2021 ASCO ANNUAL MEETING

ONCO NOUVELLE-AQUITAINE Réseau Régional de Cancérologie

BRIO BORDEAUX | Recherche Intégrée Oncologie

« En Vrac »

Pr Nicolas ISAMBERT

CHU de Poitiers

PD inhibition in soft-tissue sarcomas with tertiary lymphoid structures: a multicenter phase II trial

- PEMBROSARC
- étude de phase 2 évaluant la tolérance et l'efficacité d'un traitement associant pembrolizumab 200 mg IV et cyclophosphamide métronomique (50 mg/j 1 semaine/2) chez des patients ayant un sarcome localement avancé et/ou métastatique après une première ligne de traitement
- two-stage Simon's design
- sélection des patients sur les statut TLS (central review)
- revue centralisée de l'histologie et des évaluations radiologiques

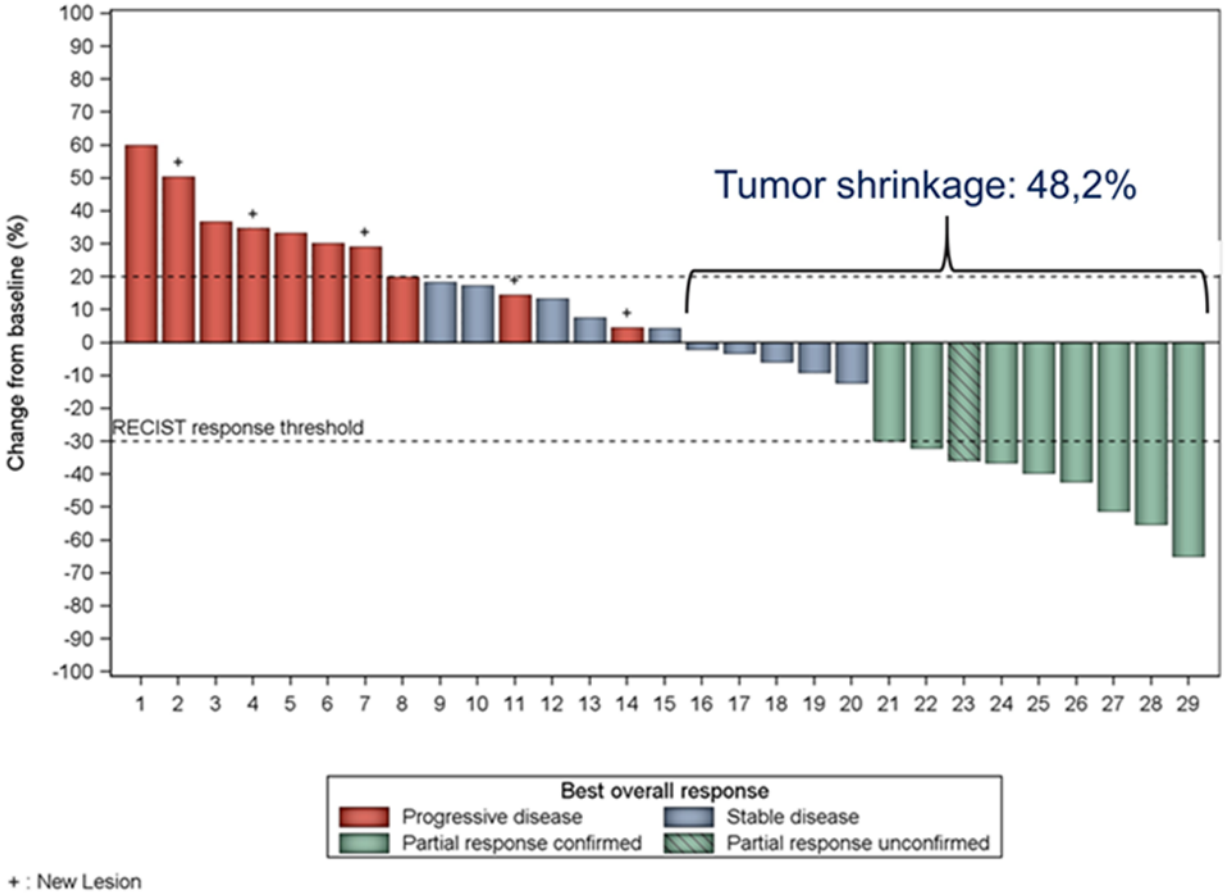
Caractéristiques de la population

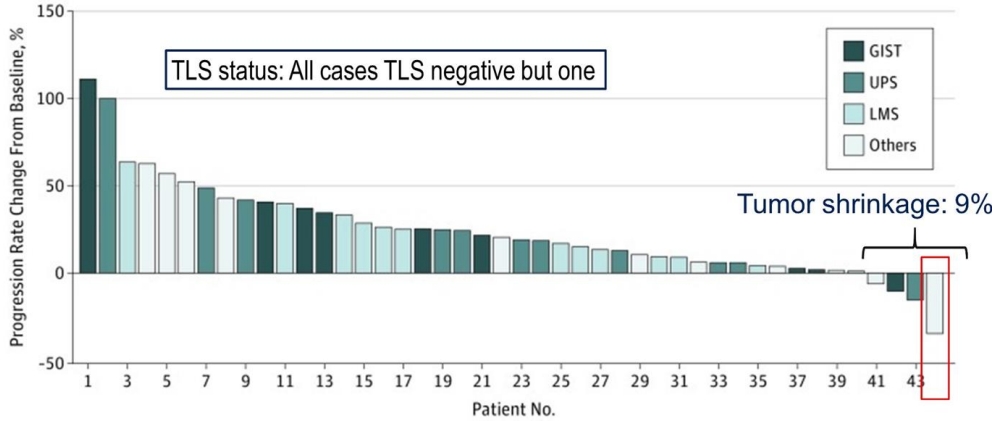
Sex, n (%)	
Male	19 (54.3%)
Female	16 (45.7%)
Age	
Median, years (range)	69 (20 – 88)
ECOG PS, n (%)	
0	20 (57,1%)
1	13 (37,1%)
ND	2 (5,7%)
Histological subtype (%)	
Well-differentiated/dedifferentiated liposarcomas	13 (37.1%)
UPS	6 (17.1%)
Epithelioid sarcomas	3 (8.7%)
Other*	13 (37.1%)
Stage n (%)	
Locally advanced	9 (17.1%)
Metastatic	26 (82.9%)
Prior lines of chemotherapy n (%)	
0	14 (40%)
1	11 (28.6%)
2	4 (11.4%)
> 2	6 (17.1%)

fibrosarcomas, solitary fibrous tumor, desmoplatic round cell tumor

Italiano A et *al.* ASCO 2021 Abst 11507

Efficacité



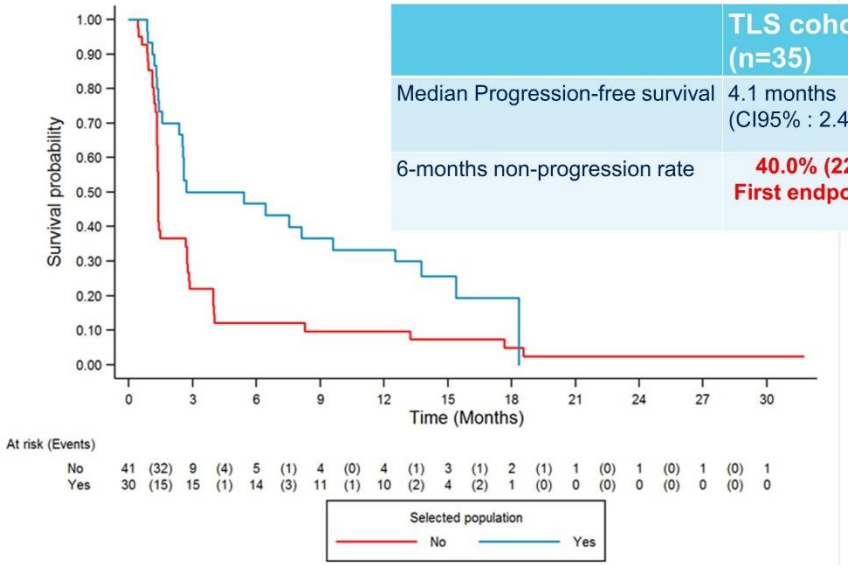


Objective response rates in previous PEMBROSARC cohorts (all comers): 2.3%

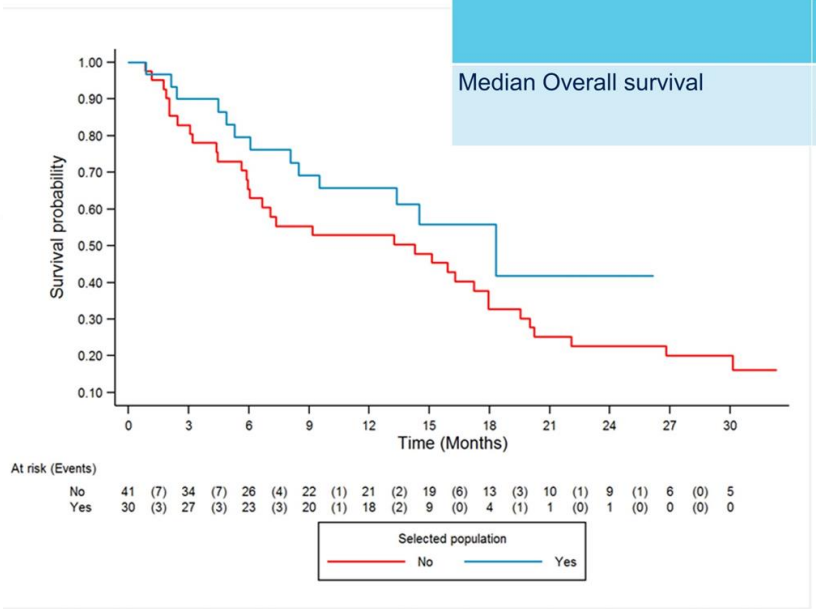
	n	%	Rate
Best overall response			
Partial response confirmed	**8**	**26.7**	**26.7%**
Partial response unconfirmed*	**1**	**3.3**	**3.3%**
Stable disease	10	33.3	33.3%
Progressive disease	10	33.3	33.3%
Not evaluable for response	1	3.3	3.3%

Italiano A et *al.* ASCO 2021 Abst 11507

Efficacité



	TLS cohort (n=35)	Previous cohorts (all comers) n=41
Median Progression-free survival	4.1 months (CI95% : 2.4-12.5)	1.4 months* (CI95% : 1.3-2.7)
6-months non-progression rate	**40.0% (22.7 – 59.4) First endpoint reached**	4.9% (0.6 – 16.5)

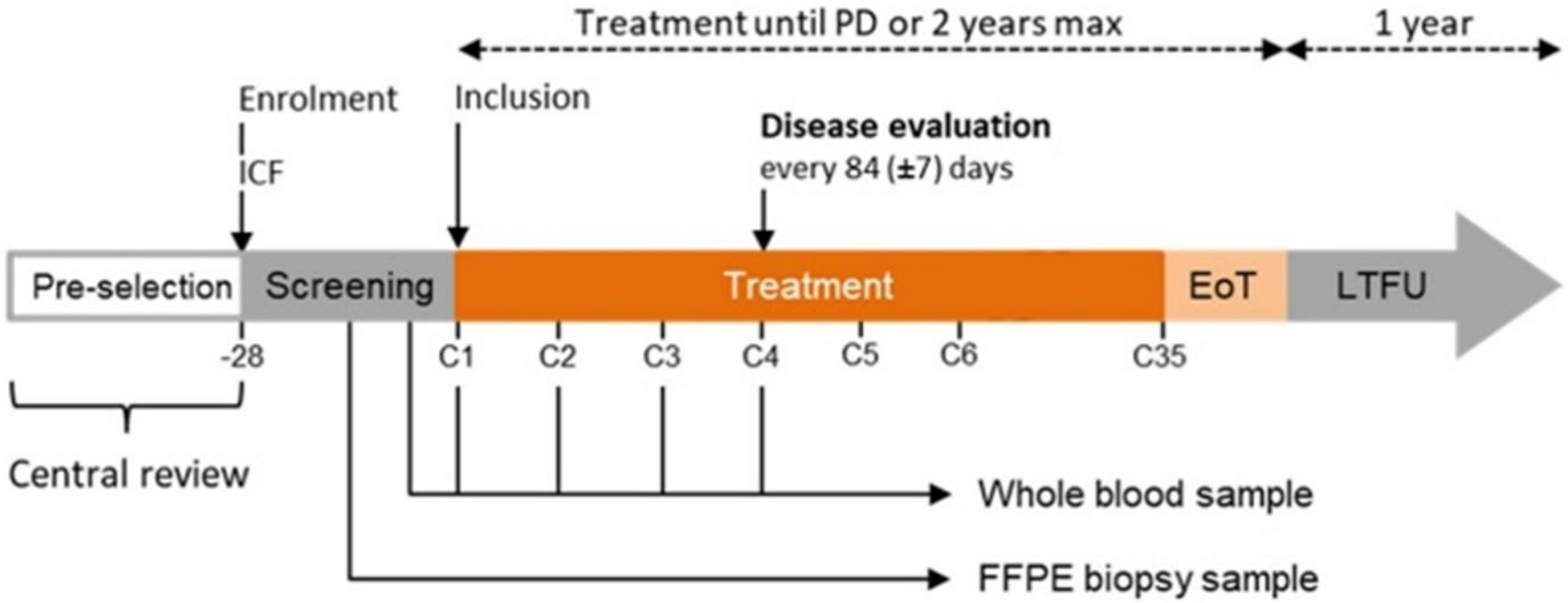


	TLS cohort (n=30)	Previous cohorts (all comers) n=41
Median Overall survival	18.3 months (CI 95% : 8.5-NA)	14.3 months* (CI 95% : 5.9-17.9)

* Toulmonde et al Jama Oncol 2017

Italiano A et *al.* ASCO 2021 Abst 11507

High clinical activity of pembrolizumab in chordoma, alveolar soft part sarcoma (ASPS) and other rare sarcoma histotypes: The French AcSé pembrolizumab study from Unicancer



Caractéristiques de la population

Parameters	Value	N	Stat
AGE		97	51 [35 ;65]
SEX	M	54	55.1 %
	F	44	44.9 %
ECOG	0	33	33.67 %
	1	64	65.31 %
	2	1	1.02 %
PREVIOUS LINES		98	2 [1 ;3]

Description of Sarcoma (N=98)	
Chordoma	34 (34.69 %)
Alveolar soft-part sarcoma (ASPS)	14 (14.29 %)
Desmoplastic tumor with little circular cells (DSRCT)	8 (8,16 %)
smarca4 deficient malignant rhabdoid tumor (SMRT)	11 (11,22 %)
Other histologies	31 (31,63 %)

Blay JY. et *al.* ASCO 2021 Abst 11520

Efficacité

Primary endpoint (at 12 weeks)

Parameters	Value	N	%
		98	
OBSERVED RESPONSE	PR	6	8 %
	SD	39	48 %
	PD	36	44 %
	Non available	17	
OVERALL RESPONSE	Non-response	92	94 %
	Response	6	6 %

Median number of cycles : 5 (range 1-35)

Best response

Parameters	Value	N	%
BEST RESPONSE	CR	1	1%
	PR	14	14%
	SD	33	34 %

Overall Survival, OS

Median OS on the overall population = 19.7 months

1-year OS rates:
- 76.6% (chordoma),
- 85.7% (ASPS),
- 30.0% (SMRT),
- 0% (DSCRT),
- 46.5% (other),

Median OS only reached for:
- SMRT = 2.1 months,
- DSRCT = 7.4 months,
- other = 7.1 months

Progression-free Survival, PFS

Median PFS on the overall population = 2.75 months

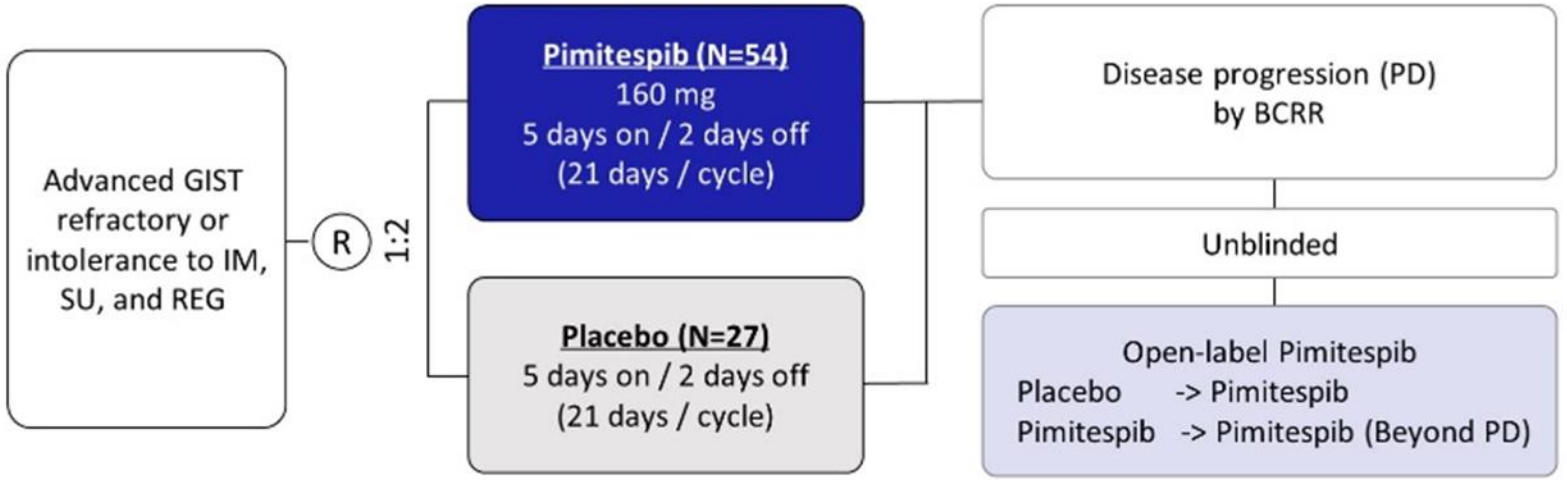
1-year PFS rates:
- 31.2% (chordoma),
- 35.7% (ASPS),
- 10.0% (SMRT),
- 0% (DSCRT)
- 6.3% (other).

Median PFS:
6.6 months (chordoma),
7.5 months (ASPS),
1.0 months (SMRT),
2.1 months (DSCRT),
2.1 months (other).

Meilleure réponse : 3 (8,8%) chordomes, 7 (50%) ASPS, 2 (20%) SMRT, 3 (9%) autres histologies
Durée médiane de réponse : 8,2 mois

Baly JY. et *al.* ASCO 2021 Abst 11520

Randomized, double-blind, placebo (PL)-controlled, phase III trial of pimitespib (TAS-116), an oral inhibitor of heat shock protein 90 (HSP90), in patients with advanced gastrointestinal stromal tumor refractory to imatinib, sunitinib and regorafenib



- **Primary endpoint:** PFS by BCRR based on modified RECIST 1.1.
- **Secondary endpoints:** overall survival (OS), PFS in the pts crossed over to pimitespib (secondary PFS), pharmacogenomics (PGx), and safety. Crossover-adjusted OS using the rank preserving structural failure time (RPSFT[9]) model.

9. Korhonen P, et al. J Biopharm Stat.2012;22:1258-1271.

Efficacité - Tolérance

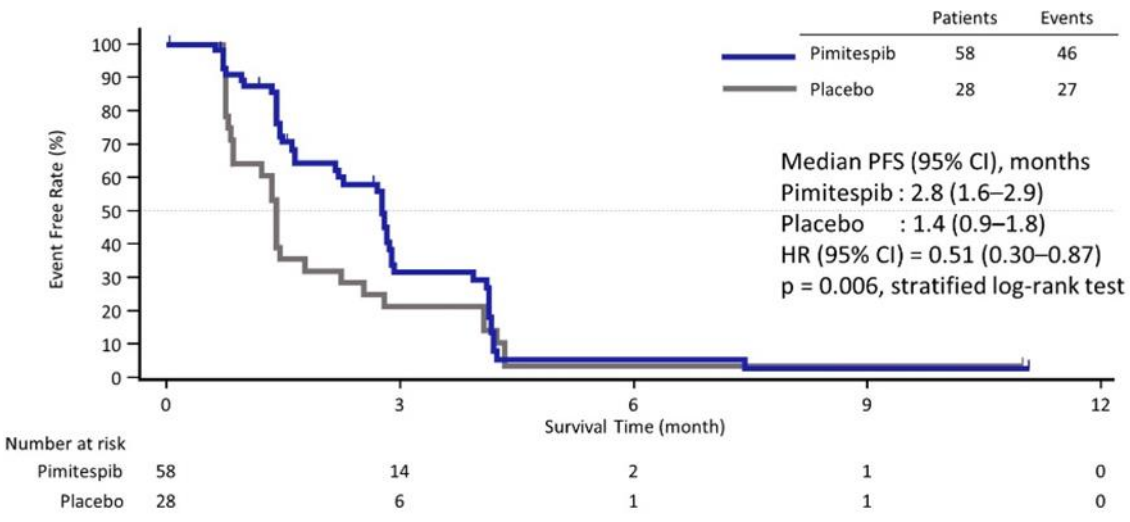
Baseline characteristics	Pimitespib (N=58)	Placebo (N=28)
Sex: Male / Female	34 (58.6%) / 24 (41.4%)	15 (53.6%) / 13 (46.4%)
Age: Median (Max-Min)	62 (32 - 83)	61.5 (26 - 81)
Age: <65 / >65	36 (62.1%) / 22 (37.9%)	17 (60.7%) / 11 (39.3%)
ECOG PS: 0 / 1	49 (84.5%) / 9 (15.5%)	24 (85.7%) / 4 (14.3%)
Number of previous therapies: 3 / >4	40 (69.0%) / 18 (31.0%)	15 (53.6%) / 13 (46.4%)
Genomic status of blood sample	**Pimitespib (N=51)**	**Placebo (N=24)**
KIT mutation detected (Exon 9, 11, 13/14, 17/18)	30 (58.8%)	15 (62.5%)
Exon 9	3 (5.9%)	5 (20.8%)
Exon 11	25 (49.0%)	12 (50.0%)
Exon 13/14, 17/18	24 (47.1%)	14 (58.3%)
PDGFRA mutation detected	6 (10.3)	0

	Adverse events (AEs)				Treatment-related AEs			
	Pimitespib (N=58)		Placebo (N=28)		Pimitespib (N=58)		Placebo (N=28)	
Preferred Term	All grades	≥ Grade3	All grades	≥ Grade3	All grades	≥ Grade3	All grades	≥ Grade3
Any Events	56 (96.6)	25 (43.1)	22 (78.6)	8 (28.6)	54 (93.1)	15 (25.9)	11 (39.3)	1 (3.6)
Diarrhea	43 (74.1)	8 (13.8)	5 (17.9)	0	43 (74.1)	8 (13.8)	4 (14.3)	0
Decreased appetite	21 (36.2)	4 (6.9)	4 (14.3)	0	18 (31.0)	1 (1.7)	2 (7.1)	0
Malaise	18 (31.0)	2 (3.4)	5 (17.9)	0	15 (25.9)	1 (1.7)	3 (10.7)	0
Nausea	16 (27.6)	0	5 (17.9)	0	14 (24.1)	0	3 (10.7)	0
Blood creatinine increased	15 (25.9)	0	3 (10.7)	0	15 (25.9)	0	2 (7.1)	0
Renal impairment	10 (17.2)	2 (3.4)	0	0	9 (15.5)	2 (3.4)	0	0
Night blindness	8 (13.8)	0	0	0	8 (13.8)	0	0	0
Tumor pain	8 (13.8)	1 (1.7)	1 (3.6)	0	0	0	0	0
Anemia	6 (10.3)	4 (6.9)	3 (10.7)	3 (10.7)	5 (8.6)	3 (5.2)	0	0

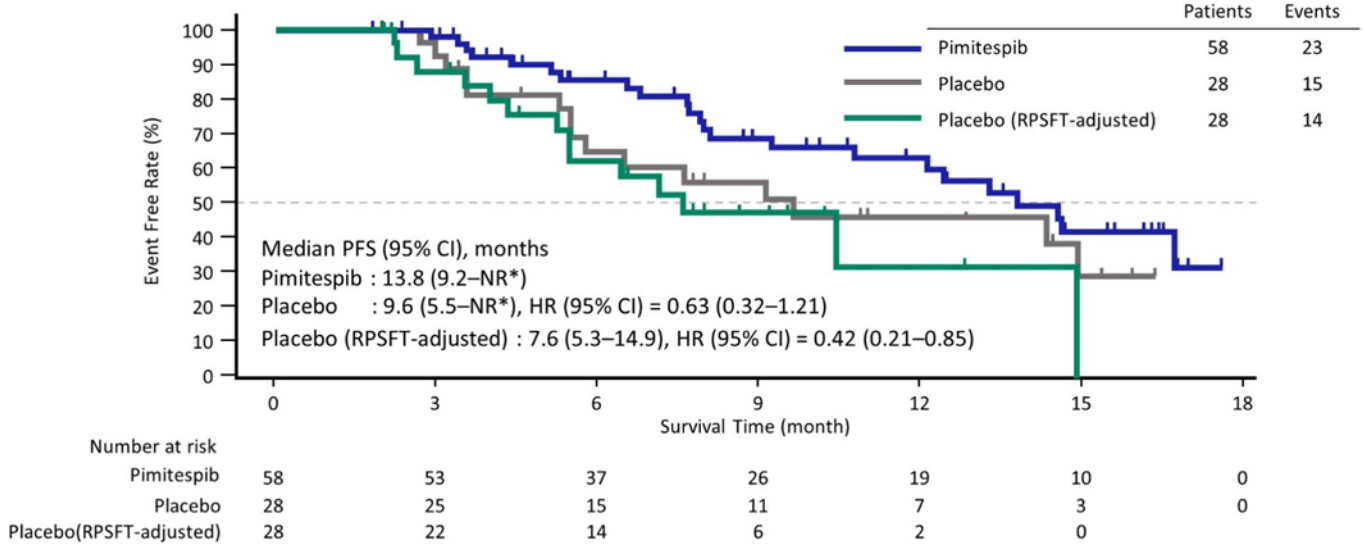
Honma Y. et *al*. ASCO 2021 Abst 11524

Survie

PFS based on BCRR

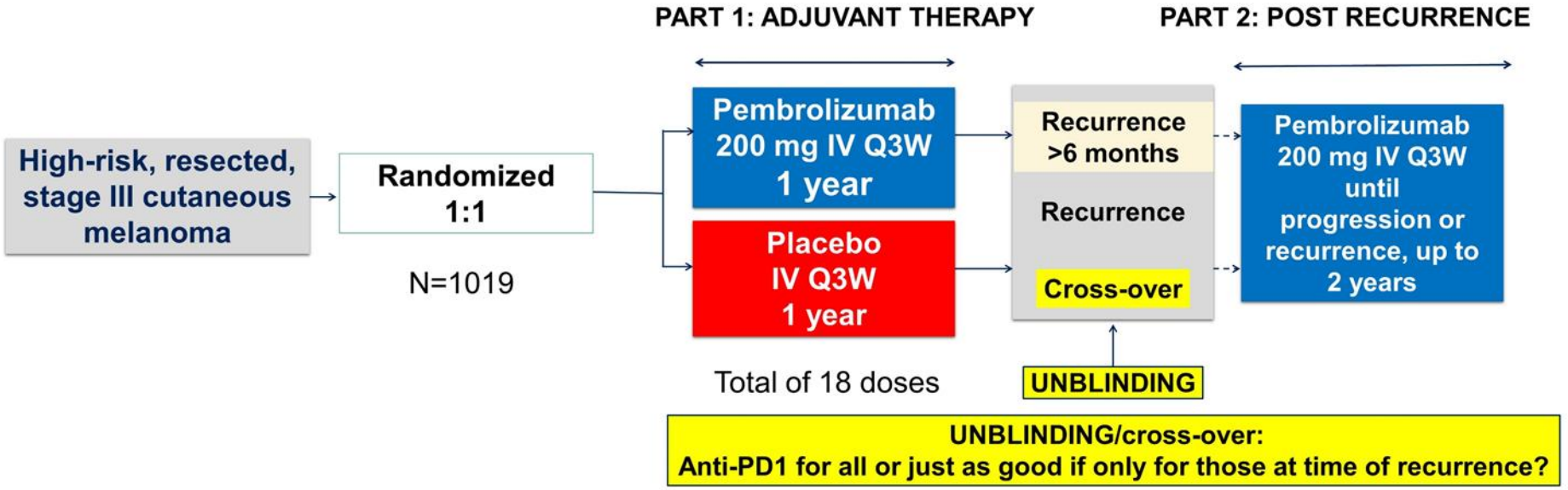


OS and OS adjusted by RPSFT model



Honma Y. et *al*. ASCO 2021 Abst 11524

Crossover and rechallenge with pembrolizumab in recurrent patients from the EORTC 1325-MG/Keynote-054 phase 3 trial, pembrolizumab versus placebo after complete resection of high-risk stage III melanoma



Stratification factors:
✓**AJCC-7 Stage**: IIIA (>1 mm metastasis) vs. IIIB vs. IIIC 1-3 positive lymph nodes vs. IIIC ≥4 positive lymph nodes
✓**Region**: North America, European countries, Australia/New Zealand, other countries

Primary Endpoints:
- **RFS (per investigator) in overall ITT population,** and **in patients with PD-L1-positive tumors**

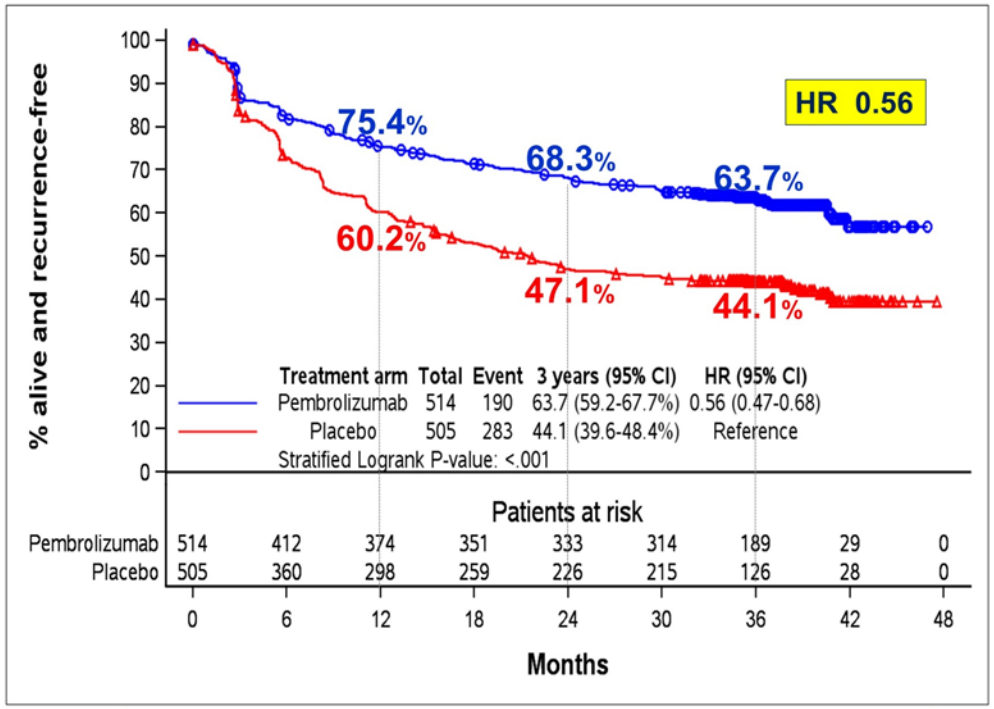
Secondary Endpoints:
- **DMFS and OS** in these 2 populations; **Safety, Health-related quality of life**

Eggermont AM et *al*. ASCO 2021 Abst 9500

Survie

RFS updated analysis @ 3YR (ASCO 2020)[1]

- ***Cut-off date*** (30-Sep-2019); median follow-up: **3** years; **473 RFS events**

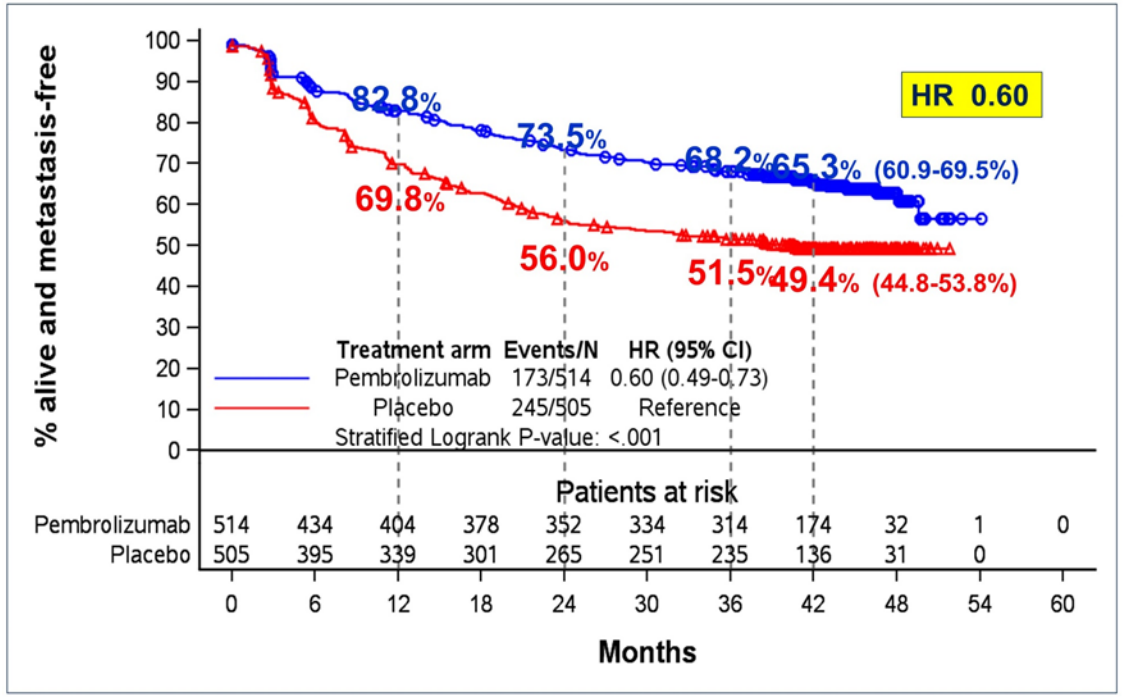


irAE: grade 1-5 (38%); grade 3-5 (7%)

[1]Eggermont AMM, et al. *J Clin Oncol* 2020;38:3925-36

DMFS final analysis @ 3.5 YR (ESMO 2020)[2]

- ***Cut-off date*** (3-Apr-2020); median follow-up: **3.5** years; **418 DMFS events** (423 planned: ~87% power HR=0.725)



[2]Eggermont AMM, et al. *Lancet Oncol.* 2021;22:643-654

Eggermont AM et *al*. ASCO 2021 Abst 9500

Caractéristiques de la population

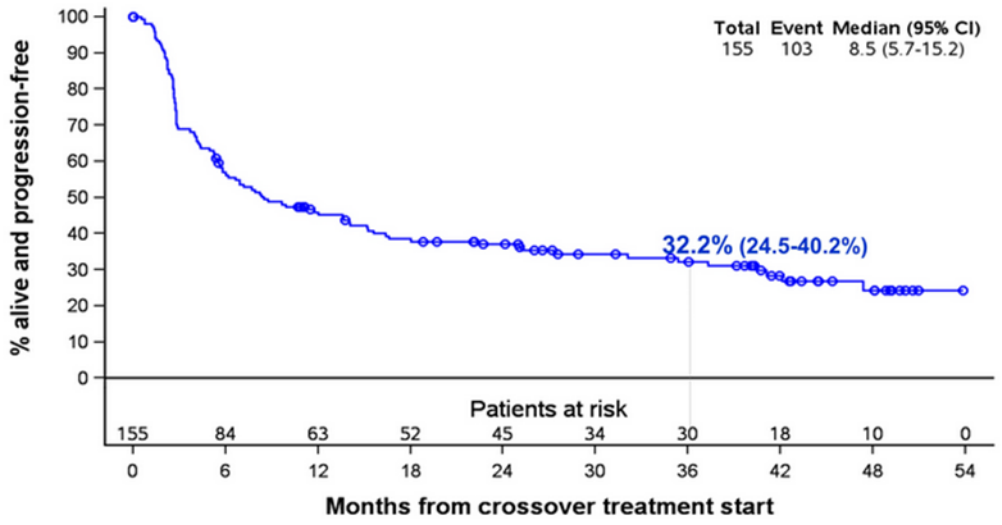
	Median follow-up (IQR) from start of Part 2, months
All patients included in Part 2 (N=175)	**39** (27-46)
Crossover patients from **placebo group (N=155)**	**41** (30-48)
Rechallenge patients from **pembrolizumab group (N=20)**	**19** (14-26)

	Randomized Placebo N=505	**Randomized pembrolizumab N=515**
Completion of 1 yr of treatment	**297**	**297**
Recurrence (before/after trt compl.)	**298**	**203**
Recurrence after 6 mts of trt compl.		**47**
Stage at baseline of Part 2, n	**Crossover population N=155**	**Rechallenge population N=20**
III resected (after local, ITM, RLN rec.)	50	7
III/IV various	105	13
III unresected (M0)	10	0
IV (M1)	95	13
IV resected/unresected	12/83	4/9
AJCC-8 M1a	22	4
AJCC-8 M1b	36	5
AJCC-8 M1c	36	4
AJCC-8 M1d	1	0

Eggermont AM et *al*. ASCO 2021 Abst 9500

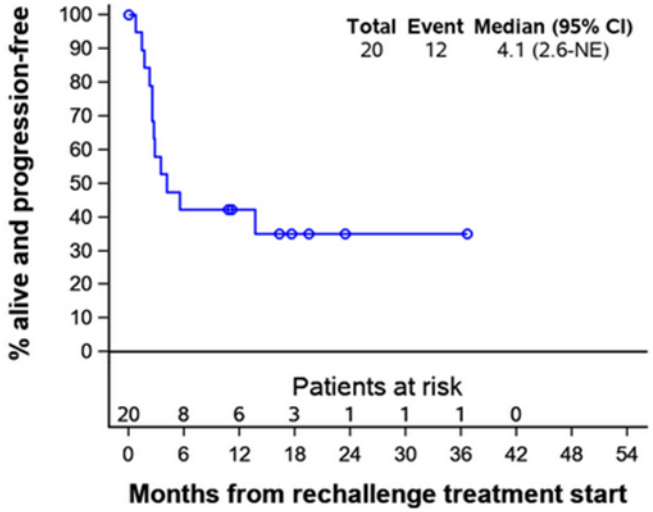
Survie

EORTC 1325/KEYNOTE-54
Crossover patients: Recurrence/Progression-free survival



EORTC 1325/KEYNOTE-54
Rechallenged patients

Recurrence/Progression-free survival (N=20)

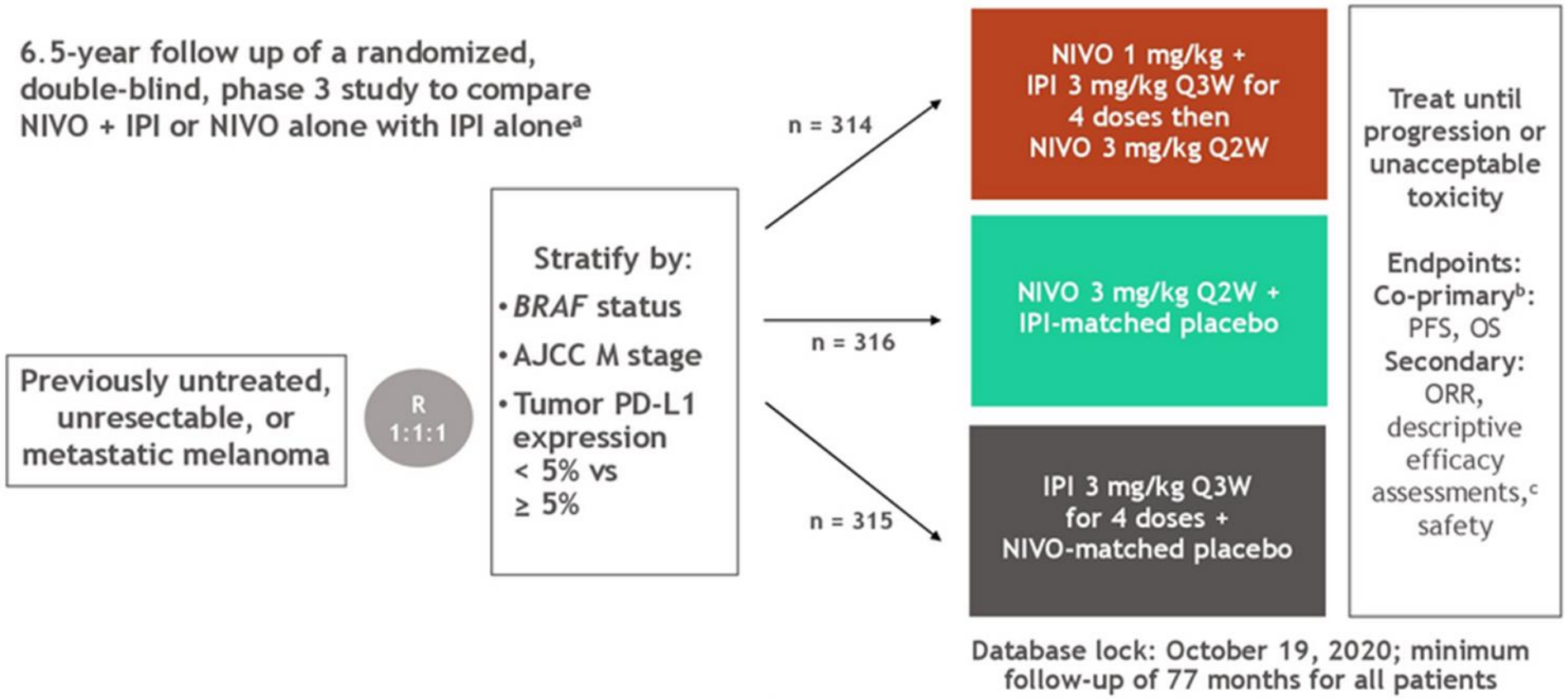


Patients with measurable advanced disease (N=9)

Best response	Advanced disease N=9 (100%)
CR	1 (11.1)
Stable disease	3 (33.3)
Progressive disease	5 (55.6)

Eggermont AM et *al*. ASCO 2021 Abst 9500

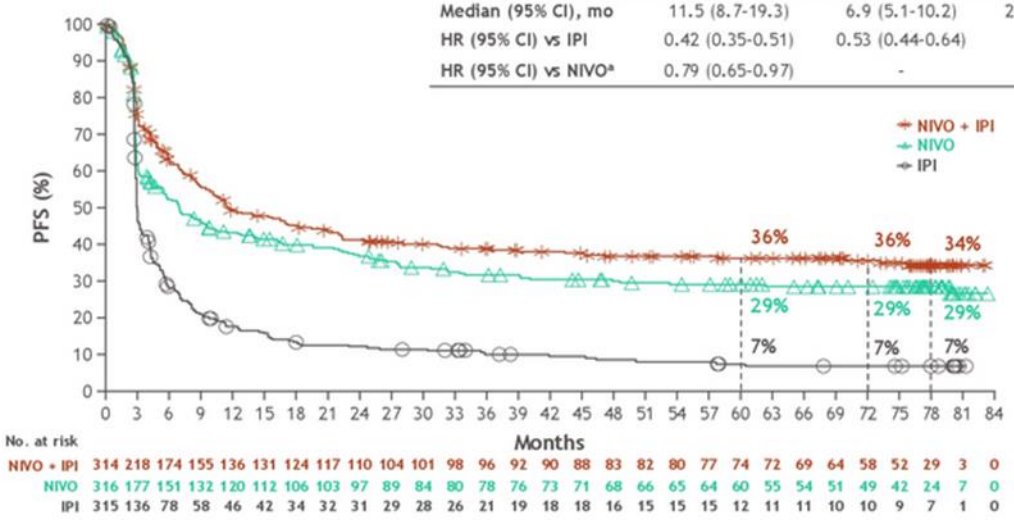
CheckMate 067: 6.5-year outcomes in patients with advanced melanoma



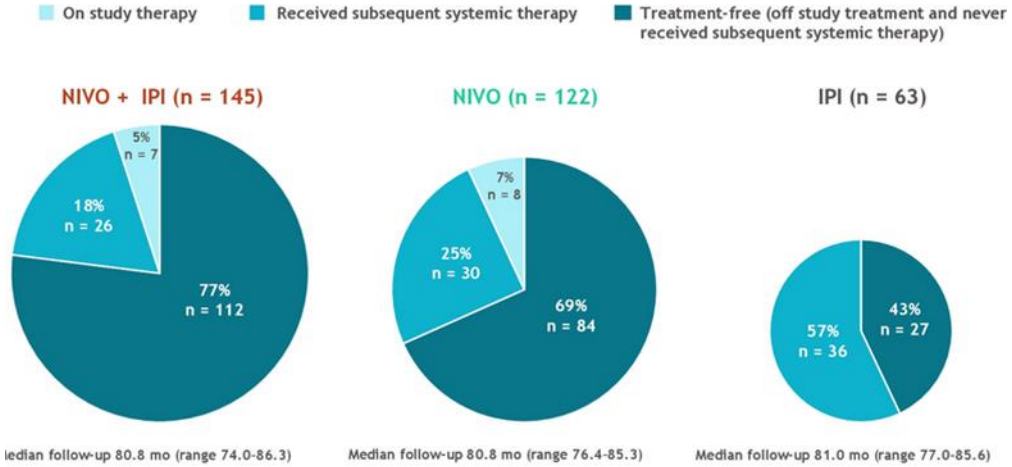
Wolchok JD et *al*. ASCO 2021 Abst 9506

Efficacité - Survie

	NIVO + IPI (n = 314)	NIVO (n = 316)	IPI (n = 315)
Median (95% CI), mo	11.5 (8.7-19.3)	6.9 (5.1-10.2)	2.9 (2.8-3.2)
HR (95% CI) vs IPI	0.42 (0.35-0.51)	0.53 (0.44-0.64)	-
HR (95% CI) vs NIVO[a]	0.79 (0.65-0.97)	-	-

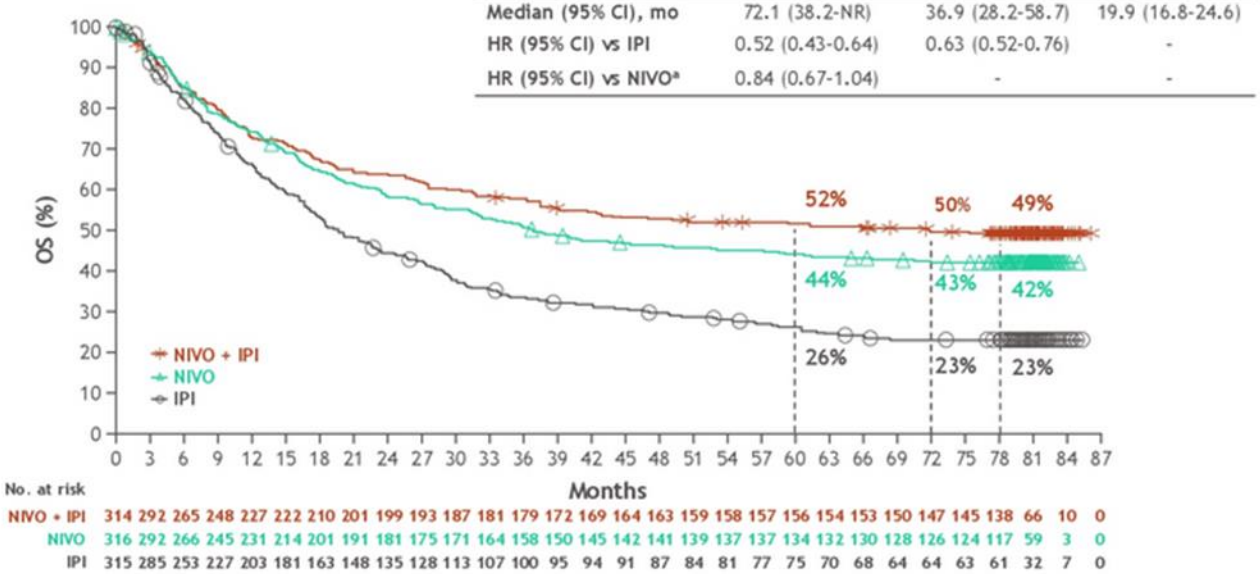


PFS



OS

	NIVO + IPI (n = 314)	NIVO (n = 316)	IPI (n = 315)
Median (95% CI), mo	72.1 (38.2-NR)	36.9 (28.2-58.7)	19.9 (16.8-24.6)
HR (95% CI) vs IPI	0.52 (0.43-0.64)	0.63 (0.52-0.76)	-
HR (95% CI) vs NIVO[a]	0.84 (0.67-1.04)	-	-



Wolchok JD et *al*. ASCO 2021 Abst 9506