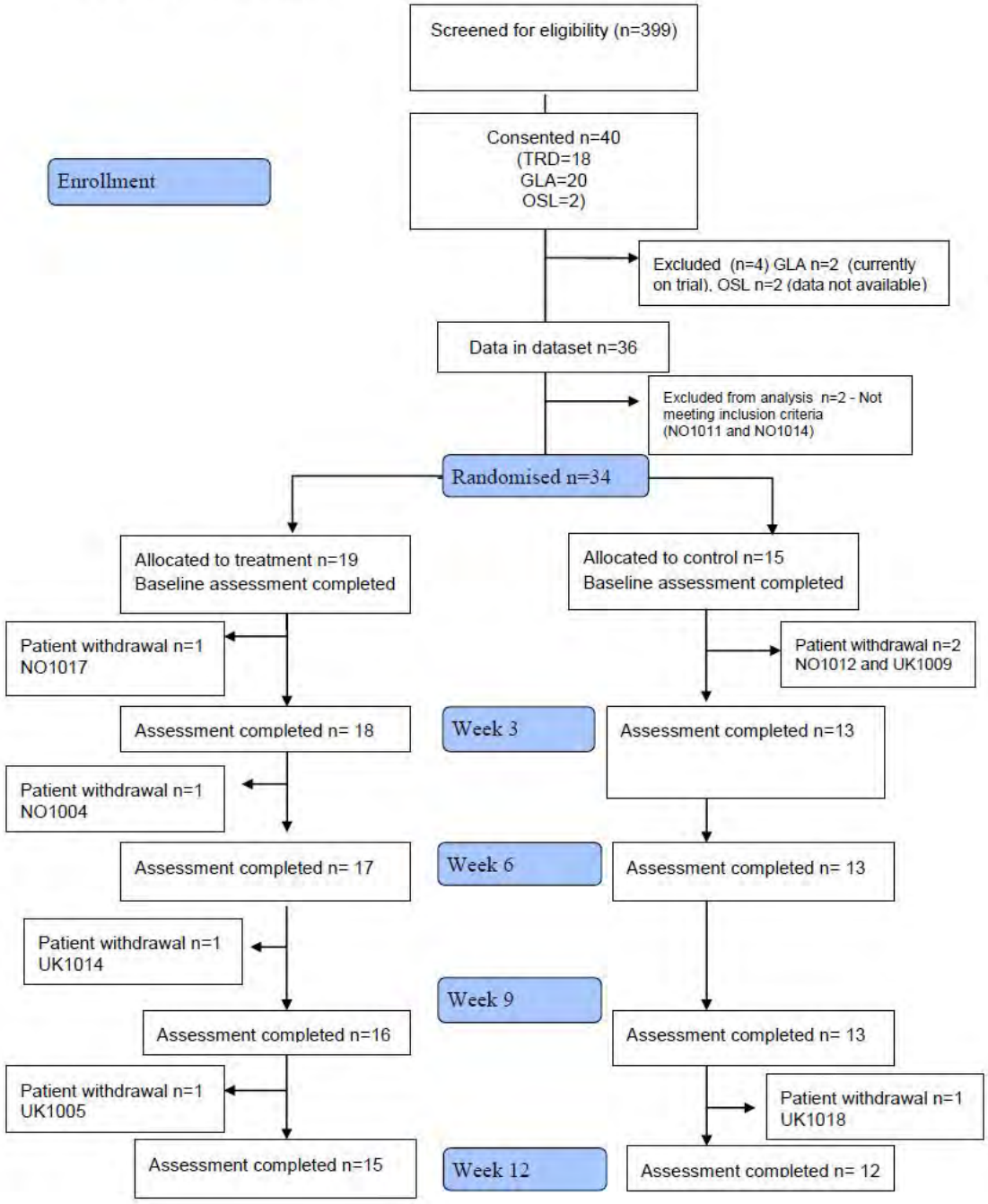
- Poor PS
- No active treatments
- Over 80 years
- Neuroendocrine ca
- Contraindications to COXII
  - Ischaemic heart disease,
  - Inflammatory disease
  - Anti-coagulants

	Glasgow	TRD	OSL
Recruited	21	19	2

Recruitment



1.1.3 CONSORT diagram

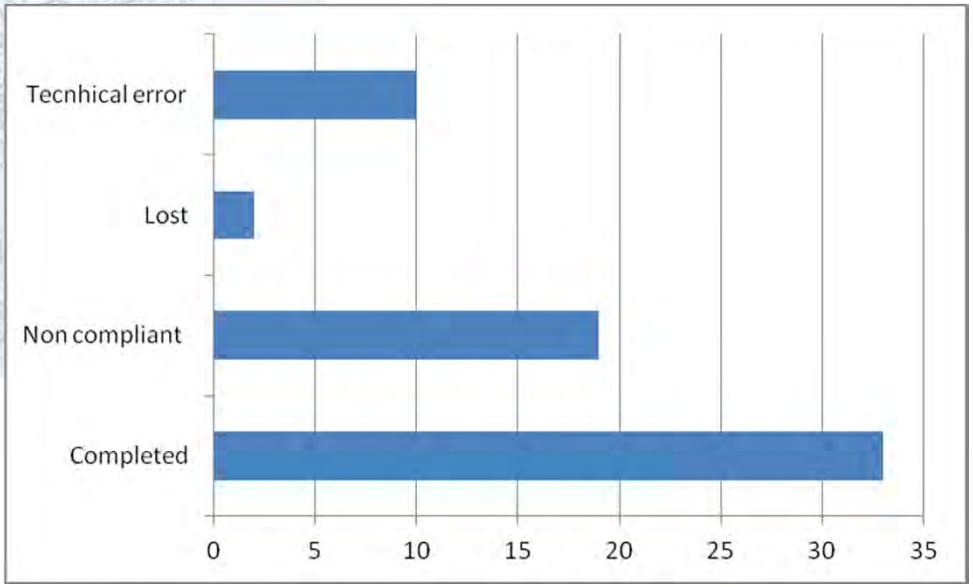


	Compliance n=19 n(%)						Summary Compliance					
							Week 3 n=18		Week 6 n=17		Total	
	<33%	33-50%	51-65%	66-75%	76-80%	>81%	Mean %	SD	Mean %	SD	Mean %	SD
Celecoxib	3 (16)	2 (11)	1 (5)		1 (5)	12 (63)	86.4	25.3	76.5	37.4	82.1	29.7
ONS	8 (42)	2 (11)				9 (47)	58.7	39.9	54.5	44.2	58.1	40.6
Exercise												
Strength	10 (53)	2 (11)	1 (5)	1 (5)		5 (26)	54.6	57.3	41.2	42.4	47.0	41.1
Aerobic	10 (53)	1 (5)				8 (42)	149.0	135.8	108.0	121.9	126.9	117.8
Nutritional Intake							**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
AveS							8.4	1.4	7.9	1.9	8.2	5.1

Summary of CT scan rates

	CT cohort	
	Treatment	Control
Baseline n (% of total patients)	19 (100)	15 (100)
Withdrawn before week 6	n=2 (NO1004 and NO1017)	n=2 (UK1009 and NO1012)
Week 6 n (% of total patients)	15/17 (88)	11/13 (84)
Completed week 6 but no CT scans	n=2 UK1013 and UK1014	n=2 UK1018 and NO1003

		Baseline		6 week		
		Yes	**No**	**Yes**	**No**	**Both**
Arm	Control - n (% of total patients)	12 (80)	3 (20)	10 (77)	3 (23)	9 (60)
	Treatment - n (% of total patients)	11 (58)	8 (42)	10 (59)	7 (41)	6 (40)
Centre	GLA - n (% of total patients)	12 (67)	6 (33)	9 (53)	8 (47)	6 (33)
	TRD - n (% of total patients)	11 (69)	5 (31)	11 (85)	2 (15)	9 (56)



6 minute walk test

	Treatment n=19	**Control n=15**	**Baseline total**	**Week 6 total**
	Completed	Completed	Treatment (n)	Control (n)
Baseline (% of total patients)	18 (95)	15 (100)	19	15
Week 6 (% of total patients)	15 (88)	13 (100)	17	13

Grip strength

	Treatment n=19	**Control n=15**	**Baseline total**	**Week 6 total**
	Completed	Completed	Treatment (n)	Control (n)
Baseline (% of total patients)	19 (100)	15 (100)	19	15
Week 6 (% of total patients)	16 (94)	12 (92)	17	13

Contamination of control group

	Baseline		**Week 6**	
	Control n=15 Mean (SD)	Treatment n=19 Mean (SD)	Control n=13 Mean (SD)	Treatment n=17 Mean (SD)
Aves	7.08 (2.66)	7.37 (2.1)	6.85 (2.23)	7.88 (1.89)
NSAID use	0		2	
HUNT 3	6.84 (1.51)	7.06 (1.67)	6.34 (1.33)	6.71 (0.99)
6MWT	473.7 (85.3)	472.5 (137.3)	454.0 (247.2)	379.8 (221.9)

Challenges of preMENAC

- Pragmatic versus homogenous design
- Multimodal intervention (multiple professionals)
- Assessments
- Compliance
- Trial running in combination with oncology intervention
- Attrition
- Recruitment!

- Trial ongoing – target 40 evaluable patients

RESULTS: Secondary endpoints…

8th World Research Congress of the European Association for Palliative Care

Lleida, Spain 5-7 June 2014

EAPC ONLUS