Supportive Care in Cancer Highlights of the Year 2015

F.Scotté

HÔPITAL EUROPÉEN GEORGES POMPIDOU

MEDICAL ONCOLOGY / SUPPORTIVE CARE IN CANCER UNIT –

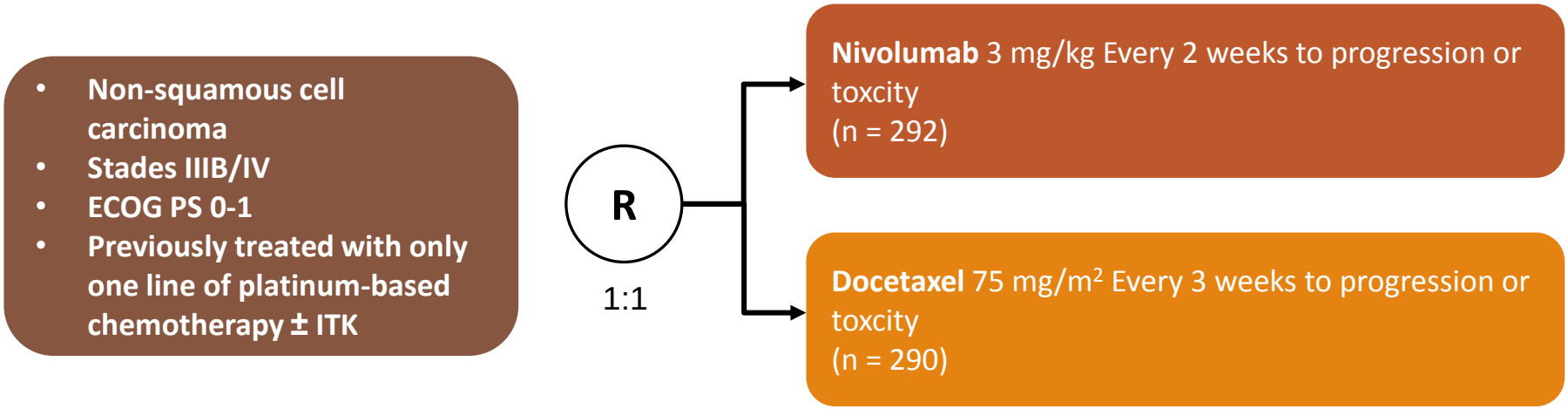
EA 4569 « ETHIQUE, POLITIQUE ET SANTÉ »

UNIVERSITÉ PARIS DESCARTES

PARIS - FRANCE

Old / New Treatment - Safety

- Phase III study (CheckMate 057) of nivolumab vs docetaxel in second_line of non-squamous cell carcinoma *(1)*



- Primary endpoint : OS

- Secondary endpoints :
  - OR RECIST v1.1
  - progression-free survival (PFS)
  - efficacy by PD-L1 expression*
  - quality of life safety

* Anti PD-L1 IHC evaluated with Daka IHC system

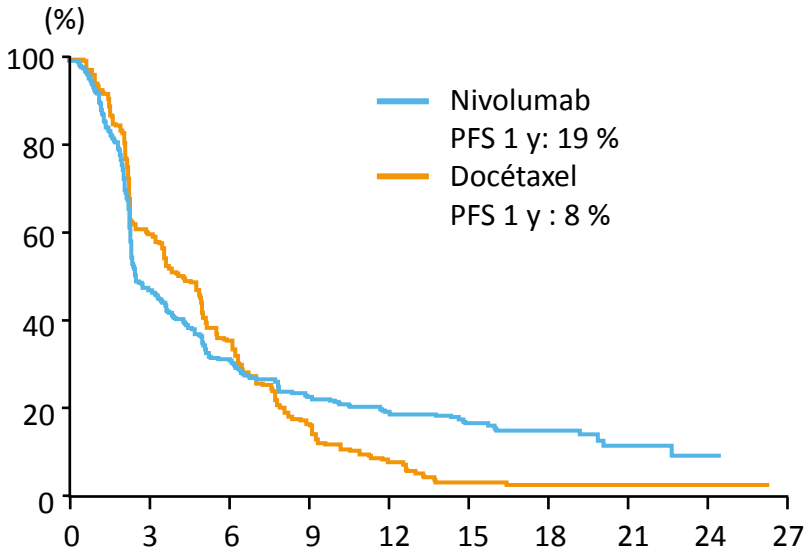
ASCO 2015 - Spigel DR et al., abstr. 8009

Old / New Treatment - Safety

- Phase III study (CheckMate 057) of nivolumab vs docetaxel in second_line of non-squamous cell carcinoma

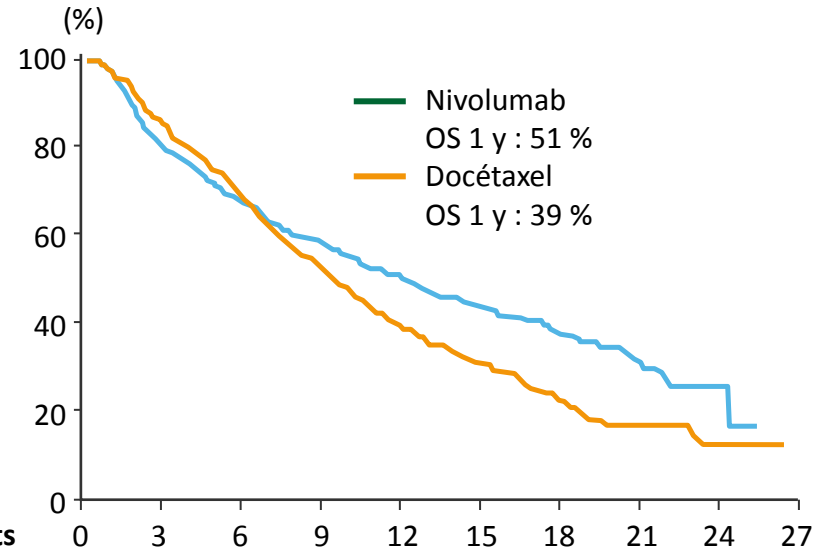
Progression-free survival

	Nivolumab (n = 292)	Docetaxel (n = 290)
Median (months)	2,3	4,2
HR = 0,92 ; IC_{95} : 0,77-1,11 ; p = 0,3932		



Overall survival

	Nivolumab (n = 292)	Docetaxel (n = 290)
Median (months)	12,2	9,4
HR = 0,73 ; IC_{96} : 0,59-0,89 ; p = 0,0015		



ASCO 2015 - Paz-Ares L et al., LBA109,

Old / New Treatment - Safety

	Nivolumab (n = 237)	Docetaxel (n = 268)
Grade 3-4 Adverse effects (%)	10	54
Graded 3-4 serious adverse effects (%)	5	18
Serious adverse effects with interuption of the treatment (%)	5	15
Ineterstitial pneumonia (%)	3	< 1
Hepatitis (%)	6	2
Diarrhea (%)	8	23
Hypothyroidism (%)	7	0

ASCO 2015 - Paz-Ares L et al., LBA109,

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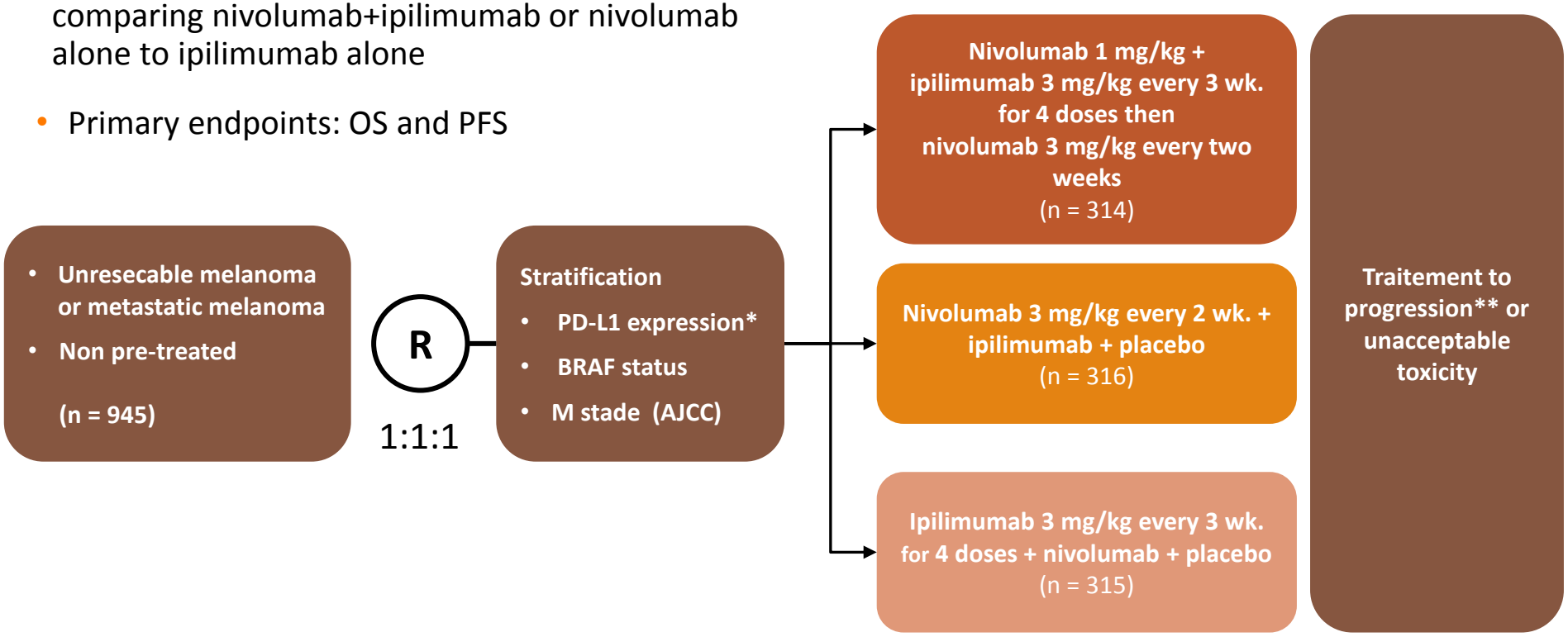
OLD SAFETY EDUCATION

ASCO 2015 - Paz-Ares L et al., LBA109,

Old / New Treatment - Safety

- Phase III trial CheckMate 067 Evaluating the interest of combined inhibition of PD-1 and CTLA-4

  - Randomized phase III trial, double-blind, comparing nivolumab+ipilimumab or nivolumab alone to ipilimumab alone
  - Primary endpoints: OS and PFS



* Stratification function of PD-L1 expression of 5%

** The patients could have been treated to progression according to condition defined by the study protocol

ASCO 2015 - Wolchok JD et al., LBA1

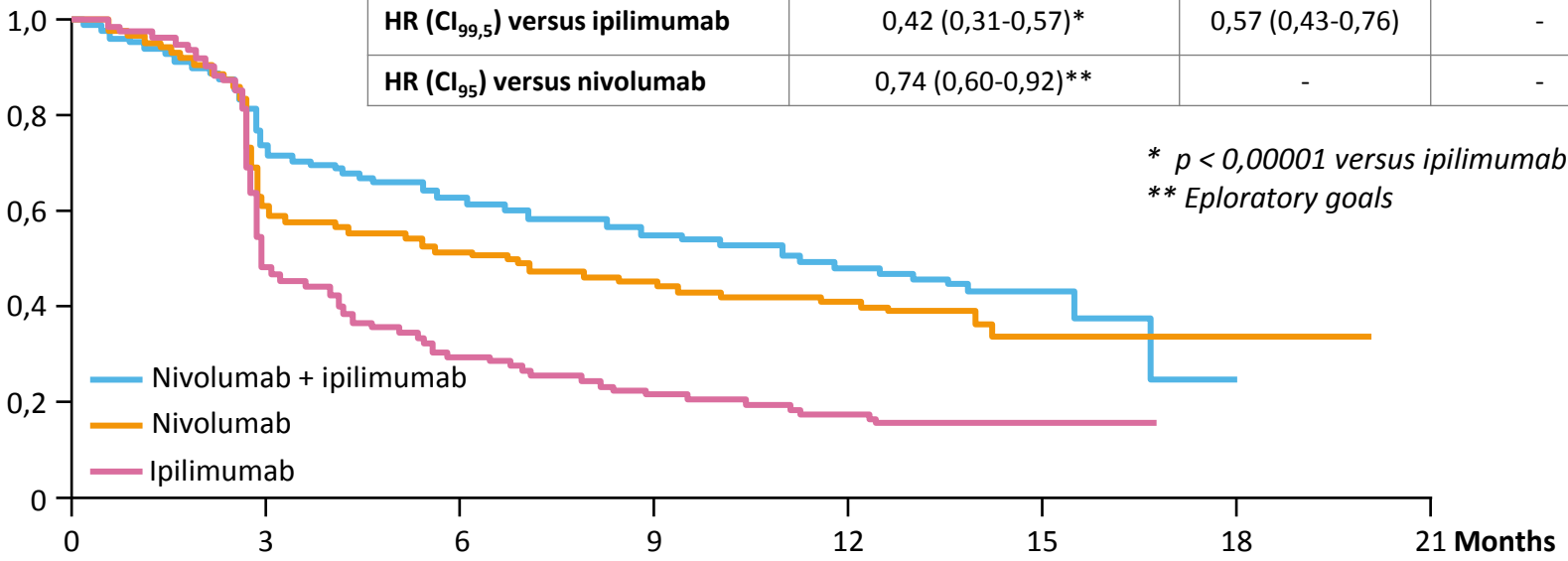
Old / New Treatment - Safety

- Phase III trial CheckMate 067 Evaluating the interest of combined inhibition of PD-1 and CTLA-4

Progression free survival

	Nivolumab + ipilimumab (n = 314)	Nivolumab (n = 316)	Ipilimumab (n = 315)
PFS médiane, months (CI_{95})	11,5 (8,9-16,7)	6,9 (4,3-9,5)	2,9 (2,8-3,4)
HR ($CI_{99,5}$) versus ipilimumab	0,42 (0,31-0,57)*	0,57 (0,43-0,76)	-
HR (CI_{95}) versus nivolumab	0,74 (0,60-0,92)**	-	-

** p < 0,00001 versus ipilimumab.*
*** Eploratory goals*



Patients at risk (n)

314	219	173	151	65	11	1	0
316	177	147	124	50	9	1	0
315	137	77	54	24	4	0	0

ASCO 2015 - Wolchok JD et al., LBA1

Old / New Treatment - Safety

- Phase III trial CheckMate 067 Evaluating the interest of combined inhibition of PD-1 and CTLA-4 *(6)*

	Nivolumab + ipilimumab (n = 313)		Nivolumab (n = 313)		Ipilimumab (n = 313)	
	All grades	**3-4 Grade**	**All grades**	**3-4 Grade**	**All grades**	**3-4 Grade**
Adverse events related to treatment	95,5	55,0	82,1	16,3	86,3	27,3
Adverse events inducing interruption of treatment	36,4	29,4	7,7	5,1	14,8	13,2
Adverse events inducing death of the patient	0		0,3		0,3	

67,5 % Of patients who stop treatment because of toxicity (81/120) had clinical response

ASCO 2015 - Wolchok JD et al., LBA1

Old / New Treatment - Safety

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NEW SAFETY EDUCATION

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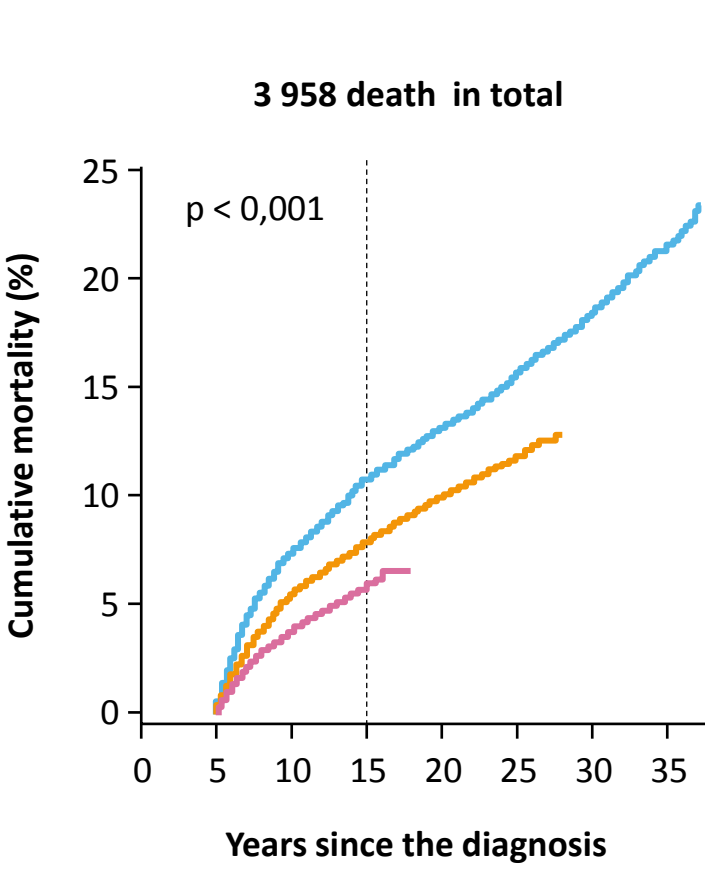
ASCO 2015 - Wolchok JD et al., LBA1

Survivorship : A story of cancer

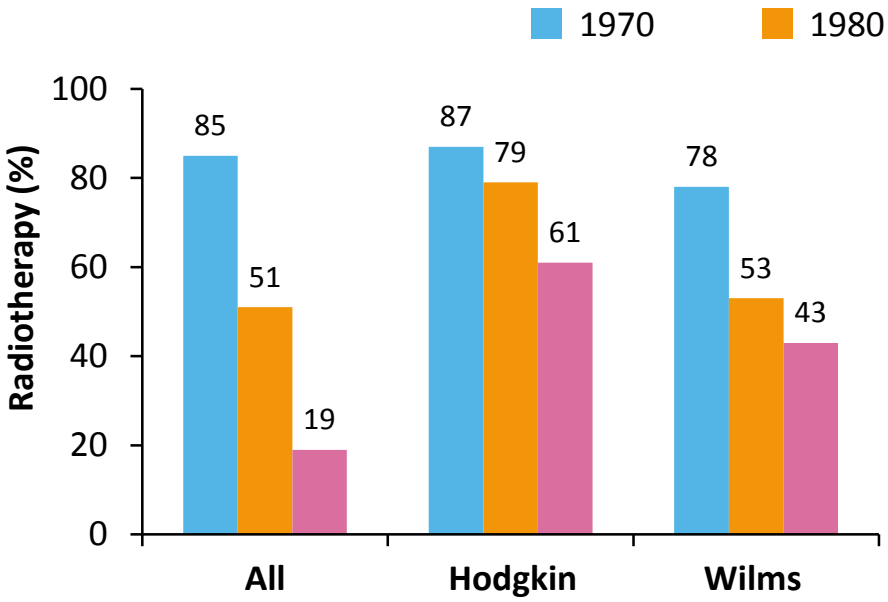
- Endpoint : Compare the causes of death of the survivors of pediatric cancers
- Evaluation of the causes of late mortalities related to treatments
- Hazard regression to estimate the mortality of every treatment



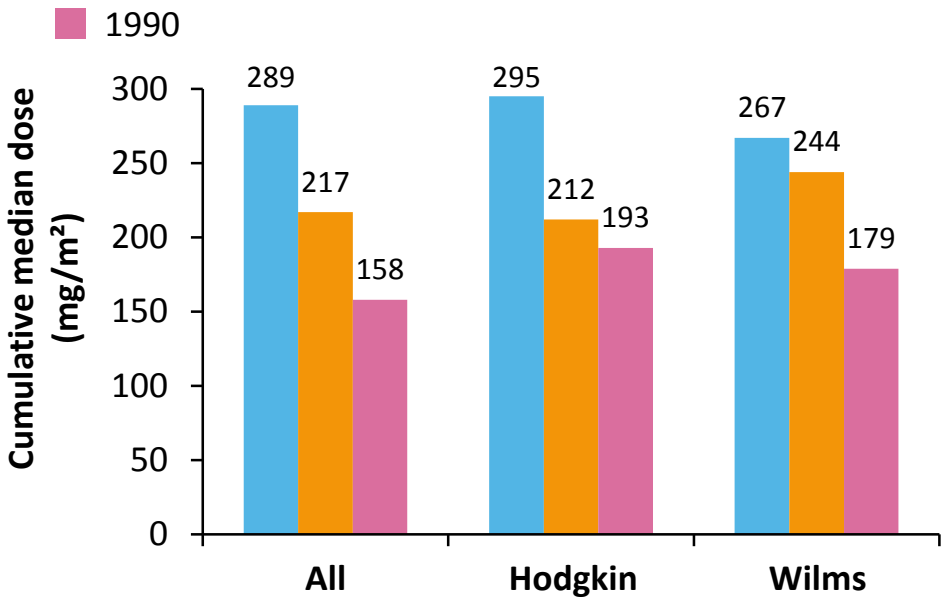
ASCO 2015 - Armstrong GT et al., LBA2

Survivorship : A story of cancer

Evolution in time of radiotherapy exposure



Evolution in time of anthracyclines exposure

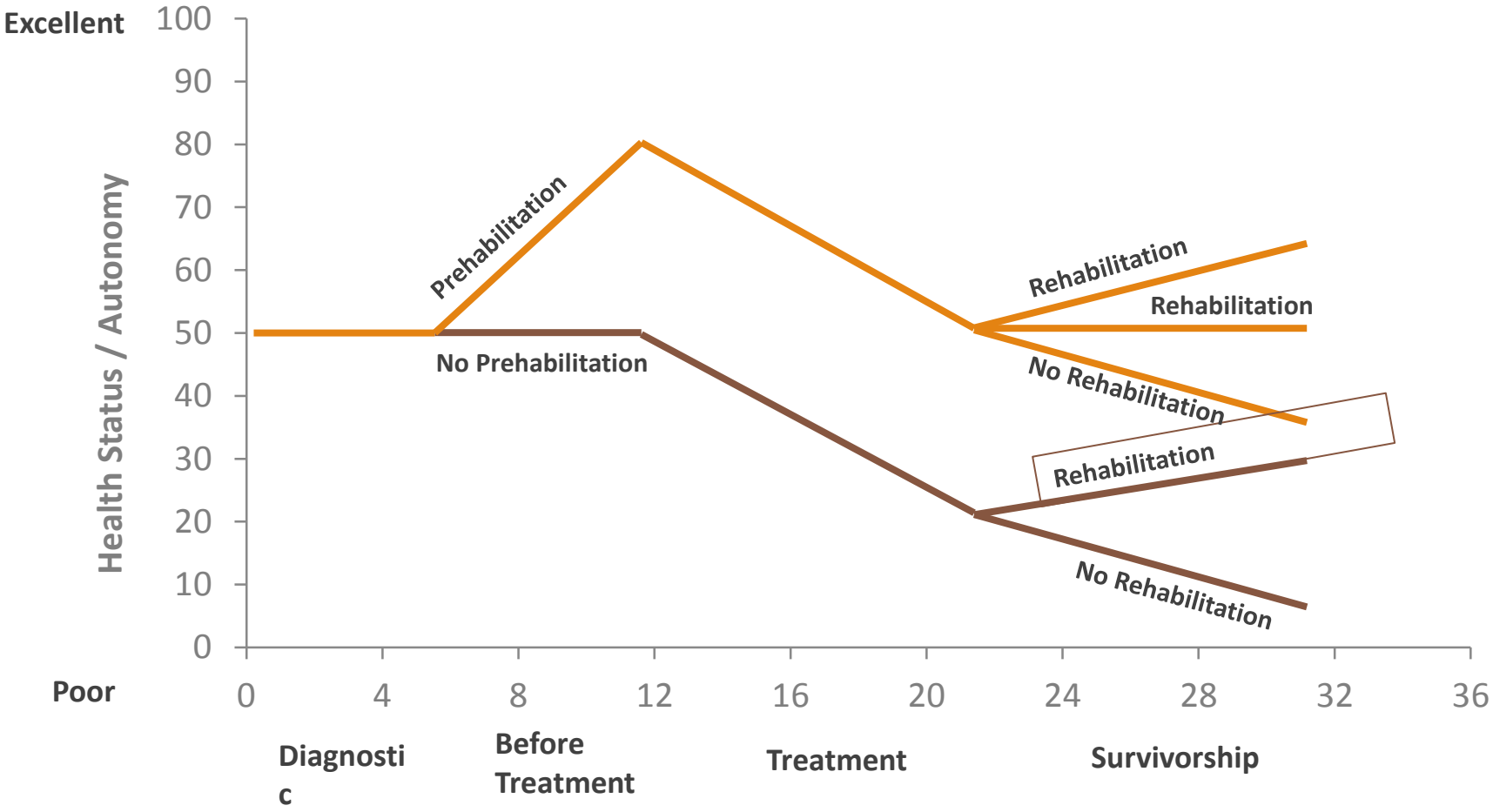


➔ The therapeutic progress and toxicity management jointly improve the survival

➔ *Supportive Care* to *Cancer Toxicity Management*

ASCO 2015 - Armstrong GT et al., LBA2,

Pre-Habilitation / Re-Habilitation
New Standard of Care ?



Zoledronic acid : 1 month vs 3 months !

- Non inferiority study
- Primary endpoint :BSE incidence

R

- Zoledronic acid/4 weeks x 2 years
- Zoledronic acid/12 weeks x 2 years

(n = 1 758)

Stratification : cancer, renal function, previous BSE and bisphosphonates

Disease	Treatment	n	≥ 1 BSE	p (CI_{95})
Breast, prostate, myeloma	ZA x 4 weeks	882	260 (29 %)	0,79 (-3,3 ; 5,1)
	ZA x 12 weeks	884	253 (29 %)	

BSE : bone secondary events

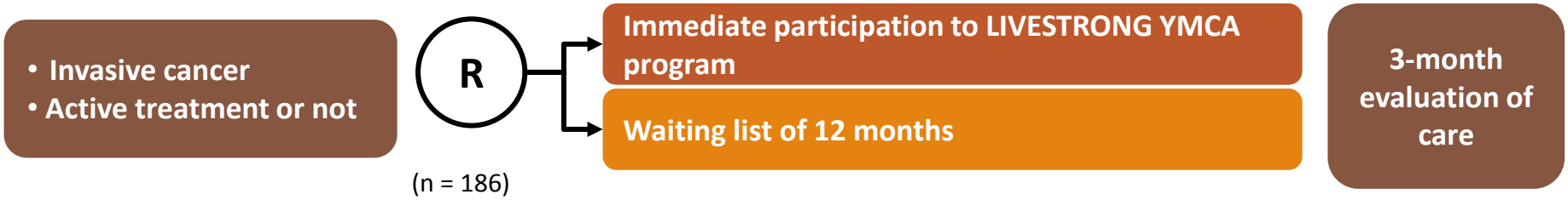
No significative difference

- Depending on tumour type : breast (p = 0,66) ; prostate (p = 0,69) ; myeloma (p = 0,39)
- On bone morbidity (p = 0,75), pain scores (p = 0,75) and general condition (p = 0,64)
- On osteonecrosis (p = 0,08) and renal function impact (p = 0,12)

➔ Zoledronic acid can be administered every 12 weeks in prevention of the bone events

ASCO 2015 - Himelstein AL et al., abstr. 9501

YMCA



Significative results ($p < 0,05$)

- Adherence to program
- Modification of physical activity level
- Quality of life score (FACT-G)

Who	Survivors with or without treatment
What	Individualised exercise program in small groups with YMCA instructor
When/Where	2 sessions of 90 min/wk./3 months in a YMCA wellness center
How	Quality of life evaluation before and after program follow by YMCA instructors

➔ Support programs improve quality of life and help to adhere

ASCO 2015 - Irwin ML et al., abstr. 9508

ENERGY : breast and obesity

- Breast cancer
- End of treatment : 6 months to 5 years before
- BMI 25-45 kg/m²

R

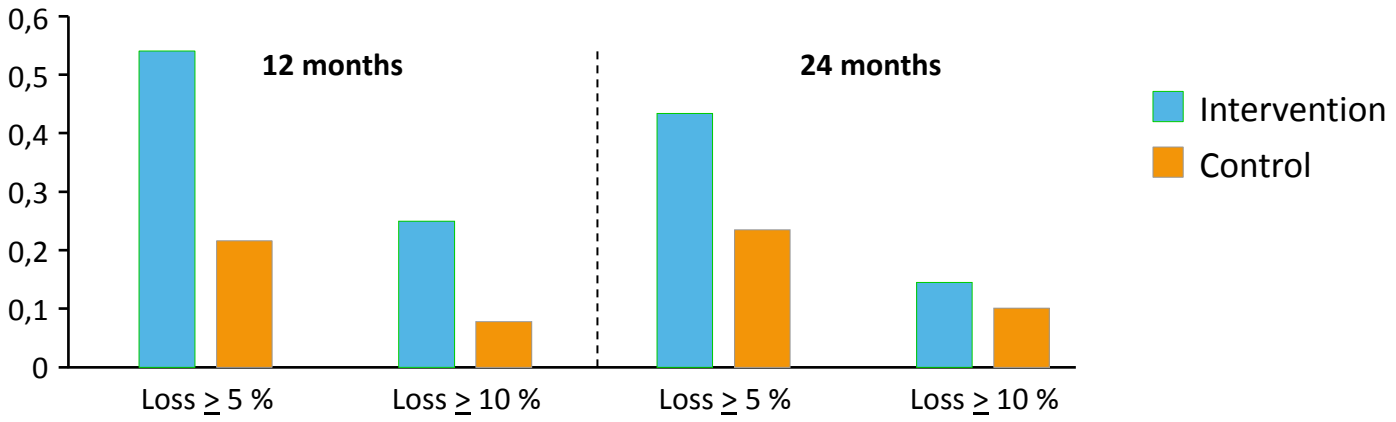
(n = 692)

Cognitive behavioural therapy, telephone support, dietary plan, adapted physical activity (APA) (n = 344)

Consultation with dietititian (inclusion and 6 months later) + telephone (n = 348)

- Evaluation at 1 and 2 years
- Loss of weight
- Impact on the quality of life

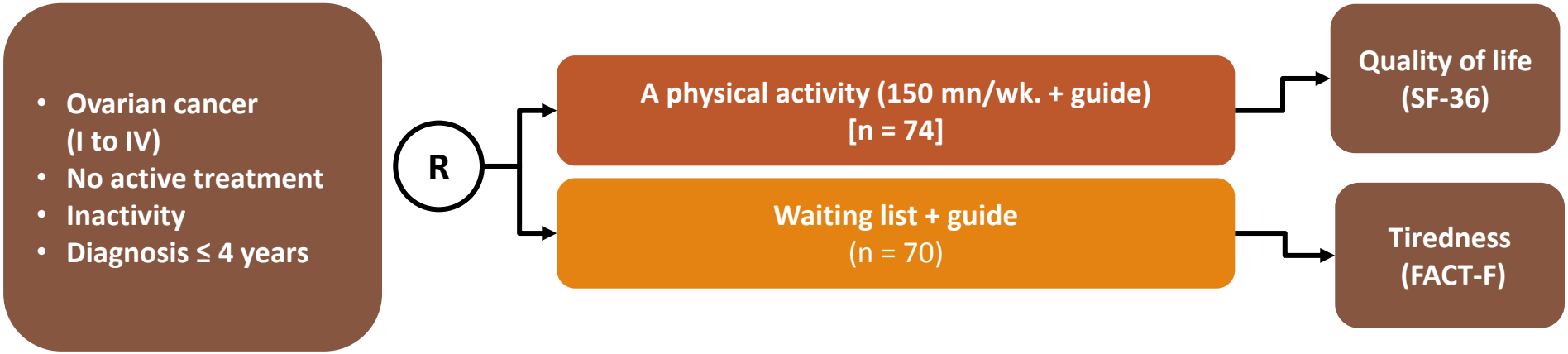
Participants' proportion in the study reaching a loss of weight ≥ 5 % and ≥ 10 % of initial weight at 12 and 24 months



➔ To care allows to reduce significantly the obesity

ASCO 2015 - Rock CL et al., abstr. 9506

Adapted physical activity in ovarian cancer

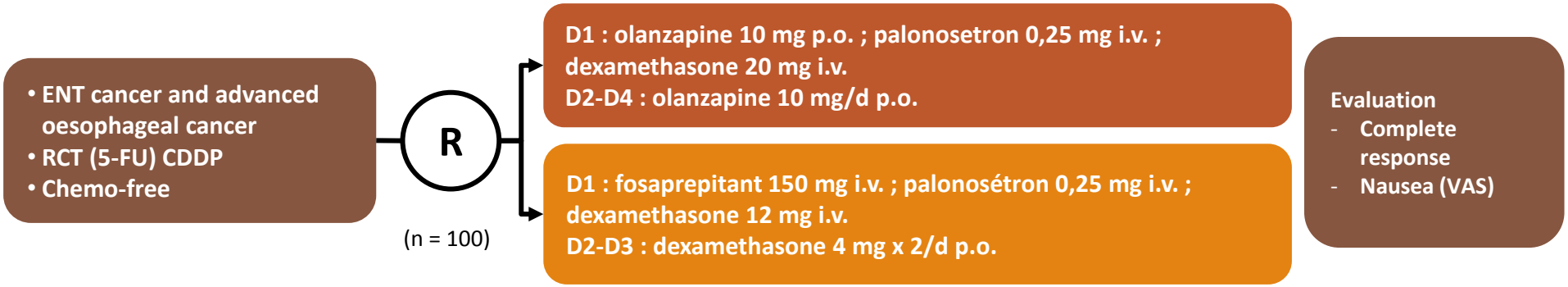


Modifications over 6 months	Change on fatigue	p	Change on quality of life	p
< 150 mn/wk. (n = 26)	0,6 (-3,4 ; 4,6)	0,76	-2,6 (-6,9 ; 1,6)	0,22
≥ 150 mn/wk. (n = 48)	5,3 (2,5 ; 8,0)	0,0003	3,5 (0,7 ; 6,4)	0,02

➔ Adhesion to APA is a security of improvement of the fatigue and of the quality of life

ASCO 2015 - Zhou Y et al., abstr. 9505

Olanzapine : Less Nausea



Period	Complete response(%)		No nausea (%)	
	Olanzapine (n = 51)	Fosaprepitant (n = 49)	Olanzapine (n = 51)	Fosaprepitant (n = 49)
Acute phase (0-24 h)	88	84 (p > 0,05)	86	77 (p > 0,05)
Delayed phase (24-120 h)	76	73 (p > 0,05)	71	41 (p < 0,01)
Overall period (0-120 h)	76	73 (p > 0,05)	71	41 (p < 0,01)

Complete response : no nausea or diziness, no backup treatment

➔ Olanzapine is effective in antiemetic prevention of highly emetogenic chemotherapies

ASCO 2015 - Navari RM et al., abstr. 9502

Olanzapine - ALLIANCE A221301

- First cycle HEC
Cisplatinum ≥ 70 mg/m2
Or
Anthracycline (60 mg/m2)
+ Cyclophosphamide (600 mg/m2)

R

Olanzapine 10mg/j/J1-4 + Standard Treatment

Placebo 1 /j/J1-4 + Standard Treatment

Standard Treatment
- Setron
- Dexamethasone
- Aprepitant

First Objective: No Nausea

Phase	Olanzapine N=192	Placebo N=188	P
Acute (0-24h)	73,8	45,3	<0,0001
Delayed (24-120h)	42,4	25,4	0,0008
Global (0-120h)	37,3	21,9	0,0015

2d Objective: Complete Response

Phase	Olanzapine N=192	Placebo N=188	P
Acute (0-24h)	85,7	64,6	<0,0001
Delayed (24-120h)	66,9	52,4	0,0073
Global (0-120h)	63,6	40,6	<0,0001

Navarri R. *et al*.- ASCO PAL 2015 - Abs 176

Anamorelin against cachexia

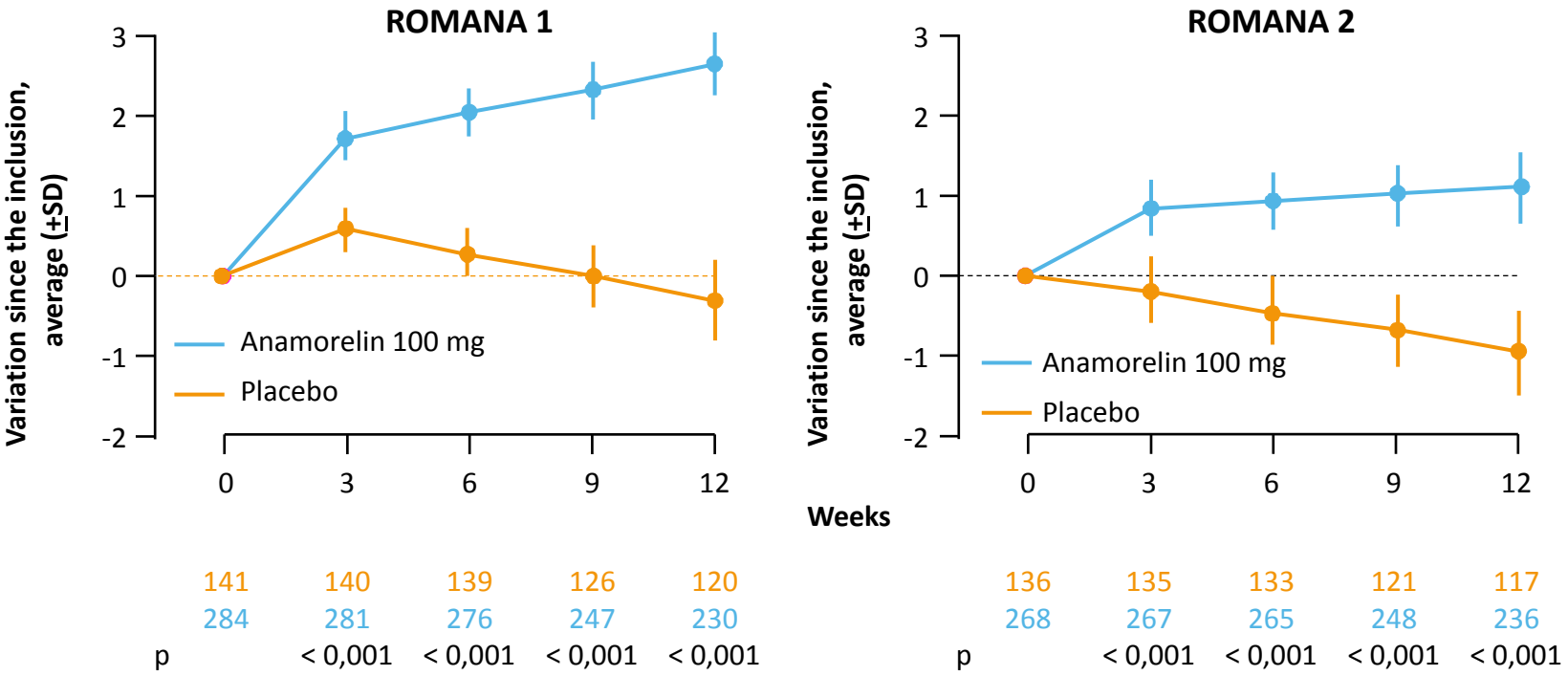
- Stages 3 and 4 NSCLC
- Anorexia/cachexia
  - Loss of weight ≥ 5 % at 6 months
  - BMI < 20 kg/m²

R (2:1)

- Anamorelin
- Placebo

Evaluation at 12 week of treatment

Evolution of weight



	141	140	139	126	120
	284	281	276	247	230
p		< 0,001	< 0,001	< 0,001	< 0,001

	136	135	133	121	117
	268	267	265	248	236
p		< 0,001	< 0,001	< 0,001	< 0,001

Anamorelin against cachexia

Primary endpoint	ROMANA 1			ROMANA 2		
	Placebo (n = 161)	Anamorelin (n = 323)	p	Placebo (n = 165)	Anamorelin (n = 330)	p
Lean mass (kg)	-0,44 (-0,88 ; 0,20)	1,10 (0,75 ; 1,42)	< 0,001	-0,96 (-1,27 ; -0,46)	0,75 (0,51 ; 1,00)	< 0,001
Wirst force (kg)	-1,45 (-2,69 ; -1,05)	-1,00 (-1,60 ; -0,30)	0,45	-0,95 (-1,60 ; 0,00)	-1,15 (-2,05 ; -0,45)	0,74

Adverse effects	ROMANA 1		ROMANA 2	
	Placebo (n = 161)	Anamorelin (n = 320)	Placebo (n = 161)	Anamorelin (n = 330)
All grades, n (%)	15 (9,3)	46 (14,4)	12 (7,5)	32 (9,7)
1-2 grades, n (%)	13 (8,1)	43 (13,4)	8 (5,0)	22 (6,7)
3-4 grades, n (%)	2 (1,2)	3 (0,9)	4 (2,5)	9 (2,7)

- Nauseas, metabolic disorders (diabetes, hyperglycemia)
- Overall survival : HR = 1,06 ; CI_{95} : 0,89-1,26 ; p = 0,47

ASCO 2015 - Temel JS et al., abstr. 9500

Kidney Failure and Mortality: What Level

CUT-OFF = GRF 70 ml/min

A Method Test	HR (CI_{95})	p	B Method Test	HR (CI_{95})	p
GFR < 90 versus GFR ≥ 90	1,02 (0,93-1,13)	> 0,05	GFR < 90 versus GFR ≥ 90	1,03 (0,93-1,14)	> 0,05
GFR < 80 versus GFR ≥ 90	1,04 (0,94-1,16)	> 0,05	GFR < 80 versus GFR ≥ 80	1,04 (0,94-1,16)	> 0,05
GFR < 70 versus GFR ≥ 90	1,16 (1,03-1,31)	0,02	GFR < 70 versus GFR ≥ 70	1,18 (1,06-1,31)	0,03
GFR < 60 versus GFR ≥ 90	1,23 (1,07-1,42)	0,04	GFR < 60 versus GFR ≥ 60	1,16 (1,03-1,27)	0,001
GFR < 50 versus GFR ≥ 90	1,27 (1,08-1,51)	0,005	GFR < 50 versus GFR ≥ 50	1,27 (1,09-1,49)	0,003
GFR < 40 versus GFR ≥ 90	1,50 (1,23-1,83)	< 0,0001	GFR < 40 versus GFR ≥ 40	1,50 (1,25-1,81)	< 0,0001
GFR < 30 versus GFR ≥ 90	1,53 (1,22-1,92)	0,0002	GFR < 30 versus GFR ≥ 30	1,53 (1,24-1,86)	0,0001

GFR : glomerular filtration rate

ASCO 2015 - Launay-Vacher V et al., abstr. 1589,

Hot Flushes : Homeopathy vs Placebo

- Localized breast cancer
- Hormone-adjuvant
- No radio- or chemotherapy
- Flushing > 10

Evaluation at 4 weeks of treatment

Evolution

Variation of flushing after 4 weeks of treatment	Actheane® (n = 65)	Placebo (n = 73)	Test
Median of absolute variation	- 2,9 (-16,9 ; 16,5)	- 2,5 (-21,8 ; 19,4)	Wilcoxon p = 0,756
Median rate of relative variation	-17,2 (-98,0 ; 76,7)	-15,4 (-99,6 ; 171,5)	Wilcoxon p = 0,629
Reduction of flushing (%)	46 (75,4)	48 (67,6)	Chi-2 p = 0,323

➔ Placebo effective against flushing, Acthéane® not superior to placebo

ASCO 2015 - Heudel PE et al., abstr. 9627

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

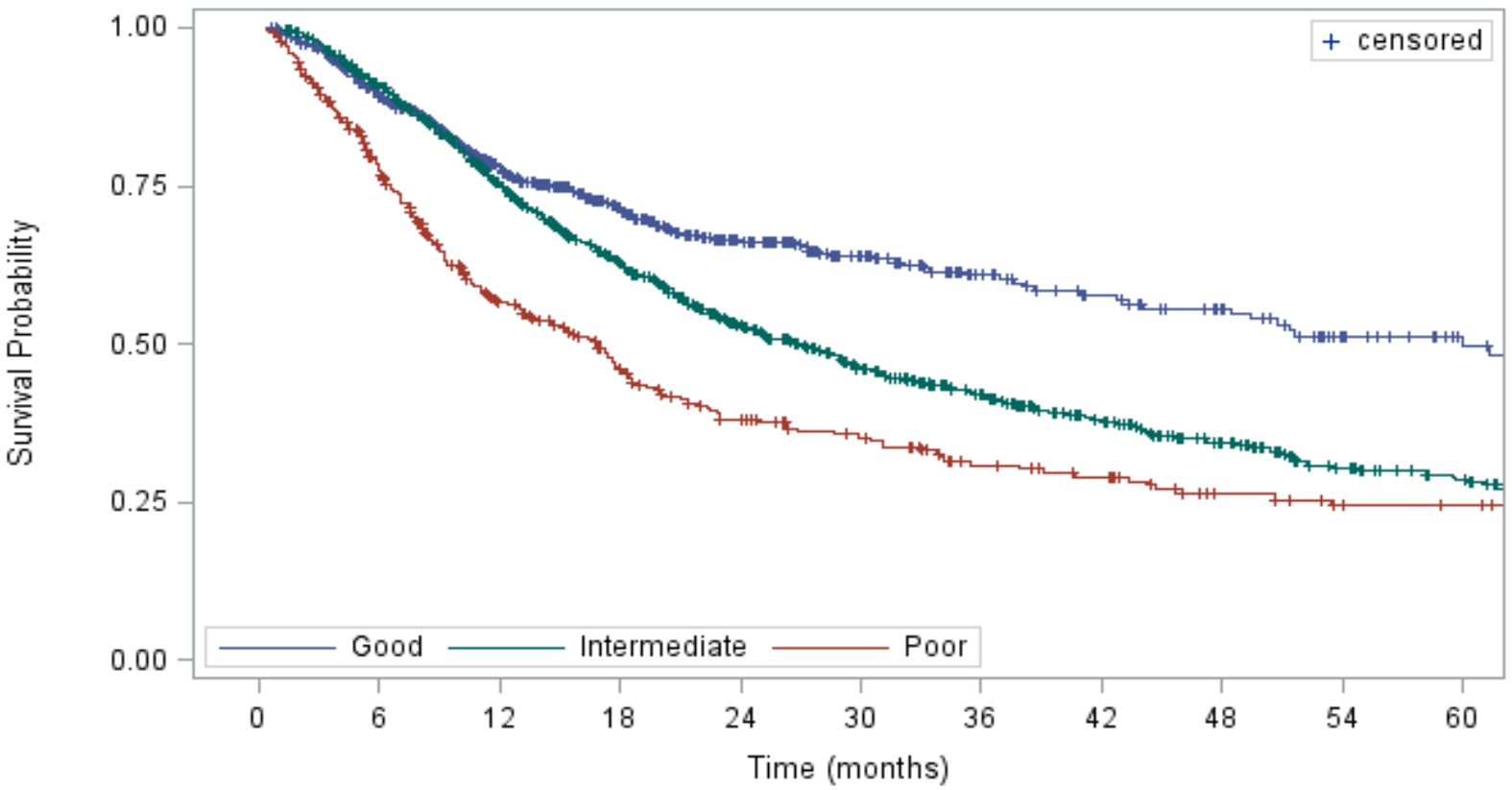
Impact of pain on overall survival in metastatic cancer patients treated with chemotherapy

Reza ELAIDI*, Florian SCOTTÉ, DUONG Khoa, Hail ABOUDAGGA, Jacques MEDIONI, Elizabeth FABRE, Bastien RANCE, Afef BOUCHOUICHA, Stephane OUDARD

***Corresponding author :** reza-thierry.elaidi@aphp.fr

ARTIC – Association pour la Recherche de Thérapeutiques Innovante en Cancérologie

Hôpital Européen Georges Pompidou, Paris, FRANCE

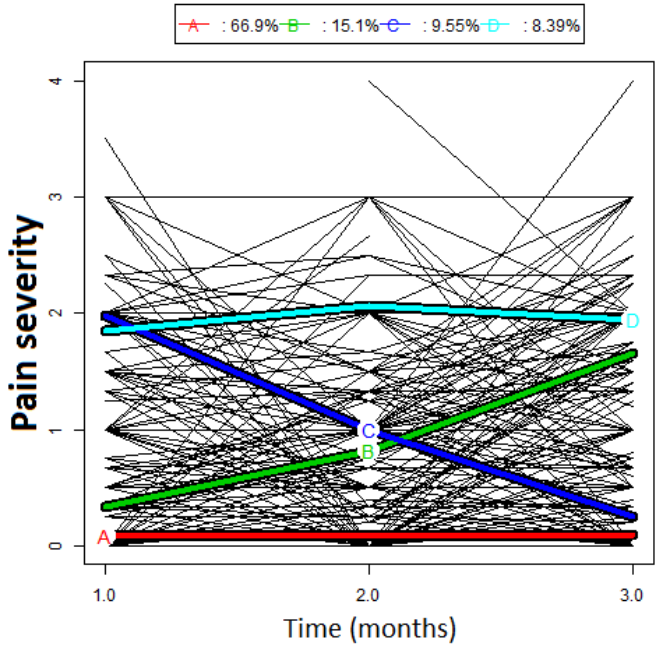


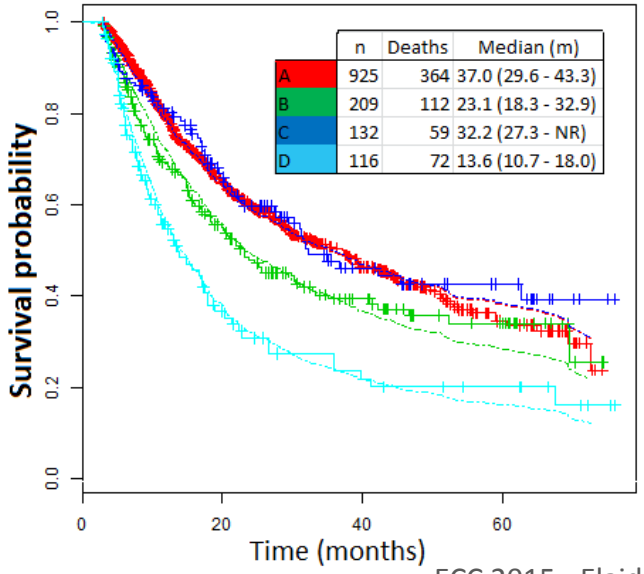
Patients at risk

Good	680	567	393	276	191	139	100	82	67	48	33
Intermediate	964	851	669	519	401	314	246	189	143	100	83
Poor	379	265	166	117	89	74	52	45	30	24	22

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

	Overall survival median (Months-95%CI)	Followup median (months)	Deaths
Overall cohort	30,2 (27,3-33,9)	31,5	47%
No pain	52,9 (49,9-NR)	20,7	31%
Low pain	29,3 (26,4-34,4)	40,0	54%
Moderate to severe pain	16,4 (12,8-18,4)	33,0	59%





ECC 2015 - Elaidi R. *and al.* Abs. 1503

"Supportive care makes excellent cancer care possible"

Dorothy M.K. Keefe,

MASCC™
Multinational Association
of Supportive Care in Cancer