Post ESMO 2019

Digestif

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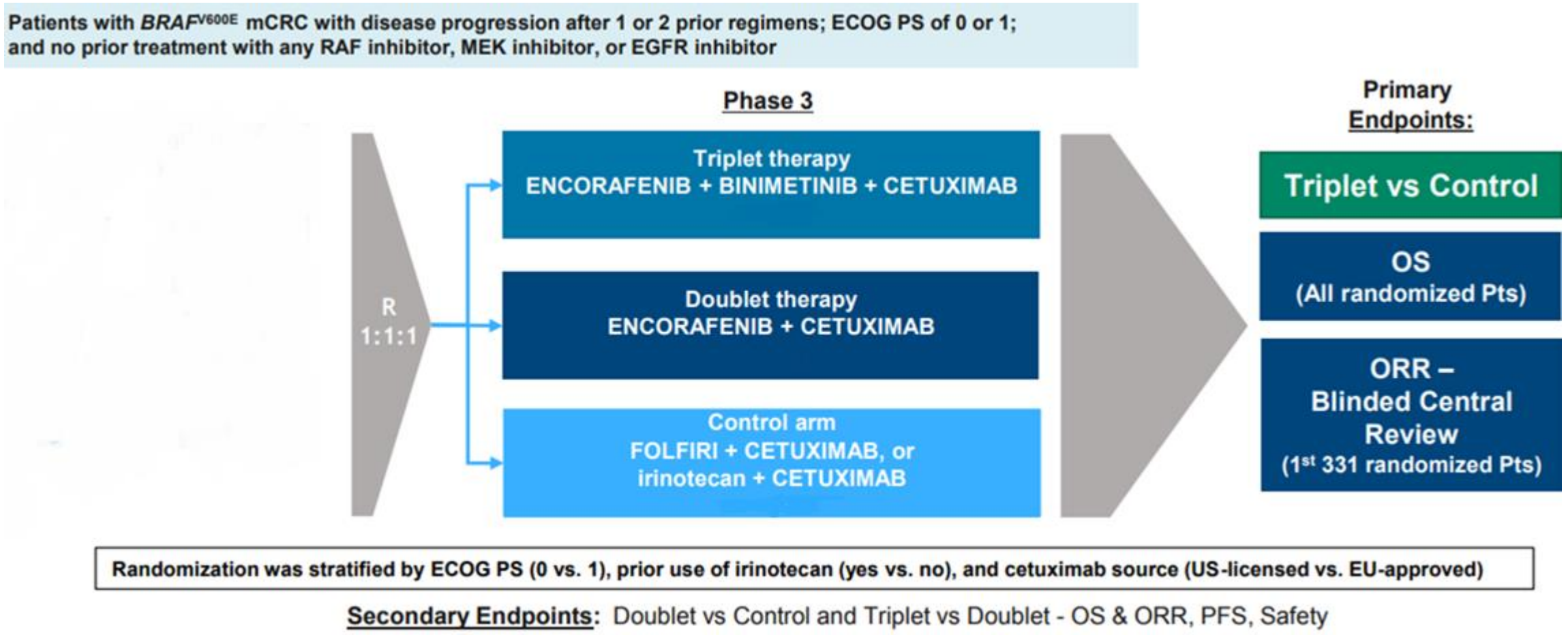
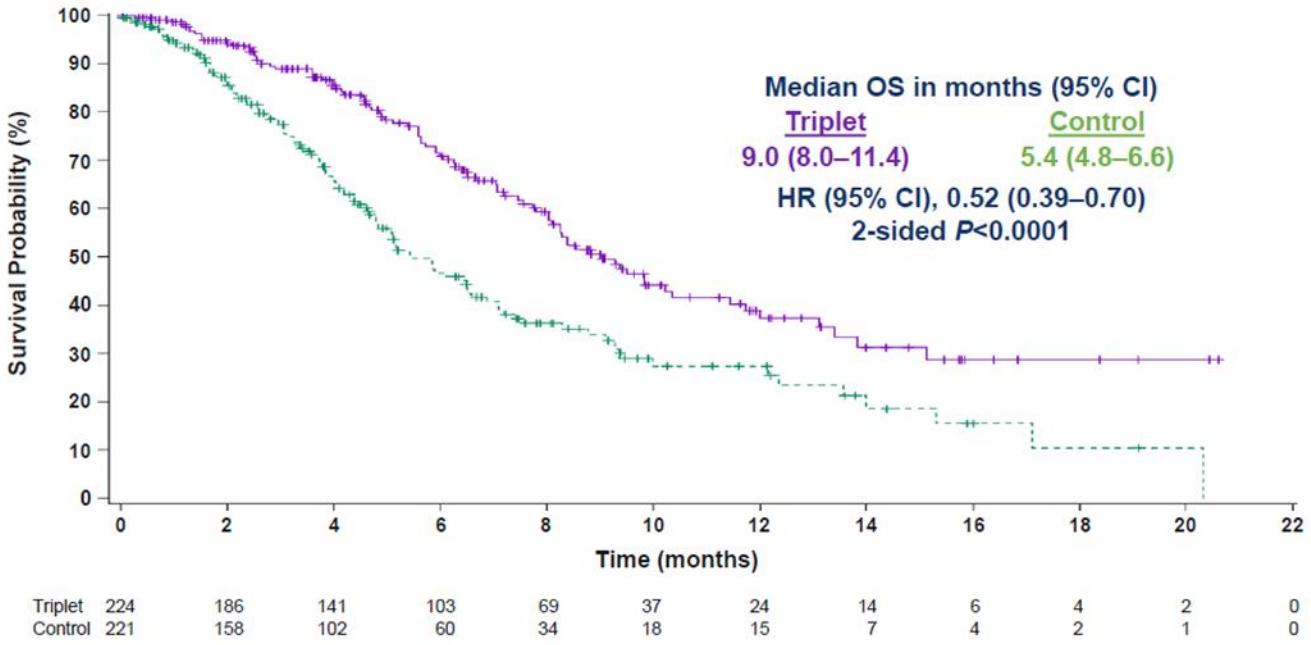
Etude BEACON: Cancer colorectal BRAF muté

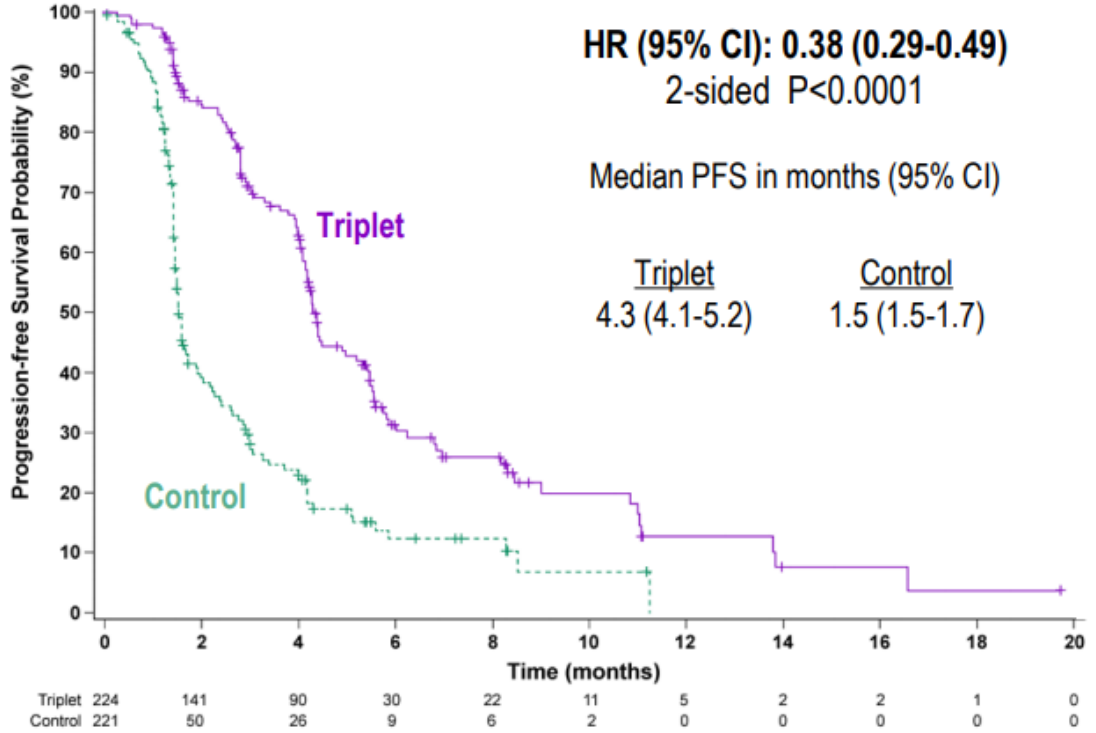


CHARACTERISTIC	Triplet N=224	Doublet N=220	Control N=221
Female	53%	48%	57%
Age, median (range), years	62 (26, 85)	61 (30, 91)	60 (27, 91)
ECOG PS 0	52%	51%	49%
Location of primary tumor*			
Left colon (includes rectum)	35%	38%	31%
Right colon	56%	50%	54%
≥3 organs involved	49%	47%	44%
Presence of liver metastases	64%	61%	58%
Prior lines of therapy			
1	65%	66%	66%
>1	35%	34%	34%
MSI-H†	10%	9%	5%
CEA Baseline Value > 5 ug/L	80%	70%	81%
CRP Baseline Value > 10mg/L	42%	37%	41%

Survie globale: trithérapie vs contrôle



Survie sans progression: trithérapie vs contrôle



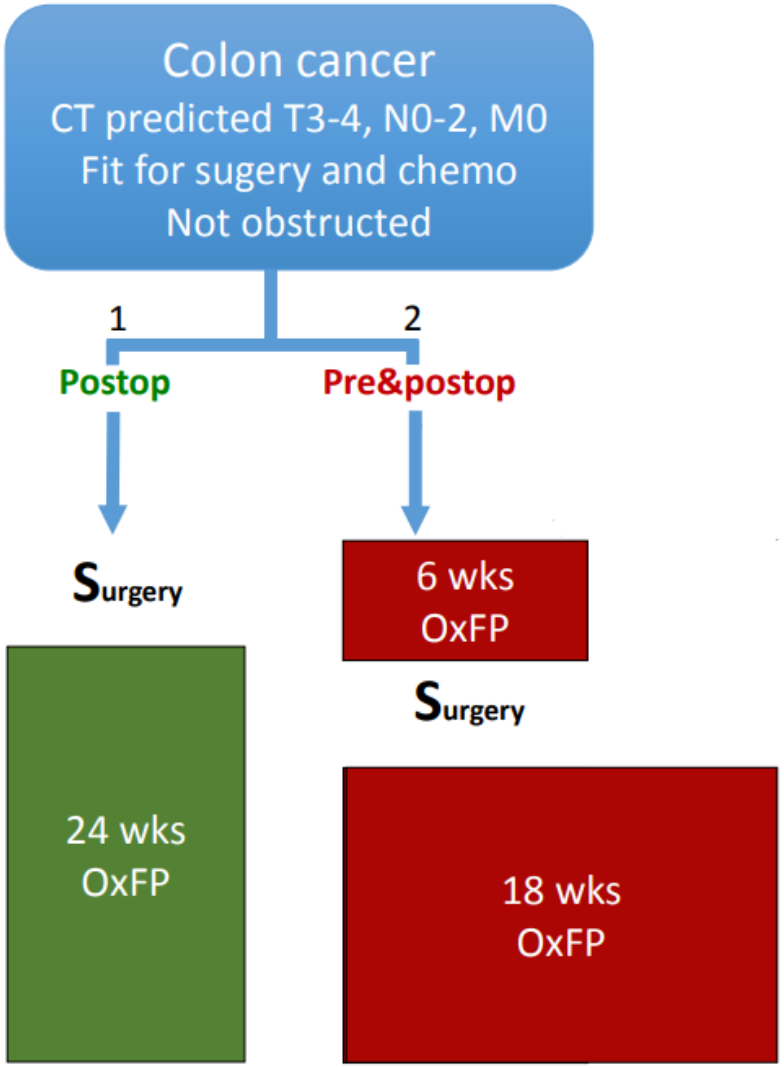
Taux de réponse (relecture centralisée)

Confirmed Response by BICR	Triplet N=111	Doublet N=113	Control N=107
Objective Response Rate	**26%**	**20%**	**2%**
95% (CI)	(18, 35)	(13, 29)	(<1, 7)
p-value vs. Control	<0.0001	<0.0001	

Event	Triplet N=222 Median Duration of Exposure: 21 weeks*	Doublet N=216 Median Duration of Exposure: 19 weeks*	Control N=193 Median Duration of Exposure: 7 weeks*
Any event	98%	98%	97%
Grade 3/4 adverse event (AE)	58%	50%	61%

Event	Triplet N=222 Grade ≥3	Doublet N=216 Grade ≥3	Control N=193 Grade ≥3
Diarrhea	10%	2%	10%
Abdominal pain	6%	2%	5%
Nausea	5%	<1%	1%
Vomiting	4%	1%	3%
Pulmonary embolism	4%	1%	4%
Intestinal obstruction	3%	4%	3%
Asthenia	3%	3%	5%
Acute kidney injury	3%	2%	<1%
Fatigue	2%	4%	4%
Dermatitis acneiform	2%	<1%	3%
Ileus	2%	1%	2%
Urinary tract infection	1%	2%	1%

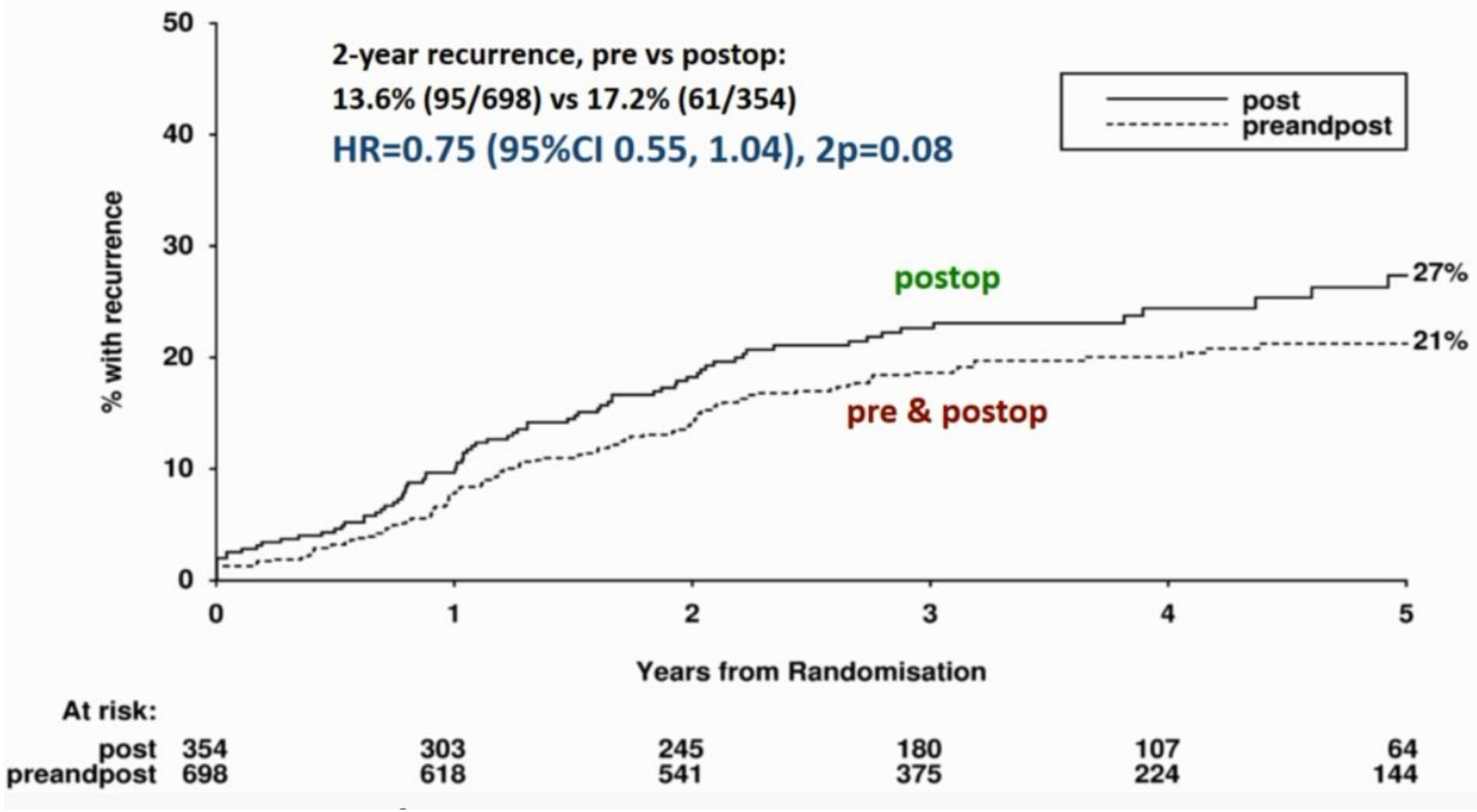
Etude FOxTROT: Cancer colique et chimiothérapie néoadjuvante



Objectifs:

- **Principal: survie sans récidive à 2 ans**
- Secondaires: taux de résection R0, réponse histologique, complications post-op

Survie sans récidive



Complications post opératoires

Underwent surgery	Pre&post n=684	Post n=351	
Procedure involved a stoma	11.7%	9.0%	p=0.18
Wound infection	8.5%	8.9%	p=0.85
Bronchopneumonia	1.8%	3.1%	p=0.16
PE ± DVT	1.6%	0.6%	p=0.18
Anastomotic leak or intra-abdo abscess	4.7%	7.4%	p=0.07
complication requiring further surgery	4.3%	7.1%	p=0.05
complication prolonging hospital stay	11.6%	14.3%	p=0.21
Death within 30 days	0.6%	0.6%	p=0.98

Local pathology	neoadj. chemo n=682	Straight to surgery n=347	
pT0	4.1%	0%	p<0.0001
pT1-2	11.7%	5.8%	
pT3	63.7%	64.5%	
pT4	20.5%	29.8%	
Max tumour diameter – median	35mm	50mm	p<0.0001
Spread beyond muscularis – median	4mm	5mm	p=0.005
EMVI+	32.3%	45.0%	p<0.0001
pN0	59.4%	48.7%	p<0.0001
pN1	25.4%	25.1%	
pN2	15.2%	25.9%	

R2 – macroscopically incomplete	0.3%	1.1%
R1 - microscopically incomplete	4.2%	8.8%
R0 - microscopically complete	93.1%	88.4%

Etude ATTRACTION-3: Nivolumab en 2ème ligne pour carcinome épidermoïde de l'œsophage

Etude de phase 3, asiatique, randomisée, en ouvert

Key eligibility criteria

- Unresectable advanced or recurrent ESCC
- Refractory to or intolerant of 1 prior fluoropyrimidine/ platinum-based therapy
- ECOG performance status 0 or 1

R
1:1

Stratification[b]:
- Region
- No. of organs with metastases
- PD-L1 expression

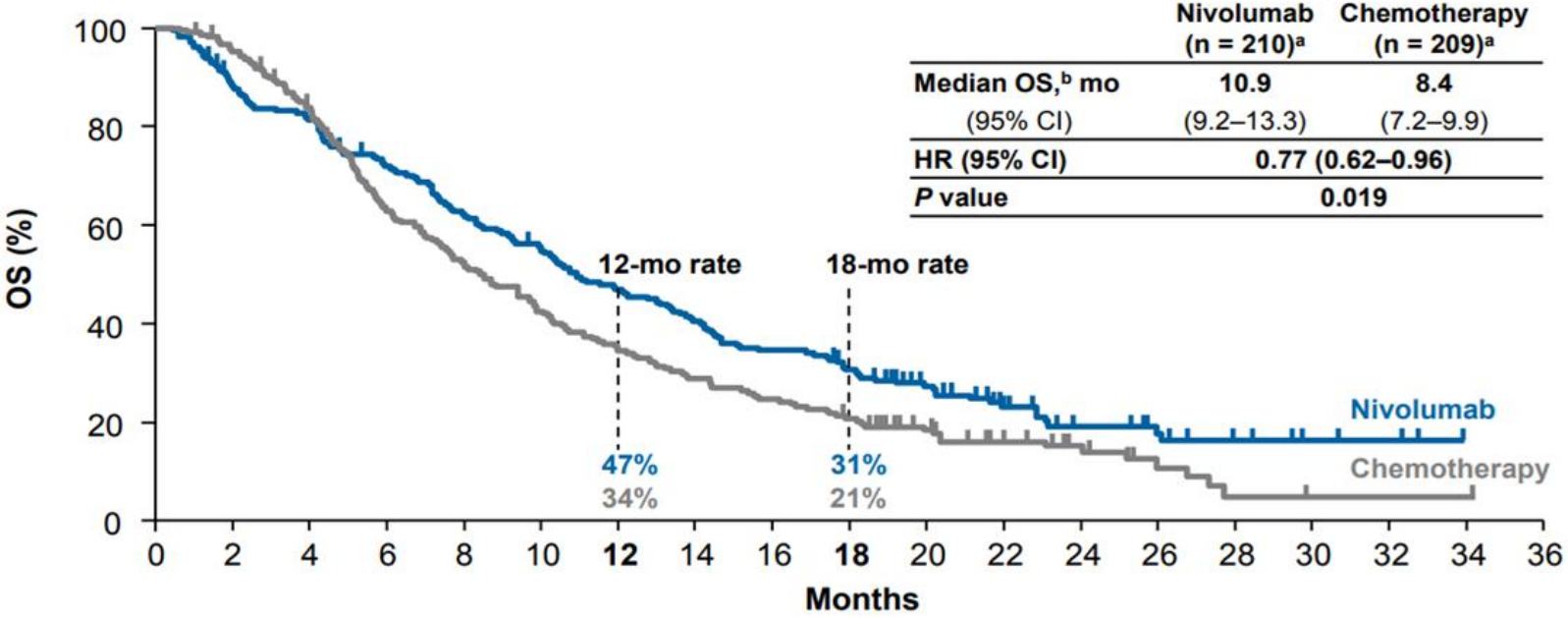
Nivolumab
240 mg IV Q2W[c]

Docetaxel 75 mg/m^2 IV Q3W[c]
or paclitaxel 100 mg/m^2 IV QW
× 6 weeks, then 1 week off[c]

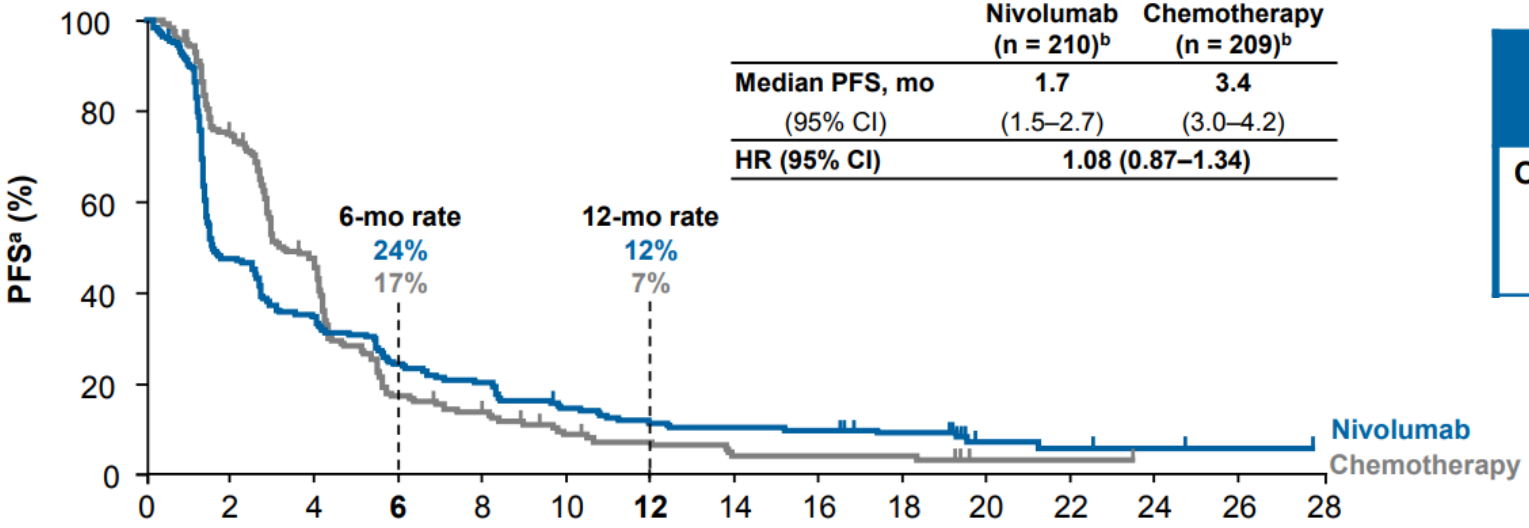
Primary endpoint:
- OS

Other key endpoints:
- PFS, ORR, DCR, TTR, DOR, HRQoL, and safety

	Nivolumab N = 210[a]	Chemotherapy N = 209[a,b]
Median age (range), years	64 (37–82)	67 (33–87)
Male, n (%)	179 (85)	185 (89)
Race, n (%)		
Asian	201 (96)	200 (96)
White	9 (4)	9 (4)
ECOG performance status, n (%)		
0	101 (48)	107 (51)
1	109 (52)	102 (49)
Disease stage[c] (TNM classification), n (%)		
II–III	8 (7)	13 (11)
IV	94 (88)	100 (83)
Prior therapies, n (%)		
Surgery	111 (53)	94 (45)
Radiotherapy	153 (73)	142 (68)
Systemic anticancer therapy	210 (100)	208 (100)
Tumor PD-L1 expression,[d] n (%)		
< 1%	109 (52)	107 (51)
≥ 1%	101 (48)	102 (49)
History of smoking, n (%)		
Never	30 (14)	32 (15)
Former	159 (76)	147 (70)
Current	21 (10)	30 (14)

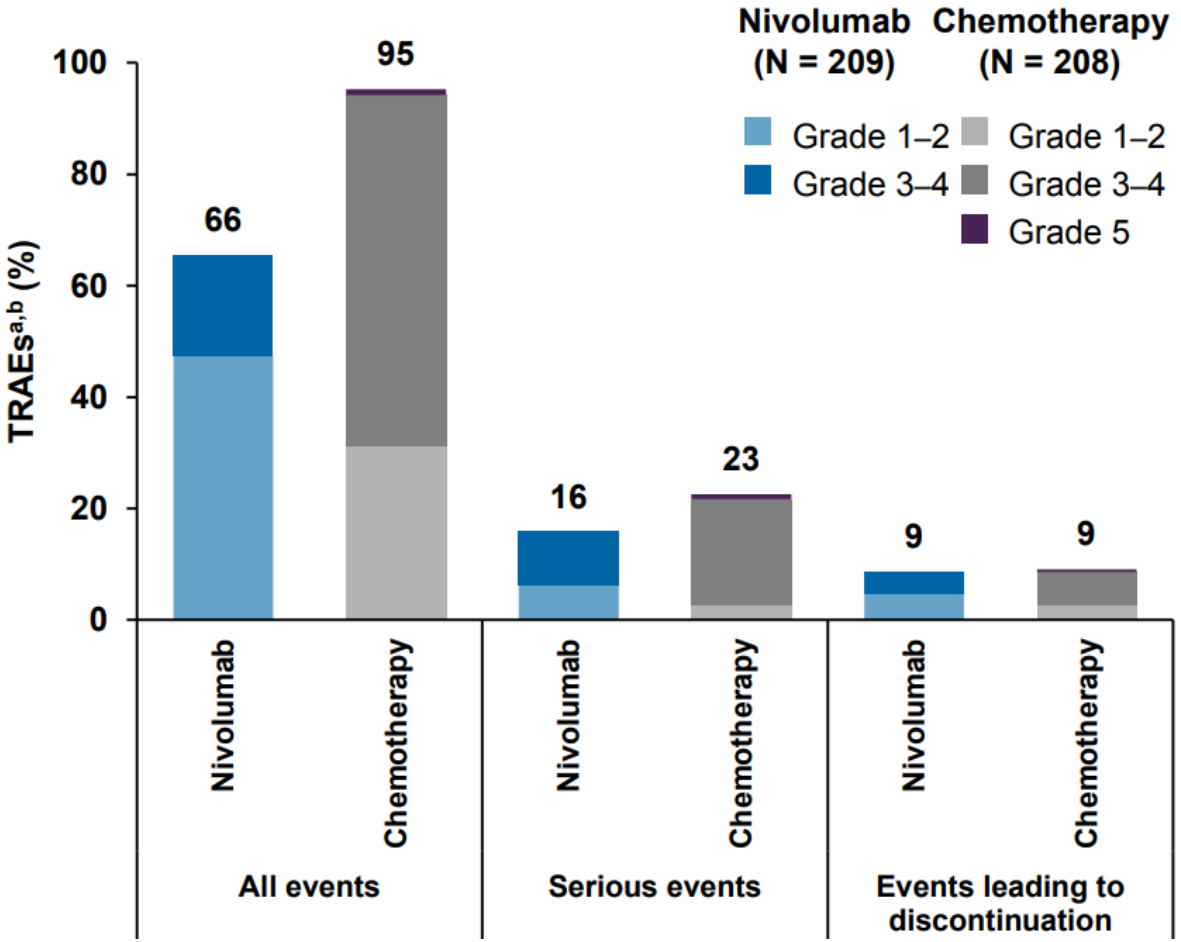


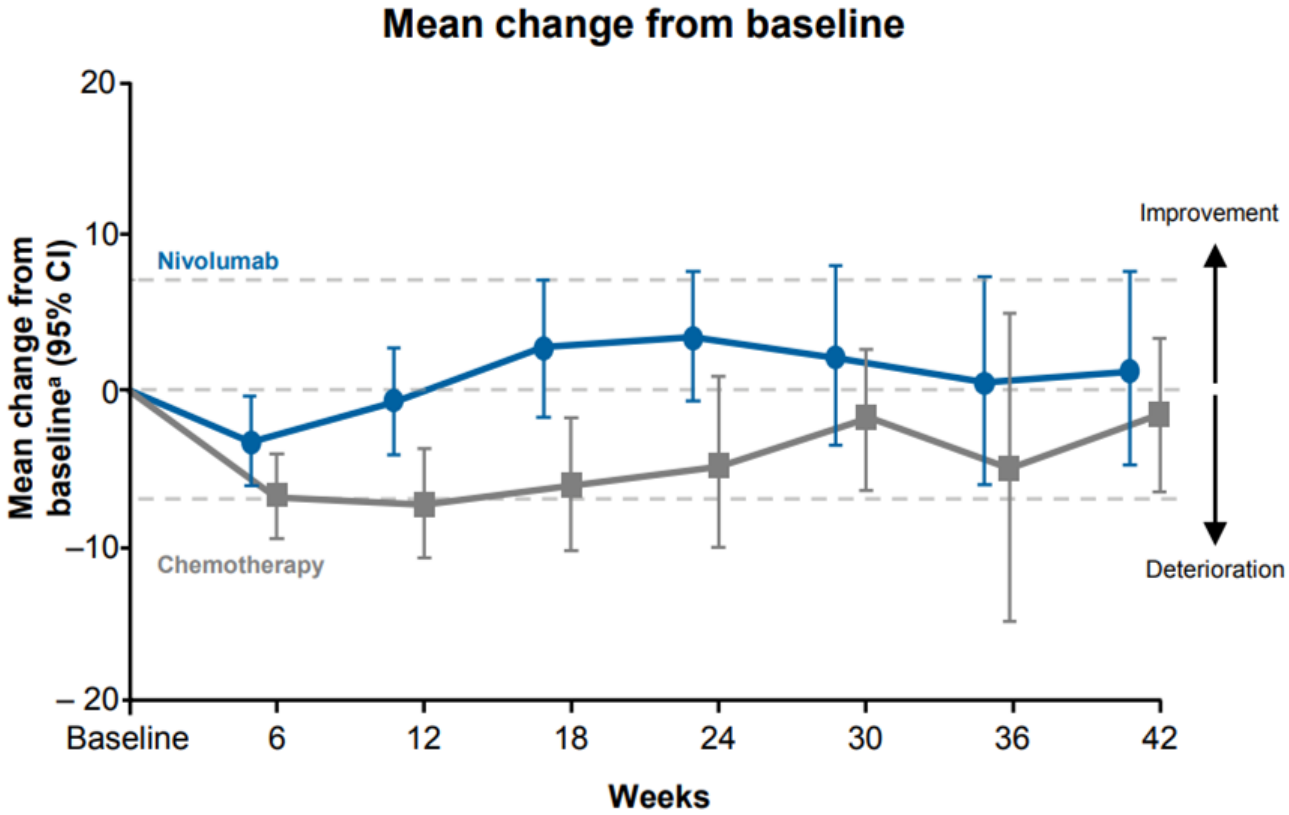
	Nivolumab (n = 210)[a]	Chemotherapy (n = 209)[a]
Median OS,[b] mo	10.9	8.4
(95% CI)	(9.2–13.3)	(7.2–9.9)
HR (95% CI)	0.77 (0.62–0.96)	
P value	0.019	



	Nivolumab (n = 210)[b]	Chemotherapy (n = 209)[b]
Median PFS, mo	1.7	3.4
(95% CI)	(1.5–2.7)	(3.0–4.2)
HR (95% CI)	1.08 (0.87–1.34)	

	Nivolumab N = 171[a]	Chemotherapy N = 158[a]
ORR,[b] n (%)	33 (19)	34 (22)
95% CI	14–26	15–29
P value	0.63	


Nivolumab (N = 209)
Chemotherapy (N = 208)
Grade 1–2
Grade 3–4
Grade 5
TRAEs[a,b] (%)
100
80
60
40
20
0
66
95
16
23
9
9
Nivolumab
Chemotherapy
All events
Serious events
Events leading to discontinuation


Mean change from baseline
Mean change from baseline[a] (95% CI)
20
10
0
–10
– 20
Nivolumab
Chemotherapy
Improvement
Deterioration
Baseline
6
12
18
24
30
36
42
Weeks

A retenir

- La **chimiothérapie néoadjuvante par FOLFOX dans les cancers du colon T3/T4**
  - améliore le taux de résection R0
  - sans augmenter la morbidité post opératoire

- Avancée majeure en **2ème ligne dans le cancer colorectal mBRAF, avec trithérapie ciblée**:
  - Encorafenib (anti BRAF) + binimetinib (anti MEK) + cetuximab (anti EGFR)
  - Doublement de la SG et de la SSP
  - Tolérance acceptable

- Traitement de **2ème ligne du carcinome épidermoïde de l'œsophage: le nivolumab** un nouveau standard?
  - Amélioration de la SG
  - Amélioration de la qualité de vie, moins d'effets secondaires